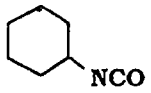
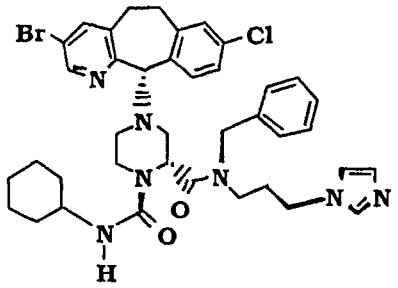
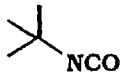
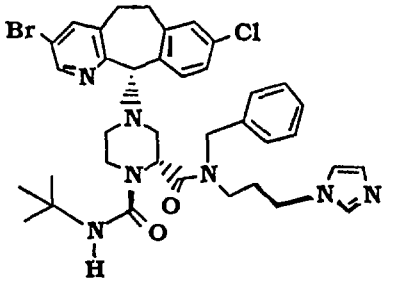
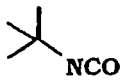
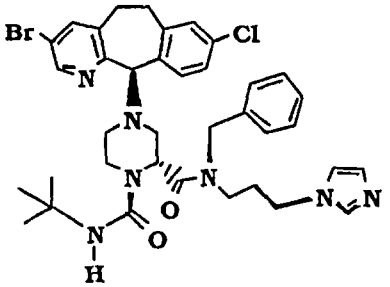
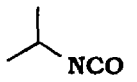
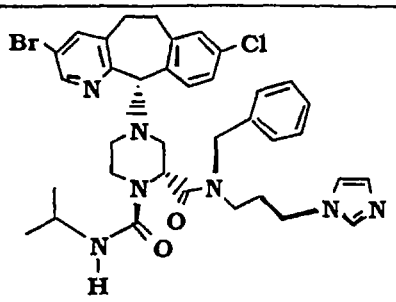
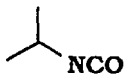
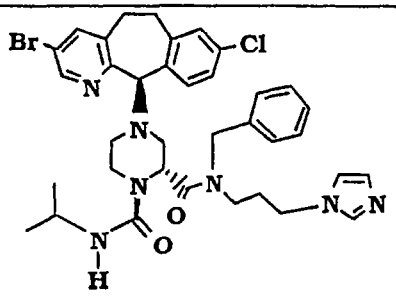
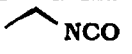
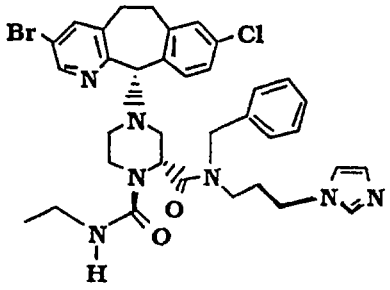
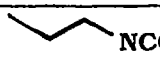
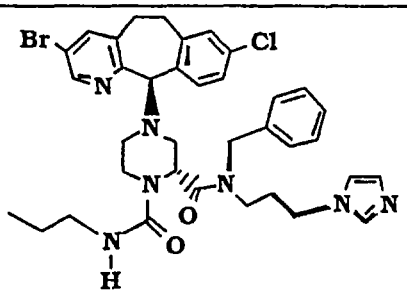
EXAMPLES 128-148

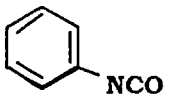
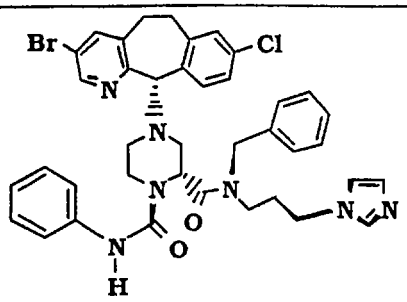
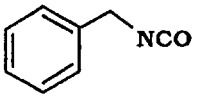
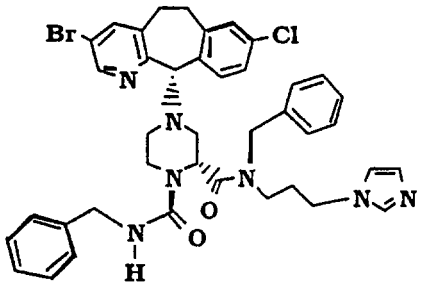
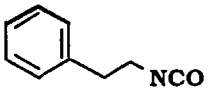
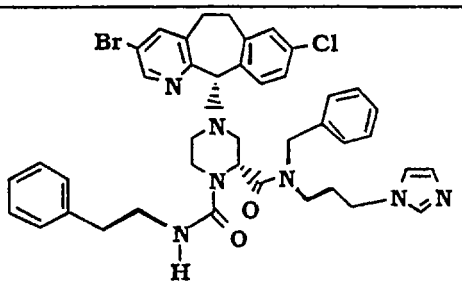
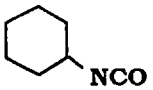
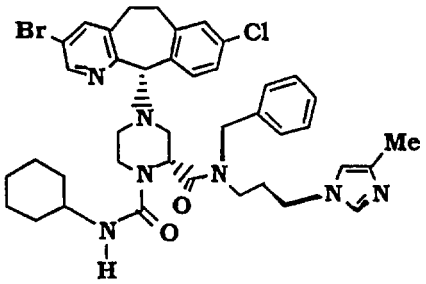
Following the procedure set forth for Example 127, but using the isocyanates and the compounds of the preparative examples given in Table 13 below, the Products given in Table 13 were obtained.

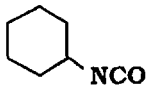
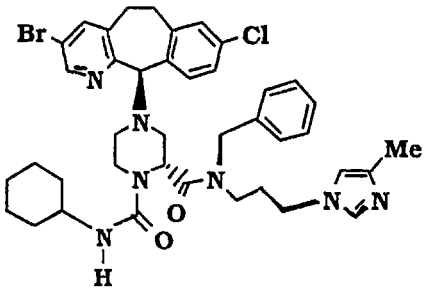
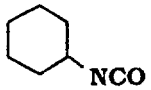
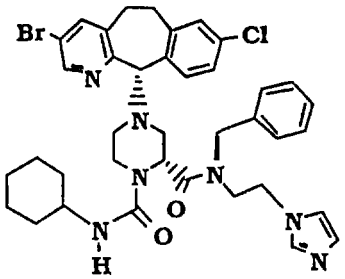
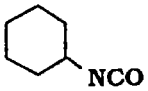
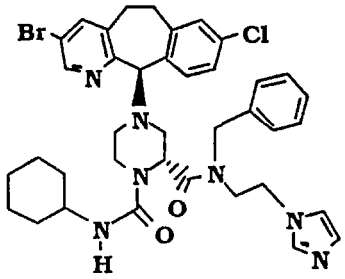
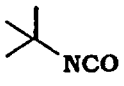
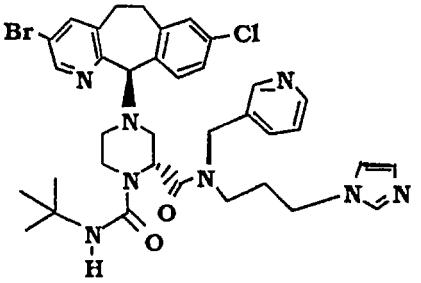
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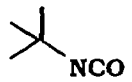
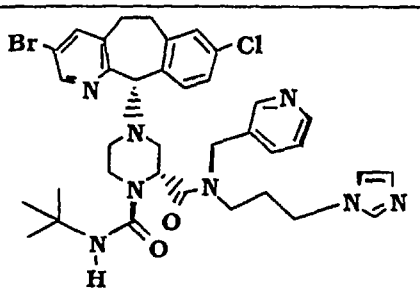
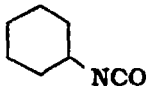
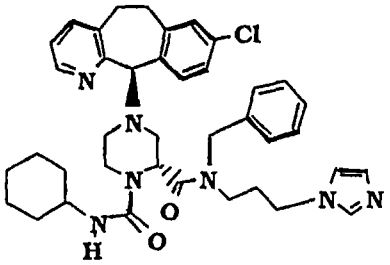
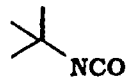
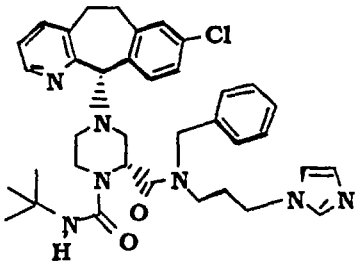
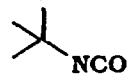
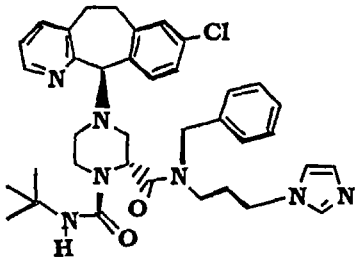
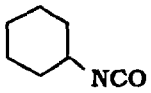
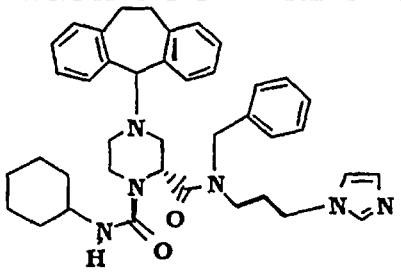
TABLE 13

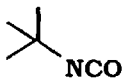
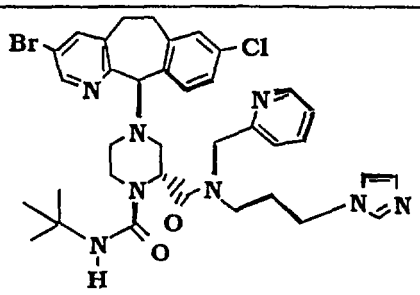
Ex.	Isocyanate and Prep. Ex. Compound	Product	1.Yield (%) 2. MH^+ 3. mp (°C)
128	 Prep. Ex. 109 Diastereomer A	 222421	1. 87 2. 760 3. 125.2
129	 Prep. Ex. 109 Diastereomer A		1. 61 2. 732 3. 126.6
130	 Prep. Ex. 109 Diastereomer B		1. 100 2. 732 3. 112.3

131	 Prep. Ex. 109 Diastereomer A		1. 95 2. 718 3. 109.8
132	 Prep. Ex. 109 Diastereomer B		1. 63 2. 718 3. 118.1
133	 Prep. Ex. 109 Diastereomer A		1. 95 2. 704 3. 93.5
134	 Prep. Ex. 109 Diastereomer B		1. 86 2. 718 3. 98.9

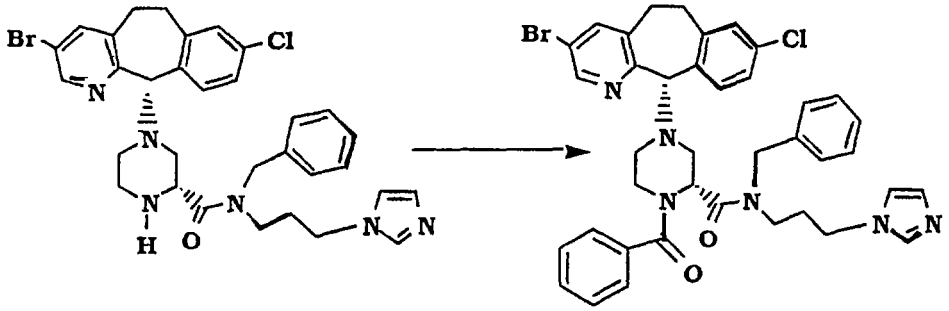
135	 Prep. Ex. 109 Diastereomer A		1. 56 2. 752 3. 81.4
136	 Prep. Ex. 109 Diastereomer A		1. 17 2. 766
137	 Prep. Ex. 109 Diastereomer A		1. 80 2. 780 3. 68.4
138	 Prep. Ex. 131 Diastereomer A		1. 68 2. 772

139	 Prep. Ex. 131 Diastereomer B		1. 53 2. 772
140	 Prep. Ex.113 Diastereomer A		1. 83 2. 744 3. 143.8
141	 Prep. Ex.113 Diastereomer B		1. 96 2. 744 3. 135.4
142	 Prep. Ex.117 Diastereomer B		1. 77 2. 733 3. 120.8

143	 Prep. Ex.117 Diastereomer A		1. 64 2. 733 3. 116.8
144	 Prep. Ex.111 Diastereomer B		1. 100 2. 680
145	 Prep. Ex.111 Diastereomer A		1. 79 2. 654 3. 61.3-69.3
146	 Prep. Ex.111 Diastereomer B		1. 97 2. 654 3. 97.0
147	 Prep. Ex.125		1. 91 2. 645

148	 Prep. Ex.130		1. 68 2. 735

EXAMPLE 149



To a solution of the title compound from Preparative Example 109 (11S,2R diastereomer A, 50 mg, 0.08 mmol) dissolved in anhydrous CH_2Cl_2 (1 mL) was added benzoyl chloride (0.02 mL, 0.16 mmol) and triethylamine (0.03 mL, 0.2 mmol) and the resulting mixture was stirred at room temperature under N_2 overnight. The solution was diluted with dichloromethane, washed with 1N aqueous NaOH and dried over anhydrous $MgSO_4$. Filtration and concentration *in vacuo* provided a residue which was purified by preparative plate chromatography (silica gel) using 5% MeOH-95% CH_2Cl_2 saturated with aqueous ammonium hydroxide to give the title compound as an off-white solid (54.4 mg, 93%, MH^+ = 737). SCH

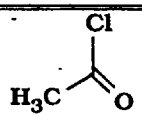
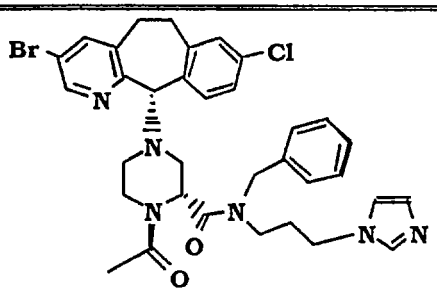
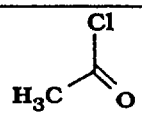
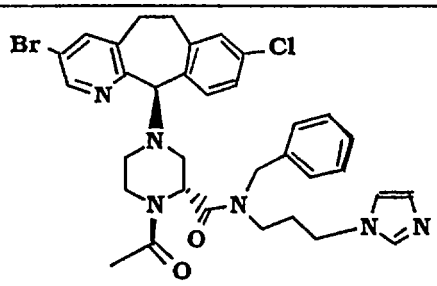
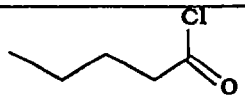
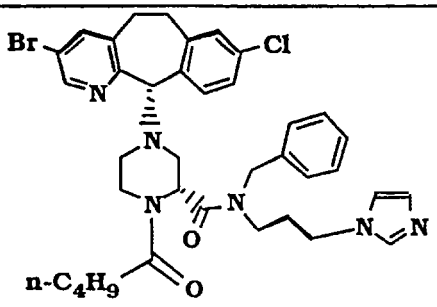
EXAMPLES 150-217

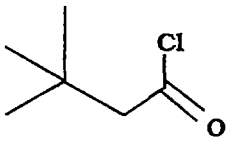
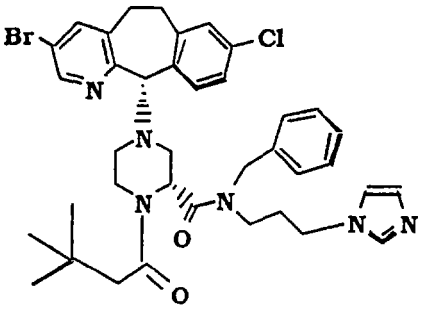
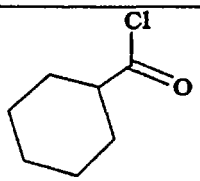
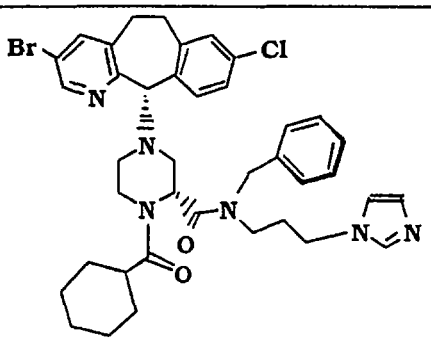
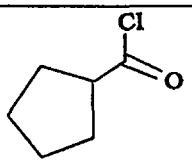
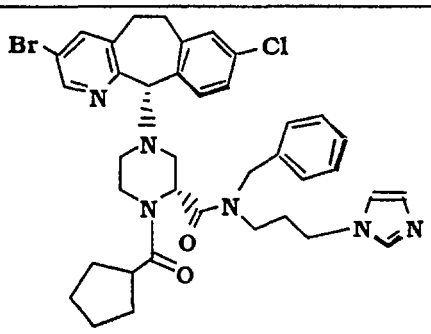
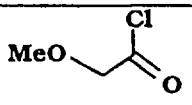
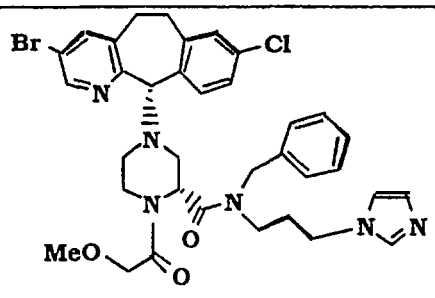
Similarly, using the procedure described for Example 149, the title compound (diastereomer A or B) from the Preparative Example given in Table 14 was treated with the corresponding acid chloride,

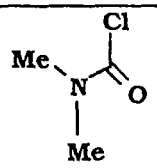
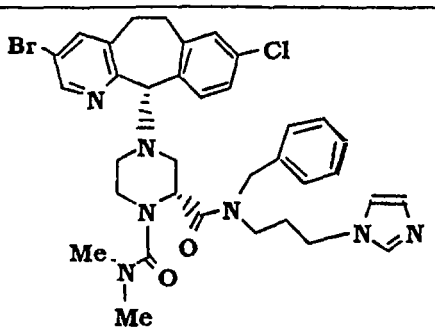
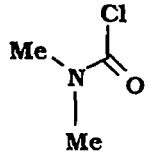
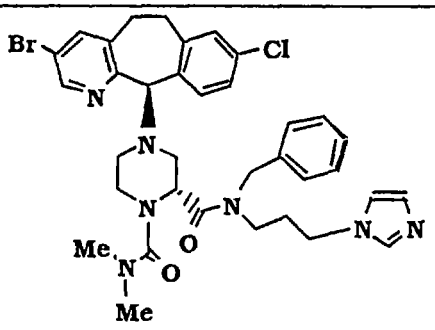
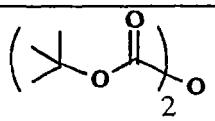
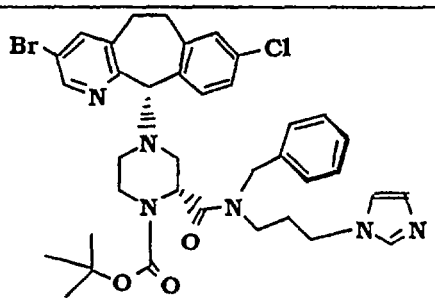
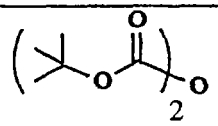
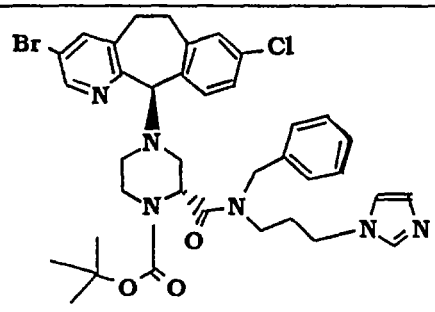
chloroformate, carbamyl chloride, dicarbonate, anhydride or sulfonyl chloride given in Table 14 below (Electrophile column) to give the N-substituted arylalkyl or heteroarylalkyl Products listed in Table 14.

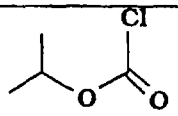
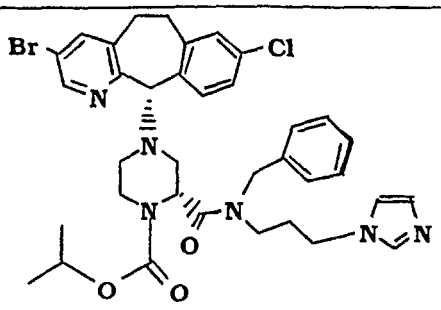
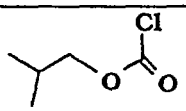
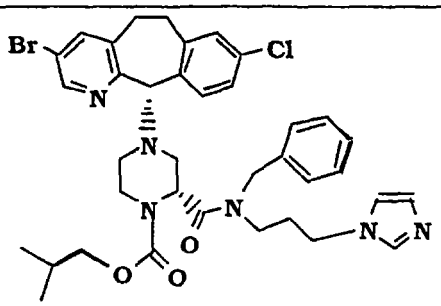
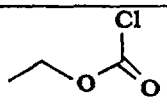
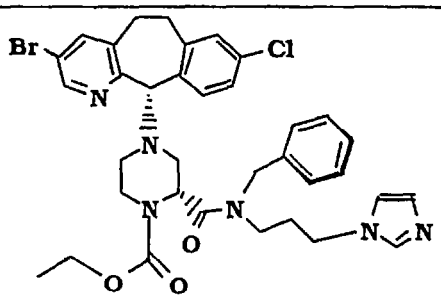
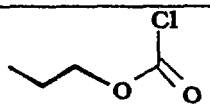
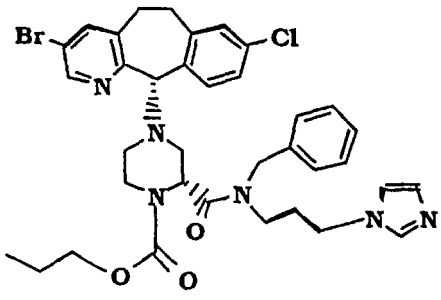
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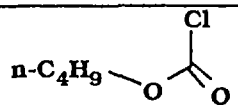
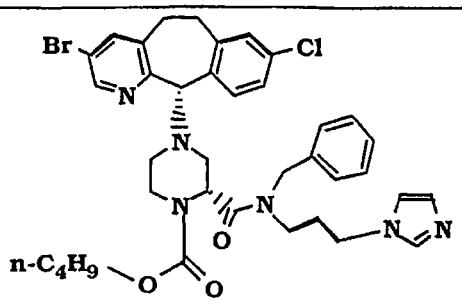
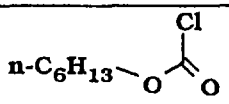
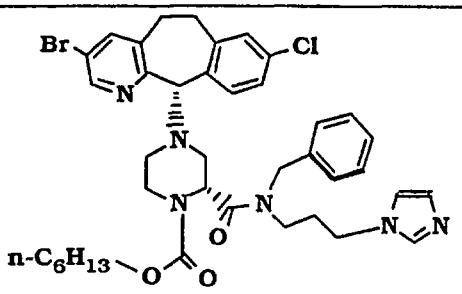
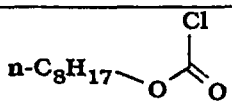
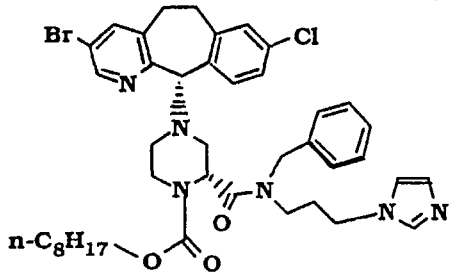
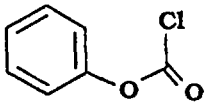
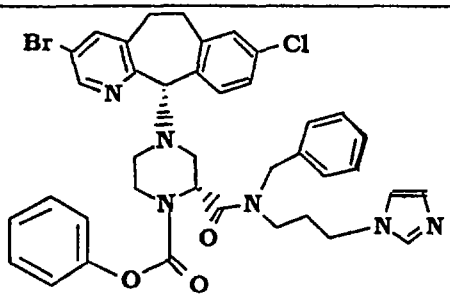
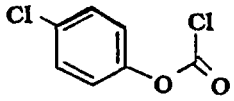
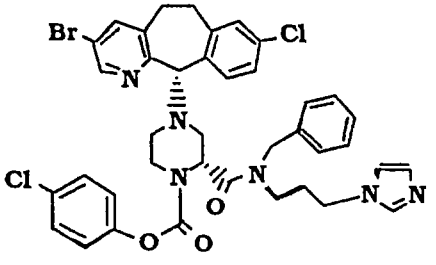
TABLE 14

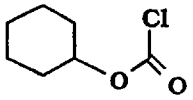
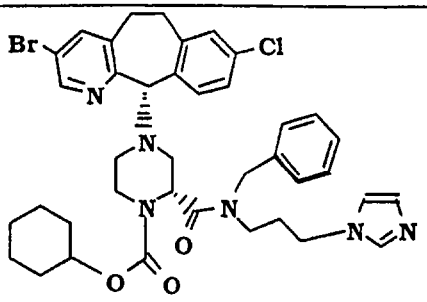
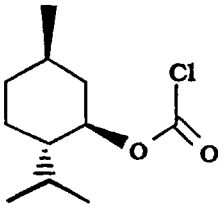
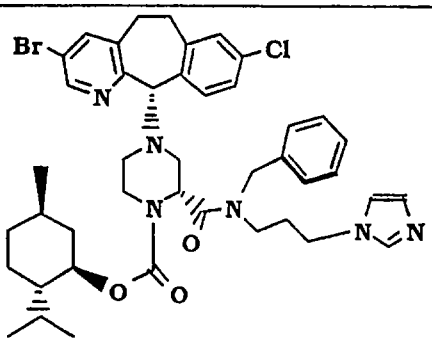
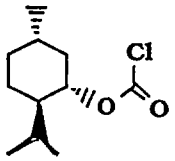
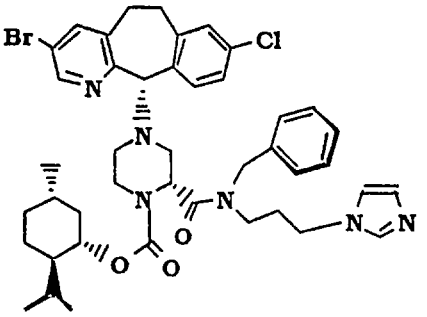
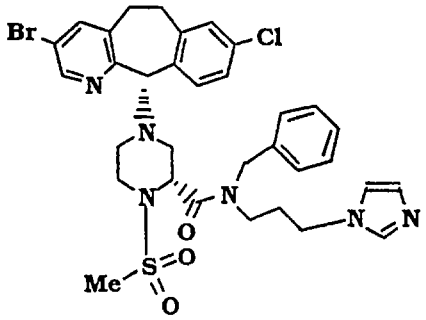
Ex.	Electrophile and Prep. Ex. Compound	Product	1. Yield (%) 2. MH^+ 3. mp (°C)
150	 Prep Ex. 109 Diastereomer A		1. 54 2. 675 3. 79.7
151	 Prep Ex. 109 Diastereomer B		1. 75 2. 675 3. 69.3
152	 Prep Ex. 109 Diastereomer A		1. 72 2. 717 3. 86.4

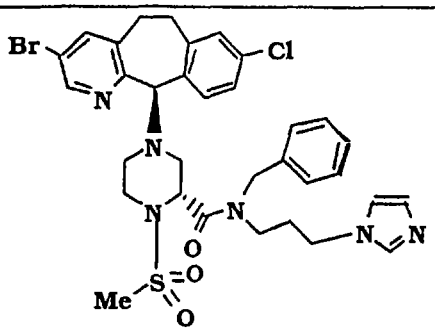
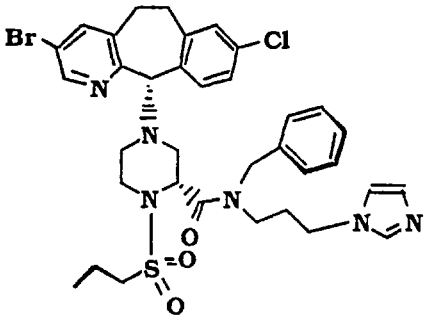
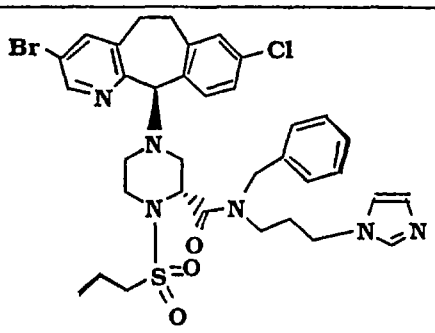
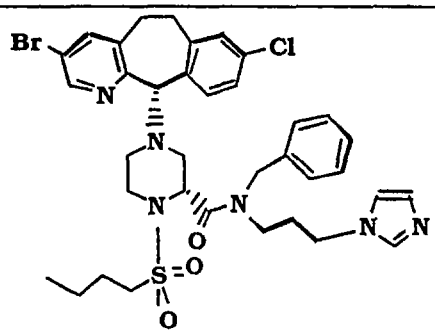
153	 Prep Ex. 109 Diastereomer A		1. 172 2. 731 3. 85.4
154	 Prep Ex. 109 Diastereomer A		1. 85 2. 743 3. 100-101
155	 Prep Ex. 109 Diastereomer A		1. 88 2. 729 3. 101-104
156	 Prep Ex. 109 Diastereomer A		1. 61 2. 705 3. 102.7

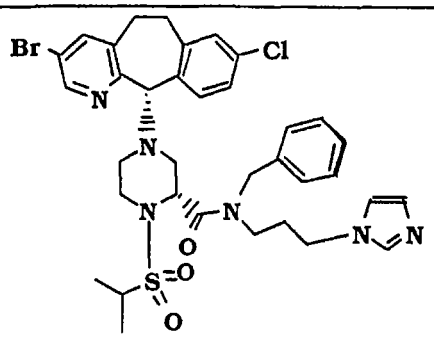
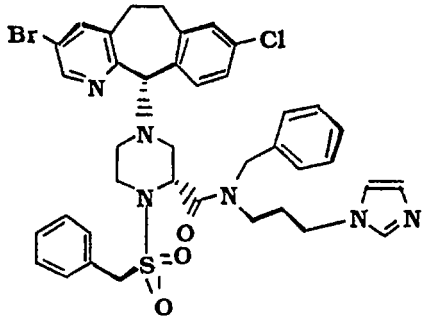
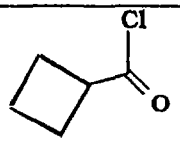
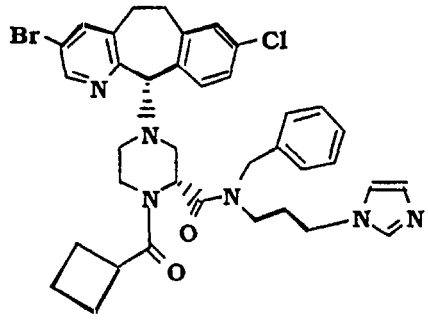
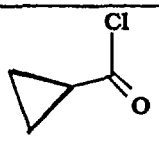
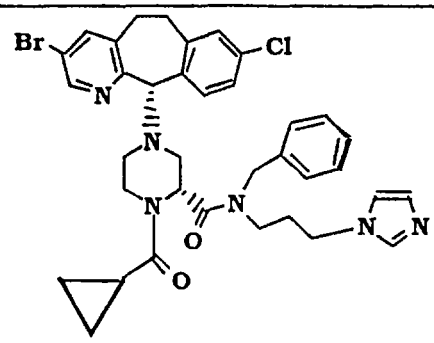
157	 Prep Ex. 109 Diastereomer A		1. 92 2. 704 3. 114.7
158	 Prep Ex. 109 Diastereomer B		1. 100 2. 704 3. 110.4
159	 Prep Ex. 109 Diastereomer A		1. 97 2. 733 3. 103.5
160	 Prep Ex. 109 Diastereomer B		1. 83 2. 733 3. 94.5

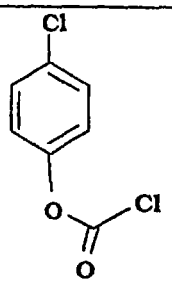
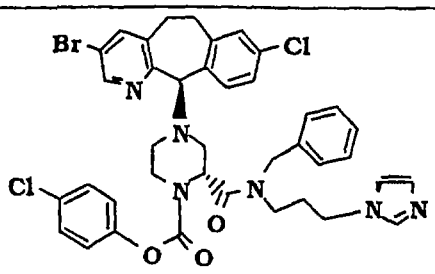
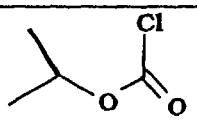
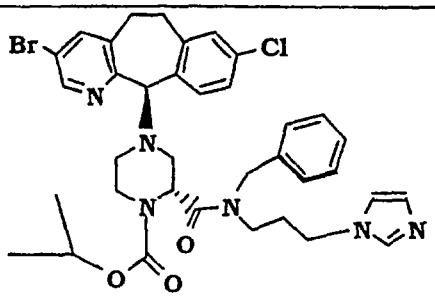
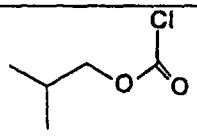
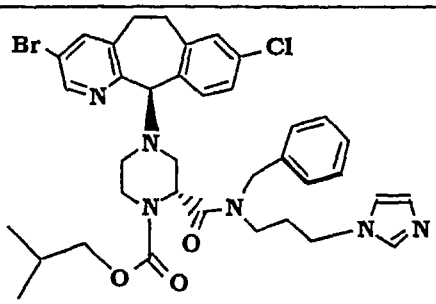
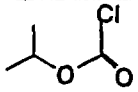
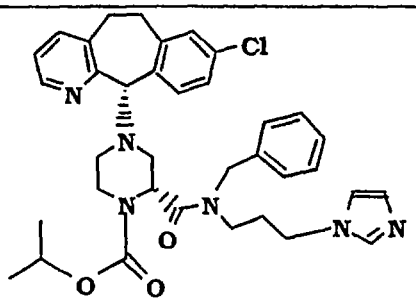
161	 Prep Ex. 109 Diastereomer A		1. 85 2. 719 3. 95.5
162	 Prep Ex. 109 Diastereomer A		1. 87 2. 733 3. 84.5
163	 Prep Ex. 109 Diastereomer A		1. 89 2. 705 3. 93.7
164	 Prep Ex. 109 Diastereomer A		1. 89 2. 719 3. 79.8

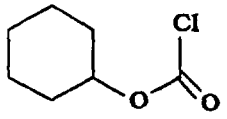
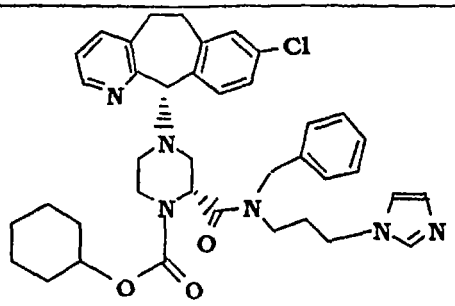
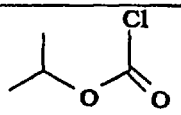
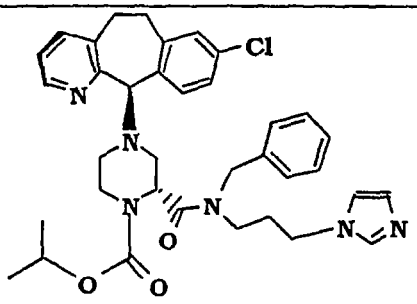
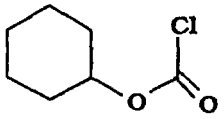
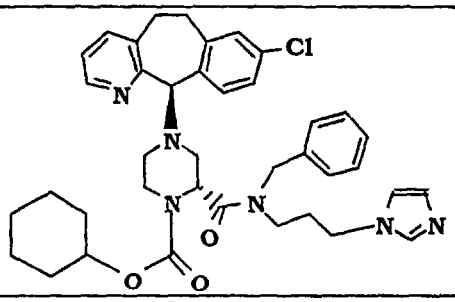
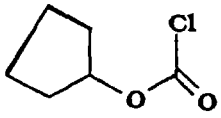
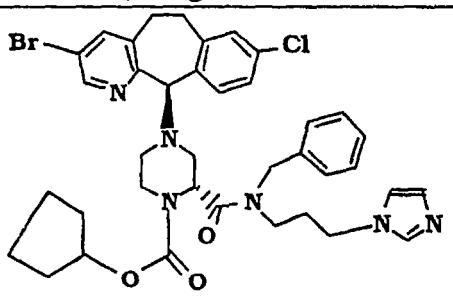
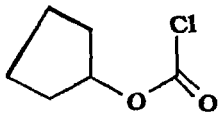
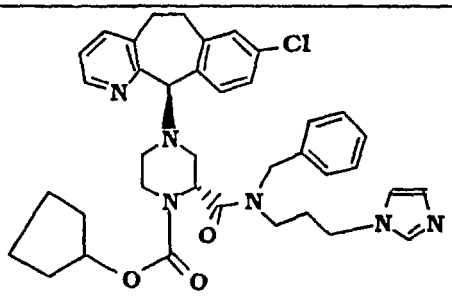
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166	 Prep Ex. 109 Diastereomer A		1. 83 2. 761 3. 60.2
167	 Prep Ex. 109 Diastereomer A		1. 86 2. 789 3. 63.1
168	 Prep Ex. 109 Diastereomer A		1. 50 2. 753 3. 91.1
169	 Prep Ex. 109 Diastereomer A		1. 91 2. 787 3. 87.3

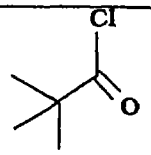
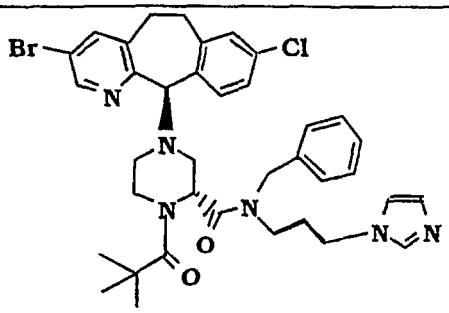
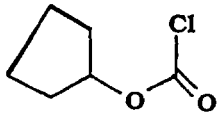
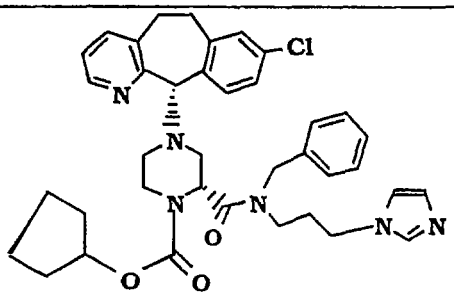
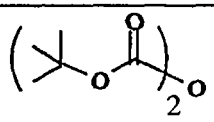
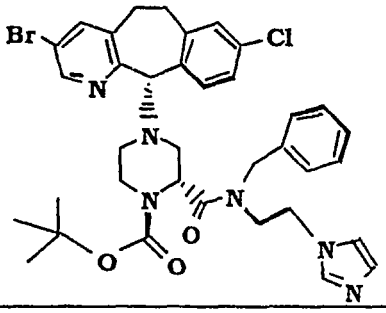
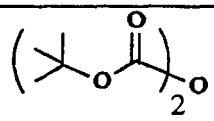
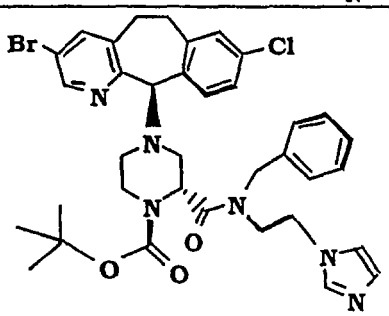
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171	 Prep Ex. 109 Diastereomer A		1. 96 2. 815 3. 96.4
172	 Prep Ex. 109 Diastereomer A		1. 88 2. 815 3. 95.8
173	$MeSO_2Cl$ Prep Ex. 109 Diastereomer A		1. 68 2. 711 3. 113.6

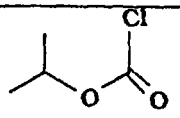
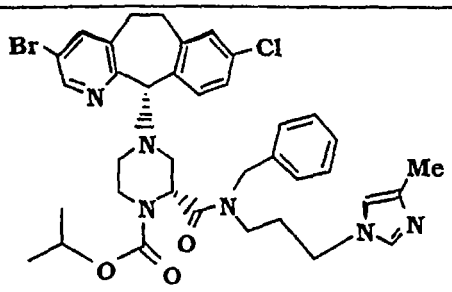
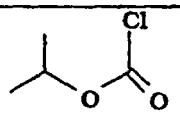
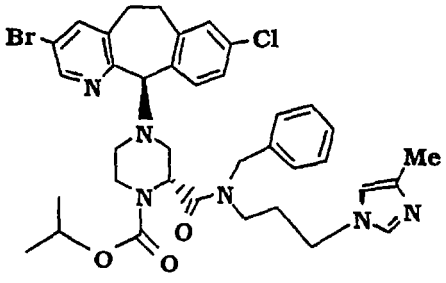
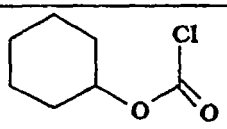
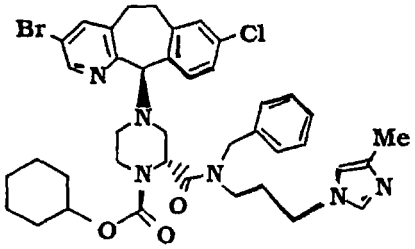
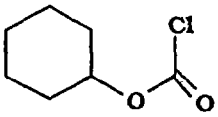
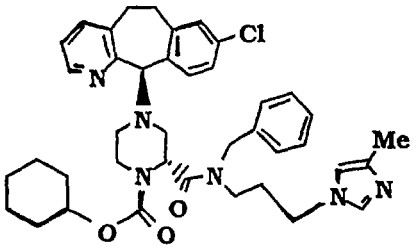
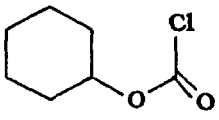
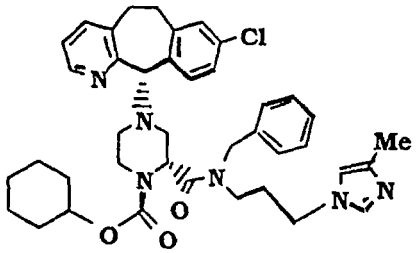
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176	n-$PrSO_2Cl$ Prep Ex. 109 Diastereomer B		1. 15 2. 739 3. 93.8
177	n-$BuSO_2Cl$ Prep Ex. 109 Diastereomer A		1. 40 2. 753 3. 87.9

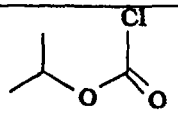
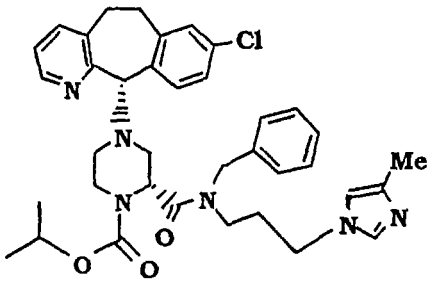
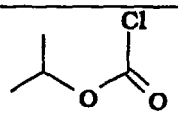
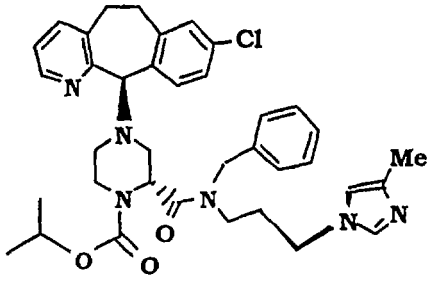
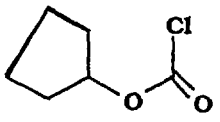
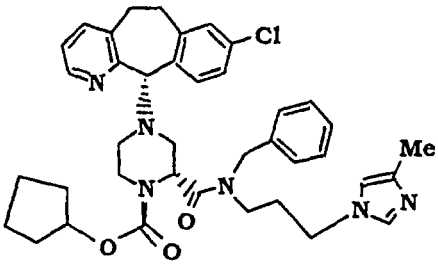
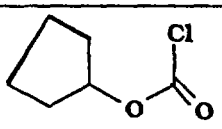
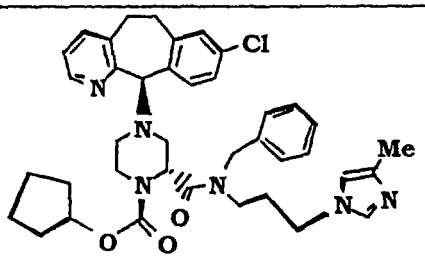
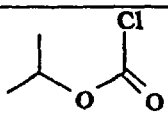
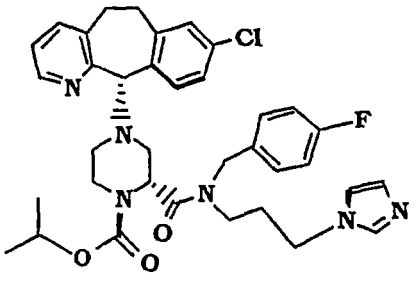
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179	$PhCH_2SO_2Cl$ Prep Ex. 109 Diastereomer A		1. 50 2. 787 3. 110.4
180	 Prep Ex. 109 Diastereomer A		1. 92 2. 715 3. 105.5
181	 Prep Ex. 109 Diastereomer A		1. 98 2. 701 3. 106.8

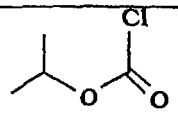
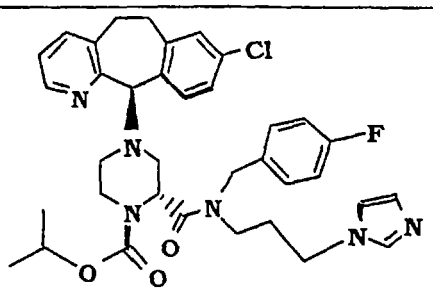
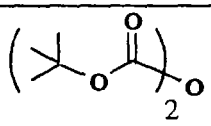
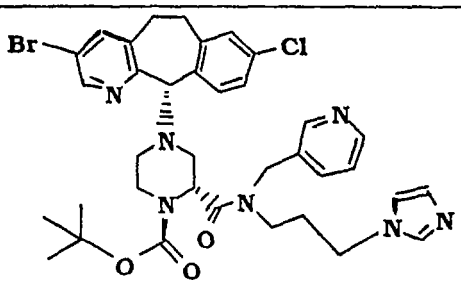
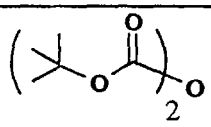
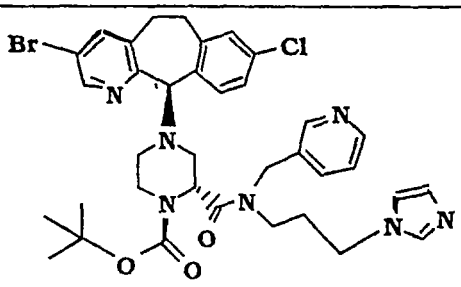
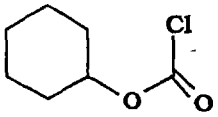
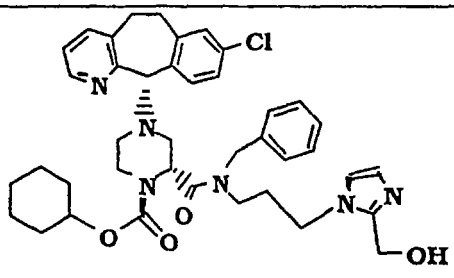
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183	 Prep Ex. 109 Diastereomer B		1. 57 2. 719 3. 95.2
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185	 Prep Ex. 111 Diastereomer A		1. 53 2. 641 3. 89.6

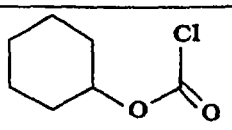
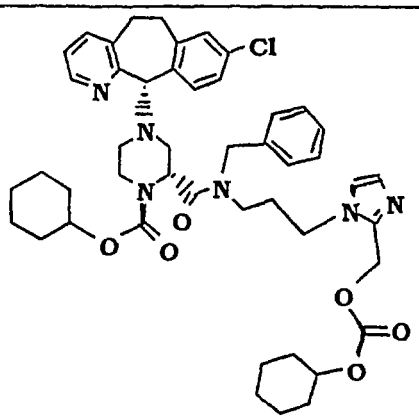
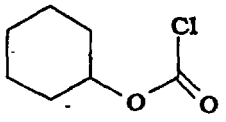
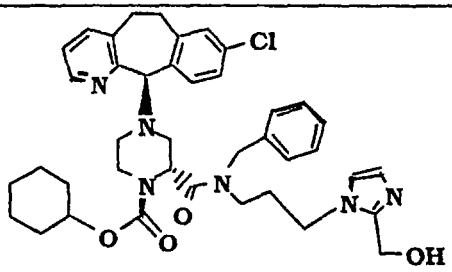
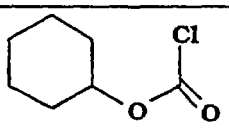
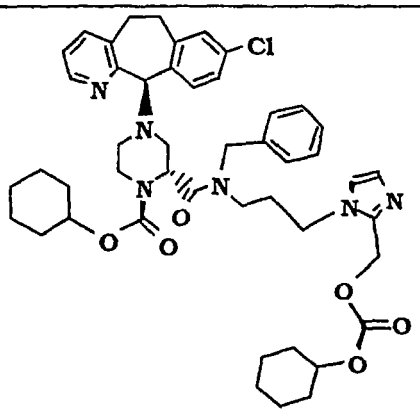
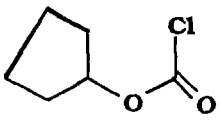
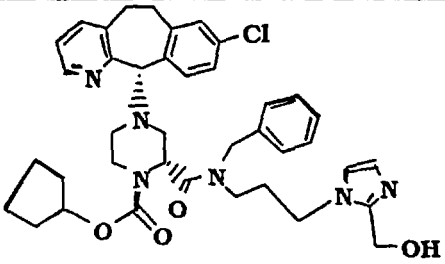
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188	 Prep Ex. 111 Diastereomer B		1. 61 2. 681 3. 87.9
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190	 Prep Ex. 111 Diastereomer B		1. 72 2. 667 3. 97.2

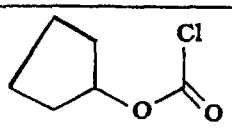
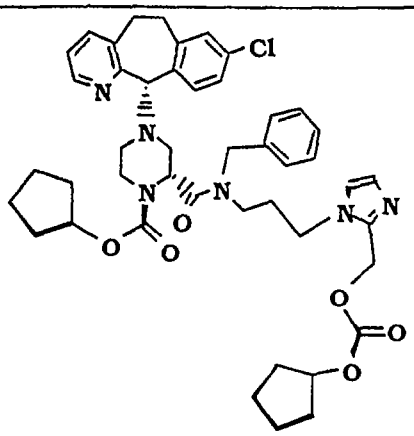
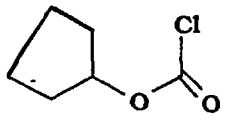
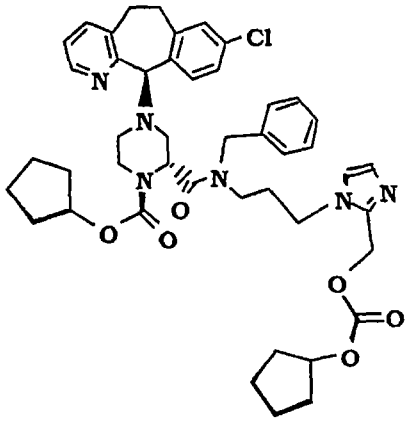
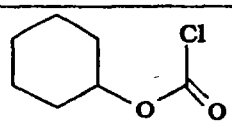
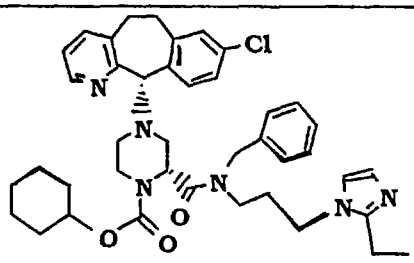
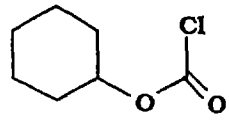
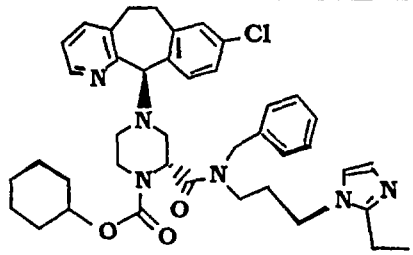
191	 Prep Ex. 109 Diastereomer B		1. 52 2. 717 3. 91.8
192	 Prep Ex. 111 Diastereomer A		1. 81 2. 667 3. 85.8
193	 Prep Ex. 113 Diastereomer A		1. 76 2. 719 3. 206.7
194	 Prep Ex. 113 Diastereomer B		1. 85 2. 719 3. 121.2-130.4

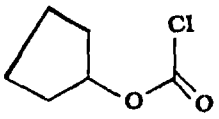
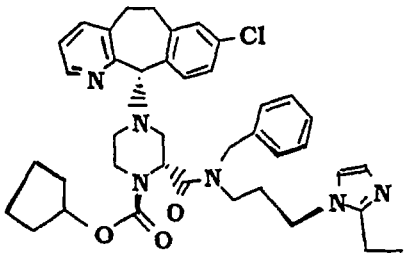
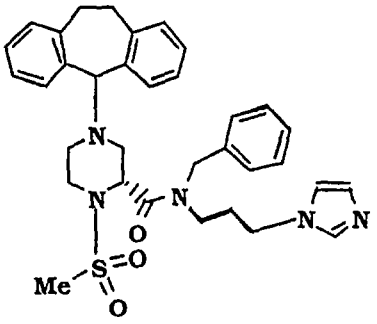
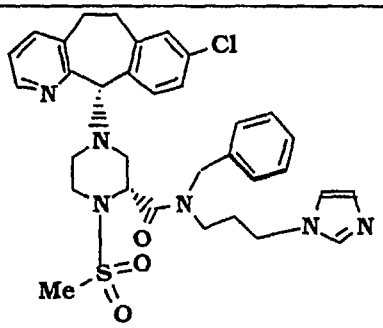
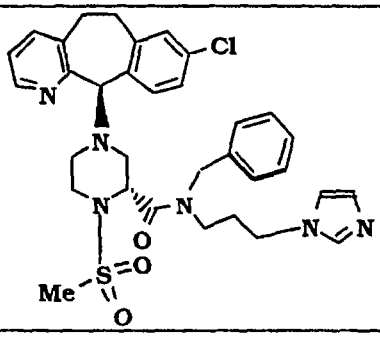
195	 Prep Ex. 131 Diastereomer A		1. 69 2. 733 3. 96.1-120.3
196	 Prep Ex. 131 Diastereomer B		1. 77 2. 733 3. 105.1-114.2
197	 Prep Ex. 131 Diastereomer B		1. 56 2. 775 3. 100.4-108.8
198	 Prep Ex. 114 Diastereomer B		1. 69 2. 695 3. 82.5
199	 Prep Ex. 114 Diastereomer A		1. 60 2. 695 3. 83.4

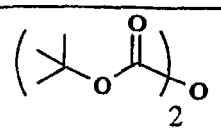
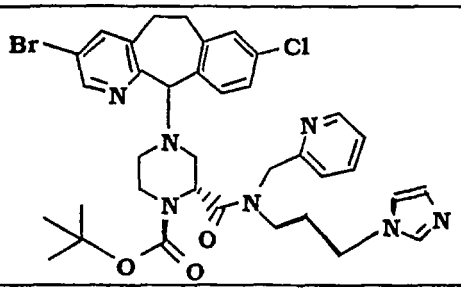
200	 Prep Ex. 114 Diastereomer A		1. 61 2. 655 3. 83.2
201	 Prep Ex. 114 Diastereomer B		1. 64 2. 655 3. 81.2
202	 Prep Ex. 114 Diastereomer A		1. 72 2. 681 3. 98.2
203	 Prep Ex. 114 Diastereomer B		1. 76 2. 681 3. 94.5
204	 Prep Ex. 108 Diastereomer A		1. 62 2. 659 3. 97.8

205	 Prep Ex. 108 Diastereomer B		1. 83 2. 56.7 3. 659
206	 Prep Ex. 117 Diastereomer A		1. 64 2. 734 3. 114.9
207	 Prep Ex. 117 Diastereomer B		1. 36 2. 734 3. 124.2
208	 Prep Ex. 121 Diastereomer A		1. 45 2. 711 3. 95.1

208 A	 Prep Ex. 121 Diastereomer A		----
209	 Prep Ex. 121 Diastereomer B		1. 39 2. 711 3. 101.8
209 A	 Prep Ex. 121 Diastereomer B		----
210	 Prep Ex. 121 Diastereomer A		1. 49 2. 697 3. 64.3

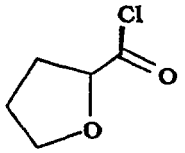
210 A	 Prep Ex. 121 Diastereomer A		----
210 B	 Prep Ex. 121 Diastereomer B		----
211	 Prep Ex. 124 Diastereomer A		1. 93 2. 709 3. 83.2
212	 Prep Ex. 124 Diastereomer B		1. 94 2. 709 3. 83.6

213	 Prep Ex. 124 Diastereomer A		1. 68 2. 695 3. 88.2
214	$MeSO_2Cl$ Prep Ex. 125		1. 81 2. 598 3. 81
215	$MeSO_2Cl$ Prep Ex. 111 Diastereomer A		1. 69 2. 633 3. 69
216	$MeSO_2Cl$ Prep Ex. 111 Diastereomer B		1. 71 2. 633 3. 106

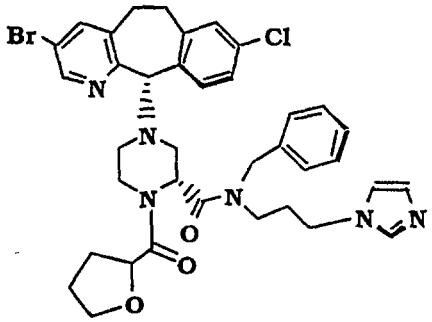
217	 Prep Ex. 130		1. 73 2. 736

EXAMPLE 218

If the procedure described in Example 149 were followed, the title compound from Preparative Example 109 (diastereomer A) could be reacted with

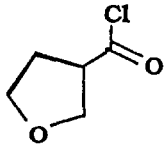


to give the compound

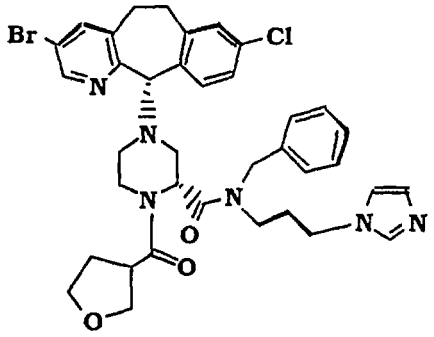


EXAMPLE 219

If the procedure described in Example 149 were followed, the title compound from Preparative Example 109 (diastereomer A) could be reacted with

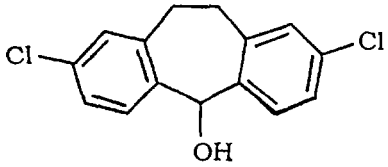


to give the compound

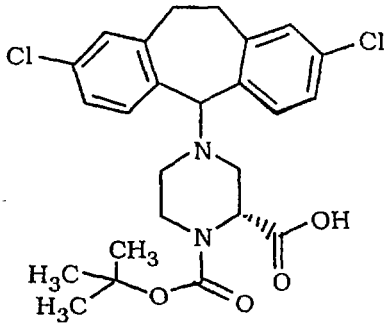


EXAMPLE 220

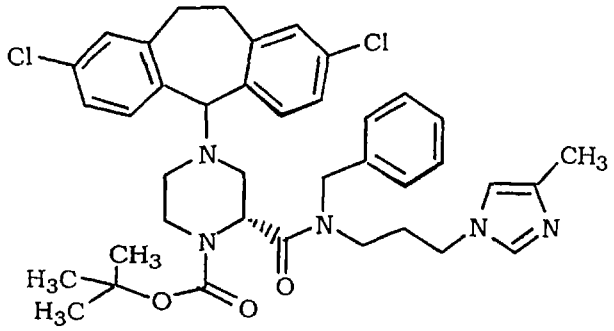
If the procedure set forth in Preparative Example 51 were followed, but substituting the 3,8-dichloro tricyclic alcohol



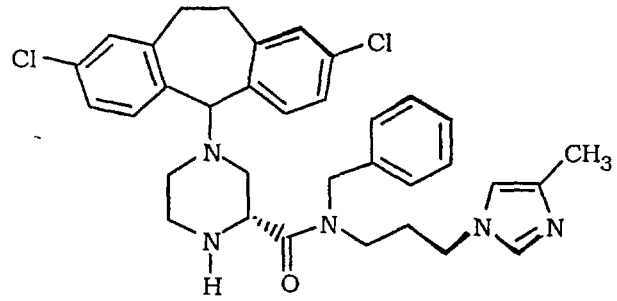
for the 3-Br-8-Cl tricyclic alcohol, the following compound could be prepared:



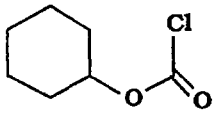
Then, if the procedure of Example 113 were followed to react the above compound with the title compound from Preparative Example 95.1 the following compound could be obtained



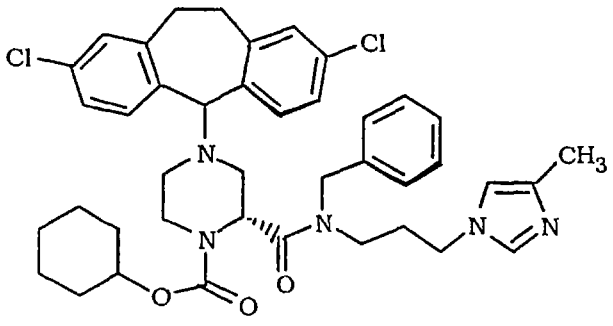
Then, if the procedure of Preparative Example 109 were followed using the above compound the following compound could be obtained:



Then if the procedure of Example 149 were followed using the above compound and



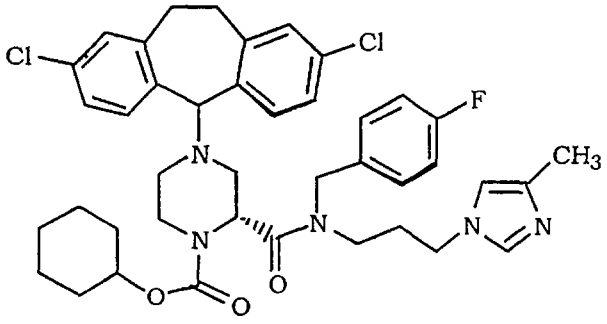
the following compound could be obtained



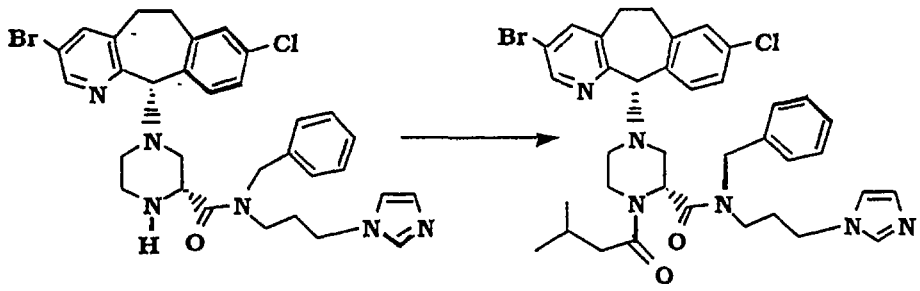
EXAMPLE 220A

If the procedure of Example 220 were followed, but the title compound from Preparative Example 90 were used instead of the

title compound from Preparative Example 95.1 in the procedural step of Example 113, the following compound could be obtained



EXAMPLE 221

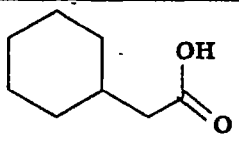
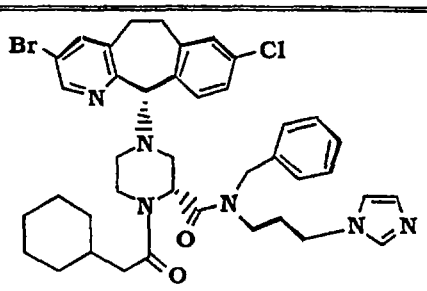
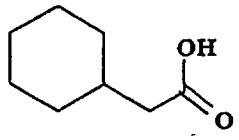
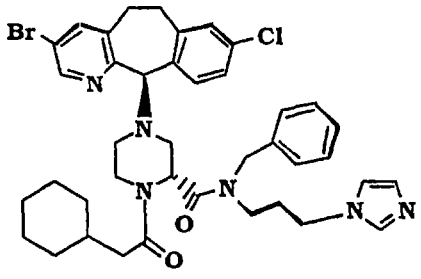
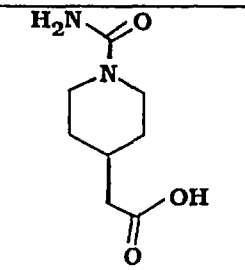
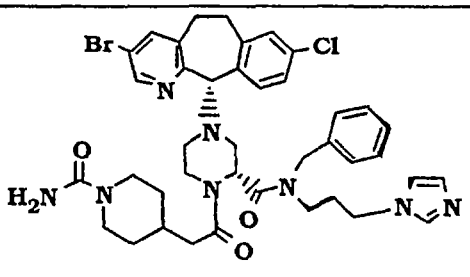


To a solution of the title compound from Preparative Example 109 (11S,2Rdiastereomer A, 75 mg, 0.12 mmol) dissolved in anhydrous DMF (1 mL) was added HOBT (32 mg, 0.24 mmol), DEC (45.4 mg, 0.24 mmol) and isovaleric acid (0.026 mL, 0.24 mmol) and the resulting solution was stirred at room temperature under N_2 overnight. The solution was concentrated in vacuo, diluted with dichloromethane, washed with 1N aqueous NaOH and dried over anhydrous $MgSO_4$. Filtration and concentration *in vacuo* provided a residue which was purified by preparative plate chromatography (silica gel) using 5% MeOH-95% CH_2Cl_2 saturated with aqueous ammonium hydroxide to give the title compound as an off-white solid (81.5 mg, 96%, MH^+ = 717).

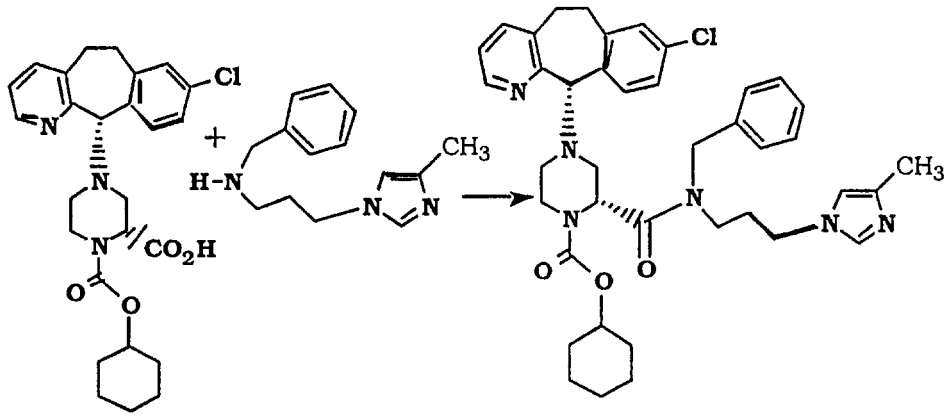
EXAMPLES 222-224

Following the procedure described for Example 221, the title compound (diastereomer A or B) from Preparative Example 109 was treated with the carboxylic acid given in Table 15 to give the N-benzyl Product listed in Table 15.

TABLE 15

Ex.	Carboxylic Acid and Diastereomer of Prep. Ex. 109	Product	1. Yield (%) 2. MH^+ 3. mp(°C)
222	 Diastereomer A		1. 74 2. 757 3. 94.7
223	 Diastereomer B		1. 85 2. 757 3. 104.2
224	 Diastereomer A		1. 59 2. 801 3. 129.3

EXAMPLE 225

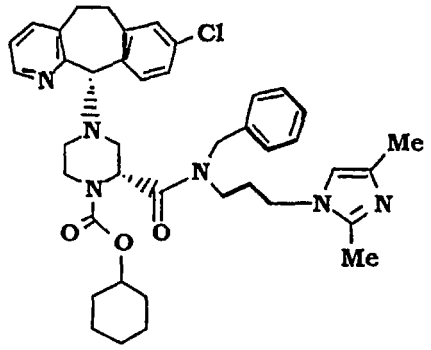
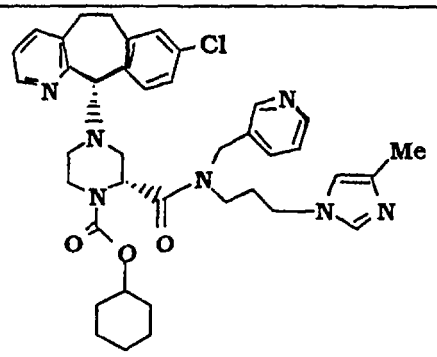
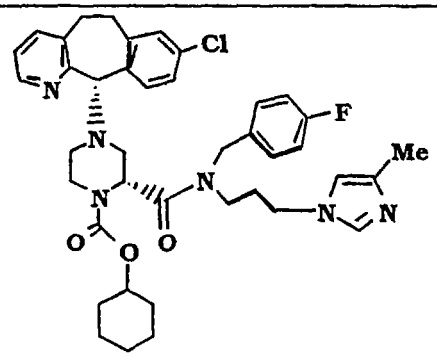


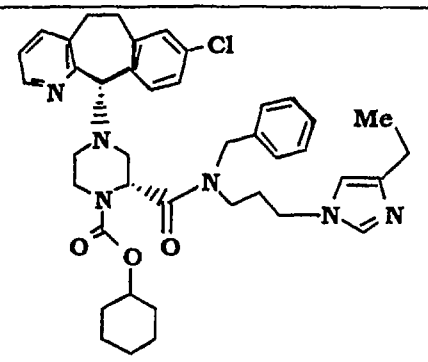
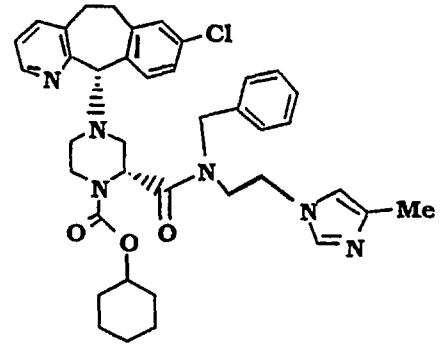
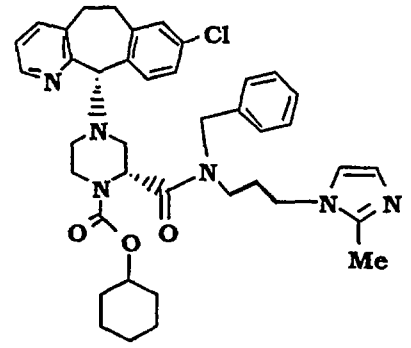
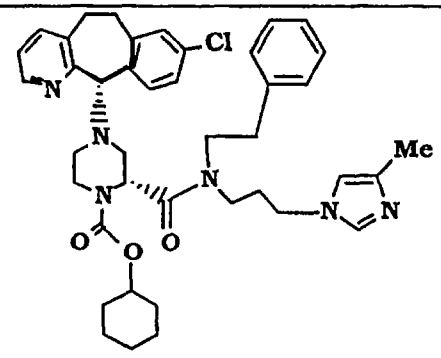
To the title compound from Preparative Example 127 Step C (11S,2R diastereomer A) (1.73 g, 3.57 mmol) were added HOBt (0.689 g, 5.1 mmol), DEC (0.98 g, 5.1 mmol), the title compound from Preparative Example 95.1 (0.9 g, 3.9 mmol), NMM (0.87 mL, 7.9 mmol) and anhydrous DMF (20 mL). The mixture was stirred at room temperature under N_2 overnight. The mixture was concentrated *in vacuo*, diluted with CH_2Cl_2 and washed with a saturated aqueous solution of $NaHCO_3$. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica gel) using 2% MeOH-98% CH_2Cl_2 saturated with aqueous ammonium hydroxide to give the title compound (1.7 g, 69%, MH^+ = 695).

EXAMPLES 226-232

Following the procedure described for Example 225, the Products listed in Table 16 below were prepared using the carboxylic acid from Preparative Example 127 Step C (diastereomer A) and the appropriate N-substituted imidazolylalkyl amine purified by preparative chiral chromatography (Chiralpack AD, 5 cm X 50 cm column, flow rate 80 mL/min, 5-13% IPA-Hexane +0.2% diethylamine).

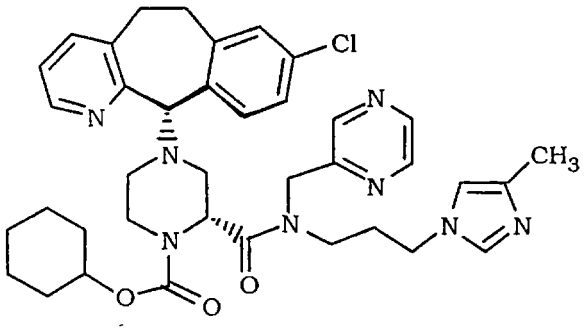
TABLE 16

Ex.	Amine of Prep Ex. No.	Product	1. Yield (%) 2. MH^+ 3. mp (°C)
226	89		1. 40 2. 709 3. 92.4
227	86		1. 43 2. 696 3. 93.7
228	90		1. 39 2. 713 3. 74.6

229	91		1. 44 2. 708 3. 85.6
230	93		1. 29 2. 681 3. 82.2
231	94		1. 71 2. 695 3. 79.7
232	101		1. 62 2. 709 3. 85.6

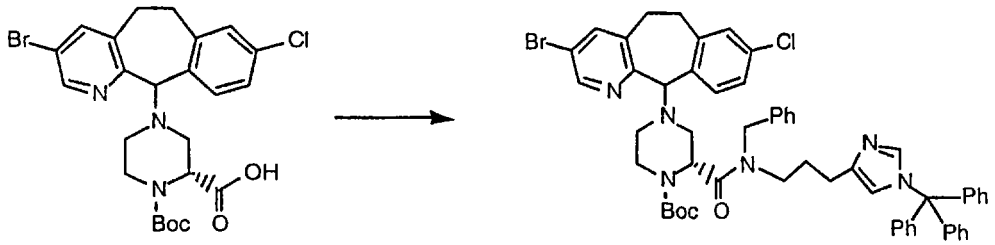
EXAMPLES 234B

If the procedure of Example 225 were followed, but the amine from Preparative Example 101.2 was to be used, then the following compound would be obtained



Example 234B

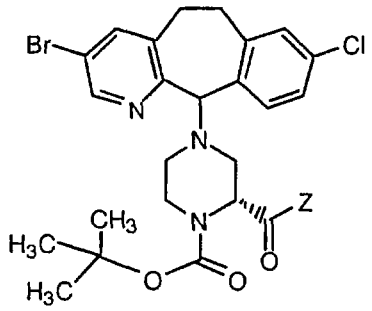
EXAMPLE 235



The title compound from Preparative Example 51 (0.184g, 0.35 mmoles.) was added to a solution of the title compound from Preprative Example 132 Step C (0.2g, 0.437 mmol), DEC (0.168g, 0.87 mmoles.), HOBT (0.118g, 0.87 mmoles.) and NMM (0.22 g, 2.19 mmoles.) in DMF (10 mL). The resulting solution was stirred at room temperature 24 hours. The reaction mixture was diluted with H_2O until precipitation ceased and the slurry filtered. The precipitate was diluted with CH_2Cl_2 ,washed with brine,dried over Na_2SO_4 and concentrated. The crude product was purified by chromatography using a 5% (10%NH_4OH in MeOH) solution in CH_2Cl_2 as eluent to give the title compound (0.18g, 42 % yield).

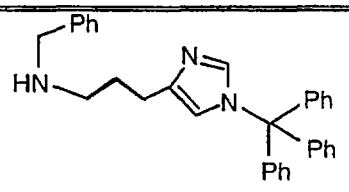
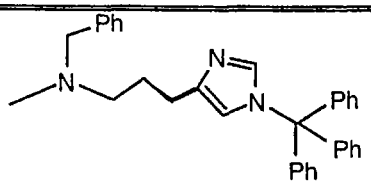
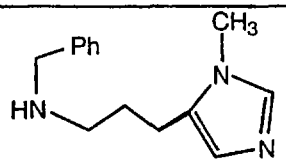
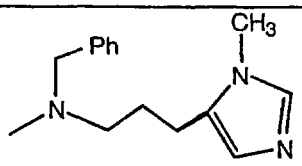
EXAMPLES 236-238

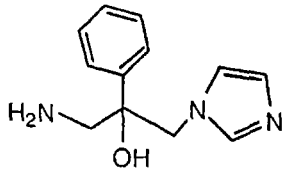
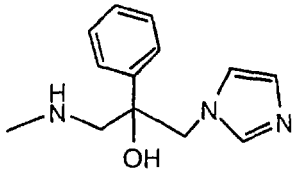
Following essentially the same procedure as set forth in Example 235, except using the amine given in Table 18, compounds of the formula



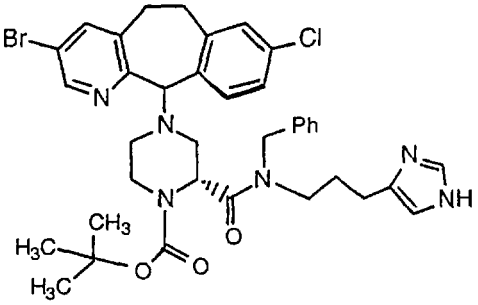
are obtained, wherein Z is as defined in Table 18.

TABLE 18

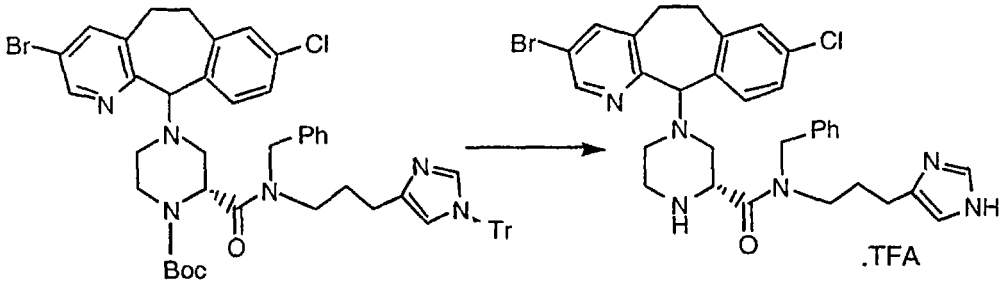
Ex.	Amine	Z
236		 FAB: MH^+ = 975
237		 FAB: MH^+ = 747

238		 FAB: MH^+ = 735

EXAMPLE 239

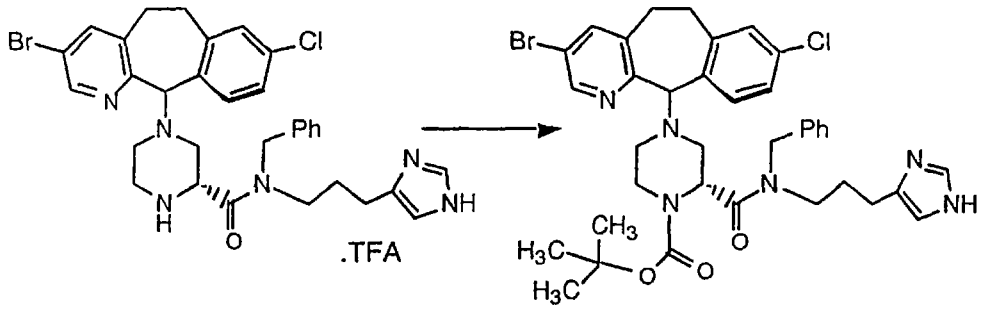


Step A



The title compound from Example 235 (0.5g, 0.517 mmoles) in CH_2Cl_2 (50 mL) was stirred with TFA (6 mL) at room temperature overnight. The reaction mixture was evaporated to give the title compound as a TFA salt (0.743g) which was used for following reactions.

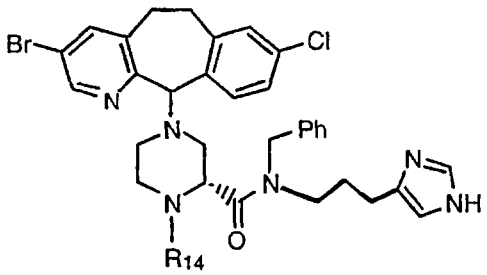
Step B



To a stirred solution of the title compound from Step A (0.102g, 0.0936 mmoles), triethyl amine (0.0798g, 0.798 mmoles) in CH_2Cl_2, di-tert-butyldicarbonate (0.0515g, 0.236 mmoles) was added and stirred overnight. Evaporated to a residue which was stirred in 2N ammonia solution in methanol (2 mL) overnight and evaporated to dryness. The residue was chromatographed on silica gel using 5% (10% conc NH_4OH in methanol) to give the title compound (0.043g).

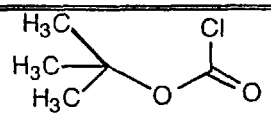
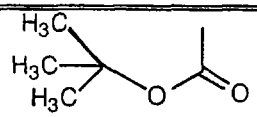
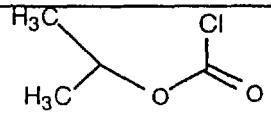
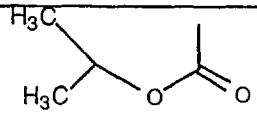
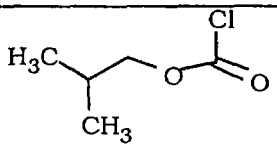
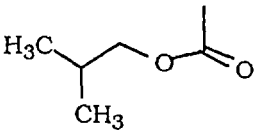
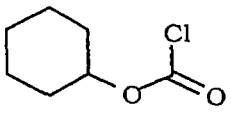
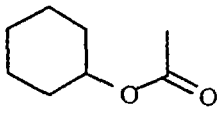
EXAMPLES 240-243

Following essentially the same procedure as that set forth in Example 239 Step B, except using the chloroformate given in Table 19 below, compounds of the formula:

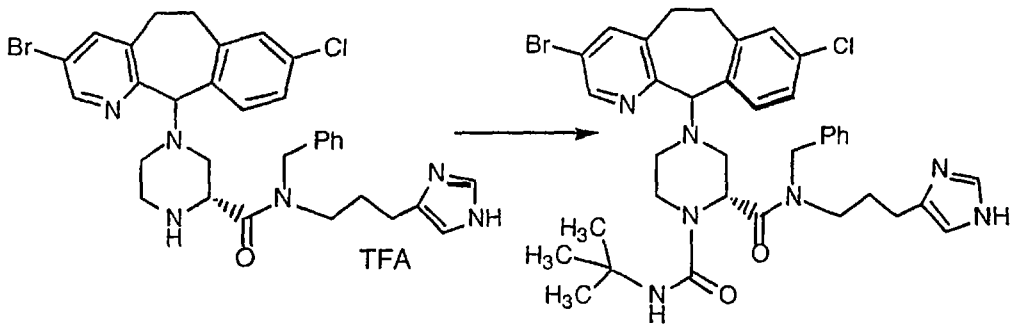


were obtained, wherein R^{14} is as defined in Table 19.

TABLE 19

Ex.	Chloroformate	R^{14}
240		 (R, S) FAB: MH^+ = 733
241		 (R, S) FAB: MH^+ = 719
242		 (R, S) FAB: MH^+ = 733
243		 (R, S) FAB: MH^+ = 759

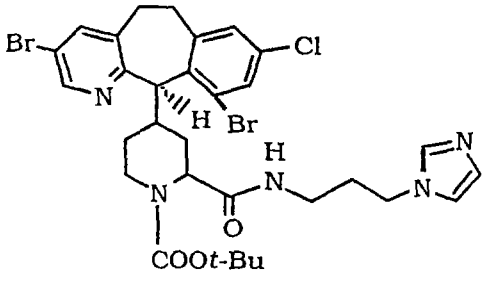
EXAMPLE 244



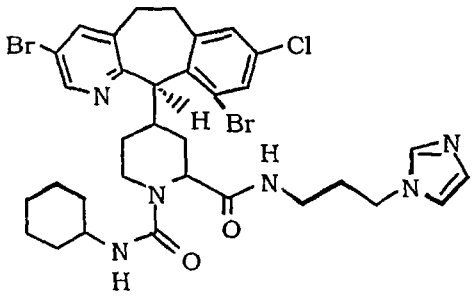
To a solution of the title compound from Step A of Example 239 (0.126g, 0.126 mmoles), triethylamine (0.071g, 0.726 mmoles) in CH_2Cl_2 (5 mL), t-butylisocyanate (0.018g, 0.189 mmoles) was added. The resulting solution was stirred at room temperature overnight. Evaporated to dryness and the residue was then stirred with 2N ammonia solution in methanol (3 mL) overnight. Evaporated to dryness and the product was chromatographed on silica gel using 5% (10% conc. NH_4OH in methanol)-CH_2Cl_2 as the eluant to give the title compound. (0.046g) CIMS: m/z (MH^+) 732.

Examples 245-254

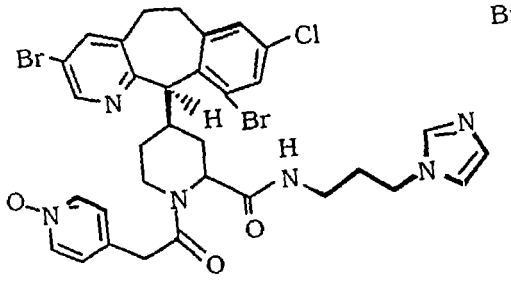
Following the procedures set forth in Examples 77-79 and 86, but using the diastereomeric mixture A and B from Preparative Example 135 and the appropriate amido-imidazole, the following compounds were prepared:



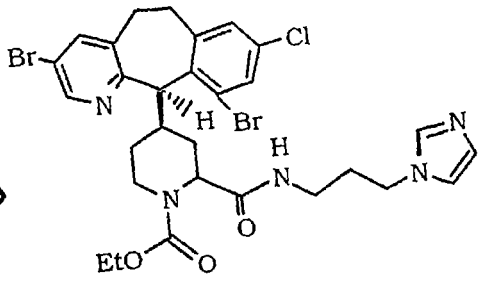
(Example 245)



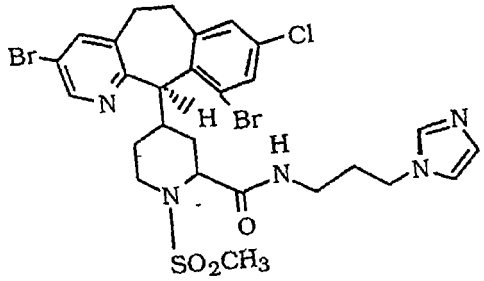
(Example 246)



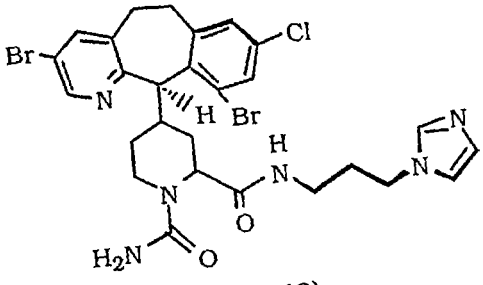
(Example 247)



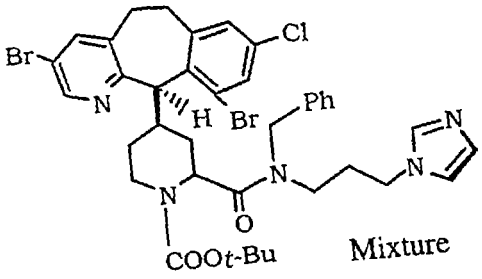
(Example 248)



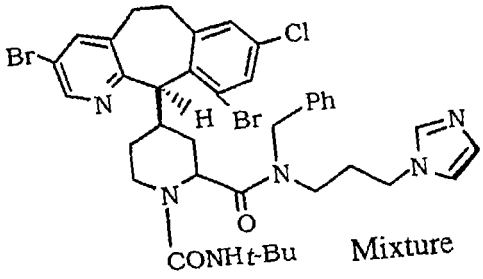
(Example 249)



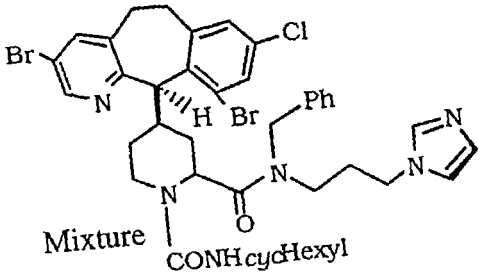
(Example 250)



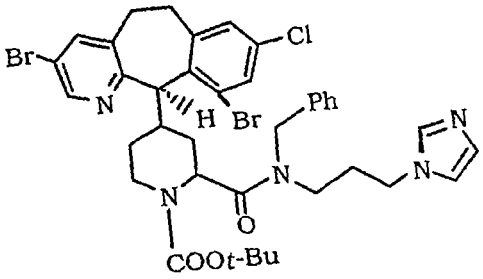
(Example 251)



(Example 252)



(Example 253)

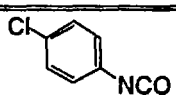
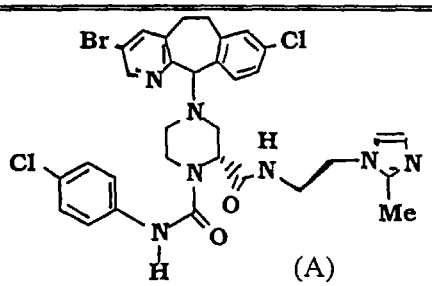
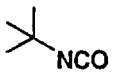
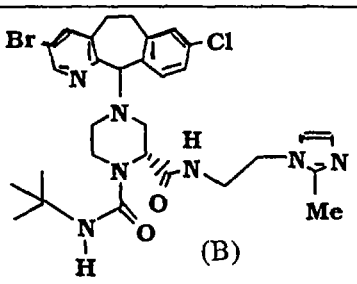
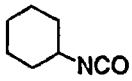
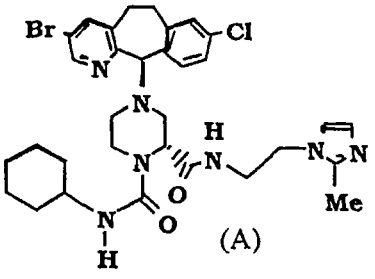


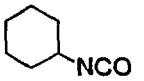
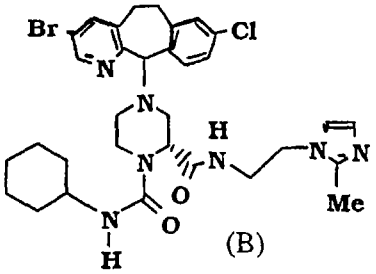
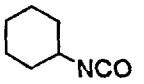
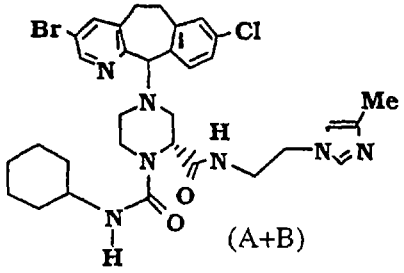
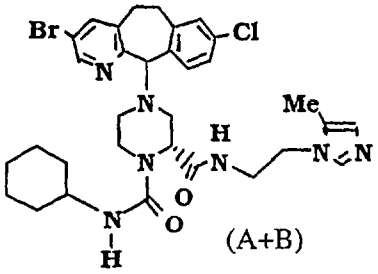
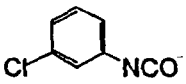
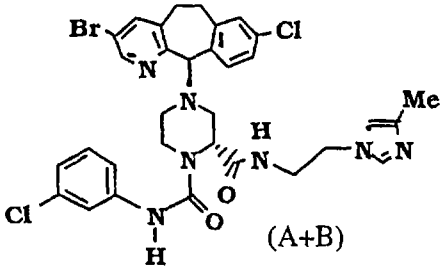
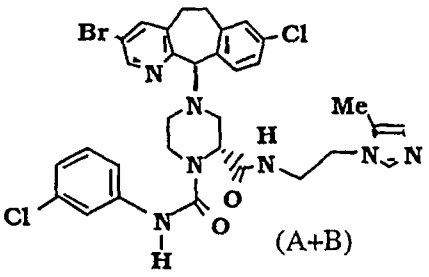
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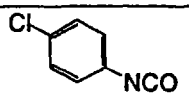
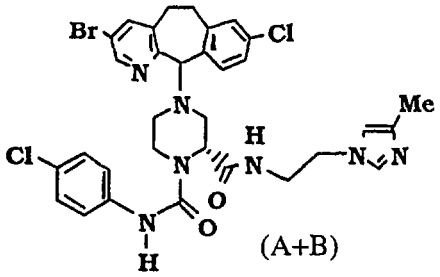
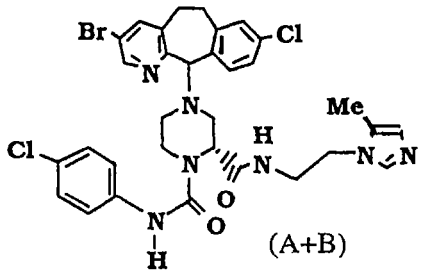
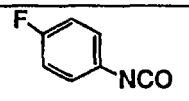
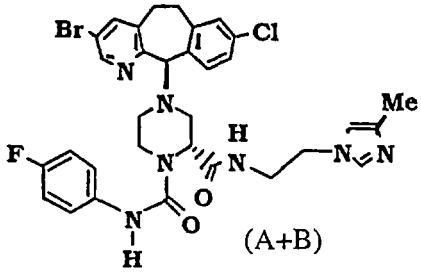
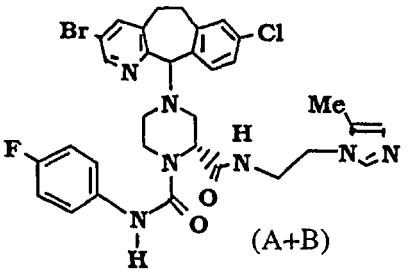
EXAMPLES 255-278

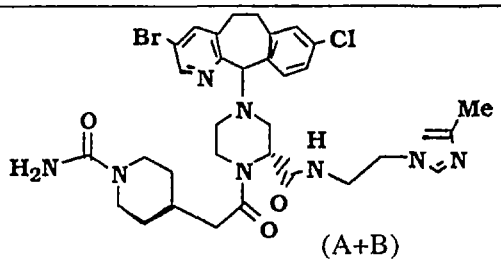
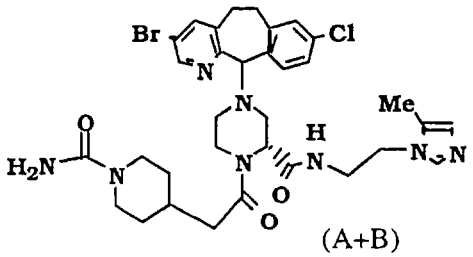
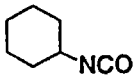
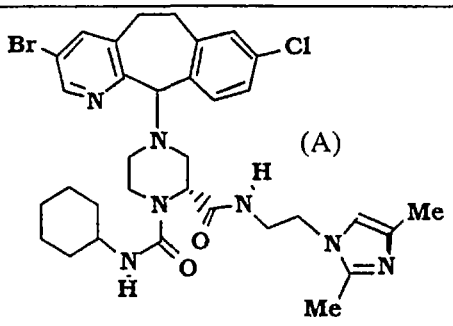
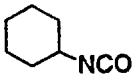
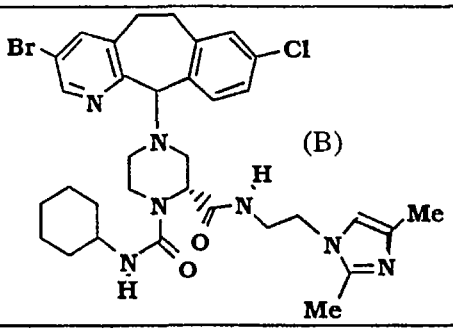
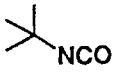
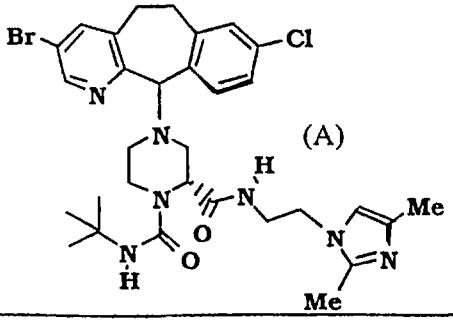
Following the procedure described for Example 127, the title compound (diastereomer A or B or A+B) from the Preparative Example indicated in Table 20 below was treated with the corresponding isocyanate to give the urea products listed in Table 20.

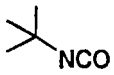
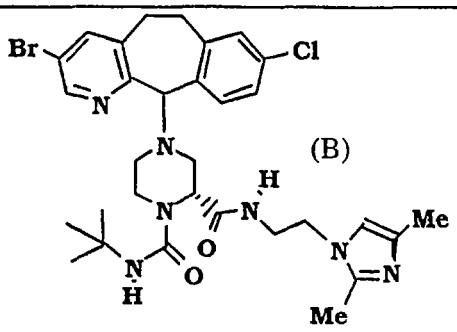
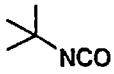
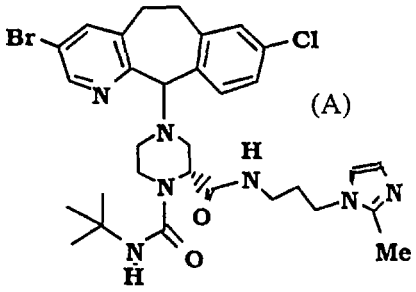
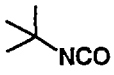
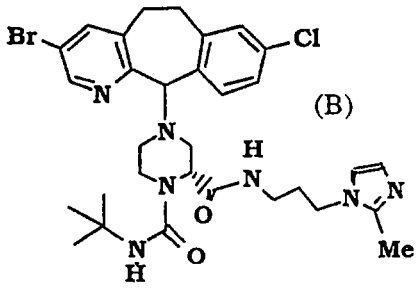
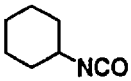
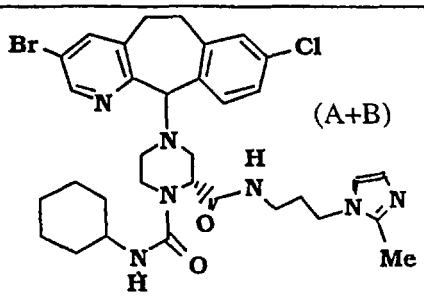
TABLE 20

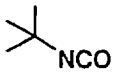
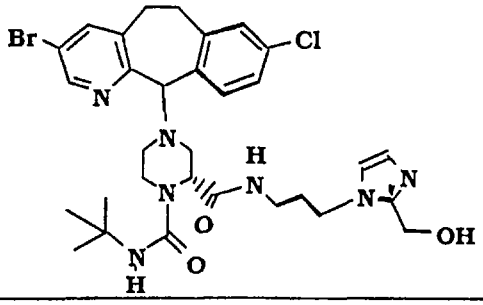
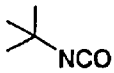
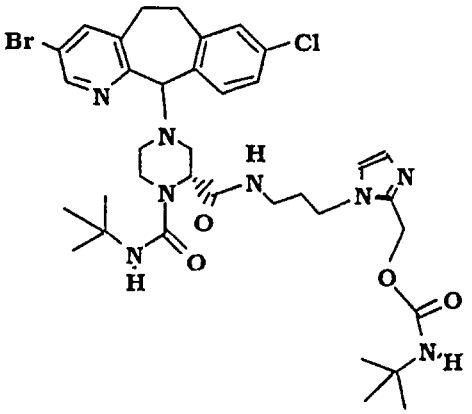
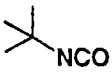
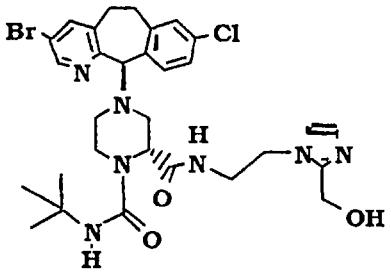
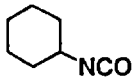
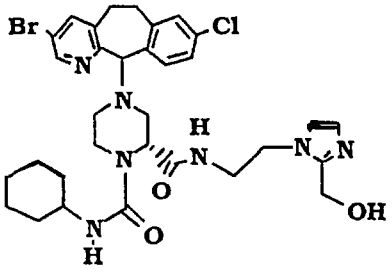
Ex.	Isocyanate and Prep. Ex.	Product	1.Yield (%) 2. MH^+ 3. mp (°C)
255	 139 diastereomer A	 (A)	1. 49 2. 695 3. 159.1
256	 139 diastereomer B	 (B)	1. 65 2. 642 3. 141.5
257	 139 diastereomer A	 (A)	1. 82 2. 668 3. 147.5

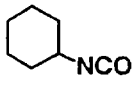
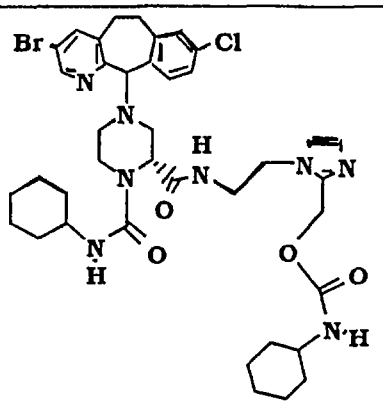
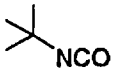
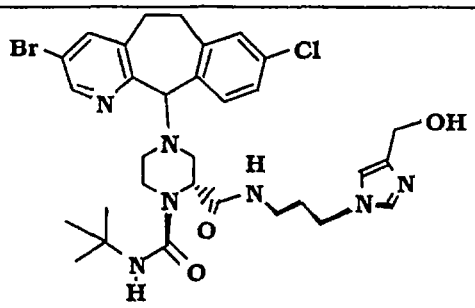
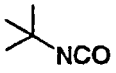
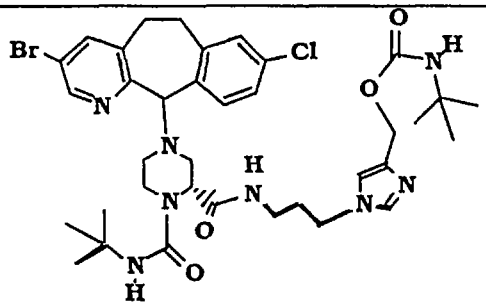
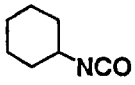
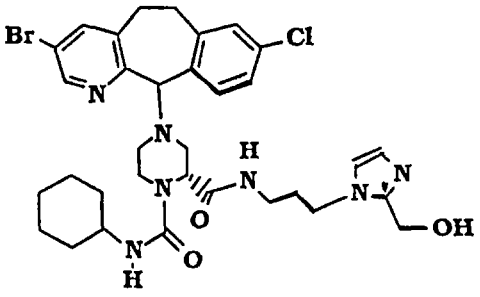
258	 139 diastereomer B	 (B)	1. 90 2. 668 3. 148.2
259	 140 diastereomer A + B	 (A+B)  (A+B)	1. 7 2. 668 3. 141.5 -146.6
260	 140 diastereomer A + B	 (A+B)  (A+B)	1. 17 2. 696 3. 136.1

261	 140 diastereomer A + B	 (A+B)  (A+B)	1. 15 2. 696 3. 140.8
262	 140 diastereomer A + B	 (A+B)  (A+B)	1. 12 2. 680 3. 130.3

263	TMS-NCO 142	 (A+B)  (A+B)	1. 25 2. 711 3. 165.5
264	 152	 (A)	1. 34 2. 682 3. 131.6
265	 153	 (B)	1. 71 2. 682 3. 120.6
266	 152	 (A)	1. 65 2. 656 3. 143.6

267	 153	 (B)	1. 64 2. 656 3. 142.9
268	 - 154 diastereomer A	 (A)	1. 83 2. 656 3. 142.8
269	 154 diastereomer B	 (B)	1. 89 2. 656 3. 146.8
270	 154 diastereomer A + B	 (A+B)	1. 43 2. 682 3. 144.6

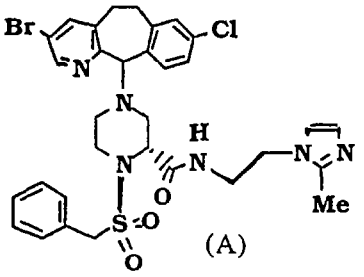
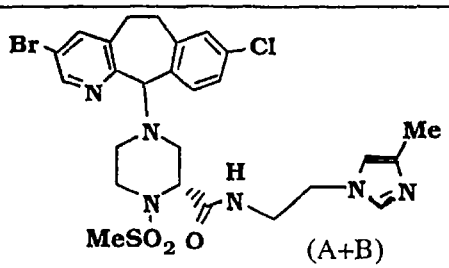
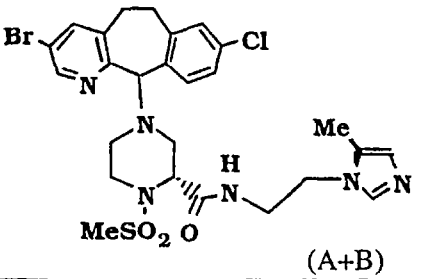
271	 158 diastereomer A + B		1. 52 2. 672 3. 122.5 - 143.6
272	 158 diastereomer A + B		1. 21 2. 769 3. 141.0
273	 159 diastereomer A + B		1. 61 2. 658 3. 151.7
274	 159 diastereomer A + B		1. 48 2. 683 3. 133.1

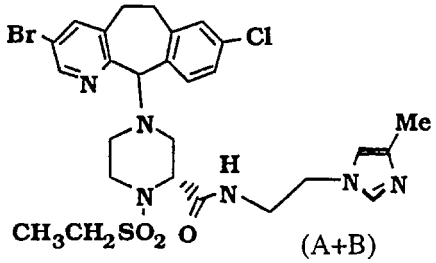
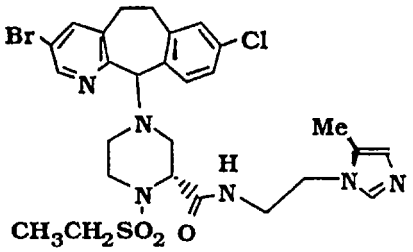
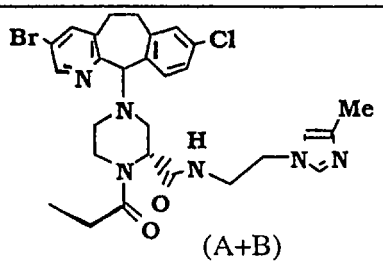
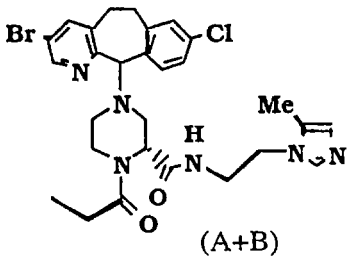
275	 159 diastereomer A + B		1. 46 2. 809 3. 131.2
276	 160 diastereomer A + B		1. 52 2. 672 3. 130.8
277	 160 diastereomer A + B		1. 38 2. 771 3. 144.6
278	 158 diastereomer A + B		1. 75 2. 698 3. 141.2

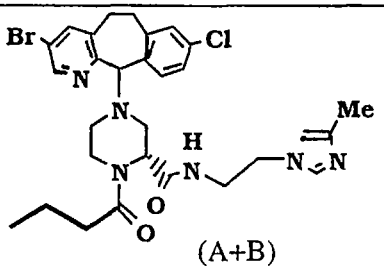
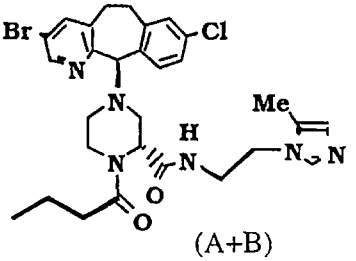
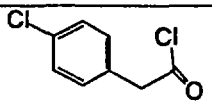
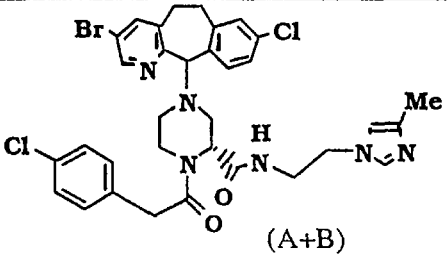
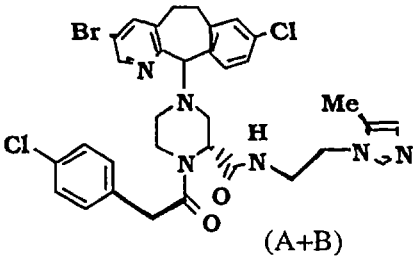
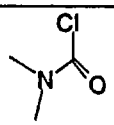
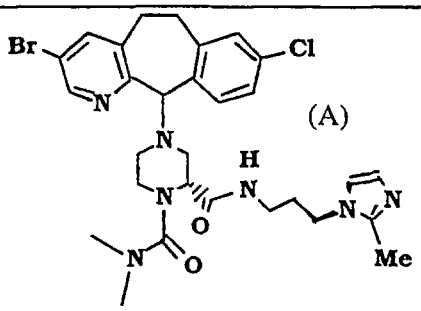
EXAMPLES 279-286

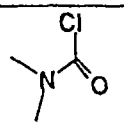
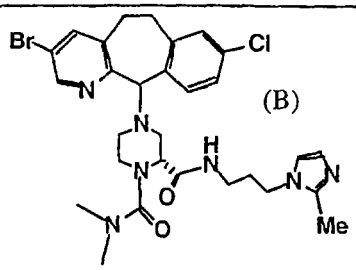
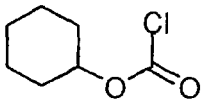
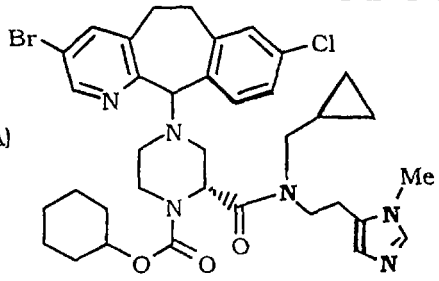
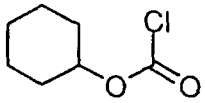
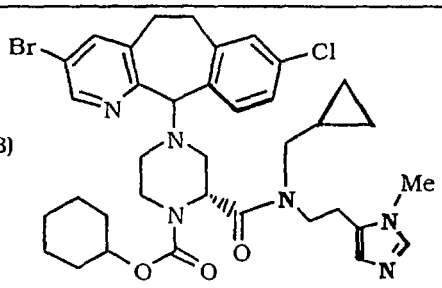
Following the procedure described for Example 149, the title compound (diastereomer A or B or A+B) from the Preparative Example indicated in Table 21 below was treated with the corresponding acid chloride, chloroformate, carbamyl chloride, dicarbonate, anhydride or sulfonyl chloride to give the products listed in the Table 21.

TABLE 21

Ex.	Electrophile and Prep. Exam.	Product	1.Yield (%) 2. MH^+ 3. mp (°C)
279	$PhCH_2SO_2Cl$ 139 diastereomer A	 (A)	1. 66 2. 697 3. 148.5
280	CH_3SO_2Cl 140 diastereomer A + B	 (A+B)  (A+B)	1. 10 2. 621 3. 134.8

281	$CH_3CH_2SO_2Cl$ 140 diastereomer A + B	 (A+B)  (A+B)	1. 11 2. 635 3. 124.8
282	CH_3CH_2COCl 140 diastereomer A + B	 (A+B)  (A+B)	1. 17 2. 599 3. 93.2

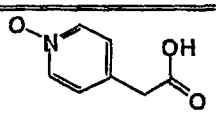
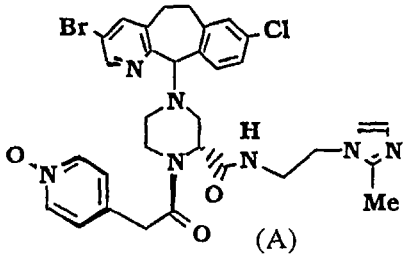
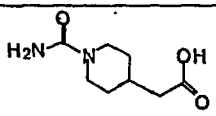
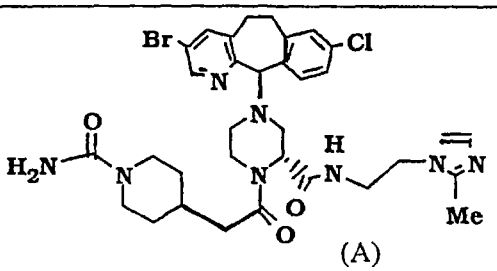
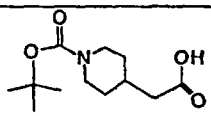
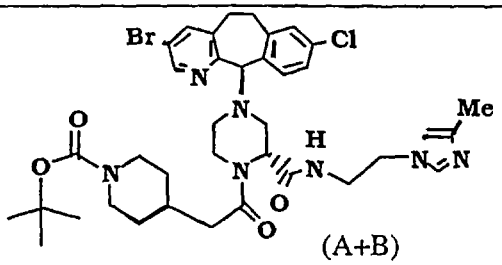
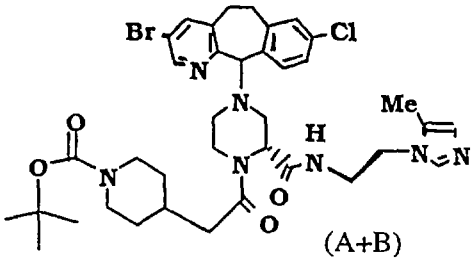
283	$CH_3CH_2CH_2COCl$ 140 diastereomer A + B	 (A+B)  (A+B)	1. 17 2. 613 3. 85.7
284	 140 diastereomer A + B	 (A+B)  (A+B)	1. 11 2. 695 3. 128.4
285	 154 diastereomer A	 (A)	1. 55 2. 628 3. 108.9

286	 154 diastereomer B	 (B)	1. 23 2. 628 3. 109.3
286 A	 166	 (A)	1. 70 2. 725 3. 88-96
286 B	 167	 (B)	1. 60 2. 725 3. 89-96

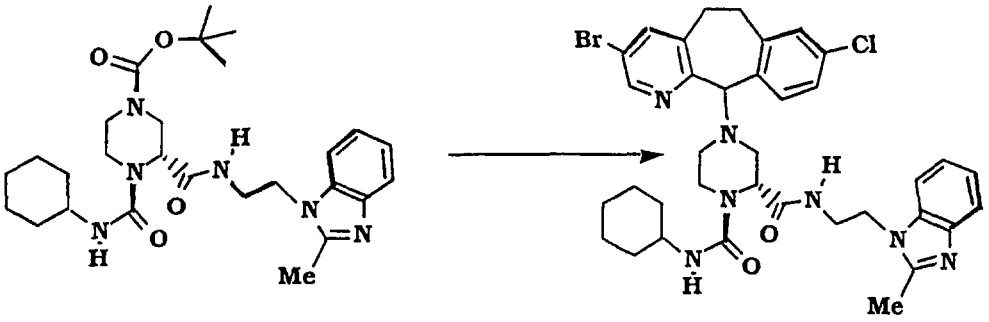
EXAMPLES 287-289

Following the procedure described for Example 221, the title compound (diastereomer A or B or A+B) from the Preparative Example indicated in Table 22 below was treated with the corresponding carboxylic acid to give the products listed in Table 22.

TABLE 22

Ex.	Carboxylic Acid and Prep. Ex.	Product	1.Yield (%) 2. MH^+ 3. mp (°C)
287	 139 diastereomer A	 (A)	1. 71 2. 678 3. 139.5
288	 139 diastereomer A	 (A)	1. 39 2. 711 3. 136.1
289	 140 diastereomer A+B	 (A+B)  (A+B)	1. 21 2. 768 3. 115.5

EXAMPLE 290

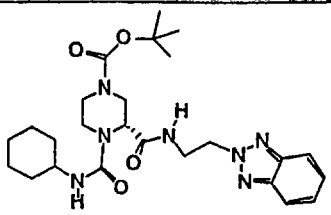
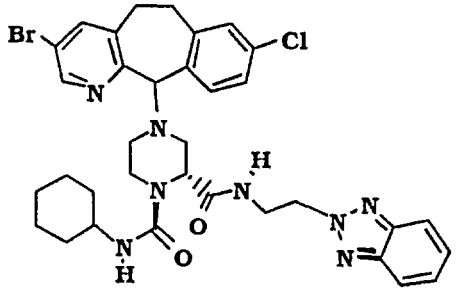
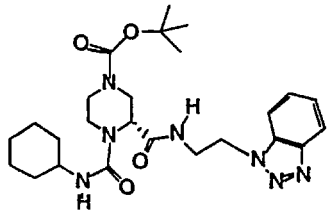
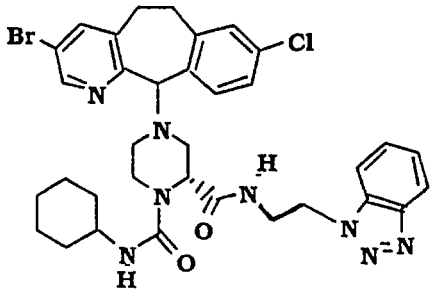
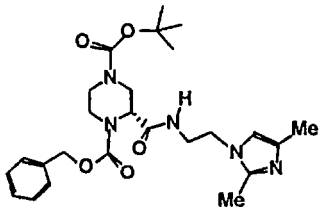
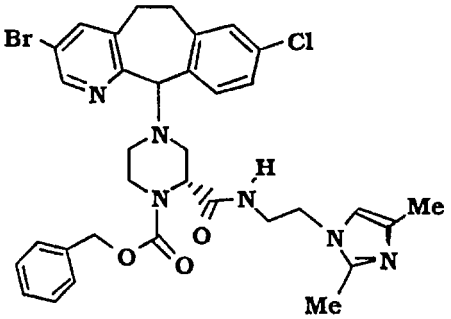


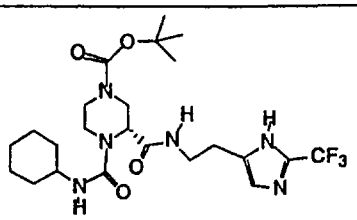
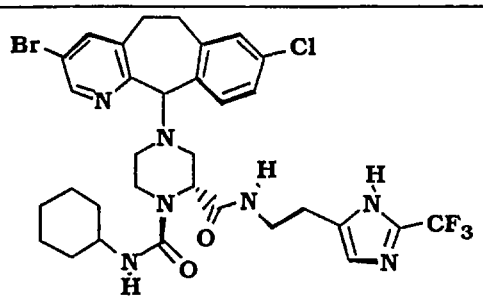
A solution of the title compound from Preparative Example 143 (0.59 g, 1.15 mmol) dissolved in anhydrous dichloromethane (10 ml) and trifluoroacetic acid (2 ml) was stirred at room temperature for 3 hrs. The resulting solution was concentrated *in vacuo*, then the residue was combined with anhydrous dichloromethane (10 ml), the tricyclic chloride (compound No. 42.0) (0.474 g, 1.38 mmol) and triethylamine (1.61 mL, 11.5 mmol) and allowed to stir at 25-40°C for 12 h. The reaction mixture was concentrated *in vacuo* and purified by flash column and preparative plate chromatography (silica gel) using 1-4% MeOH-CH_2Cl_2 saturated with aqueous ammonium hydroxide to afford the title compounds (457 mg, 55%, MH^+ = 718).

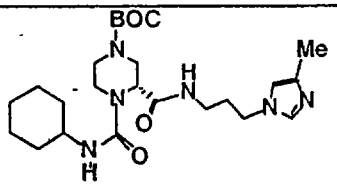
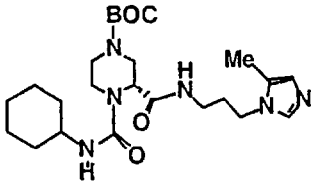
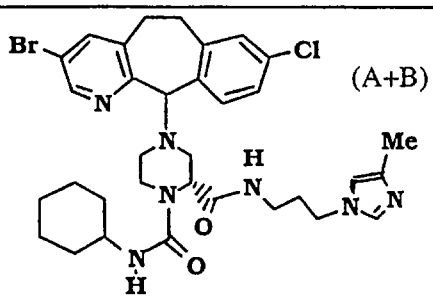
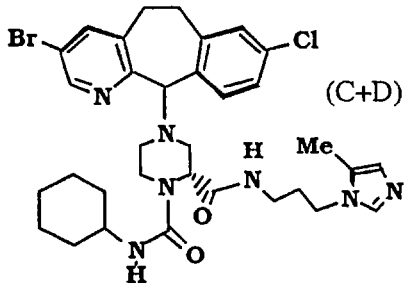
EXAMPLES 291-297

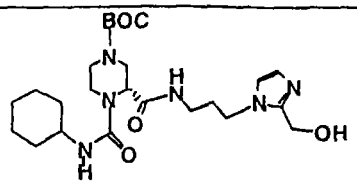
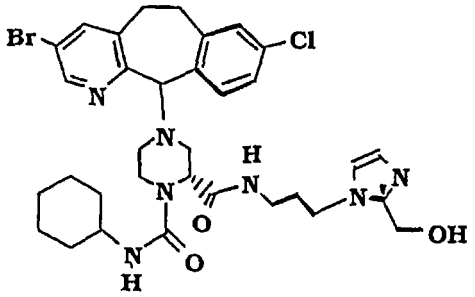
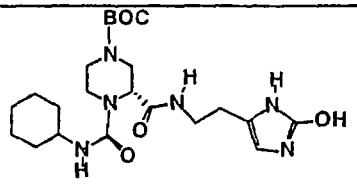
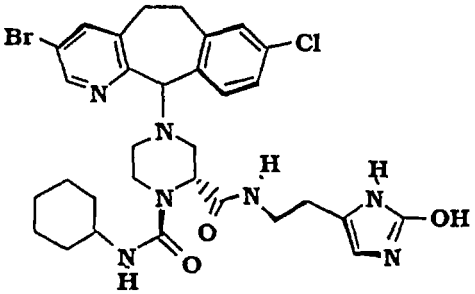
Following the procedure described for Preparative Example 290 and the BOC-protected piperazines listed in Table 23 below, the tricyclic compounds in Table 23 were prepared as diastereomeric mixtures. The diastereomers that were separated, were separated by preparative chiral chromatography (Chiralpack AD, 5 cm X 50 cm column, flow rate 80 mL/min., 7-12% IPA-Hexane +0.2% diethylamine) to give diastereomer A and diastereomer B.

TABLE 23

Ex.	BOC-Piperazine	Product
291		 1. Yield: 44% 2. MH^+ = 705 3. mp = 132-135°C
292		 1. Yield: 14% 2. MH^+ = 705 3. mp = 127-132°C
293		 For (A): For (B): 1. Yield: 38% 1. Yield: 36% 2. MH^+ = 691 2. MH^+ = 691 3. mp = 107.5°C 3. mp = 82.2°C

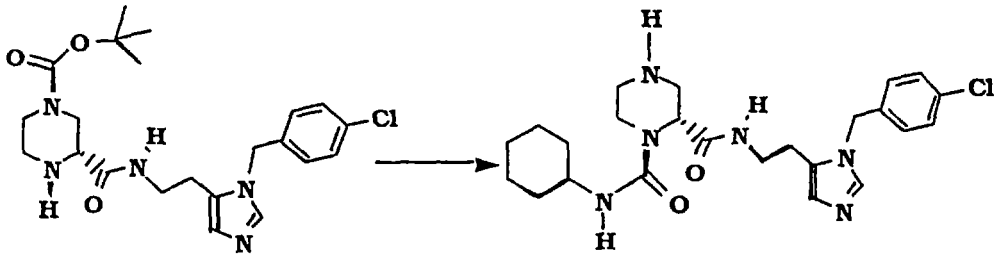
294		 1. Yield: 36% 2. MH^+ = 722 3. mp = 173.8°C

295	
	
		 (A+B)
		 (C+D)
		For (A): 1. Yield: 30% 2. MH^+ = 682
		For (B): 1. Yield: 25% 2. MH^+ = 682
		For (C): 1. Yield: 10% 2. MH^+ = 682
		For (D): 1. Yield: 13% 2. MH^+ = 682

296		 1. Yield: 75% 2. MH^+ = 698 3. mp = 141.2°C
297		 1. Yield: 13% 2. MH^+ = 670 3. mp = 182.1-219.4°C

EXAMPLE 299

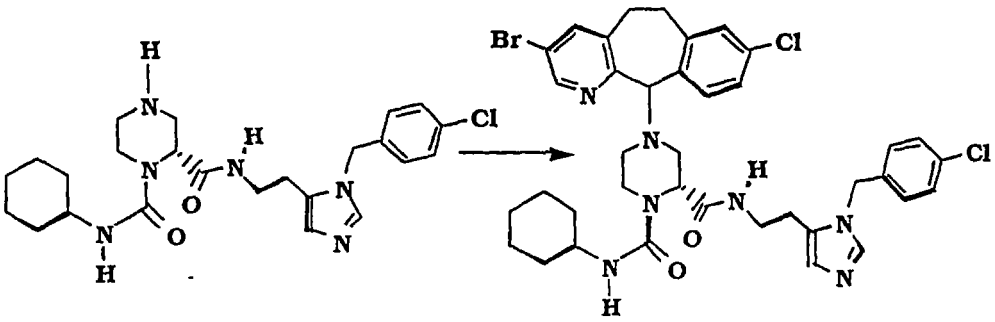
Step A



To a solution of the title compound from Preparative Example 155 Step F (0.30 g, 0.67 mmol) dissolved in anhydrous dichloromethane (3 ml) was added cyclohexylisocyanate (0.09 mL, 0.7 mmol) and the resulting solution was stirred at room temperature for 30 min, then concentrated *in vacuo*. The resulting residue was diluted with dichloromethane (3 ml) trifluoroacetic acid (3 ml). The solution was stirred at room temperature overnight,

then concentrated *in vacuo*, diluted with dichloromethane and washed with 1*N* NaOH (aq). The organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford a yellow foam (0.319 g, 100%, MH^+ = 473).

Step B

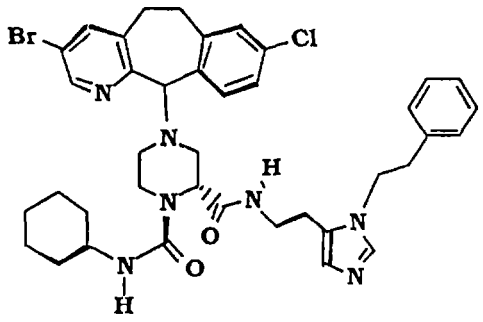


To a solution of the title compound from Step A above (0.212 g, 0.45 mmol) dissolved in anhydrous dichloromethane (10 ml) was added the tricyclic chloride (compound # 42.0) (0.154 g, 0.45 mmol) and triethylamine (0.32 mL, 2.25 mmol) and allowed to stir at 25°C for 48 h. The reaction mixture was concentrated *in vacuo* and purified by preparative plate chromatography (silica gel) using 5% MeOH-CH_2Cl_2 saturated with aqueous ammonium hydroxide to afford the title compounds (125 mg, 35%, mp = 114.8°C, MH^+ = 778).

EXAMPLE 300

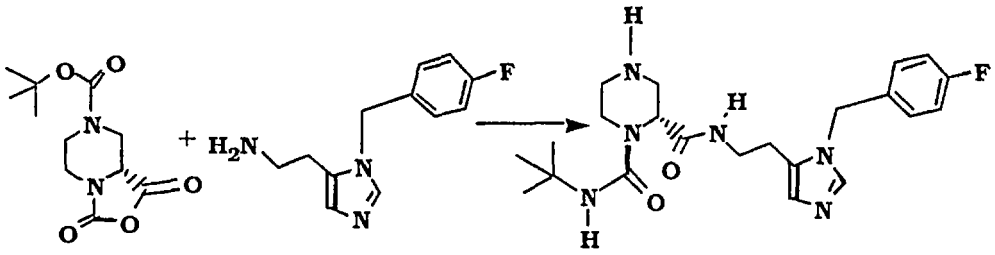
Following the procedure described for Example 299 Steps A-B, the product listed in Table 24 below was prepared using the corresponding piperazine from the indicated Preparative Example.

TABLE 24

Ex.	Prep. Ex.	Product	1.Yield (%) 2. MH^+ 3. mp (°C)
300	156		1. 38 2. 758 3. 117.3

EXAMPLE 302

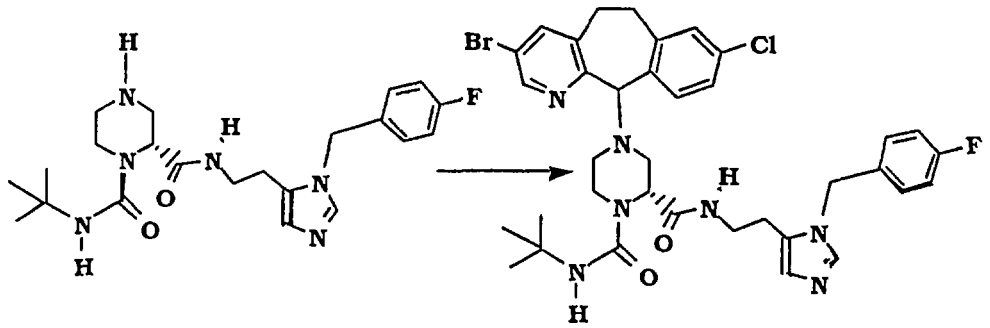
Step A



A mixture of the title compound from Preparative Example 162 (400 mg, 1.86 mmol), the anhydride from Preparative Example 44 (561 mg, 2.19 mmol) and anhydrous CH_2Cl_2 (10 mL) was stirred at 25°C for 3 hrs before tert-butylisocyanate (0.26 mL, 2.19 mmol) was added. After 12 h, the mixture was concentrated *in vacuo*, diluted with CH_2Cl_2 and washed with water. The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated. The resulting foam was diluted with anhydrous CH_2Cl_2 (10 mL) and trifluoroacetic acid (10 ml) and stirred for 3 h. Concentration *in vacuo*, redilution with CH_2Cl_2 and washing with 1*N* NaOH (0.5 M, aq) provided an organic solution which was dried over anhydrous

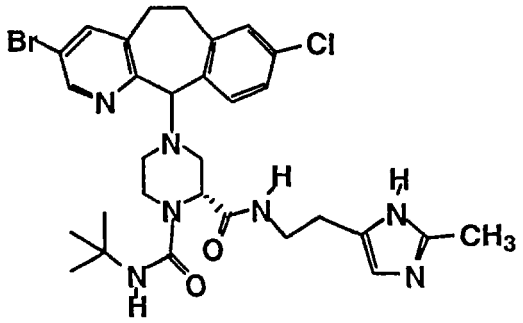
Na_2SO_4, filtered, concentrated and used without further purification (181 mg, 27%, MH^+ = 431.5).

Step B

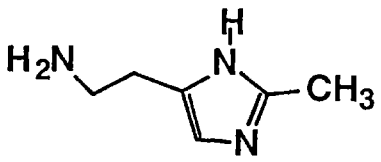


To a solution of the title compound from Step A (170 mg, 0.39 mmol) dissolved in anhydrous dichloromethane (10 ml) was added the tricyclic chloride (compound No. 42.0) (175 mg, 0.51 mmol) and triethylamine (71 μL, 0.51 mmol) and allowed to stir at 25°C for 48 h. The reaction mixture was concentrated *in vacuo* and purified by preparative plate chromatography (silica gel) using 5% MeOH-CH_2Cl_2 saturated with aqueous ammonium hydroxide to afford the title compounds (oil, 24 mg, 8%, MH^+ = 736).

EXAMPLE 303

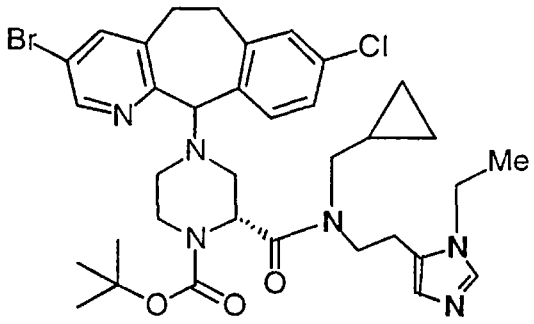


If the procedure set forth in Example 302 were followed using in Step A



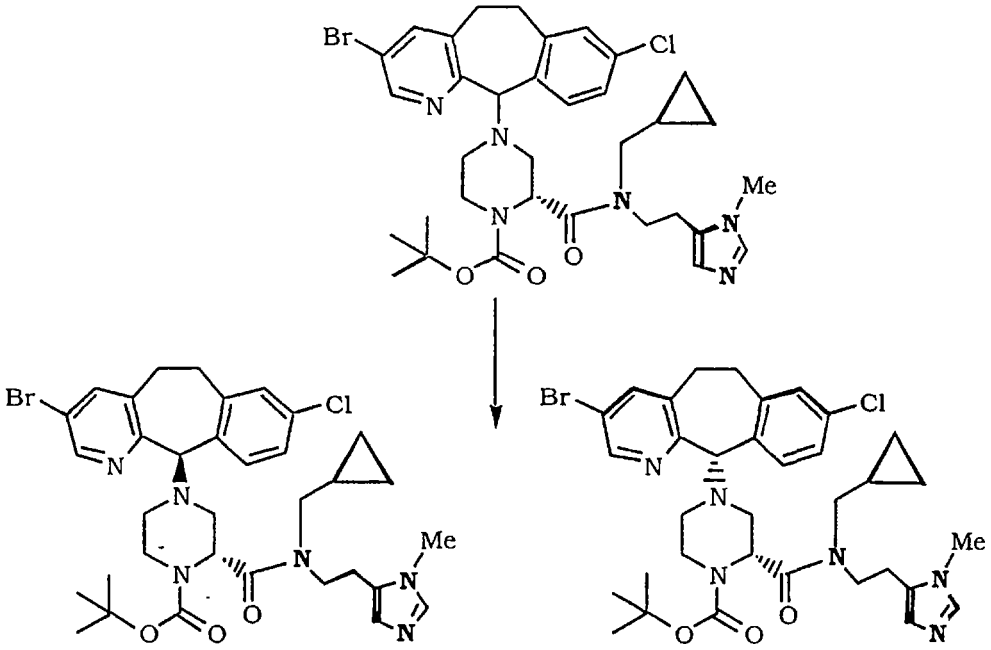
instead of the title compound from Preparative Example 162, the title compound would be obtained.

EXAMPLE 304



Following the procedure described for Example 58, except using the title compound from Preparative Example 165 instead of the title compound from Preparative Example 25, the title compound was prepared (51%, MH^+ =711, mp = 103.7-107.5).

EXAMPLE 305

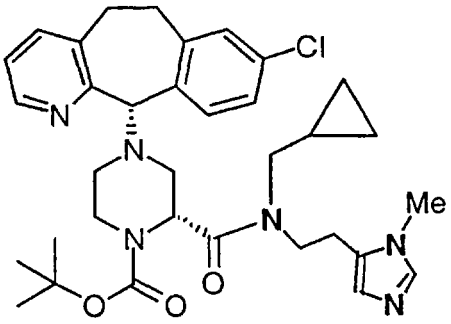


The title compound from Example 58 was separated into its two diastereomers by HPLC (Chiracel AD column) using 10% isopropanol-90% hexane-0.2% diethylamine to give the 11(R),2(R) and 11(S),2(R) isomers.

Diastereomer A : MH+ = 697; mp = 103-108°C.

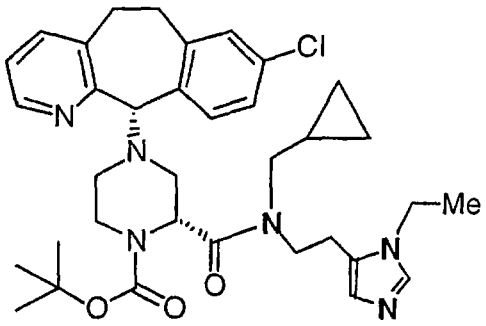
Diastereomer B : MH+ = 697; mp = 101-107°C.

EXAMPLE 306



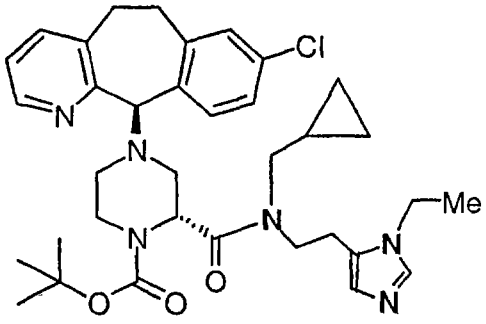
Following the procedure described for Example 58, except using the 11(S),2(R) diastereomer from Preparative Example 164 instead of the title compound from Preparative Example 51, the title compound was prepared (59%, MH^+ = 619, mp = 100-114°C).

EXAMPLE 307



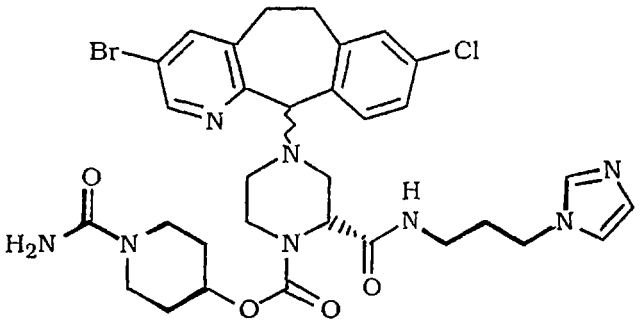
Following the procedure described for Example 306, except using the title compound from Preparative Example 165 instead of the title compound from Preparative Example 25, the title compound was prepared (73%, MH^+ = 633, mp = 89.1-96.5°C).

EXAMPLE 308



Following the procedure described for Example 58, except using the 11(R),2(R) diastereomer from Preparative Example 164 Step C instead of the title compound from Preparative Example 51, and using the title compound from Preparative Example 165 instead of the title compound from Preparative Example 25, the title compound was prepared (65%, MH^+ = 633, mp = 89.1-96.5).

EXAMPLE 309

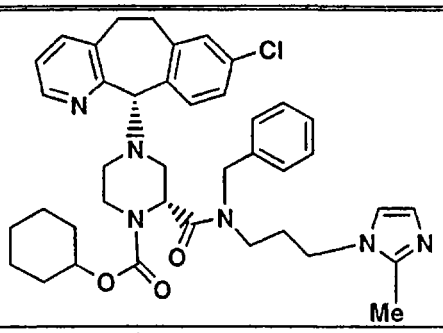
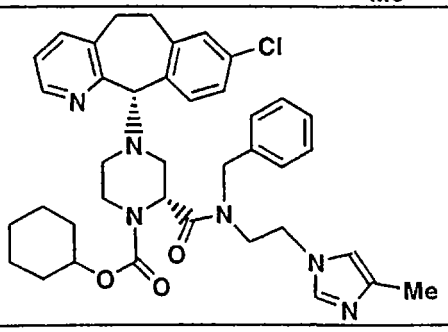
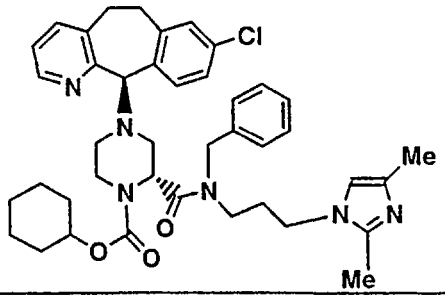
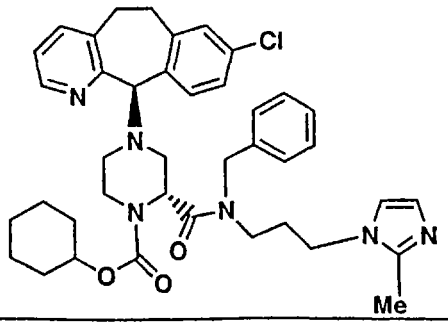


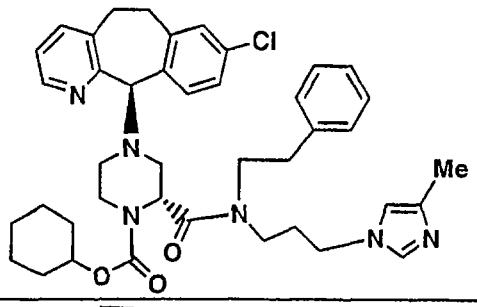
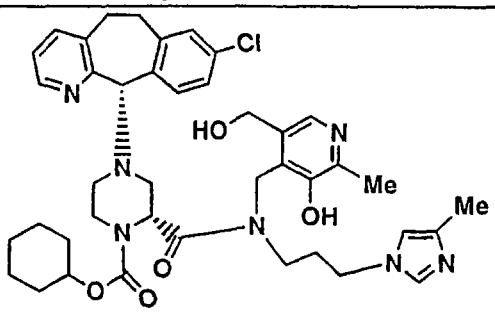
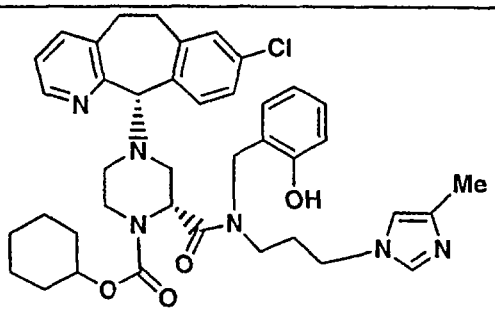
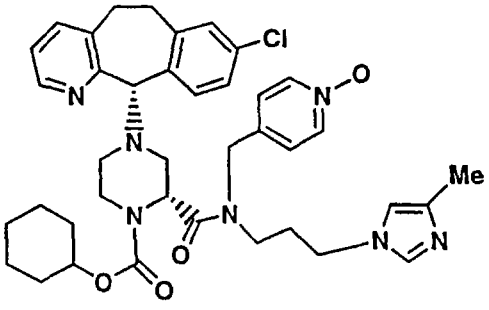
The racemic product from Preparative Example 141 (0.2g, 0.368mmoles), 4-(4-nitrophenyloxycarbonyl)piperidine-1-carboxamide (0.1706g, 0.552mmoles) (Preparative Example 36, Step B) and isopropanol (10mL) were heated under reflux and under argon at 87°C for 24h. The solution was evaporated to dryness and the residue was taken up in dichloromethane and washed with satd. aqueous $NaHCO_3$, water, dried ($MgSO_4$), filtered and evaporated to dryness. The residue was chromatographed on a silica gel column using 3%-6%-10% (10% conc. NH_4OH in methanol)-dichloromethane as the eluant to give the title compound (0.057g, 22%): FABMS; m/z 712.9 (MH^+); δ_C ($CDCl_3$) CH_2: 30.3, 30.5, 30.6, 30.6, 31.1, 36.7, 41.3, 41.3, 42.2, 44.5, 50.7/51.1, 52.3; CH: 55.4, 71.0, 78.8, ~118.9, 126.3, 129.4, 130.5, 132.5, 137.0, 141.4, 147.1; C: 120.2, 134.3, 135.0, 137.0, 141.3, 155.2, 155.2, 158.0, 170.2; δ_H ($CDCl_3$) 4.31/4.32 (1H, s, H_{11}), 4.56 (2H, broad s, $NCONH_2$), 6.93 (1H, broad s, Im-H_5), 7.07 (1H, broad s, Im-H_4), 7.10-7.16 (3H, m, Ar-H), 7.48 (1H, m, Ar-H), 7.60 (1H, broad s, Im-H_2) and 8.30ppm (1H, s, Ar-H_2).

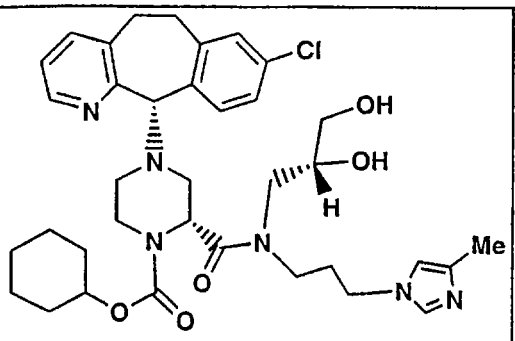
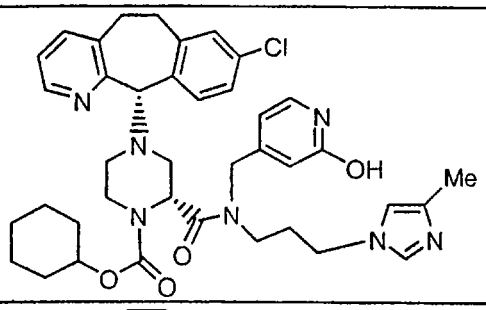
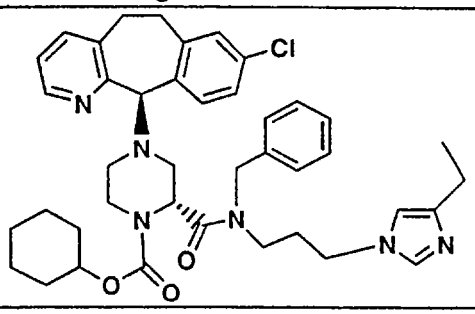
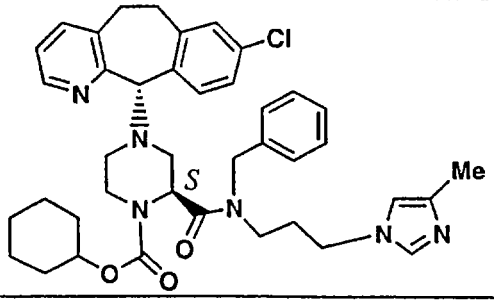
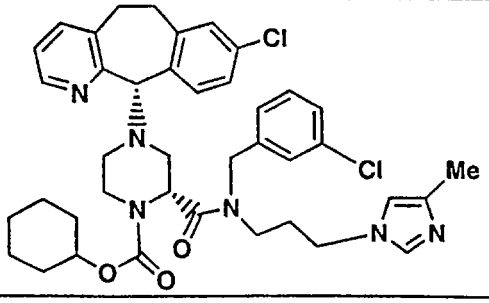
EXAMPLES 310-342

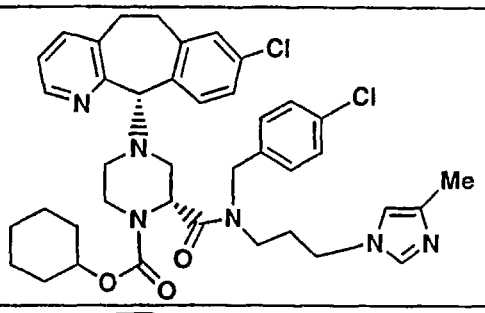
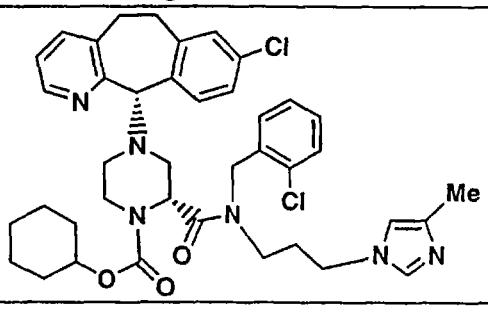
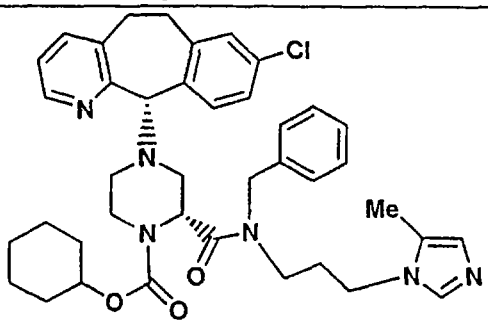
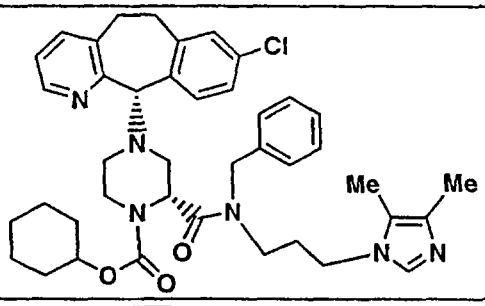
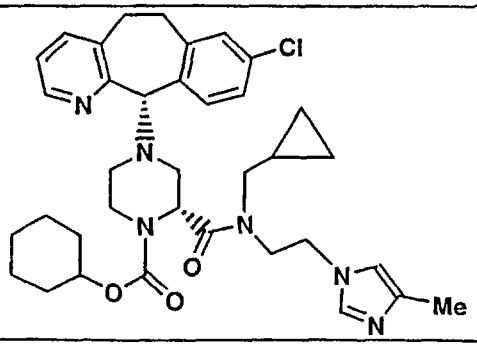
Following the procedure described for Example 225, the Products listed in Table 25 were prepared using the carboxylic acid (diastereomer A or B) from Preparative Example 127 Step C and the appropriate N-substituted imidazolylalkyl amine.

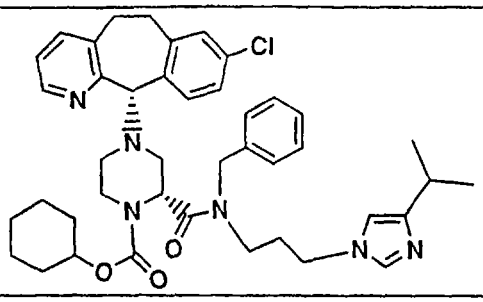
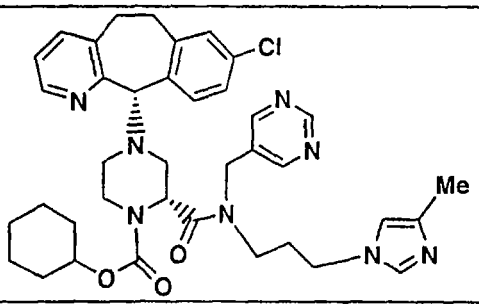
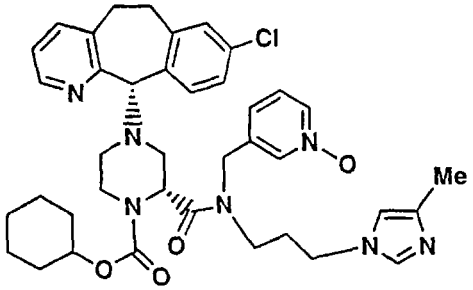
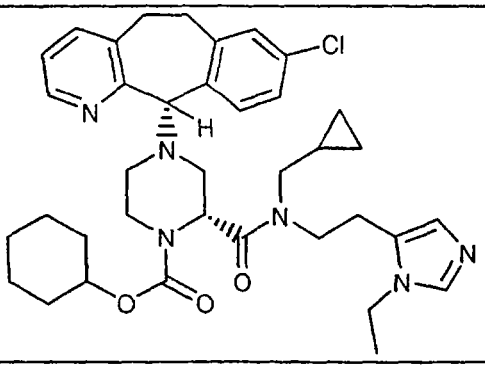
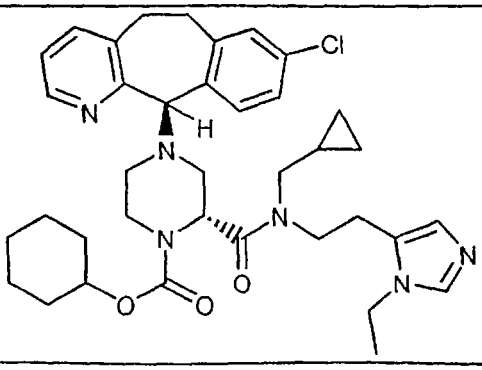
TABLE 25

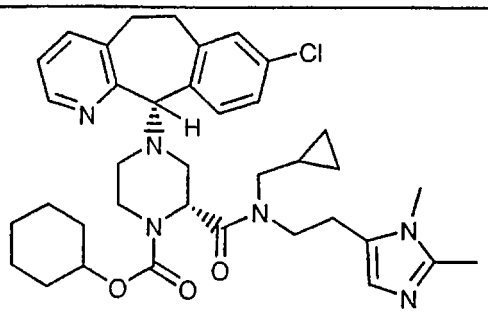
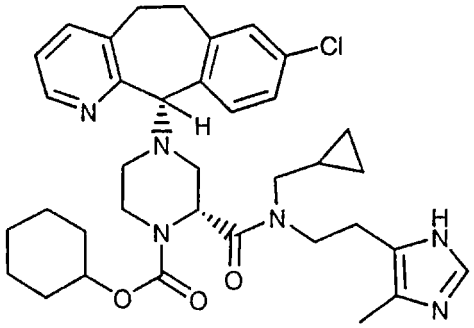
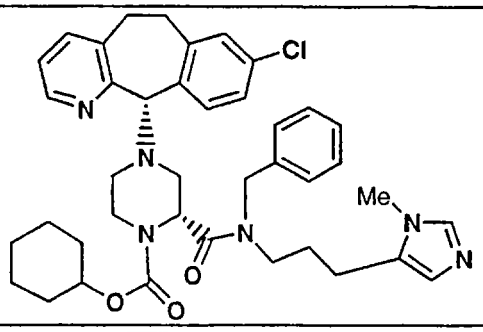
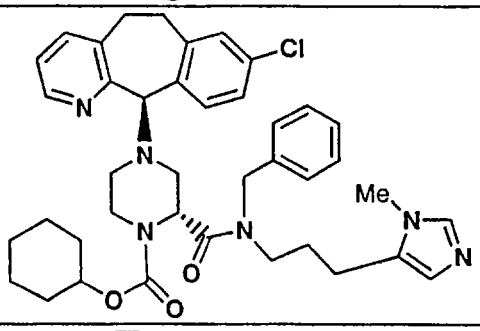
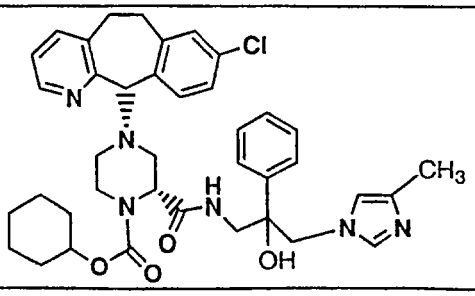
Ex.	Amine of Prep. Ex. No. Carboxylic acid diastereomer A or B	Product	1.Yield (%) 2. MH^+ 3. mp (°C)
310	94 diastereomer A		1. 71 2. 695 3. 79.7
311	93 diastereomer A		1. 29 2. 681 3. 82.2
312	89 diastereomer B		1. 43 2. 709 3. 88.4
313	94 diastereomer B		1. 47 2. 695 3. 86.3

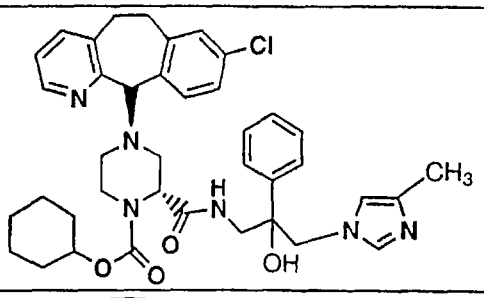
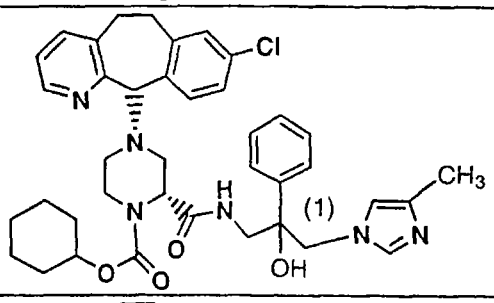
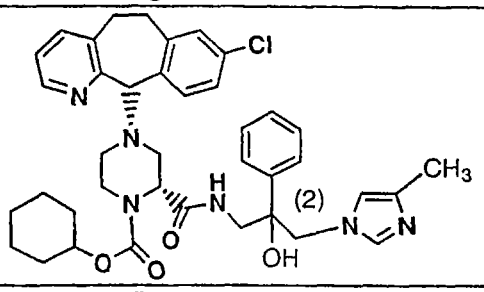
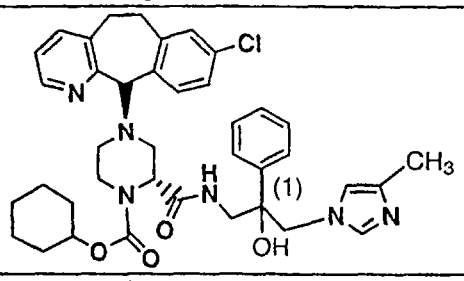
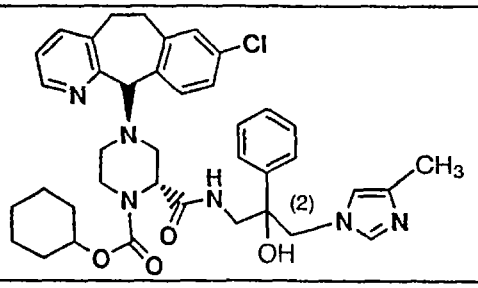
314	101 diastereomer B		1. 52 2. 709 3. 89.1
315	179 diastereomer A		1. 14 2. 756 3. semi-solid
316	172 diastereomer A		1. 65 2. 711 3. 122.2
317	173 diastereomer A		1. 27 2. 712 3. 62.9-88.2

318	174 diastereomer A		1. 19 2. 679 3. 78.3
319	199 Step B diastereomer A		1. 20 2. 712 3. 135.7
320	91 diastereomer B		1. 32 2. 709 3. 94.6
321	95.1 diastereomer A		1. 4 2. 695 3. 76.7
322	176 diastereomer A		1. 37 2. 729 3. 78-83

323	177 diastereomer A		1. 50 2. 729 3. 96-101
324	178 diastereomer A		1. 45 2. 729 3. 87-92
325	85 (B) diastereomer A		1. 55 2. 695 3. 88-93
326	180 diastereomer A		1. 53 2. 709 3. 87.7
327	183 diastereomer A		1. 63 2. 645 3. 103.6

328	181 diastereomer A		1. 40 2. 723 3. 86.5-95.2
329	184 diastereomer A		1. 16 2. 697 3. 95-100
330	182 diastereomer A		1. 7 2. 712 3. semi-solid
331	165 Diastereomer A		1. 52 2. 660 3. 90.7-101.7
332	165 Diastereomer B		1. 69 2. 660 3. 91.6-102.8

333	185 Diastereomer A		1. 29 2. 660 3. 75.9-82.8
334	186 Diastereomer A		1. 90 2. 646 3. 83-89.7
335	133 diastereomer A		1 63. 2. 696
336	133 diastereomer B		1. 59 2. 696
337	171 diastereomer A		1.15 2. 698

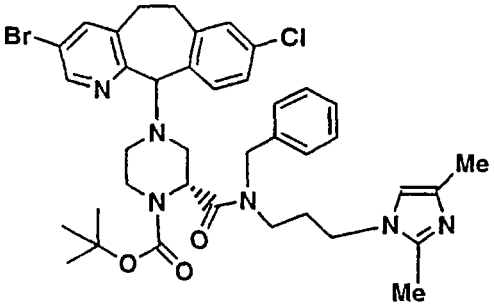
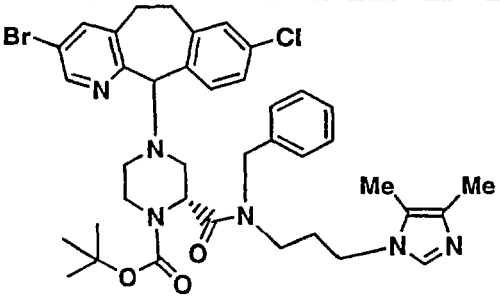
338	171 diastereomer B		1. 36 2. 698
339	171 diastereomer A		1. 26 2. 698
340	171 diastereomer A		1. 42 2. 698
341	171 diastereomer B		1. 57 2. 698
342	171 diastereomer B		1. 21 2. 698

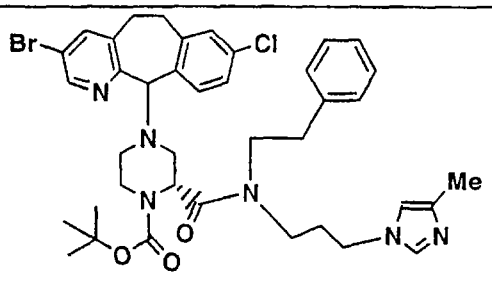
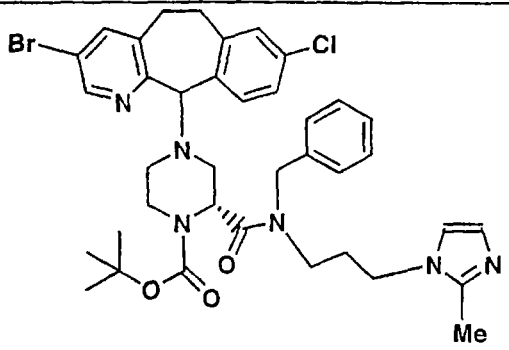
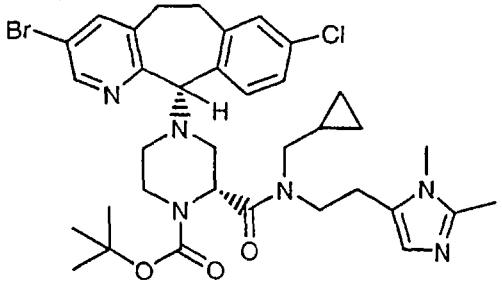
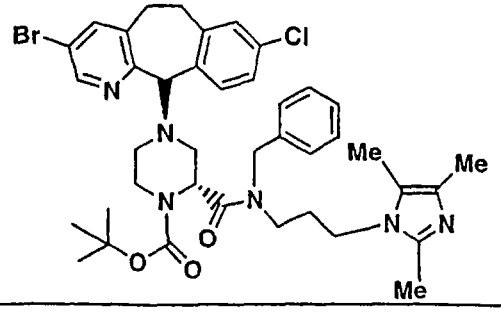
EXAMPLES 343-361

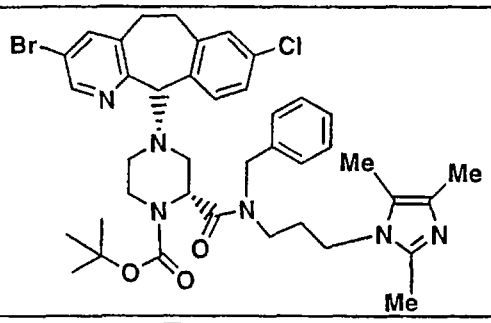
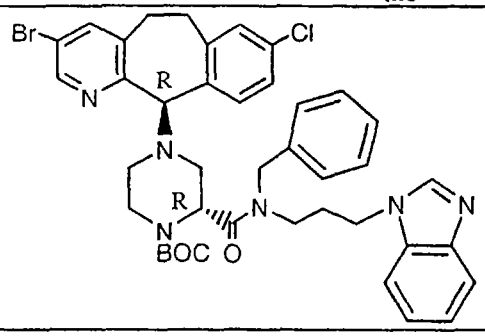
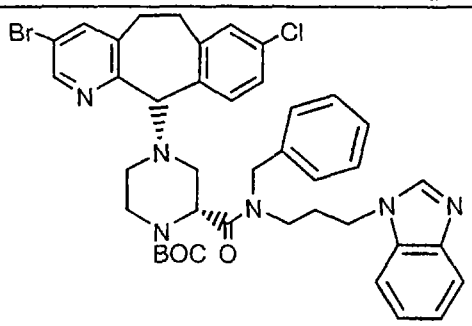
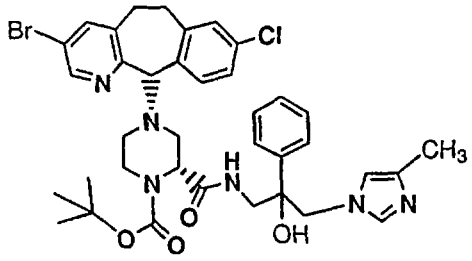
Following the procedure described for Example 40, the Products listed in Table 26 were prepared using either the mixture or the pure isomers of the carboxylic acids (diastereomer A and/or

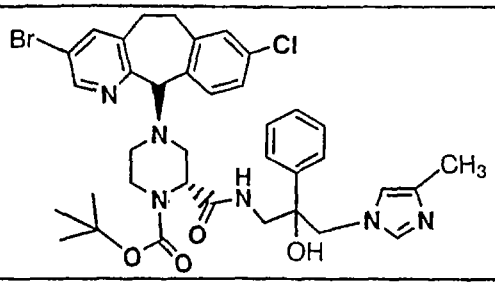
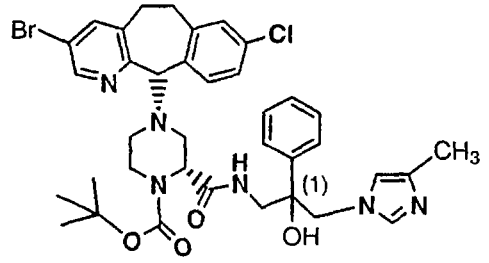
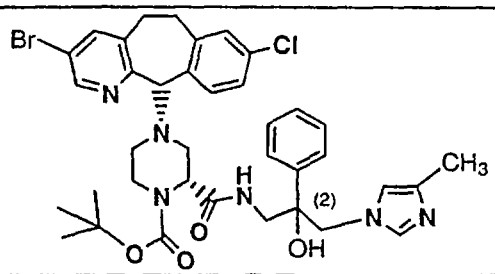
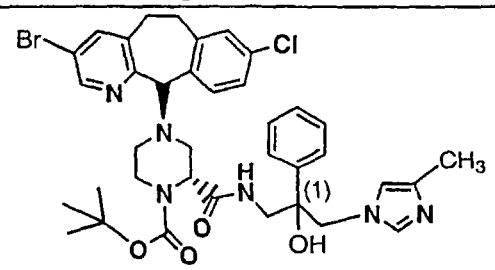
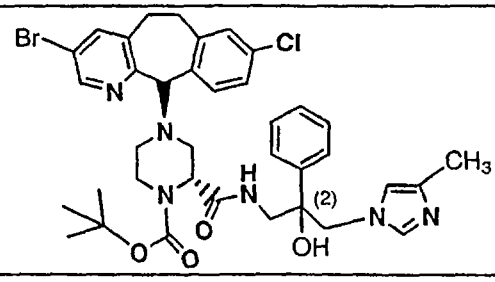
B) from Preparative Example 51 and the appropriate N-substituted imidazolylalkyl amine instead of the amine from Preparative Example 13. The resulting Products were separated by HPLC (Chiracel, AD column, 85/15 Hexane/IPA).

TABLE 26

Ex	Amine of Prep. Ex. No.	Product	1.Yield (%) 2. MH^+ 3. mp (°C)
343 and 344	89	 Isomer A (Ex. 343) And Isomer B (Ex. 344)	For (A): 1. 27 2. 761 3. 99.3 For (B): 1. 30 2. 761 3. 92.3
345 and 346	177	 Isomer A (Ex. 345) And Isomer B (Ex. 346)	For (A): 1. 16 2. 761 3. 92.4 For (B): 1. 17 2. 761 3. 96.5

347 and 348j	101	 Isomer A (Ex. 347) And Isomer B (Ex. 348)	For (A): 1. 25 2. 761 For (B): 1. 30 2. 761
349 and 350	94	 Isomer A (Ex. 349) And Isomer B (Ex. 350)	For (A): 1. 24 2. 747 For (B): 1. 26 2. 747
351	185 diastereomer A		1. 55 2. 713 3. 102.9-107.5
352	187 diastereomer B		1. 67 2. 724 3. ---

353	187 diastereomer A		1. 66 2. 724 3. ---
354	188 diastereomer B		1. 18 2. 783 3. 98-108
355	188 diastereomer A		1. 28 2. 783 3. 98-105
356	171 diastereomer A		1. 54 2. 751

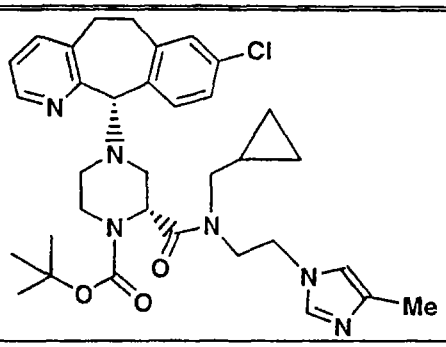
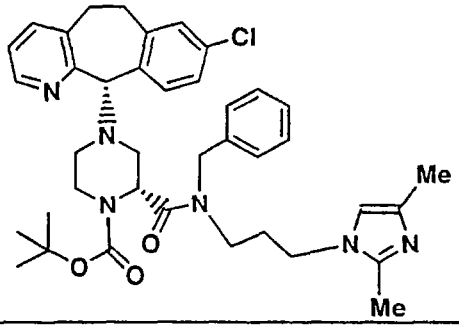
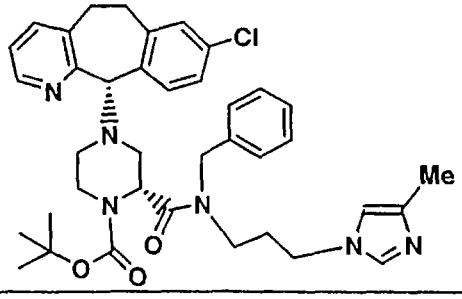
357	171 diastereomer B		1. 55 2. 751
358	171 diastereomer A		1. 17 2. 751
359	171 diastereomer A		1. 12 2. 751
360	171 diastereomer B		1. 62 2. 751
361	171 diastereomer B		1. 25 2. 751

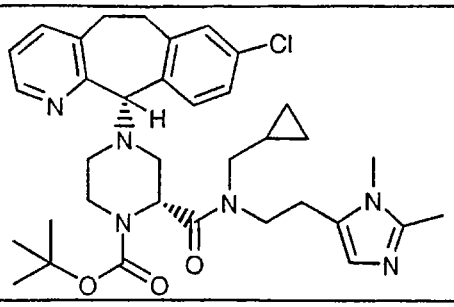
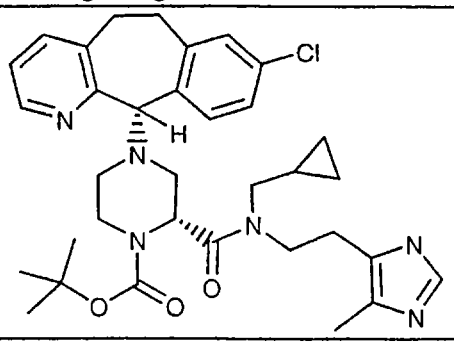
EXAMPLES 362-366

Following the procedure described for Example 225, except using the (11S, 2R(+))-carboxylic acid from Preparative Example 164 instead of that from Preparative Example 127 Step C, and using the substituted amine from the indicated Preparative Example in Table

27 instead of that from Preparative Example 95.1, the product listed in Table 27 was prepared.

TABLE 27

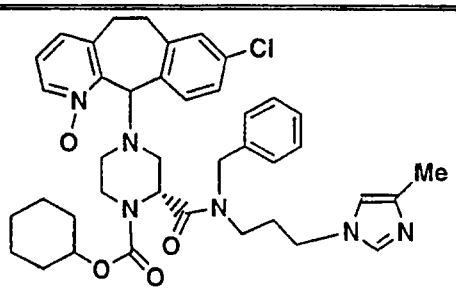
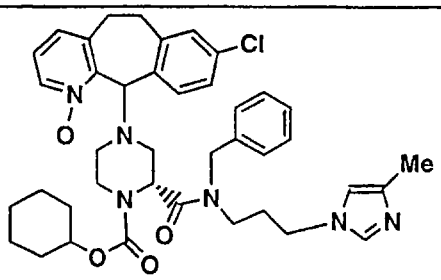
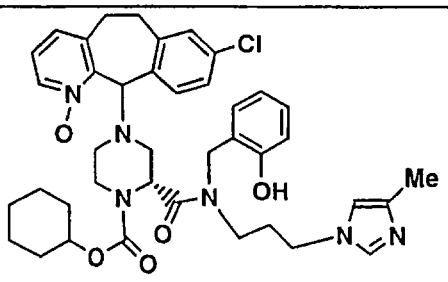
Ex.	Amine of Prep. Ex. No.	Product	1.Yield (%) 2. MH^+ 3. mp (°C)
362	183		1. 69 2. 619 3. 98.8
363	89		1. 44 2. 683 3. 91.7
364	95.1		1. 42 2. 609 3. 83.5

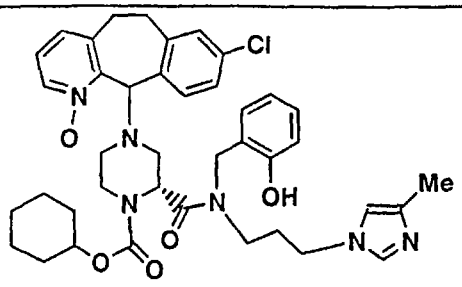
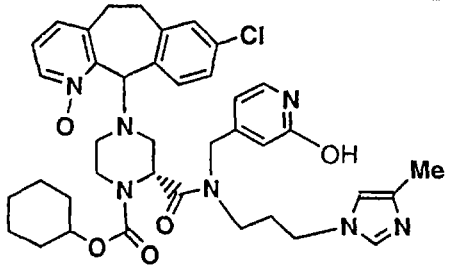
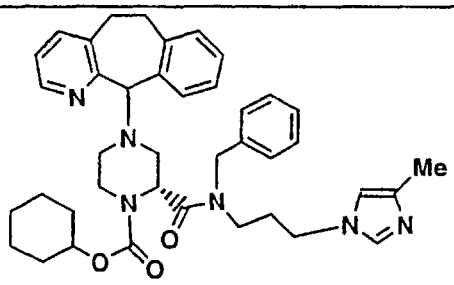
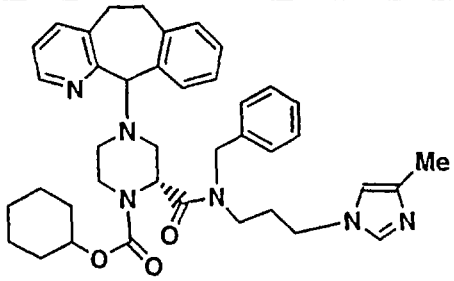
365	185		1. 57 2. 634 3. 92.1- 102.7
366	186		1. 71 2 620 3. 130.2- 140.2

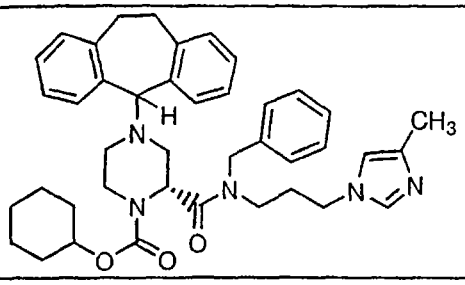
EXAMPLES 367-374

Following the procedure described for Example 225, the Products listed in Table 28 were prepared using the Carboxylic acid (diastereomer A or B) from Preparative Example listed in Table 28 below instead of the carboxylic acid from Preparative Example 127 Step C, and the appropriate imidazolylalkyl amine (Amine).

TABLE 28

Ex.	1. Prep. Ex. No. of Carboxylic acid 2. Prep. Ex. No. of Amine	Product	1.Yield (%) 2. MH^+ 3. mp (°C)
367	1. 200 diastereomer A 2. 95.1	 Isomer A	1. 46 2. 711 3. 90-95
368	1. 200 diastereomer B 2. 95.1	 Isomer B	1. 30 2. 711 3. 65-70
369	1. 200 diastereomer A 2. 172	 Isomer A	1. 61 2. 727 3. 128.5

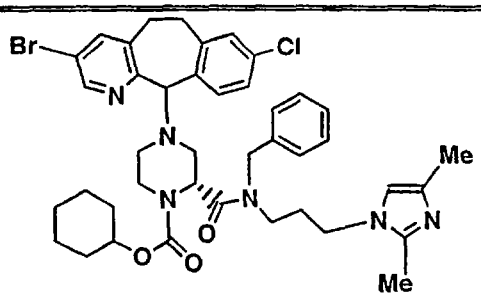
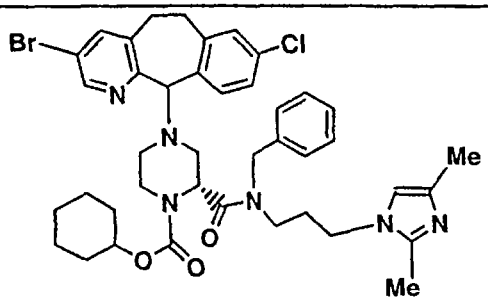
370	1. 200 diastereomer B 2. 169	 Isomer B	1. 66 2. 727 3. 133.9
371	1. 200 diastereomer B 2. 199 Step B	 Isomer B	1. 16 2. 728 3. 135.7
372	1. 201 Step B diastereomer A 2. 95.1	 Isomer A	1. 35 2. 661 3. oil
373	1. 201 Step B diastereomer B 2. 95.1	 Isomer B	1. 49 2. 661 3. oil

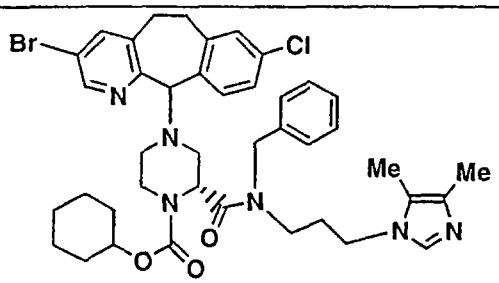
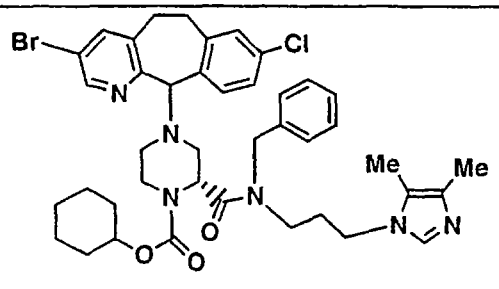
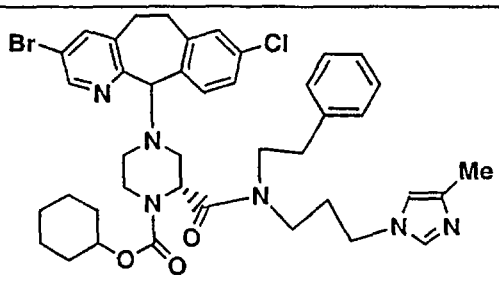
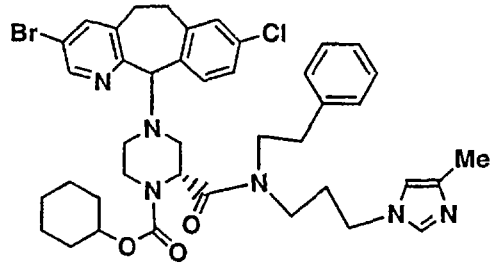
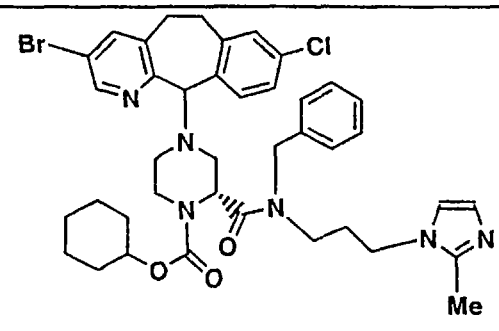
374	1. 202 2. 95.1		1. 41 2. 660 3. 80.1-88.5

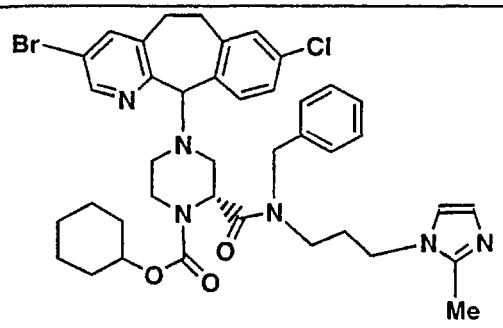
EXAMPLES 375-382

Similarly, using the procedure described for Example 149, the title compound (diastereomer A or B) from the Preparative Example given in Table 29 was treated with cyclohexyl chloroformate to give the products listed in the Table 29.

TABLE 29

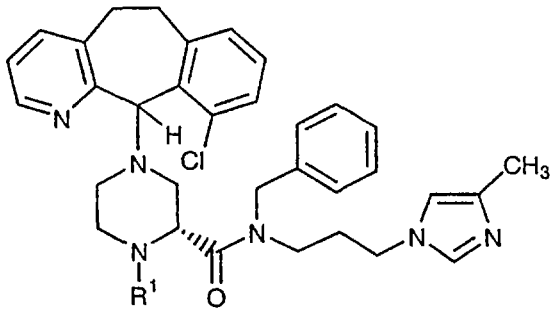
Ex.	Prep. Ex. No.	Product	1.Yield (%) 2. MH^+ 3. mp (°C)
375	190	 Isomer A	1. 76 2. 787 3. 94.7
376	191	 Isomer B	1. 67 2. 787 3. 92.3

377	192	 Isomer A	1. 87 2. 787 3. 90.8
378	193	 Isomer B	1. 85 2. 787 3. 84.2
379	194	 Isomer A	1. 72 2. 787 3. 89.7
380	195	 Isomer B	1. 62 2. 787 3. 89.7
381	196	 Isomer A	1. 74 2. 773 3. 83.9

382	197	 Isomer B	1. 73 2. 773 3. 89.8

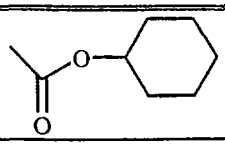
EXAMPLES 383-392

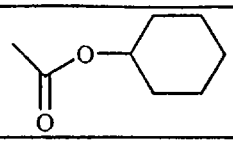
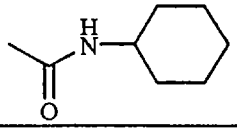
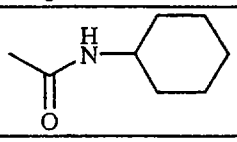
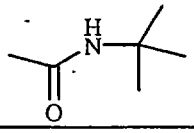
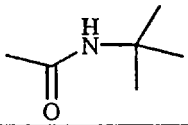
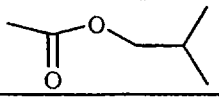
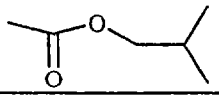
Following essentially the same procedure described for Example 149, the title compound (diastereomer A or B) from Preparative Example 170 was treated with the appropriate acylating agent (i.e cyclohexylchloroformate, or Boc dicarbonate, or cyclohexylisocyanate, or tert-butyl isocyanate or isobutyl chloroformate) to give the products of the formula:



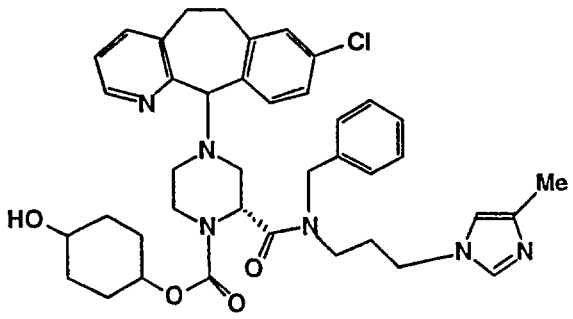
wherein R^1 is as defined in column 2 of Table 30.

TABLE 30

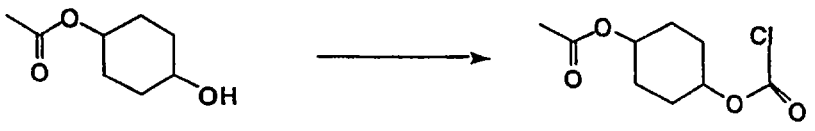
Ex.	R_1	Isomer	Mass HRMS (FABS, MH)	$[\alpha]_D^{20}$
383		A	695.3473	-29.2° c = 0.107

384		B	695.3473	+19.5° c = 0.1295
385	-$COOC(CH_3)_3$	A	669.3366	-42.5° c = 0.89
386	-$COOC(CH_3)_3$	B	669.3322	----
387		A	694.3629	-51.0° c = 0.2575
388		B	694.3642	----
389		A	668.3480	-41.0° c =0.19
390		B	668.3488	----
391		A	669.3322	-56.3° c = 0.3005
392		B	669.3330	----

EXAMPLE 393

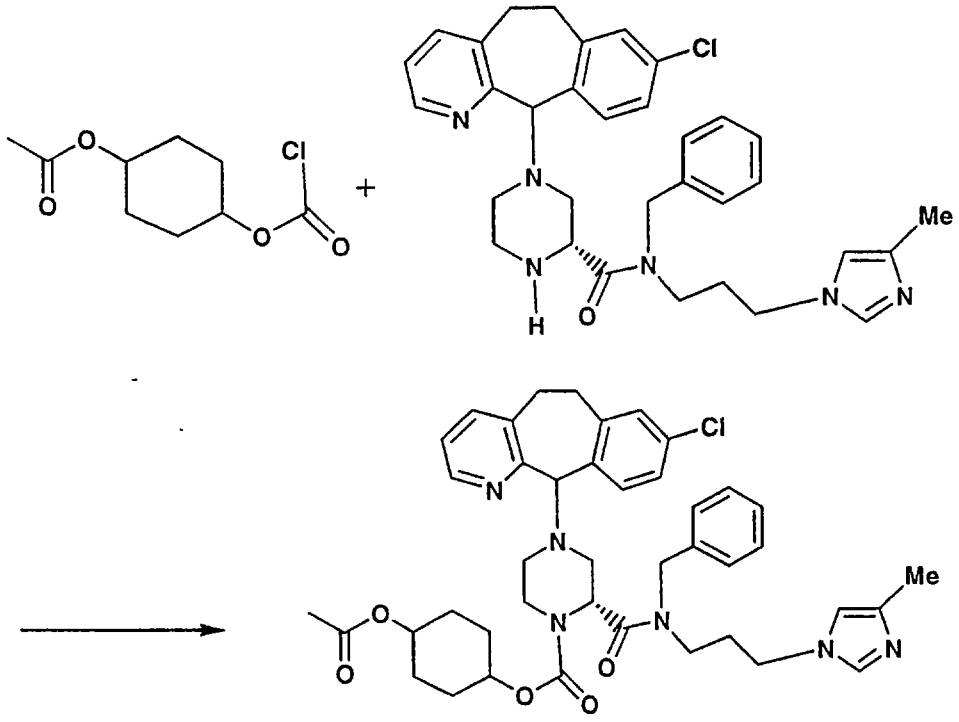


Step A



If the commercially available acetoxycyclohexanol were treated with phosgene the chloroformate would be obtained.

Step B

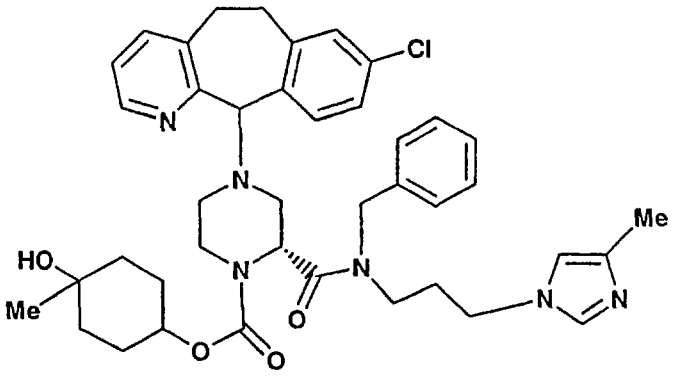


If the chloroformate from Step A were combined with the piperazine amine shown above according to the procedure described for Example 149 then the acetate would be obtained.

Step C

If the product of Step B were treated with potassium carbonate in MeOH the title compound would be obtained.

EXAMPLE 394

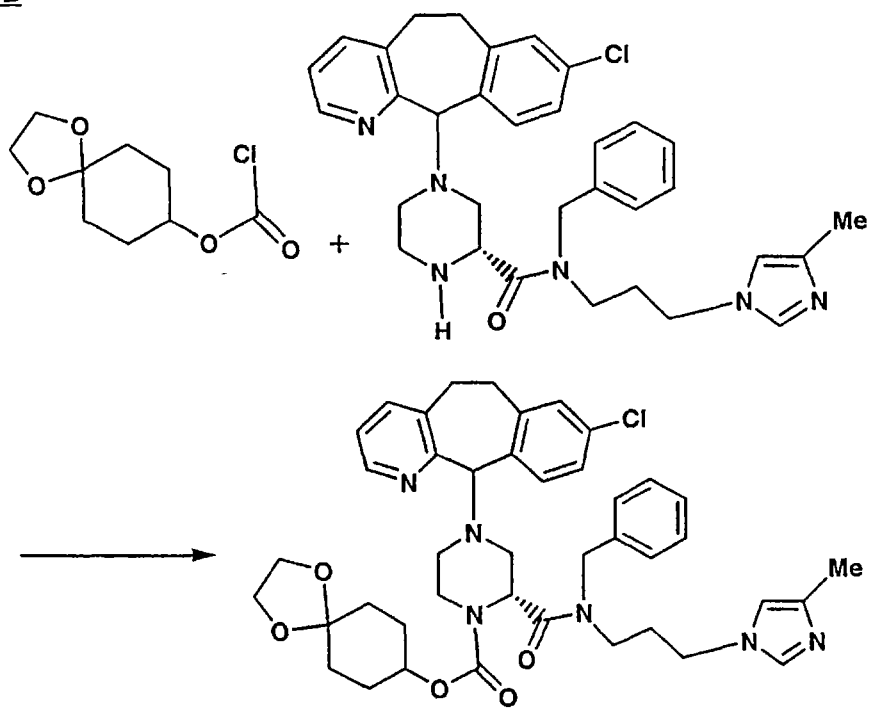


Step A



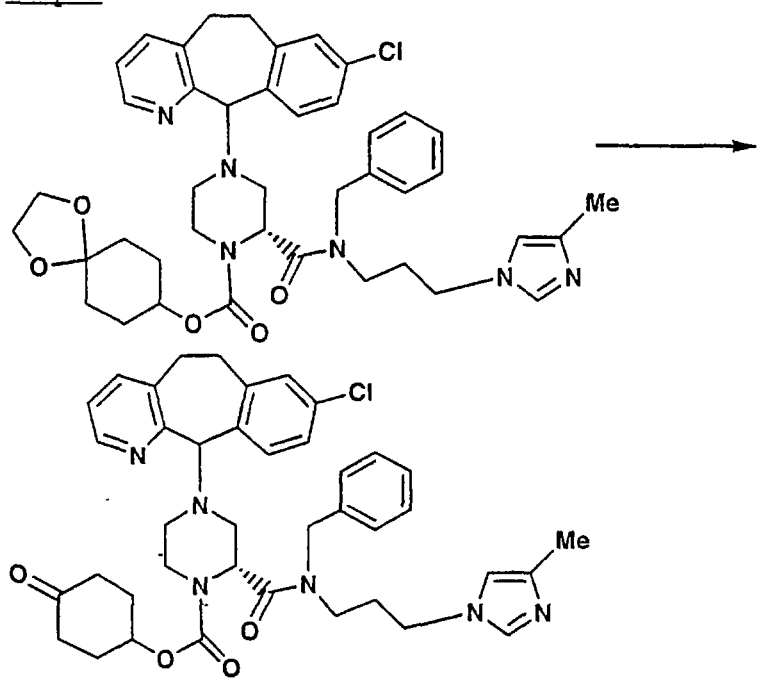
If the commercially available cyclohexanol were treated with phosgene the chloroformate would be obtained.

Step B



If the chloroformate from Step A were combined with the piperazine amine shown above according to the procedure described for Example 149 then the ketal would be obtained.

Step C

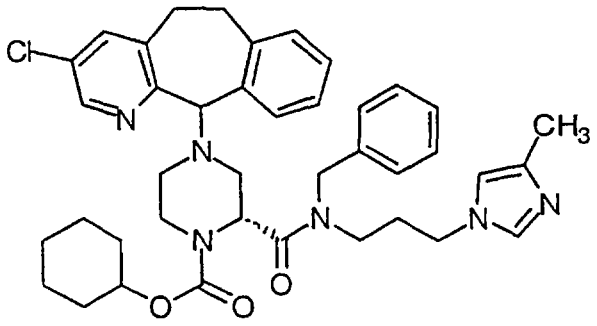


If the product of Step B were treated with aqueous acid the ketone would be obtained.

Step D

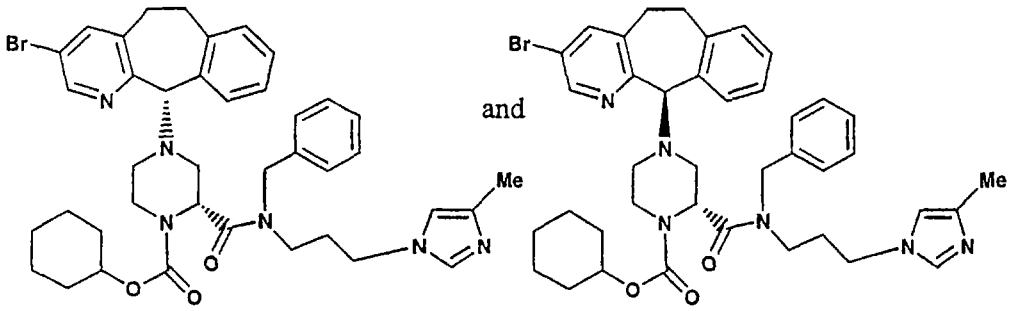
If the product of Step C were treated with MeMgBr or MeLi the title product would be obtained.

EXAMPLE 395



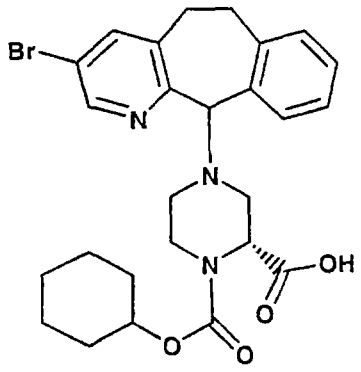
By essentially the same procedure set forth in Example 225 (coupling), only substituting the title compound from Preparative Example 212 for the acid from Preparative Example 127 Step C, the title compound was obtained. Mp 91-107 °C, LCMS MH^+=695.

EXAMPLE 397



Step A

If the 3-bromotricyclic chloride from Preparative Example 209 were used instead of the chloride in Preparative Example 127 Step C then the carboxylic acid

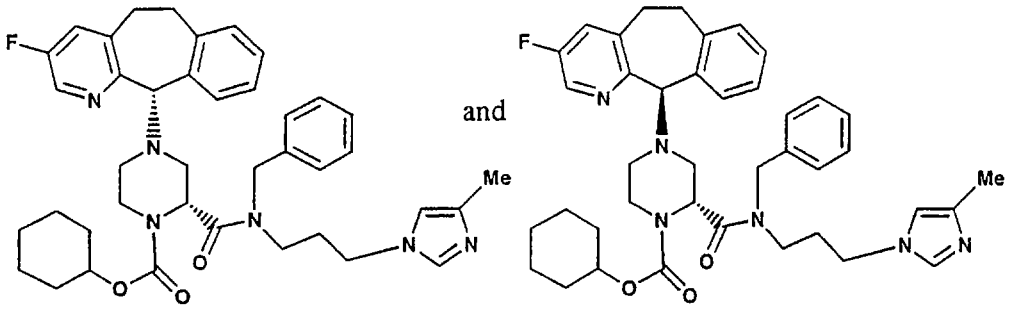


would be obtained.

Step B

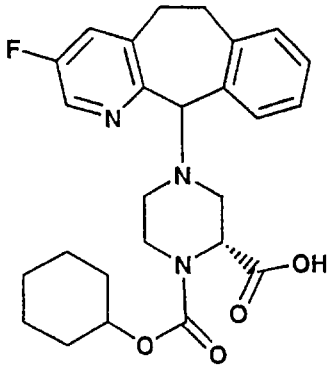
If the carboxylic acid from Step A was used in essentially the same procedure as that used for Example 225 then the title compound would be prepared. Separation of isomers could be made using chiral HPLC (AD column) using IPA-Hexane as eluent.

EXAMPLE 398



Step A

If the 3-fluorotricyclic chloride from Preparative Example 211 were used instead of the chloride in Preparative Example 127 Step C then the carboxylic acid

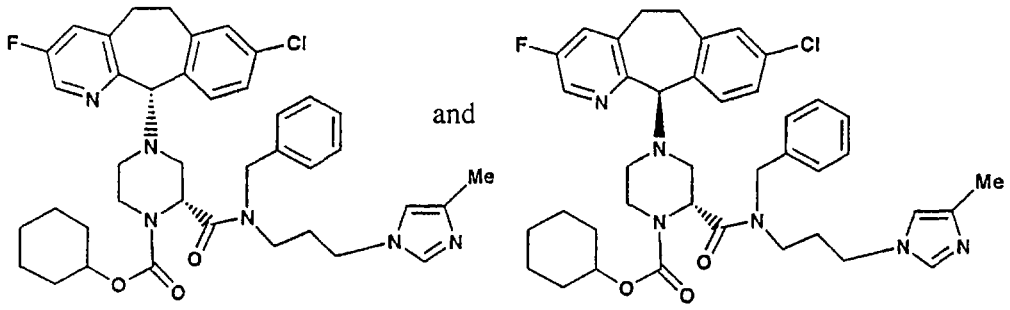


would be obtained.

Step B

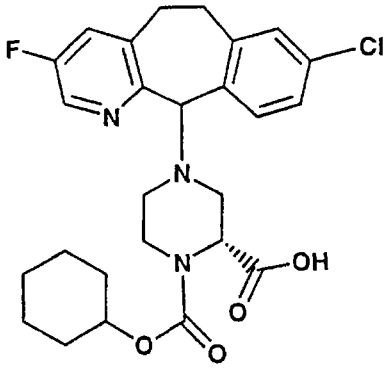
If the carboxylic acid from Step A was used in essentially the same procedure as that used for Example 225 then the title compound would be prepared. Separation of isomers could be made using chiral HPLC (AD column) using IPA-Hexane as eluent.

EXAMPLE 399



Step A

If the 3-fluoro-8-chlorotricyclic chloride from Preparative Example 204 were used instead of the chloride in Preparative Example 127 Step C then the carboxylic acid



would be obtained.

Step B

If the carboxylic acid from Step A was used in essentially the same procedure as that used for Example 225 then the title compound would be prepared. Separation of isomers could be made using chiral HPLC (AD column) using IPA-Hexane as eluent.

ASSAYS

FPT IC_{50} (inhibition of farnesyl protein transferase, in vitro enzyme assay) and COS Cell IC_{50} (Cell-Based Assay) were determined following the assay procedures described in WO 95/10516, published April 20, 1995. GGPT IC_{50} (inhibition of geranylgeranyl protein transferase, in vitro enzyme assay), Cell Mat Assay, and anti-tumor activity (in vivo anti-tumor studies) could be

determined by the assay procedures described in WO 95/10516. The disclosure of WO 95/10516 is incorporated herein by reference thereto.

Additional assays can be carried out by following essentially the same procedure as described above, but with substitution of alternative indicator tumor cell lines in place of the T24-BAG cells. The assays can be conducted using either DLD-1-BAG human colon carcinoma cells expressing an activated K-ras gene or SW620-BAG human colon carcinoma cells expressing an activated K-ras gene. Using other tumor cell lines known in the art, the activity of the compounds of this invention against other types of cancer cells could be demonstrated.

Soft Agar Assay:

Anchorage-independent growth is a characteristic of tumorigenic cell lines. Human tumor cells can be suspended in growth medium containing 0.3% agarose and an indicated concentration of a farnesyl transferase inhibitor. The solution can be overlayed onto growth medium solidified with 0.6% agarose containing the same concentration of farnesyl transferase inhibitor as the top layer. After the top layer is solidified, plates can be incubated for 10-16 days at 37°C under 5% CO_2 to allow colony outgrowth. After incubation, the colonies can be stained by overlaying the agar with a solution of MTT (3-[4,5-dimethyl-thiazol-2-yl]-2,5-diphenyltetrazolium bromide, Thiazolyl blue) (1 mg/mL in PBS). Colonies can be counted and the IC_{50}'s can be determined.

The compounds of Examples 1-19, 21-25, 67-71, 72 Step B, 72 Step C, 73-77, 78 Step B (Isomer C), 78 Step B (Isomer D), 79 Step B (Isomers A, B, and C), 80 Isomers A and B), 81-86, 86A, 87, 88, 93-104, 106, 108, 110-113, 115-211, 214-217, 221-228, 236-238, 236-238, 241-244, 255-286, 286A, 286B, 287-297, 299 Step B, 300, 302 Step B, 305 and 309 had an FPT IC_{50} within the range of <0.05nM to 20%@170nM.

The compounds of Examples 1, 2, 6-13, 15-17, 19, 78 Step B (Isomer D), 80 (Isomer A), 67-71, 72 Step B, 72 Step C, 73, 76, 81-86, 87, 88, 93, 95-101, 103, 106, 108, 110, 111, 113, 115-118, 121, 122, 124, 125 (Isomer A), 127-134, 137, 142, 144-146, 148, 151-153, 155-157, 161-162, 164, 166, 168, 173-175, 177, 180-187, 189-192, 195-196, 198-208, 210-211, 216-217, 221, 222, 225, 237, 238, 242-245, 247-263, 265, 268-286, 286A, 286B, 288-289, 292, 295-296, 299 Step B, 300, 302 StepB, 305, 309, 310-342, 343-373 and 375-382 had an FPT IC_{50} within the range of <0.04nM to 6.7nM.

The compounds of Examples 11, 16, 78 Step B (Isomers C and D), 79 Step B (Isomer A), 80 (Isomer A), 88 (Isomer A), 93 (Isomer D), 99, 100, 225, 243, 367 and 368 had an FPT IC_{50} within the range of <0.04nM to 2.7nM. The compound of Example 225 had an FPT IC_{50} of 0.36nM.

The compounds of Examples 1, 2, 8, 25, 86, 100, had a Cos Cell IC_{50} within the range of <10-920nM. The compounds of Examples 98, 101, 103, 104, 106, 108, 258, 259, 261, and 262 had a Cos Cell IC_{50} within the range of <5 to >500nM. The compounds of Examples 245-250 had a Cos Cell IC_{50} within the range of 100%@0.01 to 0.087 μM. The compounds of Examples 100, 101, 103 and 259 had a Cos Cell IC_{50} within the range of <5nM to 35nM.

The compounds of Examples 1, 2, 3, 7, 8, 10-16, 21, 25, 67-69, 70, 81, 82 86 (11R,2R Isomer), 88-95, 97, 110, 111-113, 115-119, 121-176, 178-184, 186-200, 202-204, 206-211, 214-217, 221-225, 256, 258, 259, 261, 262, 268-271, 273-274, 276, 278, 280-286, 289, 292, 295-296, 299 Step B, 305, 309-346, 351-373 and 375-382 had a Soft Agar IC_{50} within the range of <5 to >500nM.

The compounds of Examples 116, 117, 160, 170, 184, 186-188, 196-200, 202-204, 206-208, 217, 225, 305 (11s,2R isomer), 316, 321, 322, 324, 325, 335, 339, 365, 364, 372, 373, 375, and 382 had a Soft Agar IC_{50} within the range of 2 to 10nM.

The compounds of Examples 11, 16, 79 Step B (Isomer A), 80 (Isomer A), 88 (Isomer A), 93 (Isomer D), and 225 had a Soft Agar IC_{50} within the range of 2 to 300nM. The compound of Example 225 had a Soft Agar IC_{50} of 2nM.

For preparing pharmaceutical compositions from the compounds described by this invention, inert, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, dispersible granules, capsules, cachets and suppositories. The powders and tablets may be comprised of from about 5 to about 95 percent active ingredient. Suitable solid carriers are known in the art, e.g. magnesium carbonate, magnesium stearate, talc, sugar or lactose. Tablets, powders, cachets and capsules can be used as solid dosage forms suitable for oral administration. Examples of pharmaceutically acceptable carriers and methods of manufacture for various compositions may be found in A. Gennaro (ed.), Remington's Pharmaceutical Sciences, 18th Edition, (1990), Mack Publishing Co., Easton, Pennsylvania.

Liquid form preparations include solutions, suspensions and emulsions. As an example may be mentioned water or water-propylene glycol solutions for parenteral injection or addition of sweeteners and opacifiers for oral solutions, suspensions and emulsions. Liquid form preparations may also include solutions for intranasal administration.

Aerosol preparations suitable for inhalation may include solutions and solids in powder form, which may be in combination with a pharmaceutically acceptable carrier, such as an inert compressed gas, e.g. nitrogen.

Also included are solid form preparations which are intended to be converted, shortly before use, to liquid form preparations for either oral or parenteral administration. Such liquid forms include solutions, suspensions and emulsions.

The compounds of the invention may also be deliverable transdermally. The transdermal compositions can take the form of creams, lotions, aerosols and/or emulsions and can be included in a transdermal patch of the matrix or reservoir type as are conventional in the art for this purpose.

Preferably, the pharmaceutical preparation is in a unit dosage form. In such form, the preparation is subdivided into suitably sized unit doses containing appropriate quantities of the active component, e.g., an effective amount to achieve the desired purpose.

The quantity of active compound in a unit dose of preparation may be varied or adjusted from about 0.01 mg to about 1000 mg, preferably from about 0.01 mg to about 750 mg, more preferably from about 0.01 mg to about 500mg, and most preferably from about 0.01 mg to about 250mg, according to the particular application.

The actual dosage employed may be varied depending upon the requirements of the patient and the severity of the condition being treated. Determination of the proper dosage regimen for a particular situation is within the skill of the art. For convenience, the total daily dosage may be divided and administered in portions during the day as required.

The amount and frequency of administration of the compounds of the invention and/or the pharmaceutically acceptable salts thereof will be regulated according to the judgment of the attending clinician considering such factors as age, condition and size of the patient as well as severity of the symptoms being treated. A typical recommended daily dosage regimen for oral administration can range from about 0.04 mg/day to about 4000 mg/day, in two to four divided doses.

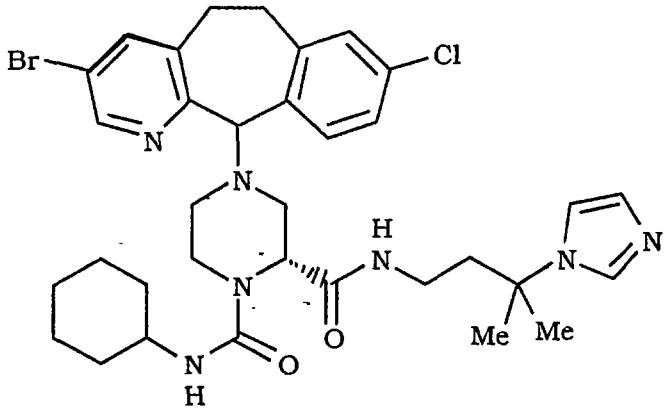
While the present invention has been described in conjunction with the specific embodiments set forth above, many

alternatives, modifications and variations thereof will be apparent to those of ordinary skill in the art. All such alternatives, modifications and variations are intended to fall within the spirit and scope of the present invention.

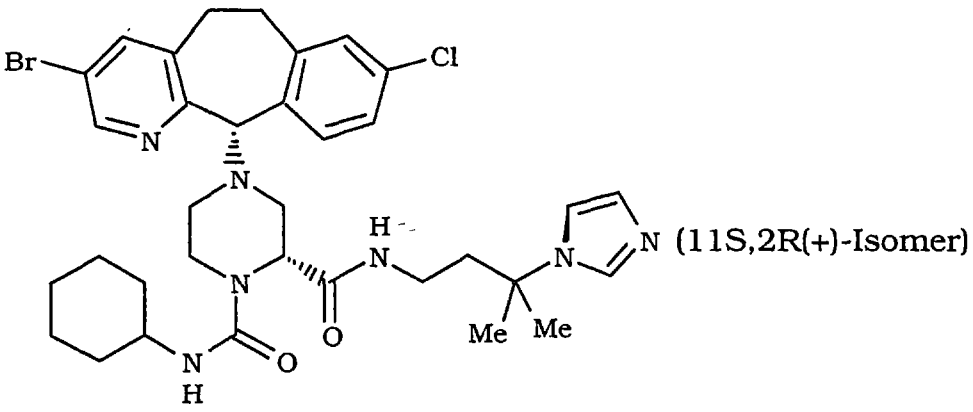
CLAIMS

WHAT WE CLAIM IS:

1. A compound selected from the group consisting of:

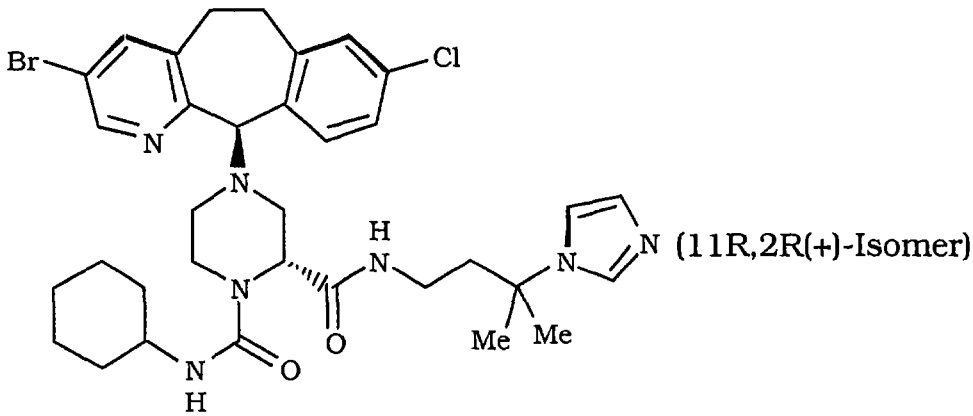


(Example 1);



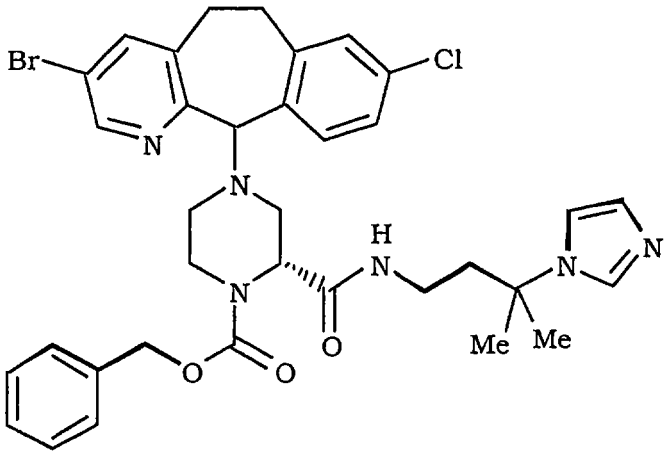
(11S,2R(+)-Isomer)

(Example 2);

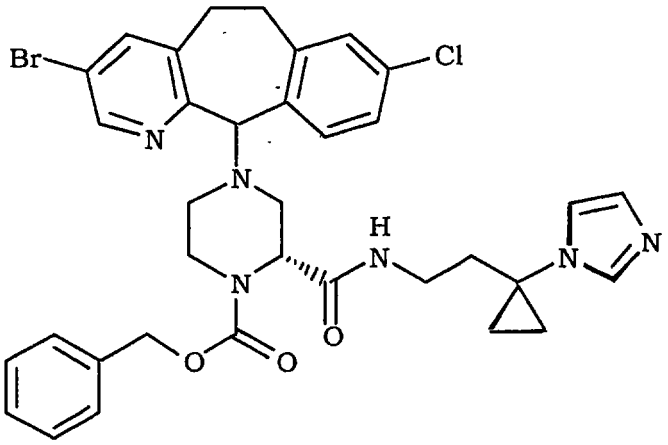


(11R,2R(+)-Isomer)

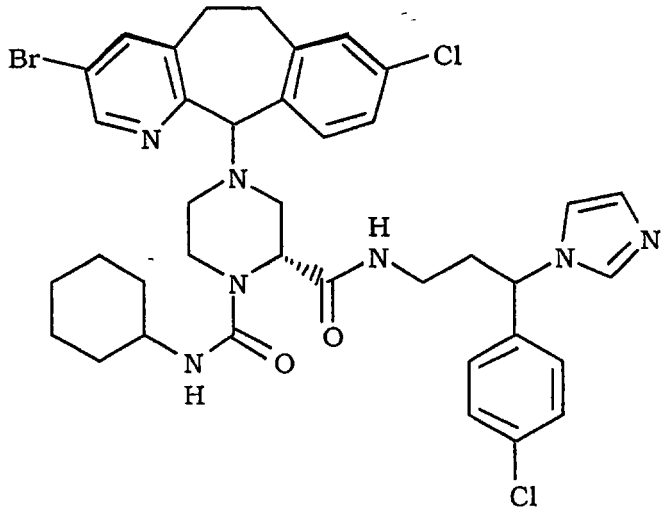
(Example 2);



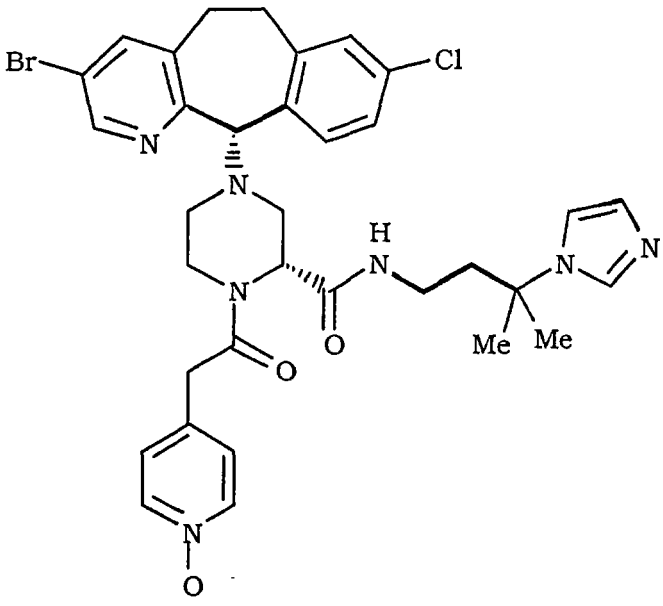
(Example 3);



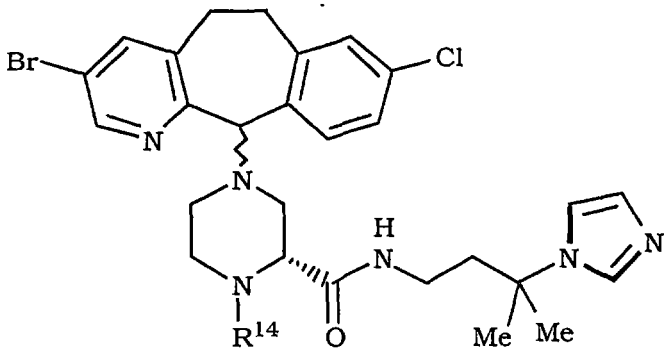
(Example 4);



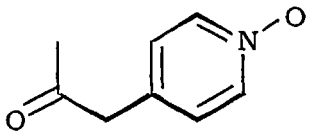
(Example 5);



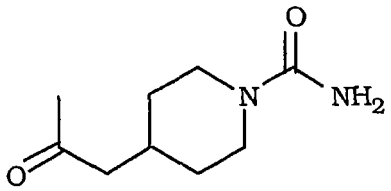
(11R,2R Isomer) (Example 6);



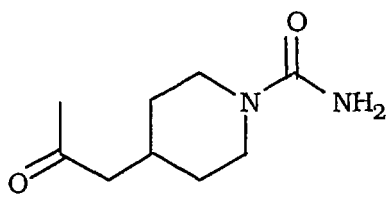
wherein R^{14} is selected from the group comprising:



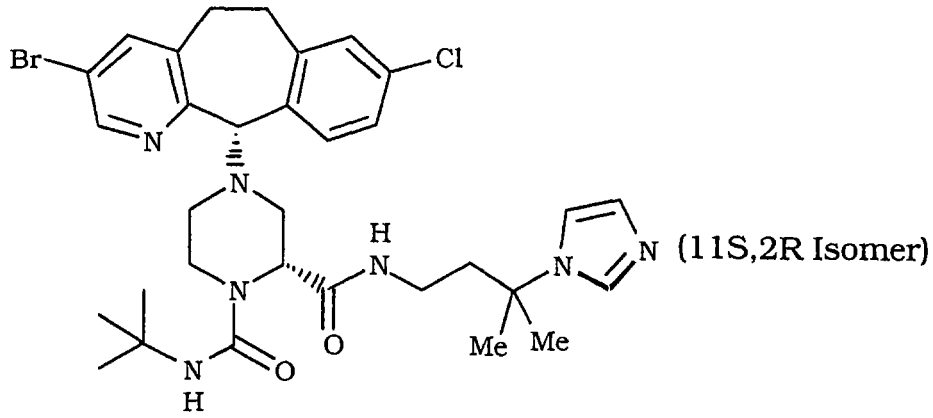
11R,2R isomer (Example 7);



11S,2R isomer (Example 8); and

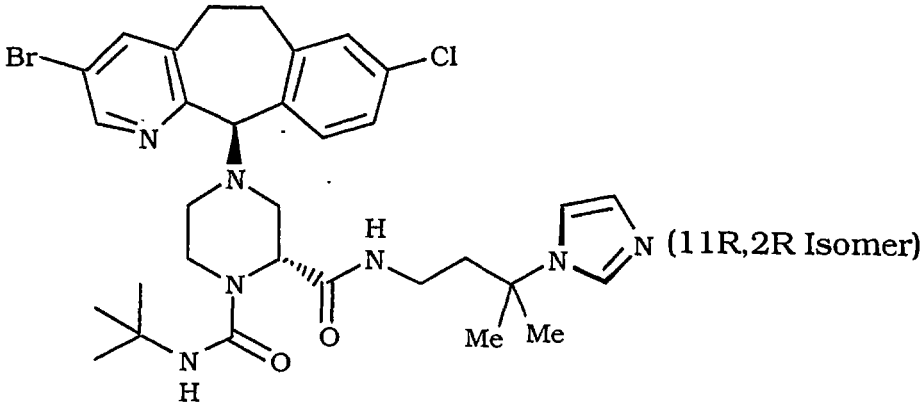


11R,2R isomer (Example 9);



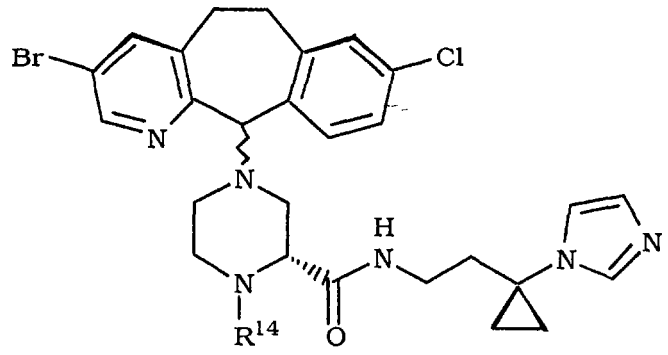
(11S,2R Isomer)

(Example 10);

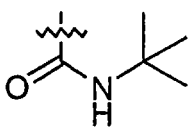


(11R,2R Isomer)

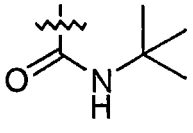
(Example 11);



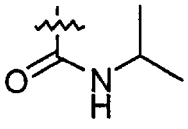
wherein R^{14} is selected from the group comprising:



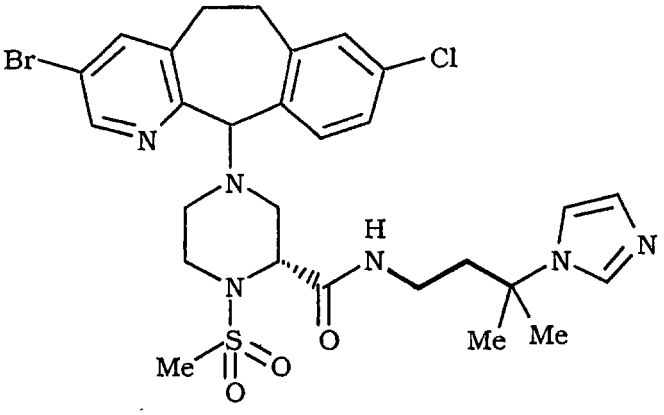
11S,2R isomer (Example 12);



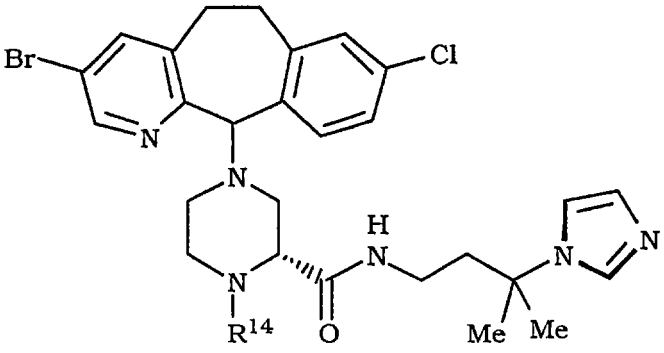
11R,2R isomer (Example 13); and



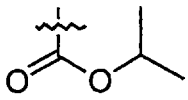
11R/S,2R isomers (Example 14);



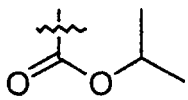
(Example 15);



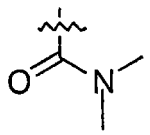
wherein R^{14} is selected from the group comprising:



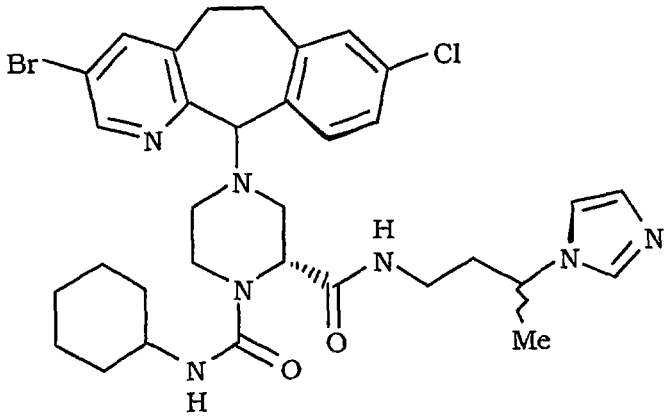
11S,2R isomer (Example 16);



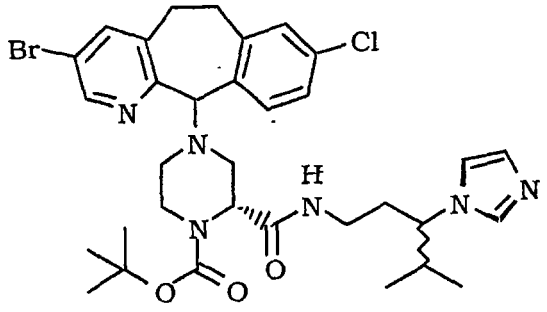
11R,2R isomer (Example 17); and



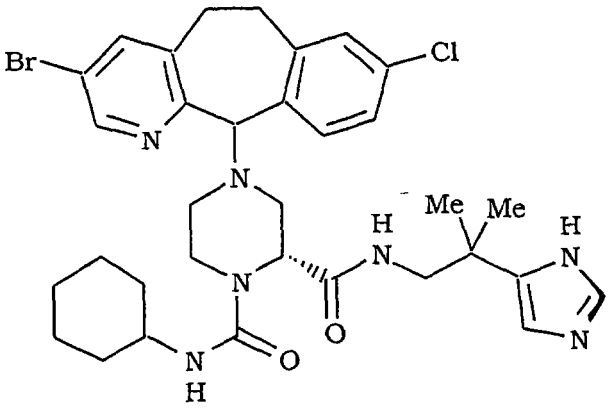
11R/S,2R isomers (Example 18);



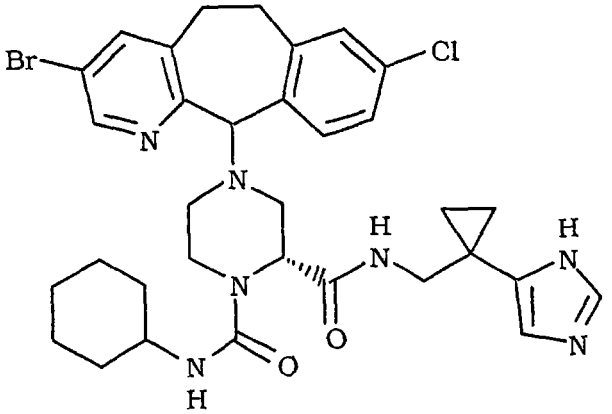
(Example 19);



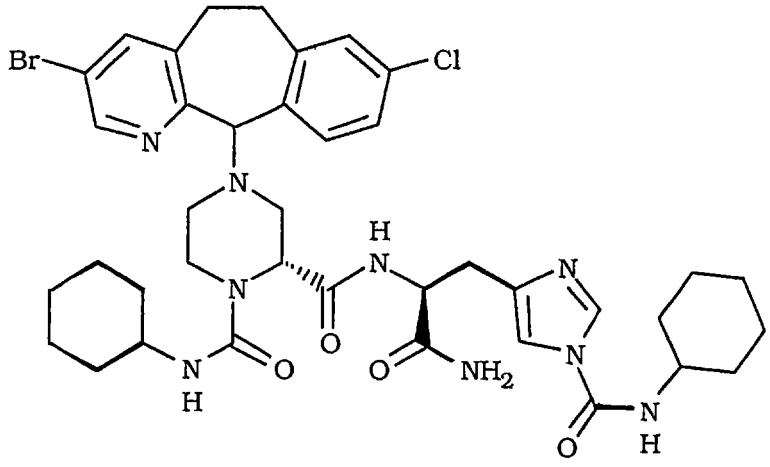
(Example 20);



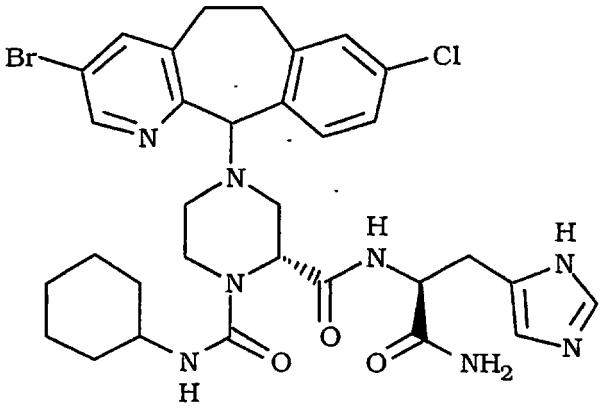
(Example 21);



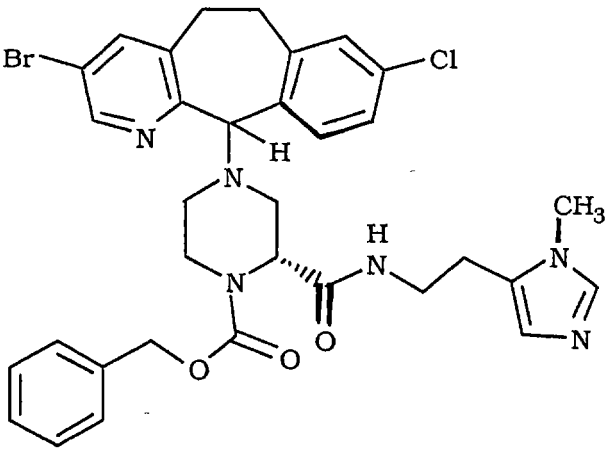
(Example 22);



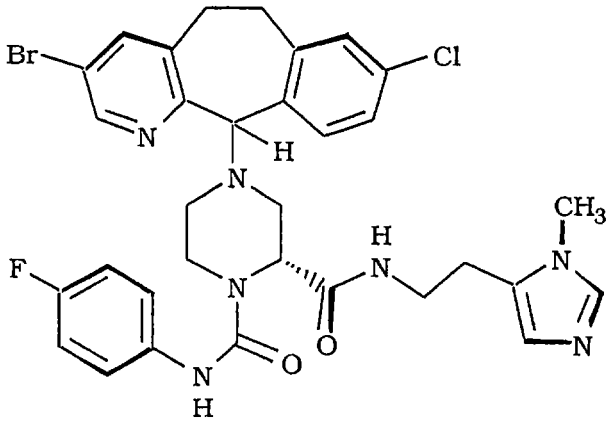
(Example 24);



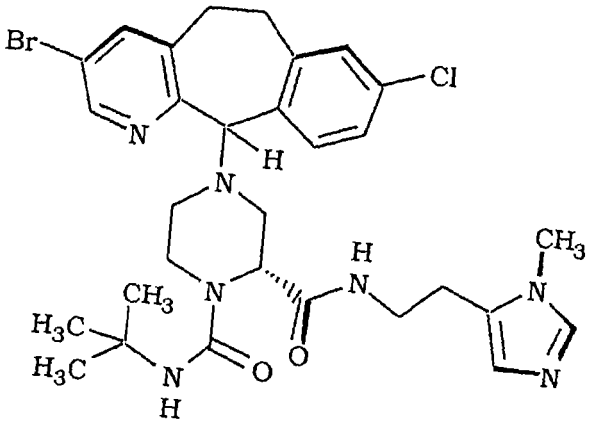
(Example 25);



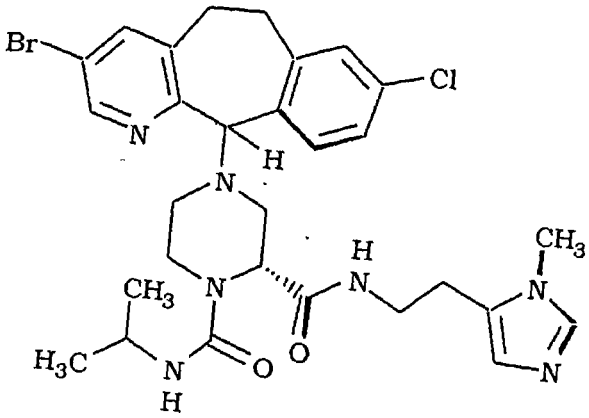
(Example 26);



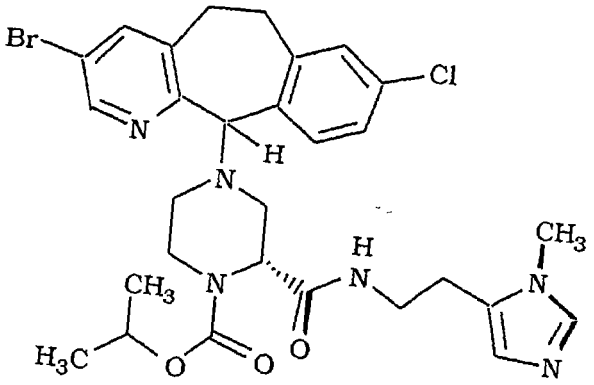
(Example 27);



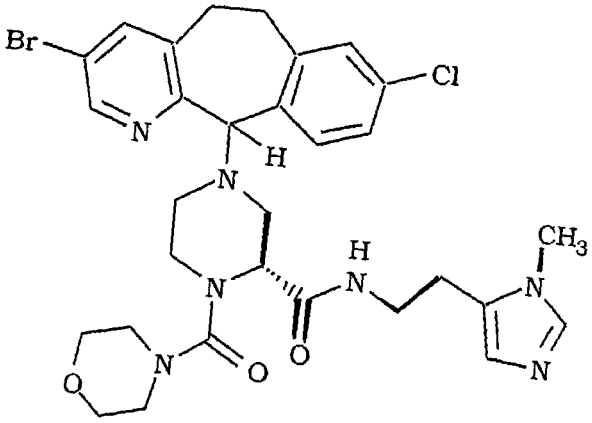
(Example 28);



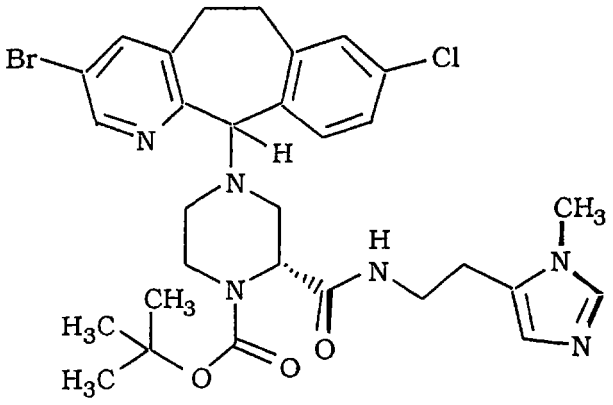
(Example 29);



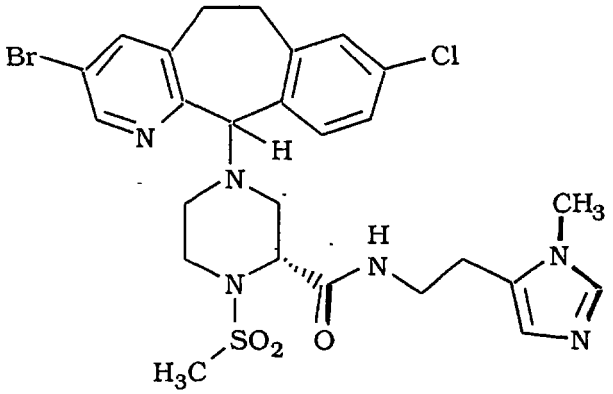
(Example 30);



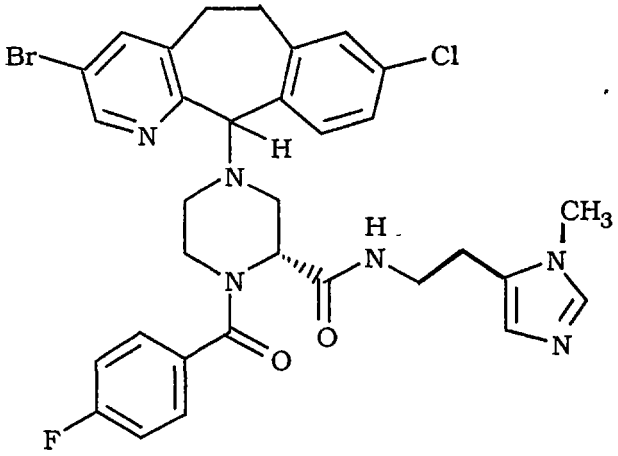
(Example 31);



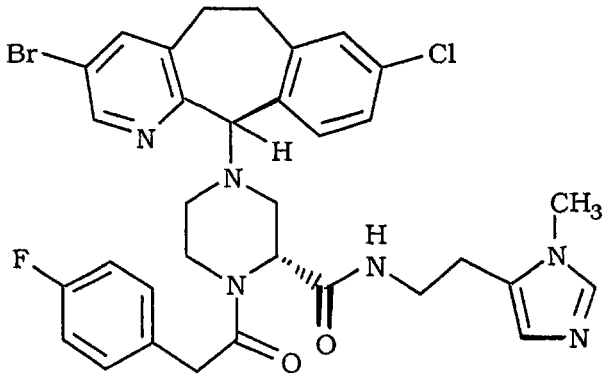
(Example 32);



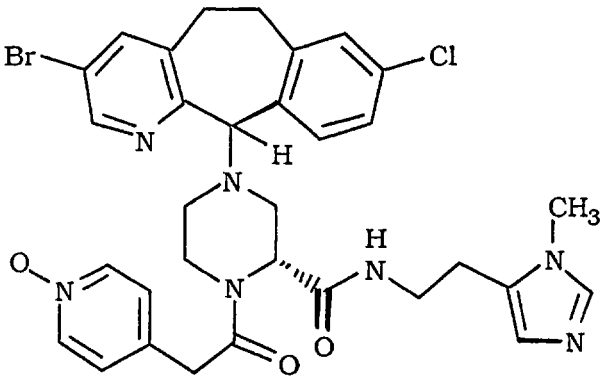
(Example 33);



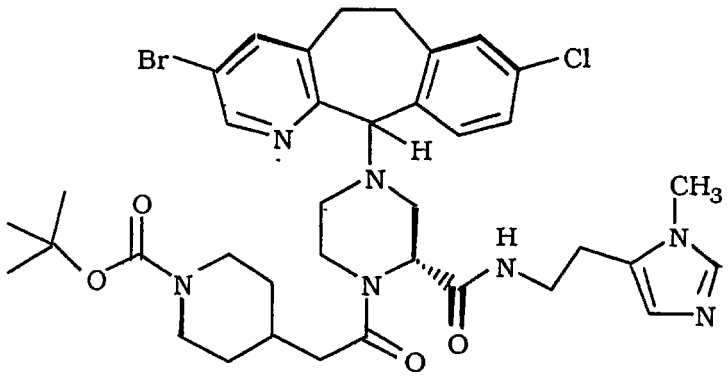
(Example 34);



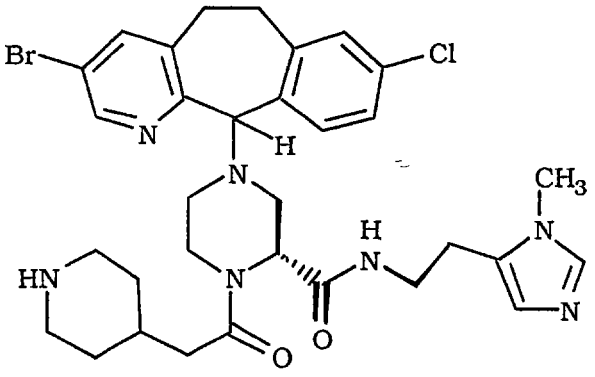
(Example 35);



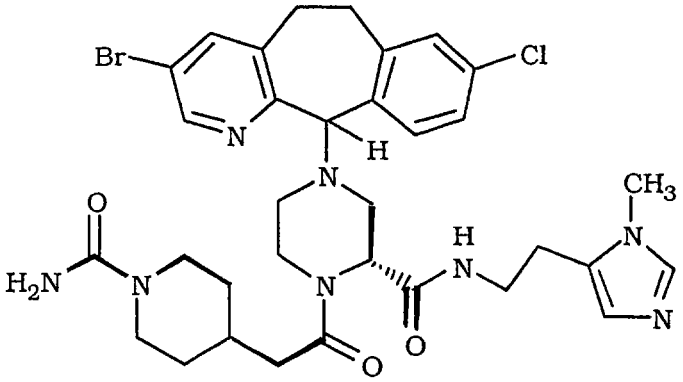
(Example 36);



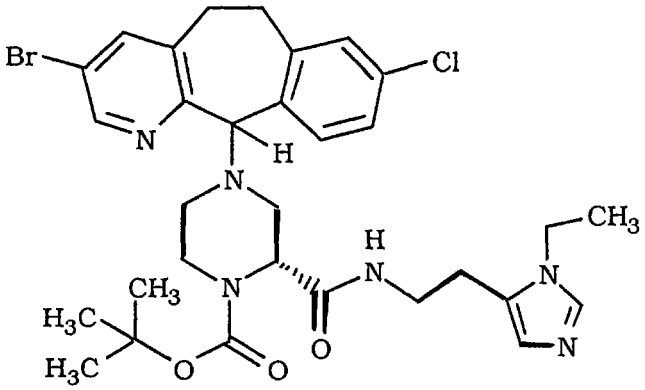
(Example 37);



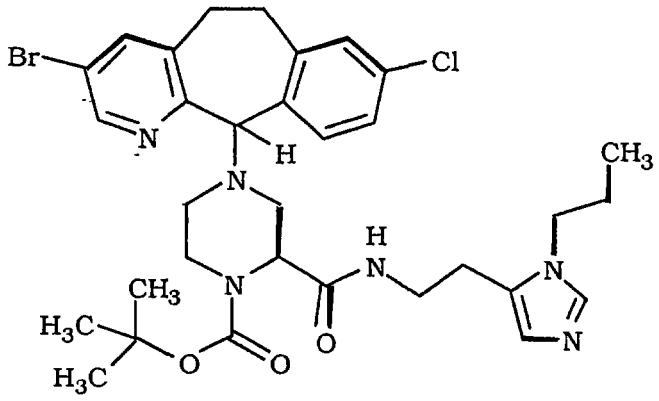
(Example 38);



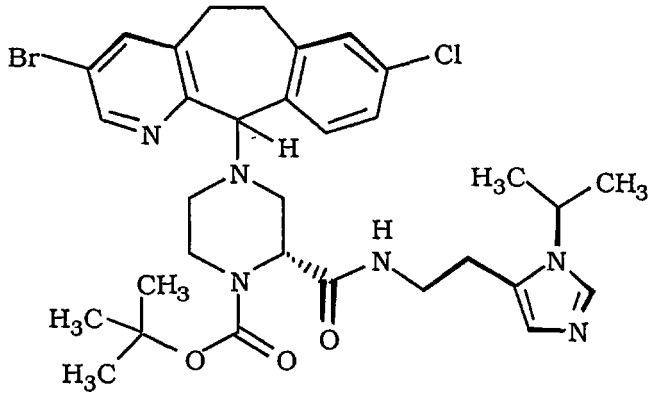
(Example 39);



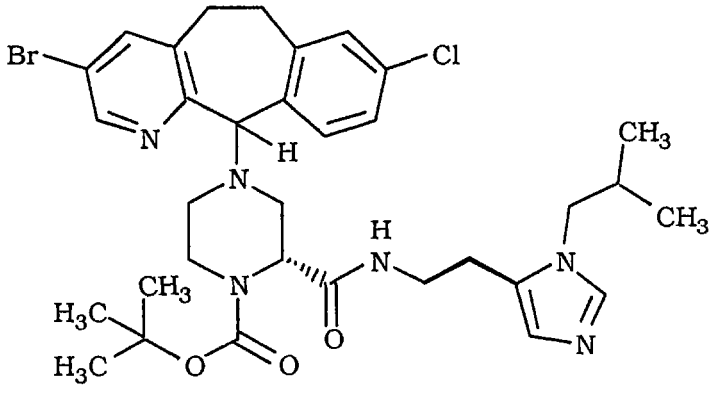
(Example 40);



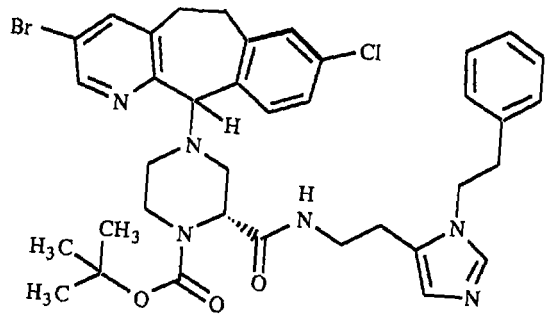
(Example 41);



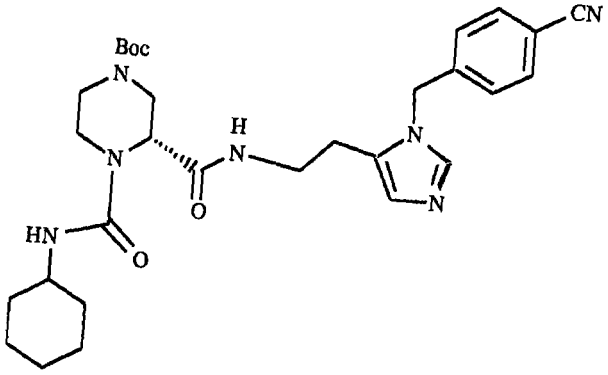
(Example 42);



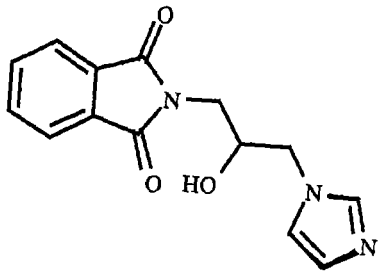
(Example 43);



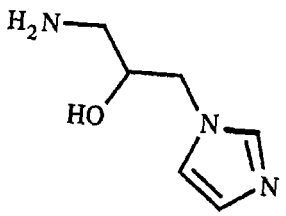
(Example 44);



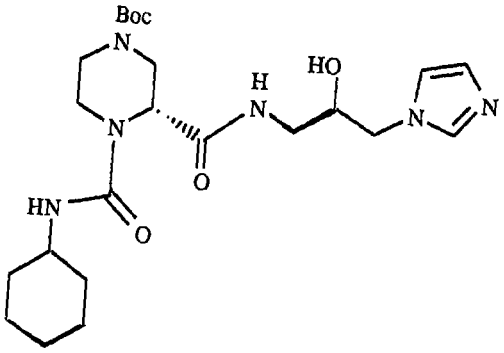
(Example 45);



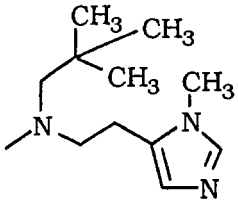
(Example 46);



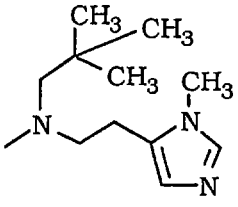
(Example 47);



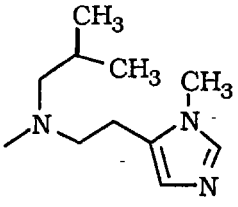
(Example 48)



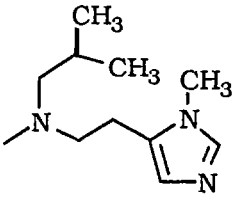
Isomer A (Example 49);



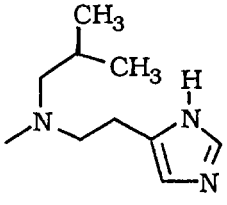
Isomer B (Example 50);



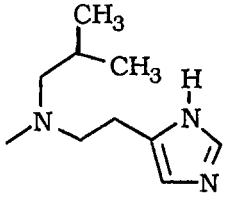
Isomer A (Example 51);



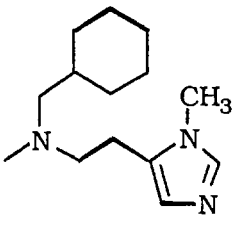
Isomer B (Example 52);



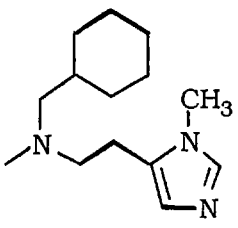
Isomer A (Example 53);



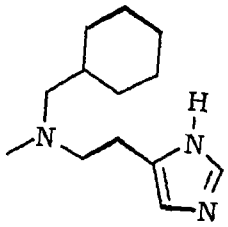
Isomer B (Example 54);



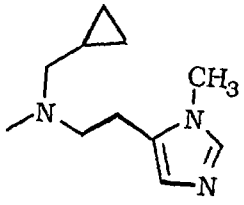
Isomer A (Example 55);



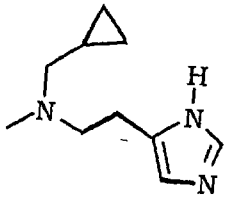
Isomer B (Example 56);



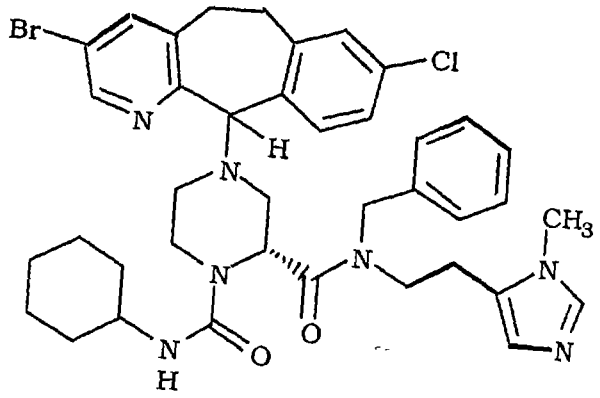
(Example 57);



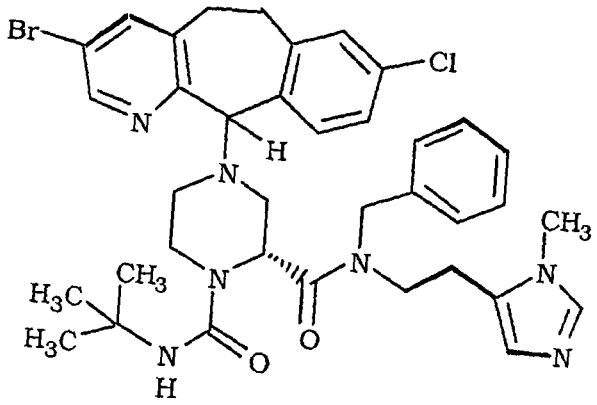
(Example 58); and



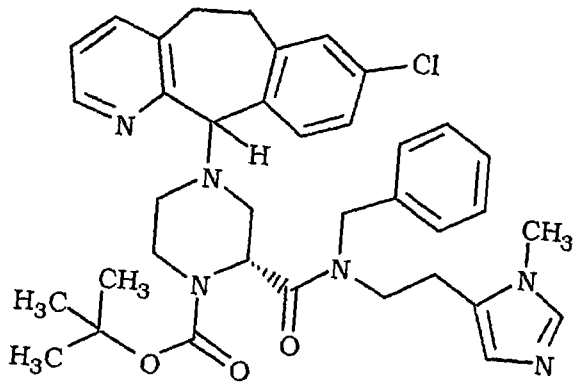
(Example 59);



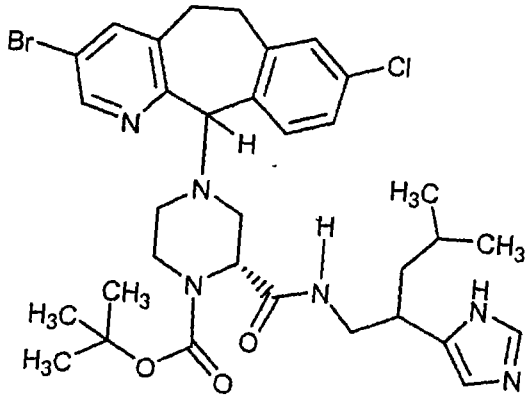
(Example 60);



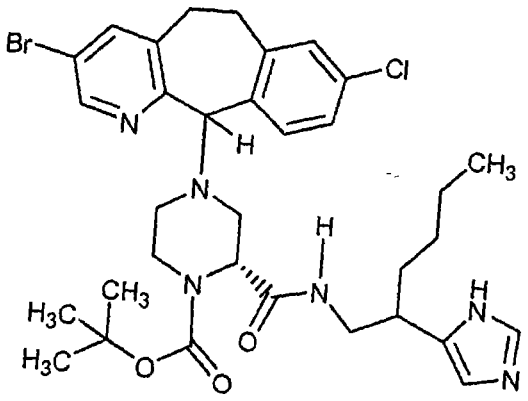
(Example 61);



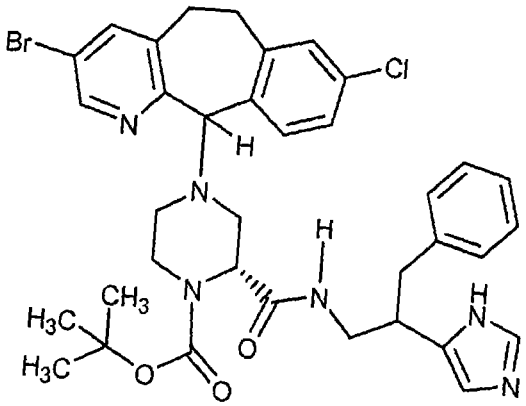
(Example 62);



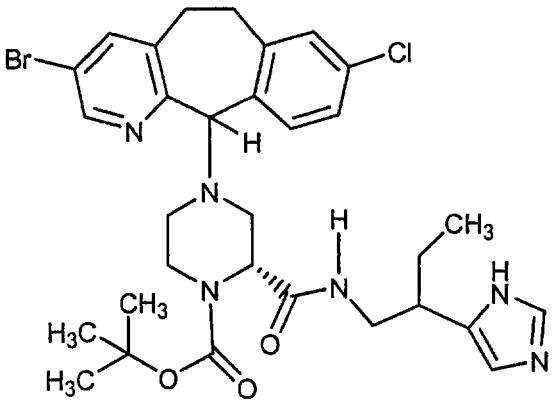
(Example 63);



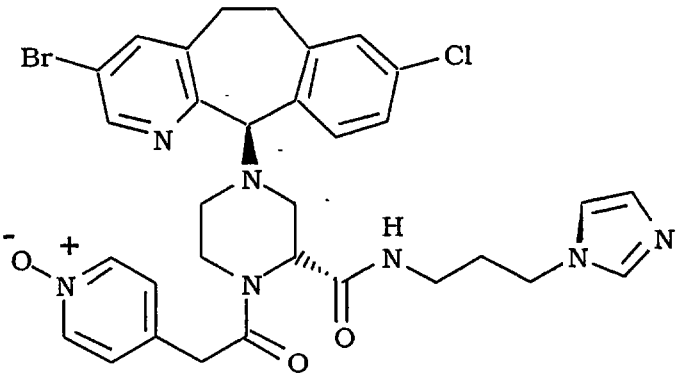
(Example 64);



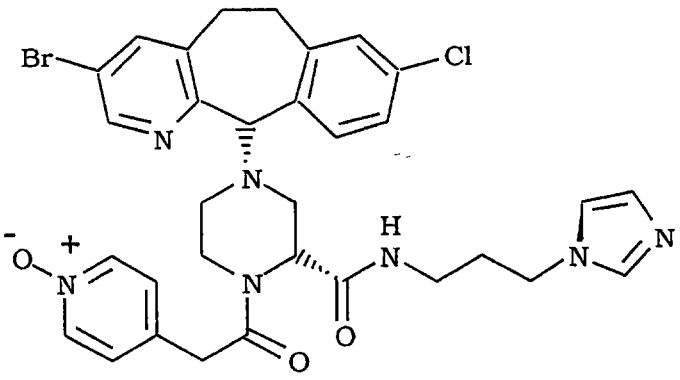
(Example 65);



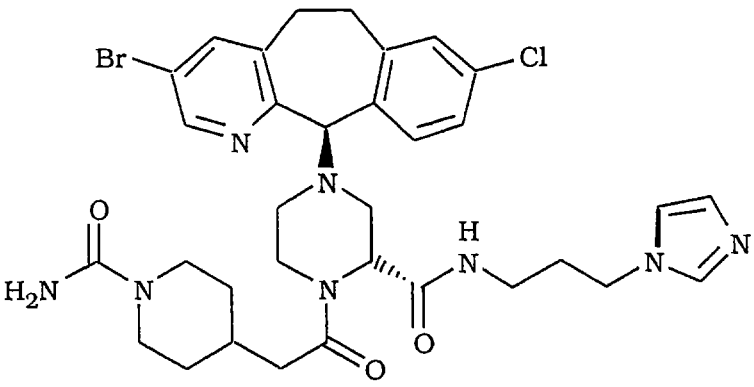
(Example 66);



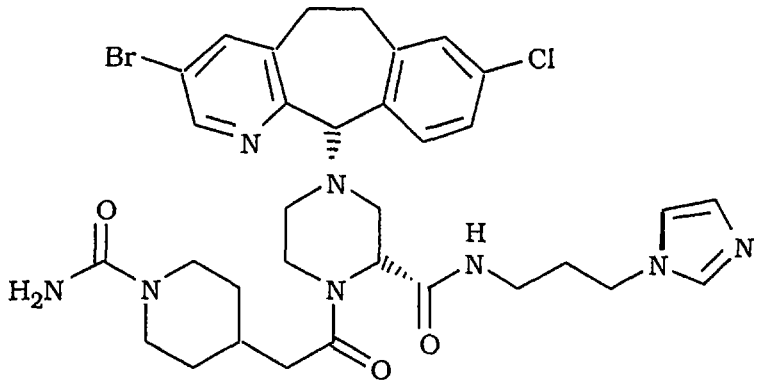
(Example 67);



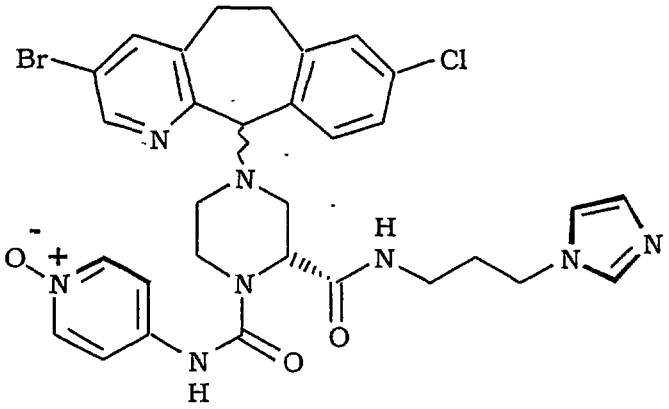
(Example 68);



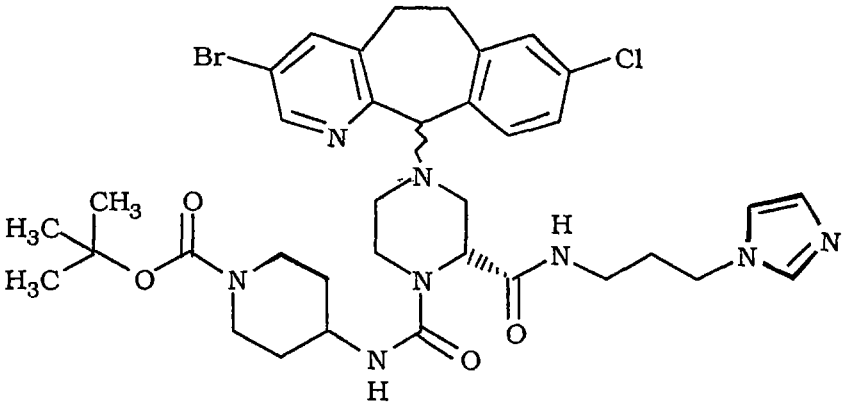
(Example 69);



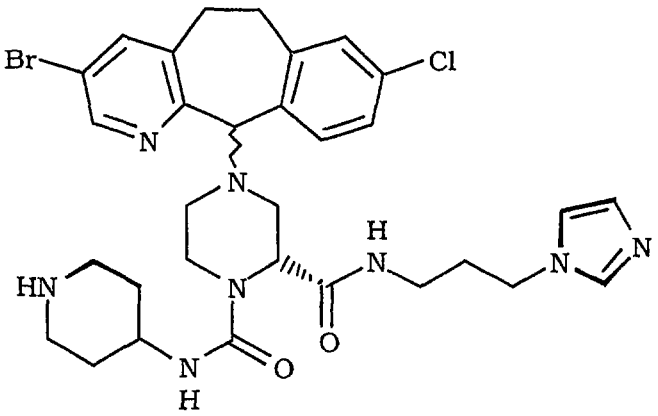
(Example 70);



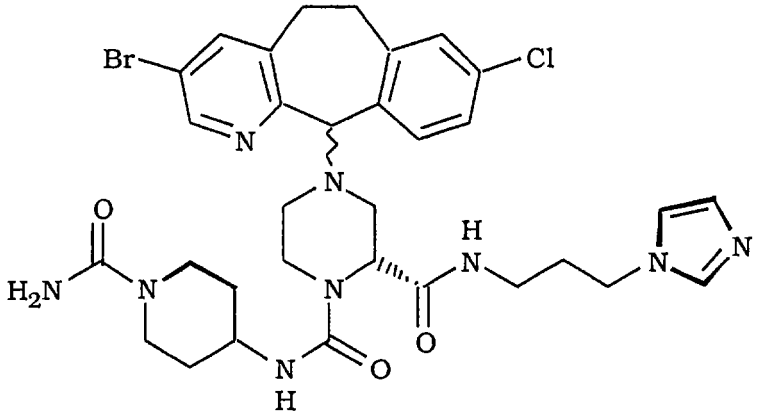
(Example 71);



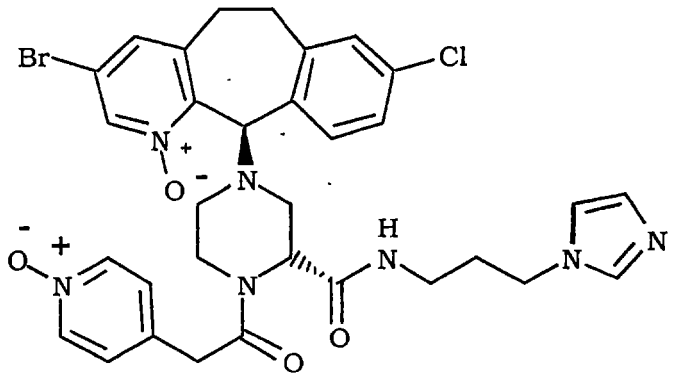
(Example 72 Step A);



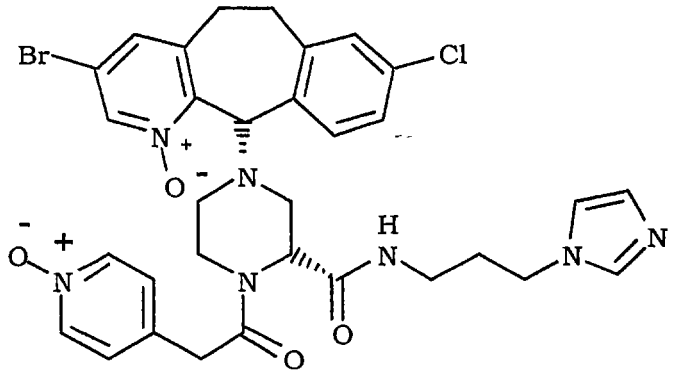
(Example 72 Step B);



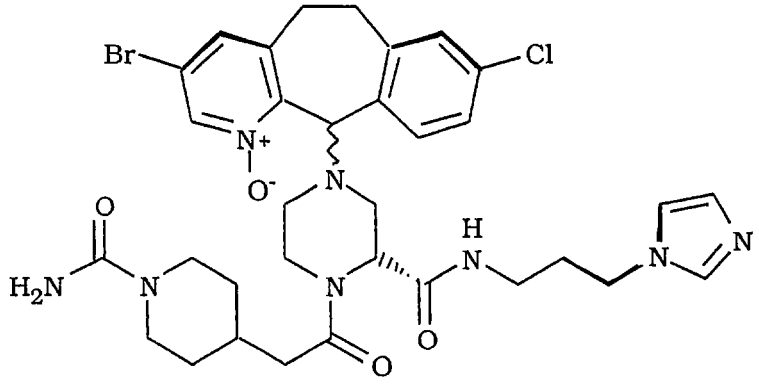
(Example 72 Step C);



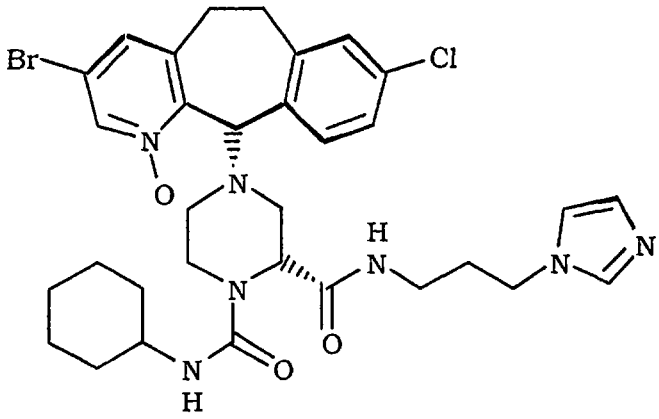
(Example 73);



(Example 74);

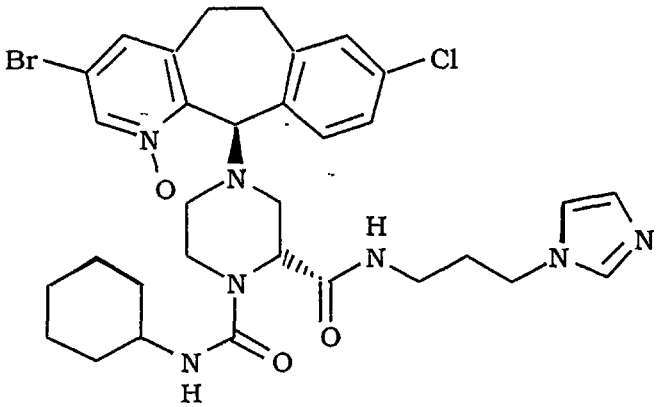


(Example 75);



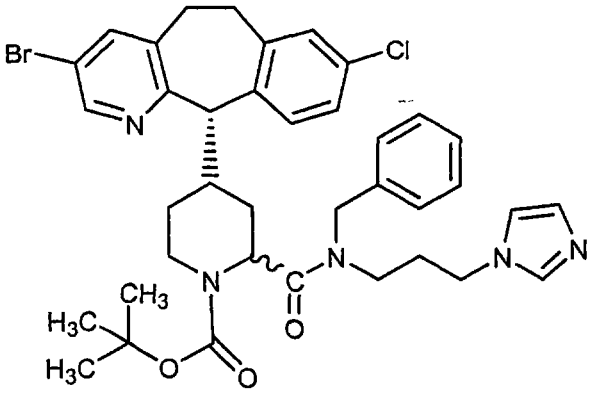
(11S,2R(-)-Isomer)

(Example 76);

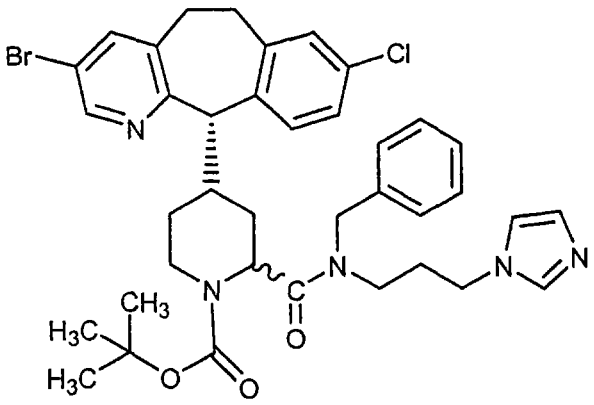


(11R,2R(+)-Isomer)

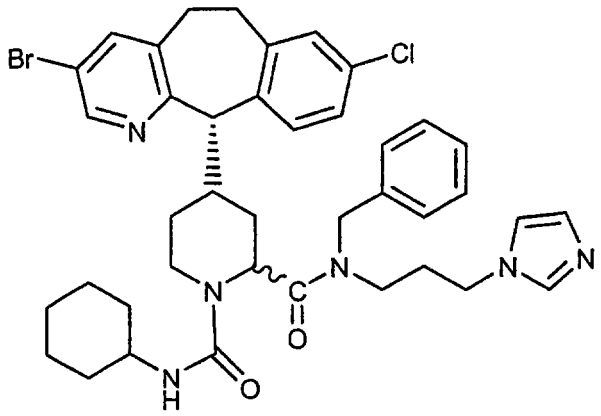
(Example 76);



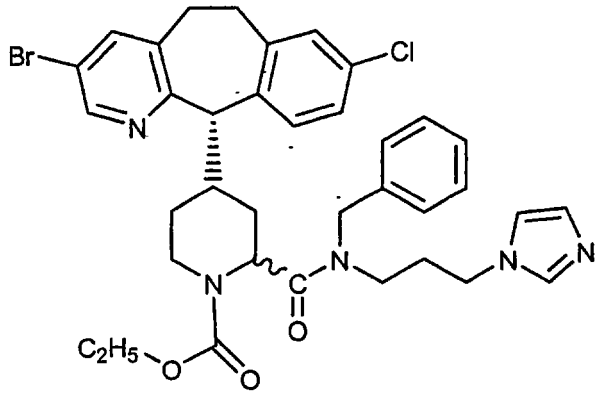
(Example 77);



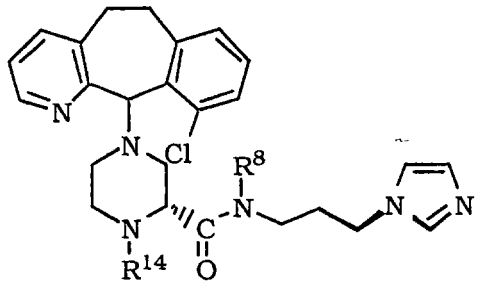
(Example 78 Step B);



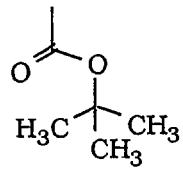
(Example 79);



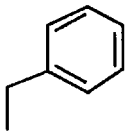
(Example 80);

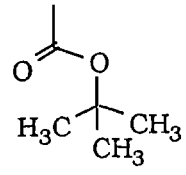


wherein R^8 is H and R^{14} is:

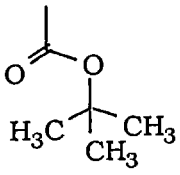


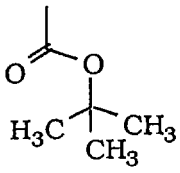
(Example 81);

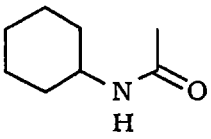
or wherein R^8 is  and R^{14} is selected from the group consisting of:

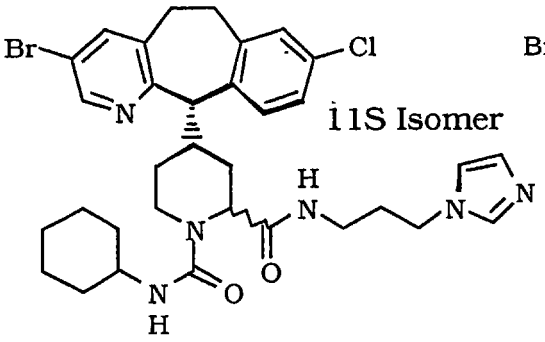


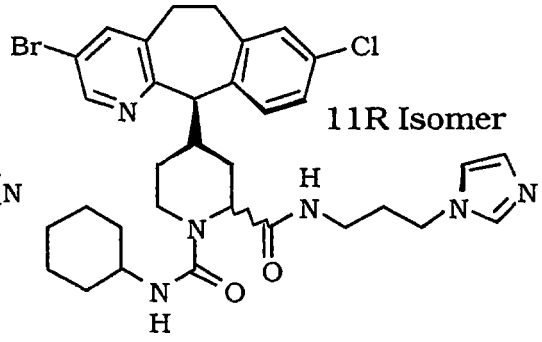
(Example 82);


Isomer A (R(+)) (Example 83);

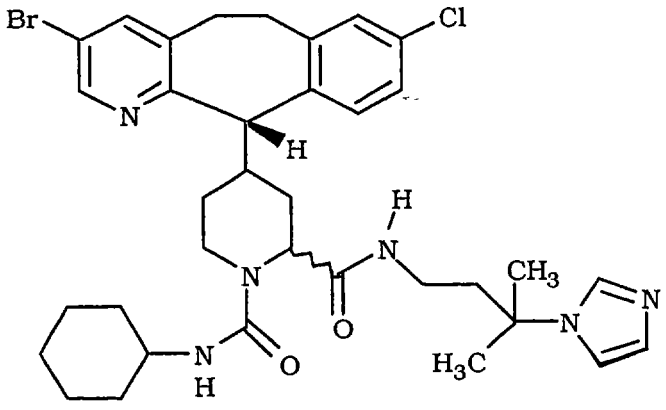

Isomer B (S(-)) (Example 84); and

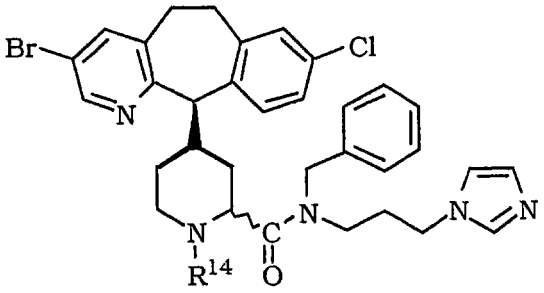

(Example 85);

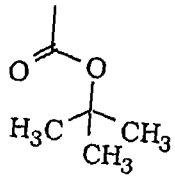




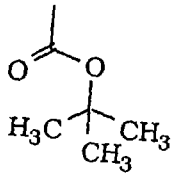
(Example 86);


(Example 86A);

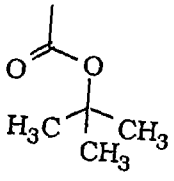

wherein R^{14} is selected from the group consisting of:



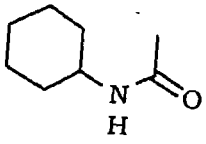
Isomers A, B, C, D (Example 87);



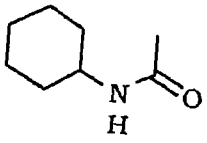
Isomer A (Example 88);



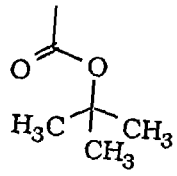
Isomer B (Example 89);



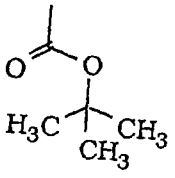
Isomer A (Example 90);



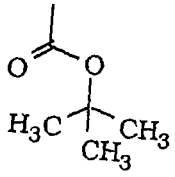
Isomer B (Example 91);



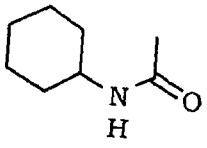
Isomer C (Example 92);



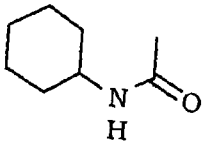
Isomer D (Example 93);



Isomer C, D (Example 94);

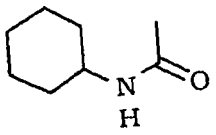


Isomer C (Example 95);

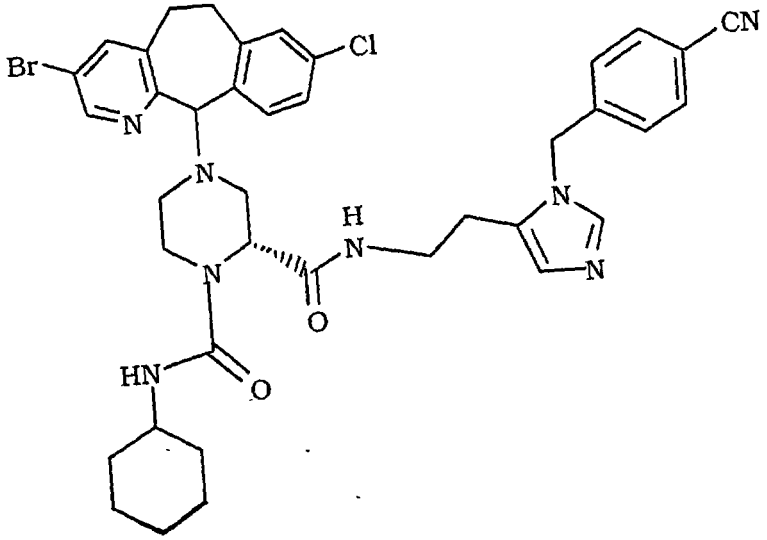


Isomer D (Example 96); and

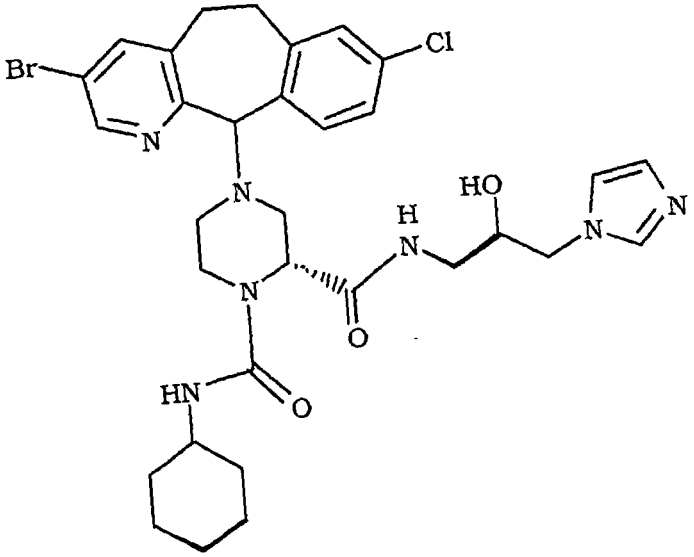
16 JUL 2003



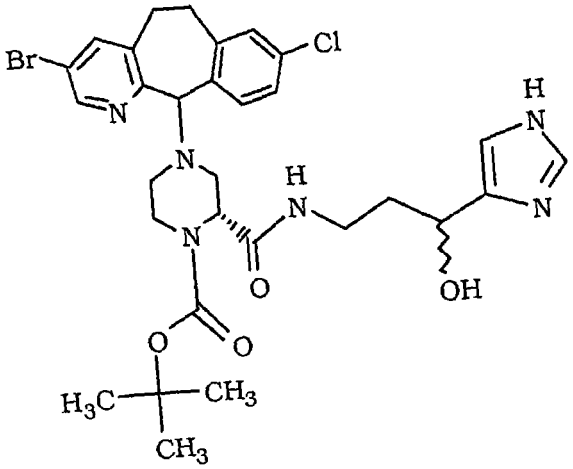
Isomers C, D (Example 97);



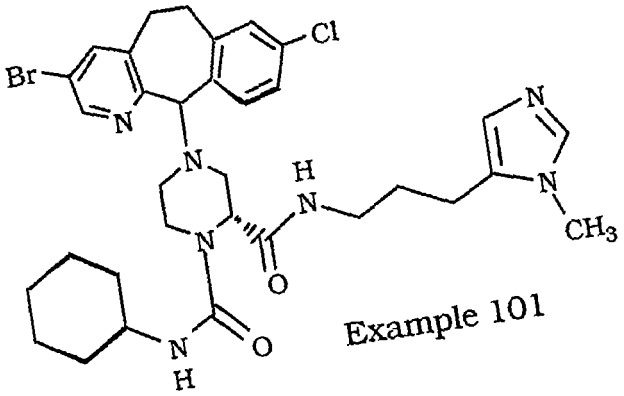
(Example 98);



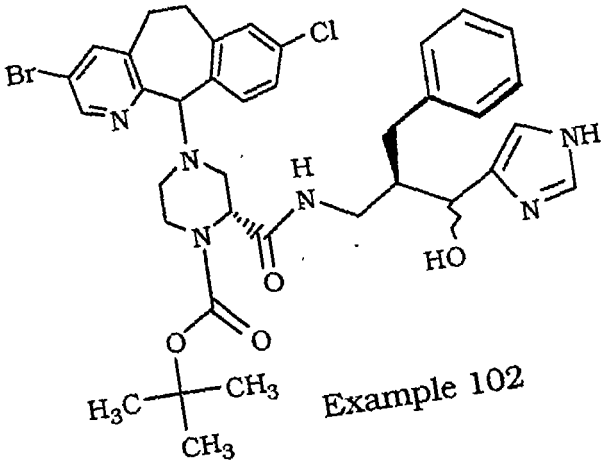
(Example 99);



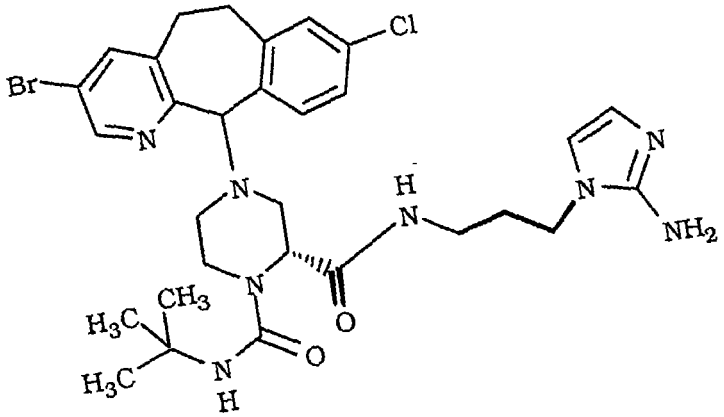
(Example 100);



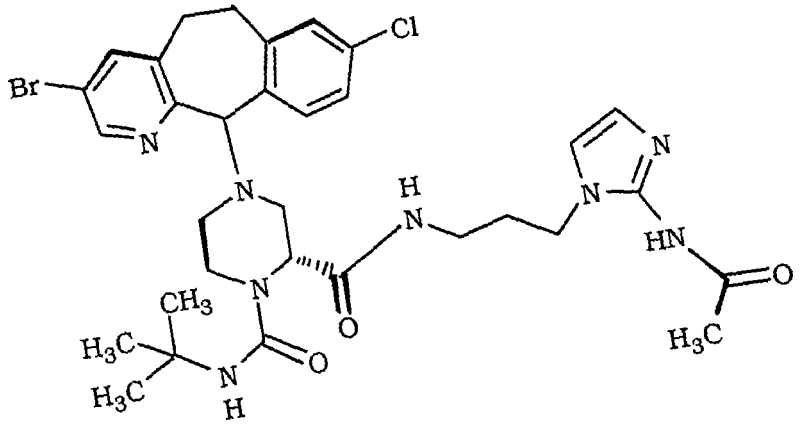
Example 101 ;



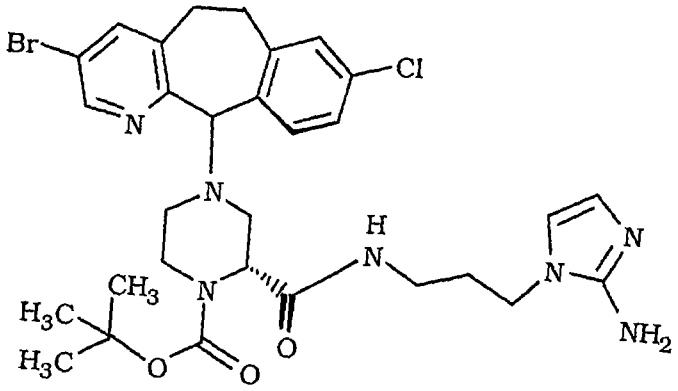
Example 102 ;



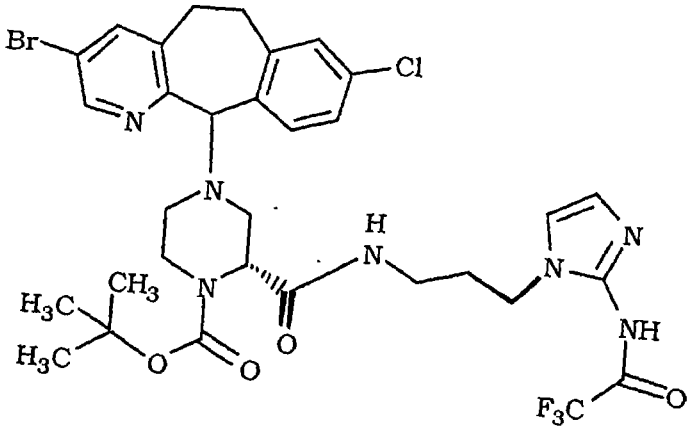
(Example 103);



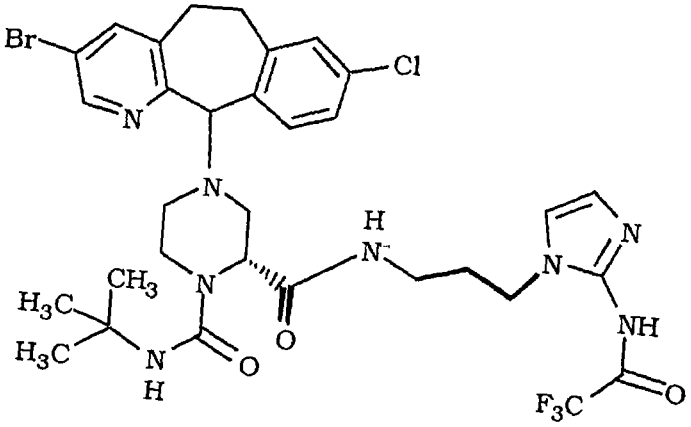
(Example 104);



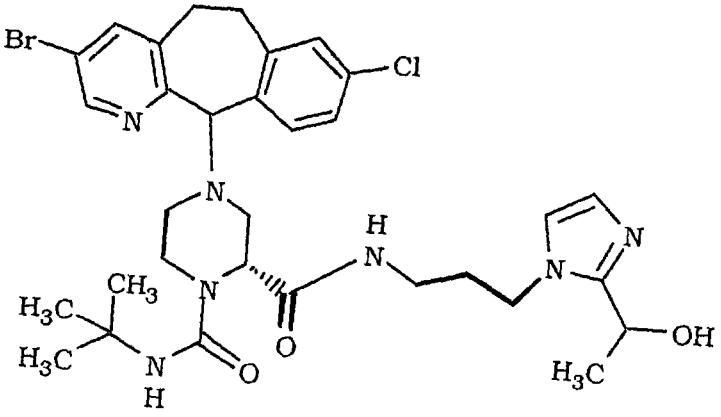
(Example 105);



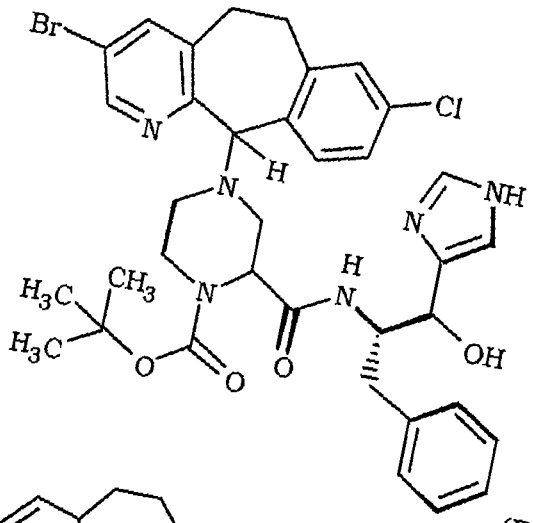
(Example 106);



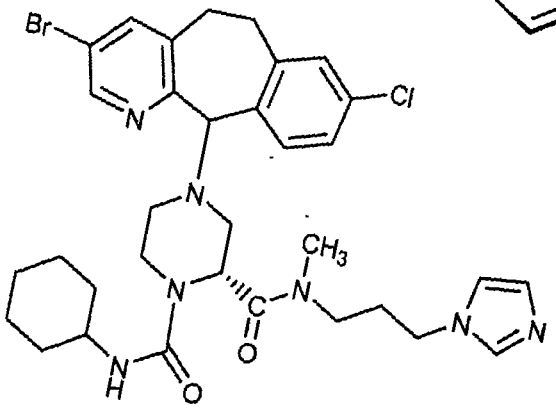
(Example 107);



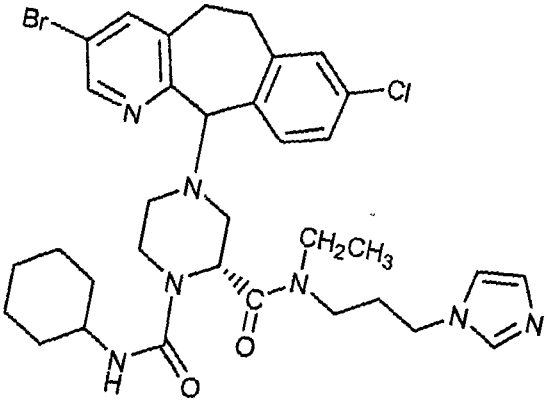
(Example 108);



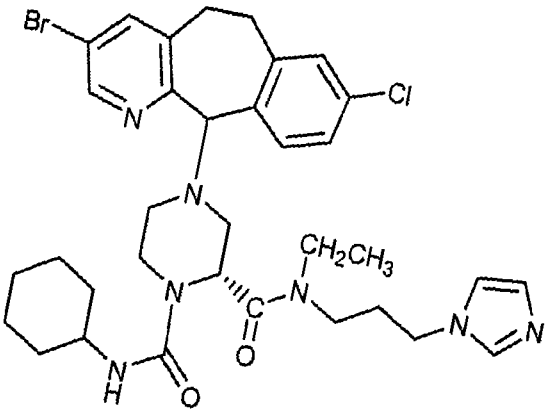
(Example 109);



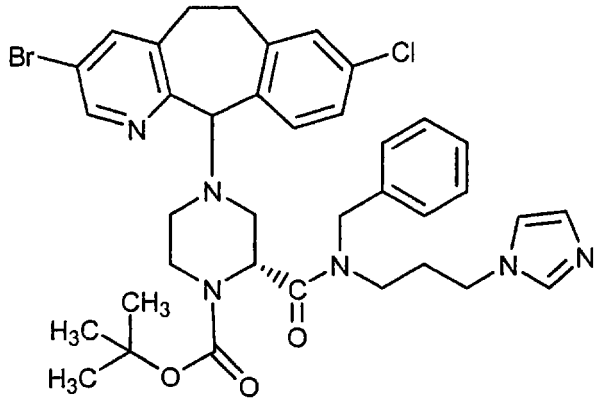
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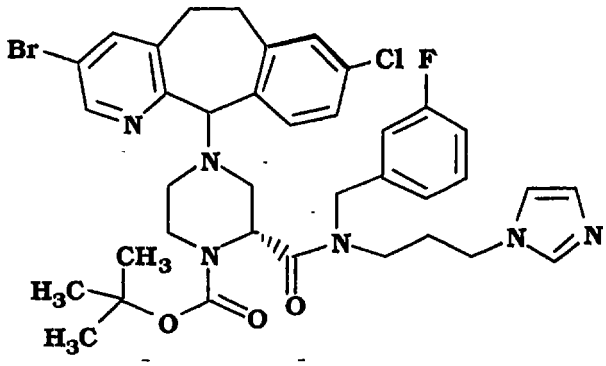
(Example 111);



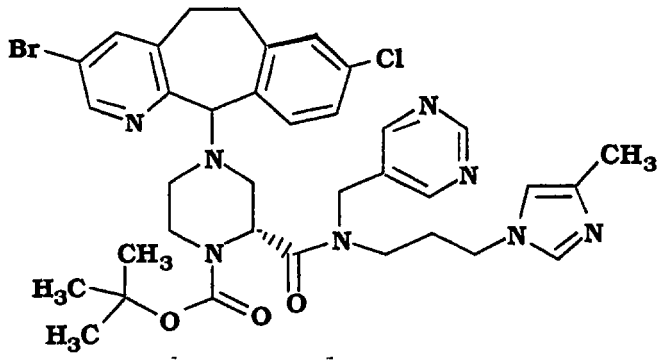
(Example 112);



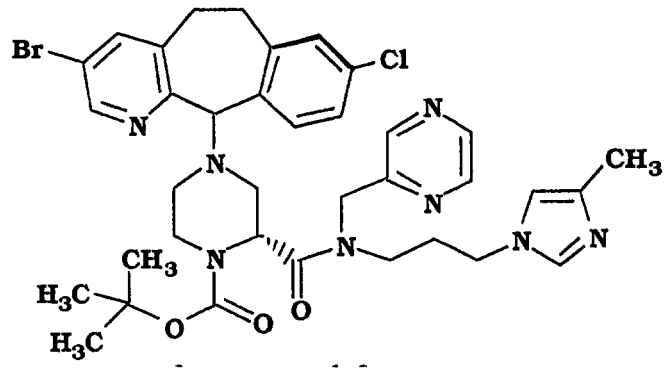
(Example 113);



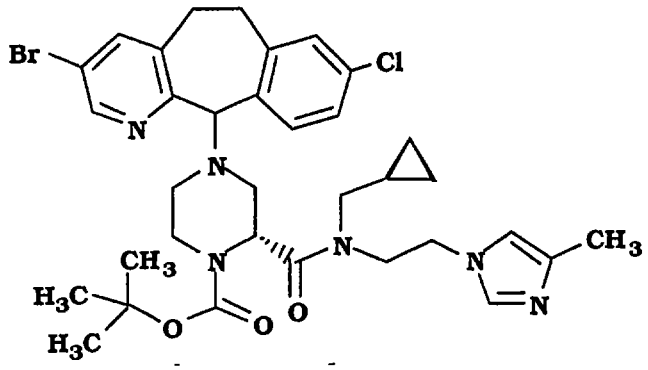
(Compound A Example 114);



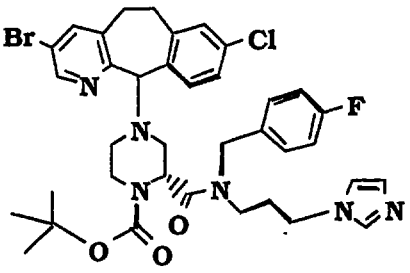
(Compound B Example 114);



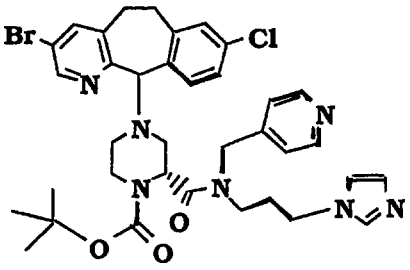
(Compound C Example 114);



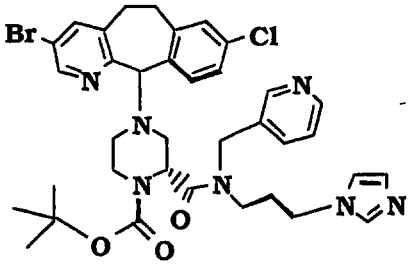
(Compound D Example 114);



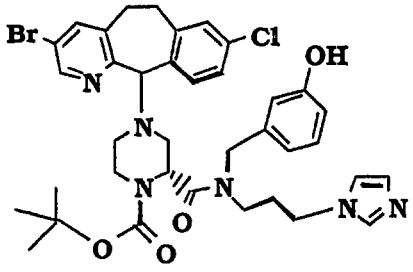
(Example 115);



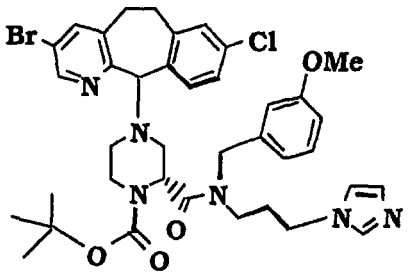
(Example 116);



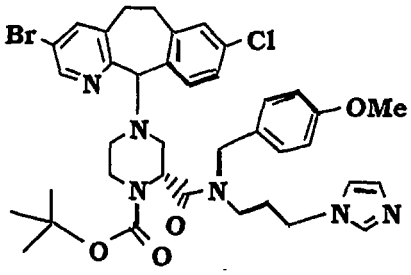
(Example 117);



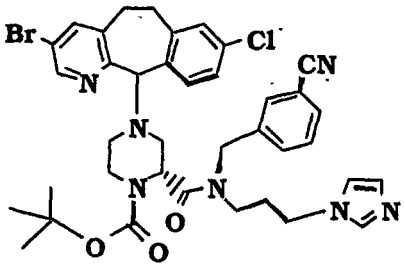
(Example 118);



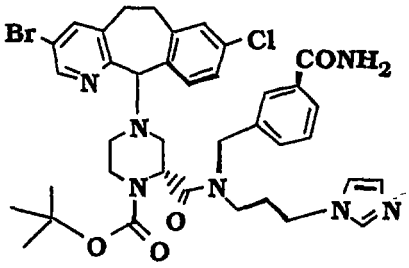
(Example 119);



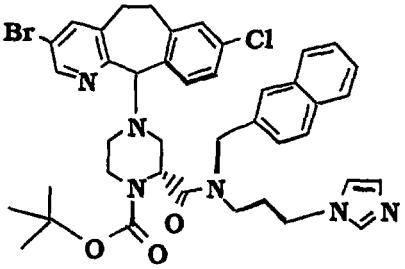
(Example 120);



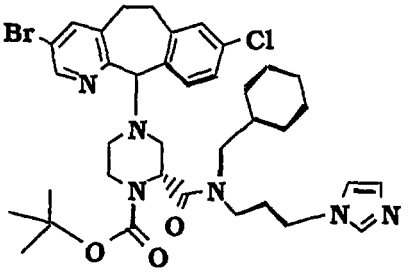
(Example 121);



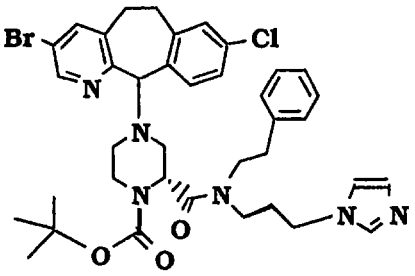
(Example 122);



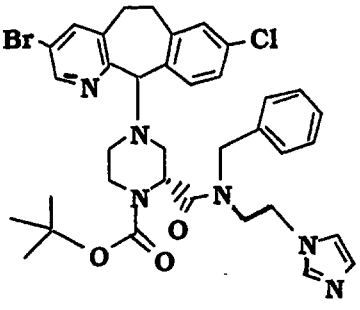
(Example 123);



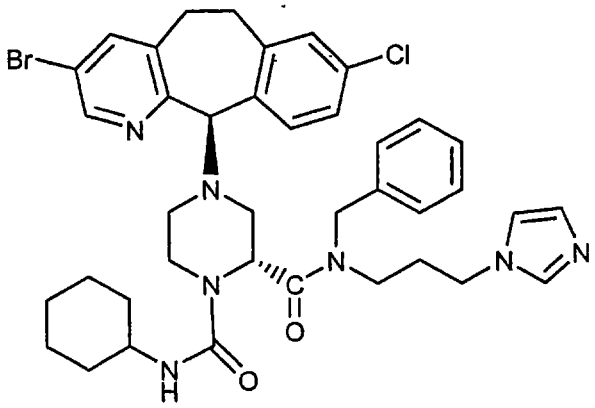
(Example 124);



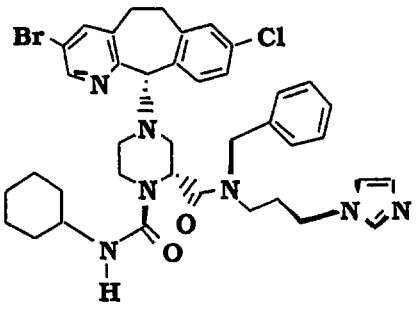
(Example 125);



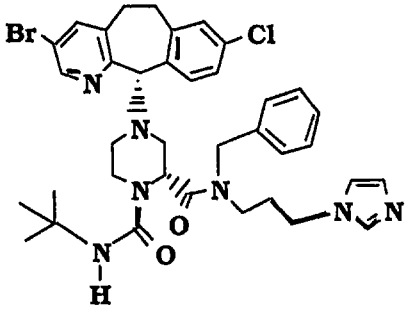
(Example 126);



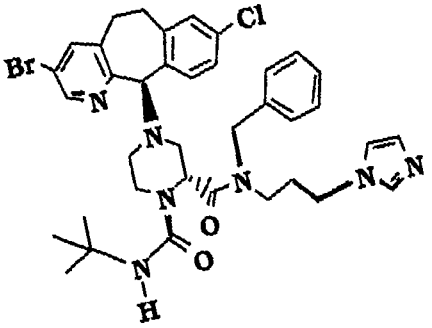
(Example 127);



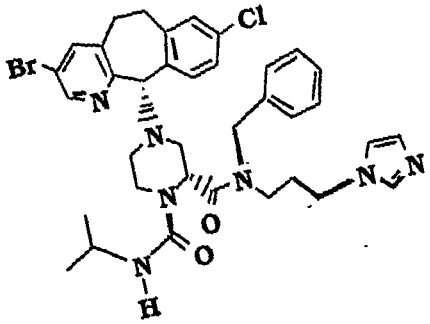
(Example 128);



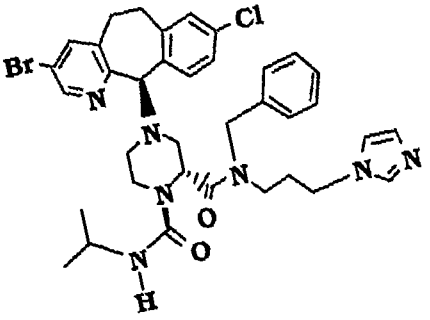
(Example 129);



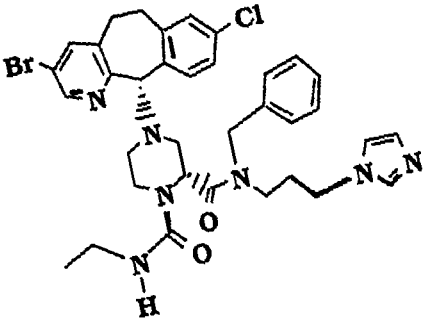
(Example 130);



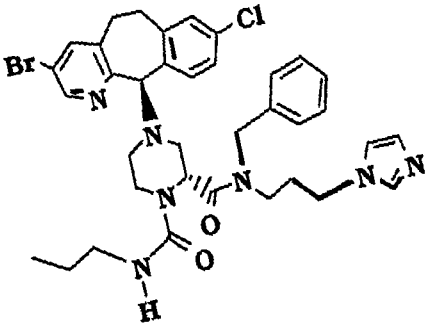
(Example 131);



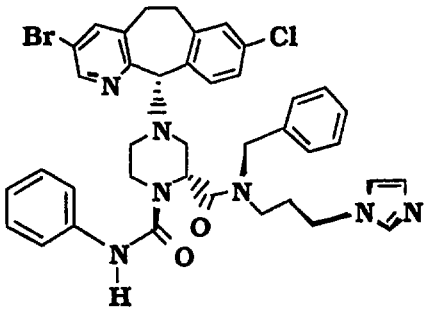
(Example 132);



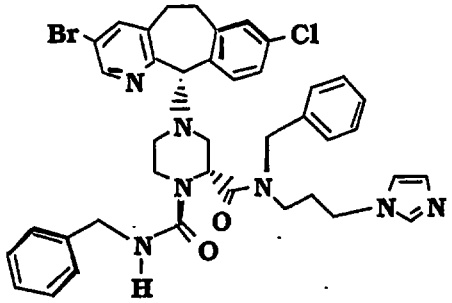
(Example 133);



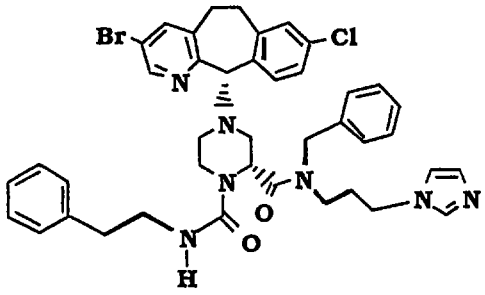
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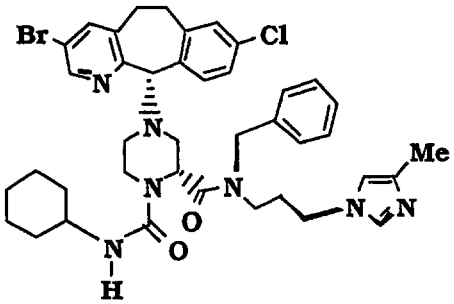
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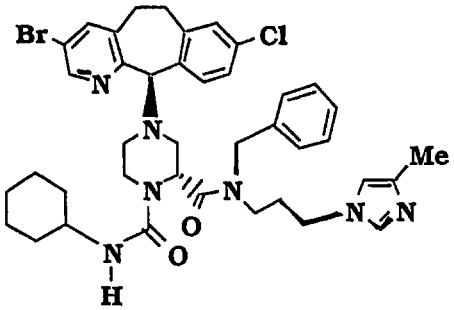
(Example 136);



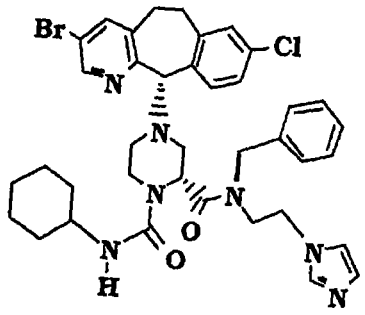
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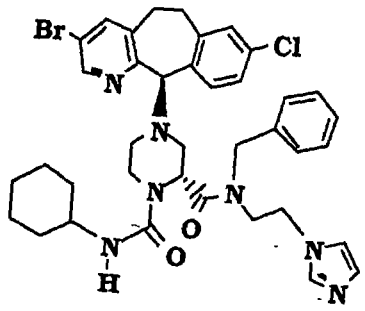
(Example 138);



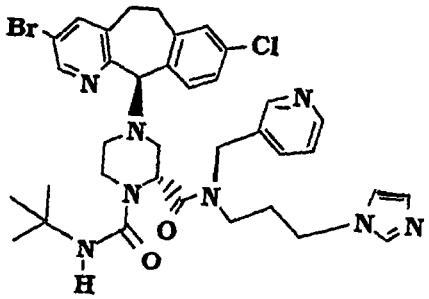
(Example 139);



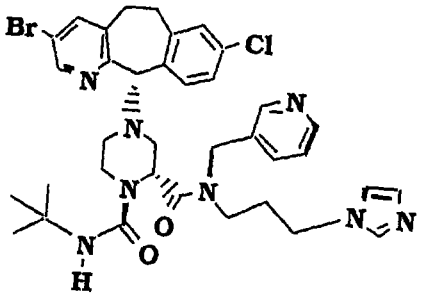
(Example 140);



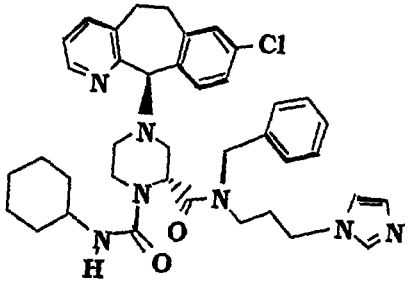
(Example 141);



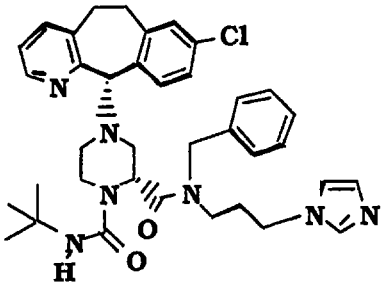
(Example 142);



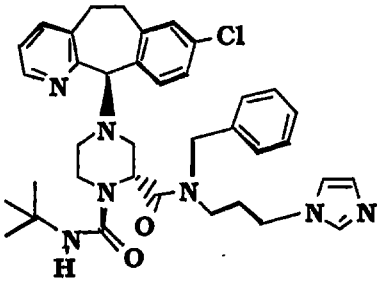
(Example 143);



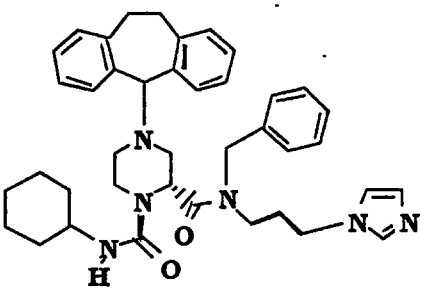
(Example 144);



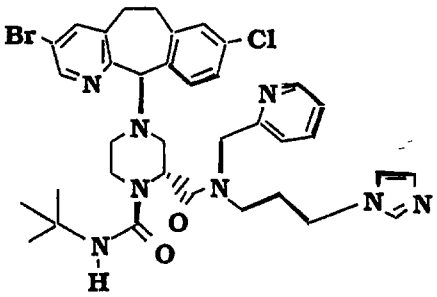
(Example 145);



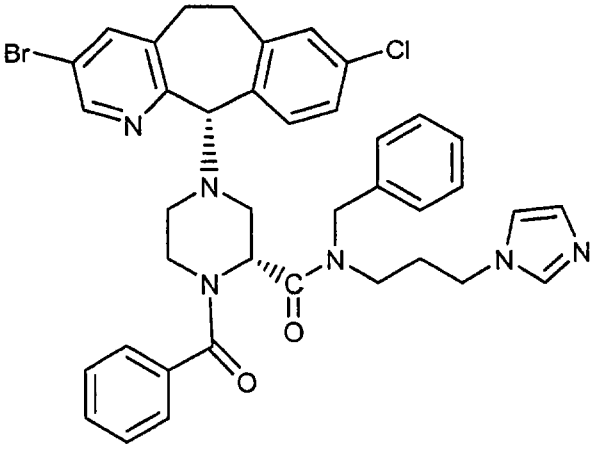
(Example 146);



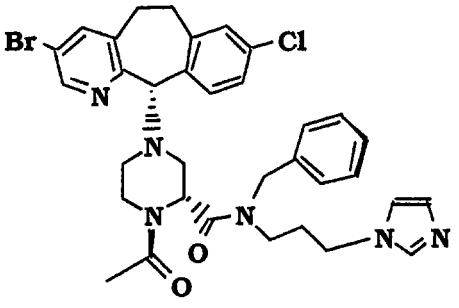
(Example 147);



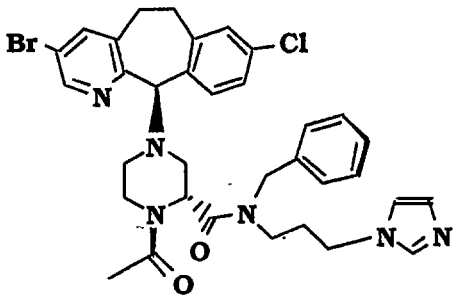
(Example 148);



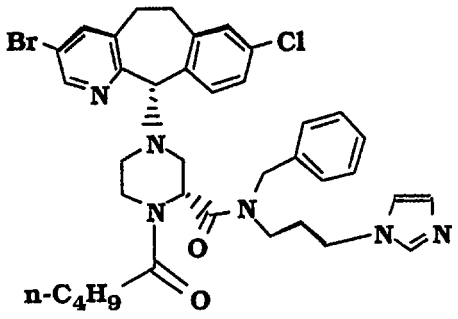
(Example 149);



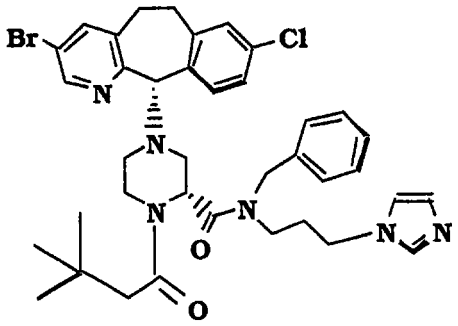
(Example 150);



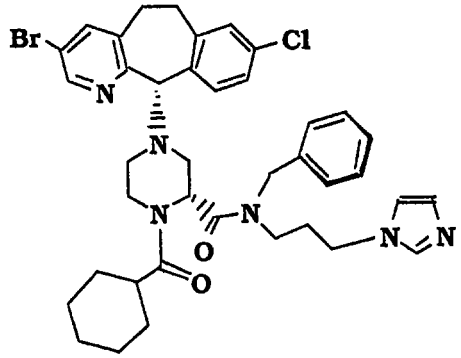
(Example 151);



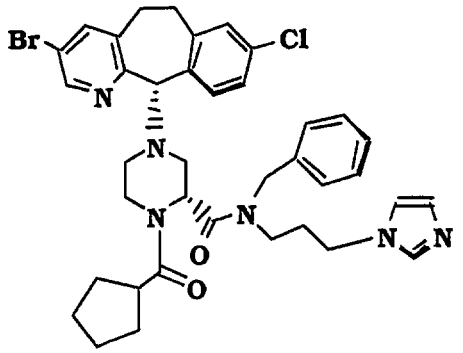
(Example 152);



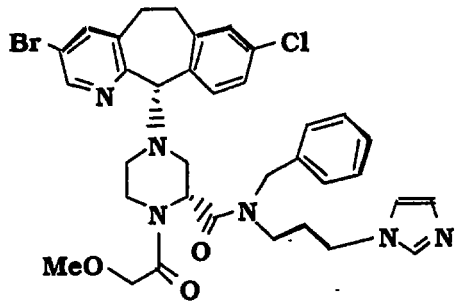
(Example 153);



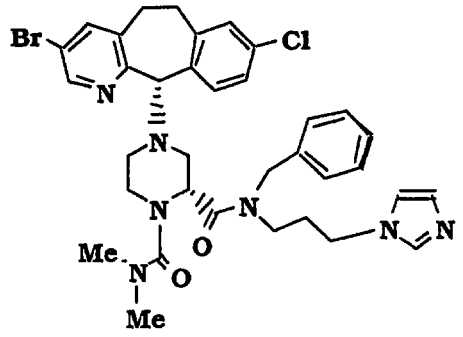
(Example 154);



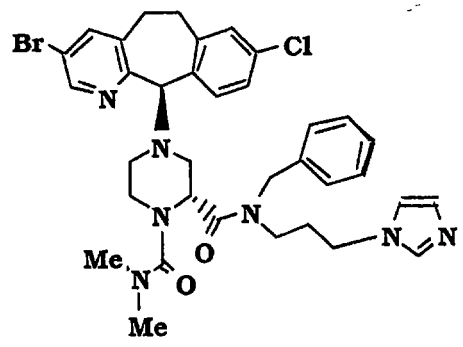
(Example 155);



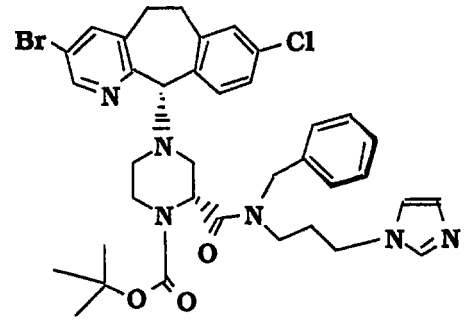
(Example 156);



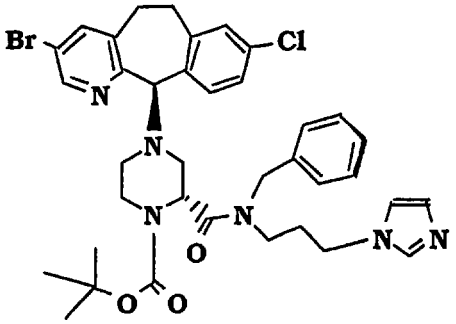
(Example 157);



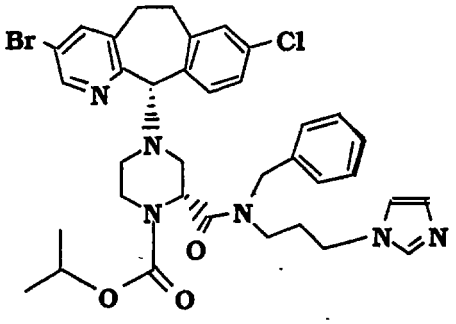
(Example 158);



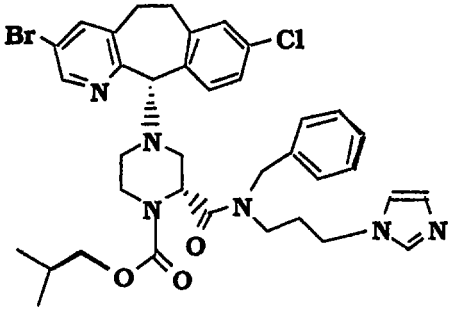
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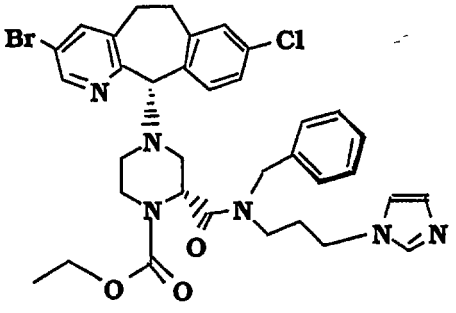
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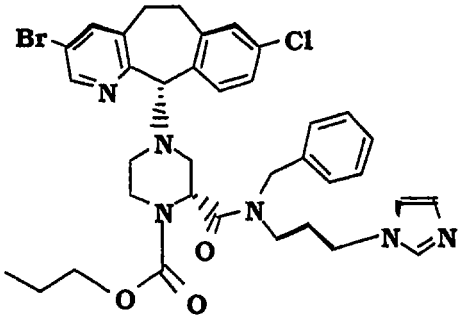
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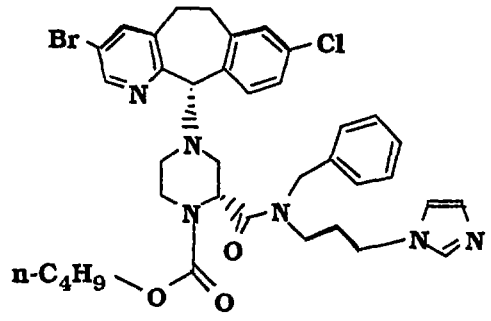
(Example 162);



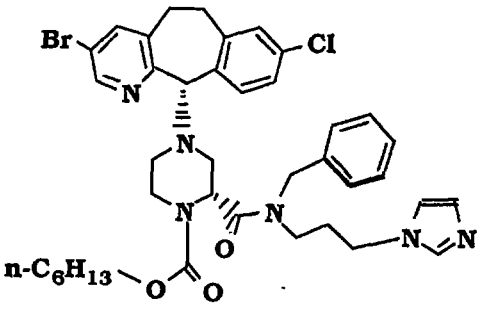
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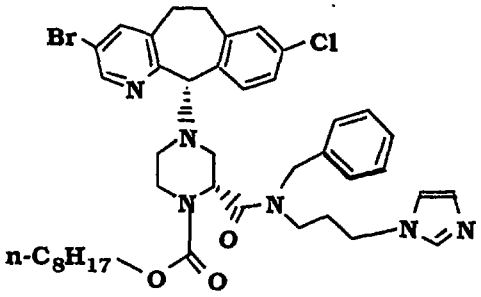
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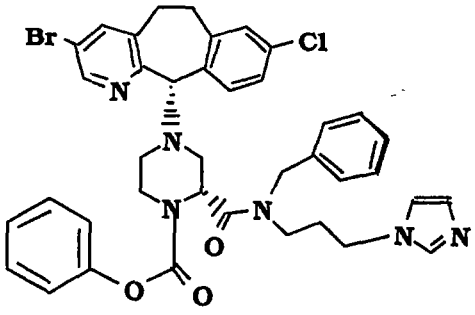
(Example 165);



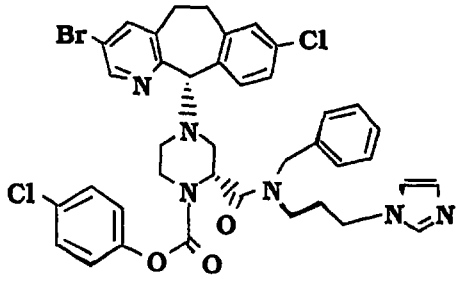
(Example 166);



(Example 167);

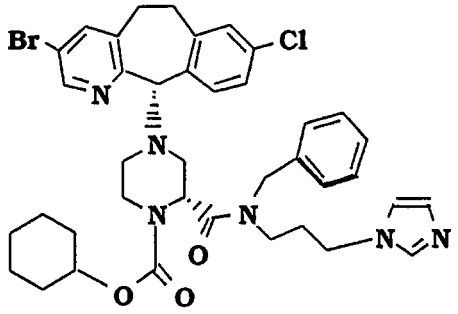


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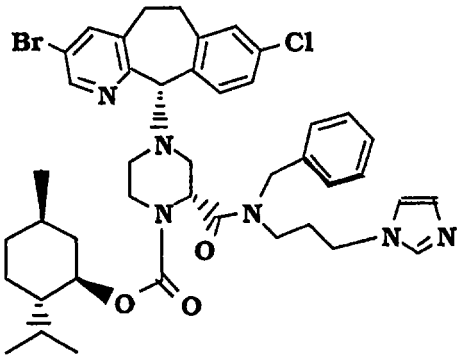


(Example 169);

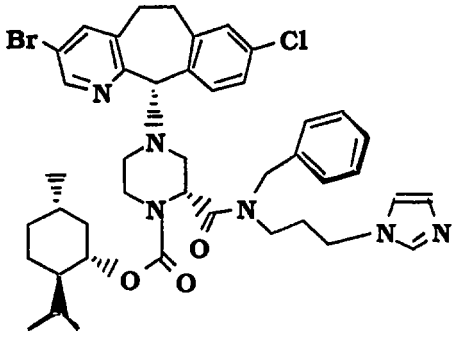
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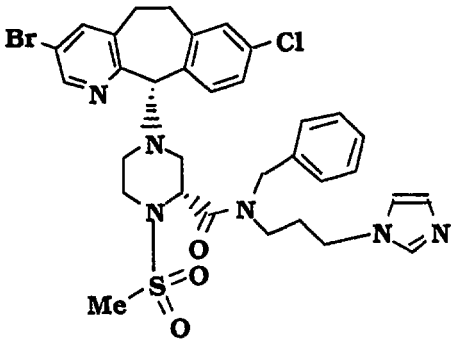
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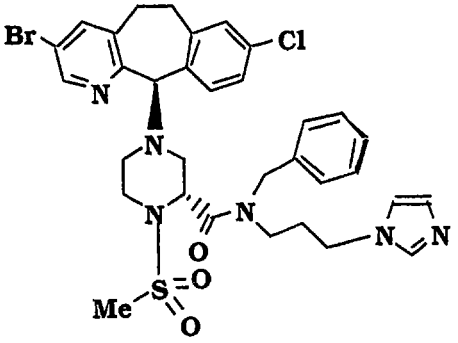
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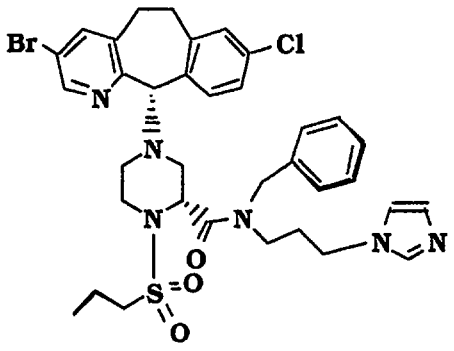
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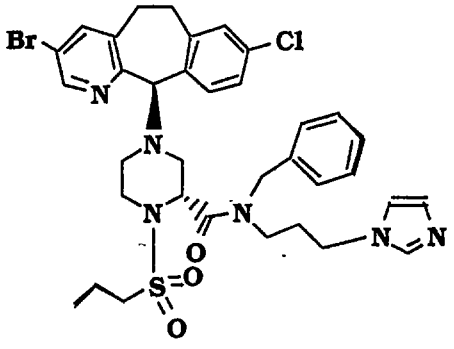
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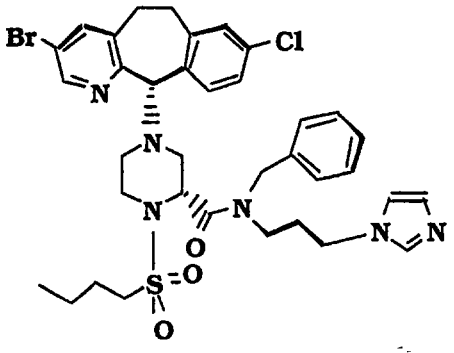
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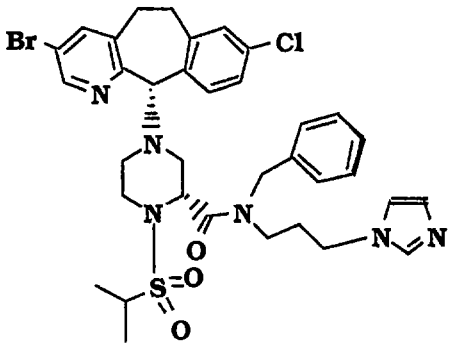
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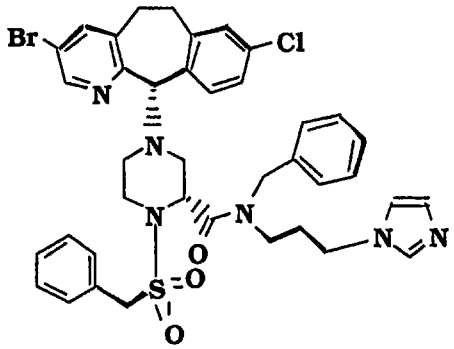
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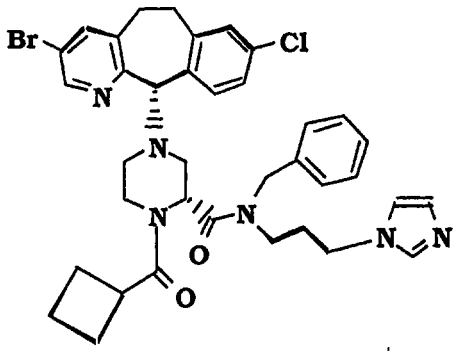
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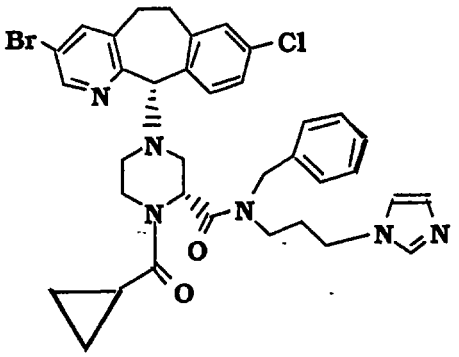
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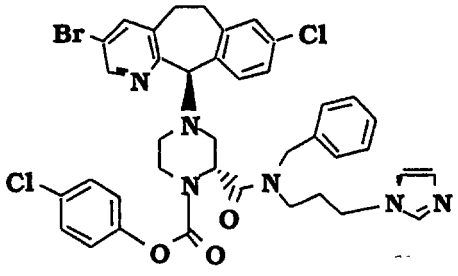
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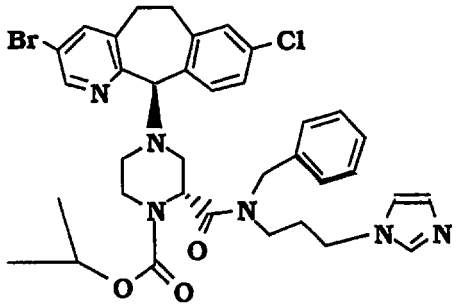
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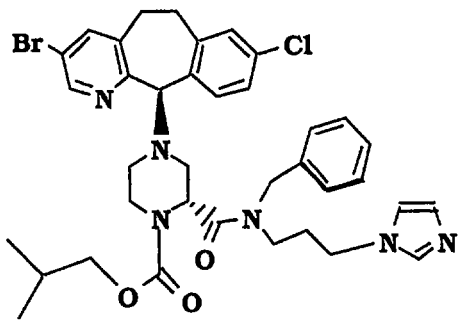
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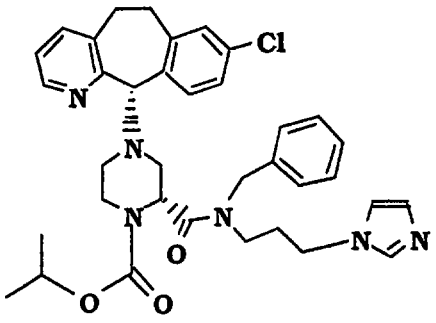
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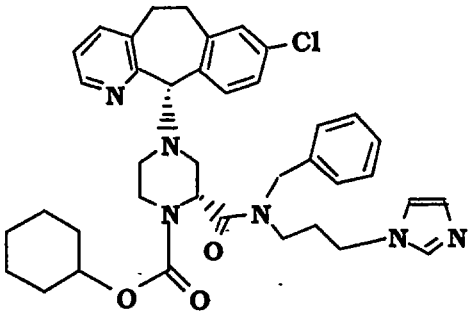
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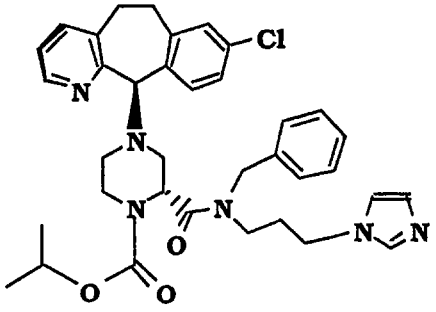
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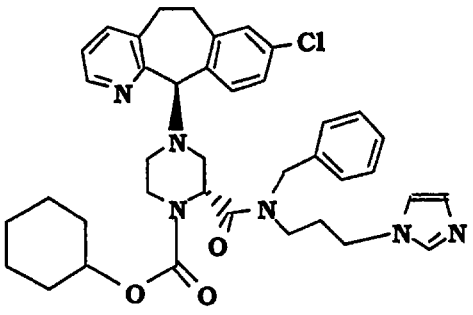
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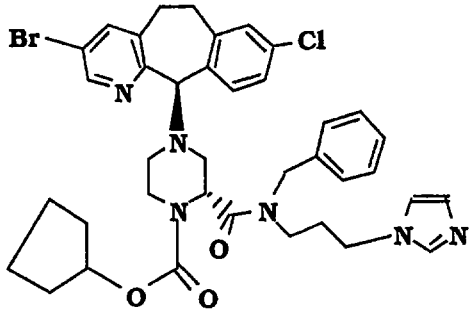
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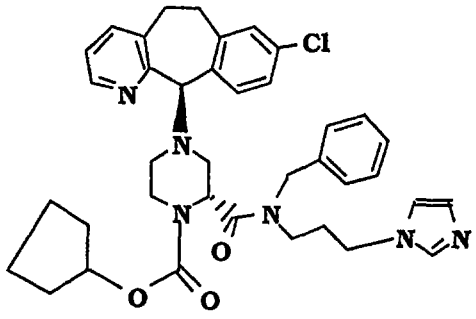
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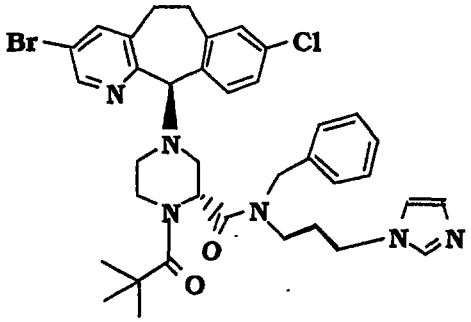
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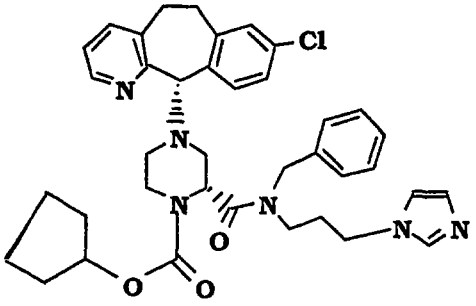
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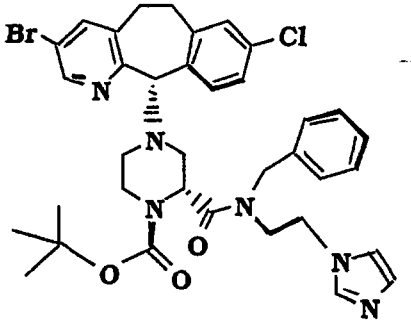
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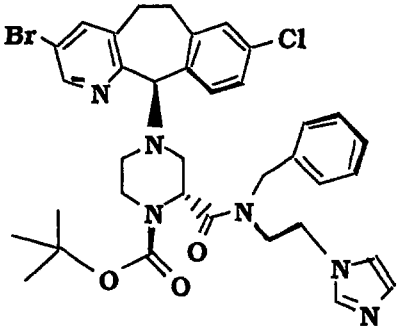
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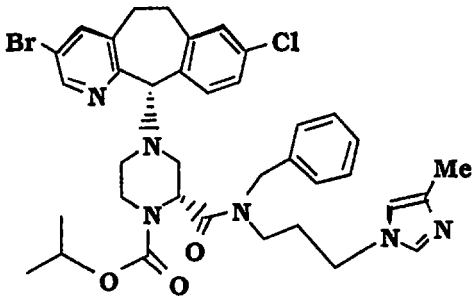
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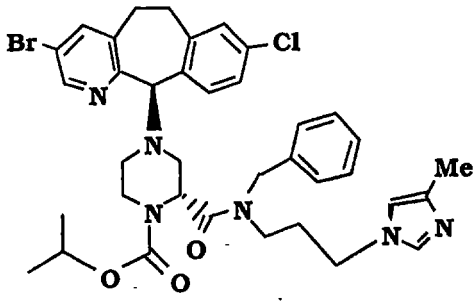
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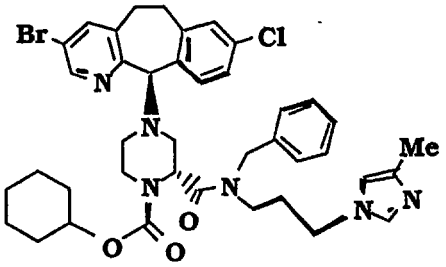
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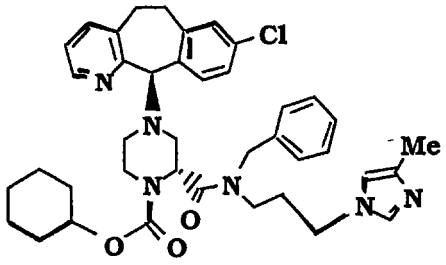
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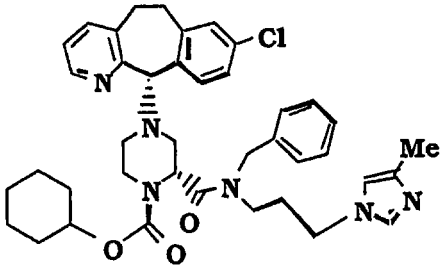
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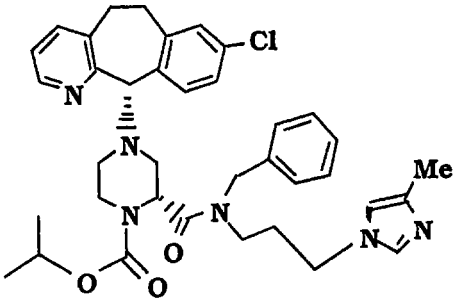
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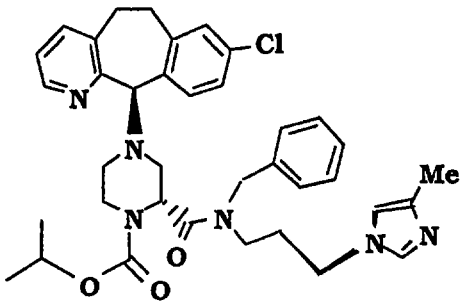
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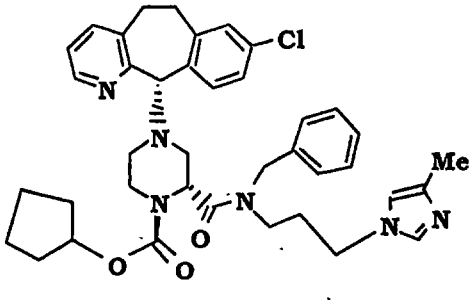
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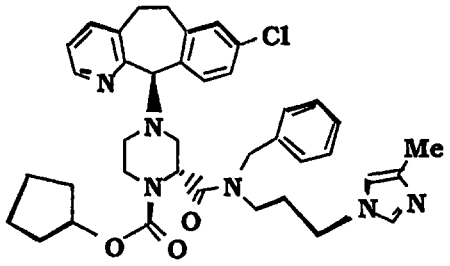
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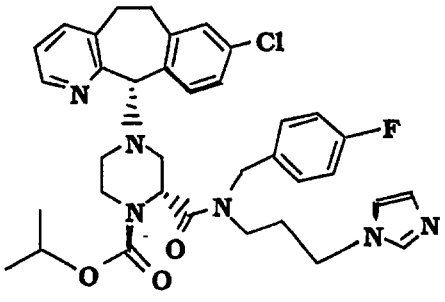
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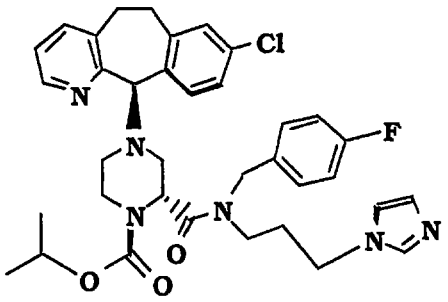
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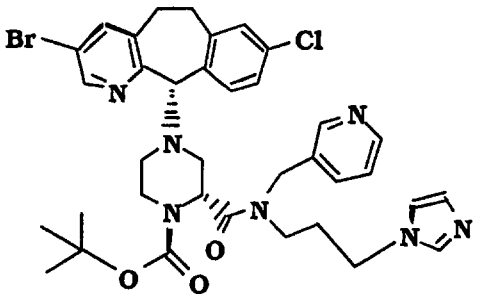
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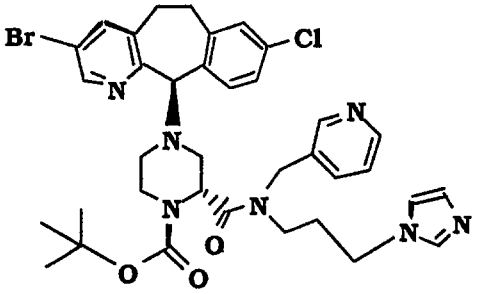
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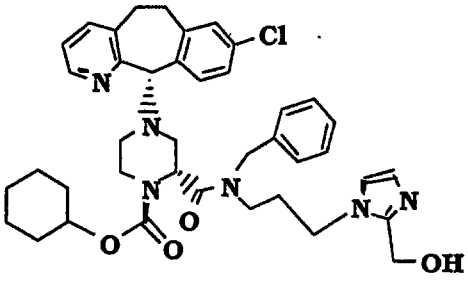
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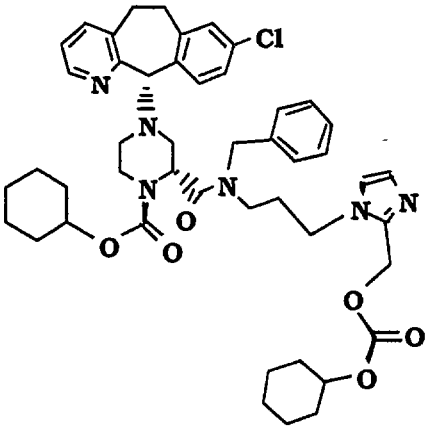
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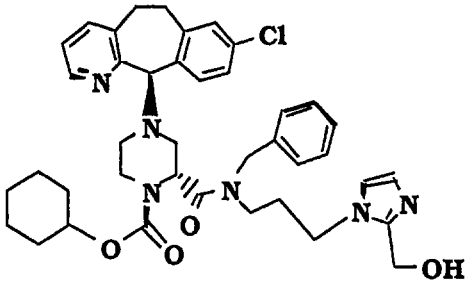
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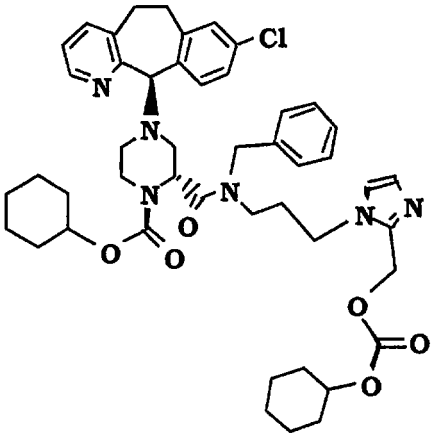
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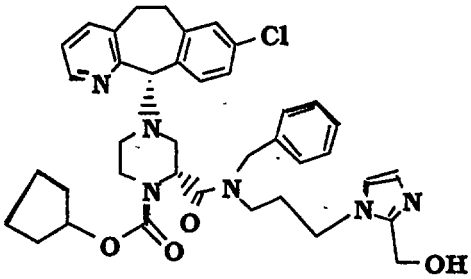
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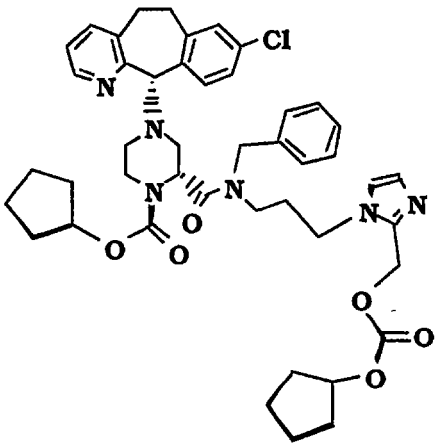
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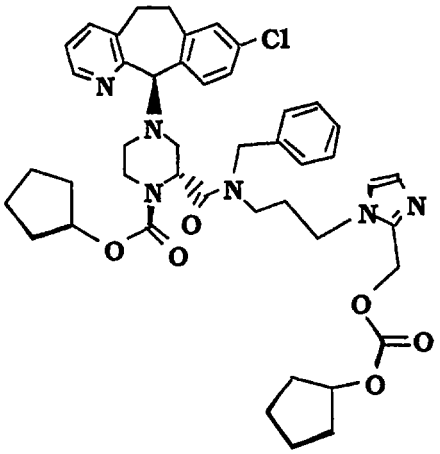
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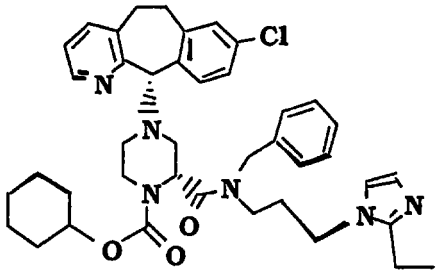
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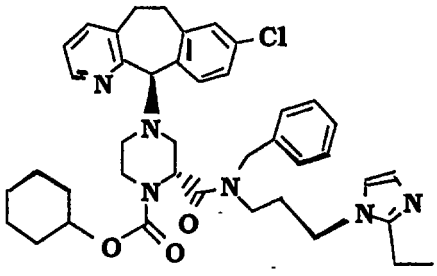
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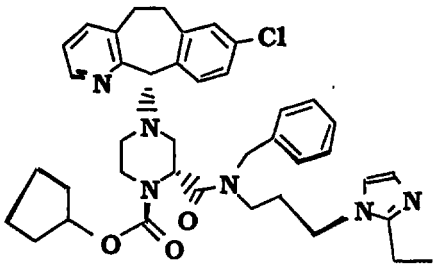
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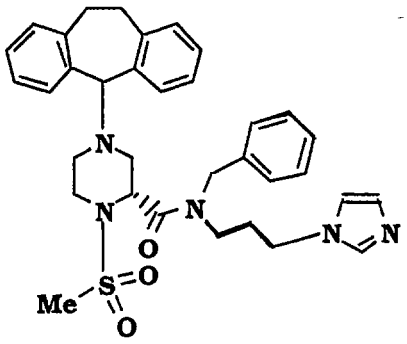
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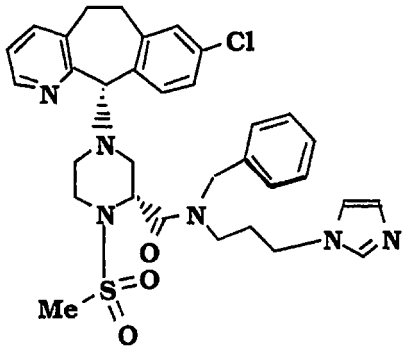
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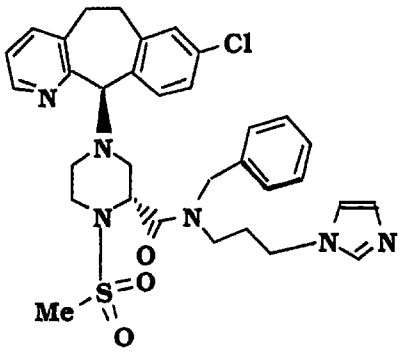
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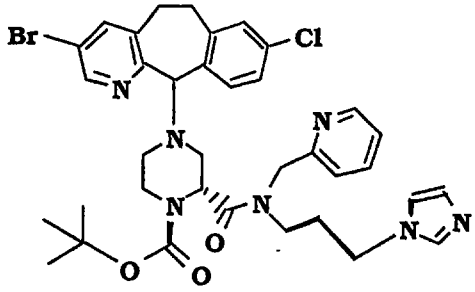
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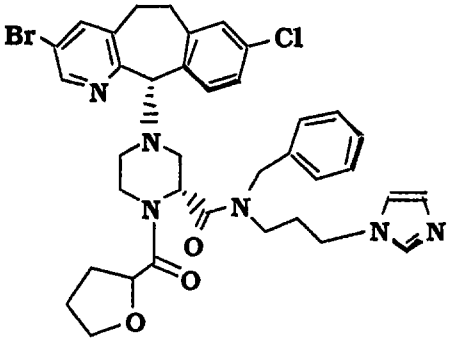
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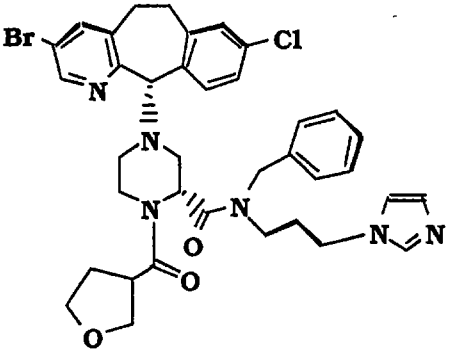
(Example 216);



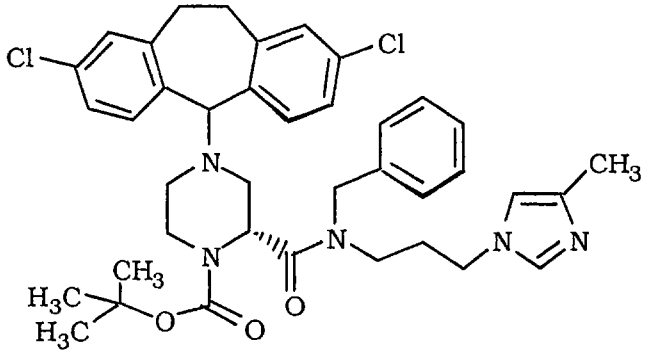
(Example 217);



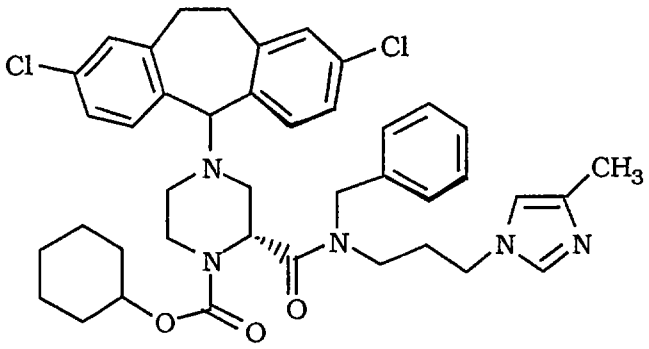
(Example 218);



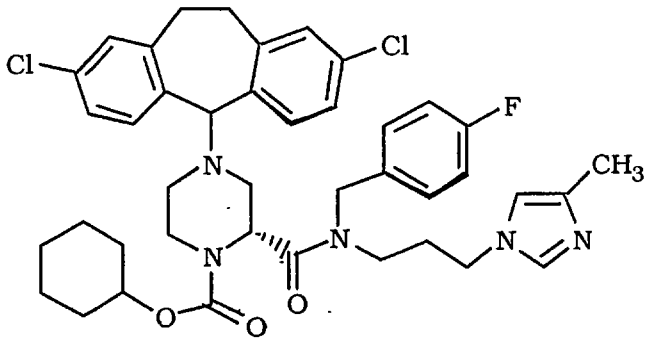
(Example 219);



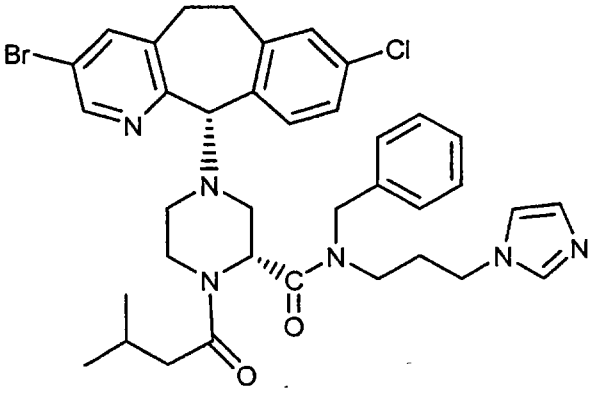
(Example 220);



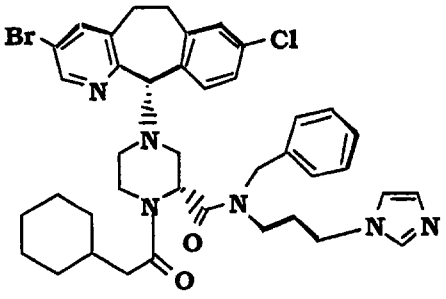
(Example 220);



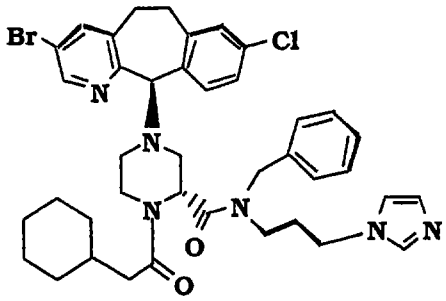
(Example 220A);



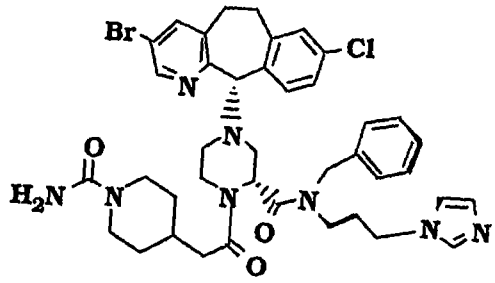
(Example 221);



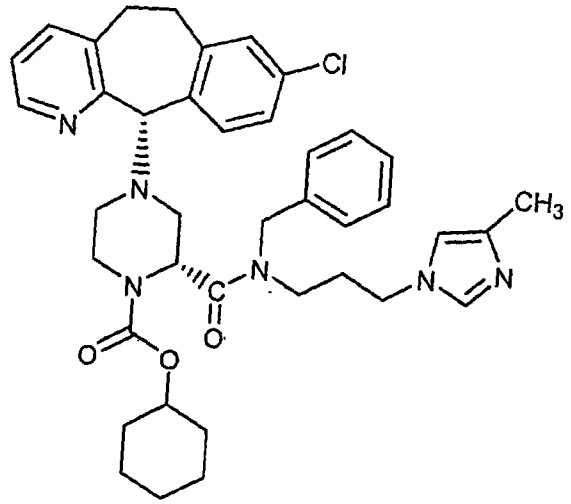
(Example 222);



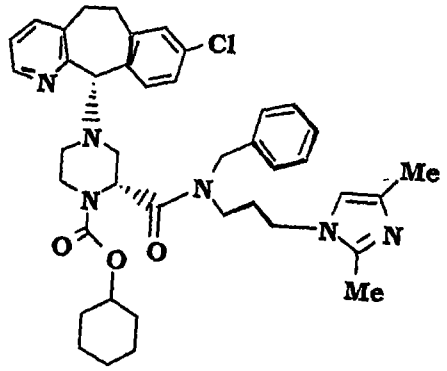
(Example 223);



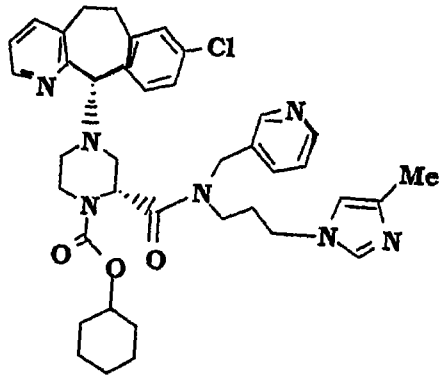
(Example 224);



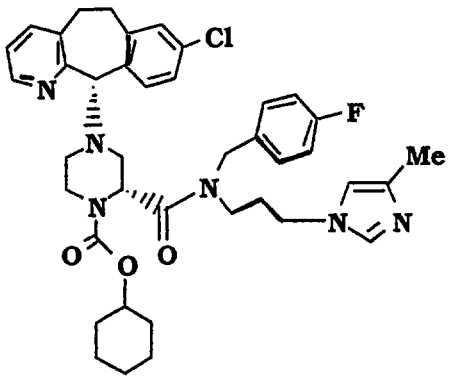
(Example 225);



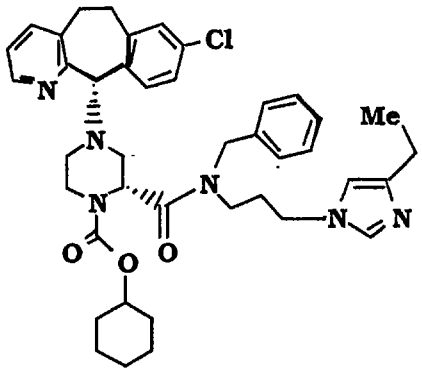
(Example 226);



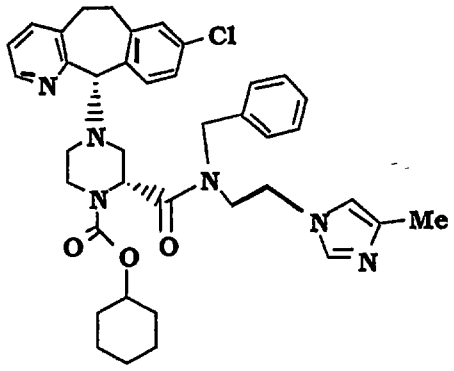
(Example 227);



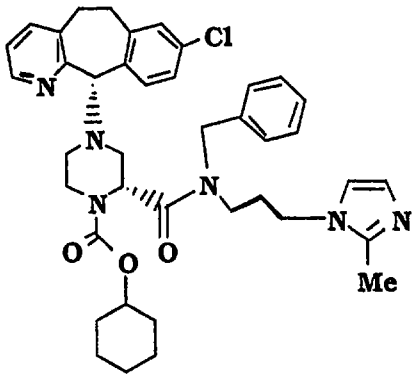
(Example 228);



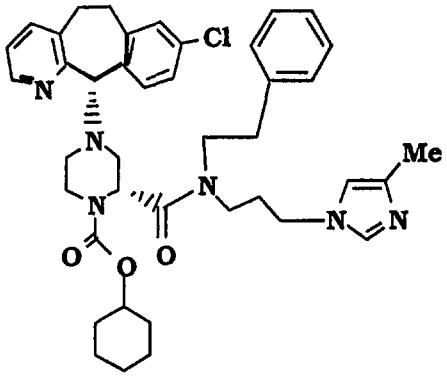
(Example 229);



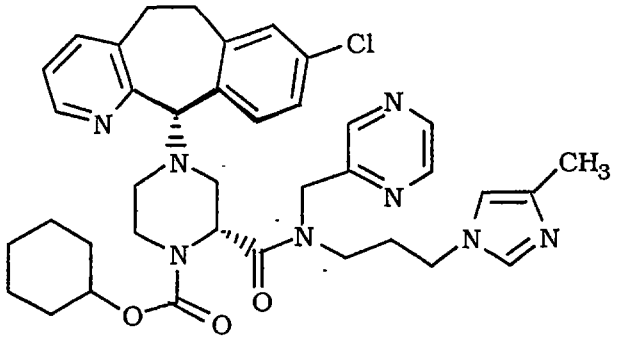
(Example 230);



(Example 231);

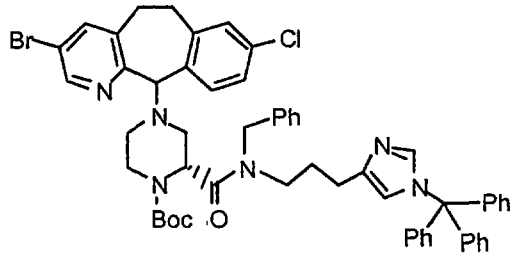


(Example 232);

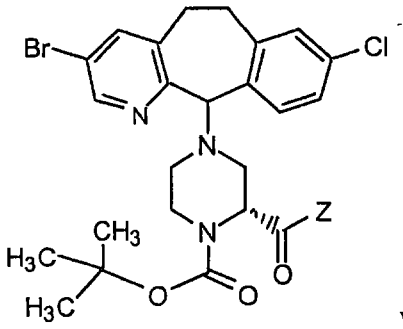


Example 234B

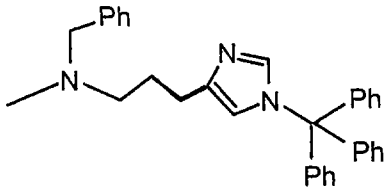
;



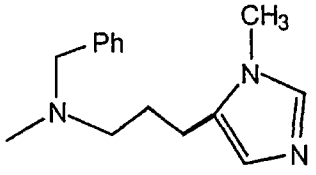
(Example 235);



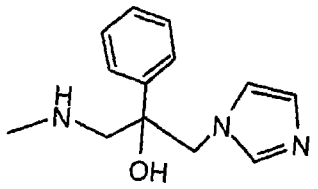
wherein Z is selected from the group consisting of:



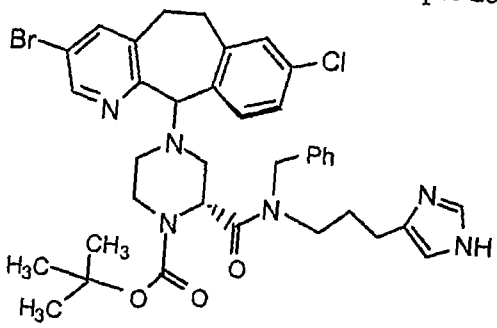
(Example 236);



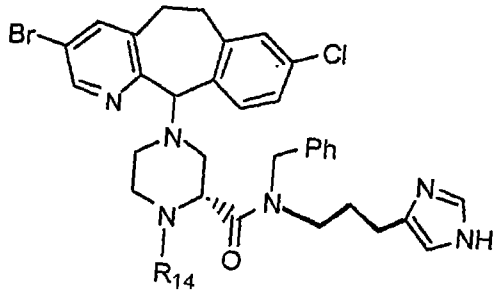
(Example 237); and



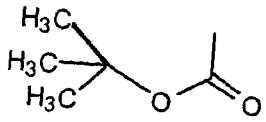
(Example 238);



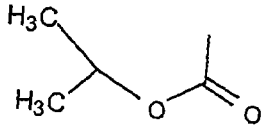
(Example 239);



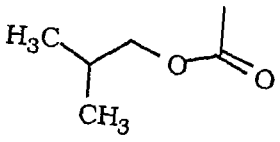
wherein R^{14} is selected from the group consisting of:



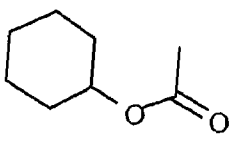
(R, S) (Example 240);



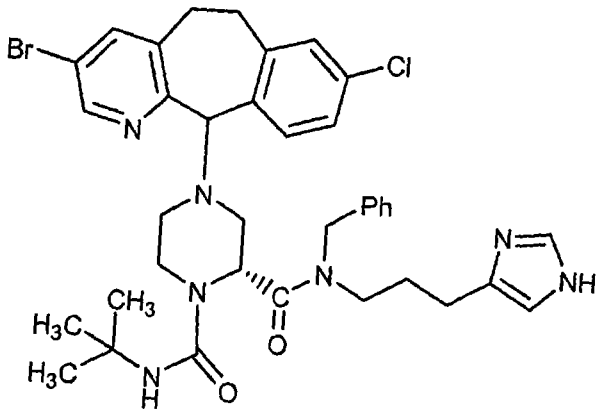
(R, S) (Example 241);



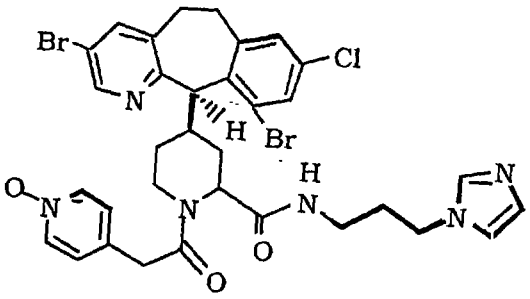
(R, S) (Example 242); and



(R, S) (Example 243);

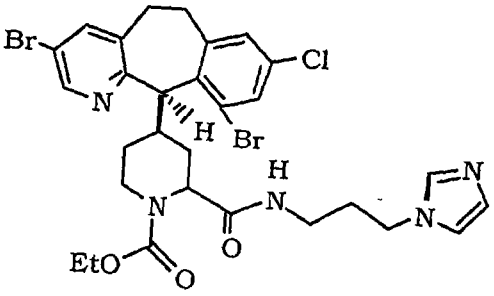


(Example 244);



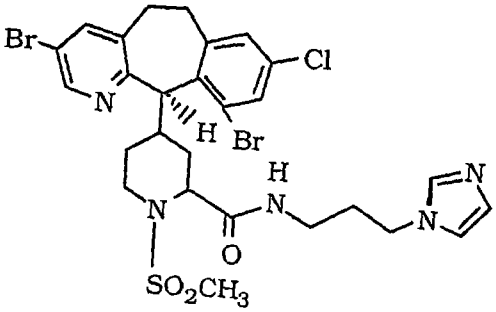
(Example 247)

;



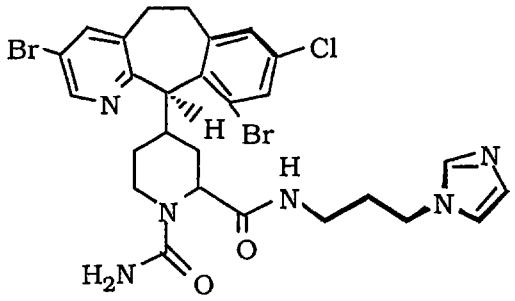
(Example 248)

;



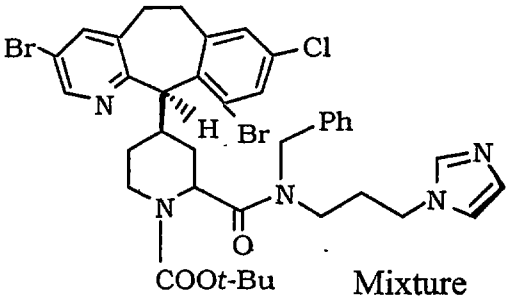
(Example 249)

;



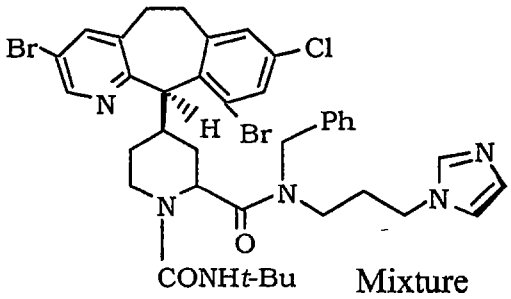
(Example 250)

;



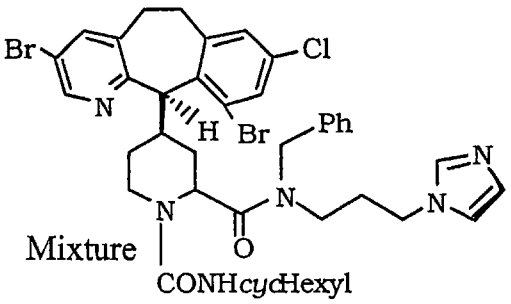
(Example 251)

;



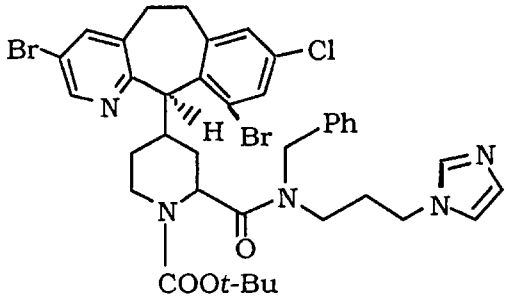
(Example 252)

;



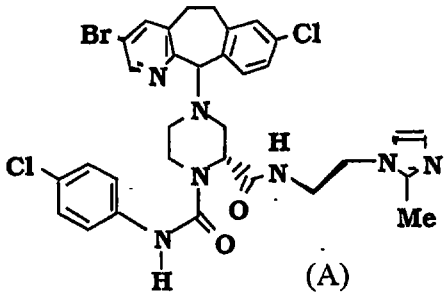
(Example 253)

;

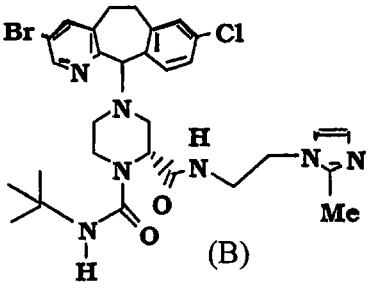


(Example 254)

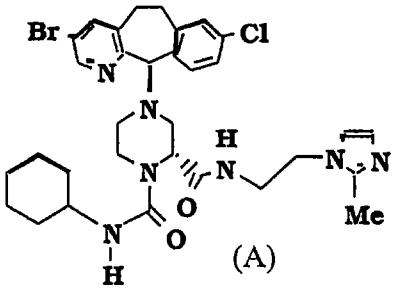
;



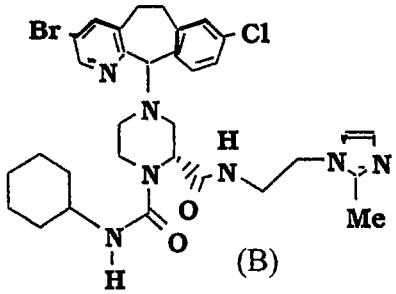
(A) (Example 255);



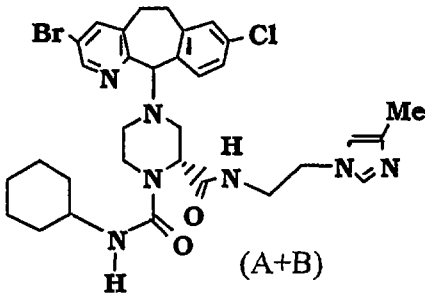
(B) (Example 256);



(A) (Example 257);

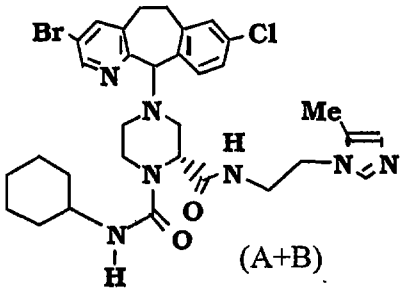


(B) (Example 258);



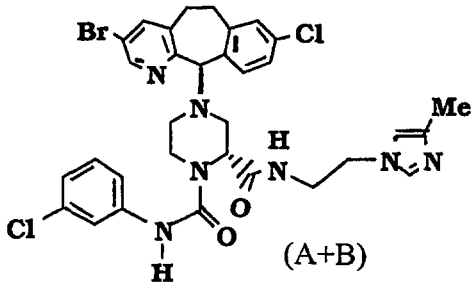
(A+B)

(Example 259);



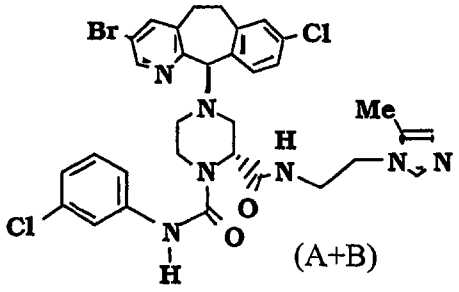
(A+B)

(Example 259);



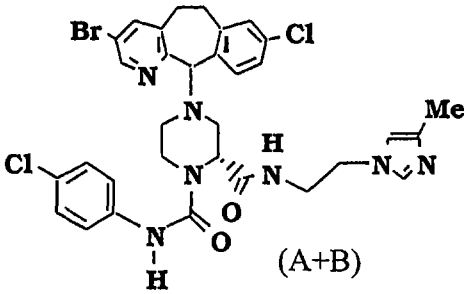
(A+B)

(Example 260);



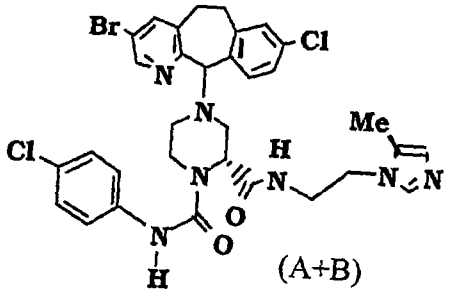
(A+B)

(Example 260);



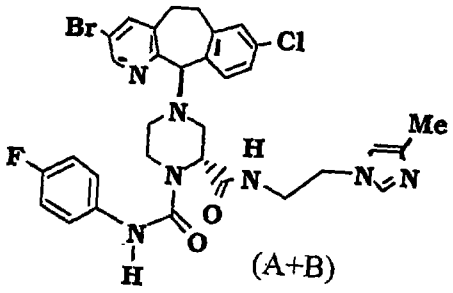
(A+B)

(Example 261);



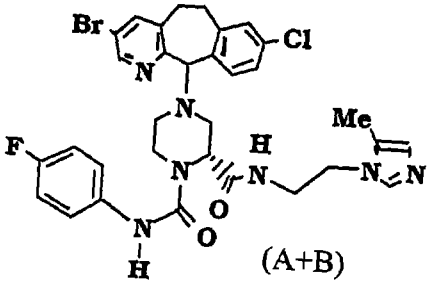
(A+B)

(Example 261);



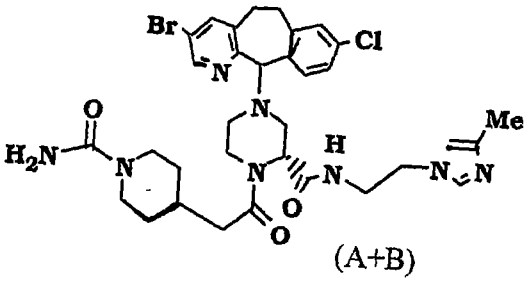
(A+B)

(Example 262);



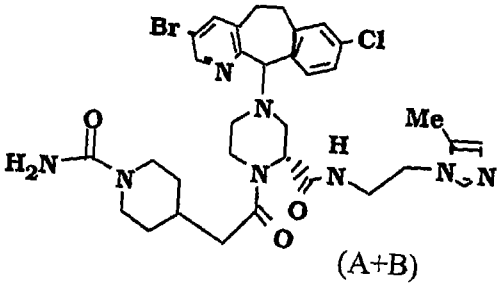
(A+B)

(Example 262);



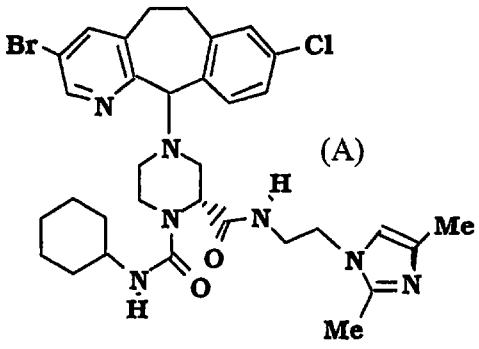
(A+B)

(Example 263);



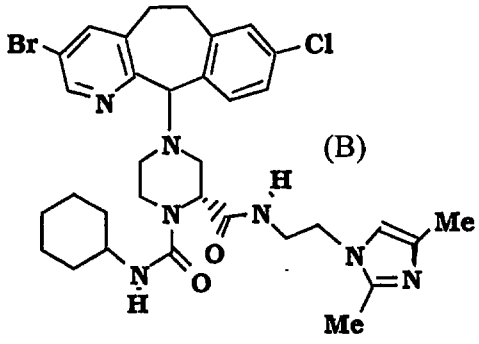
(A+B)

(Example 263);



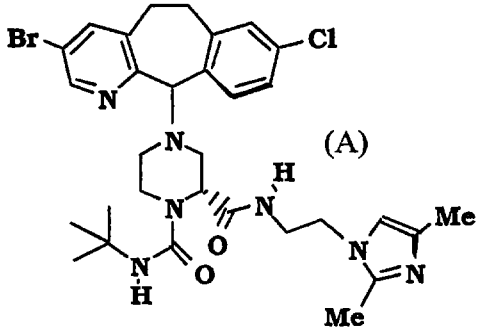
(A)

(Example 264);



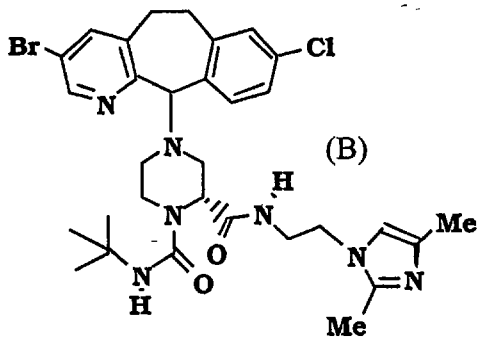
(B)

(Example 265);



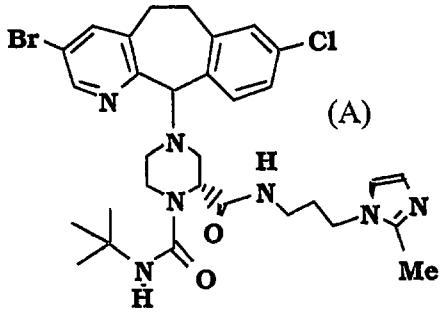
(A)

(Example 266);



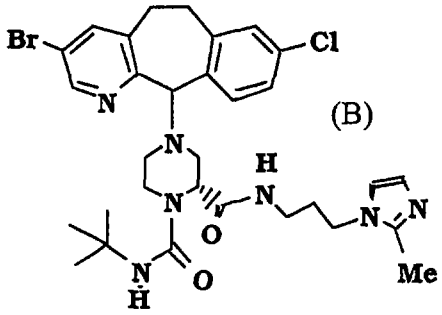
(B)

(Example 267);



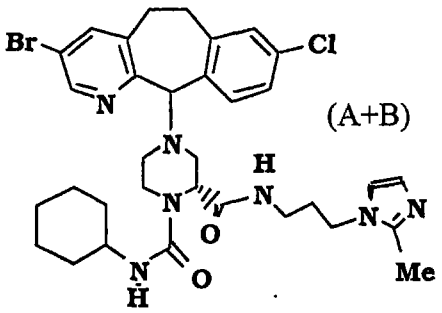
(A)

(Example 268);



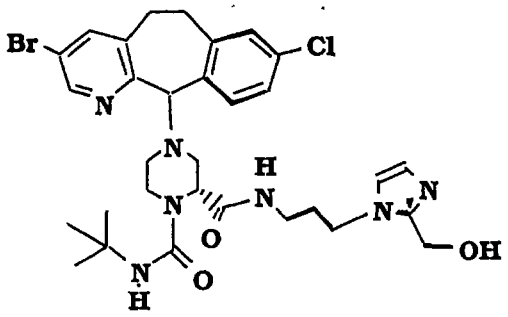
(B)

(Example 269);

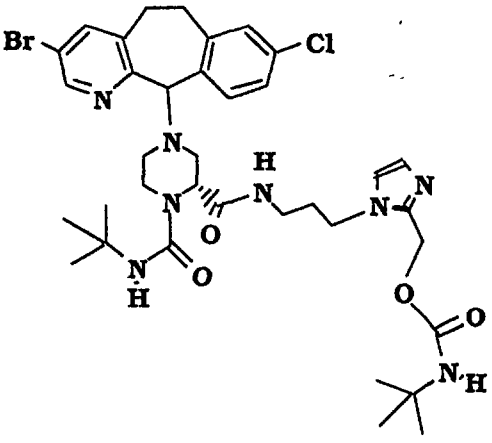


(A+B)

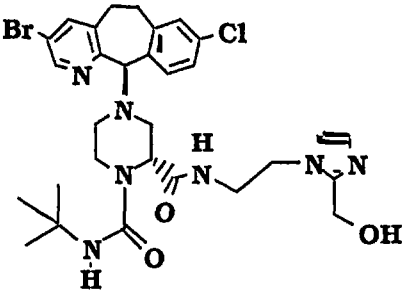
(Example 270);



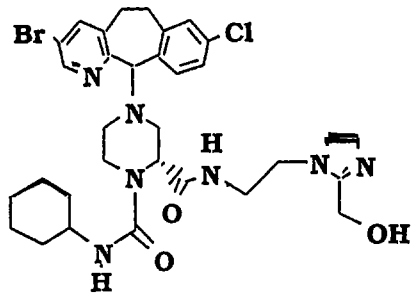
(Example 271);



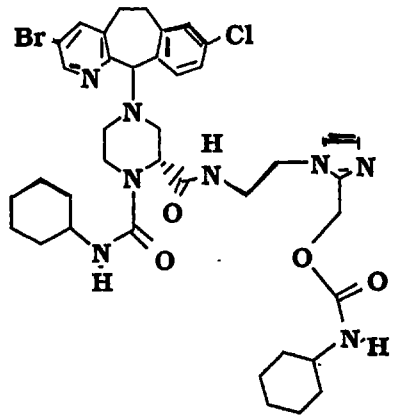
(Example 272);



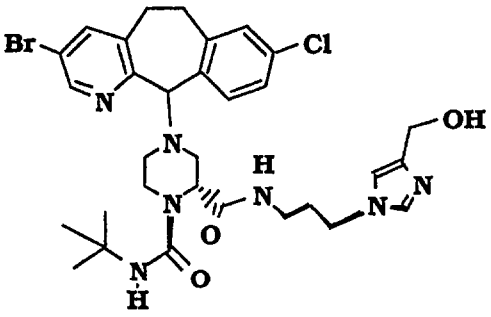
(Example 273);



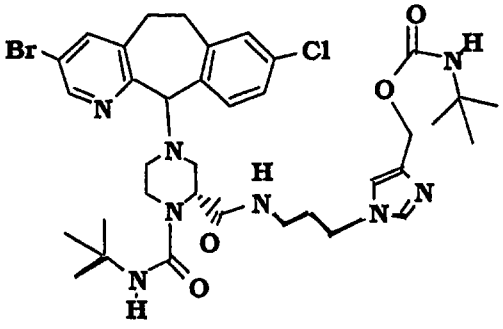
(Example 274);



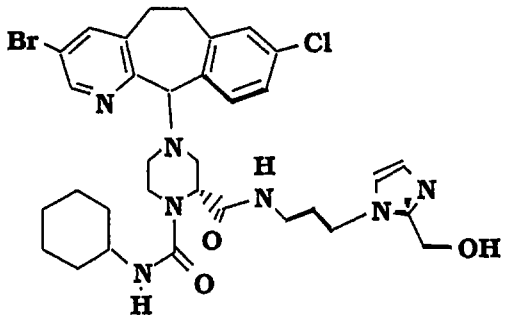
(Example 275);



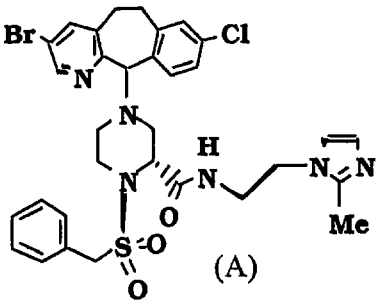
(Example 276);



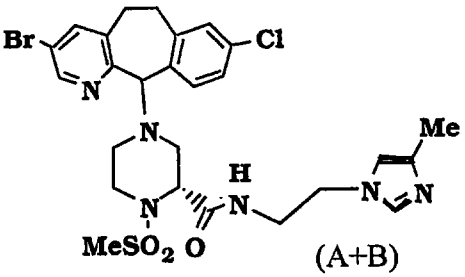
(Example 277);



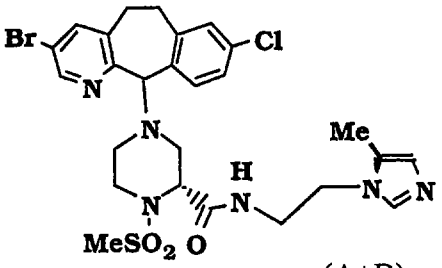
(Example 278);



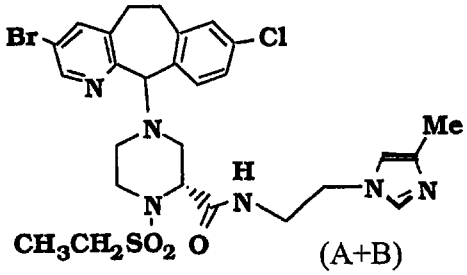
(A) (Example 279);



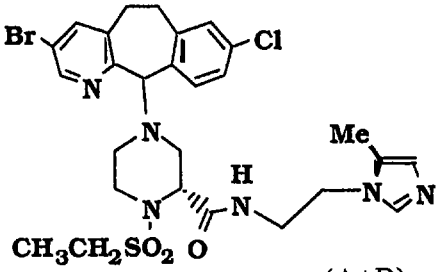
(A+B) (Example 280);



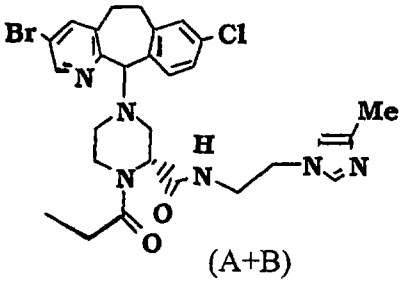
(A+B) (Example 280);



(A+B) (Example 281);

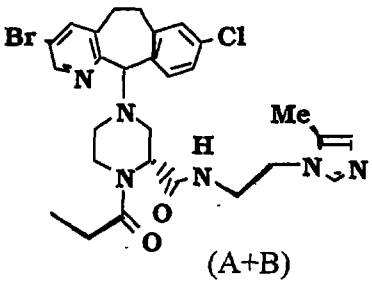


(A+B) (Example 281);



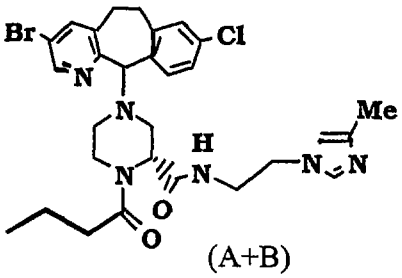
(A+B)

(Example 282);



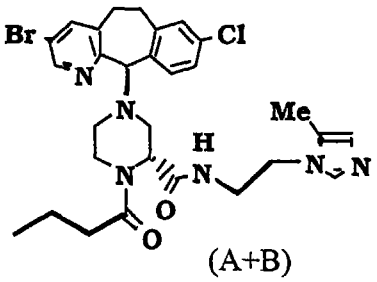
(A+B)

(Example 282);



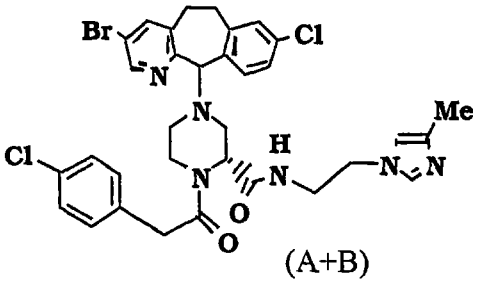
(A+B)

(Example 283);



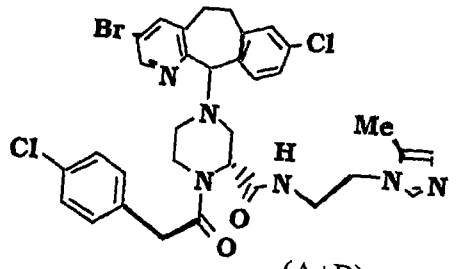
(A+B)

(Example 283);



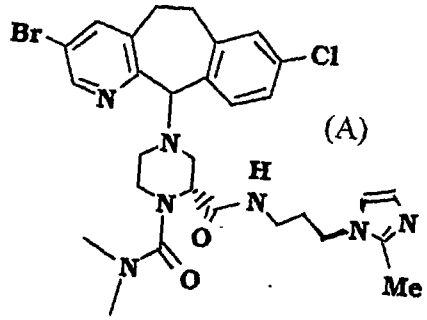
(A+B)

(Example 284);



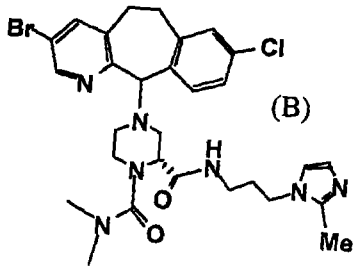
(A+B)

(Example 284);



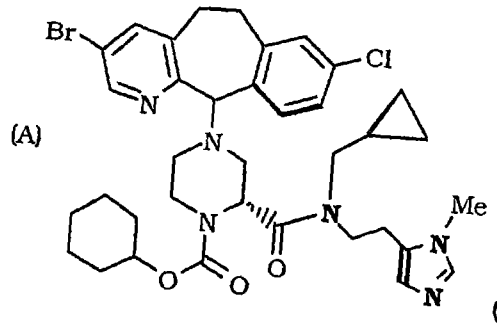
(A)

(Example 285);



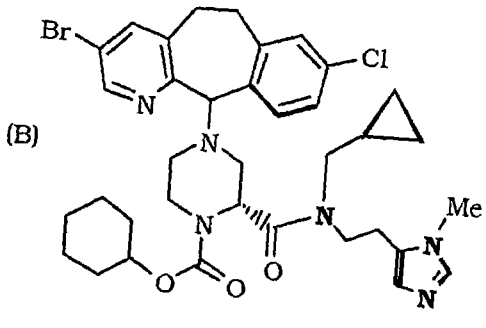
(B)

(Example 286);



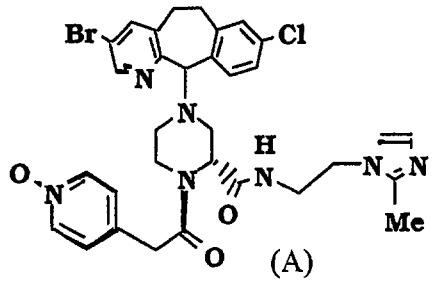
(A)

(Example 286A);

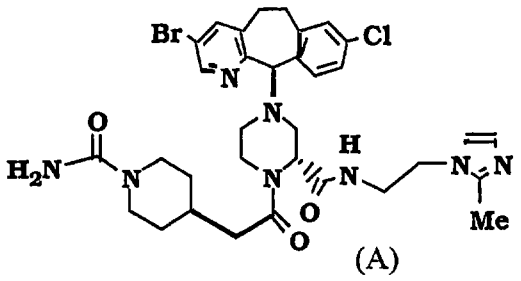


(B)

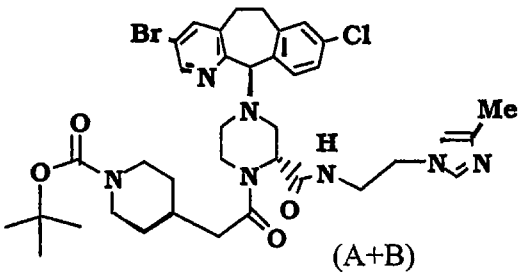
(Example 286B);



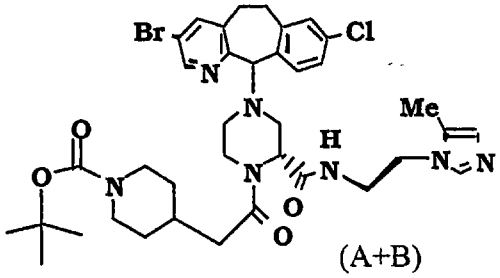
(A) (Example 287);



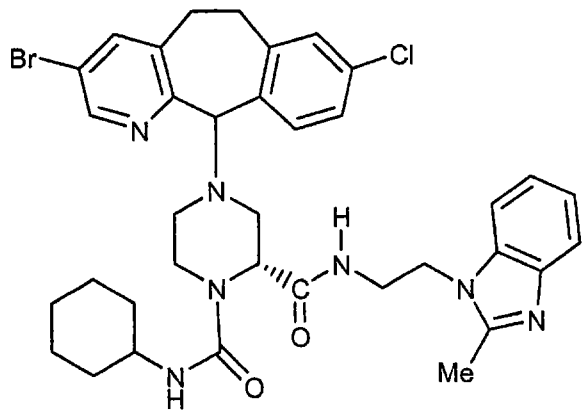
(A) (Example 288);



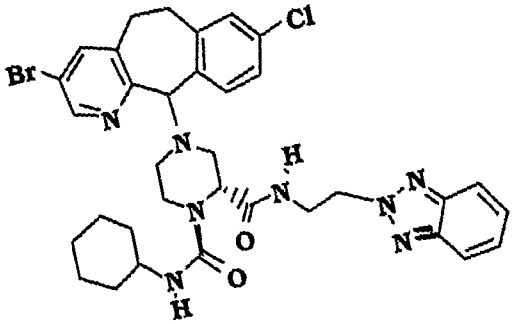
(A+B) (Example 289);



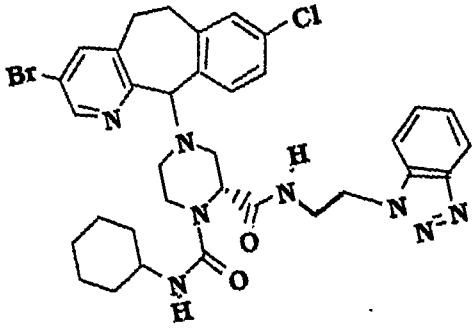
(A+B) (Example 289);



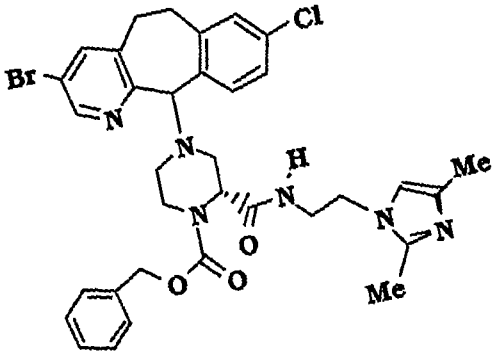
(Example 290);



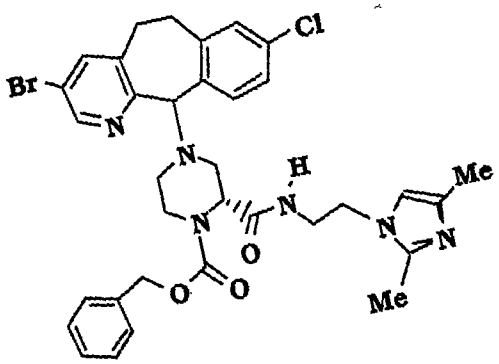
(Example 291);



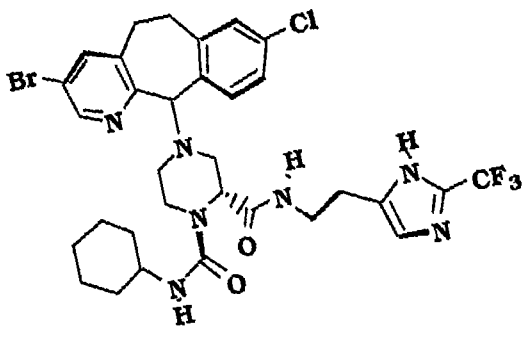
(Example 292);



Isomer A (Example 293);

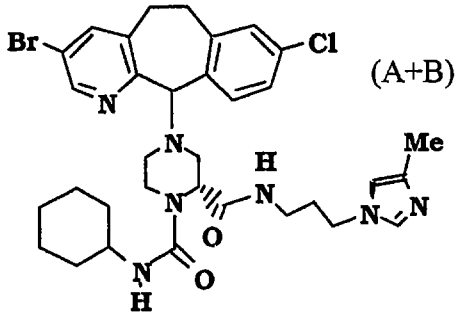


Isomer B (Example 293);



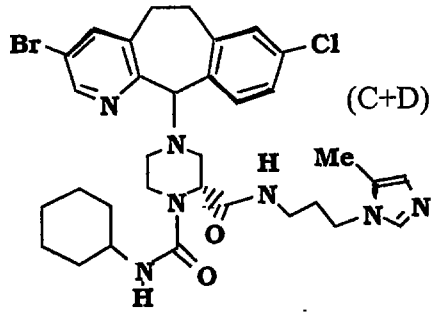
(Example 294);

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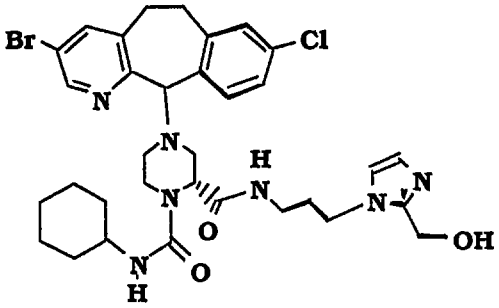
(A+B)

(Example 295);

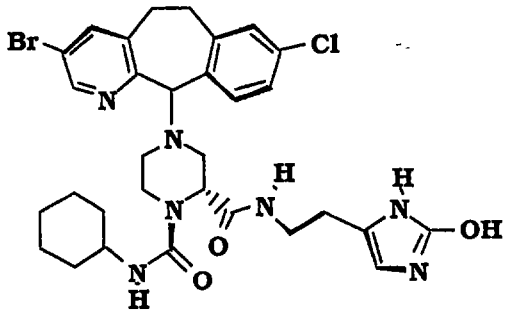


(C+D)

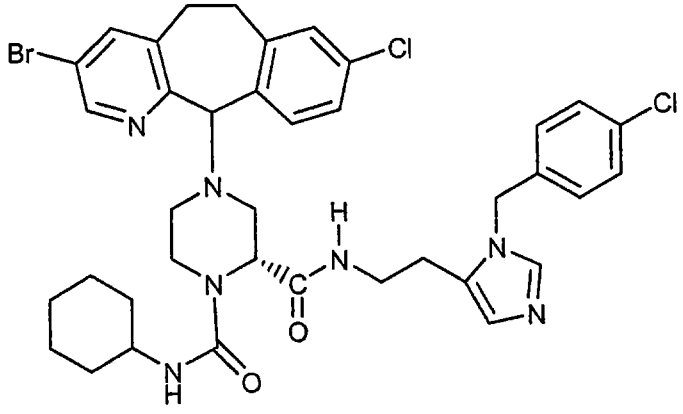
(Example 295);



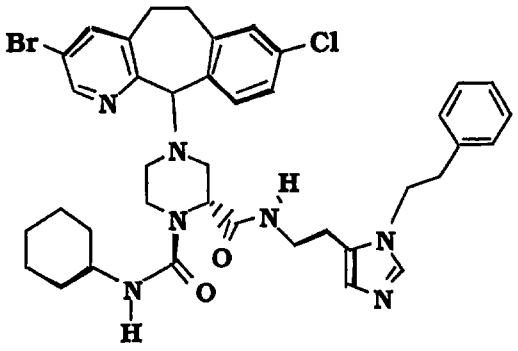
(Example 296);



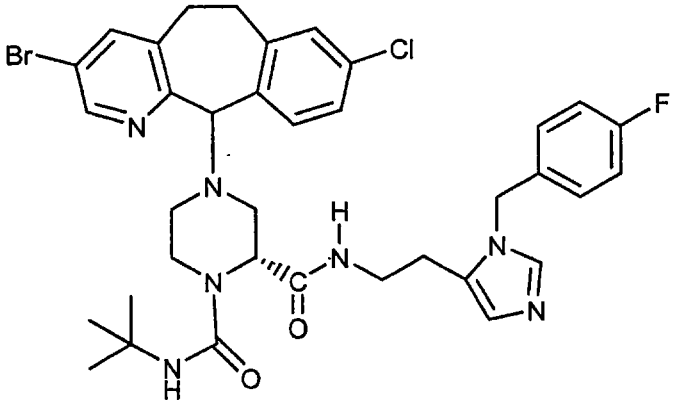
(Example 297);



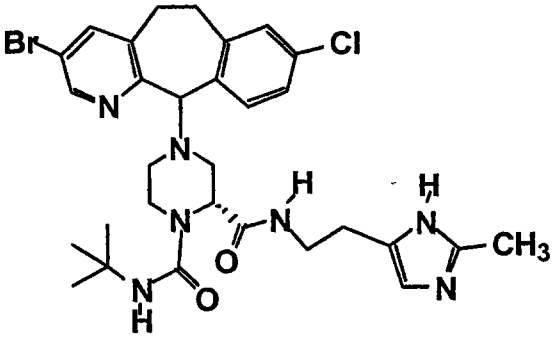
(Example 299);



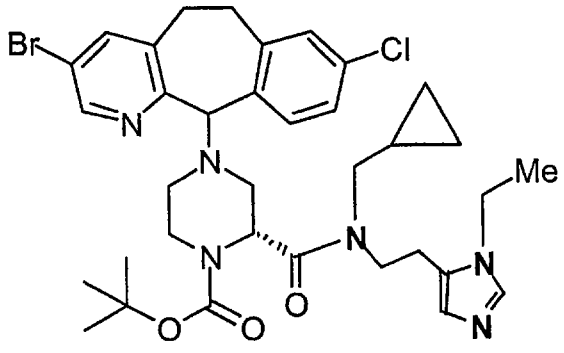
(Example 300);



(Example 302);

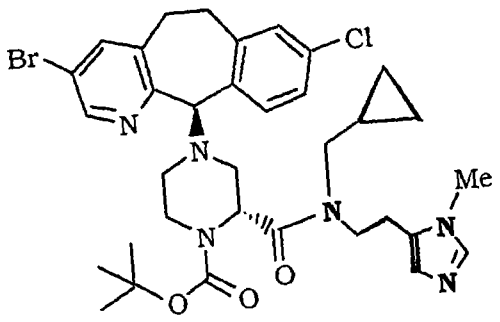


(Example 303);

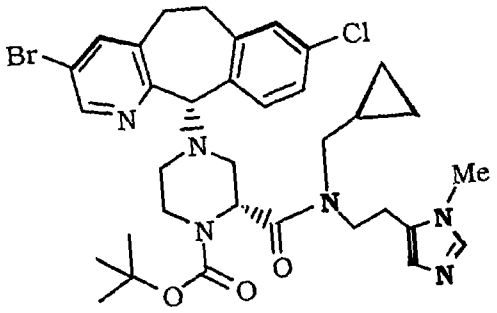


(Example 304);

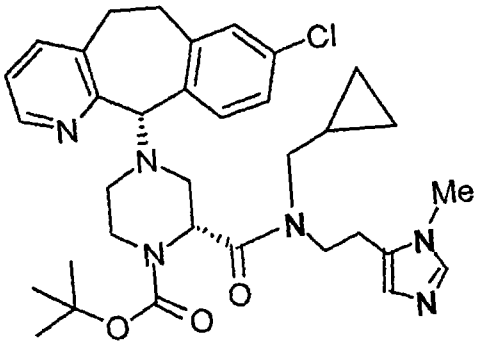
16 JUL 2003



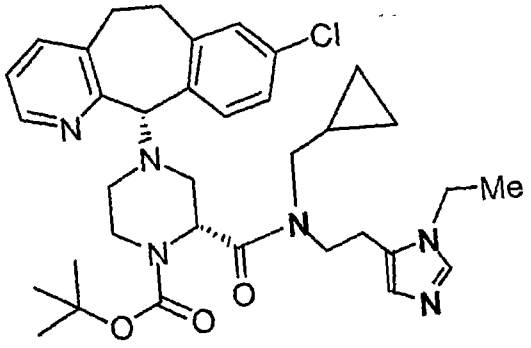
(Example 305);



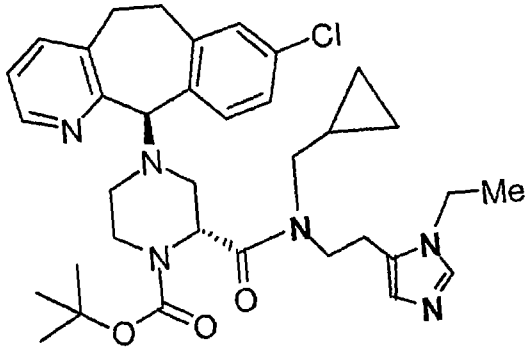
(Example 305);



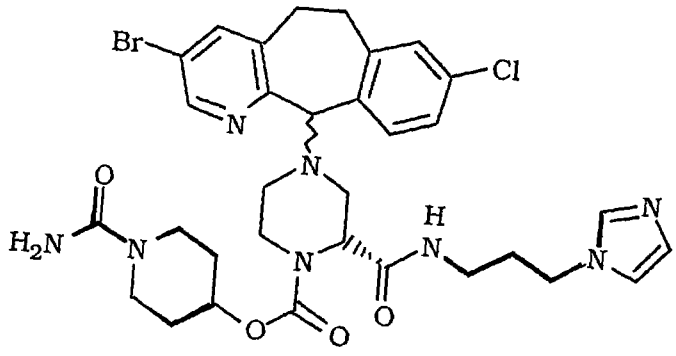
(Example 306);



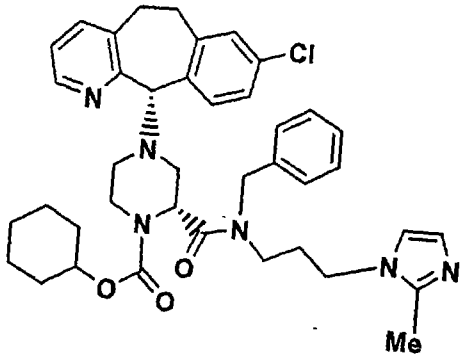
(Example 307);



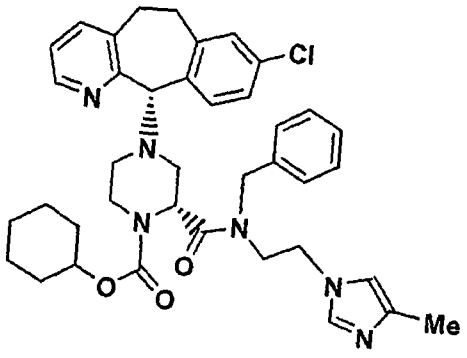
(Example 308);



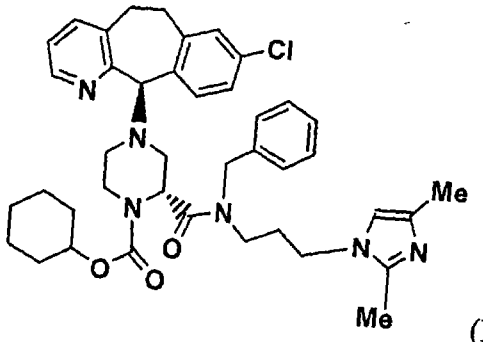
(Example 309);



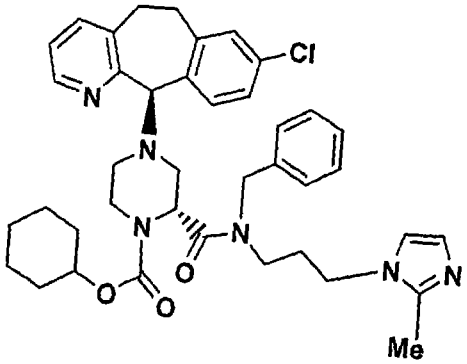
(Example 310);



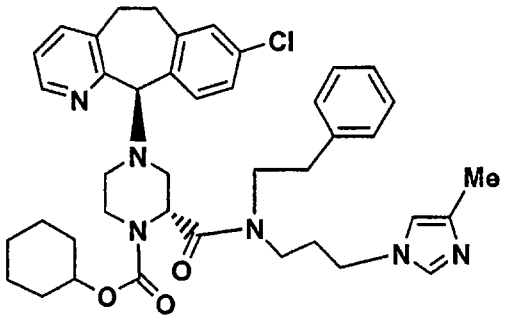
(Example 311);



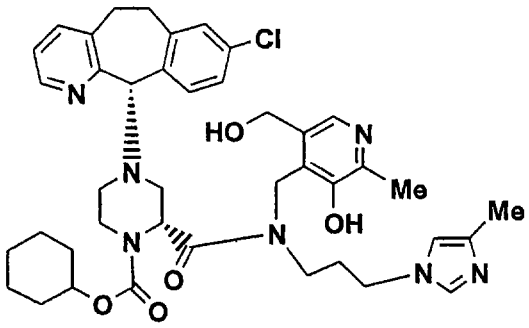
(Example 312);



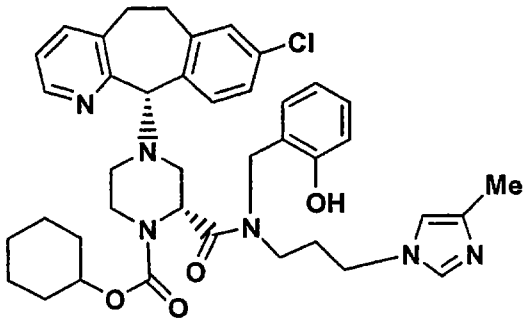
(Example 313);



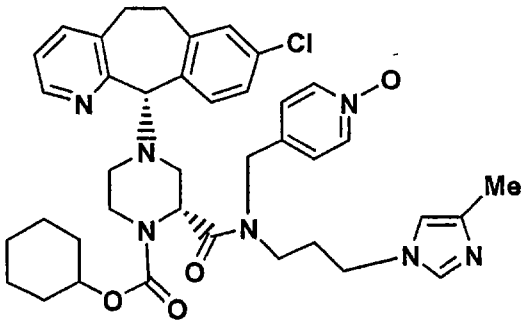
(Example 314);



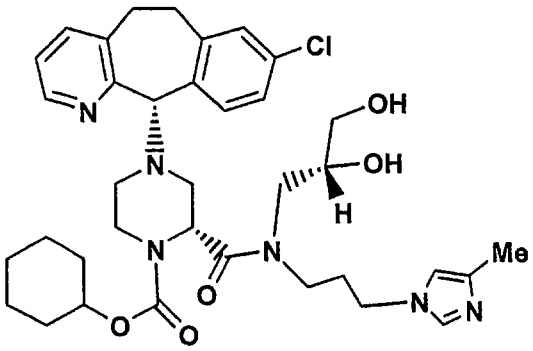
(Example 315);



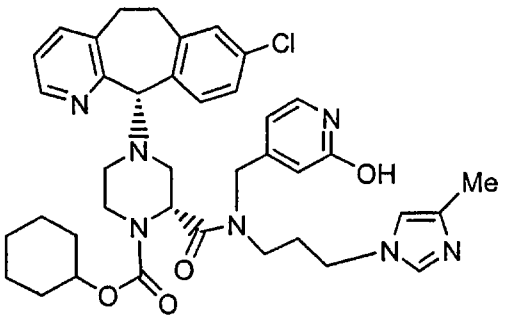
(Example 316);



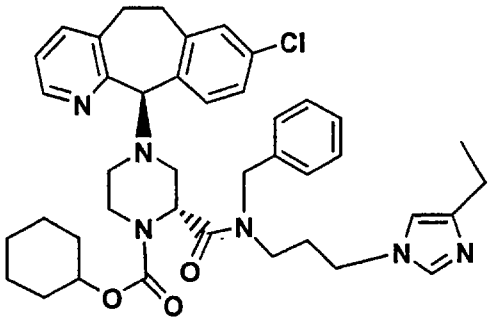
(Example 317);



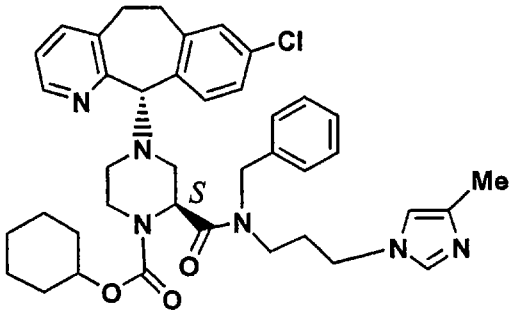
(Example 318);



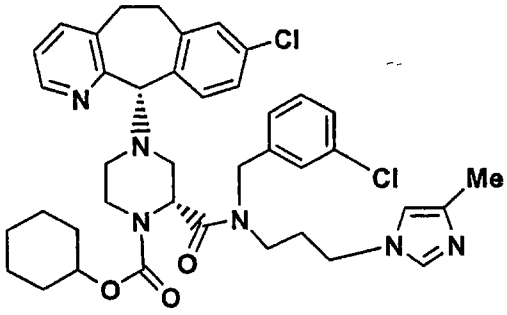
(Example 319);



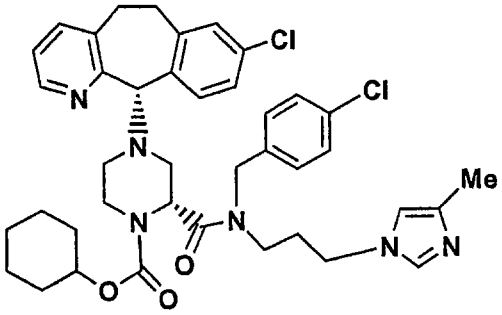
(Example 320);



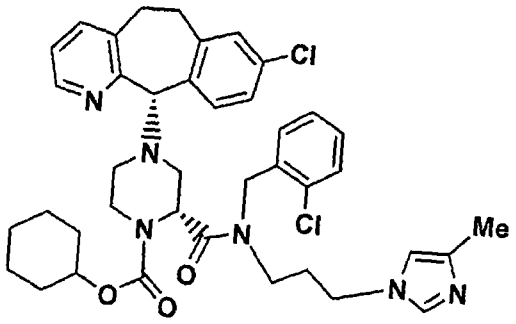
(Example 321);



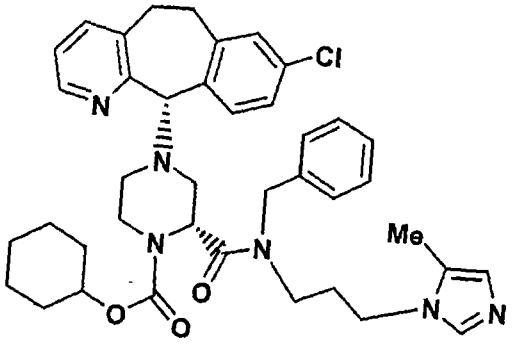
(Example 322);



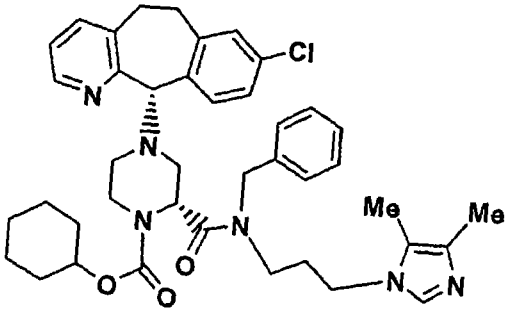
(Example 323);



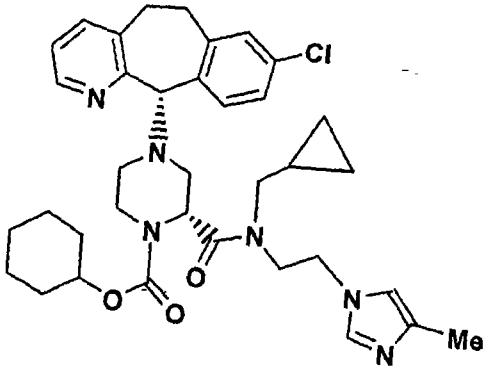
(Example 324);



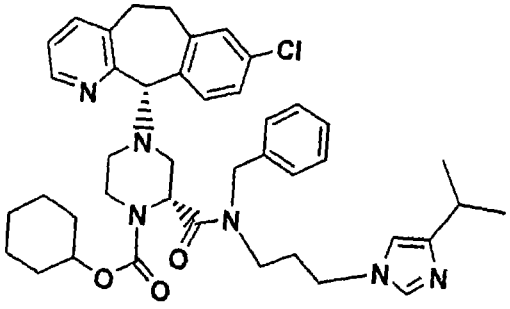
(Example 325);



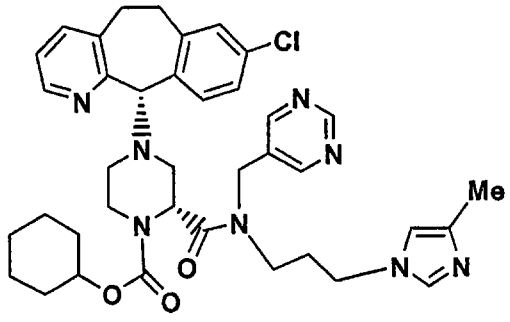
(Example 326);



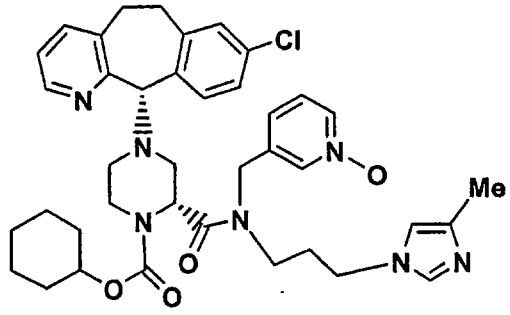
(Example 327);



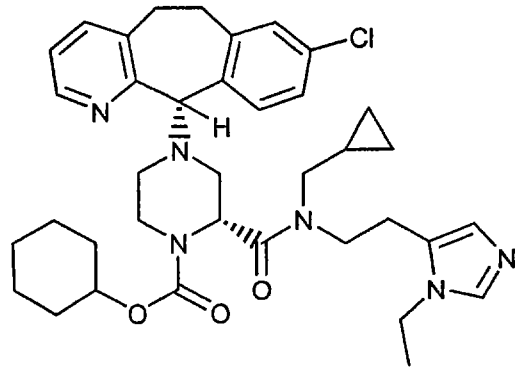
(Example 328);



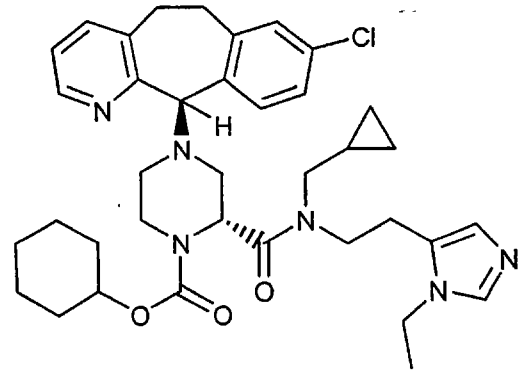
(Example 329);



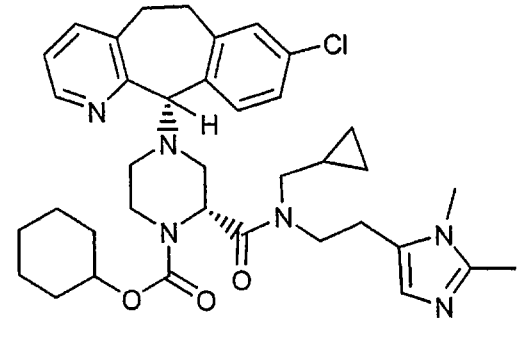
(Example 330);



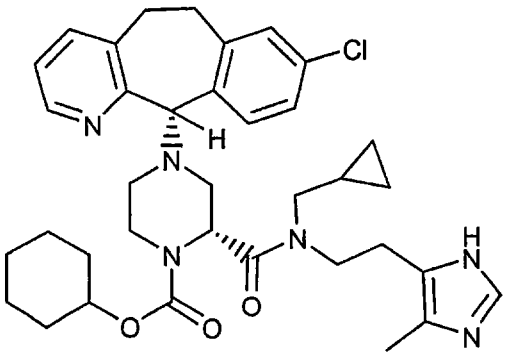
(Example 331);



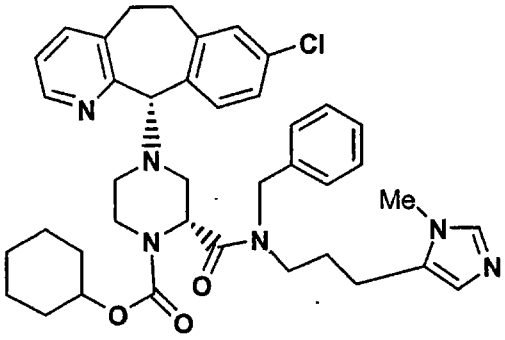
(Example 332);



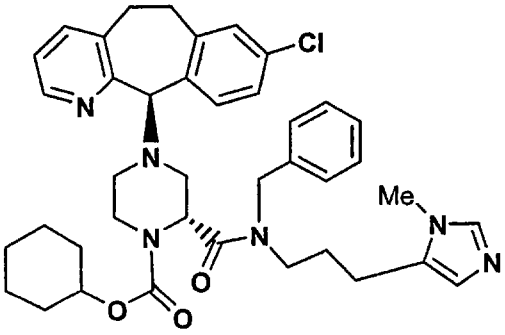
(Example 333);



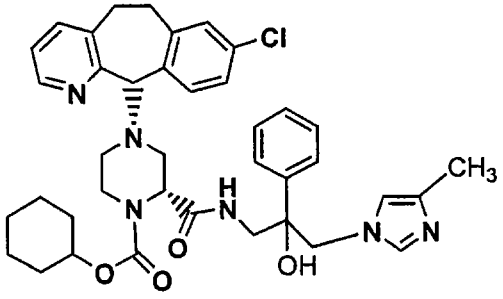
(Example 334);



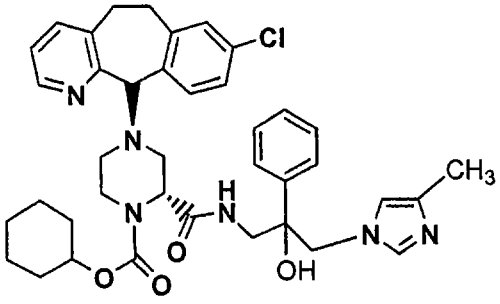
(Example 335);



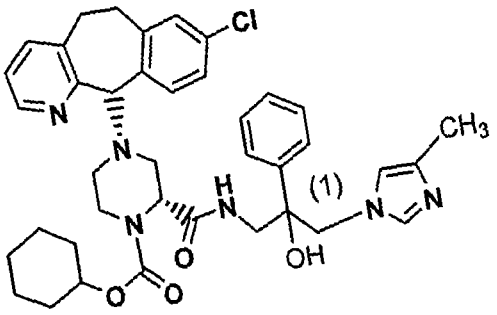
(Example 336);



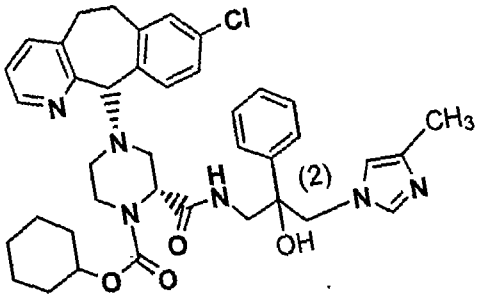
(Example 337);



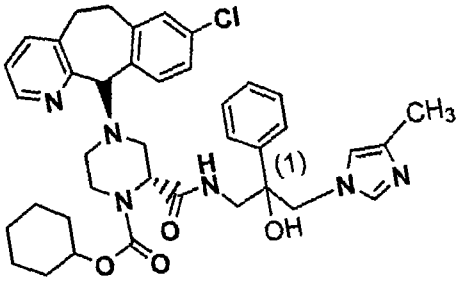
(Example 338);



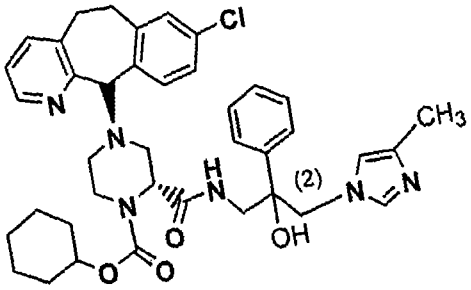
(Example 339);



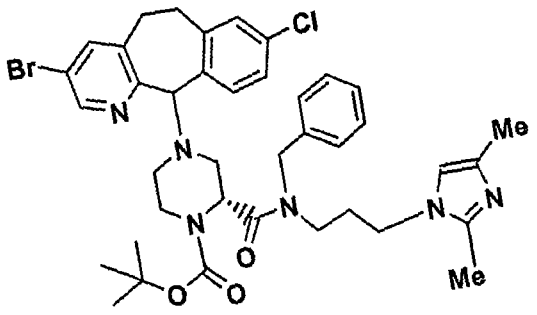
(Example 340);



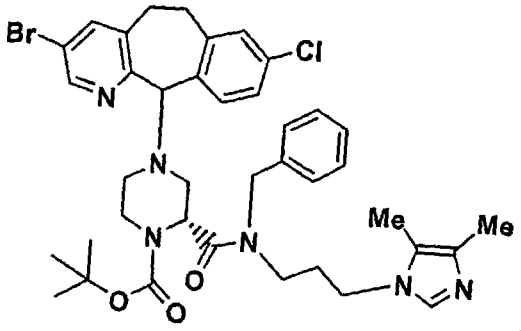
(Example 341);



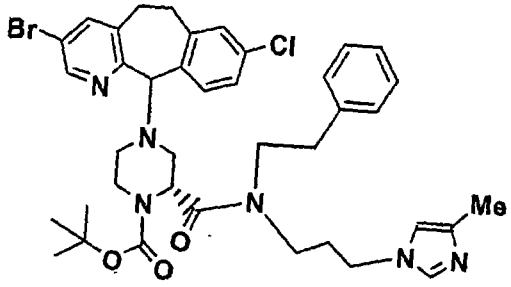
(Example 342);



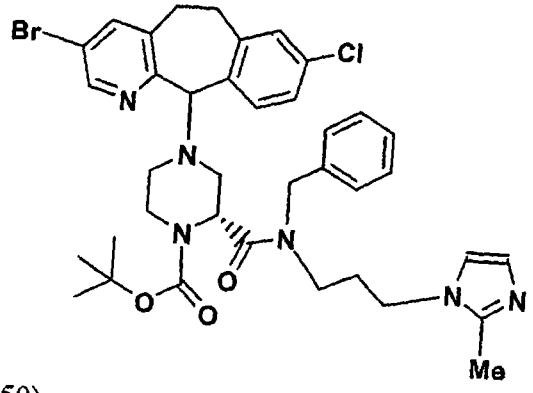
Isomer A (Example 343) and Isomer B (Example 344);



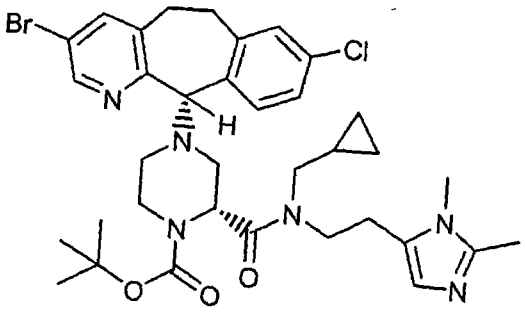
Isomer A (Example 345) and Isomer B (Example 346);



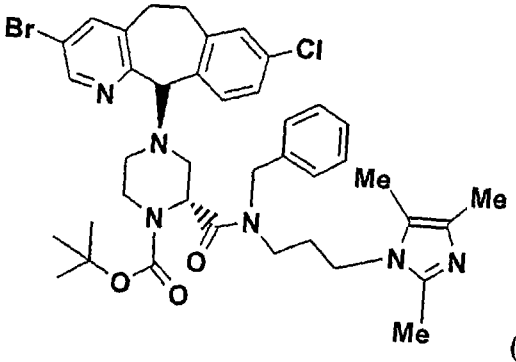
Isomer A (Example 347) and Isomer B (Example 348);



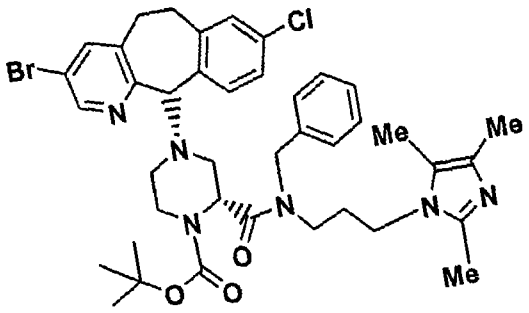
Isomer A (Example 349) and Isomer B (Example 350);



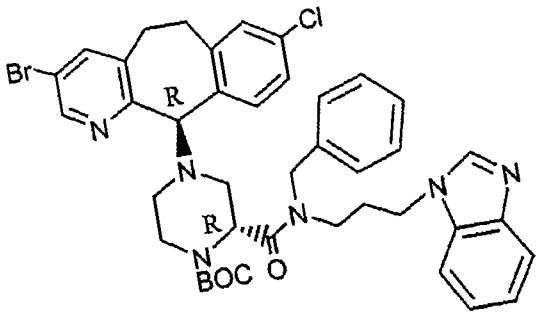
(Example 351);



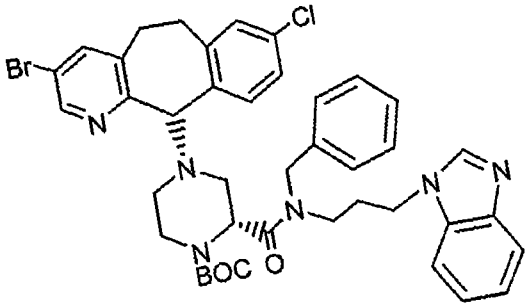
(Example 352);



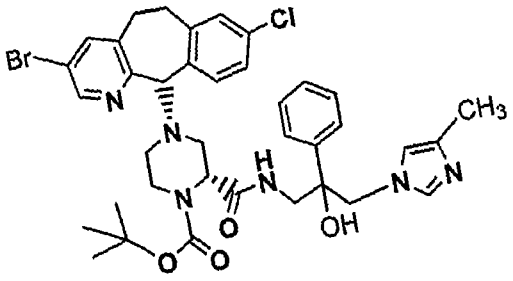
(Example 353);



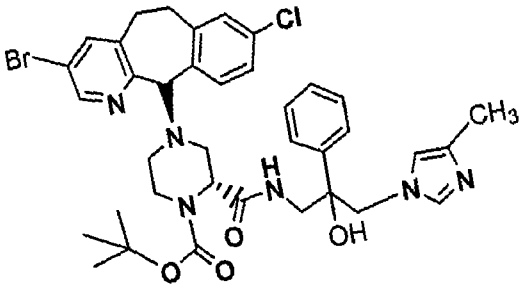
(Example 354);



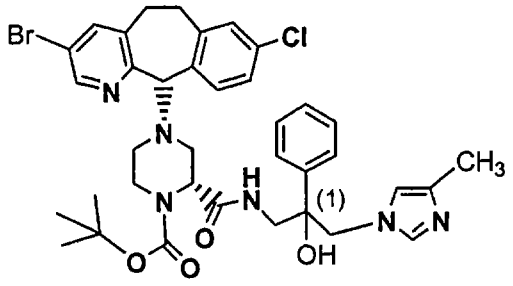
(Example 355);



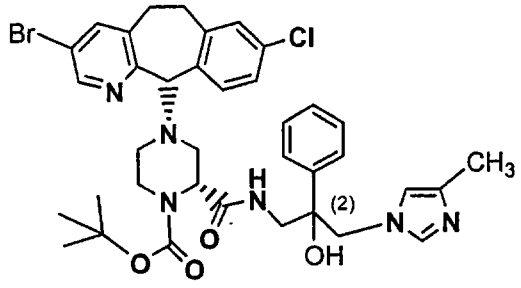
(Example 356);



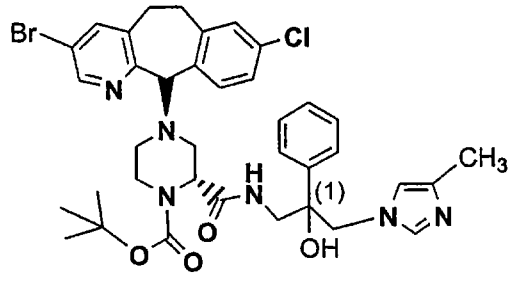
(Example 357);



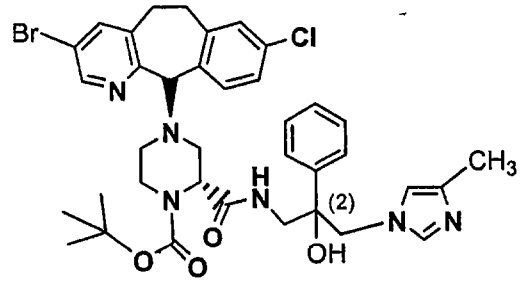
(Example 358);



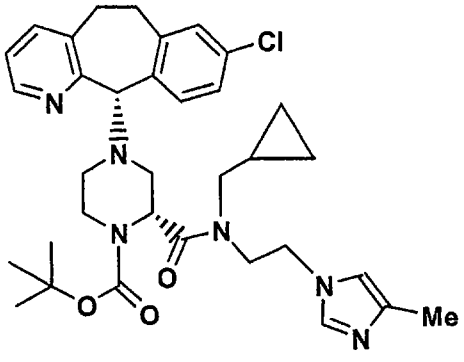
(Example 359);



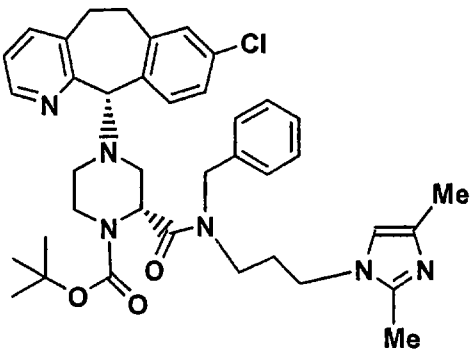
(Example 360);



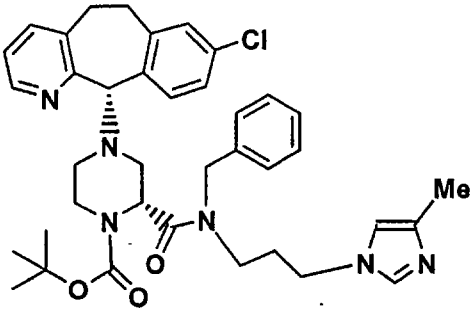
(Example 361);



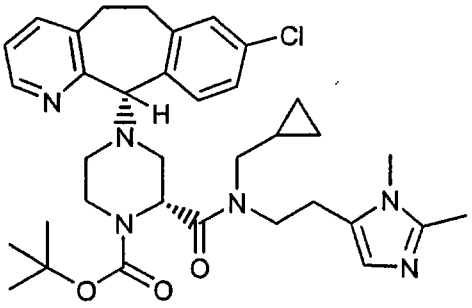
(Example 362);



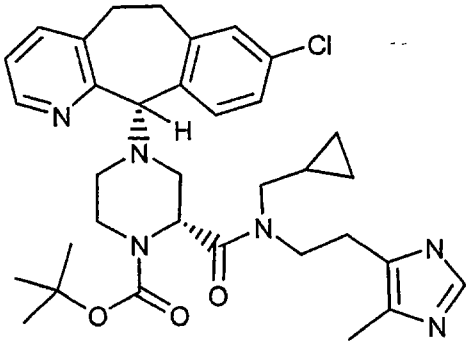
(Example 363);



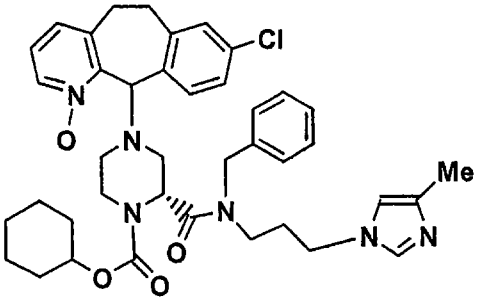
(Example 364);



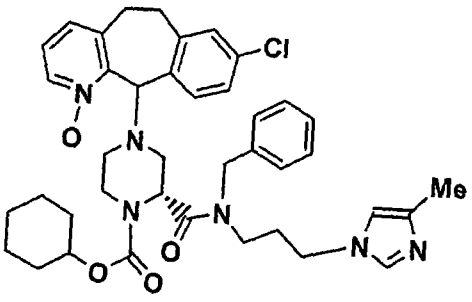
(Example 365);



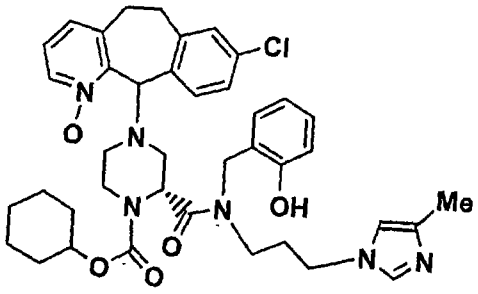
(Example 366);



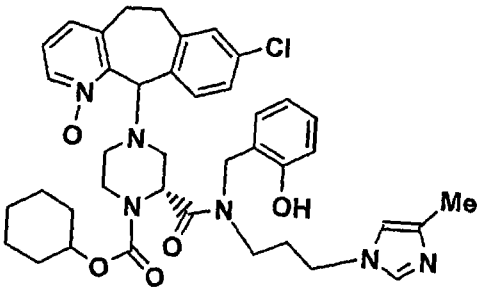
Isomer A (Example 367);



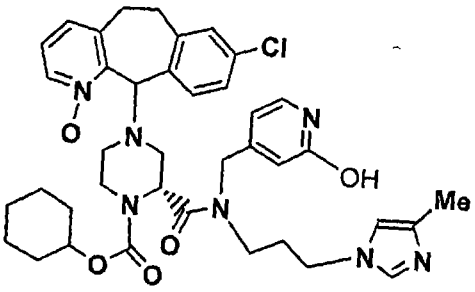
Isomer B (Example 368);



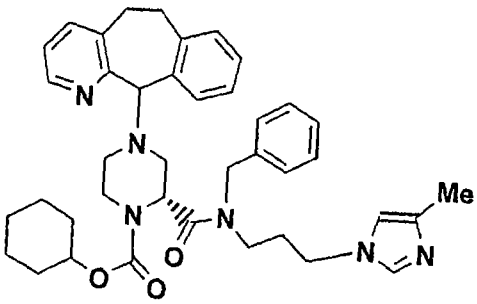
Isomer A (Example 369);



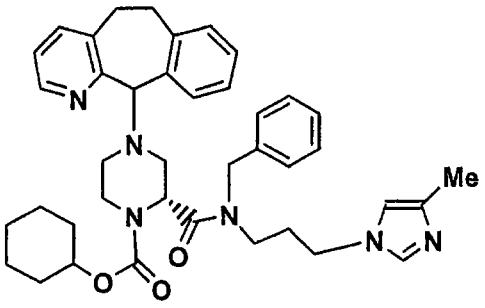
Isomer B (Example 370);



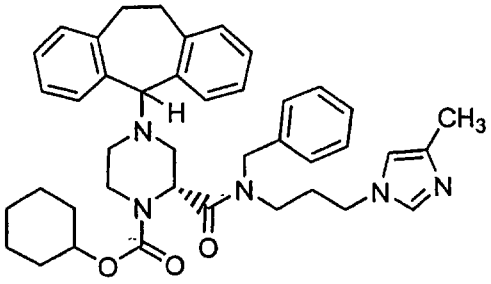
Isomer B (Example 371);



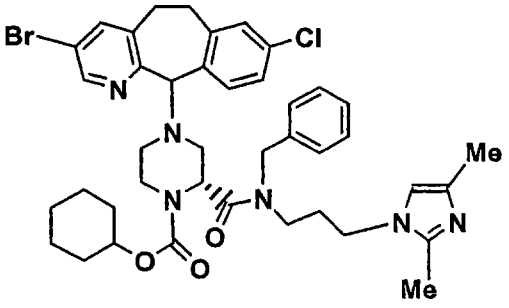
Isomer A (Example 372);



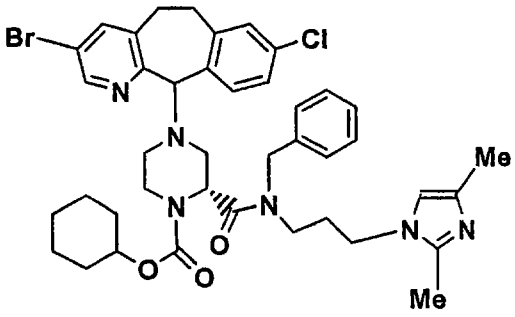
Isomer B (Example 373);



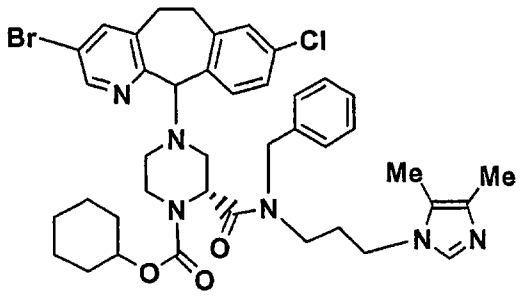
(Example 374);



Isomer A (Example 375);

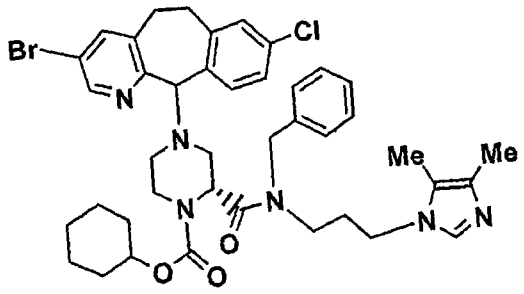


Isomer B (Example 376);

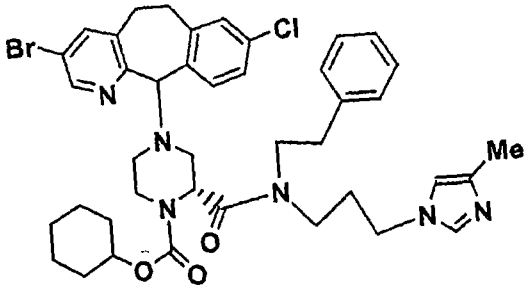


Isomer A (Example 377);

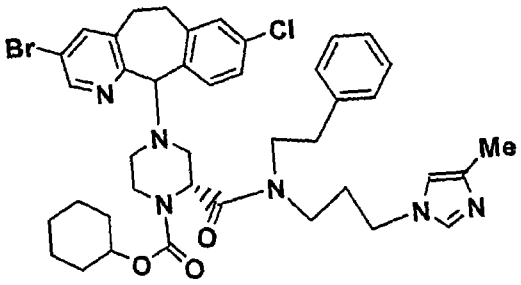
16 JUL 2003



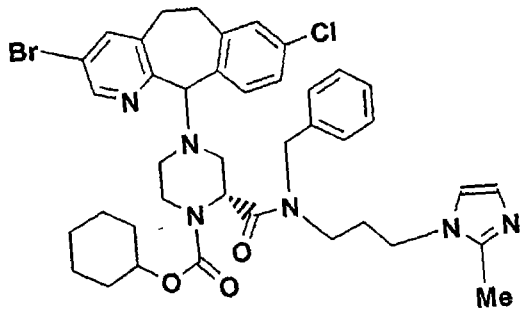
Isomer B (Example 378);



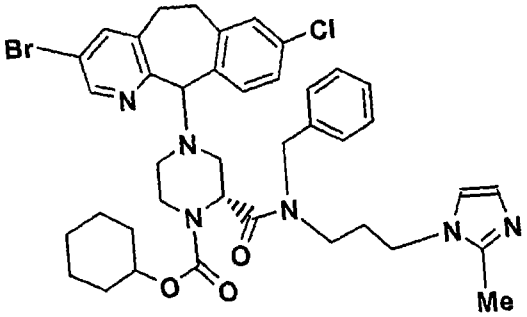
Isomer A (Example 379);



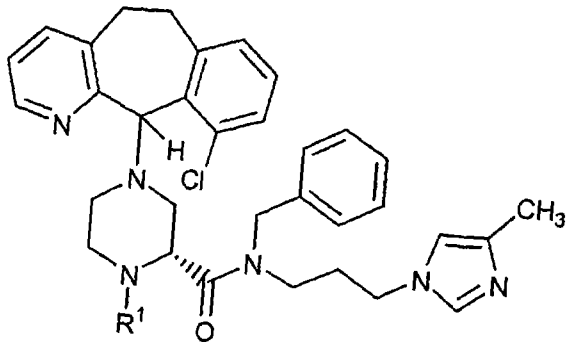
Isomer B (Example 380);



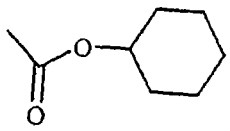
Isomer A (Example 381);



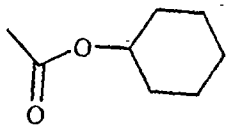
Isomer B (Example 382);



wherein R^1 is selected from the group consisting of:



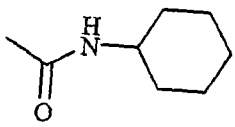
Isomer A (Example 383);



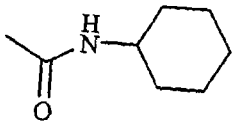
Isomer B (Example 384);

-$COOC(CH_3)_3$ Isomer A (Example 385);

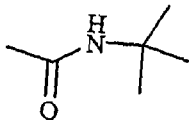
-$COOC(CH_3)_3$ Isomer B (Example 386);



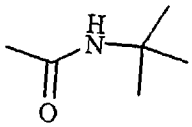
Isomer A (Example 387);



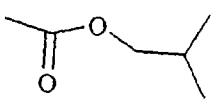
Isomer B (Example 388);



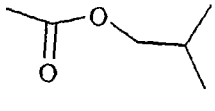
Isomer A (Example 389);



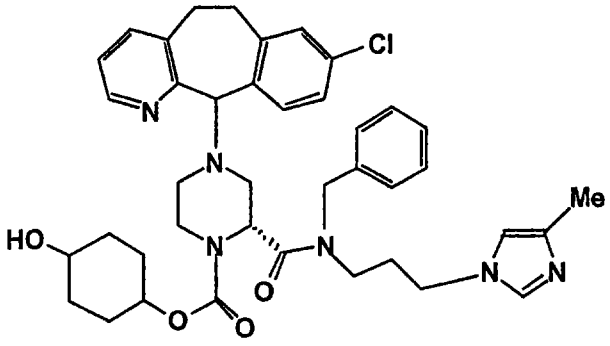
Isomer B (Example 390);



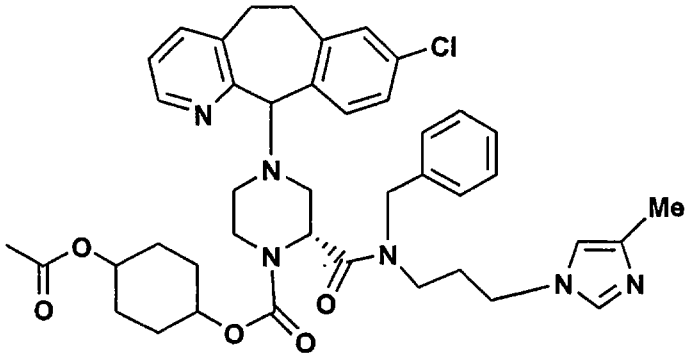
Isomer A (Example 391);



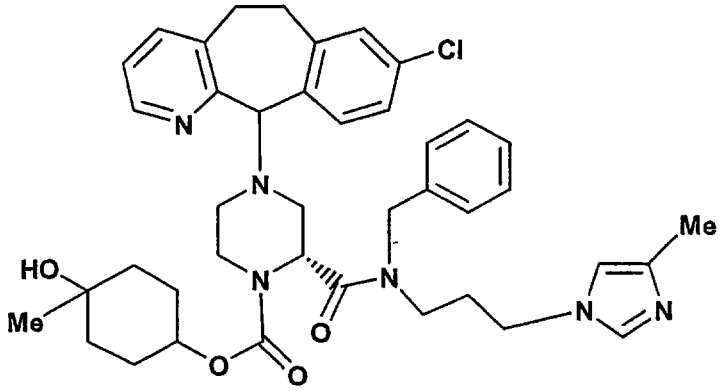
Isomer B (Example 392);



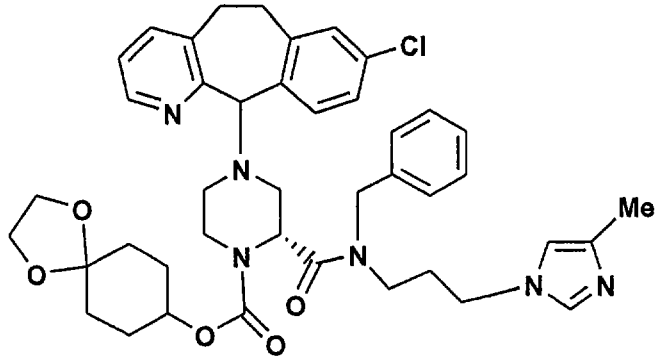
(Example 393 Step C);



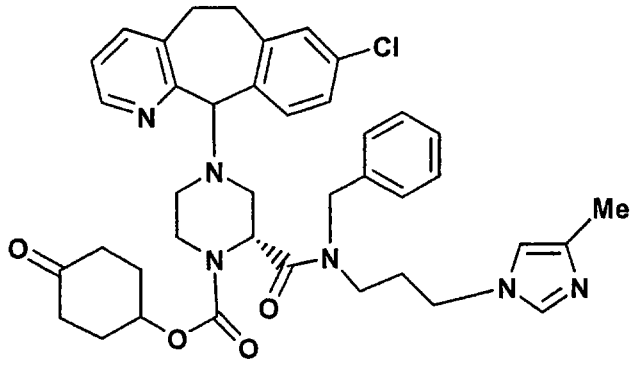
(Example 393 Step B);



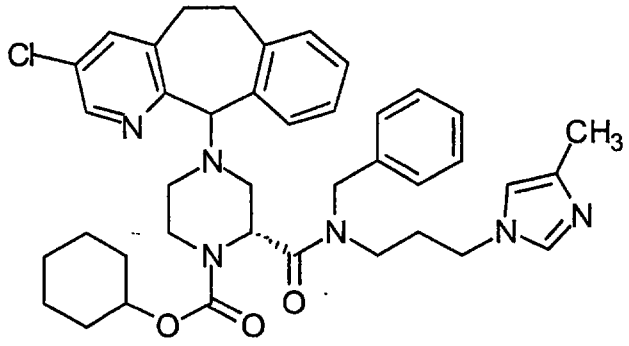
(Example 394 Step D);



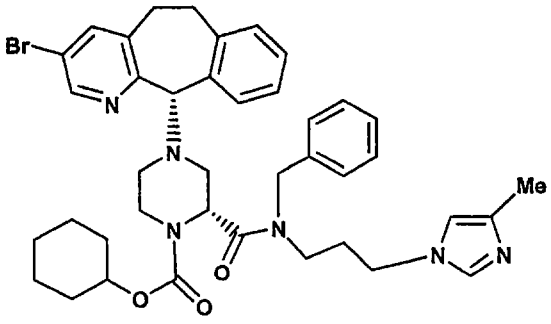
(Example 394 Step B);



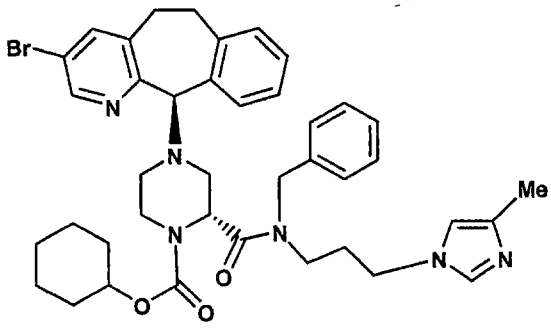
(Example 394 Step C);



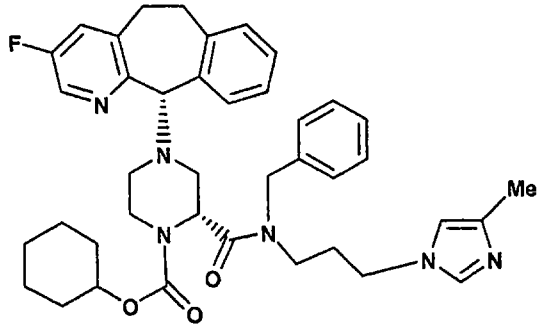
(Example 395);



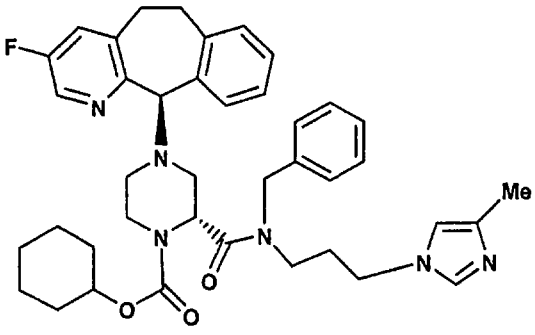
(Example 397 Step B);



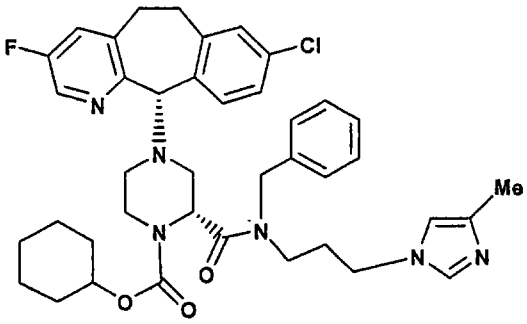
(Example 397 Step B);



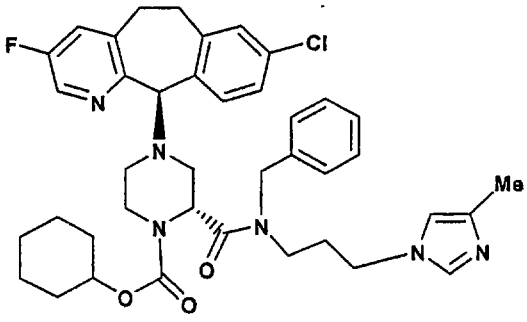
(Example 398 Step B);



(Example 398 Step B);



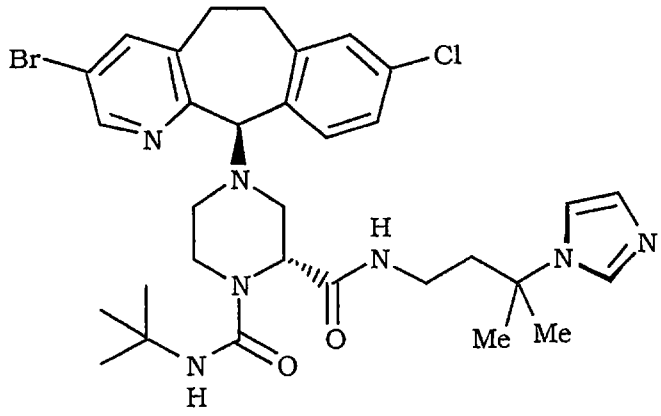
(Example 399 Step B); and



(Example 399 Step B);

and the pharmaceutically acceptable salts and solvates thereof.

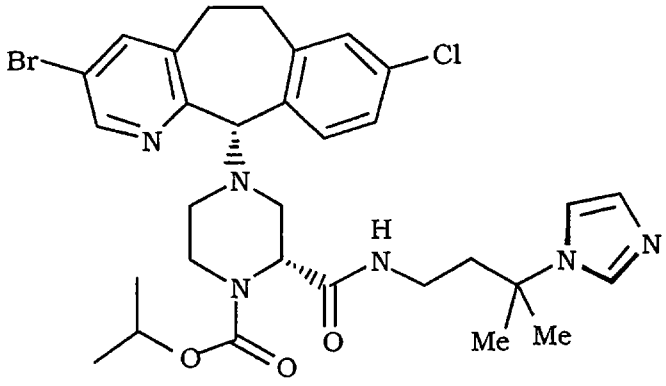
2. A compound as claimed in **Claim 1** selected from the group consisting of:



(11R,2R Isomer)

(Example 11)

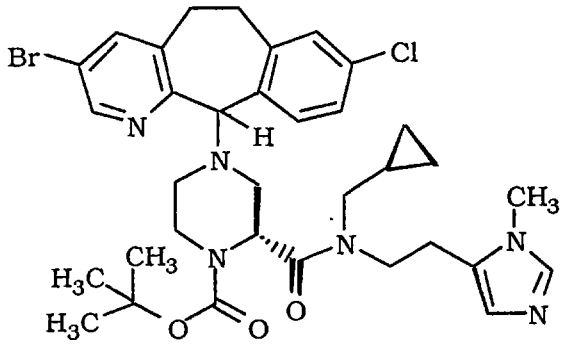
;



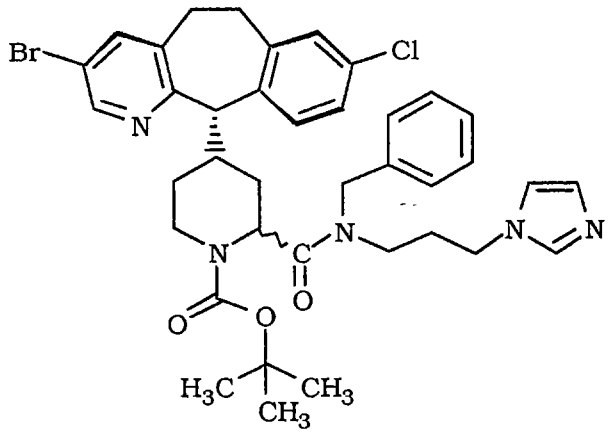
(11S,2R Isomer)

(Example 16)

;

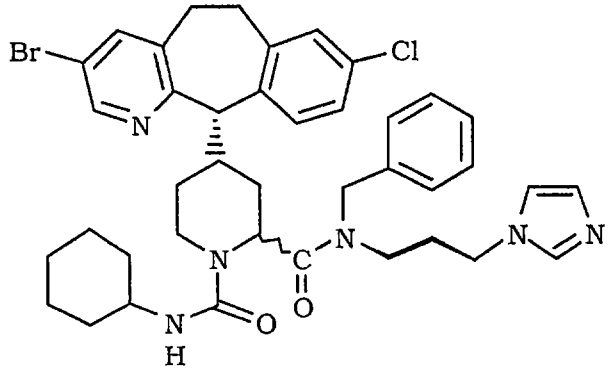


(Example 58);



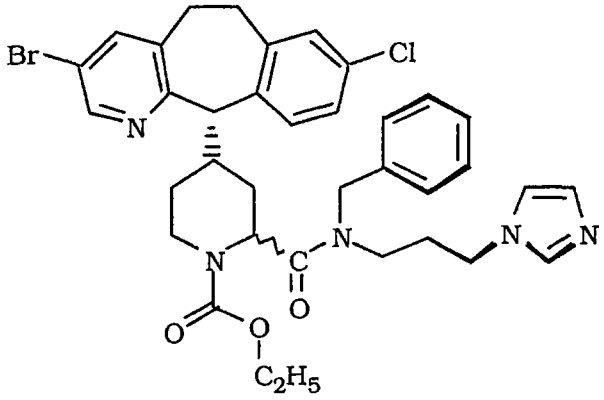
(Example 78 Step B)

;



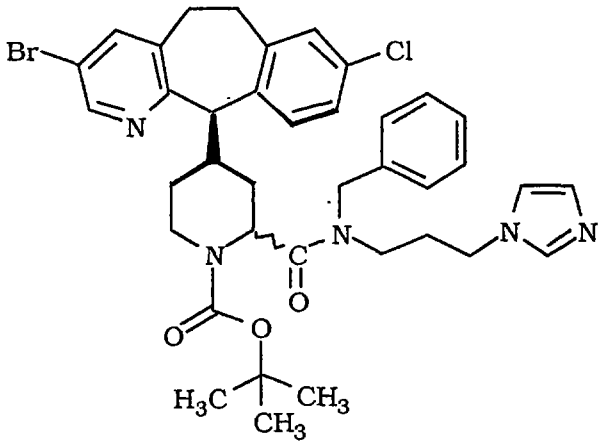
(Example 79 Isomer A)

;



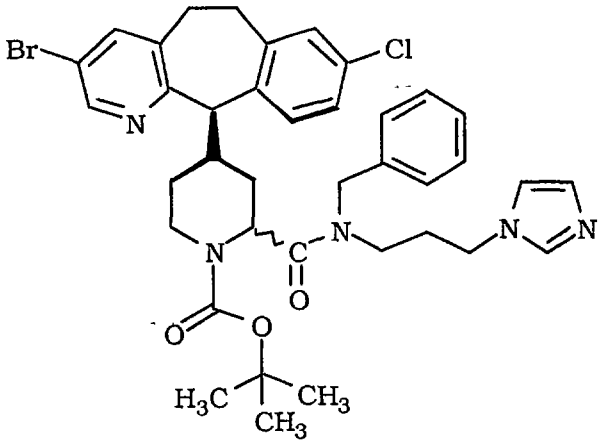
(Example 80 Isomer A)

;



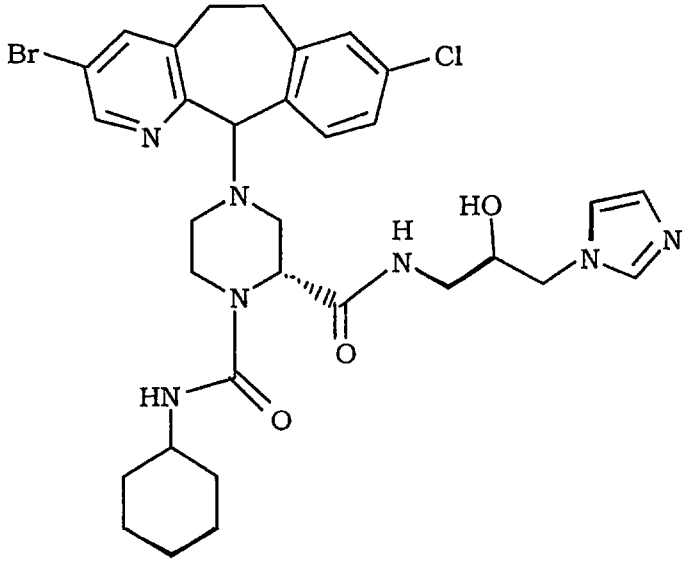
(Example 88 Isomer A)

;



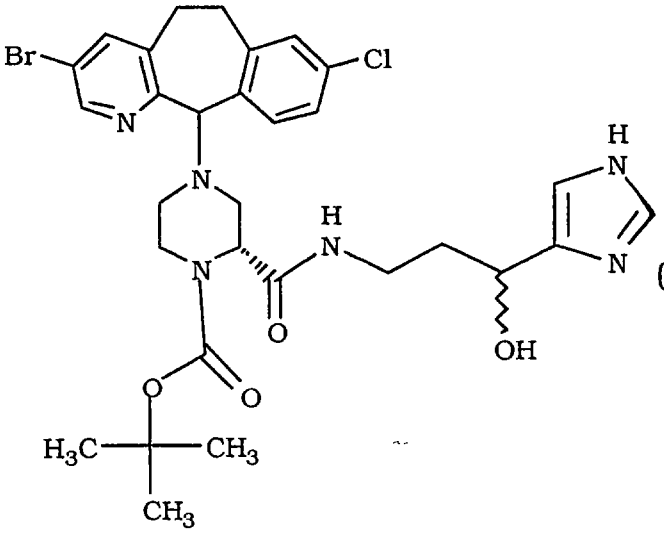
(Example 93 Isomer D)

;



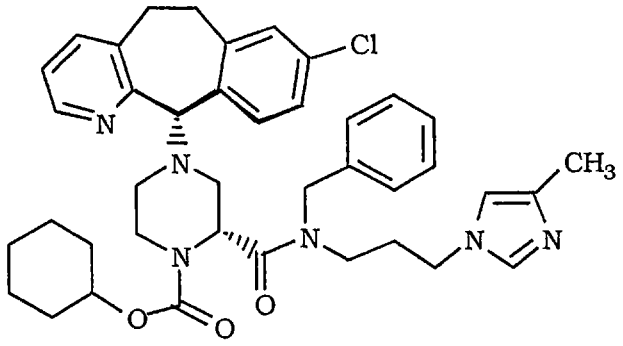
(Example 99)

;



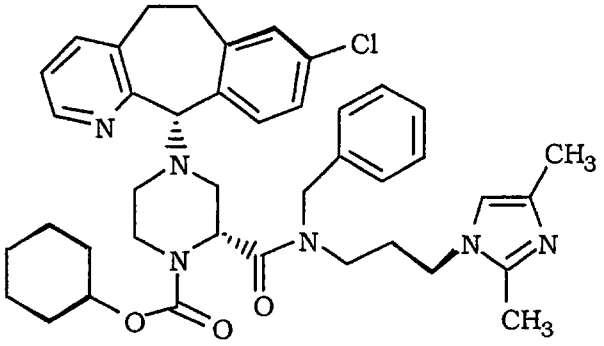
(Example 100)

;



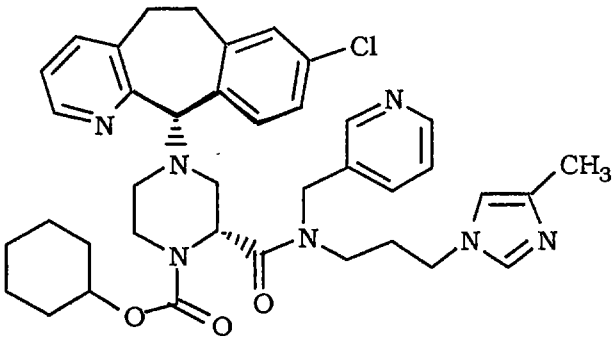
(Example 225)

;



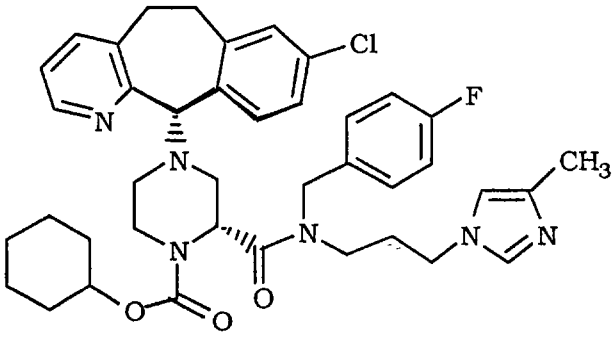
(Example 226)

;



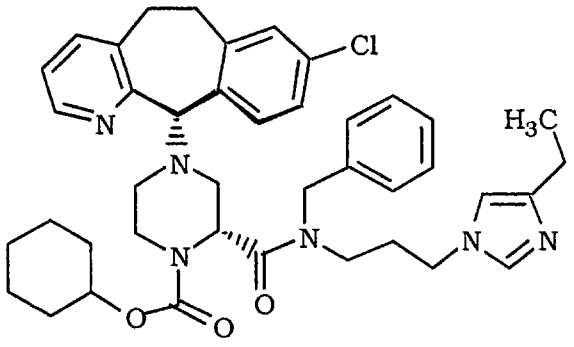
(Example 227)

;



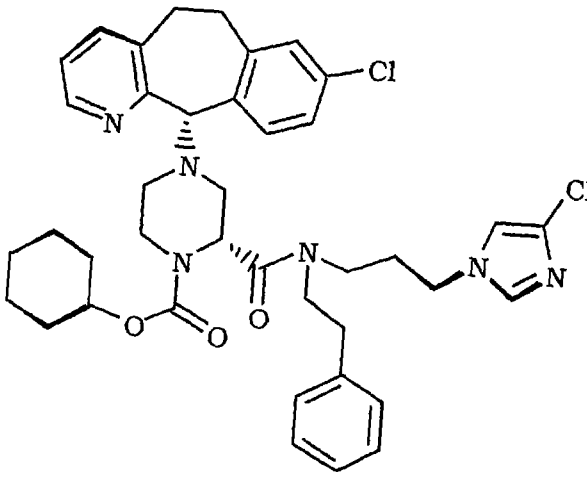
(Example 228)

;



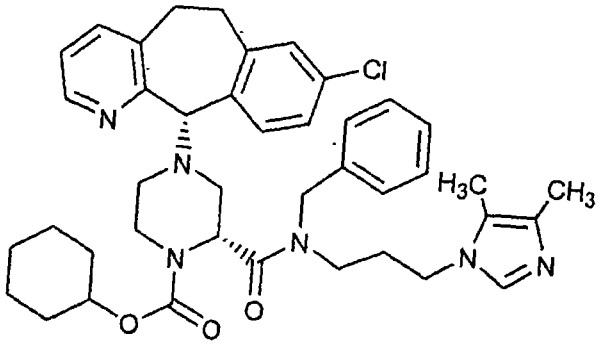
(Example 229)

;



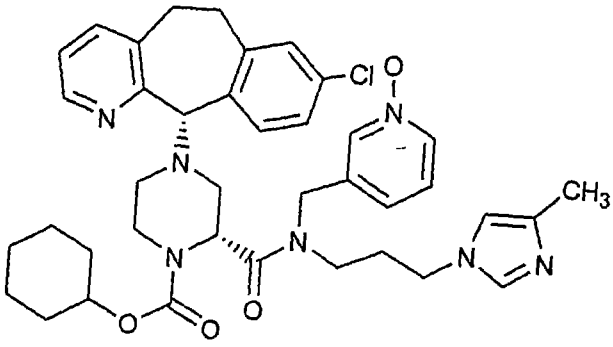
(Example 232)

;



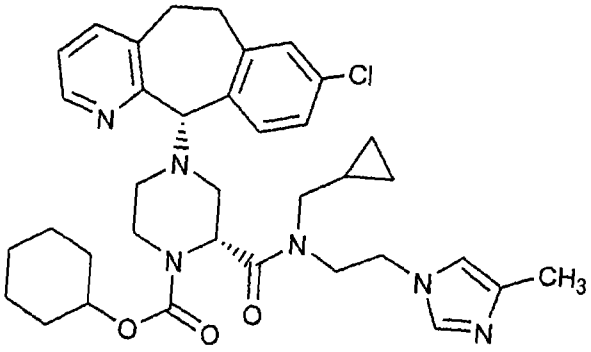
(Example 326)

;



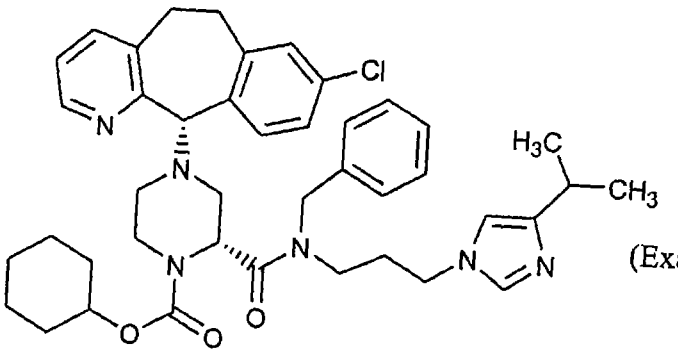
(Example 330)

;



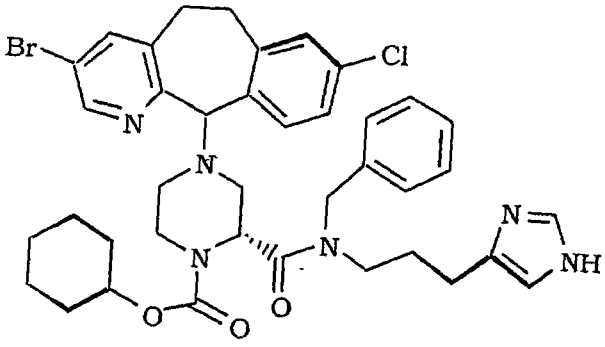
(Example 327)

;



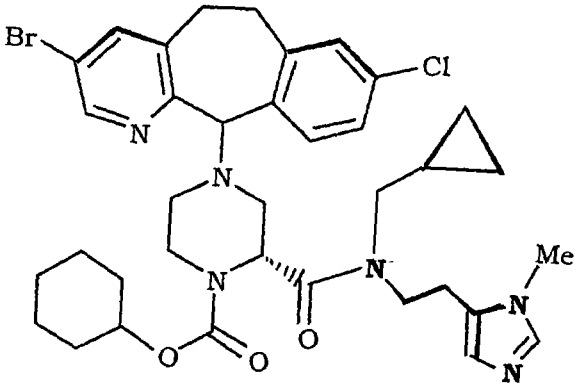
(Example 328)

;



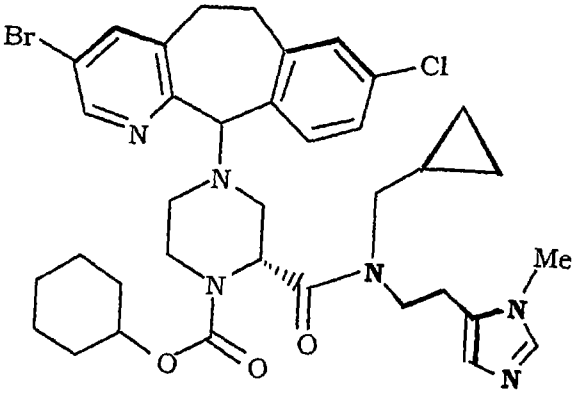
(Example 243)

;



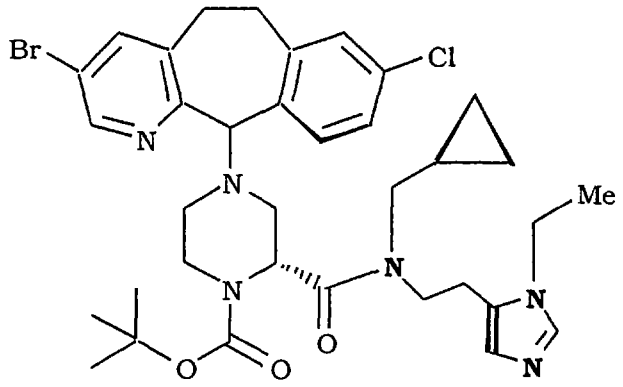
(Example 286A)

;



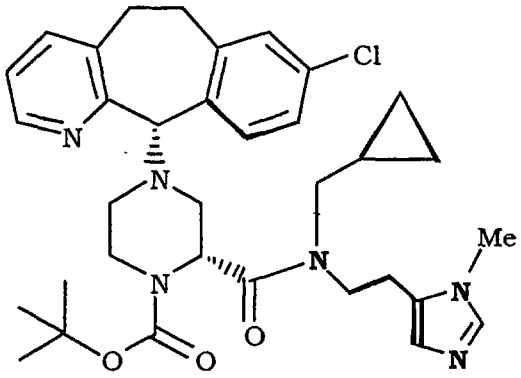
(Example 286B)

;



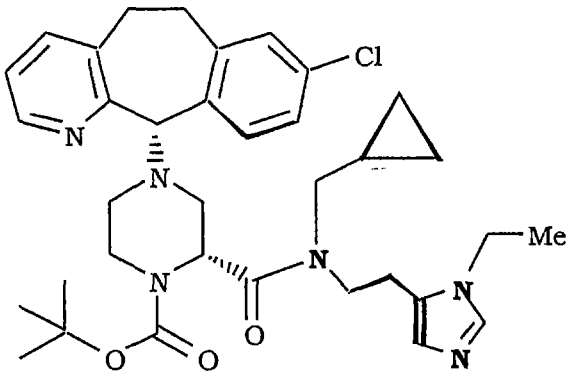
(Example 304)

;



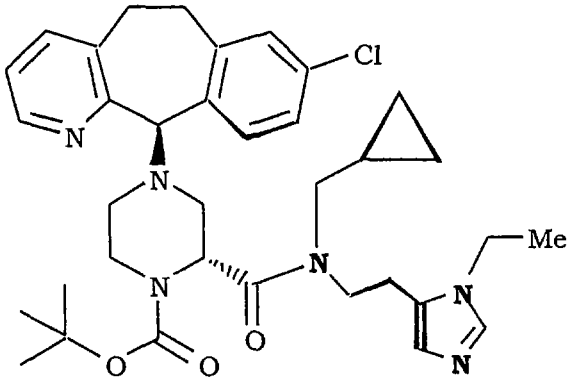
(Example 306)

;



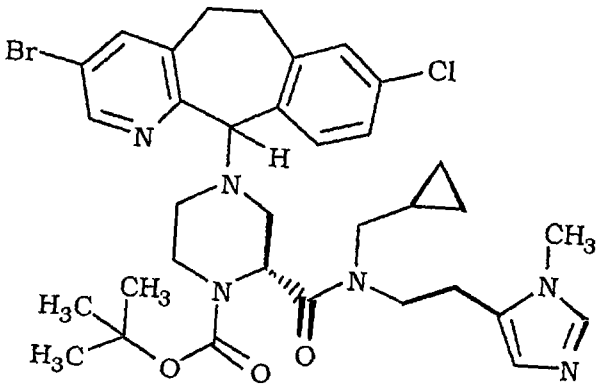
(Example 307)

; and



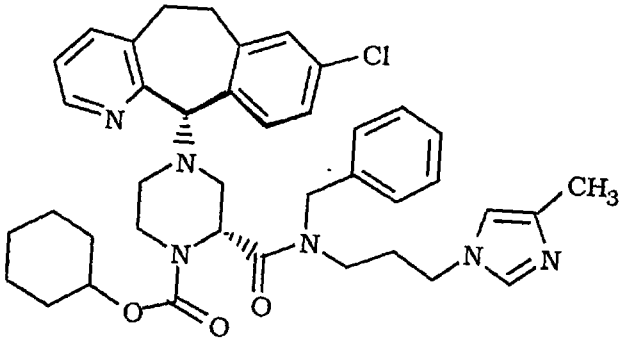
(Example 308)

3. A compound as claimed in **Claim 1** selected from the group consisting of:



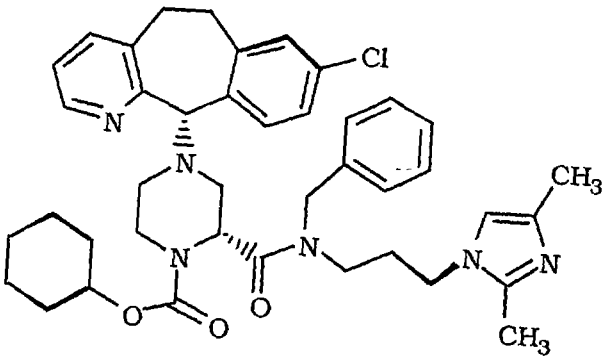
Example 58

;



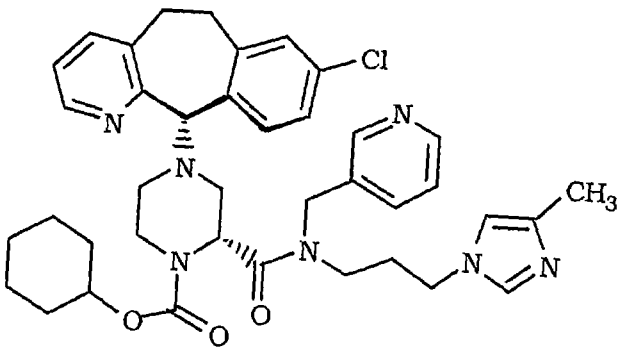
(Example 225)

;



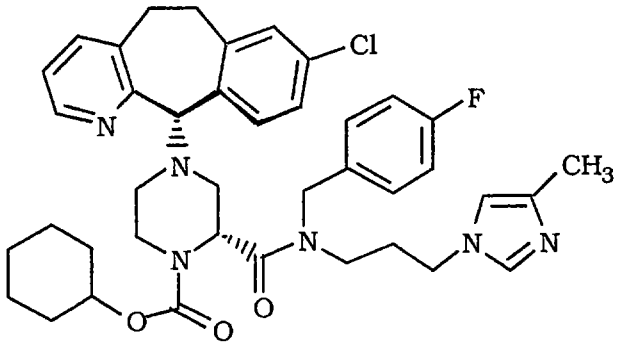
(Example 226)

;



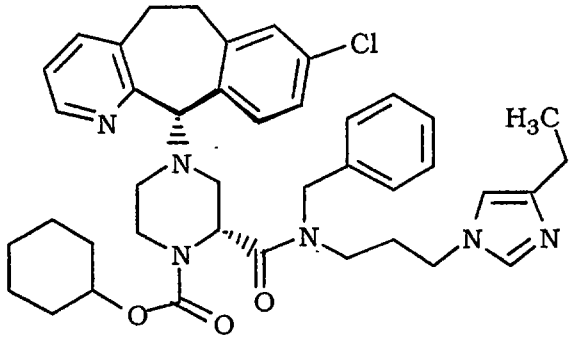
(Example 227)

;



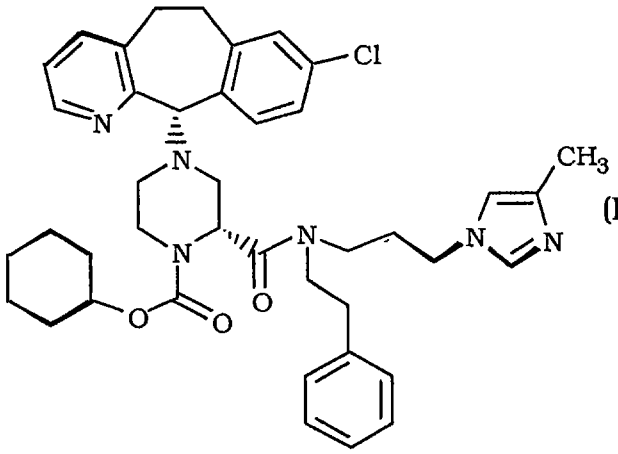
(Example 228)

;



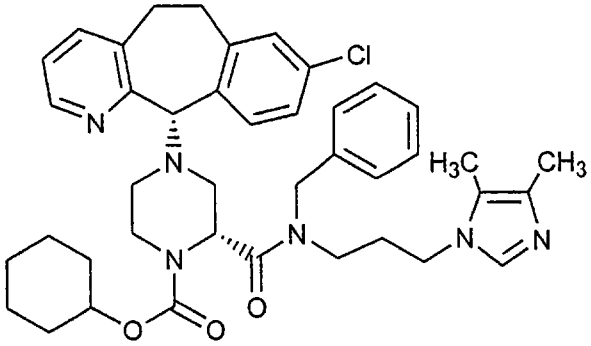
(Example 229)

;



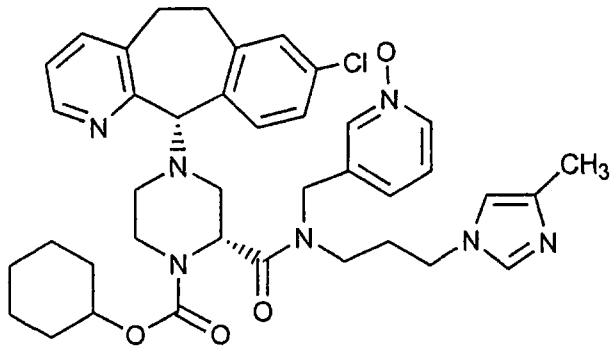
(Example 232)

;



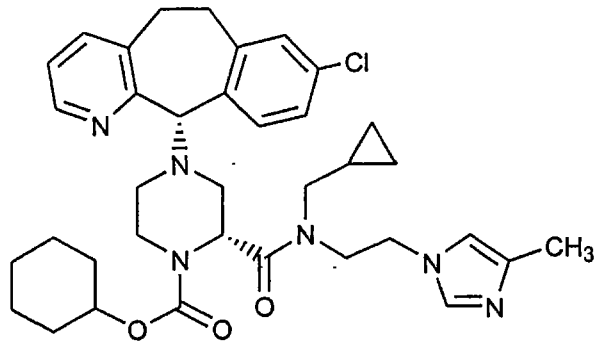
(Example 326)

;



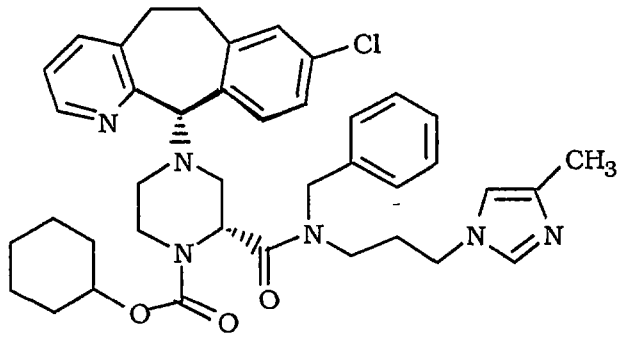
(Example 330)

; and



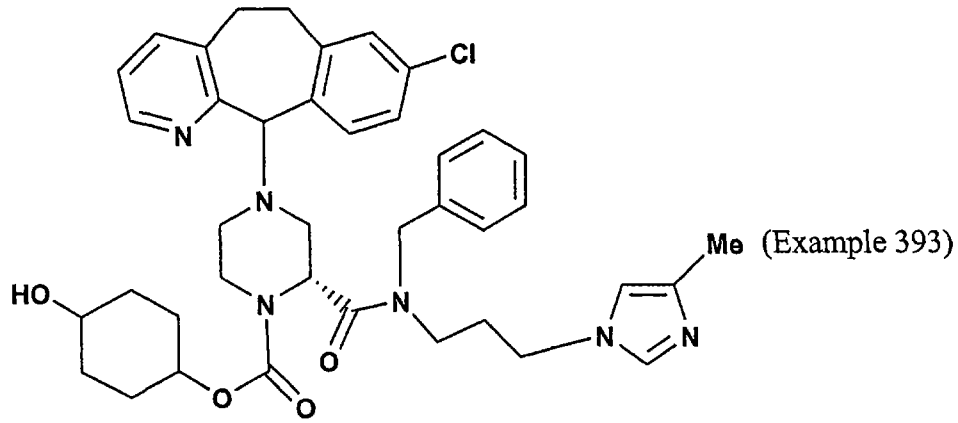
(Example 327)

4. A compound of the formula:



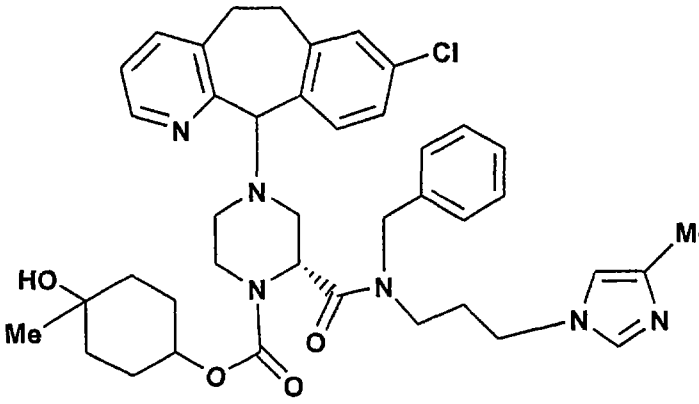
(Example 225)

5. A compound of the formula:



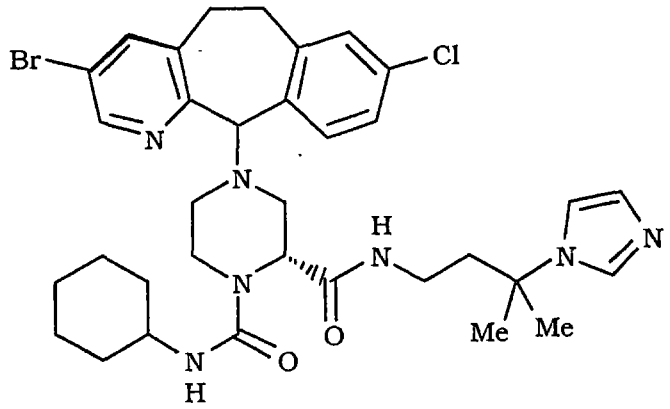
(Example 393)

or

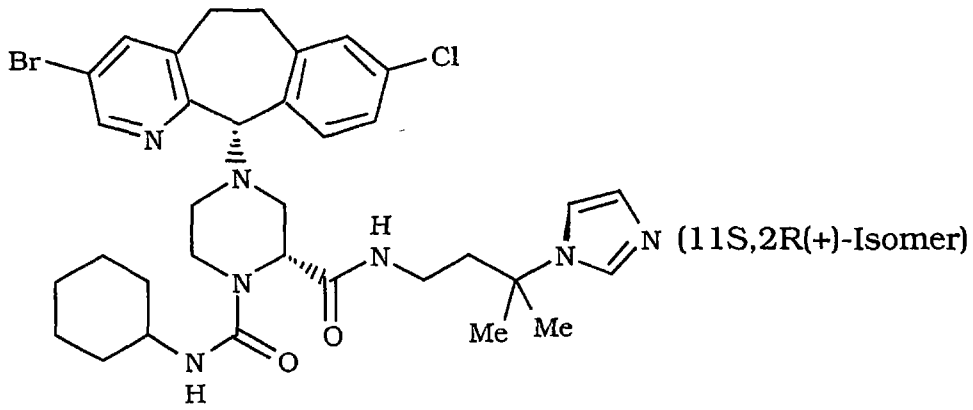


(Example 394)

6. A compound as claimed in **Claim 1** selected from the group consisting of:

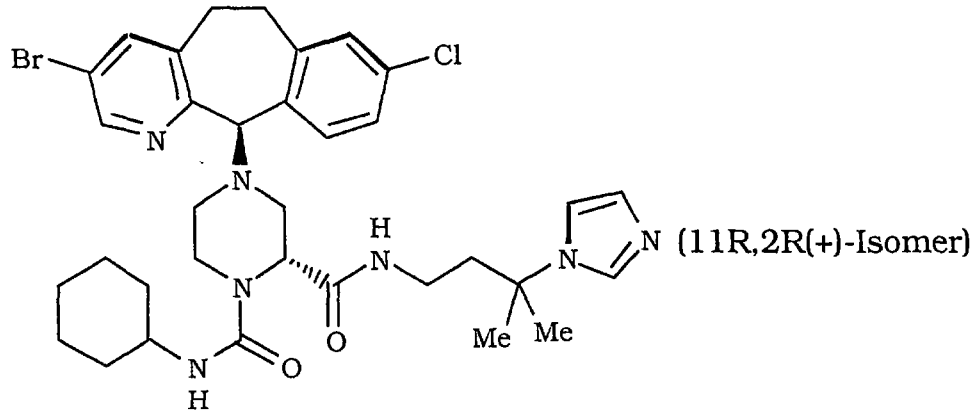


(Example 1);



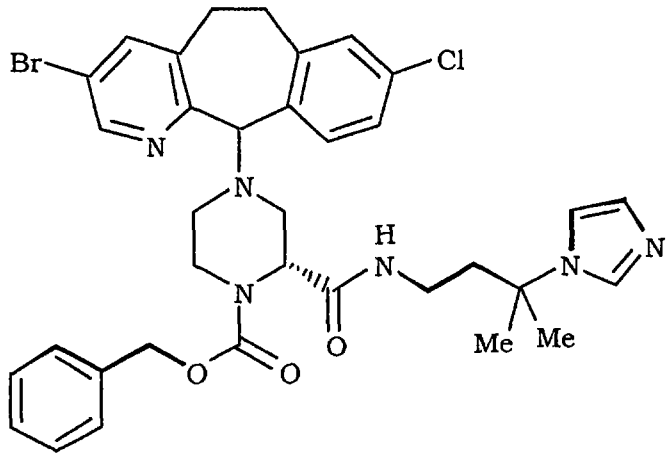
(11S,2R(+)-Isomer)

(Example 2);

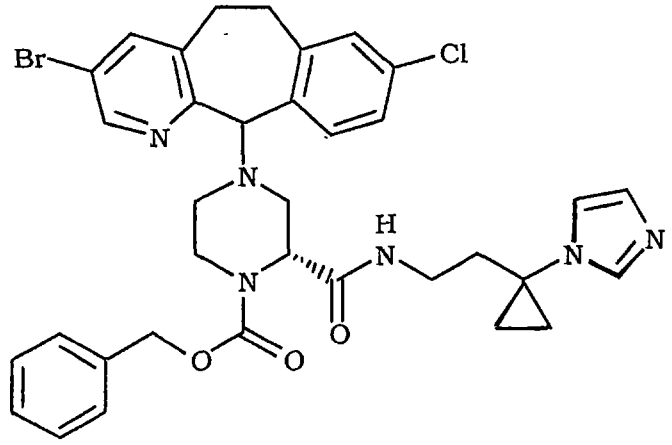


(11R,2R(+)-Isomer)

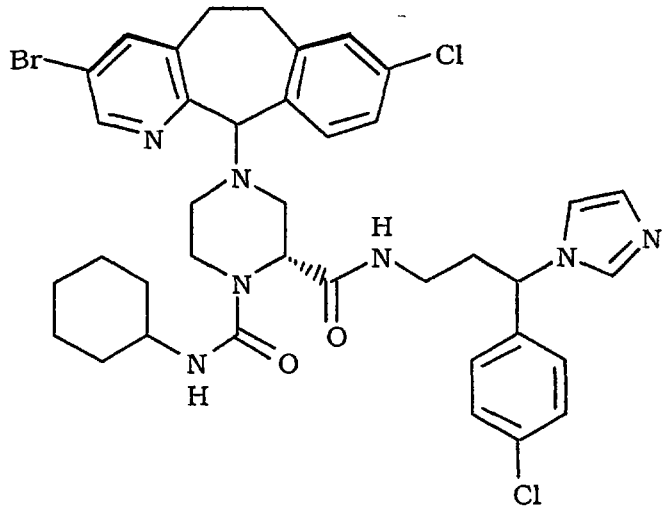
(Example 2);



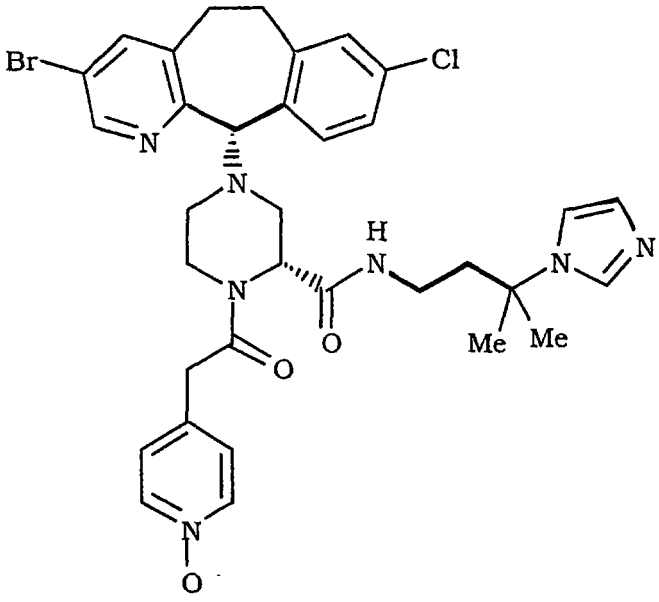
(Example 3);



(Example 4);

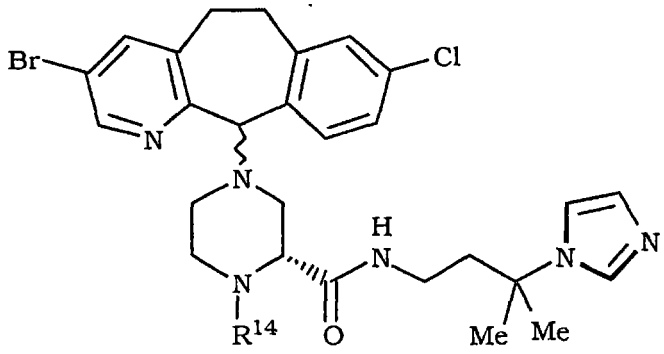


(Example 5);

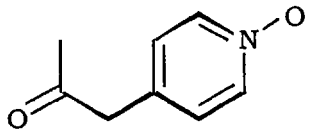


(11R,2R Isomer)

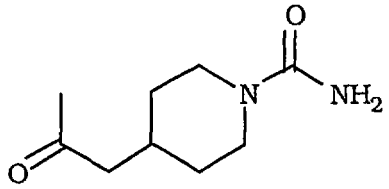
(Example 6);



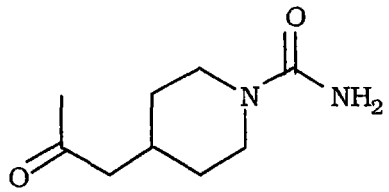
wherein R^{14} is selected from the group comprising:



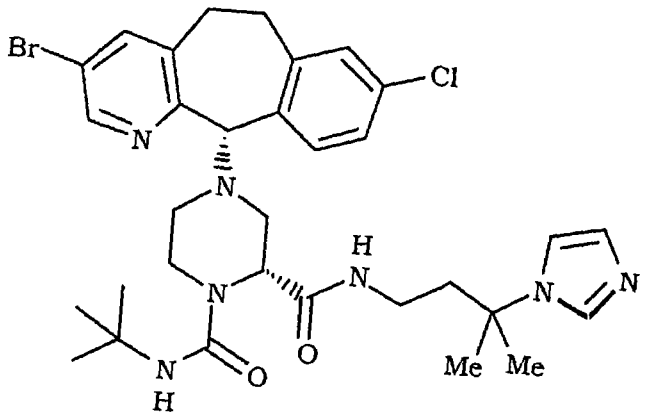
11R,2R isomer (Example 7);



11S,2R isomer (Example 8); and

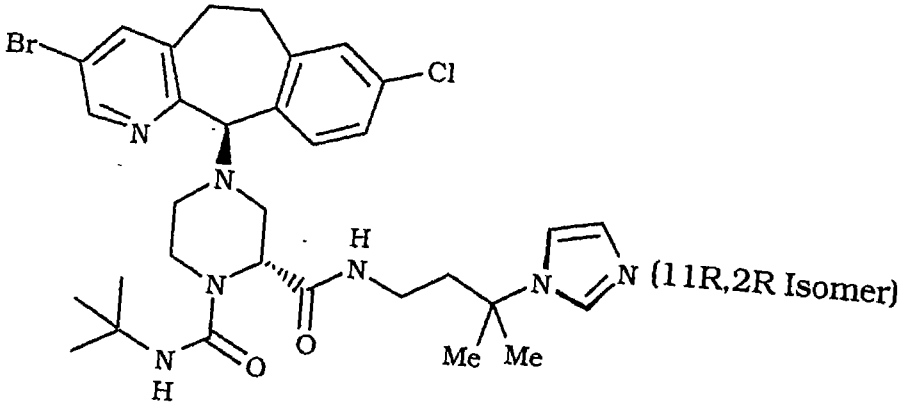


11R,2R isomer (Example 9);



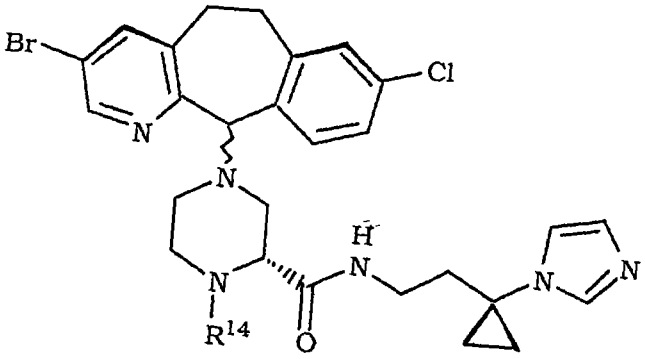
(11S,2R Isomer)

(Example 10);

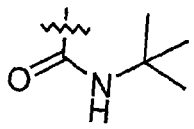


(11R,2R Isomer)

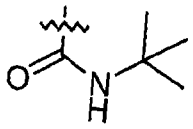
(Example 11);



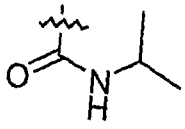
comprising: wherein R^{14} is selected from the group



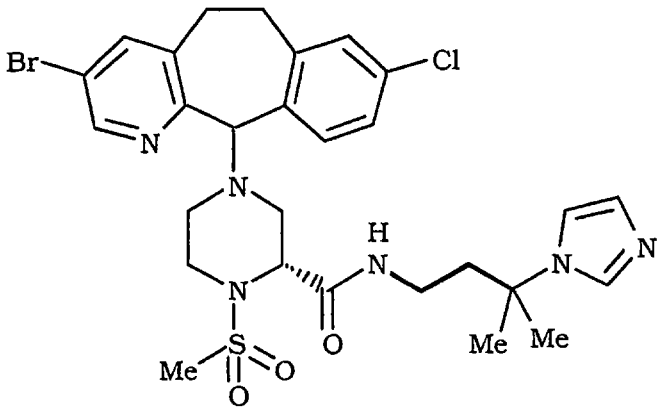
11S,2R isomer (Example 12);



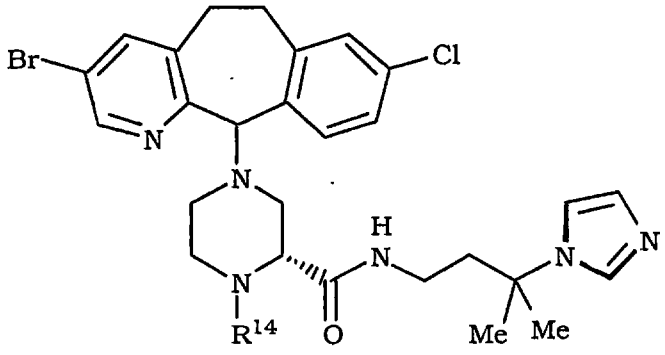
11R,2R isomer (Example 13); and



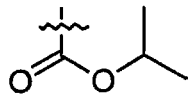
11R/S,2R isomers (Example 14);



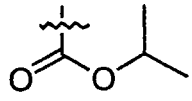
(Example 15);



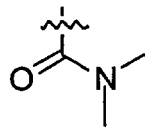
wherein R^{14} is selected from the group comprising:



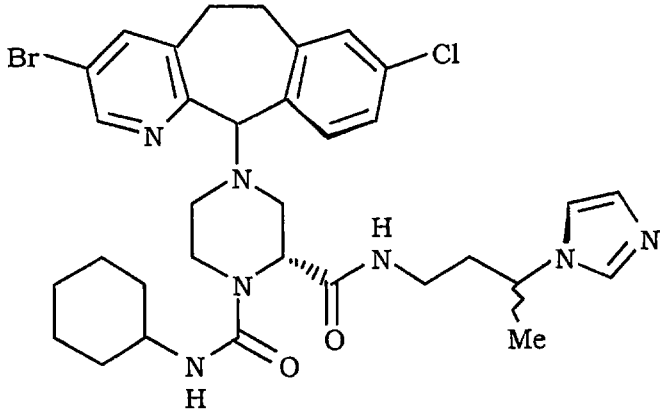
11S,2R isomer (Example 16);



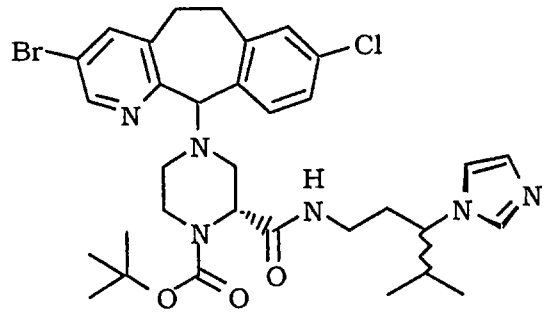
11R,2R isomer (Example 17); and



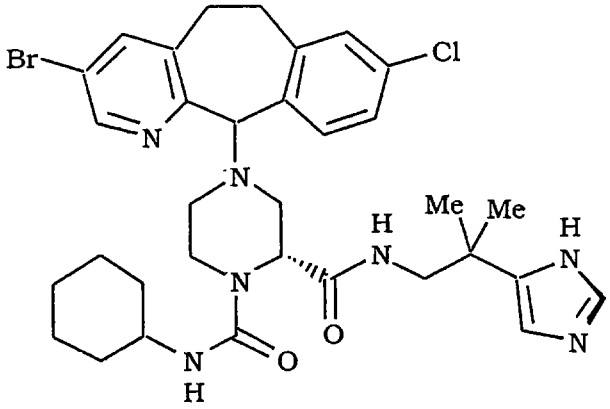
11R/S,2R isomers (Example 18);



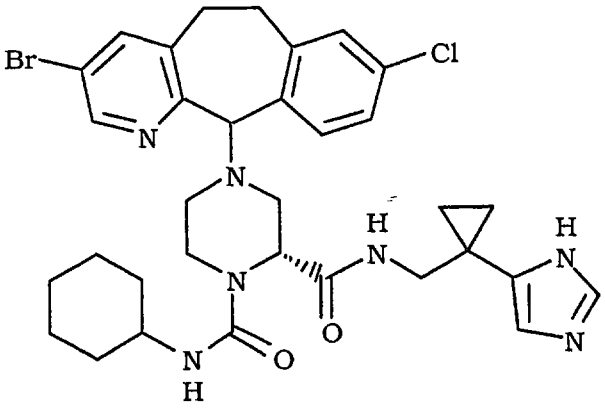
(Example 19);



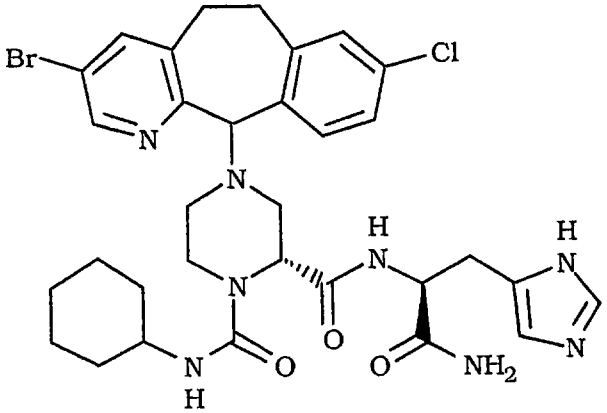
(Example 20);



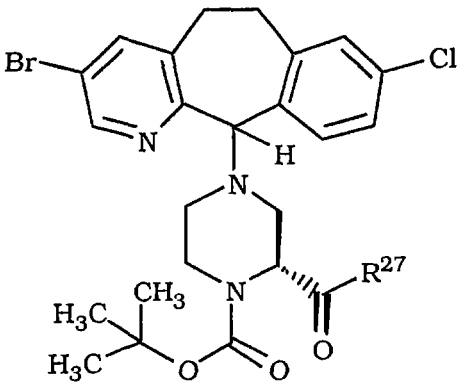
(Example 21);



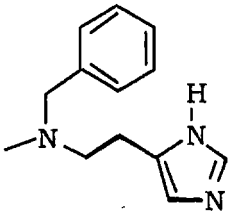
(Example 22);

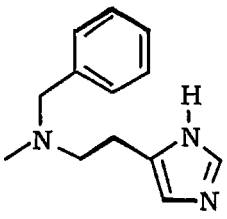


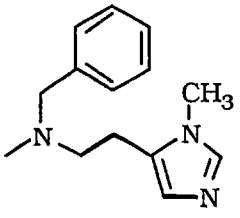
(Example 25);

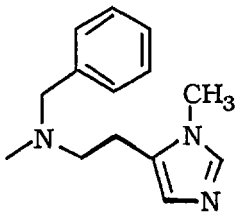


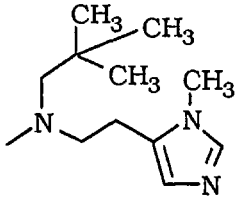
wherein R^{27} is selected from the group consisting of:

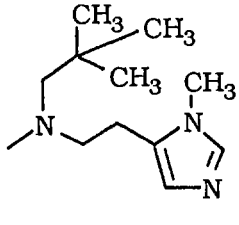
 Isomer A (Example 45);

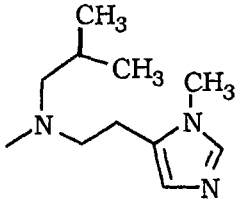
 Isomer B (Example 46);

 Isomer A (Example 47);

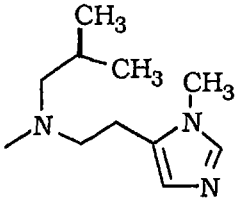
 Isomer B (Example 48);

 Isomer A (Example 49);

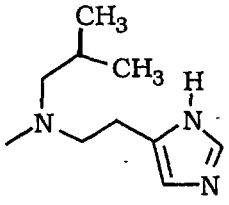
 Isomer B (Example 50);



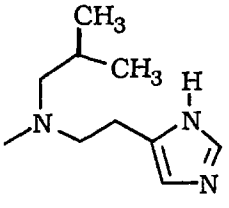
Isomer A (Example 51);



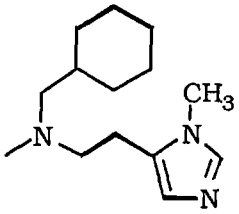
Isomer B (Example 52);



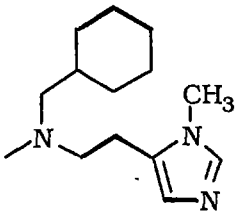
Isomer A (Example 53);



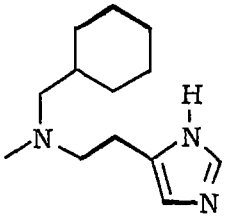
Isomer B (Example 54);



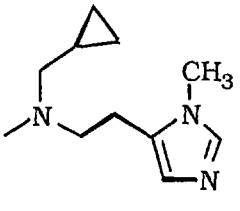
Isomer A (Example 55);



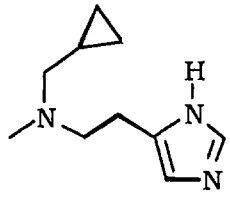
Isomer B (Example 56);



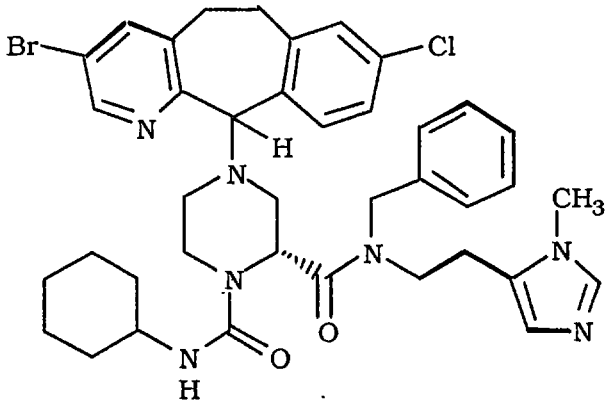
(Example 57);



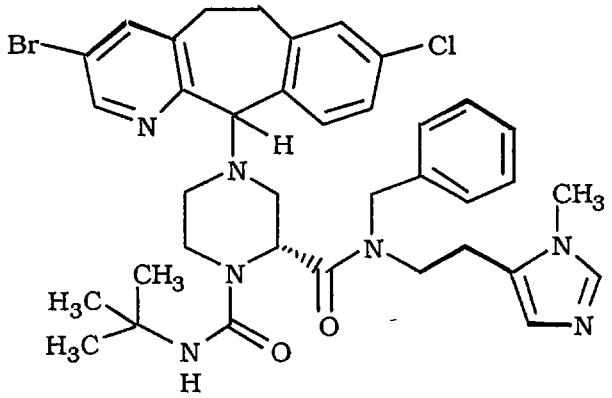
(Example 58); and



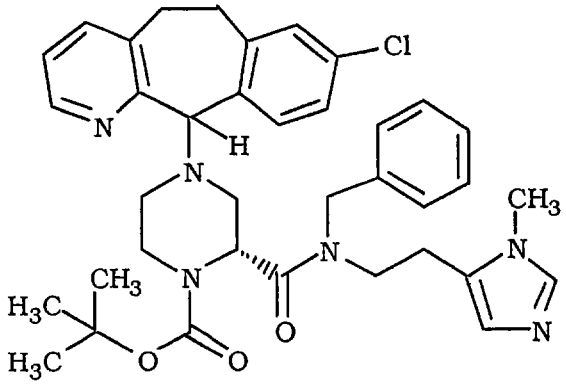
(Example 59);



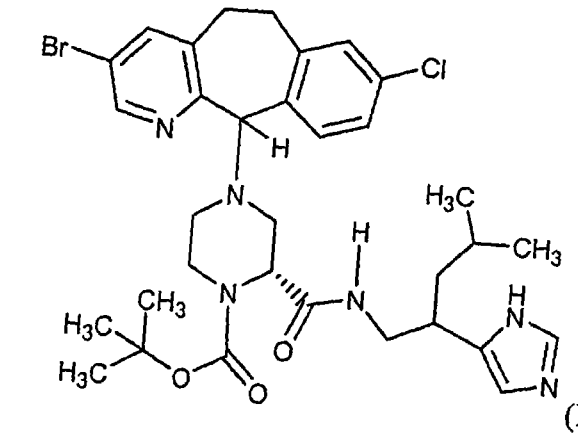
(Example 60);



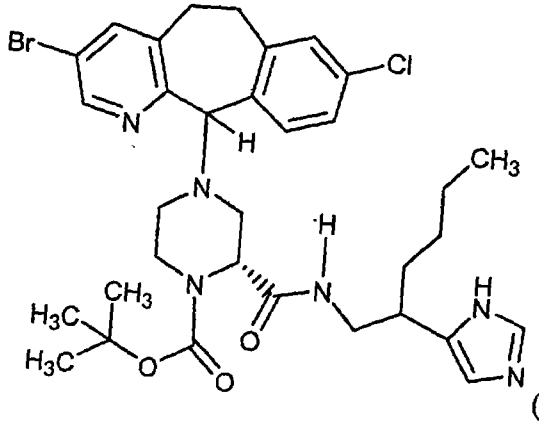
(Example 61);



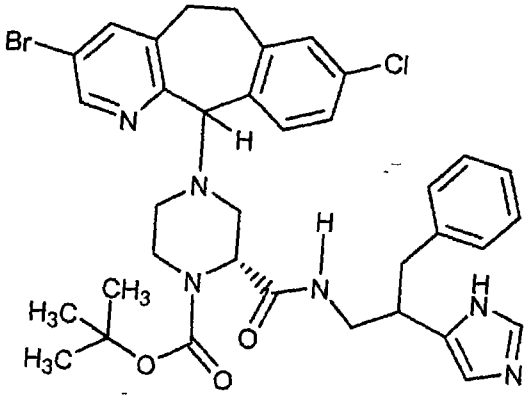
(Example 62);



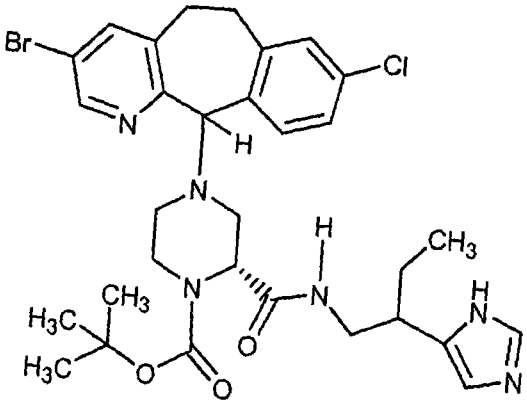
(Example 63);



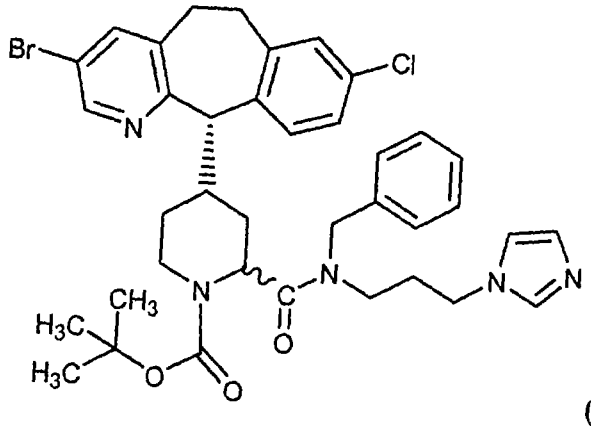
(Example 64);



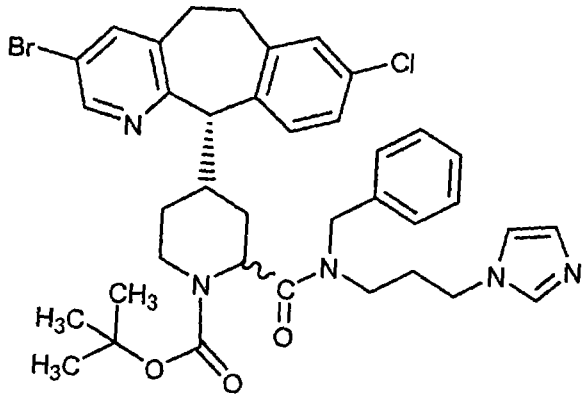
(Example 65);



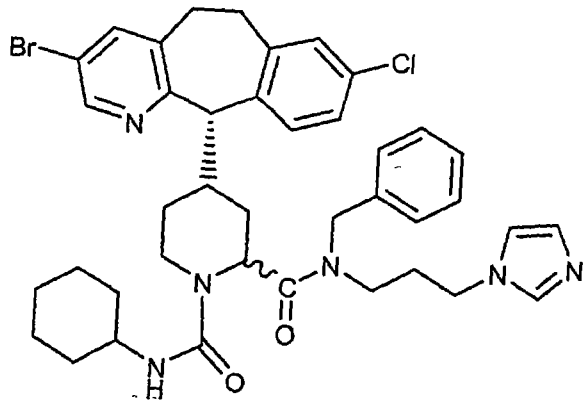
(Example 66);



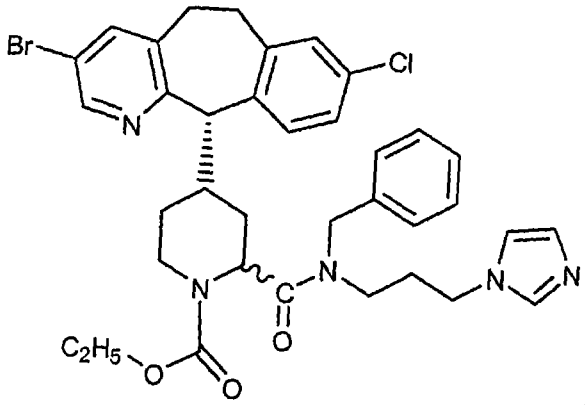
(Example 77);



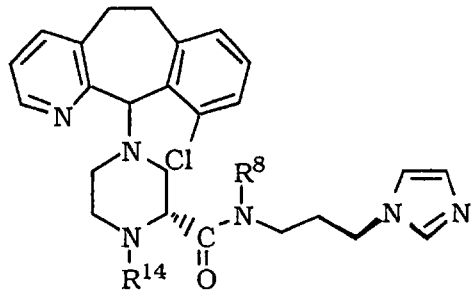
(Example 78 Step B);



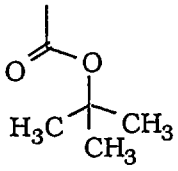
(Example 79);

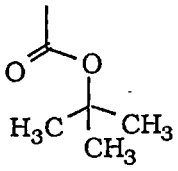


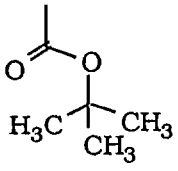
(Example 80);

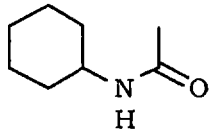


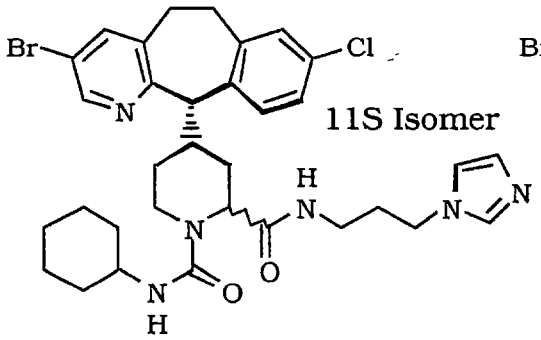
wherein R^8 is  and R^{14} is selected from the group consisting of:

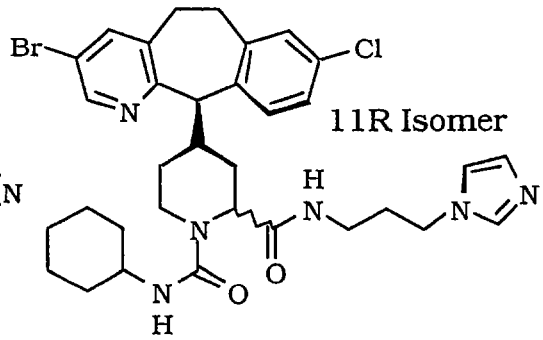
 (Example 82);

 Isomer A (R(+)) (Example 83);

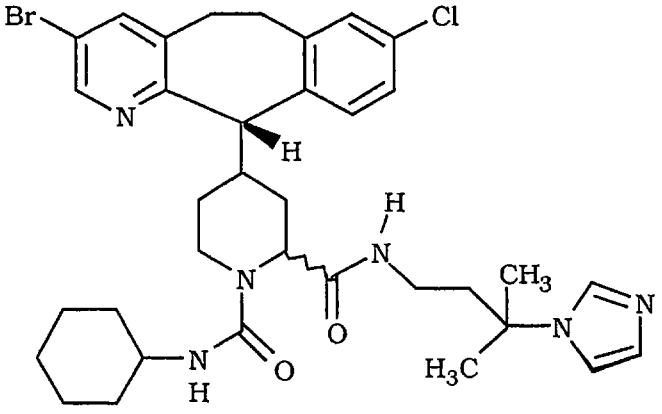
 Isomer B (S(-)) (Example 84); and

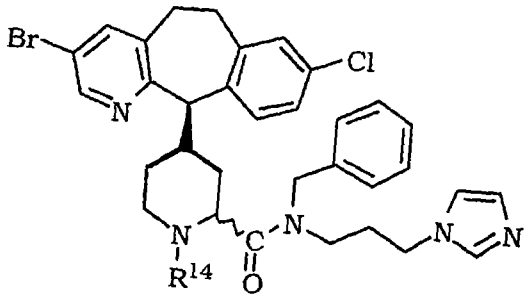
 (Example 85);



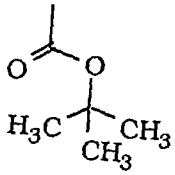


(Example 86);

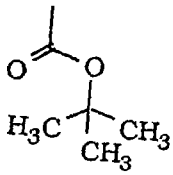
 (Example 86A);



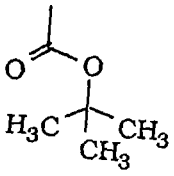
wherein R^{14} is selected from the group consisting of:



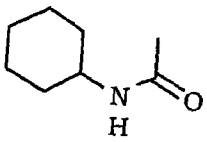
Isomers A, B, C, D (Example 87);



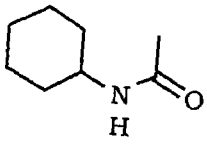
Isomer A (Example 88);



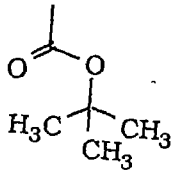
Isomer B (Example 89);



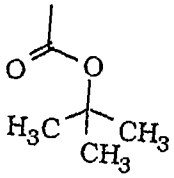
Isomer A (Example 90);



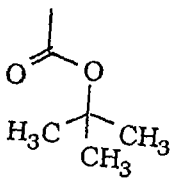
Isomer B (Example 91);



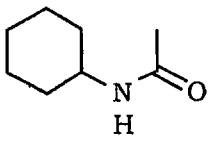
Isomer C (Example 92);



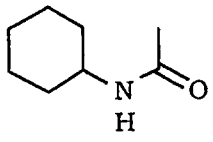
Isomer D (Example 93);



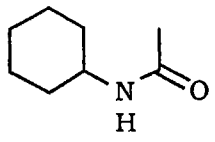
Isomer C, D (Example 94);



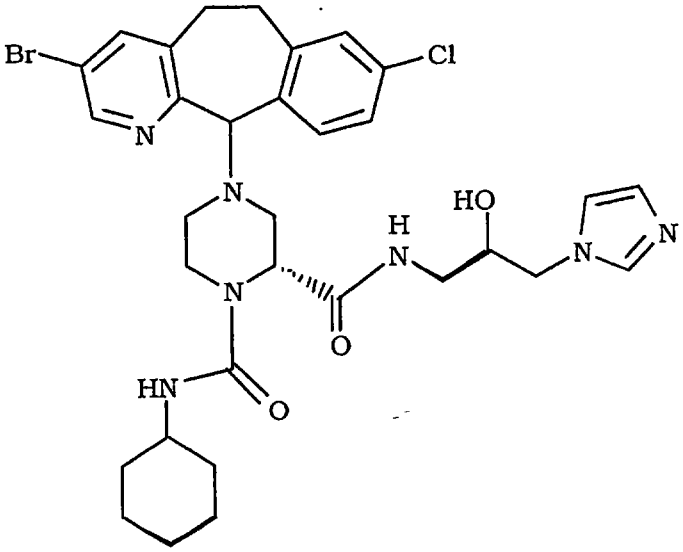
Isomer C (Example 95);



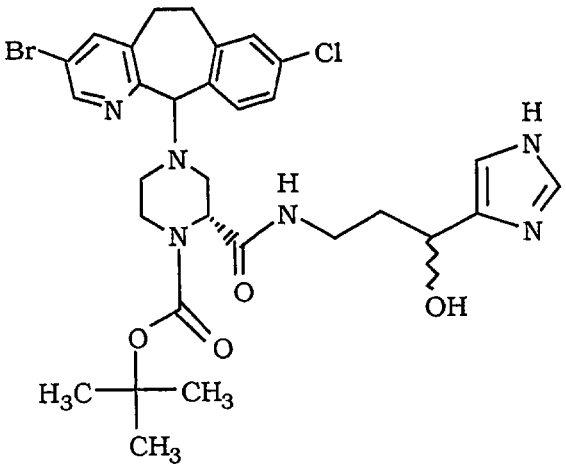
Isomer D (Example 96); and



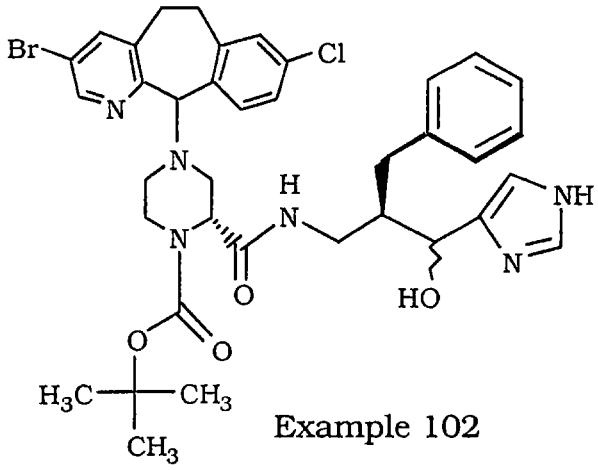
Isomers C, D (Example 97);



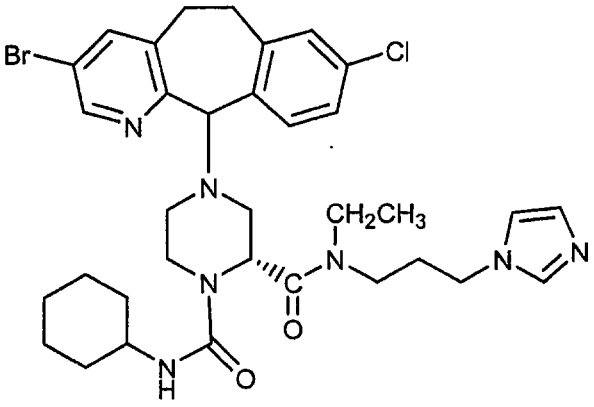
(Example 99);



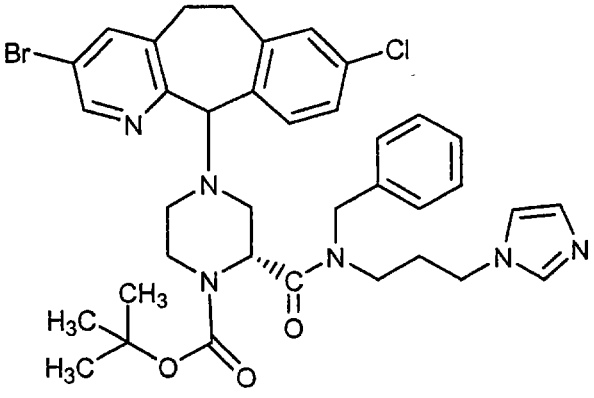
(Example 100);



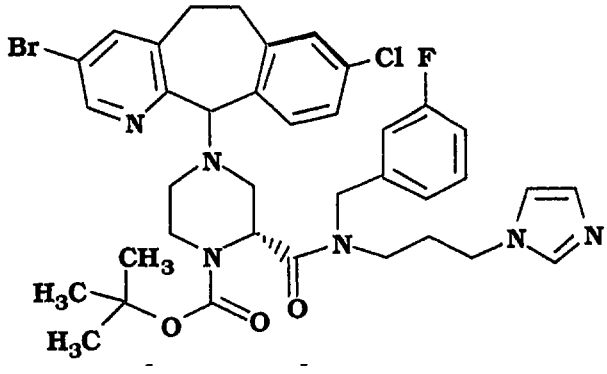
Example 102 ;



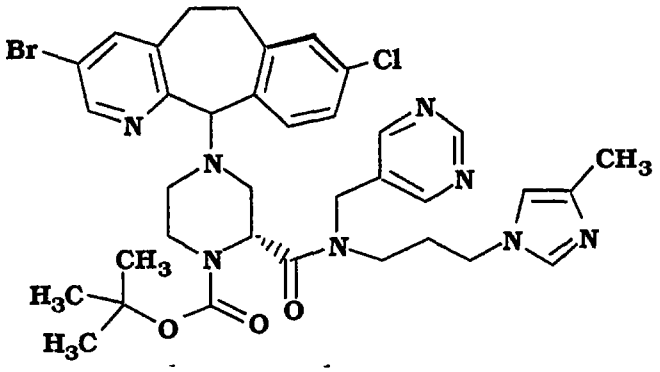
(Example 112);



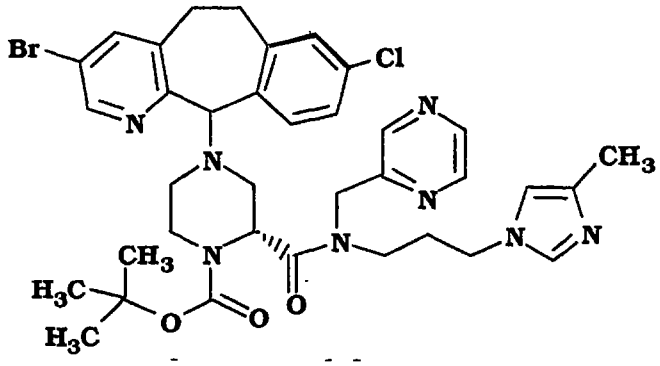
(Example 113);



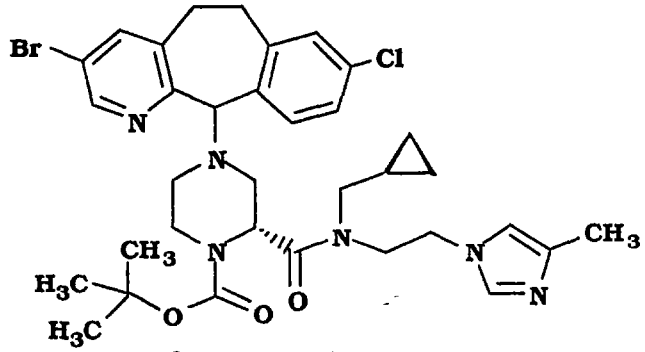
(Compound A Example 114);



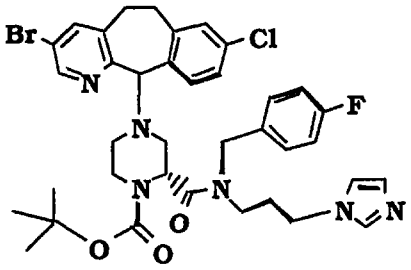
(Compound B Example 114);



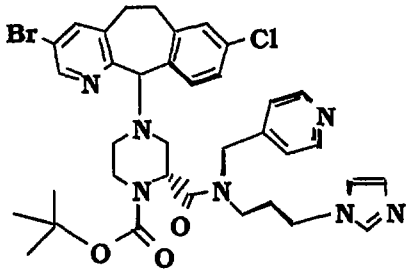
(Compound C Example 114);



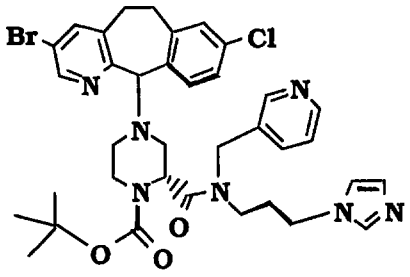
(Compound D Example 114);



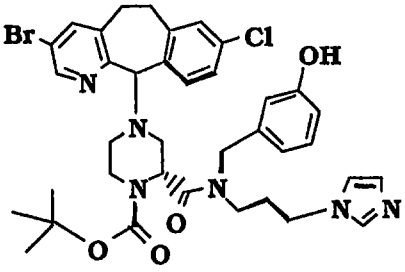
(Example 115);



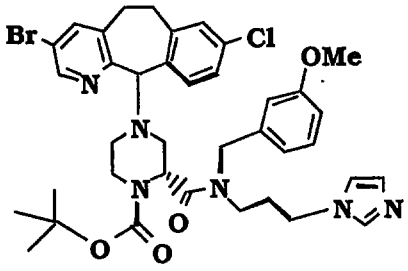
(Example 116);



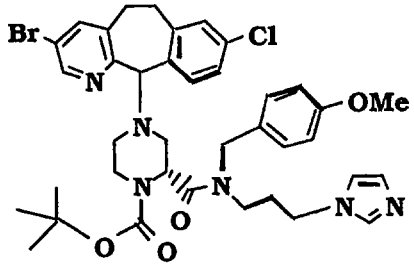
(Example 117);



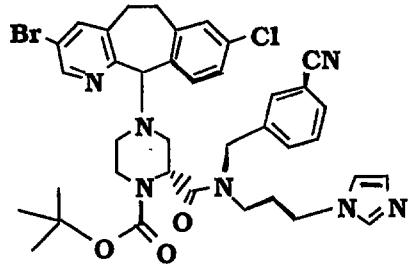
(Example 118);



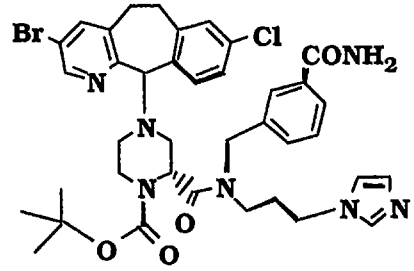
(Example 119);



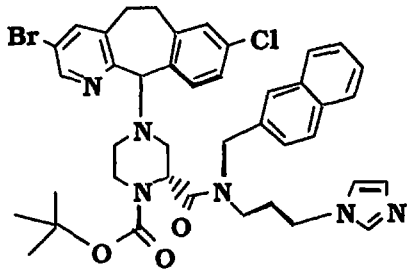
(Example 120);



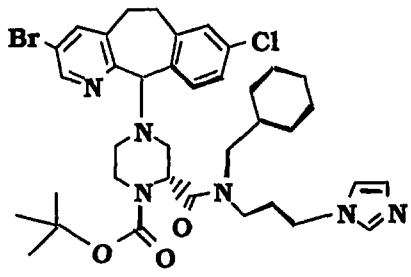
(Example 121);



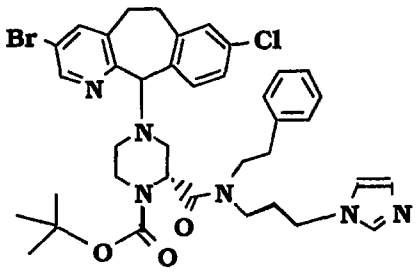
(Example 122);



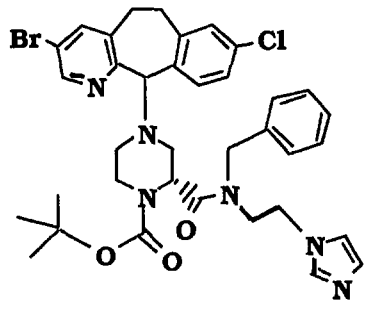
(Example 123);



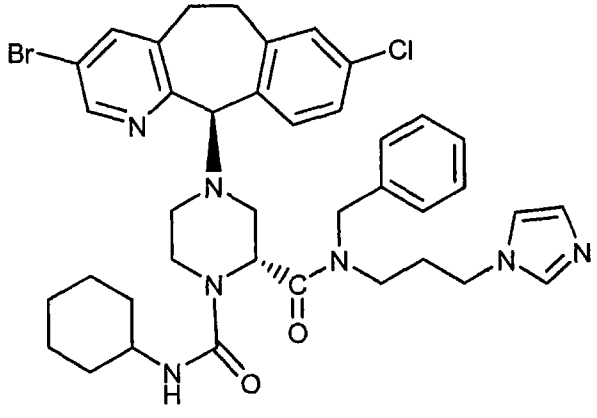
(Example 124);



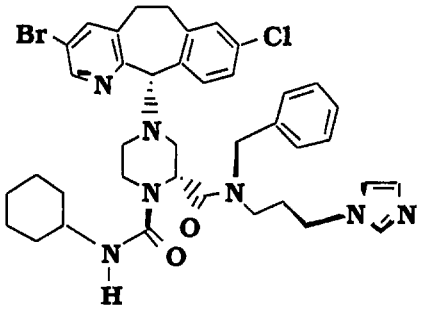
(Example 125);



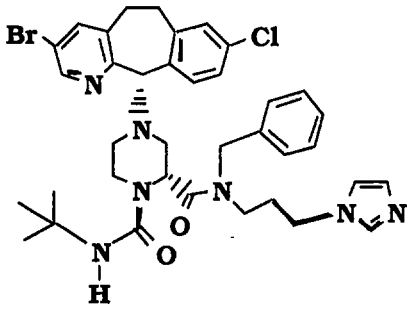
(Example 126);



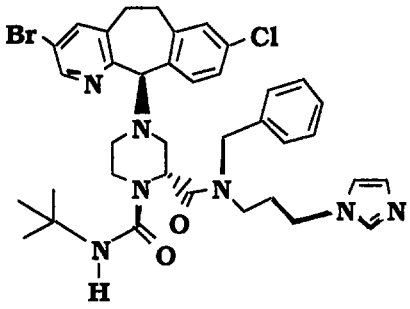
(Example 127);



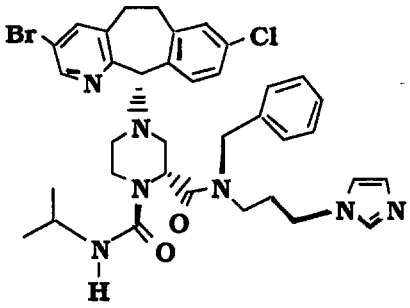
(Example 128);



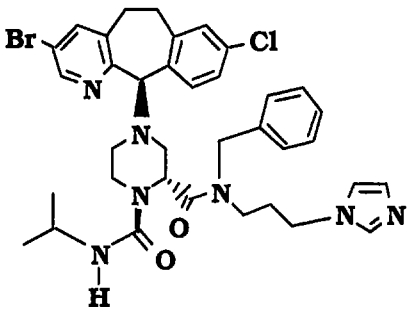
(Example 129);



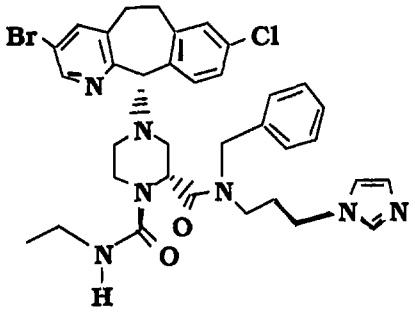
(Example 130);



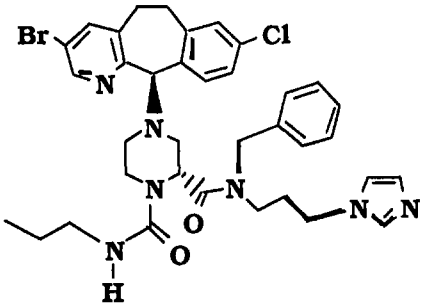
(Example 131);



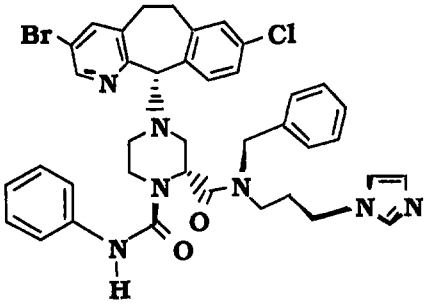
(Example 132);



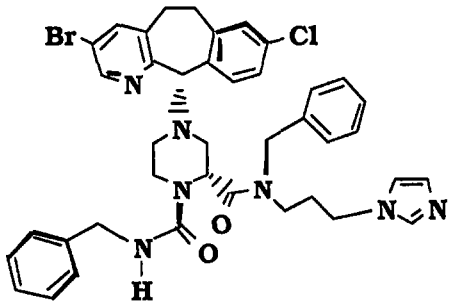
(Example 133);



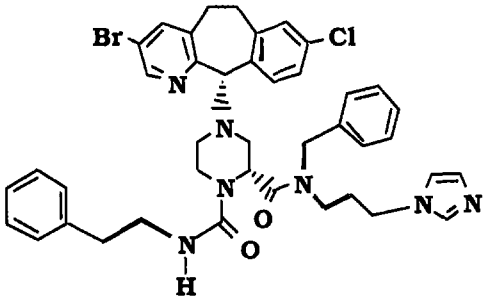
(Example 134);



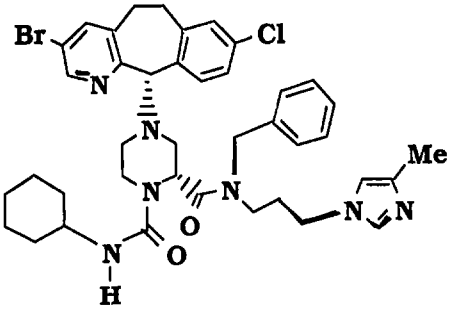
(Example 135);



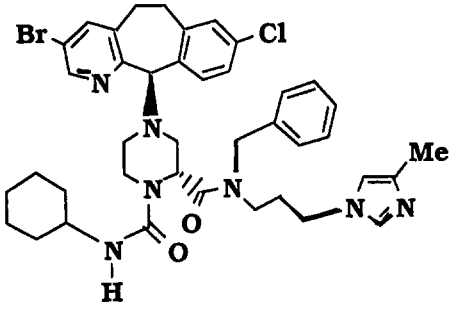
(Example 136);



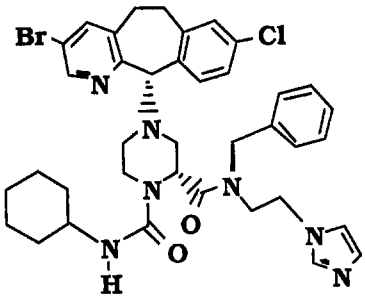
(Example 137);



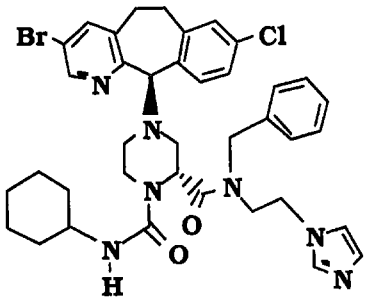
(Example 138);



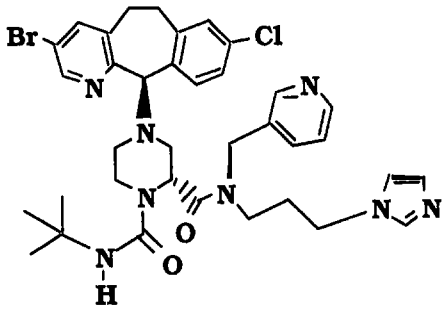
(Example 139);



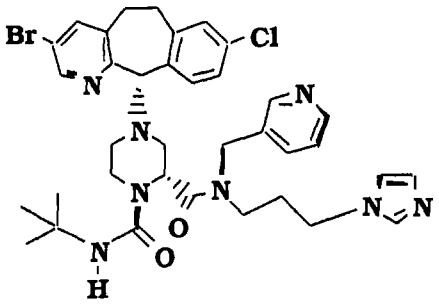
(Example 140);



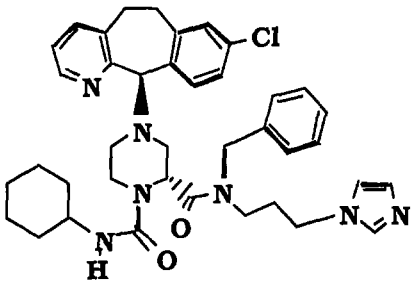
(Example 141);



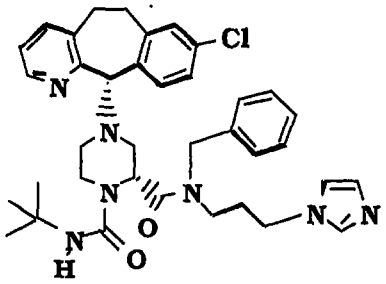
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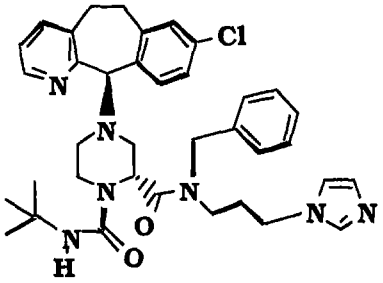
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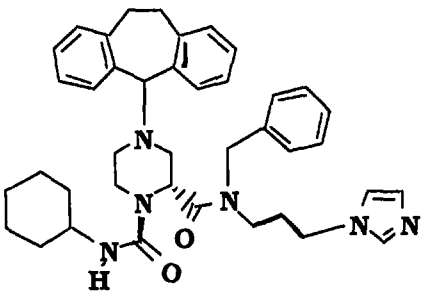
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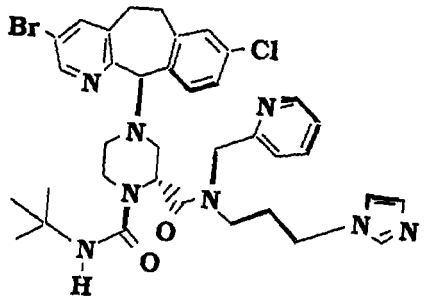
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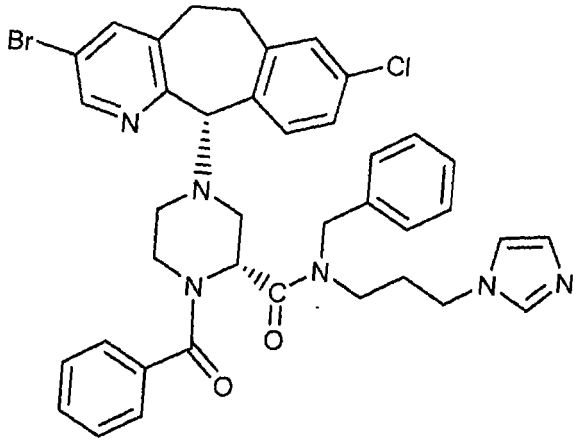
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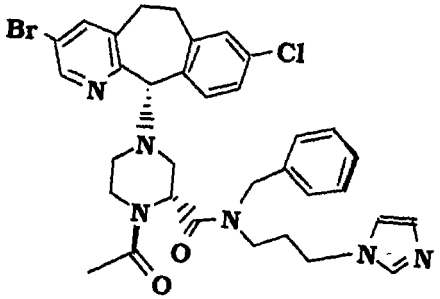
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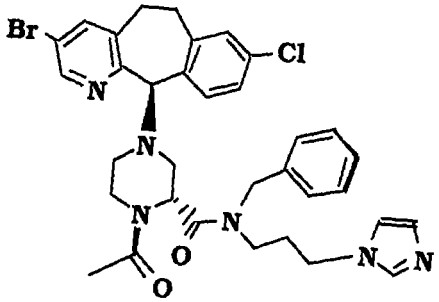
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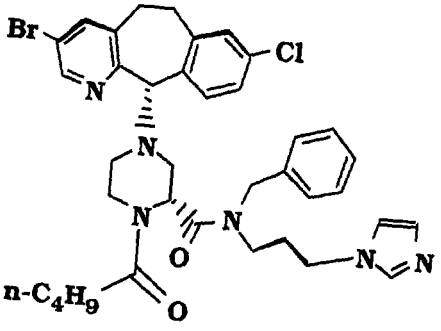
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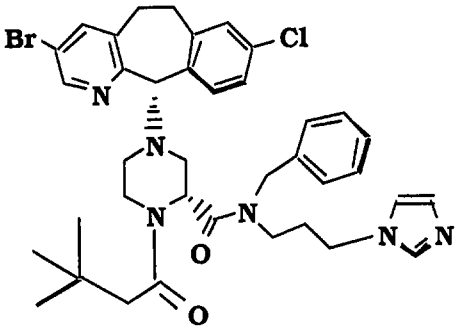
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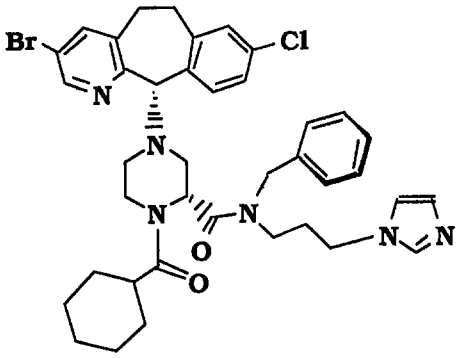
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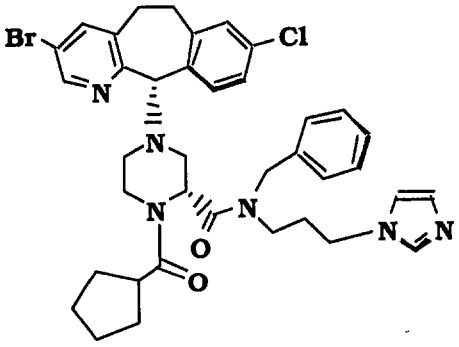
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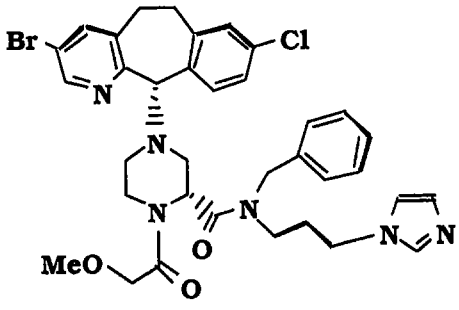
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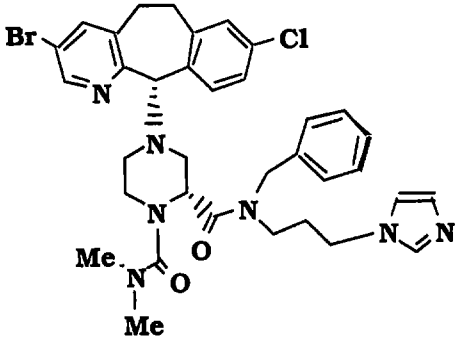
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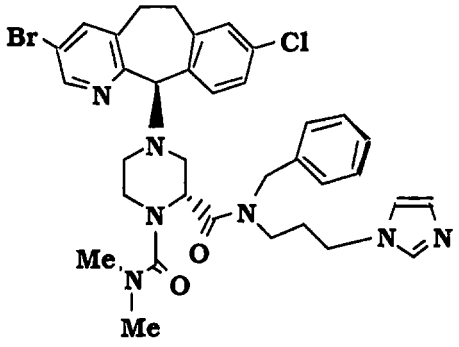
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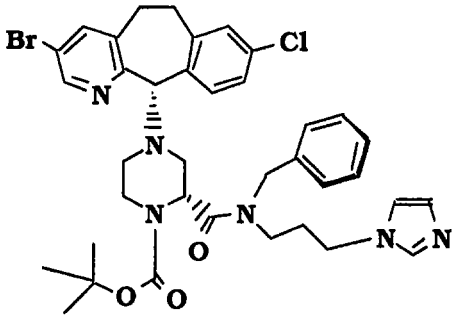
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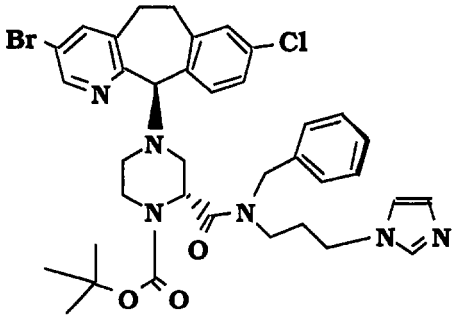
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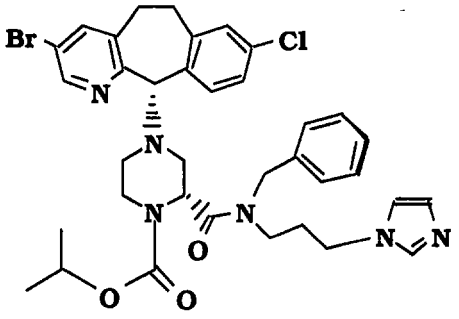
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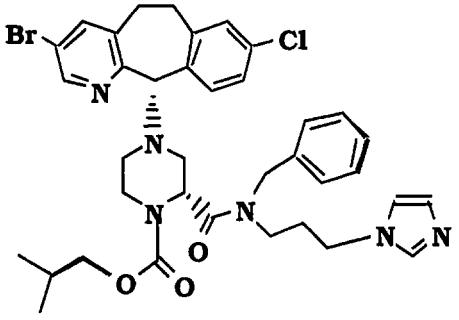
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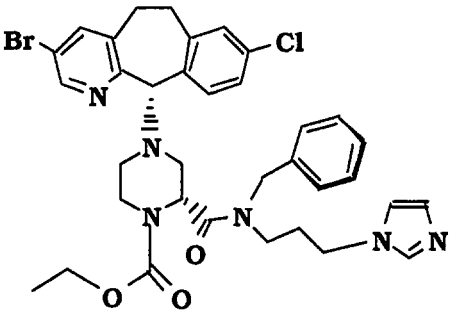
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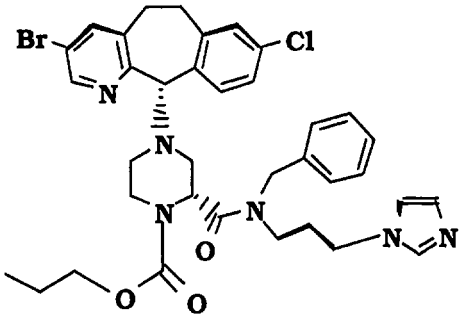
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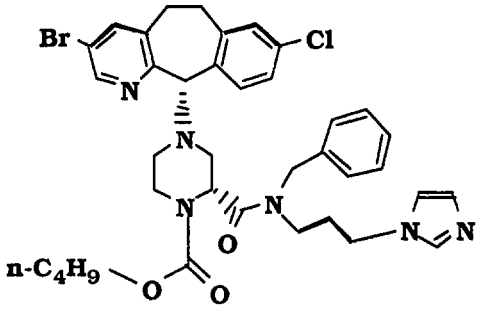
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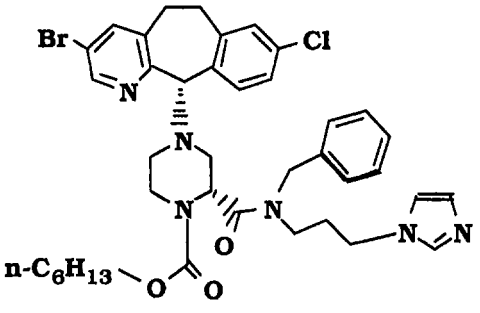
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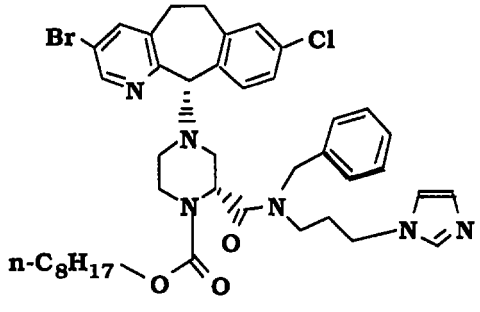
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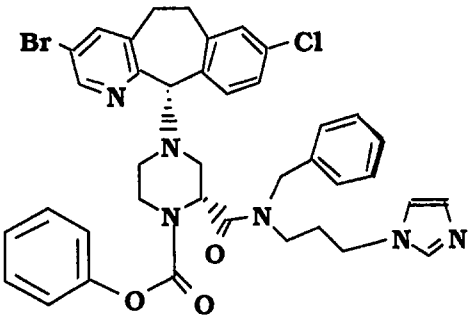
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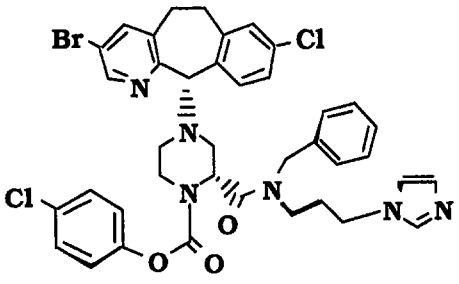
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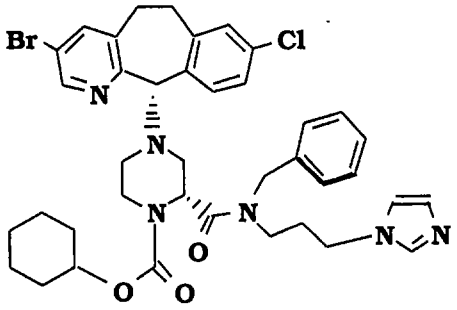
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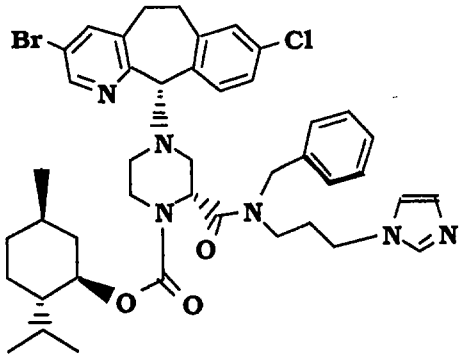
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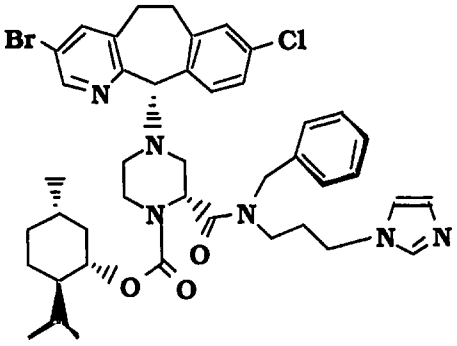
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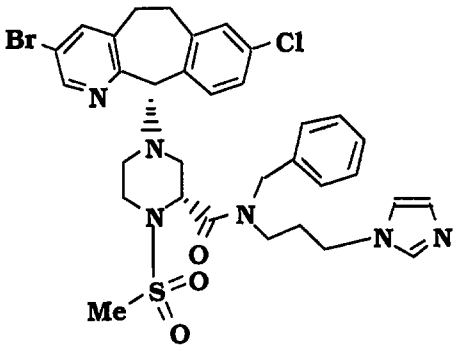
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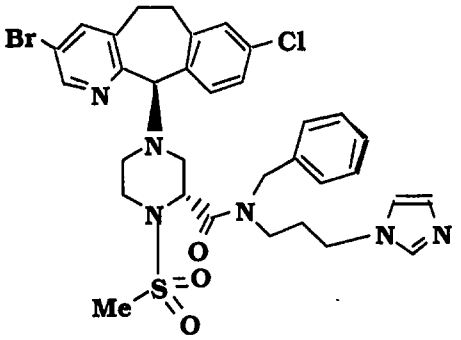
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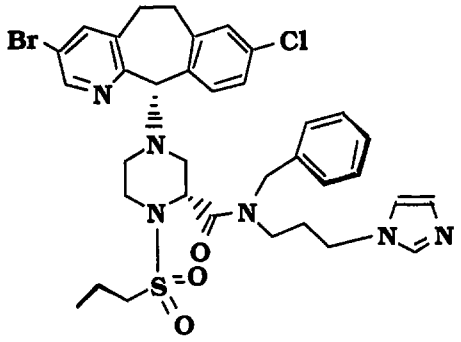
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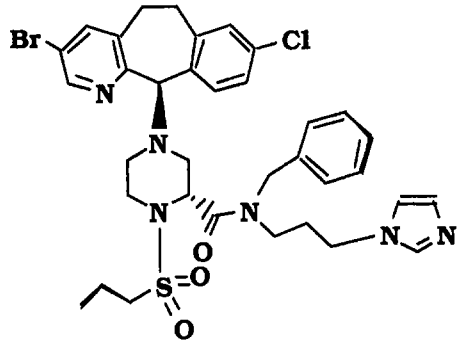
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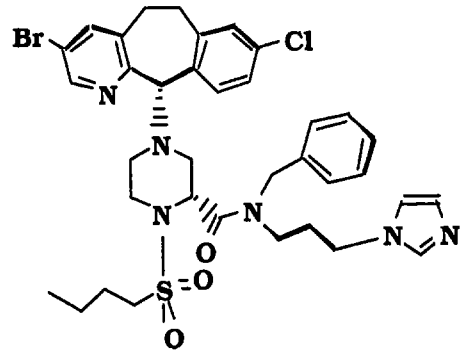
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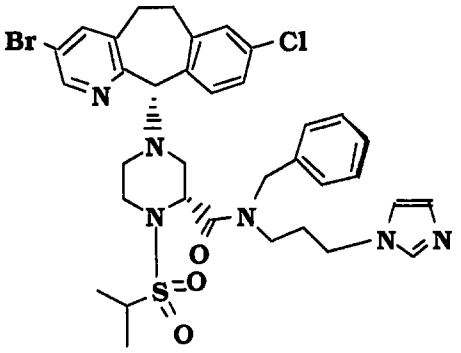
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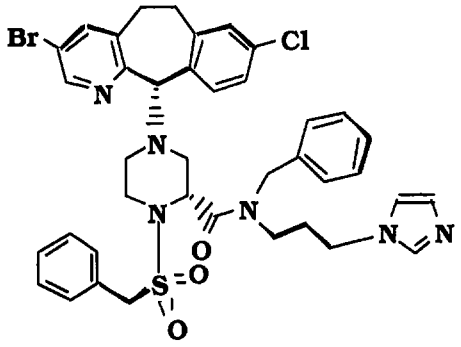
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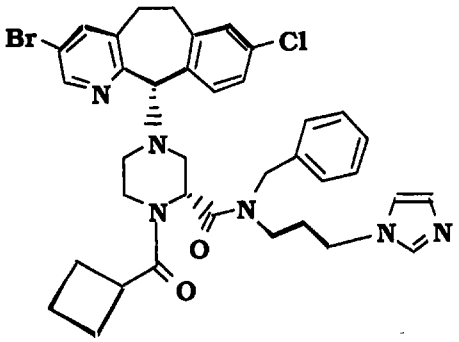
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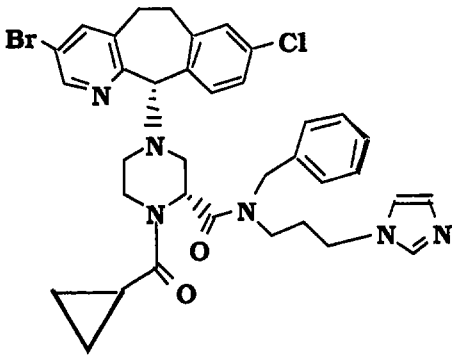
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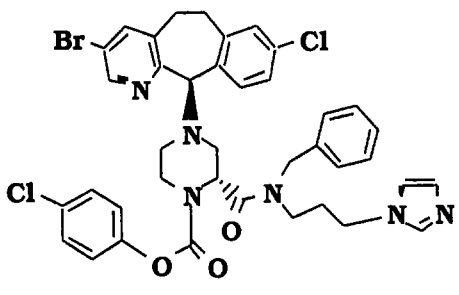
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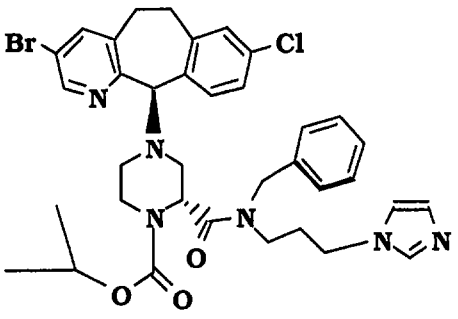
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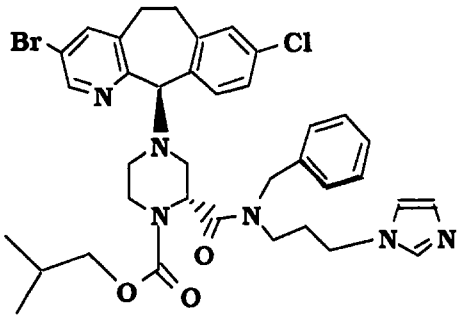
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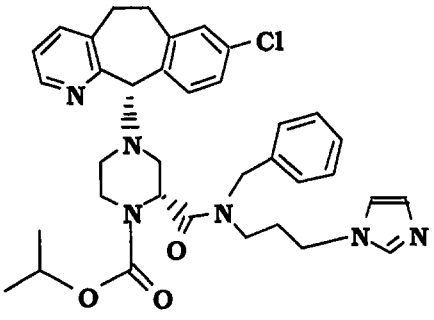
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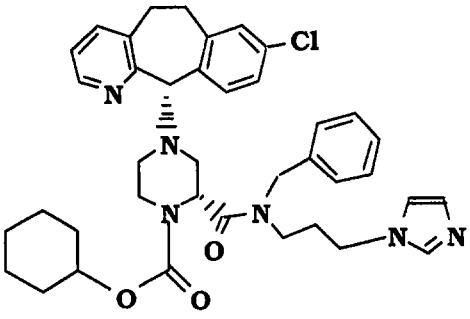
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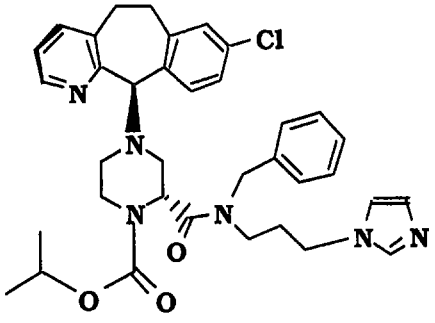
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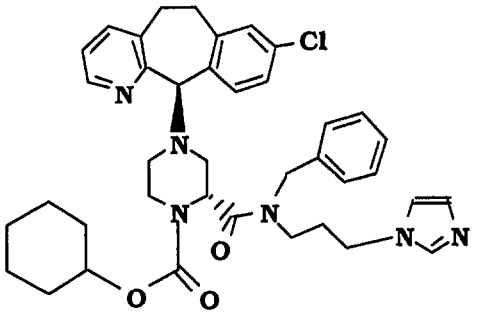
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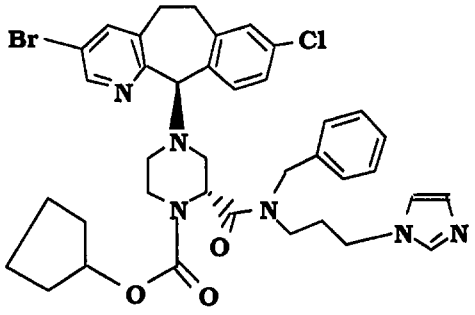
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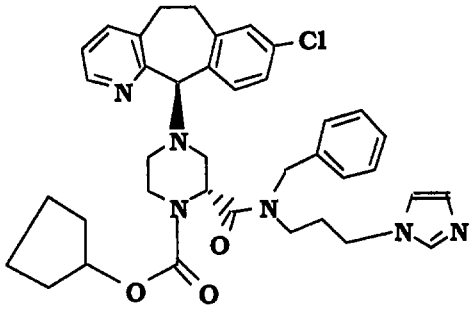
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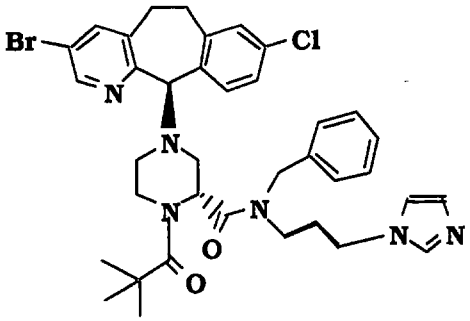
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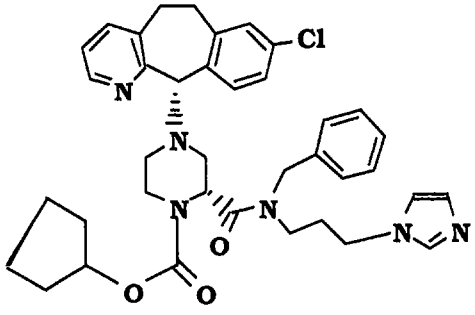
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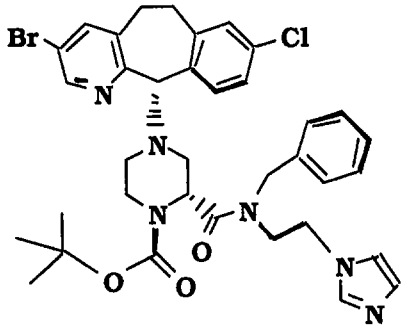
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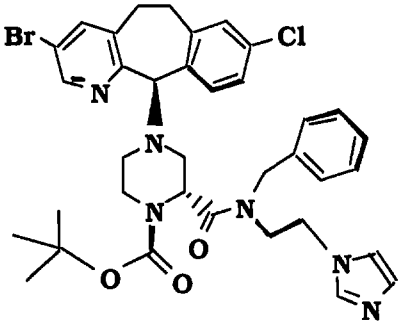
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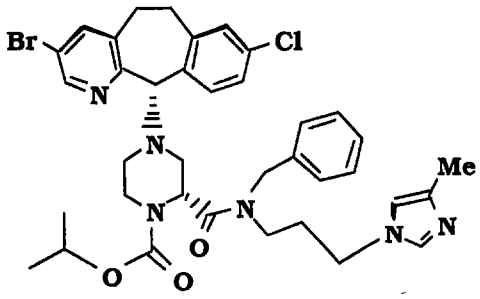
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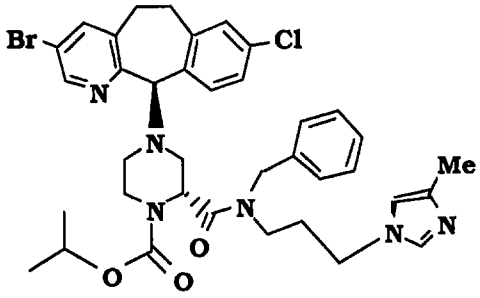
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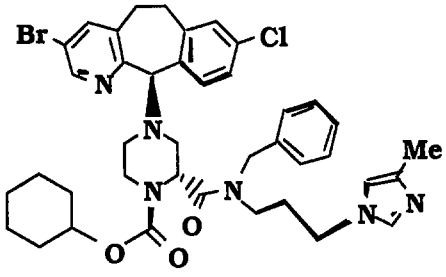
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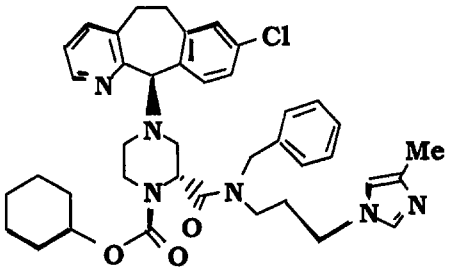
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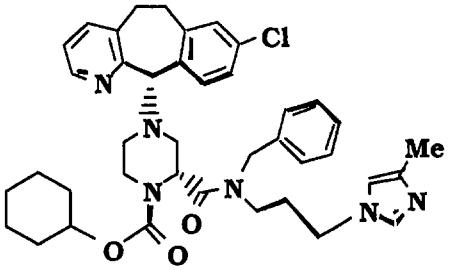
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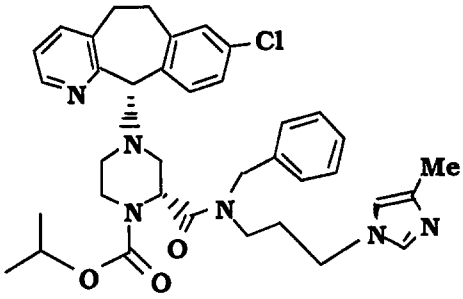
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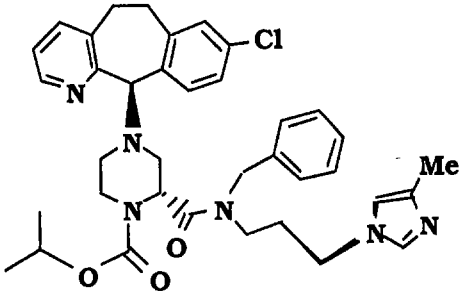
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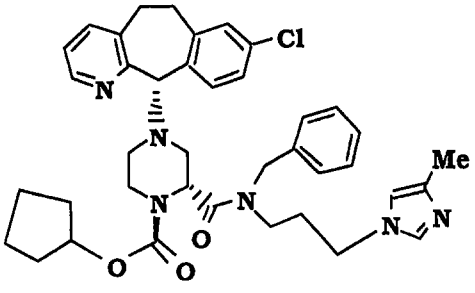
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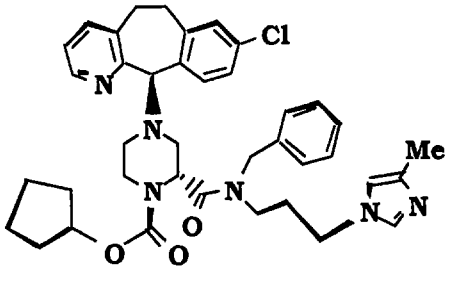
(Example 200);



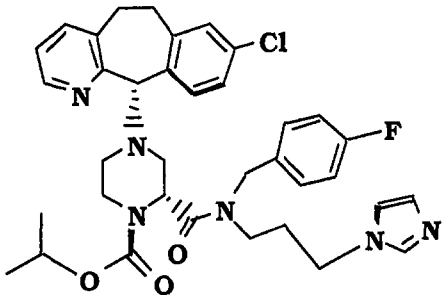
(Example 201);



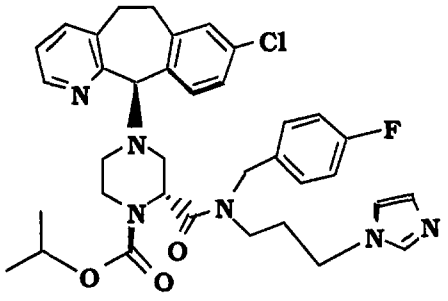
(Example 202);



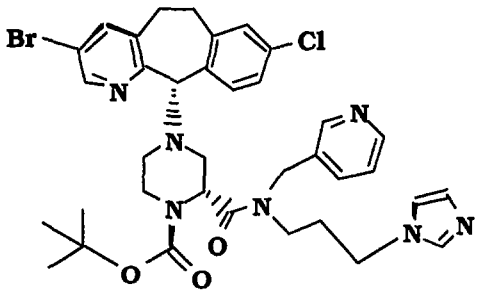
(Example 203);



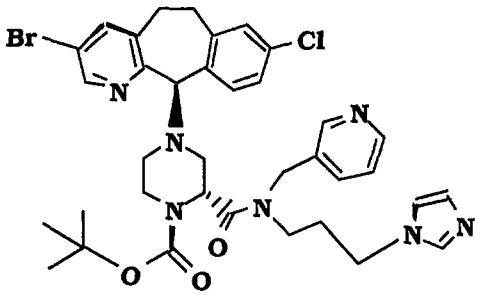
(Example 204);



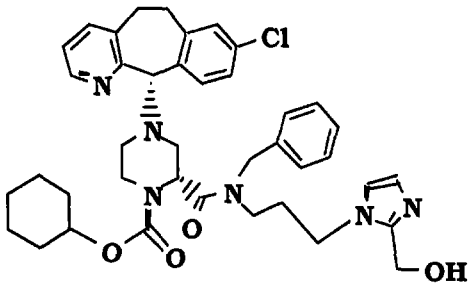
(Example 205);



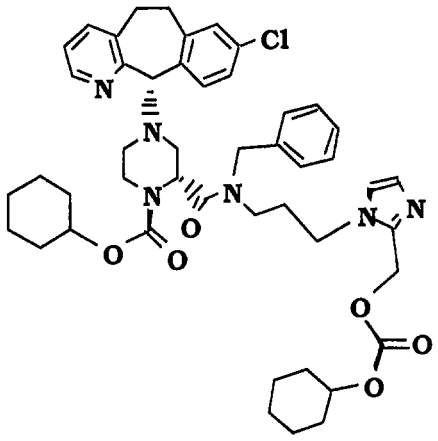
(Example 206);



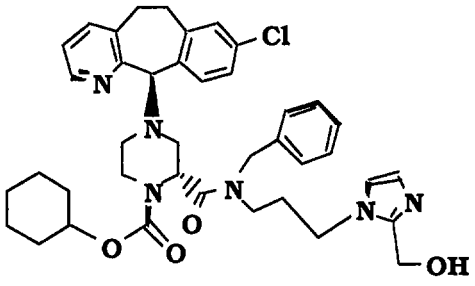
(Example 207);



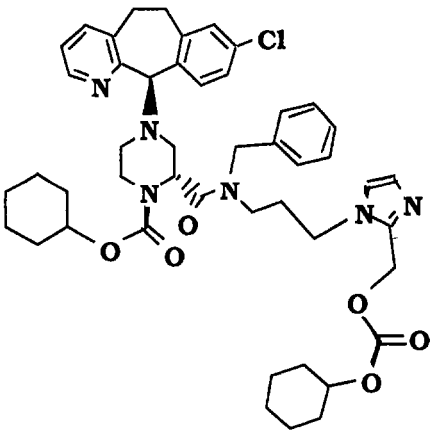
(Example 208);



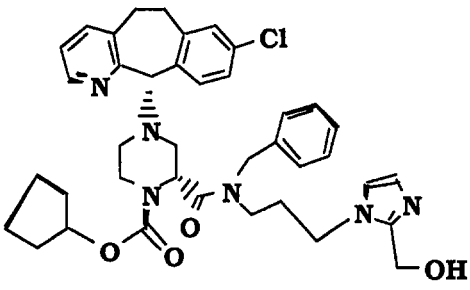
(Example 208A);



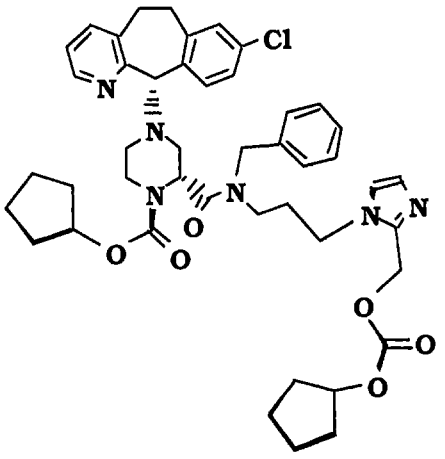
(Example 209);



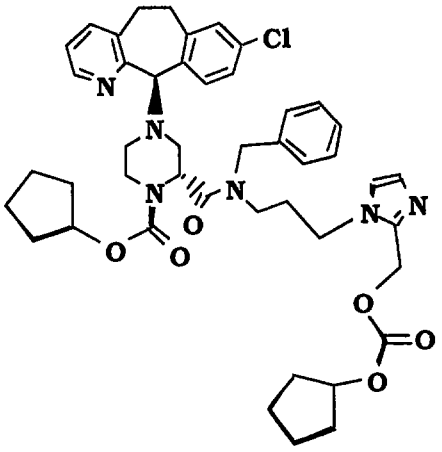
(Example 209A);



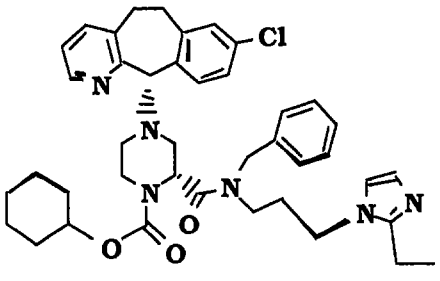
(Example 210);



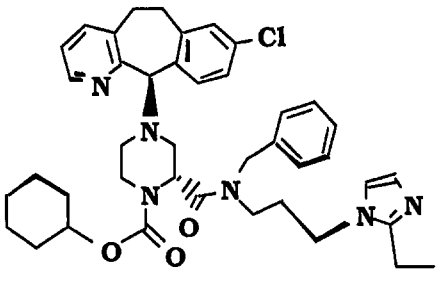
(Example 210A);



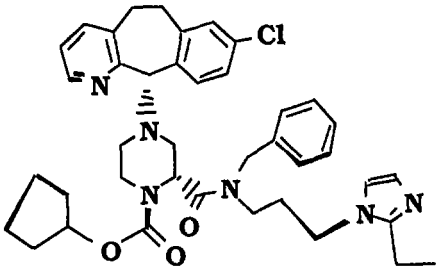
(Example 210B);



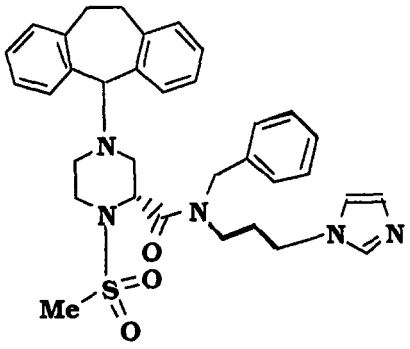
(Example 211);



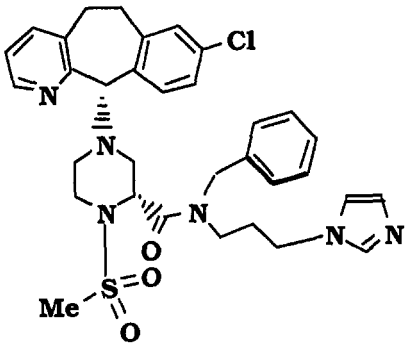
(Example 212);



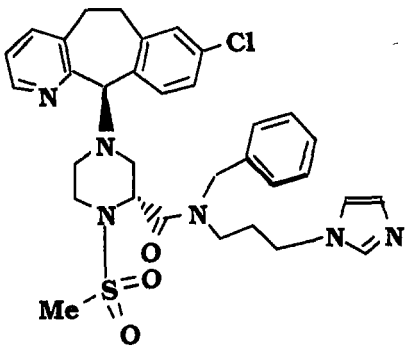
(Example 213);



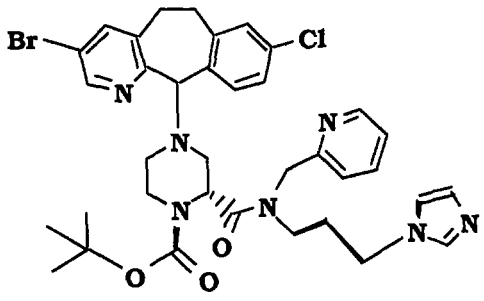
(Example 214);



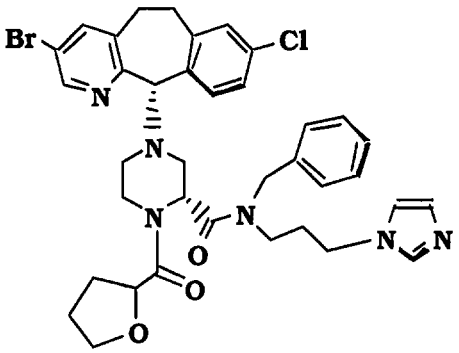
(Example 215);



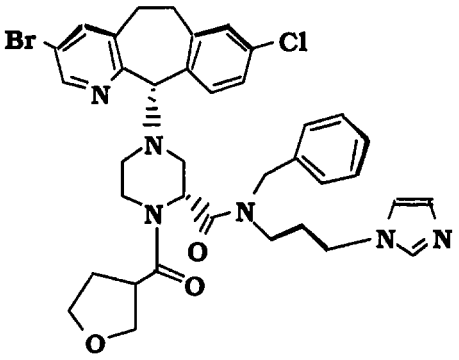
(Example 216);



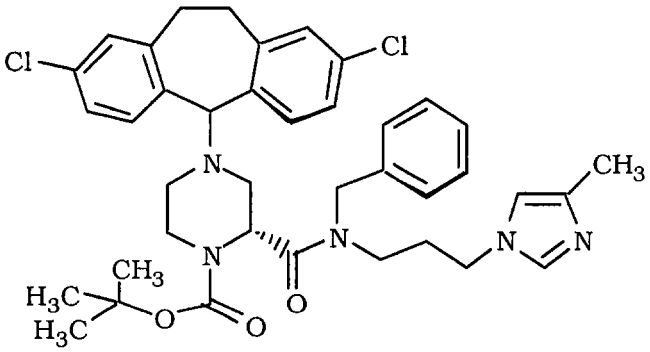
(Example 217);



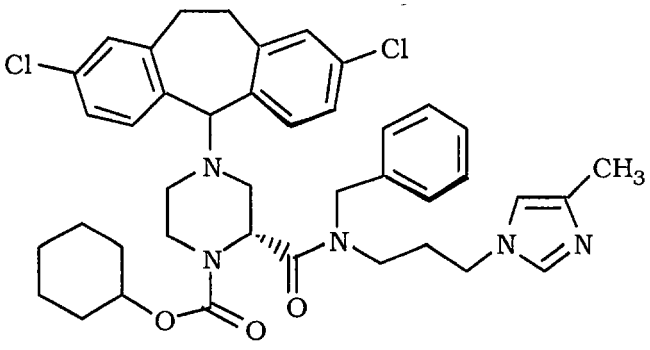
(Example 218);



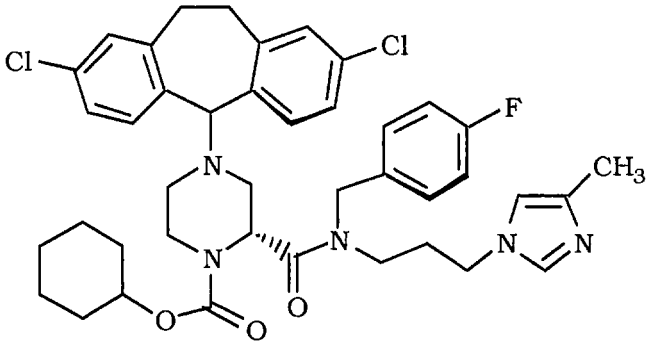
(Example 219);



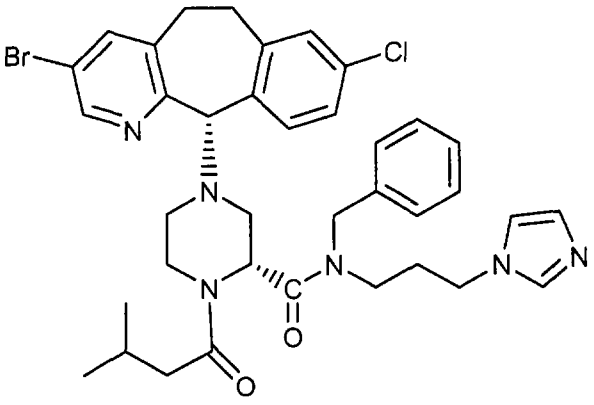
(Example 220);



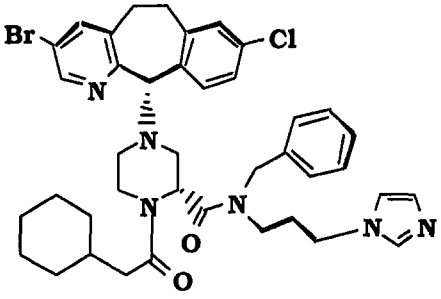
(Example 220);



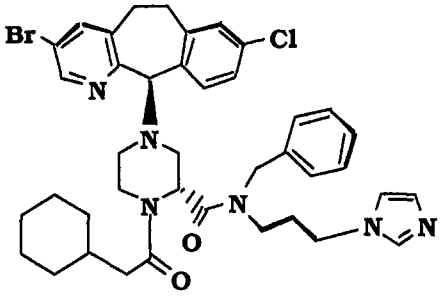
(Example 220A);



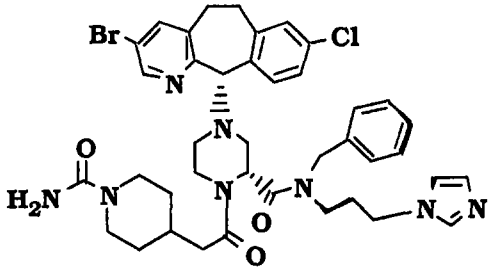
(Example 221);



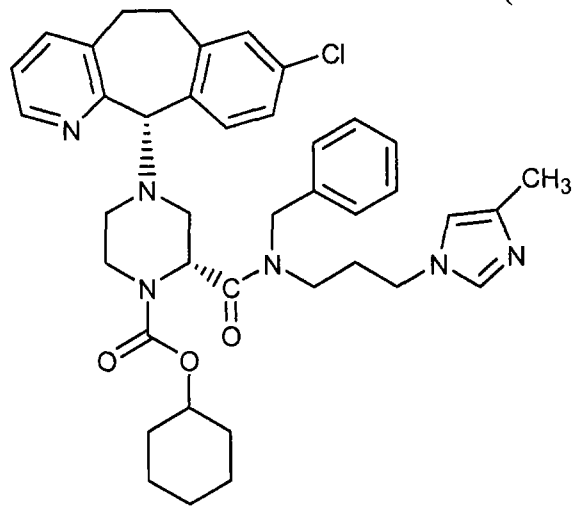
(Example 222);



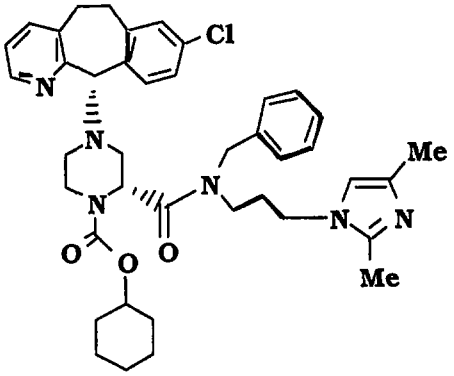
(Example 223);



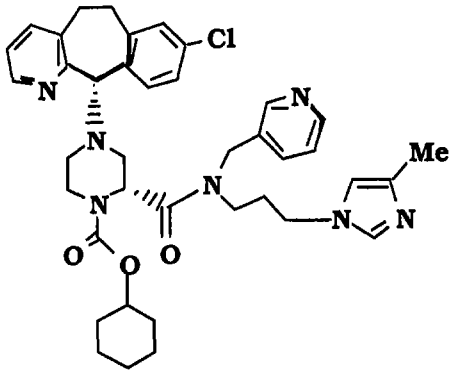
(Example 224);



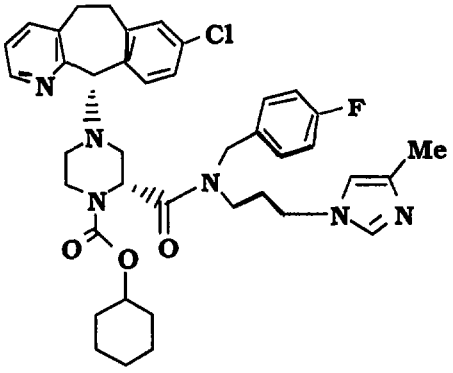
(Example 225);



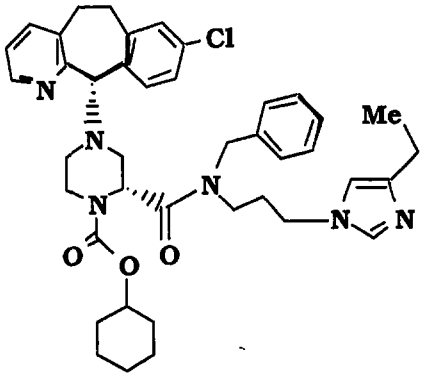
(Example 226);



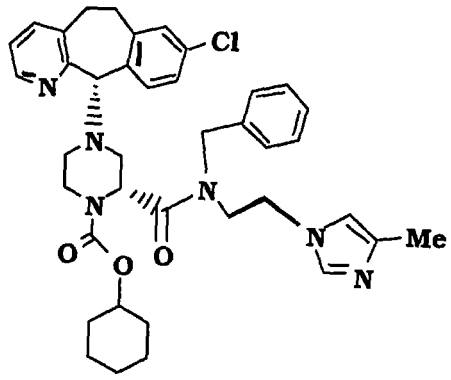
(Example 227);



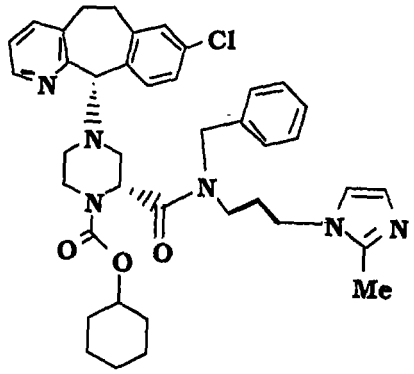
(Example 228);



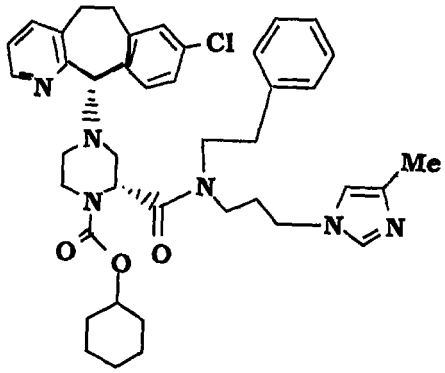
(Example 229);



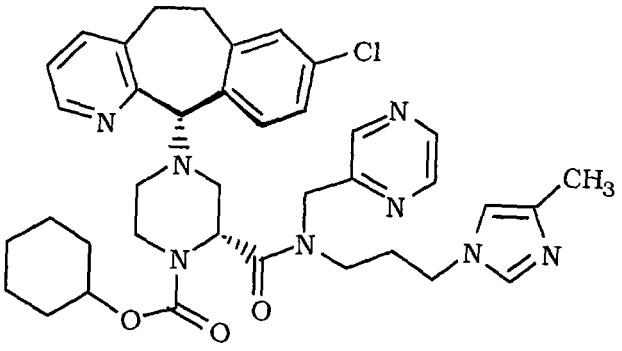
(Example 230);



(Example 231);

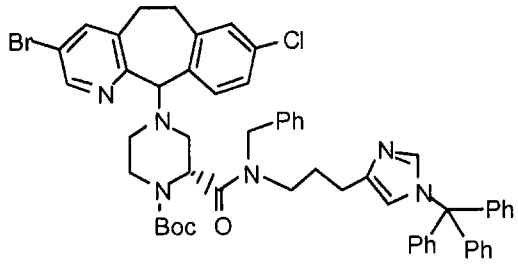


(Example 232);

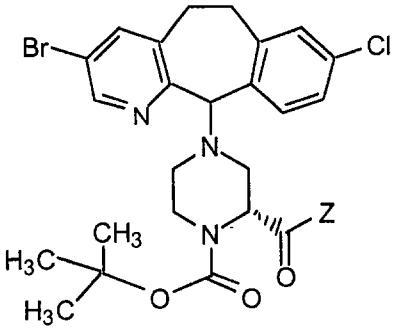


Example 234B

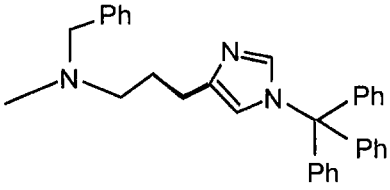
;



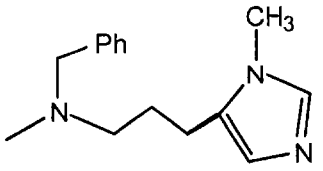
(Example 235);



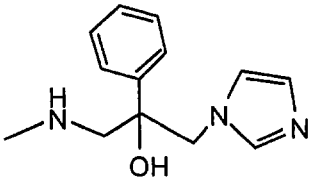
wherein Z is selected from the group consisting of:



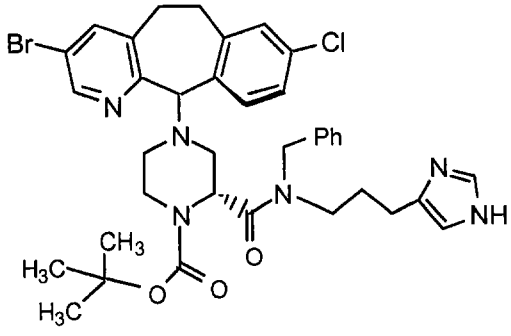
(Example 236);



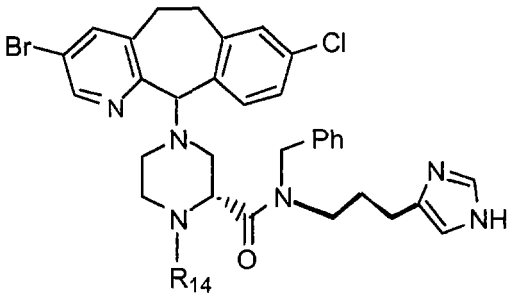
(Example 237); and



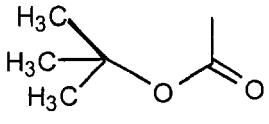
(Example 238);

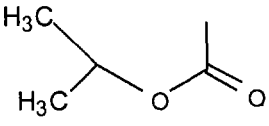


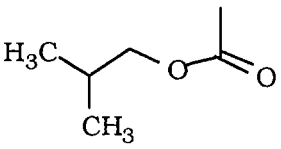
(Example 239);

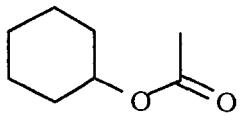


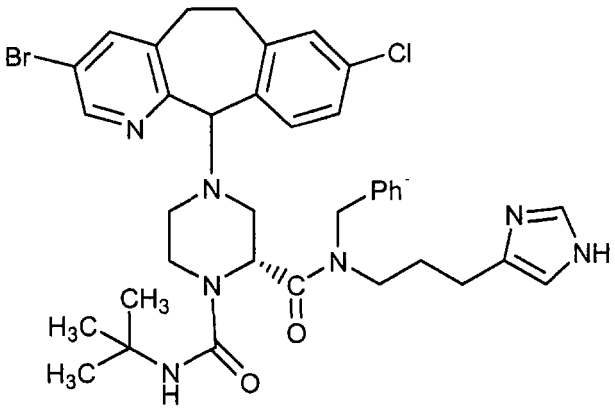
wherein R^{14} is selected from the group consisting of:

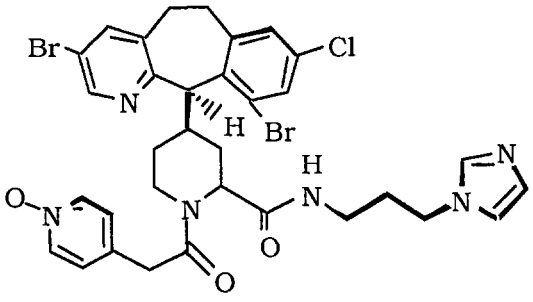
 (R, S) (Example 240);

 (R, S) (Example 241);

 (R, S) (Example 242); and

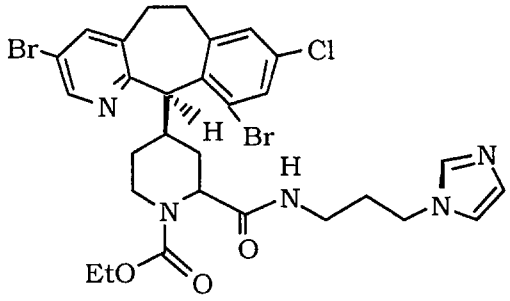
 (R, S) (Example 243);

 (Example 244);

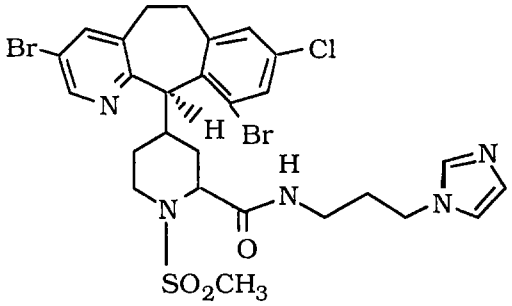


(Example 247)

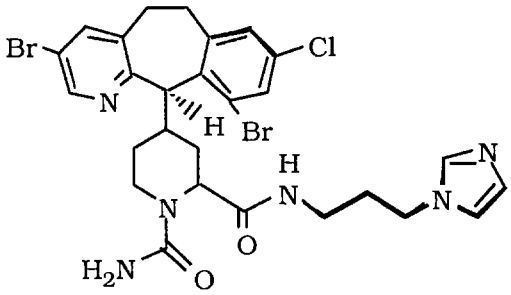
;



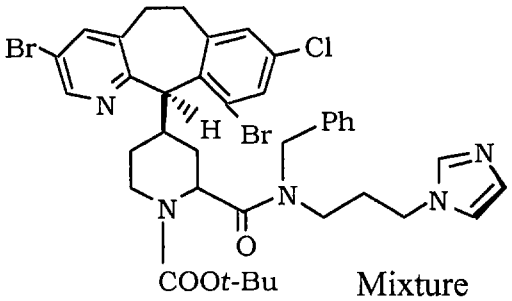
(Example 248) ;



(Example 249) ;

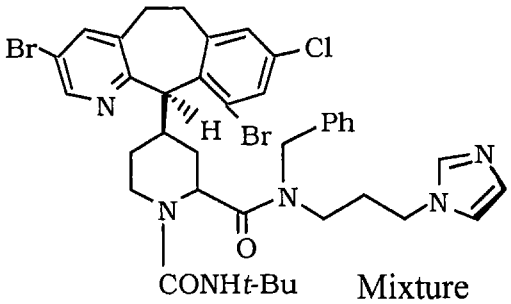


(Example 250) ;



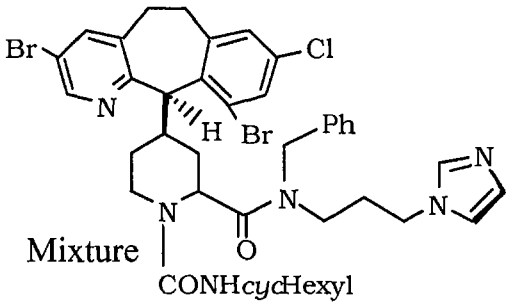
Mixture

(Example 251) ;



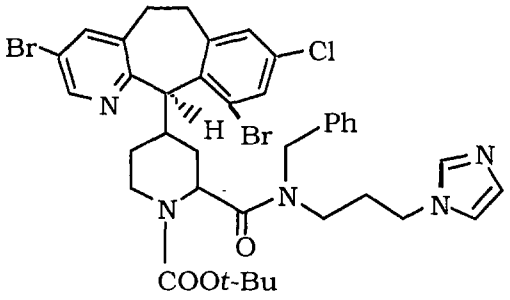
Mixture

(Example 252) ;



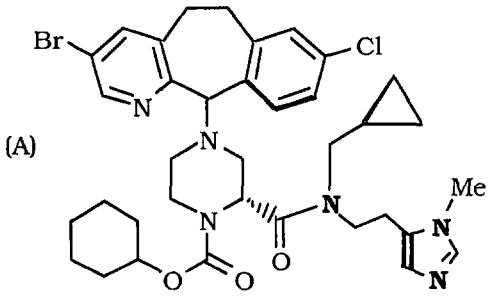
(Example 253)

;

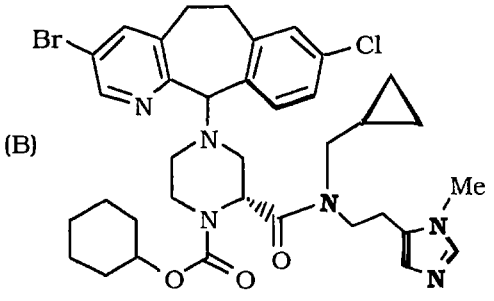


(Example 254)

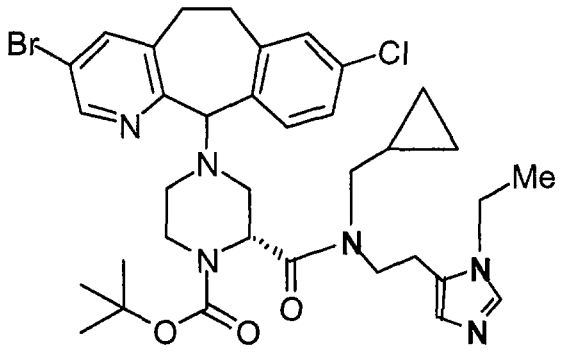
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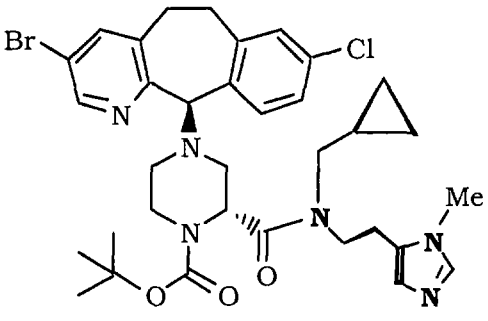
(Example 286A);



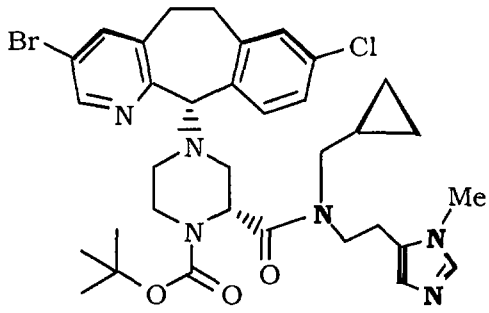
(Example 286B);



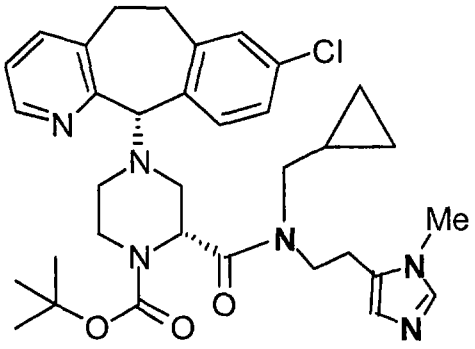
(Example 304);



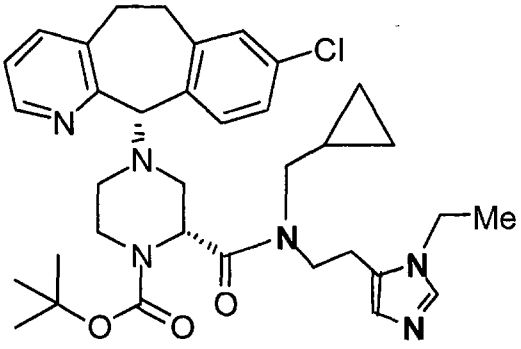
(Example 305);



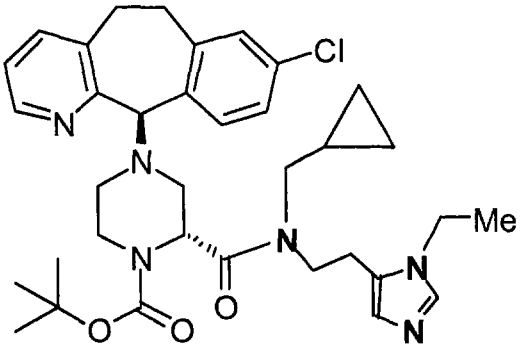
(Example 305);



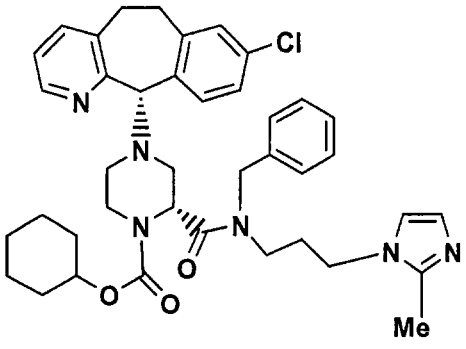
(Example 306);



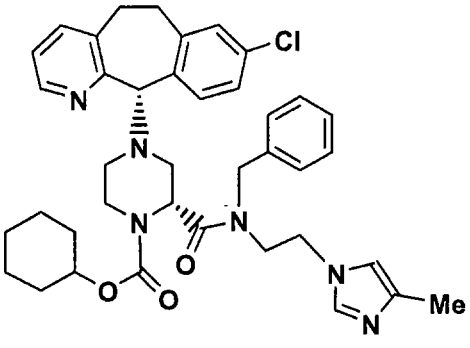
(Example 307);



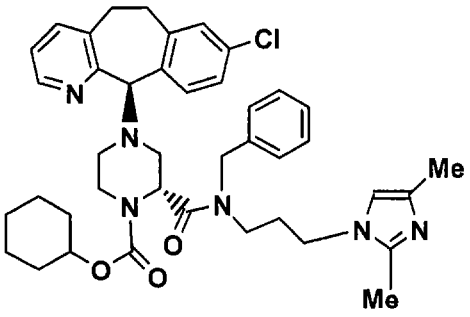
(Example 308);



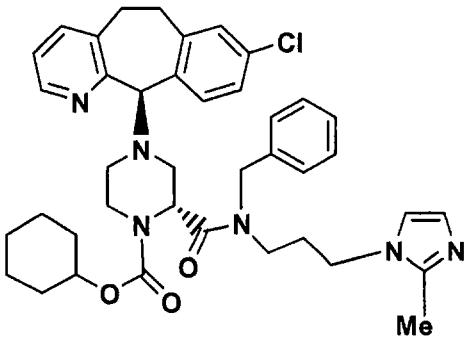
(Example 310);



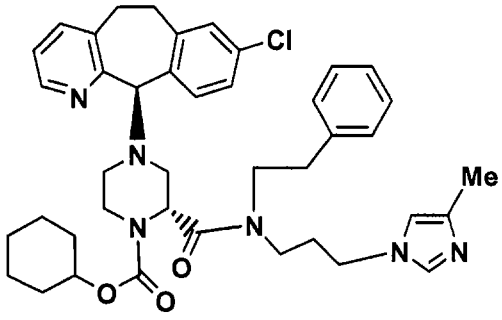
(Example 311);



(Example 312);

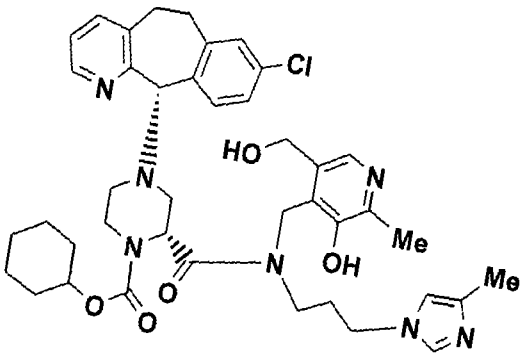


(Example 313);

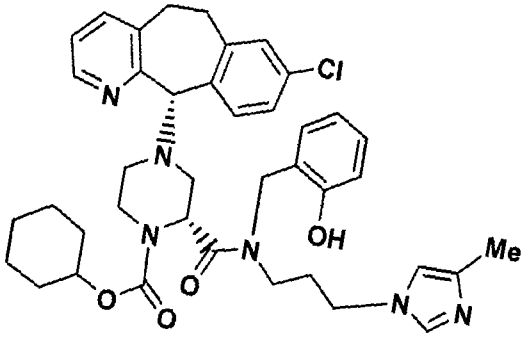


(Example 314);

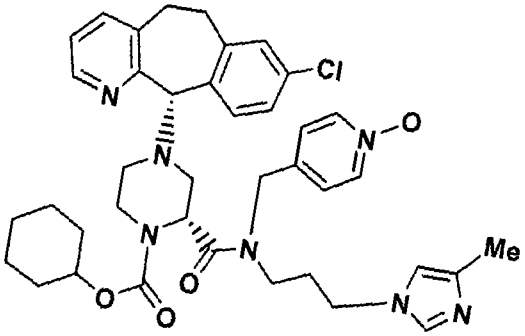
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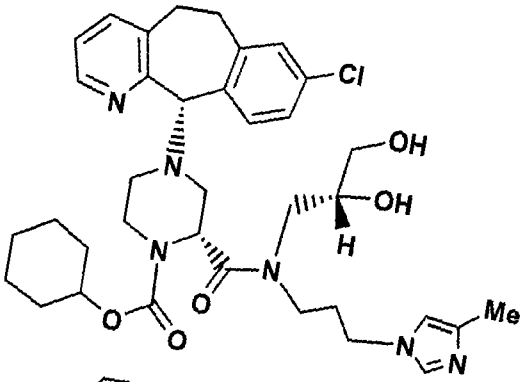
(Example 315);



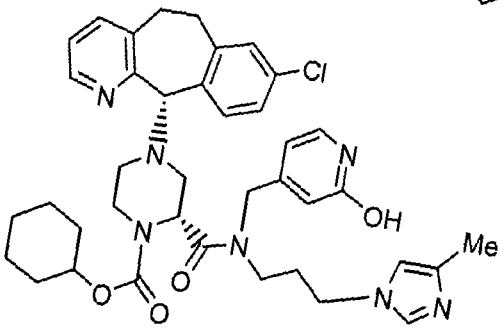
(Example 316);



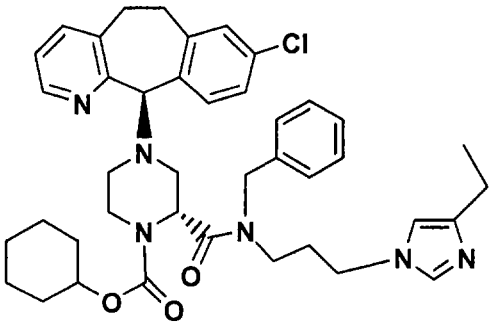
(Example 317);



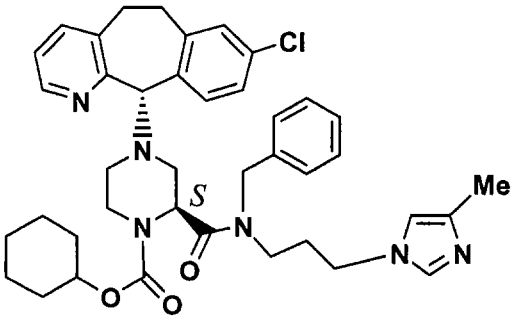
(Example 318);



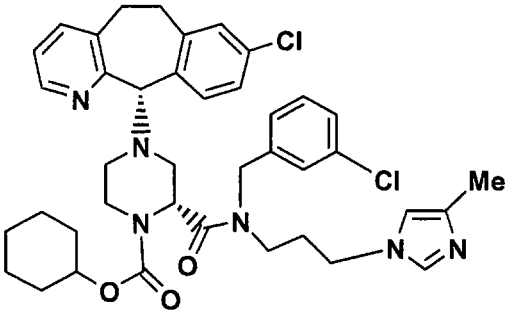
(Example 319);



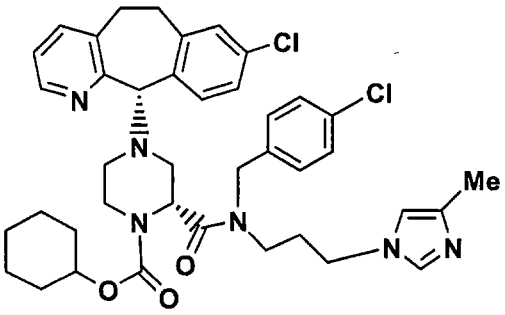
(Example 320);



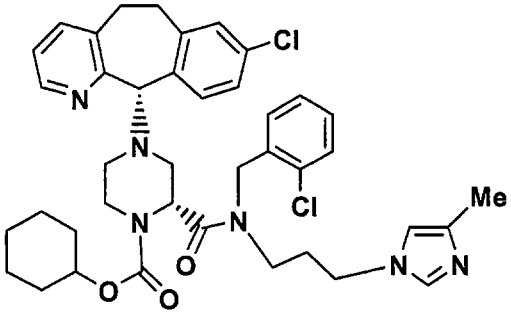
(Example 321);



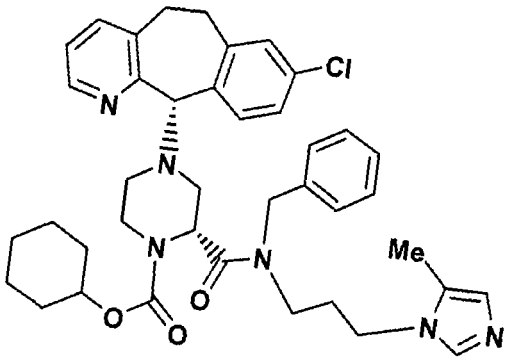
(Example 322);



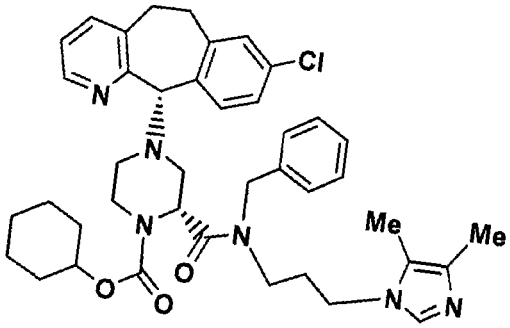
(Example 323);



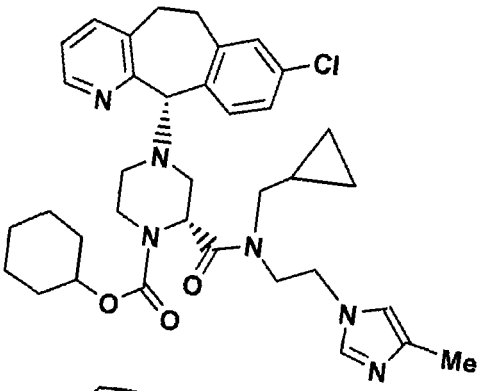
(Example 324);



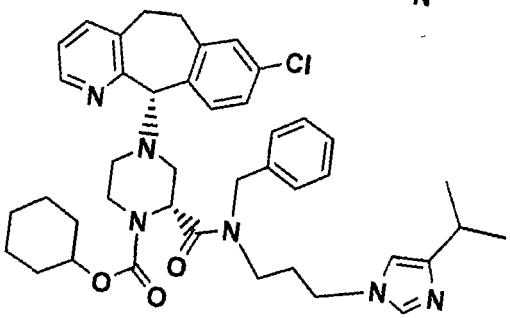
(Example 325);



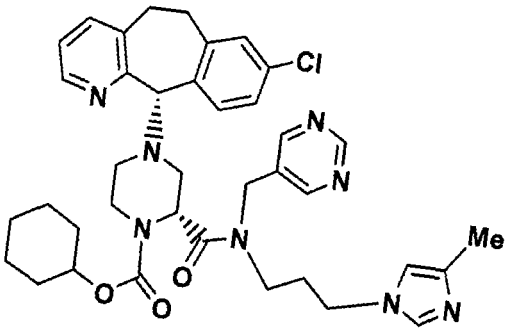
(Example 326);



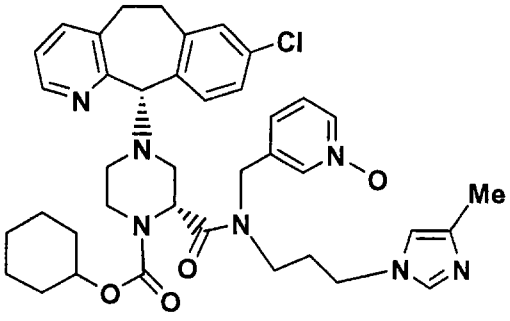
(Example 327);



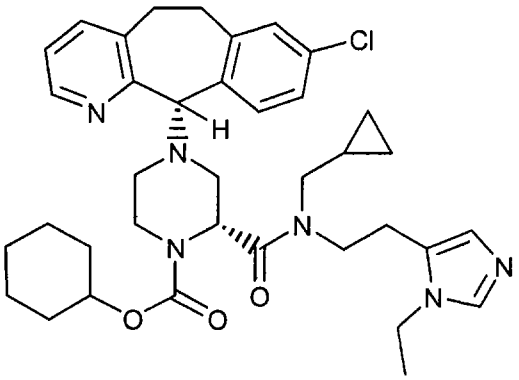
(Example 328);



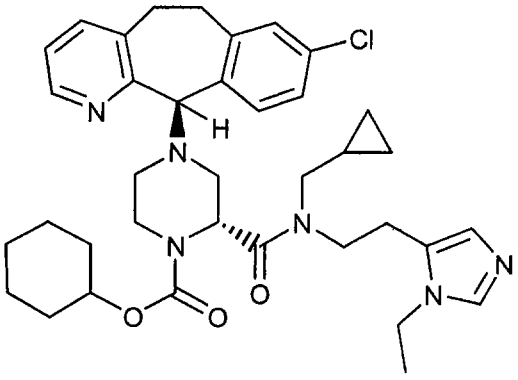
(Example 329);



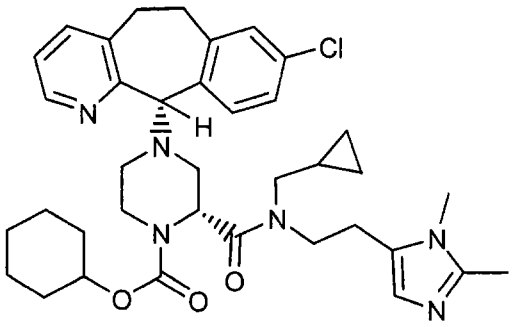
(Example 330);



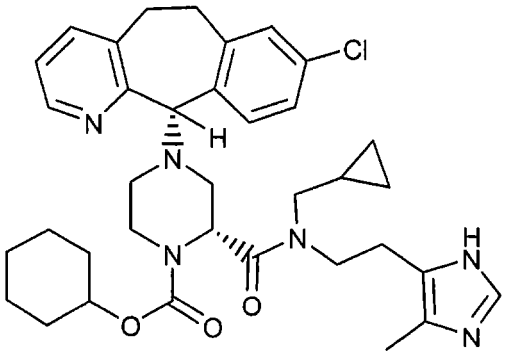
(Example 331);



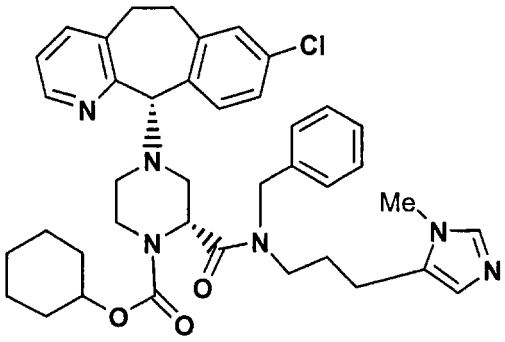
(Example 332);



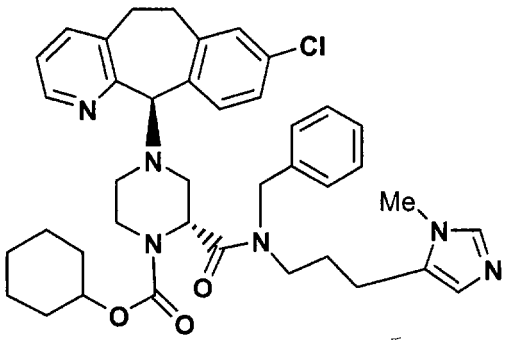
(Example 333);



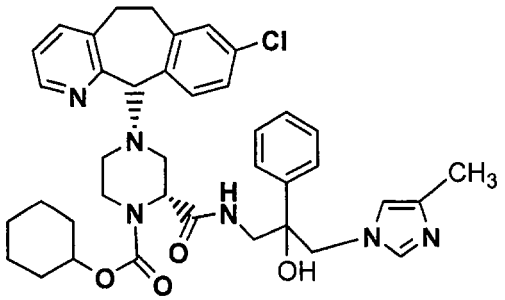
(Example 334);



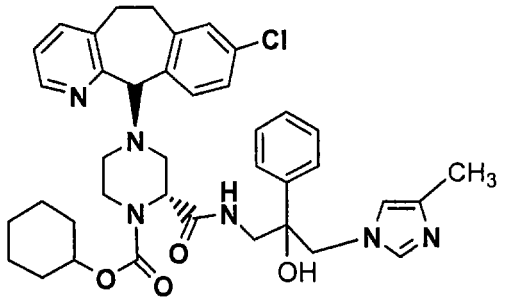
(Example 335);



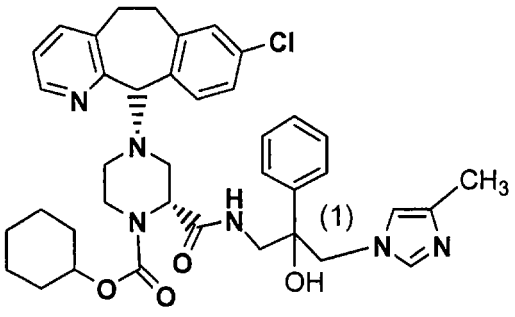
(Example 336);



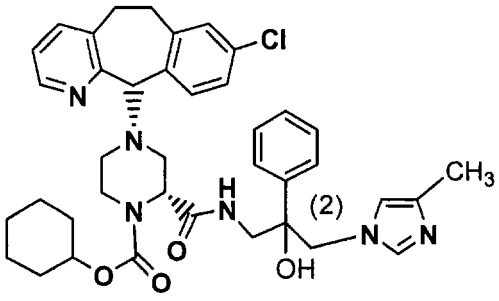
(Example 337);



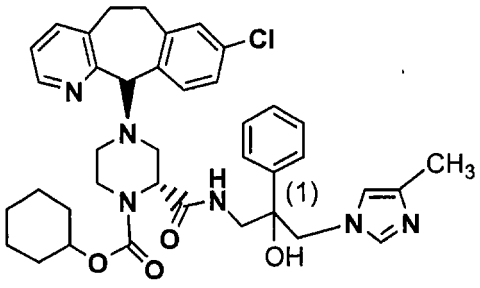
(Example 338);



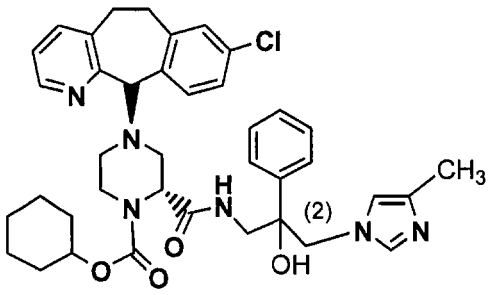
(Example 339);



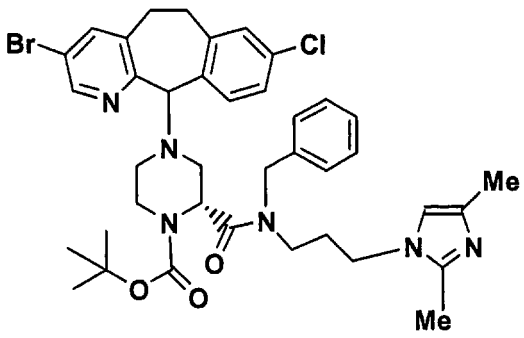
(Example 340);



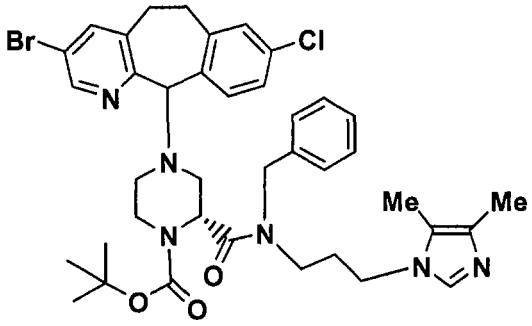
(Example 341);



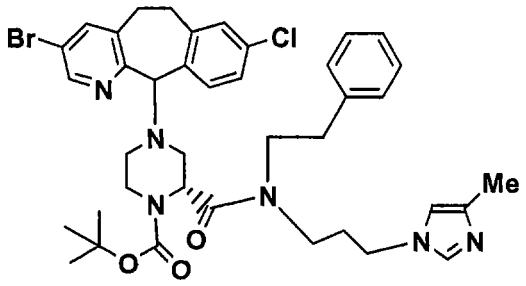
(Example 342);



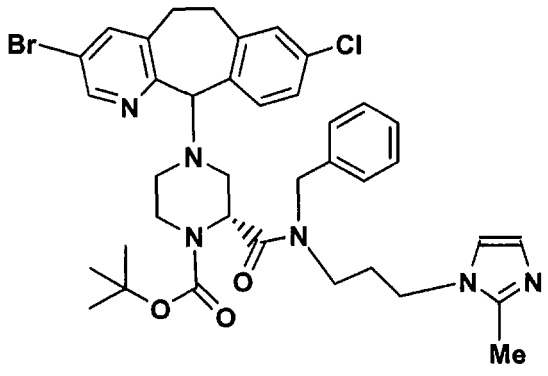
Isomer A (Example 343) and Isomer B (Example 344);



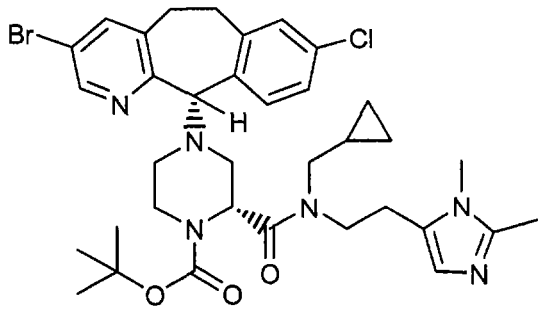
Isomer A (Example 345) and Isomer B (Example 346);



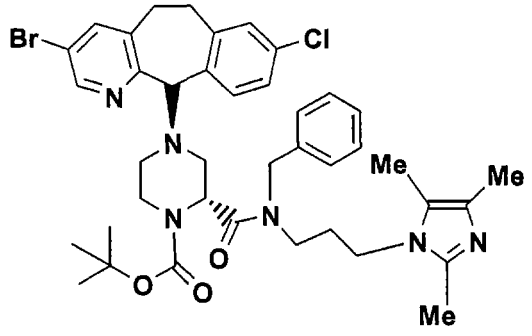
Isomer A (Example 347) and Isomer B (Example 348);



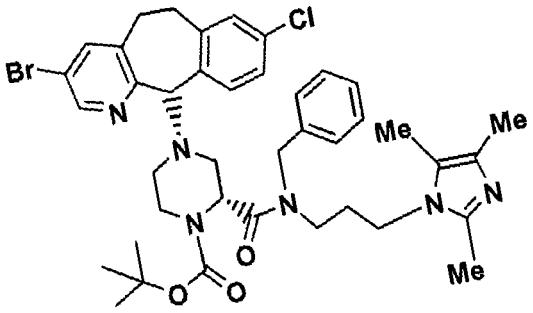
Isomer A (Example 349) and Isomer B (Example 350);



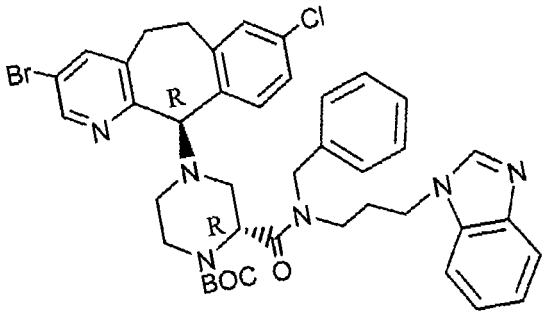
(Example 351);



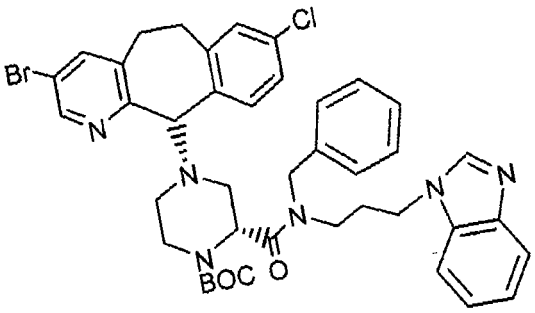
(Example 352);



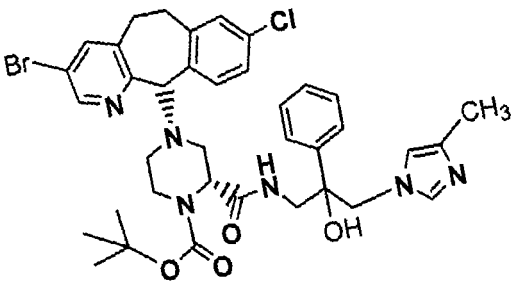
(Example 353);



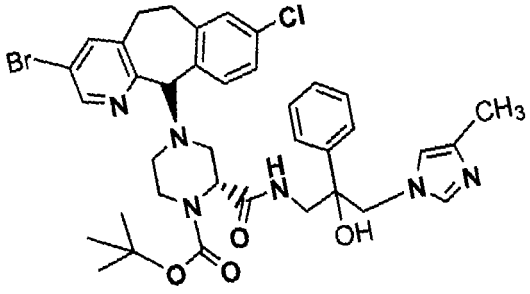
(Example 354);



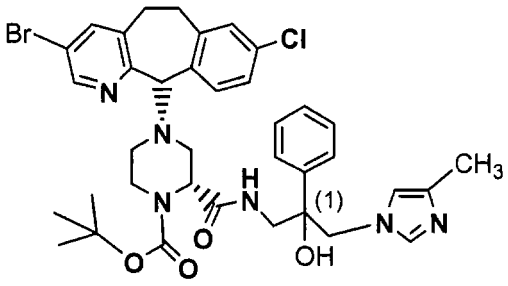
(Example 355);



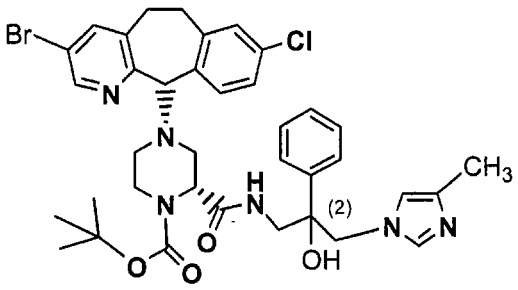
(Example 356);



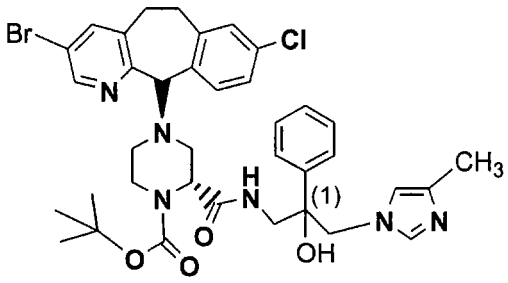
(Example 357);



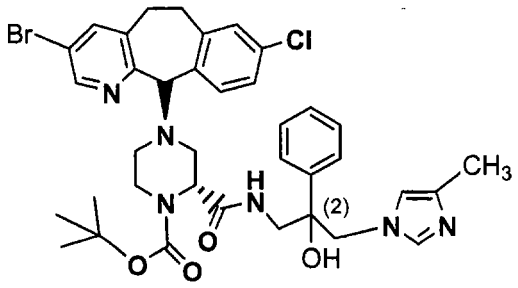
(Example 358);



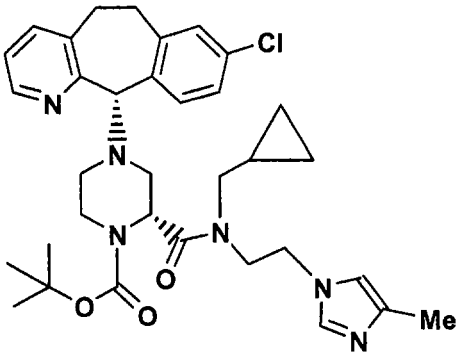
(Example 359);



(Example 360);

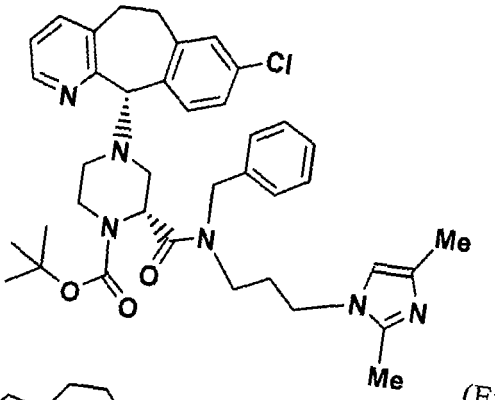


(Example 361);

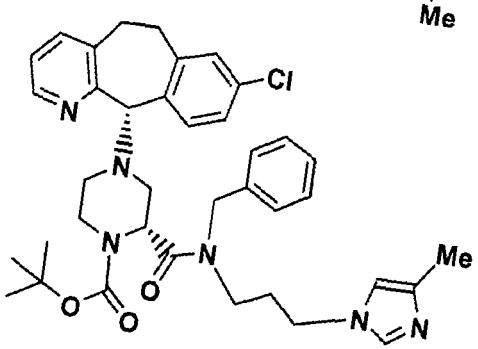


(Example 362);

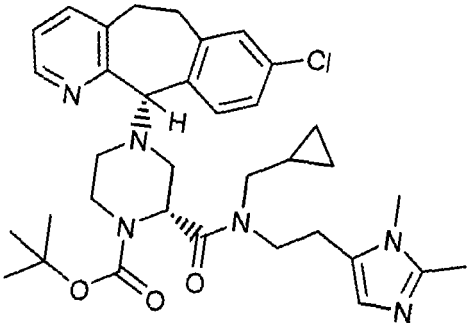
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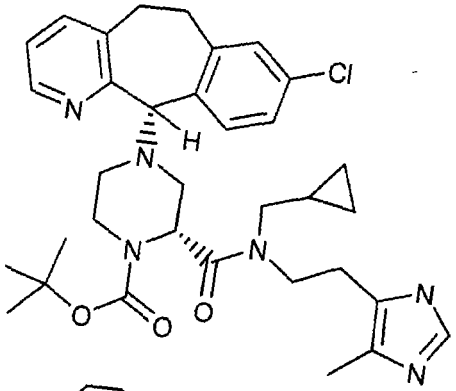
(Example 363);



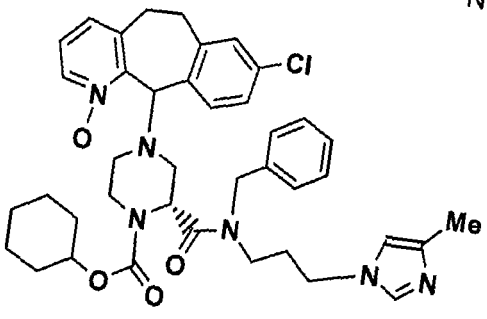
(Example 364);



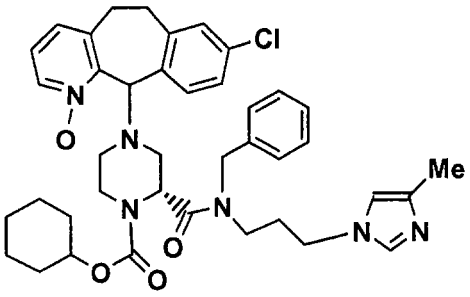
(Example 365);



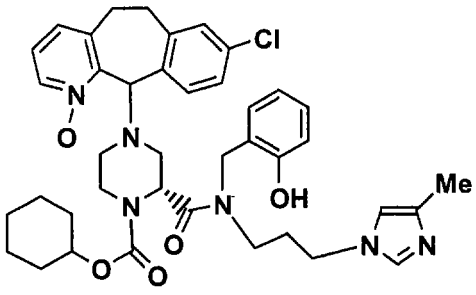
(Example 366);



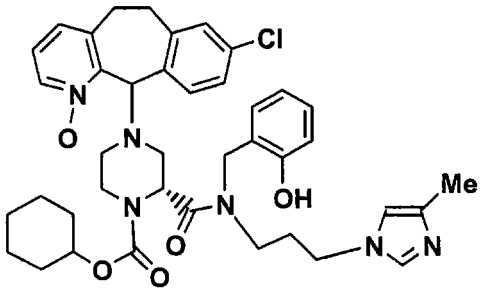
Isomer A (Example 367);



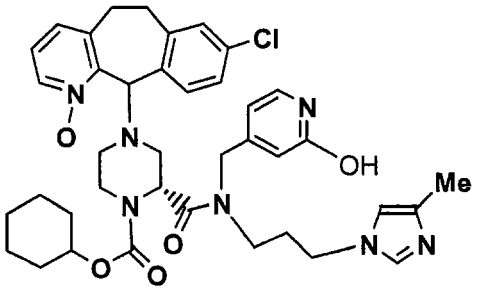
Isomer B (Example 368);



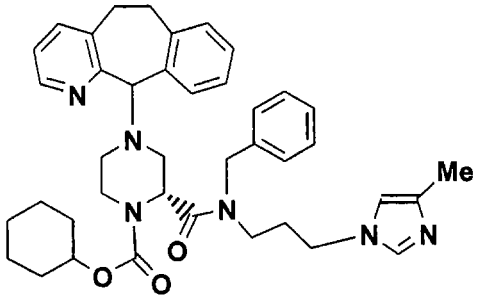
Isomer A (Example 369);



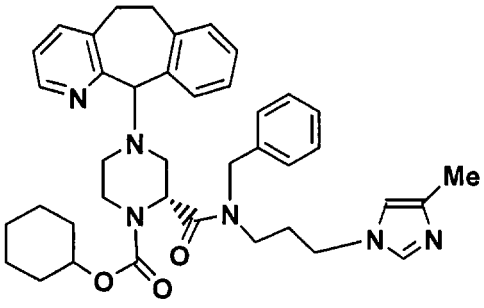
Isomer B (Example 370);



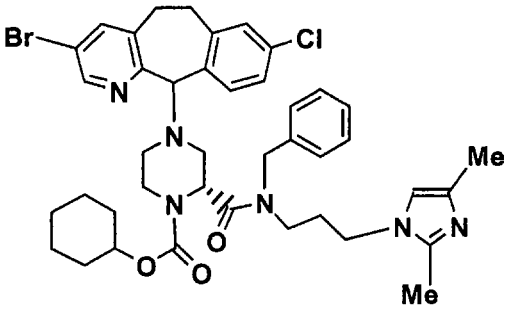
Isomer B (Example 371);



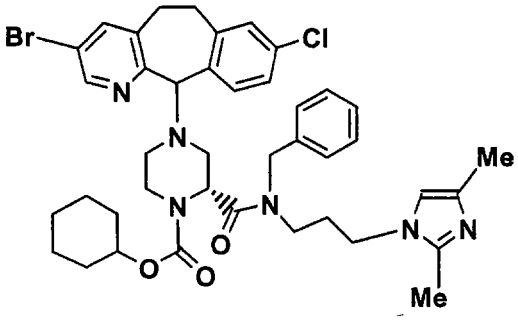
Isomer A (Example 372);



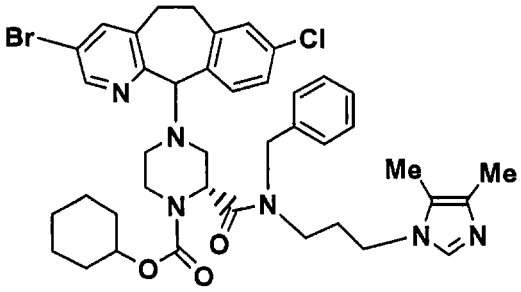
Isomer B (Example 373);



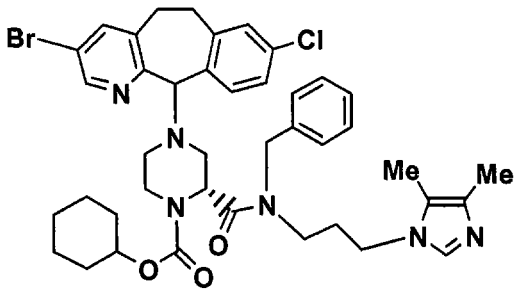
Isomer A (Example 375);



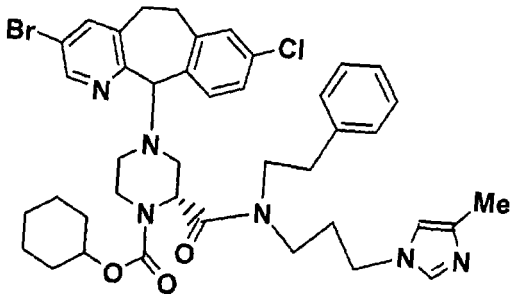
Isomer B (Example 376);



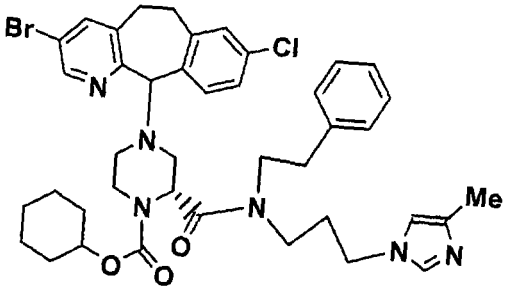
Isomer A (Example 377);



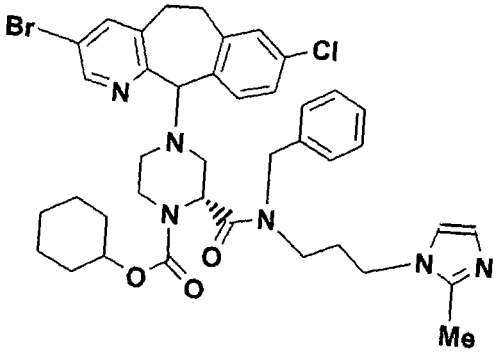
Isomer B (Example 378);



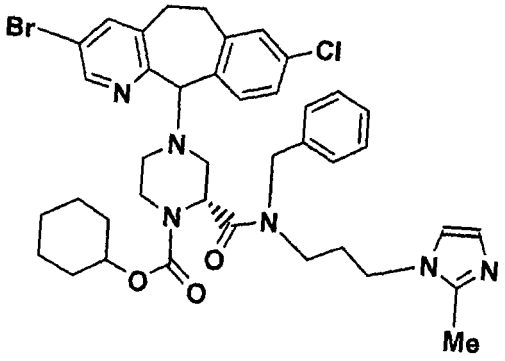
Isomer A (Example 379);



Isomer B (Example 380);



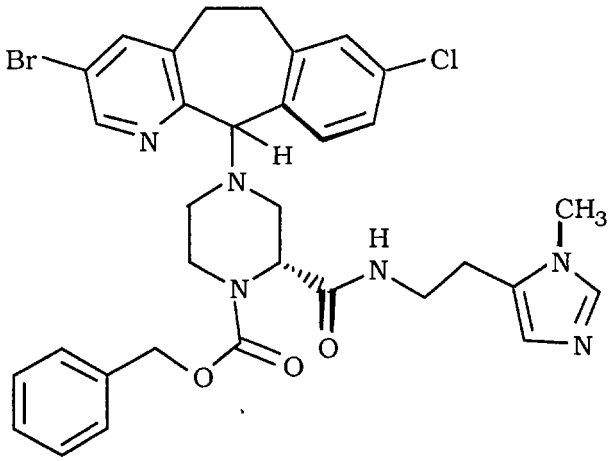
Isomer A (Example 381); and



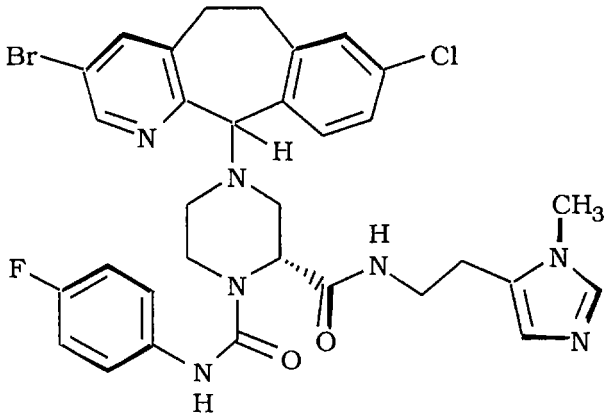
Isomer B (Example 382).

7. A compound as claimed in **Claim 1** selected from the group consisting of:

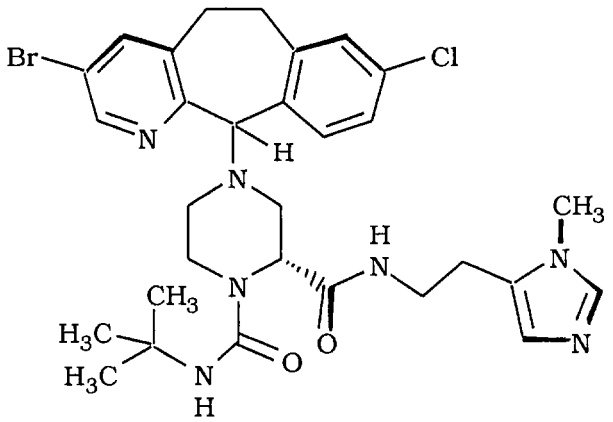
8.



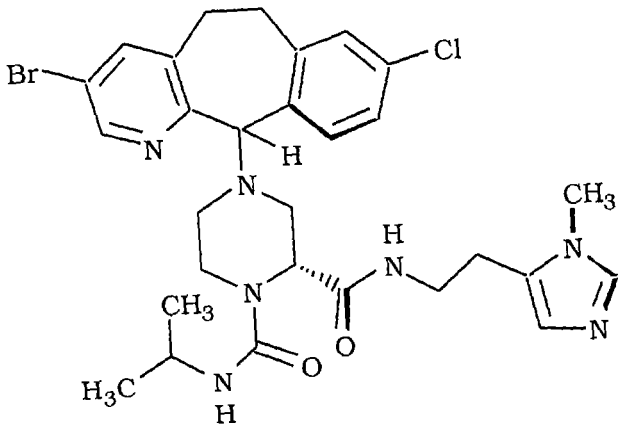
(Example 26);



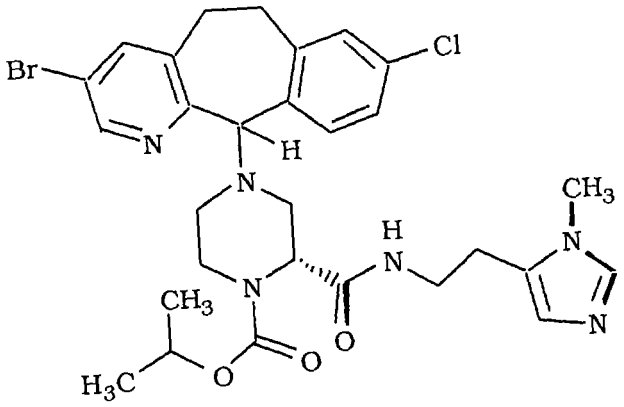
(Example 27);



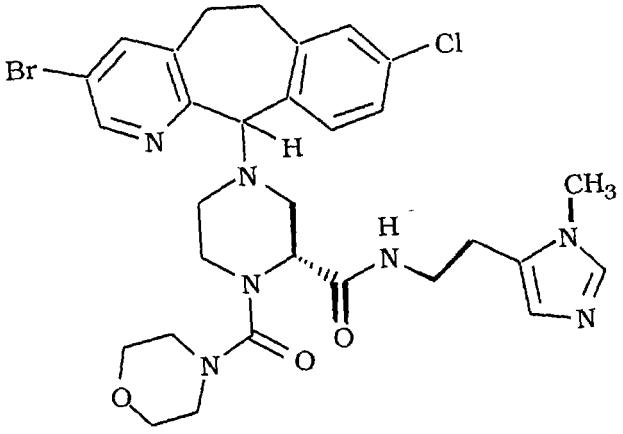
(Example 28);



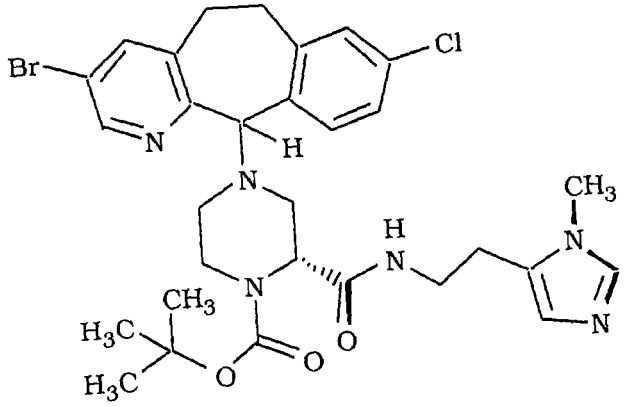
(Example 29);



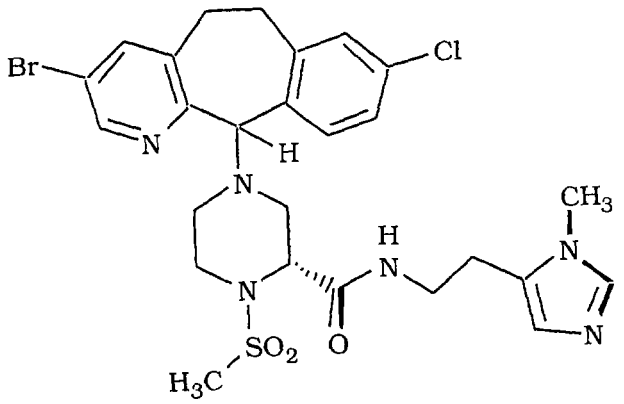
(Example 30);



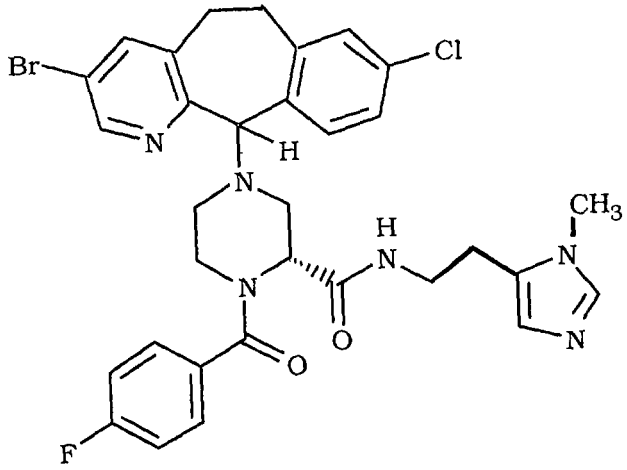
(Example 31);



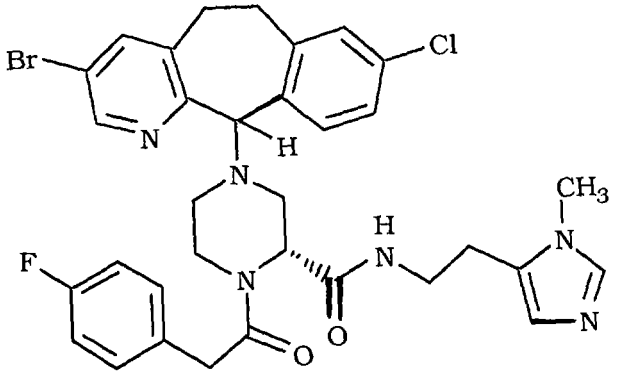
(Example 32);



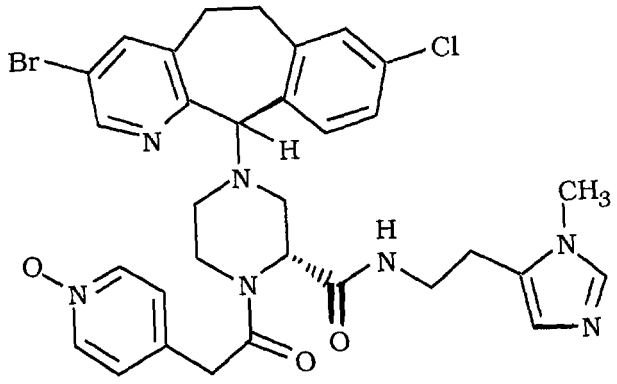
(Example 33);



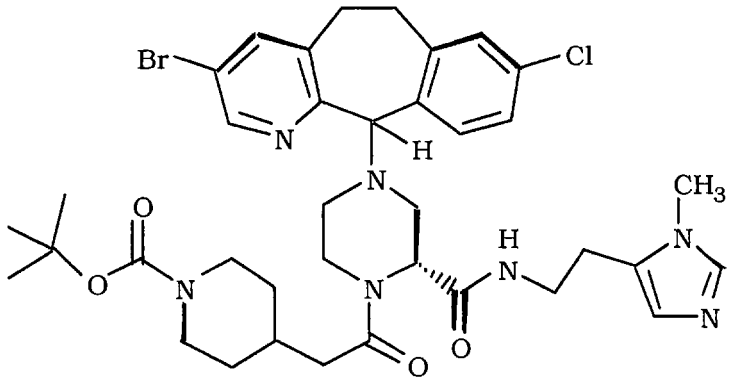
(Example 34);



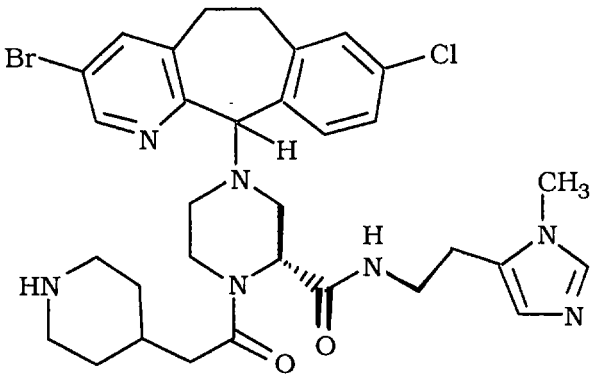
(Example 35);



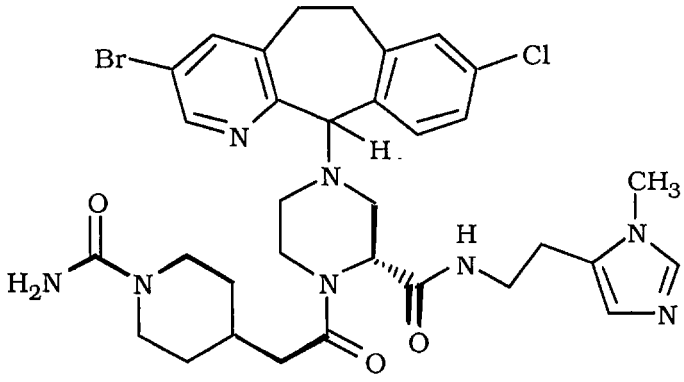
(Example 36);



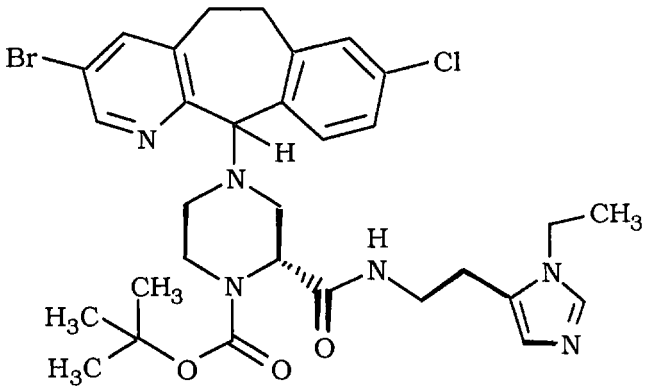
(Example 37);



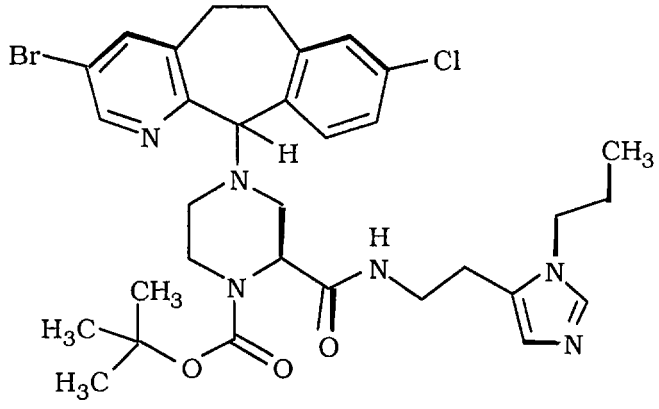
(Example 38);



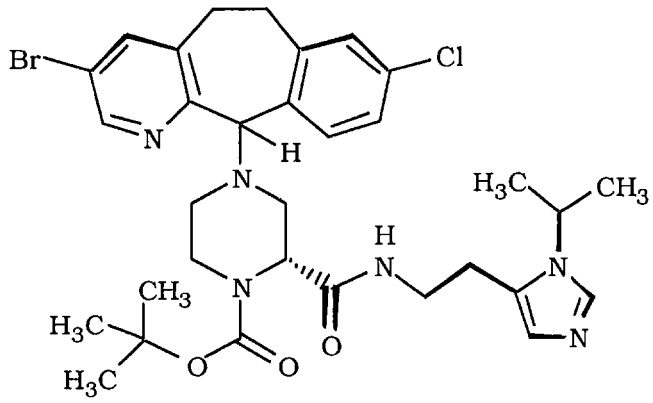
(Example 39);



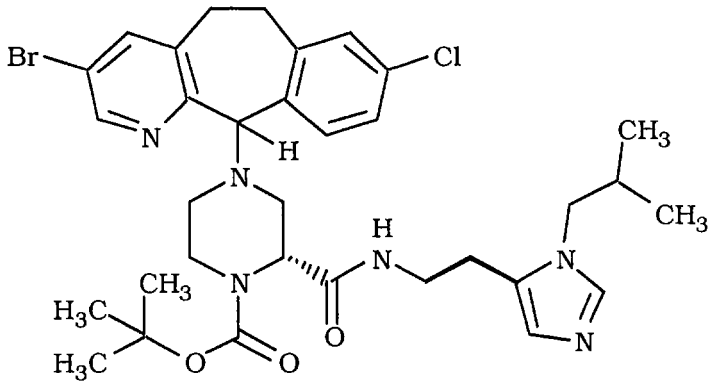
(Example 40);



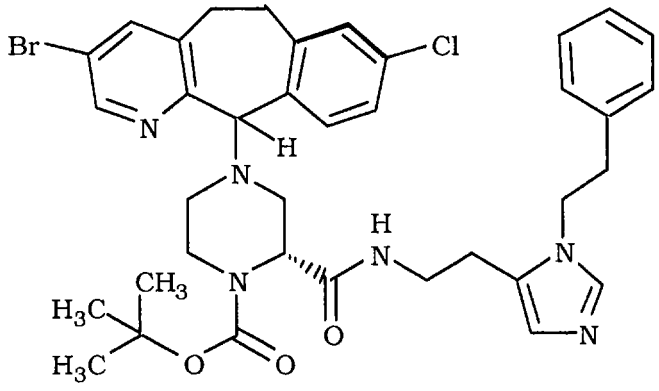
(Example 41);



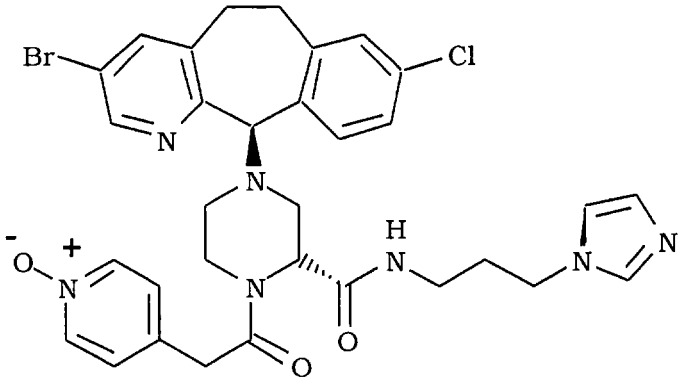
(Example 42);



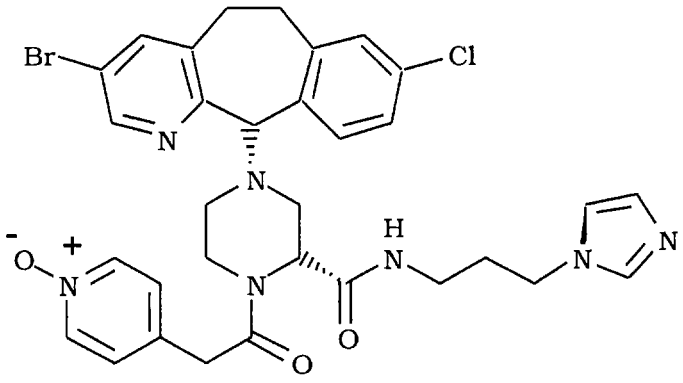
(Example 43);



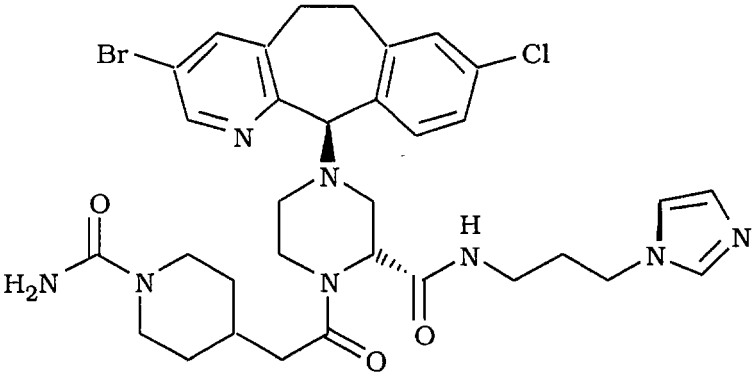
(Example 44);



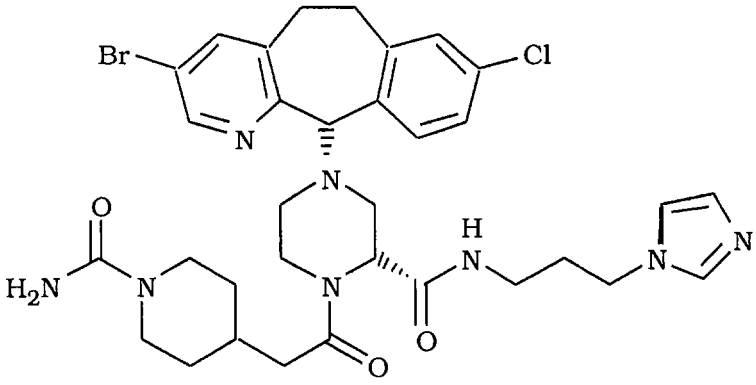
(Example 67);



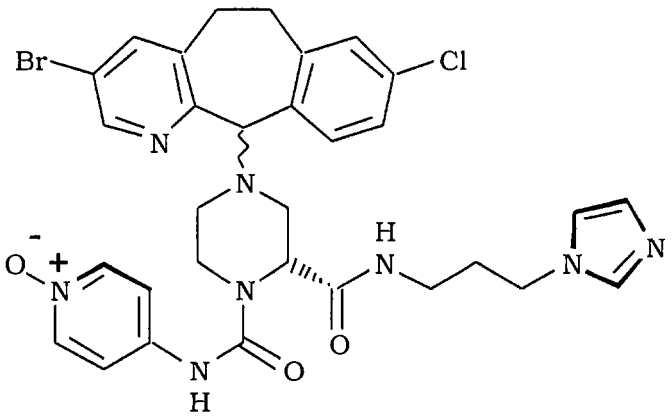
(Example 68);



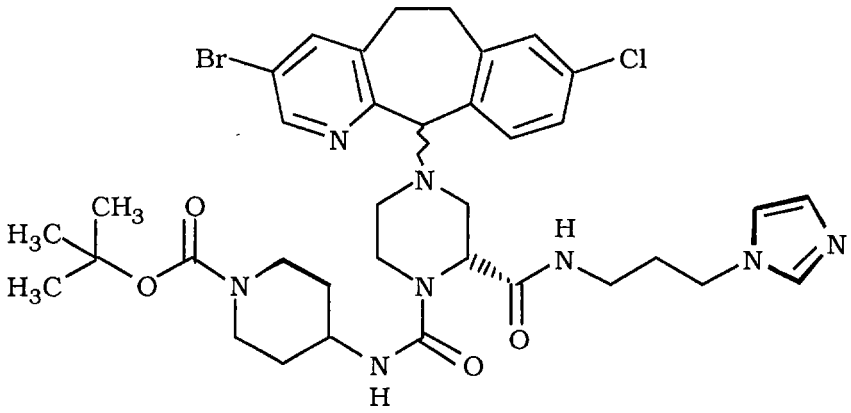
(Example 69);



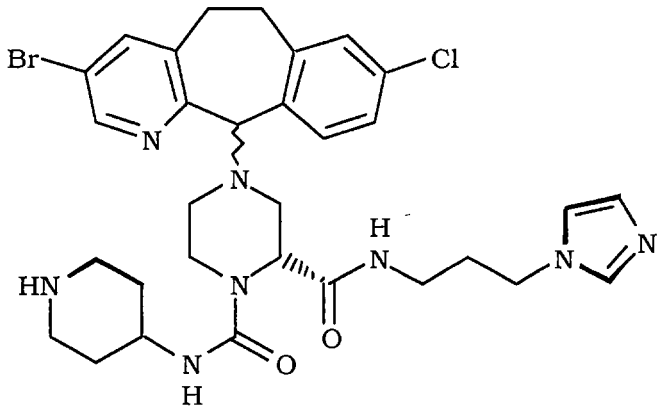
(Example 70);



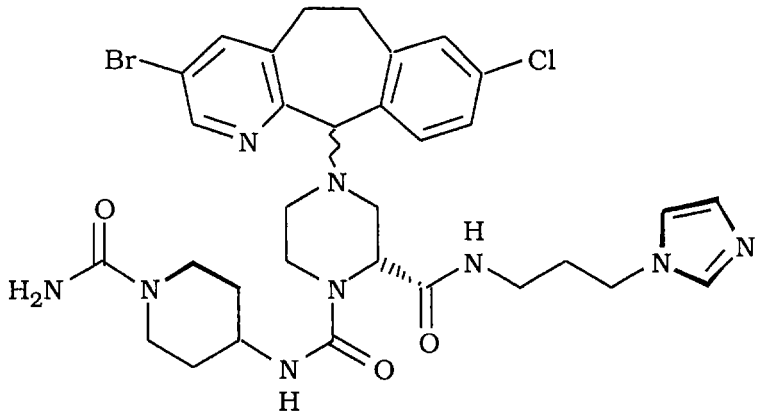
(Example 71);



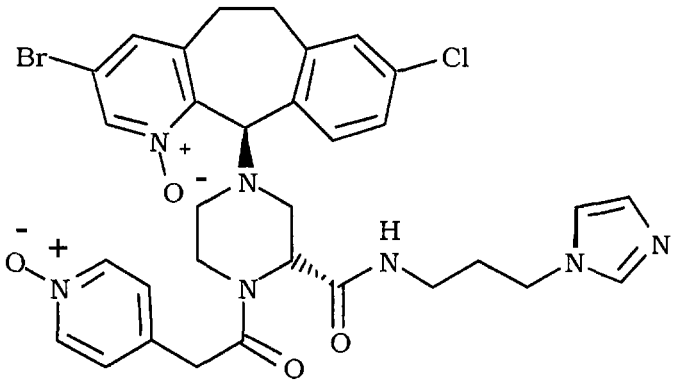
(Example 72 Step A);



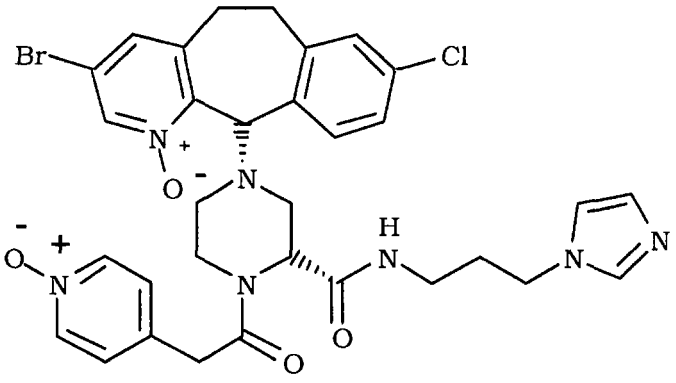
(Example 72 Step B);



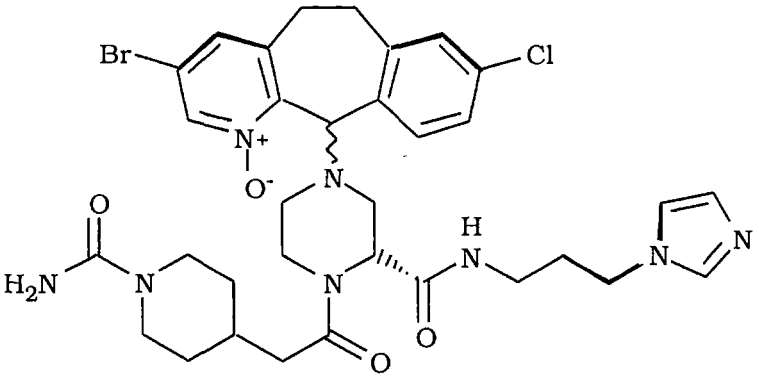
(Example 72 Step C);



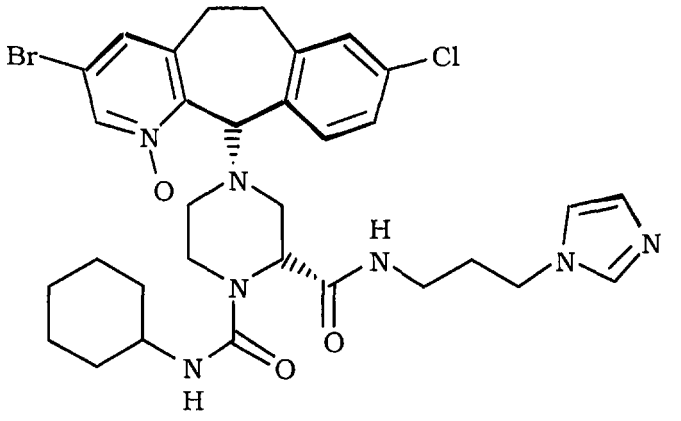
(Example 73);



(Example 74);

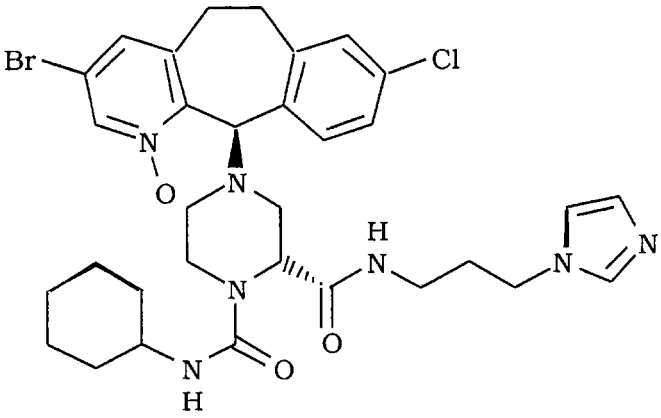


(Example 75);



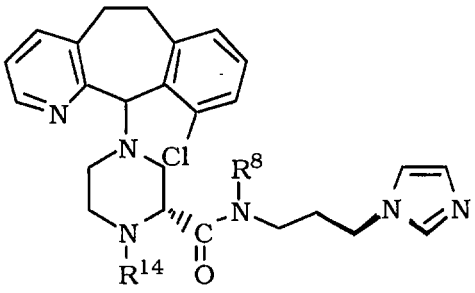
(11S,2R(-)-Isomer)

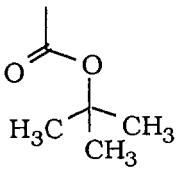
(Example 76);

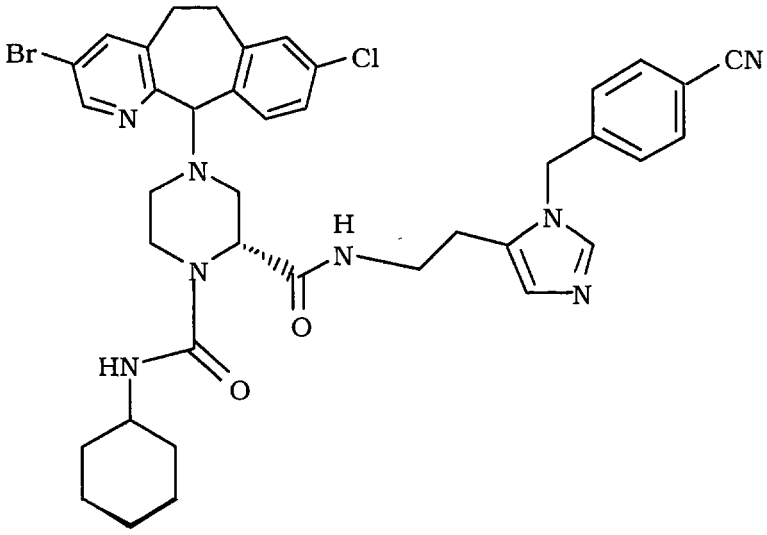


(11R,2R(+)-Isomer)

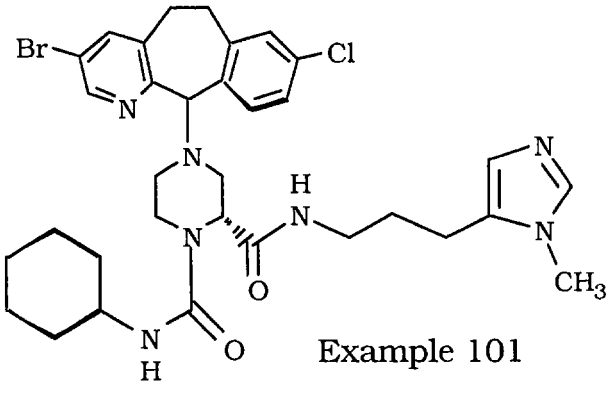
(Example 76);



wherein R^8 is H and R^{14} is  (Example 81);

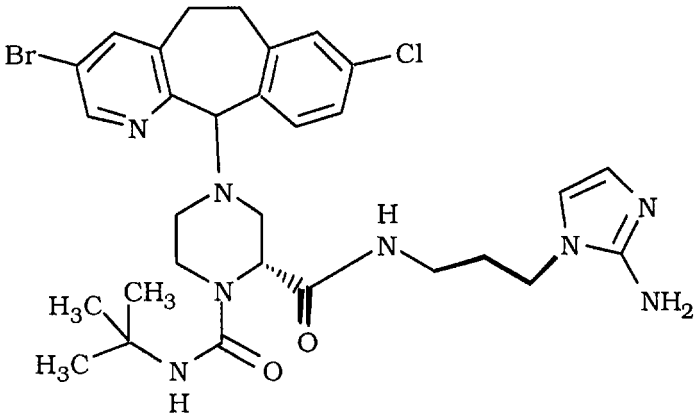


(Example 98);

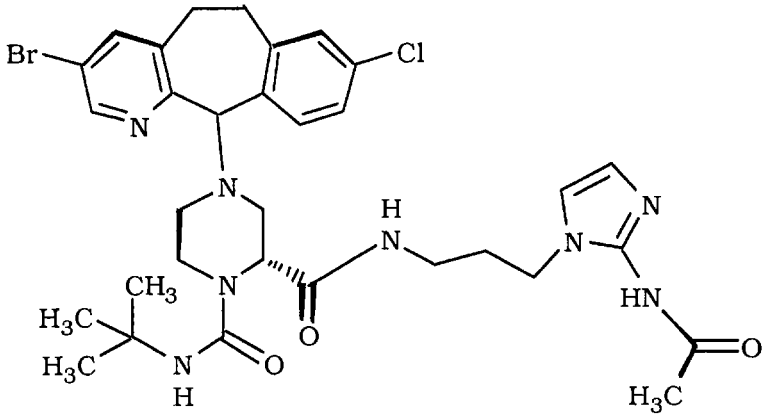


Example 101

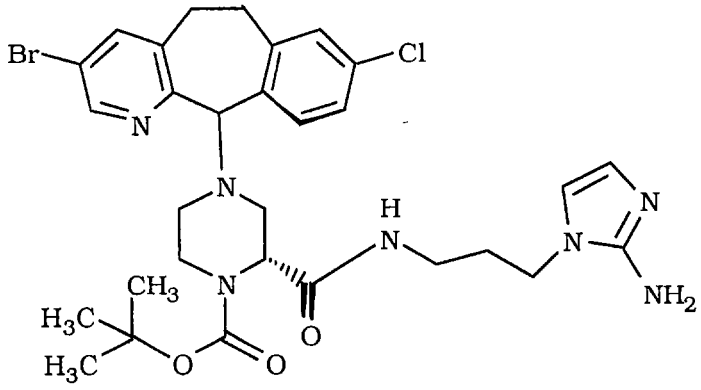
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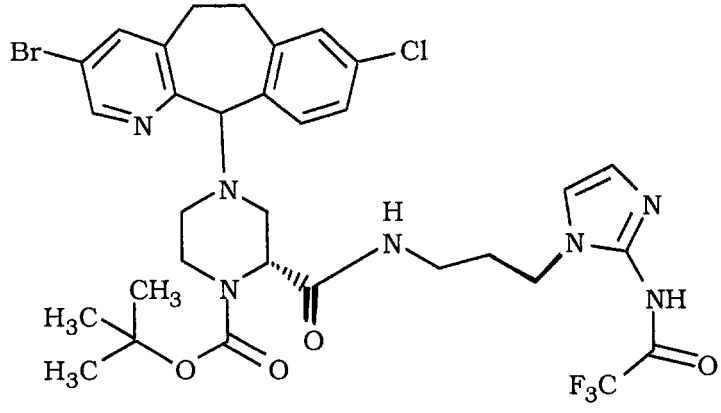
(Example 103);



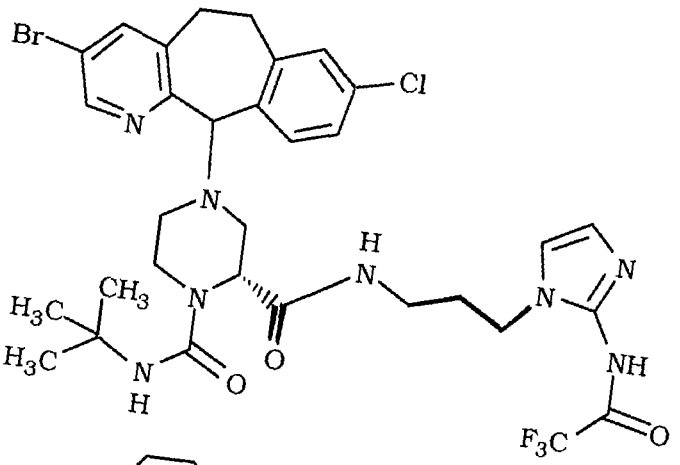
(Example 104);



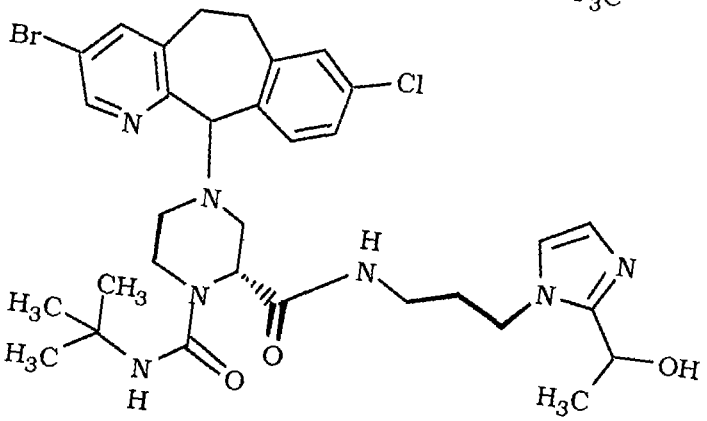
(Example 105);



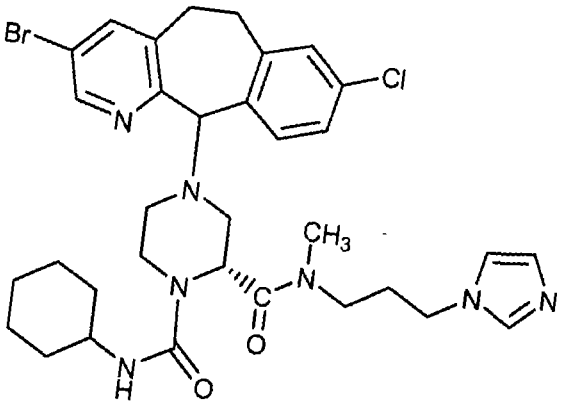
(Example 106);



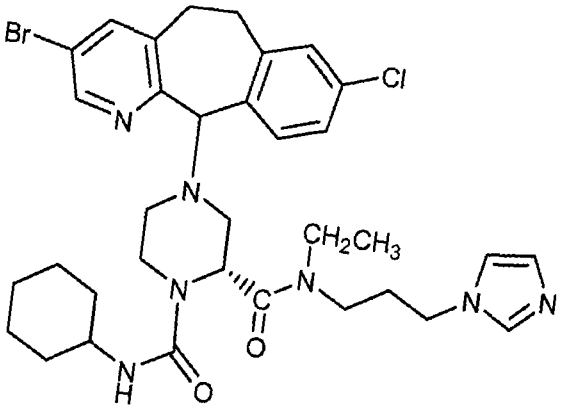
(Example 107);



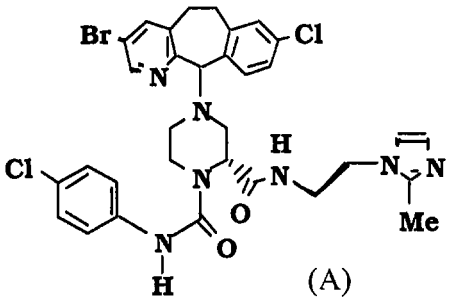
(Example 108);



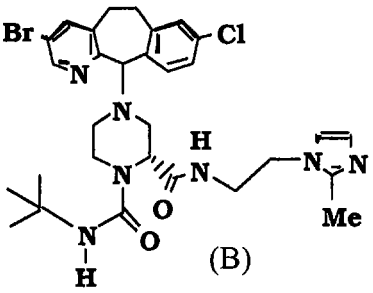
(Example 110);



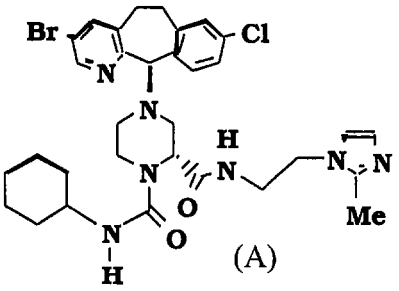
(Example 111);



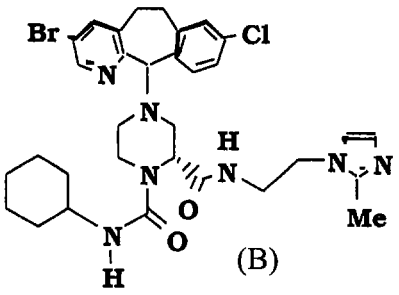
(A) (Example 255);



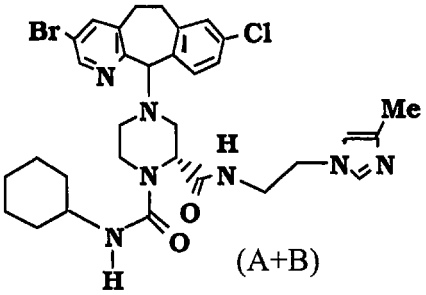
(B) (Example 256);



(A) (Example 257);

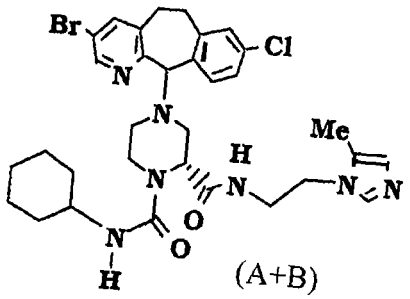


(B) (Example 258);



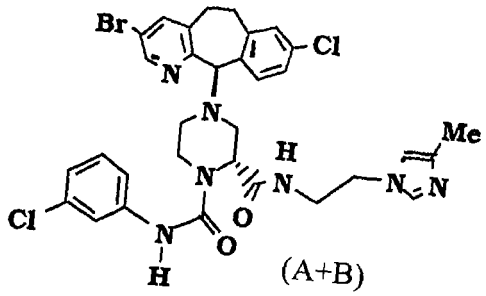
(A+B)

(Example 259);



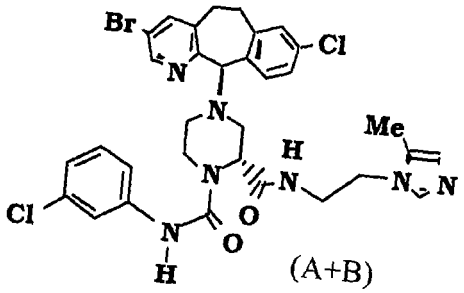
(A+B)

(Example 259);



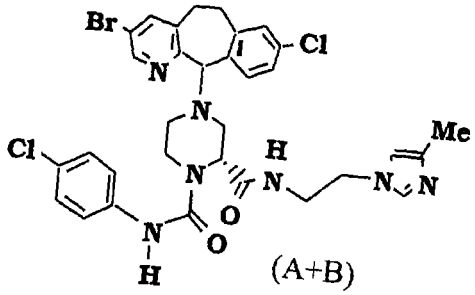
(A+B)

(Example 260);



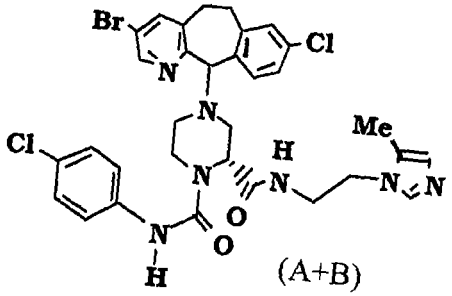
(A+B)

(Example 260);



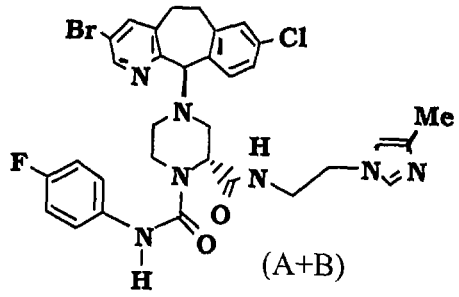
(A+B)

(Example 261);



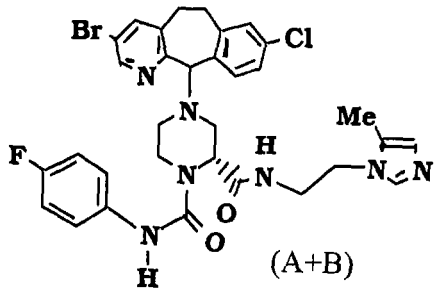
(A+B)

(Example 261);



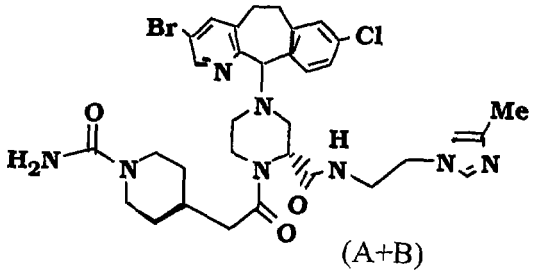
(A+B)

(Example 262);



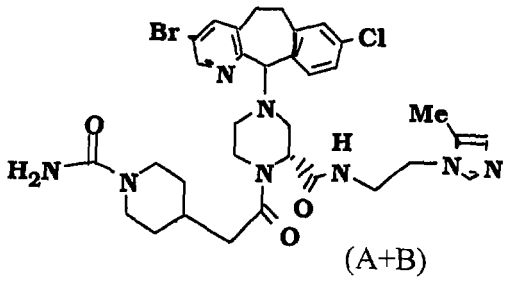
(A+B)

(Example 262);



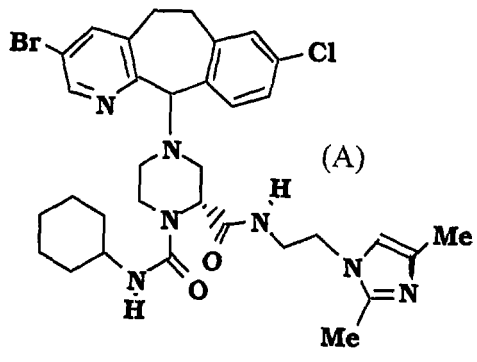
(A+B)

(Example 263);



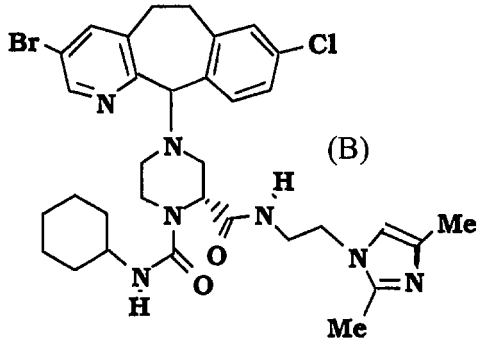
(A+B)

(Example 263);



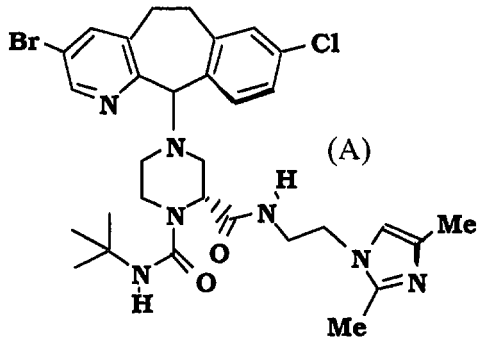
(A)

(Example 264);



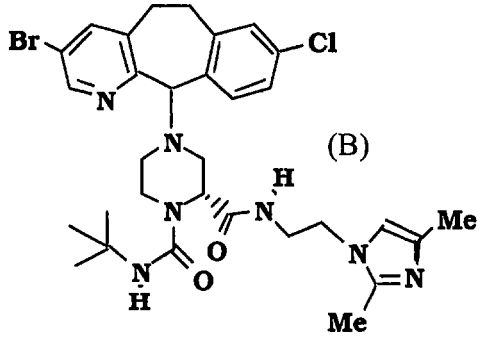
(B)

(Example 265);



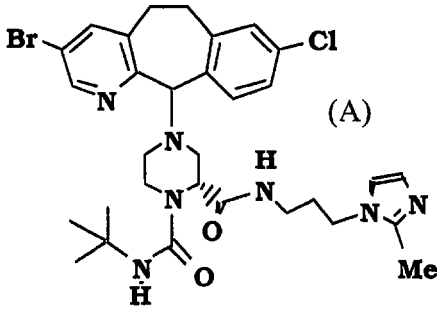
(A)

(Example 266);



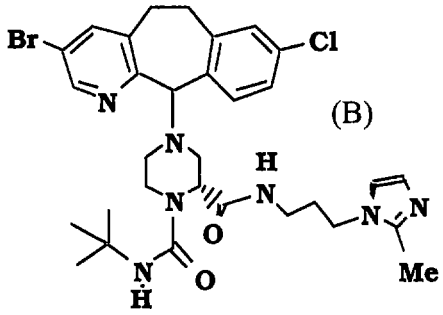
(B)

(Example 267);



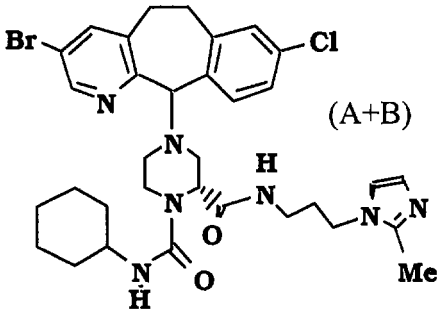
(A)

(Example 268);

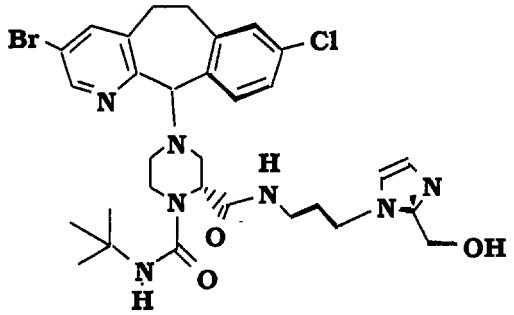


(B)

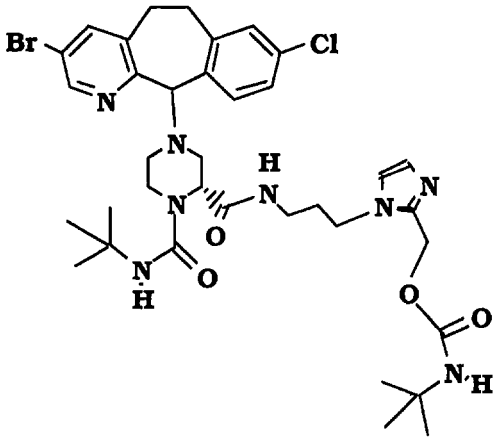
(Example 269);



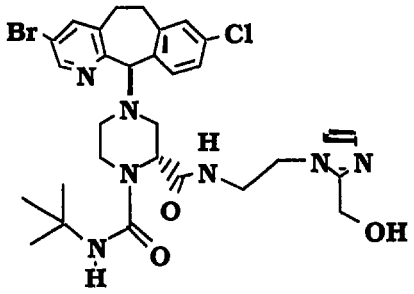
(Example 270);



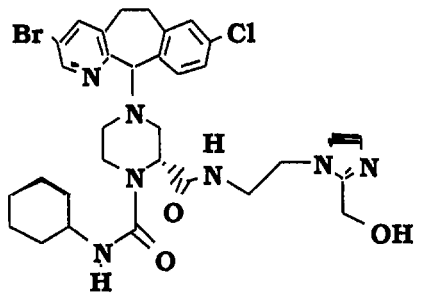
(Example 271);



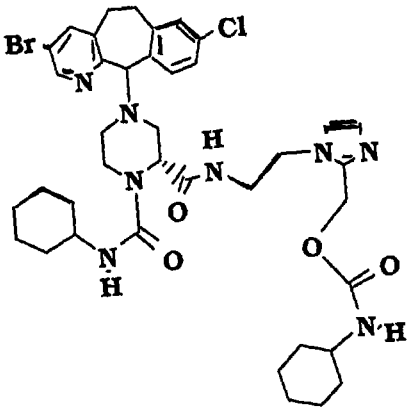
(Example 272);



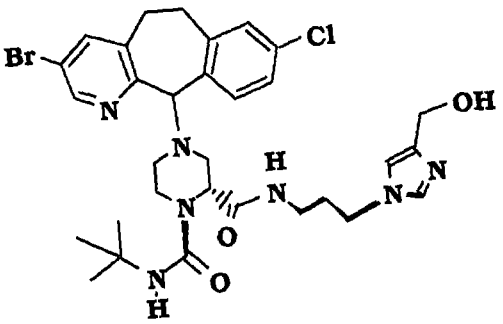
(Example 273);



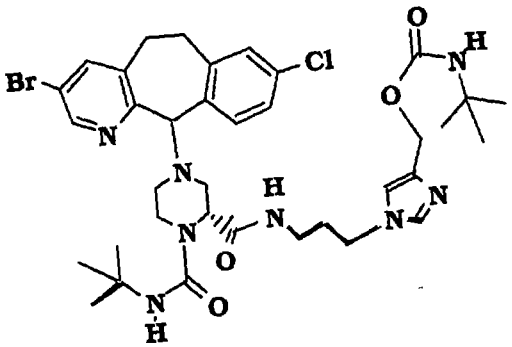
(Example 274);



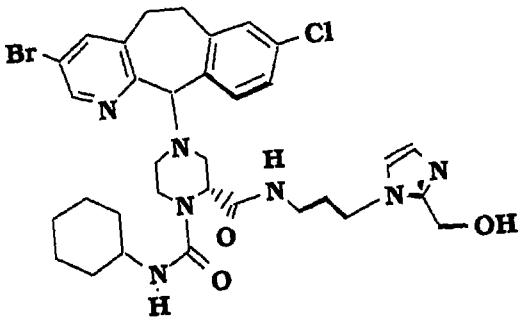
(Example 275);



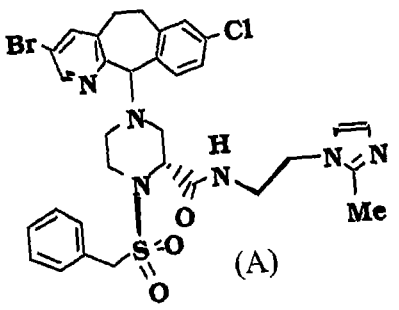
(Example 276);



(Example 277);

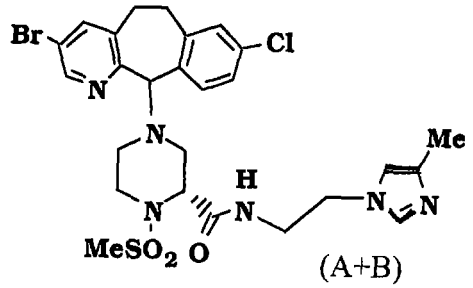


(Example 278);

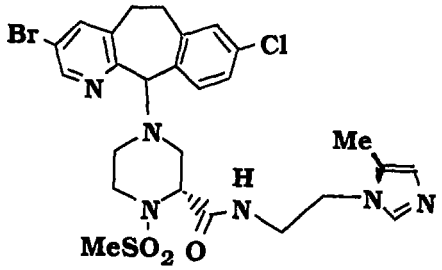


(A)

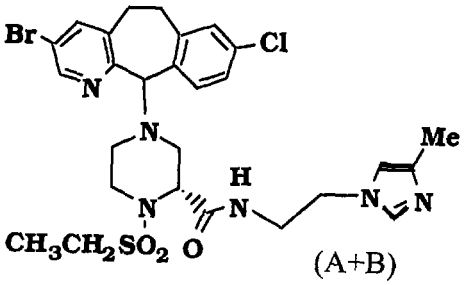
(Example 279);



(A+B) (Example 280);

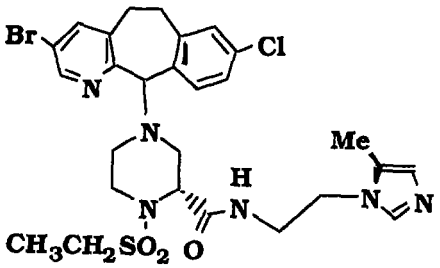


(A+B) (Example 280);

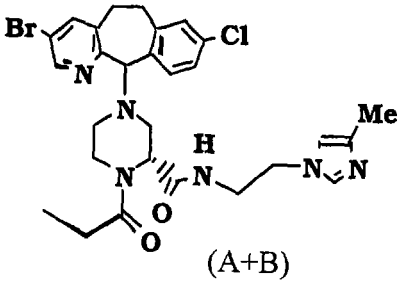


(A+B)

(Example 281);

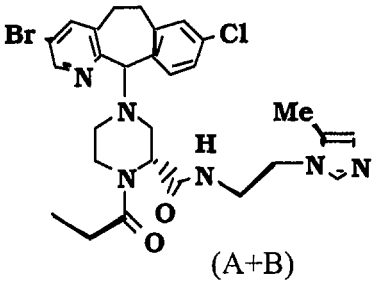


(A+B) (Example 281);

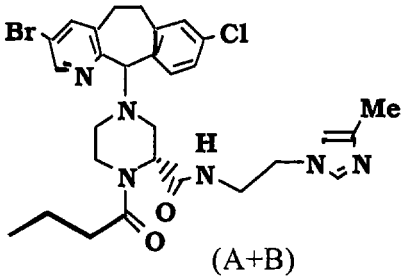


(A+B)

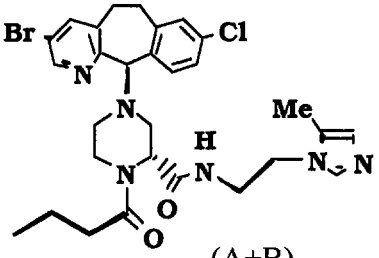
(Example 282);



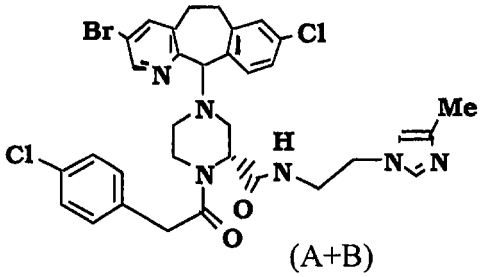
(A+B) (Example 282);



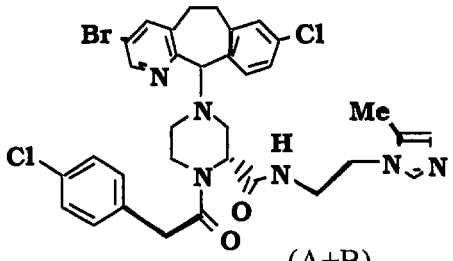
(A+B) (Example 283);



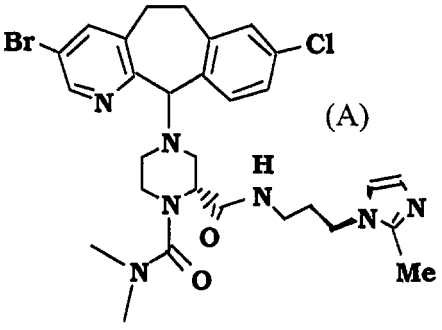
(A+B) (Example 283);



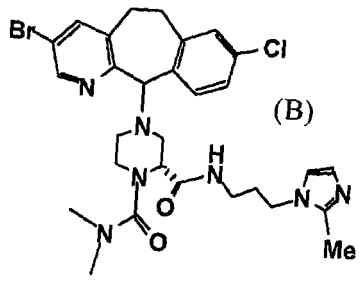
(A+B) (Example 284);



(A+B) (Example 284);

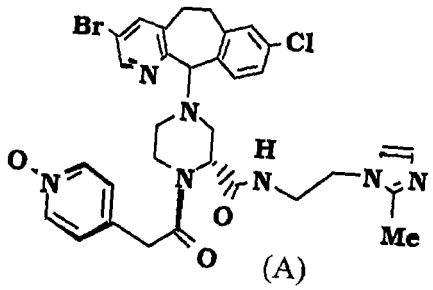


(A) (Example 285);



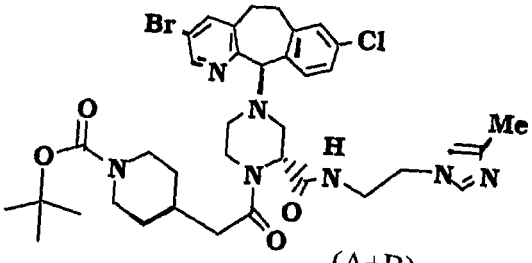
(B)

(Example 286);



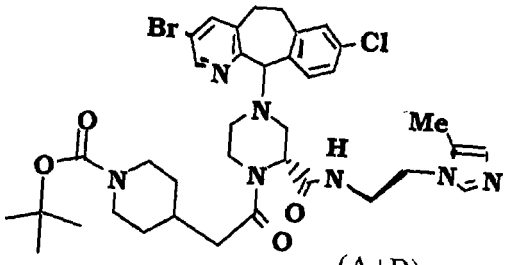
(A)

(Example 287);



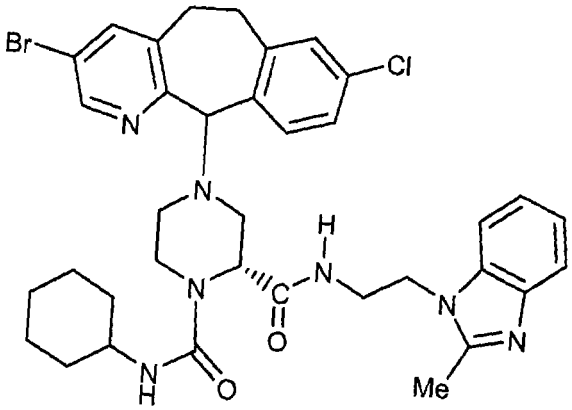
(A+B)

(Example 289);

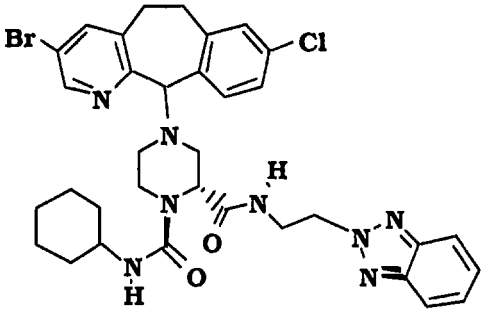


(A+B)

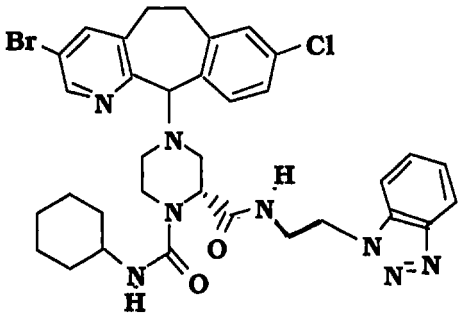
(Example 289);



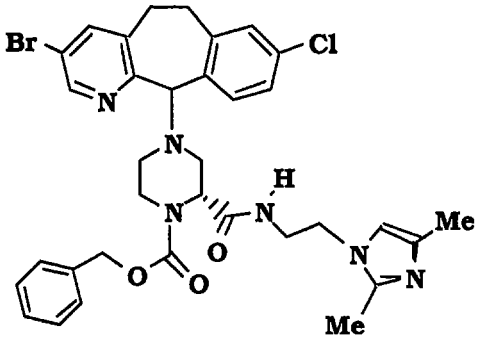
(Example 290);



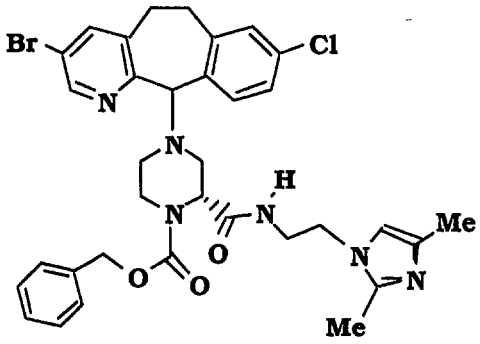
(Example 291);



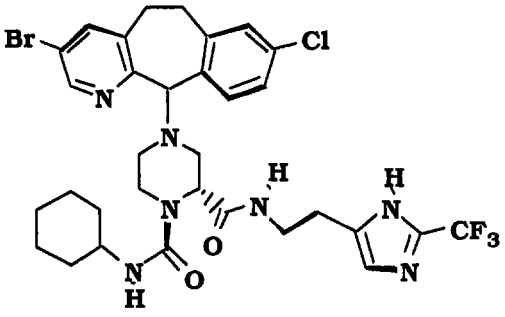
(Example 292);



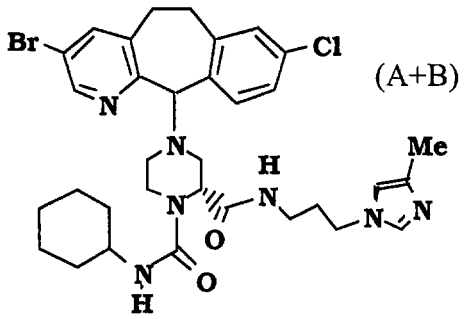
Isomer A (Example 293);



Isomer B (Example 293);

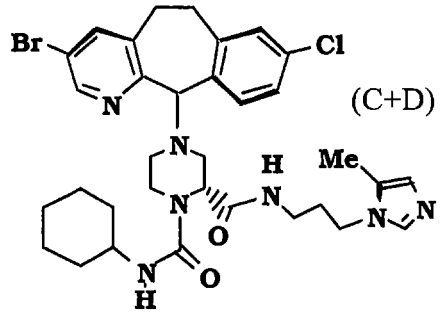


(Example 294);



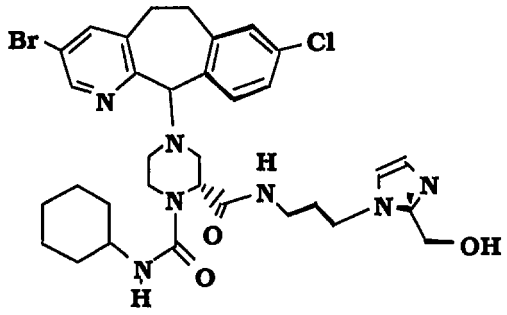
(A+B)

(Example 295);

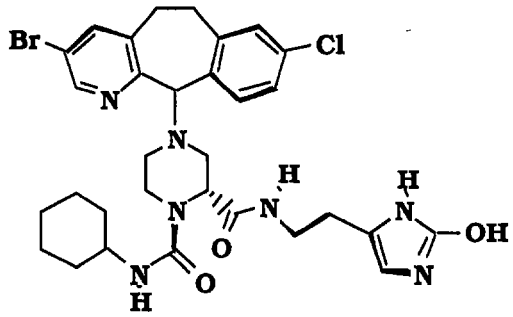


(C+D)

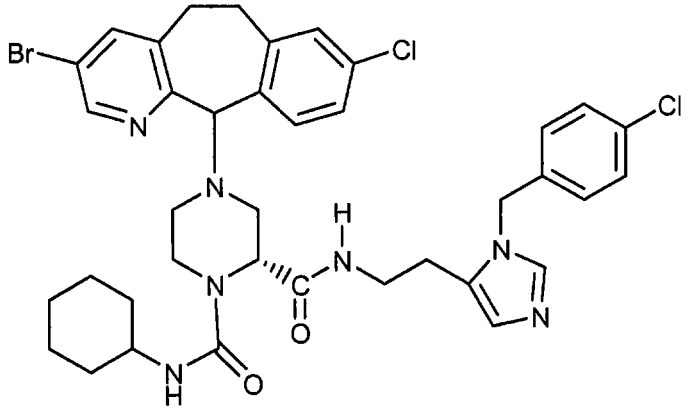
(Example 295);



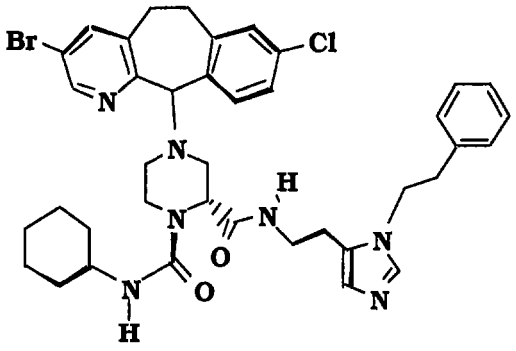
(Example 296);



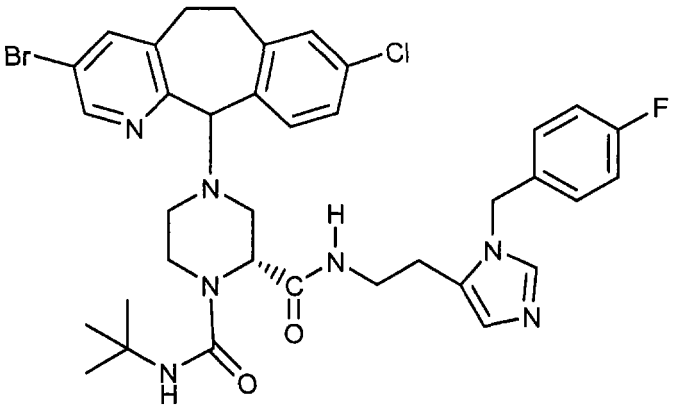
(Example 297);



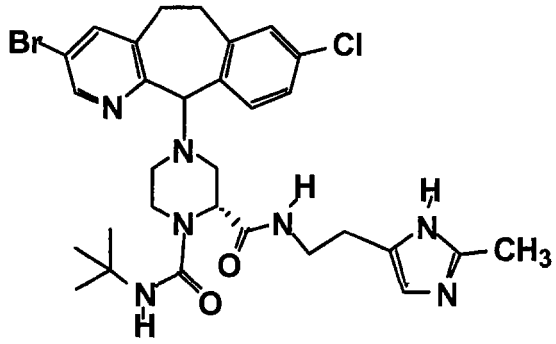
(Example 299);



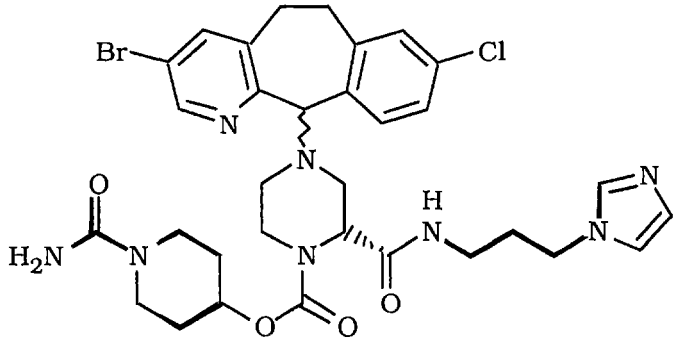
(Example 300);



(Example 302);



(Example 303); and



(Example 309).

8. A use of a compound as claimed in any one of **Claims 1 to 7** in the preparation of a medicament for treating tumor cells in a patient in need thereof.

9. A use as claimed in **Claim 8** wherein the tumor cells are selected from the group consisting of: pancreatic tumor cells; lung cancer cells; myeloid leukemia tumor cells; thyroid

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follicular tumor cells; myelodysplastic tumor cells; epidermal carcinoma tumor cells; bladder carcinoma tumor cells; colon tumors cells; melanoma; breast tumor cells and prostate tumor cells.

10. A use of a compound as claimed in any one of **Claims 1 to 7** in the preparation of a medicament for treating tumor cells in a patient in need thereof wherein the Ras protein is activated as a result of oncogenic mutation in genes other than the Ras gene.

11. A use of a compound as claimed in any one of **Claims 1 to 7** in the preparation of a medicament for inhibiting farnesyl protein transferase in a patent in need thereof.

12. A pharmaceutical composition for inhibiting farnesyl protein transferase comprising an effective amount of a compound as claimed in any one of **Claims 1 to 7** in combination with a pharmaceutically acceptable carrier.