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TITLE OF THE INVENTION:

IMIDAZOLE DERIVATIVES

BACKGROUND OF THE INVENTION

5 Field of the Invention:

This invention relates to novel imidazole derivatives and their acid addition salts, and more specifically to imidazole derivatives and their acid addition salts which have antibacterial activities against bacteria, fungi, yeasts, pathogenic plant fungi and the like and are hence usable as medicines, agricultural chemicals, antiseptics and so on.

Discussion of the Background:

15 There have already been known a variety of imidazole derivatives having antibacterial activities against fungi and the like, but their effects are still insufficient. There is thus a strong demand for the development of compounds having still better antibacterial activities.

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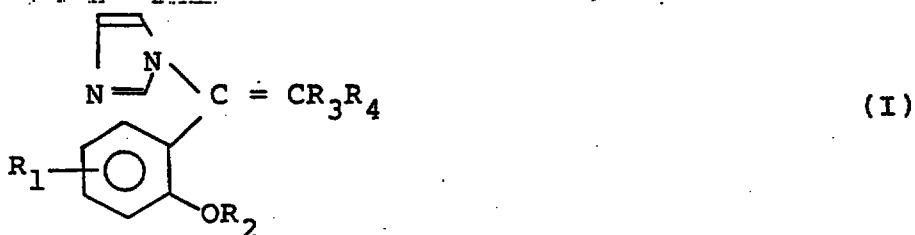
SUMMARY OF THE INVENTION

Accordingly, an object of the present invention is to provide imidazole derivatives having antibacterial activities better than conventionally-known imidazole derivatives.

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The present inventors have synthesized various imidazole derivatives and investigated their anti-bacterial activities. As a result, it has been found that imidazole derivatives represented by the following
5 general formula (I) have excellent antibacterial activities against bacteria, fungi, yeasts, pathogenic plant fungi and the like, leading to completion of this invention.

Namely, the present invention provides an
10 imidazole derivative represented by the following general formula (I):



15 wherein R₁ means a hydrogen or halogen atom or a lower alkyl group, R₂ denotes a hydrogen atom or an alkyl, alkenyl, haloalkyl or substituted or unsubstituted benzyl group, R₃ stands for a hydrogen or halogen atom, and R₄ is a substituted or unsubstituted benzylthio
20 group, a phenylthio, alkylthio, alkenylthio, furfurylthio, alkoxy or phenoxy group or a halogen atom; or an acid addition salt thereof.

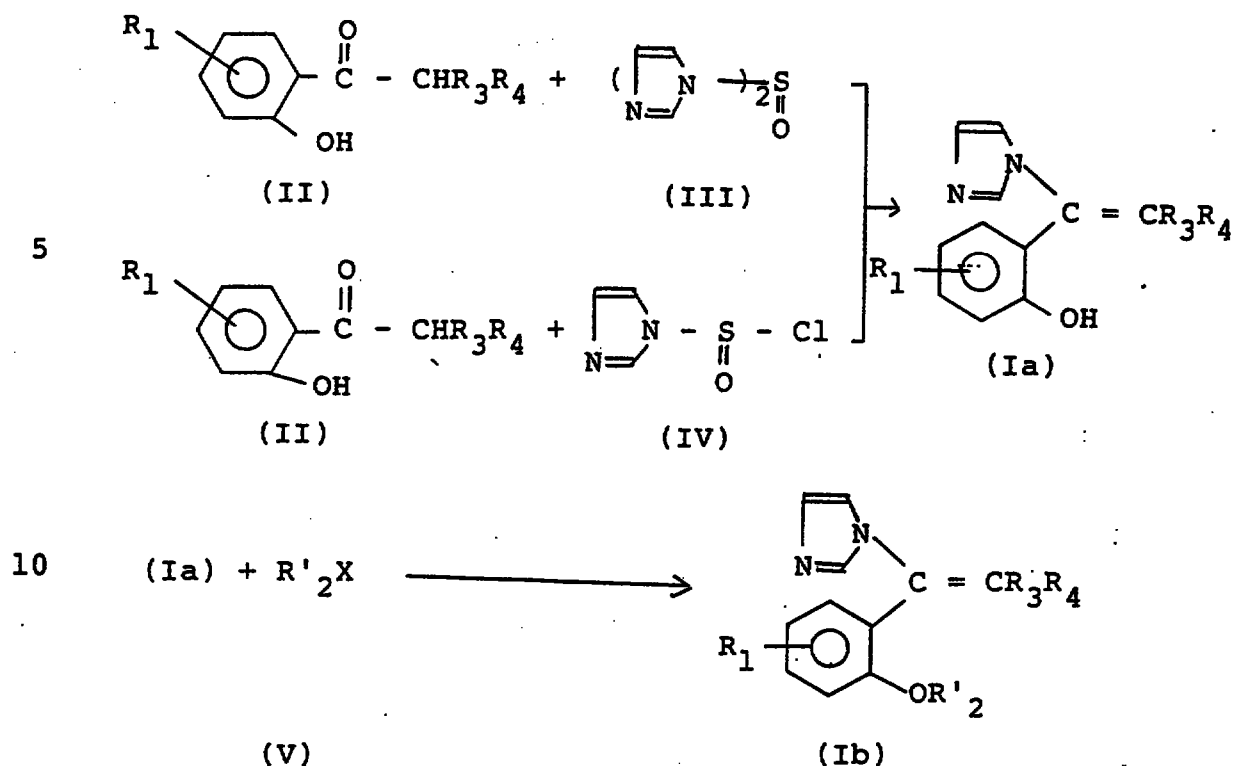
The compounds (I) of this invention, which are
25 obtained in the below-described manner, have excellent antibacterial activities against bacteria, fungi,

yeasts, pathogenic plant fungi and the like and are hence useful as medicines, agricultural chemicals, antiseptics and so on.

5 A more complete appreciation of the invention and many of the attendant advantages thereof will be readily obtained as the same becomes better understood by reference to the following detailed description.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

10 The compound (I) of this invention may be prepared, for example, in accordance with the following reaction scheme, namely, by reacting a phenol derivative (II) with an N,N'-thionyl-diimidazole (III) or
15 reacting the phenol derivative (II) with 1-imidazolyl-sulfinyl chloride (IV) in the presence of a base, e.g., triethylamine to obtain an imidazole derivative (Ia), and if desired, reacting the imidazole derivative (Ia) further with an alkylating, alkenylating, haloalkylating or substituted or unsubstituted benzylating agent
20 (V) to form another imidazole derivative (Ib).



wherein R_1 , R_2 , R_3 and R_4 have the same meaning as defined above, R'_2 denotes an alkyl, alkenyl, haloalkyl or substituted or unsubstituted benzyl group, and X means a halogen atom, benzenesulfonyloxy group, p-toluenesulfonyloxy group, methanesulfonyloxy group, trichloromethanesulfonyloxy group or the like.

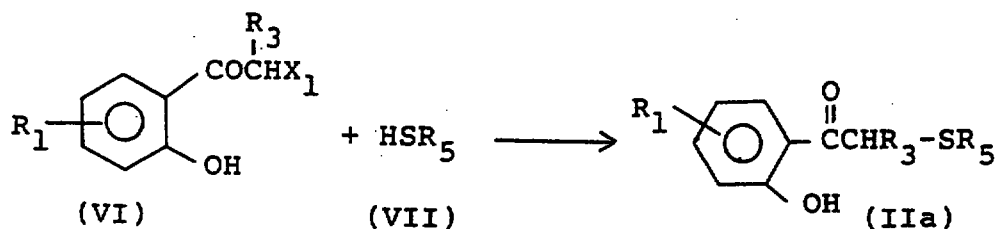
Phenol compounds (II), which are starting materials in the present invention, are either known compounds or those readily available in accordance with known processes. For example, they can each be prepared by any one of the following processes.

(1) In formula (II), R_4 : a substituted or unsubstituted benzylthio group or a phenylthio, alkylthio, alkenyl-

thio or furfurylthio group [Compound (IIa)]:

A 2'-hydroxy-2-haloacetophenone or its derivative (VI) and a thiol compound (VII) are reacted in the presence of an alkali.

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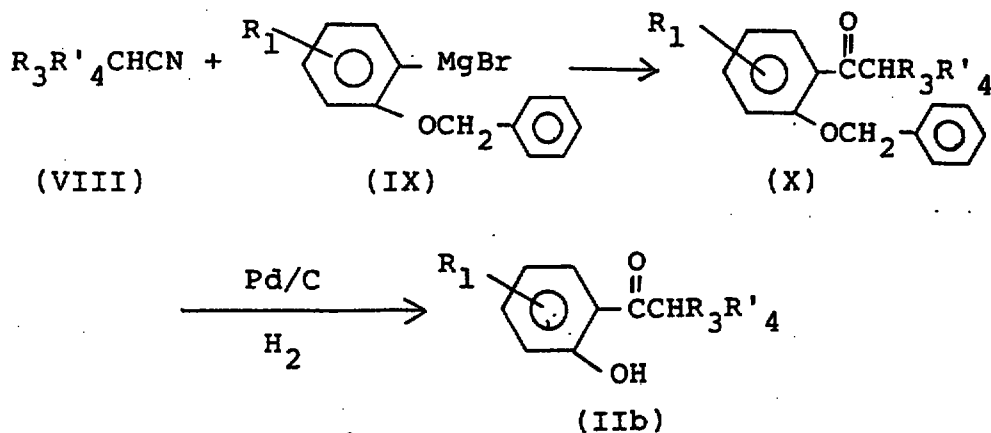


wherein R_1 and R_3 have the same meaning as defined above, and R_5 denotes a substituted or unsubstituted benzyl group or a phenyl, alkyl, alkenyl or furfuryl group, and X_1 stands for a halogen atom.

As thiol compounds (VII), may be used thiophenol, benzyl mercaptan which may contain one or more substituent groups, alkyl mercaptans, alkenyl mercaptans and furfuryl mercaptan.

(2) In formula (II), R_4 : an alkoxy or phenoxy group [Compound (IIb)]:

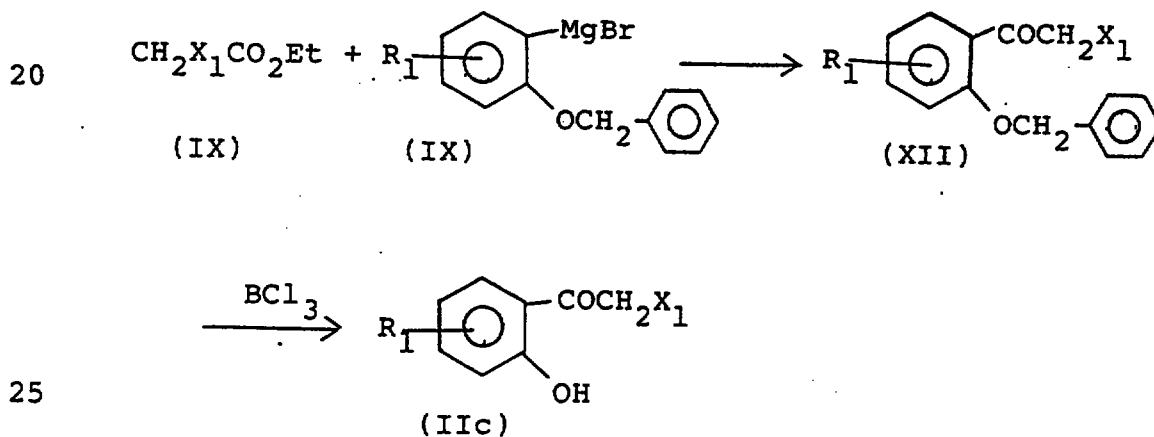
An alkoxyacetonitrile or its derivative (VIII) is reacted with 2-benzyloxyphenylmagnesium bromide or its derivative (IX) to obtain an acetophenone derivative (X), followed by its catalytic reduction to conduct debenzylation.



wherein R_1 and R_3 have the same meaning as defined above and R'_4 denotes an alkoxy or phenoxy group.

(3) In formula (II), R_4 : a halogen atom [Compound (IIc)]:

An ethyl monohaloacetate (XI) is reacted with 2-benzyloxyphenylmagnesium bromide (IX) at a low temperature (below -40°C) and the resulting acetophenone derivative (XII) is subjected to debenzoylation with boron trichloride, thereby preparing the compound (IIc).



wherein R_1 and X_1 have the same meaning as defined above.

The reaction between the compound (II) and the compound (III) or (IV) is effected by reacting them in a suitable solvent such as methylene chloride, chloroform, dimethylsulfoxide, acetonitrile, dimethylformamide or the like, at room temperature or with ice-cooling or heating, for 15 minutes - several hours. As exemplary bases useful in the reaction between the compound (II) and the compound (IV), may be mentioned, besides triethylamine referred to above, tertiary amines such as trimethylamine, tri-n-propylamine, N-methylmorpholine and N-ethylmorpholine.

On the other hand, the reaction between the compound (Ia) and the alkylating, alkenylating, haloalkylating or substituted or unsubstituted benzylating agent represented by the formula (V) is effected by reacting them in the presence of an alkali or by reacting an alkali salt of the compound (Ia) with the compound (V). As illustrative examples of the alkali employed in this reaction, may be mentioned sodium hydroxide, potassium hydroxide, sodium hydride, sodium alcoholate and the like. Illustrative examples of the alkali salt may include the sodium salt, potassium salt and so on. As a reaction solvent, may for example be mentioned dimethylformamide, benzene,

methanol, ethanol, tetrahydrofuran, ether or the like. The reaction is conducted at room temperature or with heating for several ten minutes - several ten hours. Except for the case where R_3 and R_4 are the same, the
5 thus-obtained compound (I) of this invention contains two types of isomers A and B. Each of these isomers has antibacterial activities, and they may hence be used either singly or as a mixture.

When it is desired to obtain either one of the
10 isomers of the compound (I) of this invention, it is only necessary to isolate the respective isomers by a known separation method such as column chromatography or to prepare selectively the desired isomer only by adjusting the reaction conditions.

15 The compound (I) of this invention can be converted into its acid addition salt by a method known per se in the art. As exemplary acid addition salts, may be mentioned those of acids acceptable from the standpoint of pharmacology and pharmaceutical
20 technology, for example, inorganic acids such as hydrochloric acid, sulfuric acid, nitric acid and hydrobromic acid as well as organic acids such as acetic acid, oxalic acid, fumaric acid, maleic acid, citric acid, malic acid and succinic acid.

25 Antibacterial activities of certain representa-

tive compounds of this invention, which had been
obtained in the above-described manner, were investi-
gated. Results are summarized in Table 1, in which the
compound numbers correspond to those to be given in
5 Examples which will be described herein.

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Table 1-A

Compound tested Microorganism tested	MIC ($\mu\text{g/ml}$)				
	Compound 3	Compound 4	Compound 7	Compound 8	
Bacillus subtilis ATCC 6633	1.56	6.25	25	3.12	
Staphylococcus aureus FDA 209P	12.5	25	50	25	
Staphylococcus aureus Terajima	6.25	12.5	25	6.25	
Staphylococcus aureus Smith	6.25	12.5	12.5	6.25	
Staphylococcus epidermidis ATCC 12228	3.12	12.5	25	6.25	
Sarcina lutea ATCC 9341	1.56	6.25	12.5	3.12	
Streptococcus faecalis IFO 12964	6.25	12.5	50	>100	
Micrococcus lysodeixitcus IFO 3333	0.78	3.12	6.25	1.56	
Candida albicans NHL 4019	50	25	100	>100	
Candida albicans Yu-1200	>100	>100	>100	>100	
Saccharomyces cerevisiae ATCC 9763	<0.2	<0.2	<0.2	<0.2	
Saccharomyces ruxii 6507	<0.2	<0.2	0.78	<0.2	
Aspergillus niger ATCC 9642	0.39	1.56	12.5	12.5	
Penicillium chrysogenum ATCC 6010	50	3.12	50	12.5	

Table 1-A (Cont'd)

Compound tested	MIC ($\mu\text{g/ml}$)			
	Compound 3	Compound 4	Compound 7	Compound 8
Microorganism tested				
Trichophyton mentagrophytes QM 248	<0.2	<0.2	3.12	0.39
Trichophyton mentagrophytes IFO 5812	<0.2	<0.2	0.78	0.39
Trichophyton tonsurans IFO 5928	<0.2	<0.2	<0.2	<0.2
Trichophyton rubrum NHL J	<0.2	<0.2	<0.2	<0.2
Microsporium gypseum IFO 8231	<0.2	<0.2	1.56	0.39
Microsporium audouinii IFO 6074	<0.2	<0.2	<0.2	<0.2
Microsporium cookei IFO 8303	6.25	1.56	12.5	12.5
Epidermophyton floccosum IFO 9045	3.12	1.78	6.25	6.25
Aspergillus oryzae IMF 4014	6.25	1.56	6.25	12.5
Cladosporium fulvum IAM 5006	12.5	25	100	>100
Fusarium moniliforme IAM 5062	>100	0.78	6.25	12.5
Helminthosporium sesamum IAM 5012	<0.2	<0.2	0.39	0.78
Pyricularia oryzae IAM 5016	<0.2	<0.2	<0.2	<0.2
Debaryomyces kloederi IFO 0015	6.25	6.25	25	6.25
Gibberella fujikuroi IAM 8046	25	0.78	6.25	6.25

Table 1-B

Compound tested	MIC ($\mu\text{g/ml}$)					
	Comp. 27	Comp. 34	Comp. 39	Comp. 46	Comp. 49	
Microorganism tested						
<i>Bacillus subtilis</i> ATCC 6633	6.25	3.12	12.5	6.25	3.12	
<i>Staphylococcus aureus</i> FDA 209P	12.5	12.5	25	12.5	12.5	
<i>Staphylococcus aureus</i> Terajima	6.25	12.5	25	12.5	6.25	
<i>Staphylococcus aureus</i> Smith	12.5	12.5	25	12.5	12.5	
<i>Staphylococcus epidermidis</i> ATCC 12228	6.25	3.12	25	6.25	3.12	
<i>Sarcina lutea</i> ATCC 9341	3.12	1.56	12.5	6.25	3.12	
<i>Streptococcus faecalis</i> IFO 12964	12.5	12.5	25	12.5	6.25	
<i>Micrococcus lysodeixiticus</i> IFO 3333	1.56	0.39	6.25	3.12	1.56	
<i>Candida albicans</i> NHL 4019	25	50	25	25	25	
<i>Candida albicans</i> Yu-1200	50	50	50	50	25	
<i>Saccharomyces cerevisiae</i> ATCC 9763	<0.2	<0.2	0.39	<0.2	50	
<i>Saccharomyces ruxii</i> 6507	<0.2	<0.2	0.78	0.78	<0.2	
<i>Aspergillus niger</i> ATCC 9642	0.39	0.78	1.56	1.56	<0.2	
<i>Penicillium chrysogenum</i> ATCC 6010	1.56	3.12	1.56	1.56	6.25	

Table 1-B (Cont'd)

Compound tested	MIC (µg/ml)				
	Comp. 27	Comp. 34	Comp. 39	Comp. 46	Comp. 49
Microorganism tested					
Trichophyton mentagrophytes QM 248	<0.2	<0.2	0.39	<0.2	<0.2
Trichophyton mentagrophytes IFO 5812	<0.2	<0.2	0.39	<0.2	<0.2
Trichophyton tonsurans IFO 5928	<0.2	<0.2	0.39	<0.2	<0.2
Trichophyton rubrum NHL J	<0.2	<0.2	<0.2	<0.2	<0.2
Microsporium gypseum IFO 8231	<0.2	<0.2	0.39	<0.2	<0.2
Microsporium audounii IFO 6074	<0.2	<0.2	<0.2	<0.2	<0.2
Microsporium cookei IFO 8303	<0.2	1.56	1.56	1.56	1.56
Epidermophyton floccosum IFO 9045	<0.2	1.56	1.56	1.56	0.78
Aspergillus oryzae IMF 4014	<0.2	1.56	0.78	0.78	0.78
Cladosporium fulvum IAM 5006	3.12	25	25	12.5	25
Fusarium moniliforme IAM 5062	<0.2	0.39	0.78	1.56	1.56
Helminthosporium sesamum IAM 5012	<0.2	<0.2	0.39	1.56	0.39
Pyricularia oryzae IAM 5016	<0.2	<0.2	<0.2	<0.2	<0.2
Debaryomyces kloeckeri IFO 0015	1.56	0.78	6.25	12.5	12.5
Gibberella fujikuroi IAM 8046	<0.2	<0.2	0.78	0.39	0.39

Table 1-C

Compound tested	MIC ($\mu\text{g/ml}$)					
	Comp. 64	Comp. 65	Comp. 73	Comp. 83	Comp. 93	
Microorganism tested						
<i>Bacillus subtilis</i> ATCC 6633	6.25	3.12	6.25	6.25	12.5	
<i>Staphylococcus aureus</i> FDA 209P	25	12.5	12.5	12.5	25	
<i>Staphylococcus aureus</i> Terajima	6.25	6.25	6.25	6.25	25	
<i>Staphylococcus aureus</i> Smith	12.5	6.25	12.5	12.5	25	
<i>Staphylococcus epidermidis</i> ATCC 12228	6.25	6.25	6.25	6.25	25	
<i>Sarcina lutea</i> ATCC 9341	6.25	3.12	6.25	3.12	25	
<i>Streptococcus faecalis</i> IFO 12964	25	12.5	12.5	12.5	50	
<i>Micrococcus lysodeixiticus</i> IFO 3333	1.56	1.56	3.12	1.56	6.25	
<i>Candida albicans</i> NHL 4019	>100	>100	50	50	100	
<i>Candida albicans</i> Yu-1200	>100	>100	50	12.5	>100	
<i>Saccharomyces cerevisiae</i> ATCC 9763	50	25	50	25	<0.2	
<i>Saccharomyces ruxii</i> 6507	1.56	6.25	1.56	<0.2	<0.2	
<i>Aspergillus niger</i> ATCC 9642	12.5	>100	12.5	12.5	>100	
<i>Penicillium chrysogenum</i> ATCC 6010	12.5	>100	6.25	25	>100	

Table 1-C (Cont'd)

Compound tested	MIC ($\mu\text{g/ml}$)			
	Comp. 64	Comp. 65	Comp. 73	Comp. 83
Microorganism tested	Comp. 64	Comp. 65	Comp. 73	Comp. 83
Trichophyton mentagrophytes QM 248	0.78	12.5	3.12	<0.2
Trichophyton mentagrophytes IFO 5812	<0.2	3.12	1.56	<0.2
Trichophyton tonsurans IFO 5928	3.12	12.5	3.12	<0.2
Trichophyton rubrum NHL J	<0.2	3.12	1.56	<0.2
Microsporum gypseum IFO 8231	6.25	12.5	3.12	1.56
Microsporum audouinii IFO 6074	<0.2	6.25	0.78	<0.2
Microsporum cookei IFO 8303	12.5	100	6.25	12.5
Epidermophyton floccosum IFO 9045	6.25	100	6.25	25
Aspergillus oryzae IMF 4014	6.25	>100	6.25	>100
Cladosporium fulvum IAM 5006	>100	>100	6.25	>100
Fusarium moniliforme IAM 5062	50	>100	12.5	>100
Helminthosporium sesamum IAM 5012	6.25	100	6.25	50
Pyricularia oryzae IAM 5016	<0.2	1.56	1.56	<0.2
Debaryomyces hansenii IFO 0015	>100	>100	3.12	6.25
Gibberella fujikuroi IAM 8046	25	>100	6.25	>100

Having generally described this invention, a further understanding can be obtained by reference to certain specific examples which are provided herein for purpose of illustration only and are not intended to be
5 limiting unless otherwise specified.

Example 1:

To a suspension of 4.08 g of imidazole and 30 ml of dry methylene chloride, 1.78 g of thionyl
10 chloride was added with ice-cooling. After stirring the reaction mixture for 30 minutes, 2.58 g of 2-benzylthio-2'-hydroxyacetophenone was added, followed by further stirring at room temperature for 2 hours. Ice water was added to the reaction mixture, followed
15 by extraction with methylene chloride. The organic, i.e., methylene chloride layer was washed with water, dried over magnesium sulfate and then concentrated. The residue was dissolved in chloroform and was then subjected to chromatography on a silica gel column.
20 Upon concentration of the resultant eluate, there were obtained 180 mg of Isomer A (m.p. 196 - 198°C; Compound 1) and 1.0 g of Isomer B (m.p. 136.5 - 138°C; Compound 2) of 1-(2-hydroxyphenyl)-1-imidazolyl-2-benzylthioethylene (in formula (I), $R_1, R_2, R_3 = H$,
25 $R_4 = -SCH_2C_6H_5$), both, as colorless crystals.

Example 2:

Dissolved in 2 ml of dry dimethylformamide was 100 mg of Compound 1 obtained above, to which 15 mg of 60% sodium hydride was added, followed by stirring at
5 room temperature. Thirty minutes later, 45 mg of n-propyl bromide was added. The resultant mixture was left over at room temperature for 4 hours. The reaction mixture was then added with water, followed by its extraction with ethyl ether. The ether extract was
10 dried over magnesium sulfate and the ether was then distilled off. The residue was purified by chromatography on a silica gel column. From the resulting chloroform eluate, 90 mg of Isomer A (Compound 3) of 1-(2-n-propyloxyphenyl)-1-imidazolyl-2-benzylthio-
15 ethylene (in formula (I), $R_1, R_3 = H$, $R_2 = n-C_3H_7$, $R_4 = -SCH_2C_6H_5$) was obtained as colorless crystals.

Example 3:

Two hundred milligrams of Compound 3 obtained in Example 2 were used. After an addition of hydrogen
20 chloride in an equivalent amount, the resultant precipitate was recrystallized from ethyl acetate/acetone to obtain 120 mg of Isomer A (Compound 17) of 1-(2-n-propyloxyphenyl)-1-imidazolyl-2-benzylthio-ethylene hydrochloride as colorless crystals.

25 Example 4:

Using the compound (or its isomers) obtained in

Example 1, the compounds given in Table 2-A were obtained in the same manner as in Example 2. The compounds obtained in Examples 1 - 3 are also shown in the table.

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Table 2-A

Comp. No.	Structure				Characteristics		
	Formula (I)				Appearance (m.p. °C)	NMR δ ppm in CDCl ₃	IR ν cm ⁻¹ NaCl max
	R ₁	R ₂	R ₃	R ₄			
1	H	H	H	-SCH ₂ C ₆ H ₅	Colorless crystal (196-198)	3.98(2H,s) 6.64(1H,s) 6.70-7.40(11H,m) 7.64(1H,br)	*1600, 1495, 1445, 1080
2	H	H	H	-SCH ₂ C ₆ H ₅	Colorless crystal (136.5-138)	3.90(2H,s) 6.36(1H,s) 6.70-7.60(12H,m)	*1600, 1495, 1450, 1225
3	H	n-C ₃ H ₇	H	-SCH ₂ C ₆ H ₅	Colorless crystal (82.5-84.0)	0.88(3H,t) 1.52(2H,m) 3.78(2H,t) 3.94(2H,s) 6.70(1H,s) 6.74-7.40(11H,m) 7.54(1H,s)	*3000, 1585, 1485, 1445, 1240, 1080
4	H	n-C ₃ H ₇	H	-SCH ₂ C ₆ H ₅	Oily matter	0.78(3H,t) 1.48(2H,m) 3.75(2H,t) 3.86(2H,s) 6.30(1H,s) 6.70-7.60(12H,m)	2950, 1600, 1485, 1450, 1240
5	H	CH ₃	H	-SCH ₂ C ₆ H ₅	Colorless crystal (75.0-76.5)	3.60(3H,s) 3.92(2H,s) 6.78(1H,s) 6.80-7.40(11H,m) 7.52(1H,s)	*1595, 1495, 1255, 1075, 1020
6	H	C ₂ H ₅	H	-SCH ₂ C ₆ H ₅	Colorless crystal (88.5-90.0)	1.16(3H,t) 3.78(2H,q) 3.94(2H,s) 6.70(1H,s) 6.74-7.40(11H,m) 7.54(1H,s)	*2950, 1595, 1495, 1245, 1070

Note 1: In the column under "IR", asterisk "*" indicates measurement with KBr.

Note 2: In the column under "Isomer type", "A" means compounds derived from Compound 1 or compounds having the same steric configuration as the former compounds, "B" indicates compounds derived from Compound 2 or compounds having the same steric configuration as the compounds derived from Compound 2, and "—" indicates a mixture of isomers A and B. The same definition applies to subsequent tables.

Table 2-A (Cont'd)

Comp. No.	Structure				Characteristics		
	Formula (I)				Appearance (m.p. °C)	NMR δ ppm in CDCl_3	IR ν_{max} NaCl cm^{-1}
	R_1	R_2	R_3	R_4			
7	H	C_2H_5	H	$-\text{SCH}_2\text{C}_6\text{H}_5$	Oily matter	1.10, 1.16(3H, t) 3.75, 3.78(2H, q) 3.86, 3.94(2H, s) 6.30, 6.70(1H, s) 6.70-7.60(12H, m)	1600, 1485, 1450, 1240
8	H	$\text{n-C}_4\text{H}_9$	H	$-\text{SCH}_2\text{C}_6\text{H}_5$	Colorless crystal (60.5-61.5)	0.70-1.80(7H, br) 3.78(2H, t) 3.94(2H, s) 6.70(1H, s) 6.74-7.40(11H, m) 7.54(1H, s)	*2950, 1585, 1485, 1440, 1240, 1080
9	H	$\text{n-C}_4\text{H}_9$	H	$-\text{SCH}_2\text{C}_6\text{H}_5$	Oily matter	0.70-1.80(7H, br) 3.60-3.90(4H, m) 6.30, 6.70(1H, s) 6.74-7.50(12H, m)	2950, 1600, 1485, 1450, 1240
10	H	$\text{n-C}_5\text{H}_{11}$	H	$-\text{SCH}_2\text{C}_6\text{H}_5$	Oily matter	0.70-1.80(9H, br) 3.60-3.90(4H, m) 6.30, 6.70(1H, s) 6.74-7.50(12H, m)	2950, 1600, 1485, 1450, 1240
11	H	$\text{n-C}_6\text{H}_{13}$	H	$-\text{SCH}_2\text{C}_6\text{H}_5$	Oily matter	0.70-1.80(11H, br) 3.60-3.90(4H, m) 6.30, 6.70(1H, s) 6.74-7.50(12H, m)	2950, 1600, 1485, 1450, 1240
12	H	$\text{n-C}_7\text{H}_{15}$	H	$-\text{SCH}_2\text{C}_6\text{H}_5$	Oily matter	0.70-1.80(13H, br) 3.60-3.90(4H, m) 6.30, 6.70(1H, s) 6.74-7.50(12H, m)	2950, 1600, 1485, 1450, 1245
13	H	$\text{n-C}_8\text{H}_{17}$	H	$-\text{SCH}_2\text{C}_6\text{H}_5$	Oily matter	0.70-1.80(15H, br) 3.60-3.90(4H, m) 6.30, 6.70(1H, s) 6.74-7.50(12H, m)	2950, 1600, 1485, 1450, 1245
14	H	$\text{n-C}_9\text{H}_{19}$	H	$-\text{SCH}_2\text{C}_6\text{H}_5$	Oily matter	0.70-1.80(17H, br) 3.60-3.90(4H, m) 6.30, 6.70(1H, s) 6.74-7.50(12H, m)	2950, 1600, 1485, 1450, 1245

Table 2-A (Cont'd)

Comp. No.	Structure				Characteristics		
	Formula (I)			Isomer type	Appearance (m.p. °C)	NMR δ ppm in CDCl ₃	IR ν NaCl cm ⁻¹ max
	R ₁	R ₂	R ₃	R ₄			
15	H	-CH(CH ₃) ₂	H	-SCH ₂ C ₆ H ₅	-	1.05(6H,d) 3.86,3.94(1H,s) 4.46(1H,m) 6.30,6.70(1H,s) 6.74-7.60(12H,m)	3000,1600,1485, 1450,1375,1245
16	H	-CH ₂ -CH=CH ₂	H	-SCH ₂ C ₆ H ₅	-	3.86,3.94(1H,s) 4.38(2H,d) 4.96-6.00(3H,m) 6.30,6.70(1H,s) 6.74-7.60(12H,m)	3050,1600,1490, 1450,1420,1230
17	H	n-C ₃ H ₇	H	-SCH ₂ C ₆ H ₅	A	0.86(3H,t) 1.47(2H,m) 3.76(2H,t) 4.04(2H,s) 6.75(1H,s) 6.76-7.60 (1H,m) 8.22(1H,s) (167.0-168.5)	*3000,1600,1450, 1250,1240,980

Example 5:

To a suspension of 1.02 g of imidazole, 1.52 g of triethylamine and 30 ml of dry methylene chloride, 1.78 g of thionyl chloride was added with ice-cooling.

5 The resultant mixture was stirred for 30 minutes, followed by addition of 2.42 g of 2-n-propylthio-2'-hydroxyacetophenone and a solution consisting of 1.16 g of triethylamine and 5 ml of dry methylene chloride. The reaction mixture was stirred at room temperature

10 for further 2 hours. Ice water was then added to the reaction mixture, followed by its extraction with methylene chloride. The organic, i.e., methylene chloride layer was washed with water, dried over magnesium sulfate, and then concentrated. The residue

15 was dissolved in chloroform. The chloroform solution was subjected to chromatography on a silica gel column. Upon concentration of the resulting eluate, 0.2 g of Isomer A (Compound 19; m.p. 191 - 192°C) and 1.1 g of Isomer B (Compound 18; m.p. 127 - 128°C) of 1-(2-

20 hydroxyphenyl)-1-imidazolyl-2-n-propylthioethylene were obtained respectively as colorless crystals.

Example 6:

To a suspension of 4.08 g of imidazole and 30 ml of dry methylene chloride, 1.78 g of thionyl chloride

25 was added with ice-cooling. The resultant mixture was stirred for 30 minutes, followed by an addition of

2.10 g of 2-n-propylthio-2'-hydroxyacetophenone. The thus-obtained mixture was stirred at room temperature for 2 hours. Ice water was then added to the reaction mixture, followed by its extraction with methylene chloride. The methylene chloride extract was then subjected to a post treatment in the same manner as in Example 5. The reaction product was separated by column chromatography, thereby obtaining 0.2 g of Isomer A (Compound 18) and 1.0 g of Isomer B (Compound 19) of 1-(2-hydroxyphenyl)-1-imidazolyl-2-n-propylthio-ethylene as colorless crystals respectively.

Example 7:

Dissolved in 2 ml of dry dimethylformamide was 100 mg of Compound 18 obtained in Example 5, to which 15 mg of sodium hydroxide was added. After stirring the resultant mixture at room temperature for 30 minutes, 55 mg of n-butyl bromide was added and the resulting mixture was left over at room temperature for 4 hours. Water was then added to the reaction mixture, followed by its extraction with ethyl ether. The ethyl ether extract was dried over magnesium sulfate and the ethyl ether was then distilled off. The residue was purified by chromatography on a silica gel column. From a chloroform eluate, 100 mg of Isomer A (Compound 20) of 1-(2-n-butyloxyphenyl)-1-imidazolyl-2-n-propylthioethylene was obtained as colorless crystals.

Example 8:

After adding an equivalent amount of hydrogen chloride to 200 mg of an oily substance which was Isomer B of 1-(2-n-butyloxyphenyl)-1-imidazolyl-2-n-propylthioethylene obtained from Compound 19 in the same manner as in Example 6, the resultant precipitate was recrystallized from ethyl acetate/acetone to obtain 140 mg of Isomer B (Compound 21) of 1-(2-n-butyloxyphenyl)-1-imidazolyl-2-n-propylthioethylene hydrochloride as colorless crystals.

Example 9:

Compounds 22 - 60 shown in Table 2-B were each prepared in the same manner as in any one of Examples 5 - 8. Physical properties of Compounds 18 - 21 are also given in the table.

Table 2-B

Comp. No.	Structure				Characteristics		
	Formula (I)				Appearance (m.p. °C)	NMR δ ppm in CDCl ₃	IR ν NaCl cm ⁻¹ max
	R ₁	R ₂	R ₃	R ₄			
18	H	H	H	-S-n-C ₃ H ₇	Colorless crystal (191-192)	1.01(3H,t) 1.72(2H,m) 2.77(2H,t) 6.70(1H,s) 6.80-7.40(6H,m) 7.69(1H,s)	*2970, 1590, 1495, 1445, 1090
19	H	H	H	-S-n-C ₃ H ₇	Colorless crystal (127-128)	0.98(3H,t) 1.66(2H,m) 2.68(2H,t) 6.40(1H,s) 6.80-7.40(6H,m) 7.46(1H,s)	*2970, 1595, 1495, 1455, 1230, 1080
20	H	n-C ₄ H ₉	H	-S-n-C ₃ H ₇	Colorless crystal (77-78)	0.80-1.90(12H,m) 2.72(2H,t) 3.88(2H,t) 6.84(1H,s) 6.80-7.30(6H,m) 7.68(1H,s)	*2940, 1585, 1495, 1245
21	H	n-C ₄ H ₉	H	-S-n-C ₃ H ₇	Colorless crystal (HCl) (109.5-111)	0.70-1.90(12H,m) 2.84(2H,t) 3.82(2H,t) 6.80-7.60(7H,m) 8.75(1H,s)	*2940, 1650, 1560, 1455, 1240
22	H	CH ₃	H	-SCH ₃	Oily matter	2.28(3H,s) 3.68(3H,s) 6.38(1H,s) 6.70-7.50(7H,m)	2930, 1600, 1490, 1250, 1025
23	H	C ₂ H ₅	H	-SCH ₃	Colorless crystal (96-97)	1.14(3H,t) 2.28(3H,s) 3.88(2H,q) 6.36(1H,s) 6.70-7.50(7H,m)	*3000, 1595, 1485, 1255, 1050
24	H	n-C ₃ H ₇	H	-SCH ₃	Colorless crystal (67-68)	0.82(3H,t) 1.52(2H,m) 2.28(3H,s) 3.78(2H,t) 6.36(1H,s) 6.70-7.50(7H,m)	*2950, 1595, 1485, 1255, 1045

Table 2-B (Cont'd)

Comp. No.	Structure				Characteristics		
	Formula (I)				Appearance (m.p. °C)	NMR δ ppm in CDCl ₃	IR ν NaCl cm ⁻¹ max
	R ₁	R ₂	R ₃	R ₄			
25	H	n-C ₄ H ₉	H	-SCH ₃	Colorless crystal (63.5-64.5)	0.86(3H,t) 1.00-1.70(4H,m) 2.28(3H,s) 3.83(2H,t) 6.36(1H,s) 6.70-7.50(7H,m)	*2950, 1595, 1485, 1255
26	H	n-C ₅ H ₁₁	H	-SCH ₃	Colorless crystal (38.5-39.5)	0.86(3H,t) 1.01-1.70(6H,m) 2.28(3H,s) 3.80(2H,t) 6.34(1H,s) 6.70-7.50(7H,m)	*2950, 1595, 1485, 1255, 1070
27	H	n-C ₆ H ₁₃	H	-SCH ₃	Colorless crystal (65.5-66.5)	0.70-1.70(11H,m) 2.28(3H,s) 3.80(2H,t) 6.34(1H,s) 6.70-7.50(7H,m)	*2940, 1600, 1485, 1235, 1115
28	H	n-C ₇ H ₁₅	H	-SCH ₃	Colorless crystal (67.5-68.5)	0.70-1.70(13H,m) 2.28(3H,s) 3.80(2H,t) 6.34(1H,s) 6.70-7.50(7H,m)	*2930, 1595, 1485, 1230, 1150
29	H	n-C ₈ H ₁₇	H	-SCH ₃	Colorless crystal (37-38)	0.70-1.70(15H,m) 2.28(3H,s) 3.80(2H,t) 6.34(1H,s) 6.70-7.50(7H,m)	*2930, 1595, 1480, 1240, 1110
30	H	CH ₃	H	-SC ₂ H ₅	Oily matter	1.31(3H,t) 2.72(2H,q) 3.68(3H,s) 6.43(1H,s) 6.70-7.50(7H,m)	2970, 1600, 1490, 1250, 1030
31	H	C ₂ H ₅	H	-SC ₂ H ₅	Colorless crystal (79-80)	1.14(3H,t) 1.31(3H,t) 2.72(2H,q) 3.88(2H,q) 6.40(1H,s) 6.70-7.50(7H,m)	*2980, 1595, 1485, 1450, 1245, 1040
32	H	n-C ₃ H ₇	H	-SC ₂ H ₅	Colorless crystal (48-49)	0.83(3H,t) 1.32(3H,t) 1.20-1.70(2H,m) 2.72(2H,q) 3.78(2H,t) 6.40(1H,s) 6.70-7.50(7H,m)	*2950, 1600, 1490, 1455, 1250

Table 2-B (Cont'd)

Comp. No.	Structure					Characteristics		
	Formula (I)					Appearance (m.p. °C)	NMR δ ppm in CDCl ₃	IR ν max NaCl cm ⁻¹
	R ₁	R ₂	R ₃	R ₄	Isomer type			
33	H	n-C ₄ H ₉	H	-SC ₂ H ₅	B	Colorless crystal (33.5-34.5)	0.86(3H,t) 1.00-1.70(4H,m) 1.30(3H,t) 2.71(2H,q) 3.82(2H,t) 6.39(1H,s) 6.70-7.50(7H,m)	*2950, 1595, 1480, 1240, 1105
34	H	n-C ₅ H ₁₁	H	-SC ₂ H ₅	B	Colorless crystal (51-52)	0.70-1.70(12H,m) 2.70(2H,q) 3.80(2H,t) 6.39(1H,s) 6.70-7.50(7H,m)	*2950, 1595, 1480, 1240, 1230, 1105
35	H	n-C ₆ H ₁₃	H	-SC ₂ H ₅	B	Colorless crystal (51.5-53)	0.70-1.70(14H,m) 2.71(2H,q) 3.80(2H,t) 6.39(1H,s) 6.70-7.50(7H,m)	*2930, 1595, 1485, 1245, 1230, 1110
36	H	n-C ₇ H ₁₅	H	-SC ₂ H ₅	B	Colorless crystal (56-57)	0.70-1.70(16H,m) 2.70(2H,q) 3.80(2H,t) 6.40(1H,s) 6.70-7.50(7H,m)	*2930, 1595, 1490, 1450, 1250, 1110
37	H	CH ₃	H	-S-n-C ₃ H ₇	B	Colorless crystal (71-72)	0.96(3H,t) 1.64(2H,m) 2.64(2H,t) 3.66(3H,s) 4.38(1H,s) 6.70-7.50(7H,m)	*2970, 1600, 1490, 1250, 1055
38	H	C ₂ H ₅	H	-S-n-C ₃ H ₇	B	Colorless crystal (68-69)	0.99(3H,t) 1.14(3H,t) 1.66(2H,m) 2.68(2H,t) 3.88(2H,q) 6.38(1H,s) 6.70-7.50(7H,m)	*2960, 1595, 1485, 1245, 1040
39	H	n-C ₃ H ₇	H	-S-n-C ₃ H ₇	B	Oily matter	0.70-1.90(10H,m) 2.68(2H,t) 3.78(2H,t) 6.40(1H,s) 6.70-7.50(7H,m)	2960, 1595, 1485, 1245, 980
40	H	n-C ₅ H ₁₁	H	-S-n-C ₃ H ₇	B	Colorless crystal (HCl) (112.5-124)	0.70-1.90(14H,m) 2.84(2H,t) 3.82(2H,t) 6.80-7.60(7H,m) 8.75(1H,s)	*2950, 1600, 1565, 1445, 1255

Table 2-B (Cont'd)

Comp. No.	Structure				Characteristics		
	Formula (I)				Appearance (m.p. °C)	NMR δ ppm in CDCl ₃	IR ν cm ⁻¹ NaCl max
	R ₁	R ₂	R ₃	R ₄			
41	H	n-C ₆ H ₁₃	H	-S-n-C ₃ H ₇	Oily matter	0.70-1.90(16H,m) 2.68(2H,t) 3.78(2H,t) 6.40,6.80(1H,s) 6.80-7.60(7H,m)	2970,2940,1600,1485,1245,1110
42	H	n-C ₇ H ₁₅	H	-S-n-C ₃ H ₇	Oily matter	0.70-1.90(18H,m) 2.68(2H,t) 3.78(2H,t) 6.40,6.80(1H,s) 6.80-7.60(7H,m)	2940,1600,1485,1245
43	H	n-C ₈ H ₁₇	H	-S-n-C ₃ H ₇	Oily matter	0.70-1.90(20H,m) 2.68(2H,t) 3.78(2H,t) 6.40,6.80(1H,s) 6.70-7.60(7H,m)	2940,1595,1485,1450,1245,1050
44	H	CH ₃	H	-S-n-C ₄ H ₉	Colorless crystal (72-73.5)	0.90(3H,t) 1.10-1.80(4H,m) 2.68(2H,t) 3.68(3H,s) 6.41(1H,s) 6.70-7.50(7H,m)	*2950,1595,1490,1245,1070
45	H	C ₂ H ₅	H	-S-n-C ₄ H ₉	Oily matter	0.70-1.80(10H,m) 2.68(2H,t) 3.86(2H,q) 6.39(1H,s) 6.70-7.60(7H,m)	2970,2940,1600,1495,1450,1250,1120
46	H	n-C ₃ H ₇	H	-S-n-C ₄ H ₉	Oily matter	0.70-1.80(12H,m) 2.68(2H,t) 3.80(2H,t) 6.37(1H,s) 6.70-7.50(7H,m)	2970,1595,1490,1450,980
47	H	n-C ₄ H ₉	H	-S-n-C ₄ H ₉	Oily matter	0.70-1.80(14H,m) 2.68(2H,t) 3.80(2H,t) 6.37(1H,s) 6.70-7.50(7H,m)	2960,1595,1485,1450,1245,1110
48	H	n-C ₅ H ₁₁	H	-S-n-C ₄ H ₉	Oily matter	0.70-1.80(16H,m) 2.68(2H,t) 3.80(2H,t) 6.37(1H,s) 6.70-7.50(7H,m)	2960,1595,1490,1450,1250,1110
49	H	C ₂ H ₅	H	-S-n-C ₅ H ₁₁	Oily matter	0.70-1.80(12H,m) 2.68(2H,t) 3.86(2H,q) 6.38(1H,s) 6.80-7.60(7H,m)	2940,1595,1485,1450,1245

Table 2-B (Cont'd)

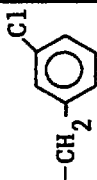
Comp. No.	Structure				Characteristics		
	Formula (I)			Isomer type	Appearance (m.p. °C)	NMR δ ppm in CDCl ₃	IR ν NaCl max cm^{-1}
	R ₁	R ₂	R ₃	R ₄			
50	H	-CH ₂ -CH=CH ₂	H	-S-n-C ₆ H ₁₃	B	Oily matter 0.70-1.80(1H,m) 2.68(2H,t) 4.32(2H,m) 5.02(2H,m) 5.60(1H,m) 6.38(1H,s) 6.80-7.60(7H,m)	2940, 1595, 1485, 1450, 1245, 1045
51	H	-CH ₂ CF ₃	H	-S-n-C ₃ H ₇	B	Oily matter 0.98(3H,t) 1.66(2H,m) 2.68(2H,t) 4.20(2H,q) 6.45(1H,s) 6.80-7.60(7H,m)	2980, 1600, 1490, 1240, 1165
52	H	-CH ₂ CF ₃	H	-S-n-C ₄ H ₉	B	Oily matter 0.90(3H,t) 1.10-1.80(4H,m) 2.68(2H,t) 4.20(2H,q) 6.44(1H,s) 6.80-7.60(7H,m)	2970, 1600, 1490, 1240, 1165
53	H	-CH ₂ C ₆ H ₅	H	-SCH ₃	B	Colorless crystal (85.5-86.5) 2.27(3H,s) 4.94(2H,s) 6.36(1H,s) 6.80-7.50(12H,m)	*3130, 2940, 1595, 1485, 1240, 1220 1110
54	H		H	-SCH ₃	B	Oily matter 2.27(3H,s) 4.95(2H,s) 6.36(1H,s) 6.80-7.50(11H,m)	3130, 2940, 1600, 1490, 1245, 1120
55	H	n-C ₃ H ₇	H	-SCH ₂ CH=CH ₂	B	Oily matter 0.80(3H,t) 1.52(2H,m) 3.28(2H,d) 3.76(2H,t) 5.00-5.32(2H,m) 5.60-6.06(1H,m) 6.32(1H,s) 6.70-7.60(7H,m)	2970, 1600, 1490, 1455, 1245, 1120
56	H	C ₂ H ₅	H	-SC(CH ₃) ₃	B	Oily matter 1.12(3H,t) 1.36(9H,s) 3.85(2H,q) 6.55(1H,s) 6.70-7.60(7H,m)	2970, 1600, 1485, 1450, 1250, 1050

Table 2-B (Cont'd)

Comp. No.	Structure				Characteristics		
	Formula (I)				Appearance (m.p. °C)	NMR δ ppm in CDCl ₃	IR ν NaCl cm ⁻¹ max
	R ₁	R ₂	R ₃	R ₄			
57	H	n-C ₃ H ₇	H	-SC(CH ₃) ₃	B	Oily matter 0.80(3H,t) 1.36(9H,s) 1.54(2H,m) 3.76(2H,t) 6.55(1H,s) 6.70-7.60 (7H,m)	2970, 1600, 1490, 1455, 1250, 1160
58	H	n-C ₃ H ₇	H	-SCH ₃	A	Oily matter 0.94(3H,t) 1.66(2H,m) 2.32(3H,s) 3.84(2H,t) 6.72(1H,s) 6.76-7.40 (6H,m) 7.56(1H,s)	2940, 1595, 1490, 1250, 1070
59	H	n-C ₄ H ₉	H	-SCH ₃	A	Oily matter 0.92(3H,t) 1.10-1.80(4H,m) 2.32 (3H,s) 3.88(2H,t) 6.74(1H,s) 6.76-7.40(6H,m) 7.56(1H,s)	2940, 1595, 1490, 1250, 1070
60	H	n-C ₅ H ₁₁	H	-SCH ₃	A	Oily matter 0.90(3H,t) 1.10-1.80(6H,m) 2.32 (3H,s) 3.86(2H,t) 6.74(1H,s) 6.76-7.40(6H,m) 7.54(1H,s)	2940, 1595, 1490, 1250, 1070

Example 10:

To a suspension of 1.02 g of imidazole, 1.52 g of triethylamine and 30 ml of dry methylene chloride, 1.78 g of thionyl chloride was added with ice-cooling.

5 The resultant mixture was stirred for 30 minutes, followed by addition of 2.44 g of 2-phenylthio-2'-hydroxyacetophenone and a solution consisting of 1.16 g of triethylamine and 5 ml of dry methylene chloride. The reaction mixture was stirred at room temperature

10 for further 2 hours. Ice water was then added to the reaction mixture, followed by its extraction with methylene chloride. The organic, i.e., methylene chloride layer was washed with water, dried over magnesium sulfate, and then concentrated. The residue

15 was dissolved in chloroform. The chloroform solution was subjected to chromatography on a silica gel column. Upon concentration of the resulting eluate, 0.2 g of Isomer A (Compound 61; m.p. 235.5 - 237°C) and 0.9 g of Isomer B (Compound 62; m.p. 152.5 - 154°C) of 1-(2-

20 hydroxyphenyl)-1-imidazolyl-2-phenylthioethylene were obtained respectively as colorless crystals.

Example 11:

To a suspension of 4.08 g of imidazole and 30 ml of dry methylene chloride, 1.78 g of thionyl chloride

25 was added with ice-cooling. The resultant mixture was stirred for 30 minutes, followed by an addition of

2.10 g of 2-phenylthio-2'-hydroxyacetophenone. The thus-obtained mixture was stirred at room temperature for 2 hours. Ice water was then added to the reaction mixture, followed by its extraction with methylene chloride. The methylene chloride extract was then subjected to a post treatment in the same manner as in Example 10. The reaction product was separated by column chromatography, thereby obtaining 0.2 g of Isomer A (Compound 61) and 1.0 g of Isomer B (Compound 62) of 1-(2-hydroxyphenyl)-1-imidazolyl-2-phenylthio-ethylene as colorless crystals respectively.

Example 12:

Dissolved in 2 ml of dry dimethylformamide was 100 mg of Compound 61 obtained in Example 10, to which 15 mg of sodium hydroxide was added. After stirring the resultant mixture at room temperature for 30 minutes, 45 mg of ethyl bromide was added and the resulting mixture was left over at room temperature for 4 hours. Water was then added to the reaction mixture, followed by its extraction with ethyl ether. The ethyl ether extract was dried over magnesium sulfate and the ethyl ether was then distilled off. The residue was purified by chromatography on a silica gel. From a chloroform eluate, 100 mg of Isomer A (Compound 63) of 1-(2-ethyloxyphenyl)-1-imidazolyl-2-phenylthioethylene was obtained as colorless crystals.

Example 13:

After adding an equivalent amount of hydrogen chloride to 100 mg of an oily substance which was Isomer B (Compound 66) of 1-(2-n-butyloxyphenyl)-1-imidazolyl-2-phenylthioethylene obtained from Compound 62 in the same manner as in Example 10, the resultant precipitate was recrystallized from ethyl acetate/acetone to obtain 75 mg of Isomer B (Compound 95) of 1-(2-n-butyloxyphenyl)-1-imidazolyl-2-phenylthioethylene hydrochloride as colorless crystals.

Example 14:

Compounds 64, 65 and 67 - 94 shown in Table 2-C were each prepared in the same manner as in any one of Examples 10 - 13. Physical properties of Compounds 61 - 63, 66 and 95 are also given in the table.

Table 2-C

Comp. No.	Structure				Characteristics		
	Formula (I)				Appearance (m.p. °C)	NMR δ ppm in CDCl_3	IR ν NaCl cm^{-1} max
	R_1	R_2	R_3	R_4			
61	H	H	H	$-\text{SC}_6\text{H}_5$	Colorless crystal (235.5-237)	6.85(1H, s) 7.00-7.50(12H, m)	*3130, 1590, 1440, 1245, 1080
62	H	H	H	$-\text{SC}_6\text{H}_5$	Colorless crystal (152.5-154)	6.65(1H, s) 6.70-7.45(11H, m) 7.50(1H, s)	*3130, 1595, 1450, 1230, 1090
63	H	C_2H_5	H	$-\text{SC}_6\text{H}_5$	Colorless crystal (96-97)	1.25(3H, t) 3.87(2H, q) 6.70-7.50 (12H, m) 7.70(1H, s)	*3070, 1585, 1480, 1235, 1080
64	H	$n\text{-C}_3\text{H}_7$	H	$-\text{SC}_6\text{H}_5$	Oily matter	0.83(3H, t) 1.54(2H, m) 3.80(2H, t) 6.62(1H, s) 6.70-7.50(12H, m)	2970, 1595, 1480, 1240, 1070
65	H	$n\text{-C}_3\text{H}_7$	H	$-\text{SC}_6\text{H}_5$	Colorless crystal (75-76)	0.88(3H, t) 1.65(2H, m) 3.87(2H, t) 6.70-7.50(12H, m) 7.70(1H, s)	*2970, 1585, 1480, 1230, 1065
66	H	$n\text{-C}_4\text{H}_9$	H	$-\text{SC}_6\text{H}_5$	Oily matter	0.70-1.80(7H, m) 3.80(2H, t) 6.45(1H, s) 6.70-7.50(12H, m)	2960, 1595, 1580, 1480, 1220, 1015
67	H	$n\text{-C}_4\text{H}_9$	H	$-\text{SC}_6\text{H}_5$	Colorless crystal (97-98)	0.70-1.80(7H, m) 3.88(2H, t) 6.73-7.50(12H, m) 7.70(1H, s)	*2960, 1590, 1440, 1240, 1060
68	H	$-\text{CH}_2\text{CH}=\text{CH}_2$	H	$-\text{SC}_6\text{H}_5$	Oily matter	4.32(2H, m) 5.02(2H, m) 5.60(1H, m) 6.45(1H, s) 6.70-7.50(12H, m)	3080, 1595, 1580, 1480, 1240

Table 2-C (Cont'd)

Comp. No.	Structure				Characteristics		
	Formula (I)				Isomer type	Appearance (m.p. °C)	NMR δ ppm in CDCl ₃
	R ₁	R ₂	R ₃	R ₄			
69	H	C ₂ H ₅	H	-OC ₆ H ₅	B	Oily matter	1.20(3H,t) 3.86(2H,q) 6.70-7.50(12H,m) 7.48(1H,s)
70	H	n-C ₃ H ₇	H	-OC ₆ H ₅	B	Oily matter	0.88(3H,t) 1.62(2H,m) 3.78(2H,t) 6.70-7.50(12H,m) 7.48(1H,s)
71	H	n-C ₄ H ₉	H	-OC ₆ H ₅	B	Oily matter	0.88(3H,t) 1.00-1.70(4H,m) 3.80(2H,t) 6.70-7.50(12H,m) 7.50(1H,s)
72	H	n-C ₅ H ₁₁	H	-OC ₆ H ₅	B	Oily matter	0.86(3H,t) 1.00-1.70(6H,m) 3.80(2H,t) 6.70-7.50(12H,m) 7.50(1H,s)
73	H	n-C ₆ H ₁₃	H	-OCH ₃	B	Oily matter	0.88(3H,t) 1.00-1.70(8H,m) 3.74(3H,s) 3.84(2H,t) 6.48(1H,s) 6.70-7.50(6H,m) 7.56(1H,s)
74	H	n-C ₃ H ₇	H	-OCH ₃	B	Oily matter	0.88(3H,t) 1.60(2H,m) 3.72(3H,s) 3.80(2H,t) 6.48(1H,s) 6.70-7.50(6H,m) 7.56(1H,s)
75	H	n-C ₄ H ₉	H	-OCH ₃	B	Oily matter	0.90(3H,t) 1.00-1.70(4H,m) 3.74(3H,s) 3.84(2H,t) 6.50(1H,s) 6.70-7.50(6H,m) 7.56(1H,s)
76	H	n-C ₅ H ₁₁	H	-OCH ₃	B	Oily matter	0.88(3H,t) 1.00-1.70(6H,m) 3.74(3H,s) 3.84(2H,t) 6.50(1H,s) 6.70-7.50(6H,m) 7.56(1H,s)
77	H	n-C ₄ H ₉	H	Br	B	Oily matter	0.86(3H,t) 1.00-1.70(4H,m) 3.78(2H,t) 6.48(1H,s) 6.70-7.50(7H,m)
							IR $\nu_{\text{max}}^{\text{NaCl}}$ -1 3070, 3000, 1670, 1600, 1490, 1230 3070, 2970, 1670, 1600, 1490, 1230 3070, 2970, 1670, 1600, 1490, 1230 3070, 2970, 1670, 1600, 1490, 1230 2950, 1680, 1600, 1495, 1450, 1240 2950, 1680, 1600, 1495, 1450, 1240 2950, 1680, 1600, 1495, 1450, 1240 2950, 1680, 1600, 1495, 1450, 1240 2970, 1600, 1490, 1450, 1110

Table 2-C (Cont'd)

Comp. No.	Structure				Characteristics		
	Formula (I)				Appearance (m.p. °C)	NMR δ ppm in CDCl_3	IR ν_{max} NaCl cm^{-1}
	R_1	R_2	R_3	R_4			
78	H	$\text{n-C}_6\text{H}_{13}$	H	Br	B	0.86(3H,t) 1.00-1.70(8H,m) 3.78(2H,t) 6.47(1H,s) 6.70-7.50(7H,m)	2950, 1600, 1490, 1450, 1250, 1050
79	H	$\text{n-C}_8\text{H}_{17}$	H	Br	B	0.88(3H,t) 1.00-1.70(12H,m) 3.78(2H,t) 6.48(1H,s) 6.70-7.50(7H,m)	2950, 1600, 1490, 1450, 1250, 1030
80	H	C_2H_5	H	Cl	B	1.18(3H,t) 3.88(2H,q) 6.50(1H,s) 6.70-7.50(6H,m) 7.64(1H,s)	*3070, 1630, 1600, 1485, 1255, 1070
81	H	$\text{n-C}_4\text{H}_9$	H	Cl	B	0.90(3H,t) 1.00-1.70(4H,m) 3.82(2H,t) 6.48(1H,s) 6.70-7.50(6H,m) 7.64(1H,s)	2970, 1600, 1485, 1250, 1070
82	H	$\text{n-C}_5\text{H}_{11}$	H	Cl	B	0.90(3H,t) 1.00-1.70(6H,m) 3.82(2H,t) 6.49(1H,s) 6.70-7.50(6H,m) 7.64(1H,s)	2950, 1600, 1485, 1250, 1070
83	H	$\text{n-C}_6\text{H}_{13}$	H	Cl	B	0.88(3H,t) 1.00-1.70(8H,m) 3.82(2H,t) 6.49(1H,s) 6.70-7.50(6H,m) 7.64(1H,s)	2950, 1600, 1485, 1250, 1070
84	H	$\text{n-C}_3\text{H}_7$	H	F	B	0.84(3H,t) 1.56(2H,m) 3.82(2H,t) 6.92(1H,d) 6.70-7.50(6H,m) 7.56(1H,s)	2970, 1680, 1600, 1490, 1450, 1250
85	H	$\text{n-C}_4\text{H}_9$	H	F	B	0.88(3H,t) 1.00-1.70(4H,m) 3.84(2H,t) 6.90(1H,d) 6.70-7.50(6H,m) 7.56(1H,s)	2940, 1680, 1600, 1490, 1450, 1250

Table 2-C (Cont'd)

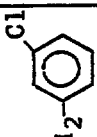
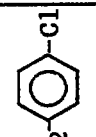
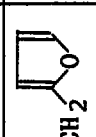
Comp. No.	Structure				Characteristics		
	Formula (I)				Appearance (m.p. °C)	NMR δ ppm in CDCl ₃	IR ν NaCl -1 cm ^{max}
	R ₁	R ₂	R ₃	R ₄			
86	H	n-C ₅ H ₁₁	H	F	B	Oily matter 0.88(3H, t) 1.00-1.70(6H, m) 3.84(2H, t) 6.90(1H, d) 6.70-7.50(6H, m) 7.56(1H, s)	2940, 1680, 1600, 1490, 1450, 1250
87	H	n-C ₆ H ₁₃	H	F	B	Oily matter 0.88(3H, t) 1.00-1.70(8H, m) 3.84(2H, t) 6.90(1H, d) 6.70-7.50(6H, m) 7.56(1H, s)	2940, 1680, 1600, 1490, 1450, 1250
88	5-Cl	n-C ₅ H ₁₁	H	-SCH ₃	-	Oily matter 0.88(3H, t) 1.00-1.70(6H, m) 2.32, 2.35(3H, s) 3.78(2H, t) 6.36(1H, s) 6.70-7.50(5H, m) 7.45, 7.50(1H, s)	2940, 1595, 1490, 1250, 1080
89	5-CH	n-C ₄ H ₉	H	-SCH ₃	B	Oily matter 0.88(3H, t) 1.00-1.70(4H, m) 2.30(6H, s) 3.78(2H, t) 6.36(1H, s) 6.70-7.50(5H, m) 7.45(1H, s)	2970, 1610, 1490, 1250, 1080
90	H	n-C ₃ H ₇	H	-SCH ₂ - 	B	Colorless crystal (96-97) 0.80(3H, t) 1.50(2H, m) 3.76(2H, t) 3.80(2H, s) 6.28(1H, s) 6.70-7.50(11H, m)	*2970, 1600, 1490, 1245, 1050
91	H	n-C ₃ H ₇	H	-SCH ₂ - 	-	Oily matter 0.78, 0.86(3H, t) 1.20-1.70(2H, m) 3.60-3.90(4H, m) 6.26, 6.62(1H, s) 6.70-7.50(11H, m)	2970, 1600, 1490, 1250
92	H	n-C ₄ H ₉	H	-SCH ₂ - 	-	Oily matter 0.70-1.70(7H, m) 3.70-4.00(4H, m) 6.30(2H, m) 6.42, 6.85(1H, s) 6.80-7.60(8H, m)	3120, 2970, 1600, 1490, 1450, 1250

Table 2-C (Cont'd)

Comp.	Structure					Characteristics		
	Formula (I)				Isomer type	Appearance (m.p. °C)	NMR δ ppm in CDCl ₃	IR ν NaCl cm ⁻¹ max
	R ₁	R ₂	R ₃	R ₄				
No.								
93	H	n-C ₄ H ₉	Br	Br	No isomer	Colorless crystal (69-70)	0.95(3H,t) 1.10-1.80(4H,m) 3.83(2H,t) 6.60-7.40(6H,m) 7.50(1H,s)	*2970,1600,1485, 1450,1280,1260, 1050
94	H	n-C ₆ H ₁₃	Br	Br	No isomer	Oily matter	0.70-1.90(11H,m) 3.83(2H,t) 6.60-7.40(6H,m) 7.50(1H,s)	2950,1600,1485, 1450,1250,1050
95	H	n-C ₄ H ₉	H	-SC ₆ H ₅	B	Colorless crystal (HCl) (143-145)	0.88(3H,t) 1.00-1.70(4H,m) 3.86(2H,t) 6.80-7.60(12H,m) 8.34(1H,s)	*3000,1595,1490, 1450,1240,1070

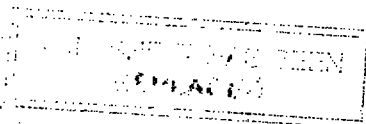
Having now fully described the invention, it
will be apparent to one of ordinary skill in the art
that many changes and modifications can be made thereto
without departing from the spirit or scope of the
5 invention as set forth herein.

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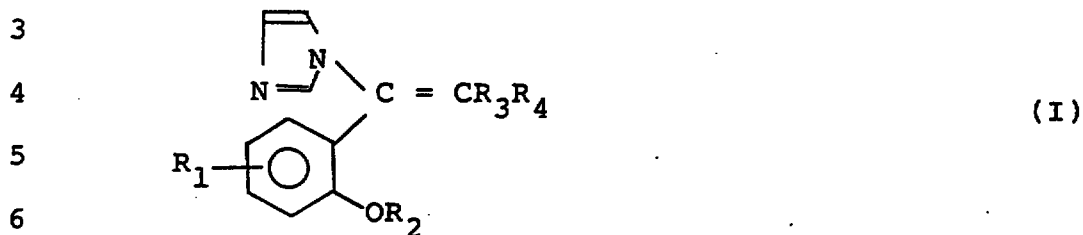
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WHAT IS CLAIMED AS NEW AND IS SECURED BY LETTERS
PATENT IS:

1 1. An imidazole derivative represented by the
2 following general formula (I):



7 wherein R_1 means a hydrogen or halogen atom or a lower
8 alkyl group, R_2 denotes a hydrogen atom or an alkyl,
9 alkenyl, haloalkyl or substituted or unsubstituted
10 benzyl group, R_3 stands for a hydrogen or halogen atom,
11 and R_4 is a substituted or unsubstituted benzylthio
12 group, a phenylthio, alkylthio, alkenylthio, furfuryl-
13 thio, alkoxy or phenoxy group or a halogen atom; or an
14 acid addition salt thereof.

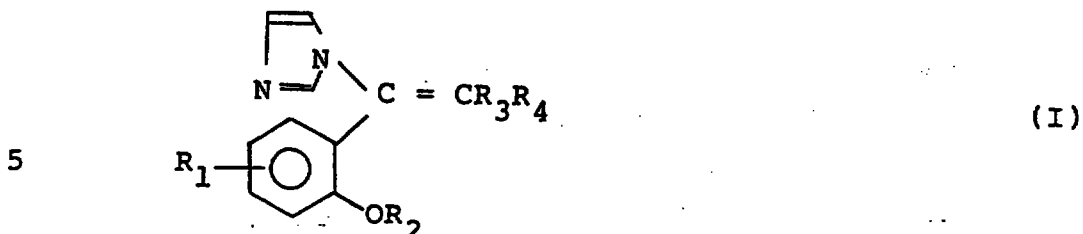
This Sheet Has Been Replaced



THIS SHEET HAS BEEN
REPLACED

ABSTRACT OF THE DISCLOSURE

An imidazole derivative represented by the following general formula (I):



wherein R_1 means a hydrogen or halogen atom or a lower alkyl group, R_2 denotes a hydrogen atom or an alkyl, alkenyl, haloalkyl or substituted or unsubstituted benzyl group, R_3 stands for a hydrogen or halogen atom, and R_4 is a substituted or unsubstituted benzylthio group, a phenylthio, alkylthio, alkenylthio, furfurylthio, alkoxy or phenoxy group or a halogen atom; or an acid addition salt thereof.

10

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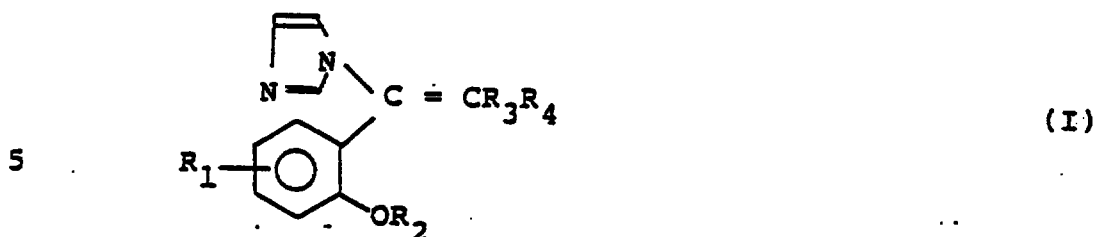


Replacement Sheet - 10 September 1996

ABSTRACT OF THE DISCLOSURE

IMIDAZOLE DERIVATIVES

An imidazole derivative represented by the following general formula (I):

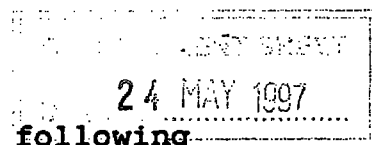


wherein R_1 means a hydrogen or halogen atom or a lower alkyl group, R_2 denotes a hydrogen atom or an alkyl, alkenyl, haloalkyl or substituted or unsubstituted benzyl group, R_3 stands for a hydrogen or halogen atom, and R_4 is a substituted or unsubstituted benzylthio group, a phenylthio, alkylthio, alkenylthio, furfurylthio, alkoxy or phenoxy group or a halogen atom; or an acid addition salt thereof.

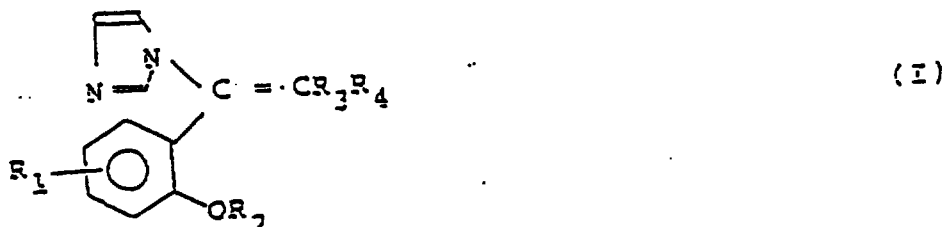
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Claims

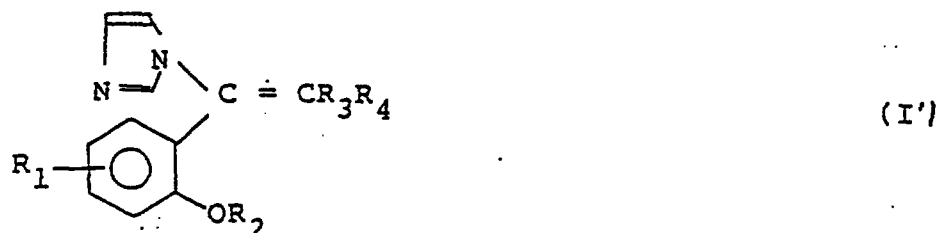


1. An imidazole derivative represented by the following general formula (I):

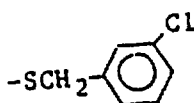


wherein R_1 means a hydrogen or halogen atom or a methyl group, R_2 denotes a hydrogen atom or an alkyl, alkenyl or haloalkyl group, R_3 stands for a hydrogen or halogen atom and R_4 is an unsubstituted benzylthio group or a phenylthio, alkylthio, alkenylthio, furfurylthio, methoxy or phenoxy group or a halogen atom; or an acid addition salt thereof.

2. An imidazole derivative represented by the following formula (I'):



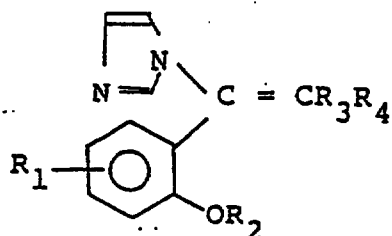
wherein R_1 is a hydrogen atom, R_2 is $n\text{-C}_3\text{H}_7$, R_3 is a hydrogen atom, R_4 is a group of the following formula





24 MAY 1997

3. An imidazole derivative represented by the following formula (I''):



(I'')

wherein R_1 is hydrogen, R_2 is $n\text{-C}_3\text{H}_7$, R_3 is hydrogen atom and R_4 is a group of the following formula

