The title compound was prepared according to the method of Example 128 substituting 2-methylcyclopentanol in place of 2-indanol (yield: 230 g, 86%). mp 180-181 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.75 (d, J=7 Hz, 3H), 1.60 (m, 2H), 1.89 (m, 2H), 2.10 (m, 1H), 2.21 (m, 1H), 2.40 (m, 1H), 3.23 (s, 3H), 5.37 (q, J=7 Hz, 1H), 7.12 (t, J=9 Hz, 2H), 7.21 (m, 2H), 7.47 (d, J=9 Hz, 2H), 7.86 (d, J=9 Hz, 2H), 8.11 (s, 1H). MS (APCI+) m/z 427 $(M+H)^+$ and (APCI-) m/z 461 $(M+Cl)^-$. Anal. calc. for $C_{23}H_{23}FN_2O_3S$: C, 64.77; H, 5.43; N, 6.56. Found: C, 64.71; H, 5.34; N, 6.28.

Example 132

2-(2-Adamantyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 128 substituting 2-adamantanol in place of 2-indanol, (yield: 75 g, 25%).mp 195-197 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.60 (m, 2H), 1.77 (m, 2H), 1.94 (m, 6H), 2.35 (m, 4H), 3.23 (s, 3H), 4.83 (m, 1H), 7.11 (t, J=9 Hz, 2H), 7.22 (m, 2H), 7.47 (d, J=9 Hz, 2H), 7.87 (d, J=9 Hz, 2H), 8.11 (s, 1H). MS (APCI+) m/z 479 $(M+H)^+$ and (APCI-) m/z 478 (M-H)-, m/z 513 $(M+Cl)^-$. Anal. calc. for $C_{27}H_{27}FN_2O_3S.0.25\ H_2O$: C, 67.13; H, 5.73; N, 5.79. Found: C, 67.06; H, 5.76, N, 5.06.

Example 133

2-(3-Methylcyclopentyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 128 substituting 3-methylcyclopentanol in place of 2-indanol (yield: 155 g, 73%). mp 169-171 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.05 (dd, 2:1, 3H), 1.24 (m, 1H), 1.63 (m, 1H), 2.00 (m, 3H), 2.22 (m, 2H), 3.23 (s, 3H), 5.43 (m, 1H), 7.1 (t, J=9 Hz, 2H), 7.21 (m, 2H), 7.46 (d, J=9 Hz, 2H), 7.86 (d, J=9 Hz, 2H), 8.12 (two s, 2:1, 1H). MS (APCI−) m/z 27 $(M+H)^+$ and (APCI-) m/z 426 (M-H)-, m/z 461 $(M+Cl)^-$. Anal. calc. for $C_{27}H_{27}FN_2O_3S.0.25\ H_2O$: C, 64.09; H, 5.49; N, 6.49 Found: C, 64.27; H, 5.62; N, 6.46.

ACTION

Example 134

2-(1-Methylcyclopentyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

A solution of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (206 mg, 0.6 mmol), prepared according to the method of Example 11, 1-methyl-1-cyclopentanol (60 mg, 0.6 mmol), DMAP (18 mg, 0.12 mmol) and Ph_3P (262 mg, 1 mmol) in toluene (30 mL) in ethyl acetate (5 mL) was prepared and added dropwise to a solution of DIAD (0.2 mL, 1 mmol) in 10 mL of toluene. The mixture was stirred at room temperature for 6 hours and then concentrated in vacuo. The residue was chromatographed (silica gel, 19:1 CH_2Cl_2-ethyl acetate) to provide 80 mg of product (contaminated with reduced DIAD). A second column chromatography (hexanes-ethyl acetate 1:1) furnished the title product, (yield: 50 mg, 19%). mp 107-110 °C. ^1H NMR (DMSO-d_6, 300 MHz) δ 1.55 (s, 3H), 1.70 (m, 4H), 2.08 (m, 2H), 2.32 (m, 2H), 3.22 (s, 3H), 7.10 (t, J=9 Hz, 2H), 7.20 (m, 2H), 7.45 (d, J=9 Hz, 2H), 7.86 (d, J=9 Hz, 2H), 8.03 (s, 1H). MS (APCI+) m/z 427 $(M+H)^+$ and (APCI-) m/z 426 (M-H)-, m/z 461 $(M+Cl)^-$.

Example 135

2-(3,4-Difluorophenyl)-4-(4-fluoro-3-vinylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone.

Exampel 135A

5-Bromo-2-fluorostyrene.

A mixture of methyltriphenylphosphonium bromide (2.14 g, 6 mmol) and potassium t-butoxide (672 mg, 6 mmol) in 50 mL of THF was refluxed for 30 minutes under N_2 and then cooled to room temperature. 5-Bromo-2-fluorobenzaldehyde (1.02 g, 5 mmol) was added and the resulting mixture was refluxed for 2 hours (until the TLC showed the disappearance of starting aldehyde). The reaction was concentrated in vacuo and partitioned between water and ethyl acetate. The acetate layer was washed with water and brine. The solution was dried over $MgSO_4$ and concentrated in vacuo. The residue

was purified by chromatography (silica gel, 15:1 hexanes-diethyl ether) to provide 900 mg (90%) of 5-bromo-2-fluorostyrene.

Example 135B

2-(3,4-Difluorophenyl)-4-(4-fluoro-3-vinylphenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone.

The bromo-styrene compound, Example 135A, in 10 mL of THF was added dropwise to a heated mixture of magnesium turnings (120 mg, 5 mmol) and a few drops of 1,2-dibromoethane in THF (20 mL) at a rate to maintain a gentle reflux. The mixture was refluxed for the next 30 minutes and cooled to room temperature The Grignard reagent solution was cooled to -78 °C and added, dropwise, to a solution of 2-(3,4-difluorophenyl)-4-methoxy-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone (540 mg, 1.5 mmol) in THF (20 mL). The reaction mixture was allowed to warm to room temperature for 12 hours. Afterwards, a saturated solution of NH_4Cl was added and the mixture was extracted with ethyl acetate to provide 320 mg of crude sulfide.

Example 135C

2-(3,4-Difluorophenyl)-4-(4-fluoro-3-vinylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone.

The sulfide, Example 135B, was dissolved in CH_2Cl_2 (20 mL) and at 0 °C was treated with 30% CH_3CO_3H in CH_3CO_2H (0.5 mL). After 1.5 hours, 10% $NaHCO_3$ was added and the mixture extracted with CH_2Cl_2. The extract was concentrated in vacuo and the residue purified by chromatography (silica gel, 1:1 hexanes-ethyl acetate) to provide the title compound (yield: 270 mg, 37%). ^1H NMR (DMSO-d_6, 300 MHz) δ 3.22 (s, 3H), 5.37 (d, J=12 Hz, 1H), 5.65 (d, J=18 Hz, 1H), 6.77 (dd, J=12 Hz and 18 Hz, 1H), 7.15 (m, 2H), 7.57 (m, 5H), 7.90 (m, 3H), 8.28 (s, 1H). MS (APCI+) m/z 483 $(M+H)^+$ and (APCI-) m/z 517 $(M+Cl)^-$ Anal. calc. for $C_{25}H_{17}F_3N_2O_3S.0.5\ H_2O$: C, 61.09; H, 3.69; N, 5.69 Found: C, 61.04; H, 3.71; N, 5.34

Example 136

2-(3,4-Difluorophenyl)-4-(6-methyl-3-heptenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

A Grignard, prepared as described in Example 135 , substituting 2-(2-bromoethyl)-1,3-dioxane (586 mg, 3 mmol) in place of 5-bromo-2-fluorostyrene, was added to a solution of 2-(3,4-difluorophenyl)-4-methoxy-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone (720 mg, 2 mmol) in THF (30 mL) at -78 °C. The mixture was left at room temperature for 14 hours, quenched with a saturated solution of NH_4Cl and extracted with ethyl acetate to obtain 900 mg of crude sulfide.

The intermediate sulfide product was dissolved in CH_2Cl_2 (10 mL) and treated at 0 °C with 33% solution of CH_3CO_3H in CH_3CO_2H (0.7 mL) for 1 hour. The mixture was concentrated in vacuo and the residue was partitioned between saturated $NaHCO_3$ and ethyl acetate. The acetate layer was dried over $MgSO_4$ and concentrated in vacuo to provide 950 mg of crude sulfonyl derivative.

The sulfonyl compound, prepared above, was dissolved in acetone (50 mL) and treated with 2 N HCl (10 mL). The resulting mixture was refluxed for 16 hours and concentrated in vacuo. The residue was extracted with ethyl acetate to provide 900 mg of 2-(3,4-difluorophenyl)-4-(2-formylethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (crude aldehyde, contaminated with some unreacted starting dioxane derivative).

A mixture of isoamyltriphenylphosphonium bromide (414 mg, 1 mmol) and potassium t-butoxide (112 mg, 1 mmol) in toluene (25 mL) was refluxed for 30 minutes and then cooled to room temperature. The crude aldehyde was added and the mixture was refluxed for 14 hours. The reaction mixture was then cooled to room temperature and concentrated in vacuo. The residue was dissolved in ethyl acetate and was washed with water, 10% citric acid, brine, dried over $MgSO_4$ and concentrated in vacuo. Purification by column chromatography (silica gel, 1:1 hexanes-ethyl acetate) provided the title compound as an oil (yield: 120 mg, 13%) ^1H NMR (300 MHz, DMSO-d_6) δ 0.74 (d, J=7 Hz, 6H), 1.44 (m, 1H), 1.70 (t, J=7 Hz, 2H), 2.22 (m, 2H), 2.54 (m, 2H); 3.30 (s, 3H), 5.29

(m, 2H), 7.51 (m, 1H), 7.63 (m, 1H), 7.74 (d, J=9 Hz, 2H), 7.82 (m, 1H), 8.02 (s, 1H), 8.10 (d, J=9 Hz, 2H). MS (APCI+) m/z 473 $(M+H)^+$ and (APCI-) m/z 471 (M-H)-, m/z 507 $(M+Cl)^-$. Anal. calc. for $C_{25}H_{26}F_2N_2O_3S$: C, 63.54; H, 5.54; N. 5.92. Found: C, 63.74; H, 5.67; N, 5.58.

Example 137

2-(3,4-Difluorophenyl)-4-(3-cyclopropylidenepropyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 136 substituting cyclopropyltriphenylphosphonium bromide in place of isoamyltriphenylphosphonium bromide (yield: 55 mg, 12%). mp 128-129 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.81 (m, 2H), 0.97 (m, 2H), 2.34 (m, 2H), 2.65 (m, 2H), 3.32 (s, 3H), 5.64 (m, 1H), 7.52 (m, 1H), 7.63 (m, 1H), 7.73 (d, J=9 Hz, 2H), 7.81 (m, 1H), 8.02 (s, 1H), 8.10 (d, J=9 Hz, 2H). MS (APCI+) m/z 443 $(M+H)^+$ and (APCI-) m/z 441 (M-H)-, m/z 477 $(M+Cl)^-$. Anal. calc. for $C_{23}H_{20}F_2N_2O_3S.0.5\ H_2O$: C, 61.18; H, 4.68; N, 6.20. Found: C, 61.48; H, 4.60; N, 6.02.

Example 138

2-(3,4-Difluorophenyl)-4-(5-methyl-3-hexenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound, an oil, was prepared according to the method of Example 136 substituting isobutyltriphenylphosphonium bromide in place of isoamyltriphenylphosphonium bromide (yield: 170 mg, 74%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.75 (d, J=7 Hz, 6H), 2.22 (m, 3H), 2.54 (m, 2H), 3.32 (s, 3H), 5.12 (m, 2H), 7.52 (m, 1H), 7.60 (m, 1H), 7.72 (d, J=9 Hz, 2H), 7.80 (m, 1H), 8.02 (s, 1H), 8.10 (d, J=9 Hz, 2H). MS (APCI+) m/z 459 $(M+H)^+$ and (APCI-) m/z 457 (M-H)-, m/z 493 $(M+Cl)^-$. Anal. calc. for $C_{24}H_{24}F_2N_2O_3S$: C, 62.86; H, 5.27, N, 6.10. Found: C, 62.57; H, 5.32; N, 5.81.

Example 139

2-(3,4-Difluorophenyl)-4-(5-methylhexyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound, an oil, was prepared according to the method of Example 135B , substituting 5-methylhexylmagnesium bromide for 3-fluoro-4-vinylphenylmagnesium bromide, (yield: 28 mg, 10%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.77 (d, J=7 Hz, 6H), 0.88 (m, 1H), 1.03 (m, 2H), 1.20 (m, 1H), 1.46 (m, 5H), 3.32 (s, 3H), 7.52 (m, 1H), 7.62 (m, 1H), 7.75 (d, J=9 Hz, 2H), 7.82 (m, 1H), 8.02 (s, 1H), 8.11 (d, J=9 Hz, 2H). MS (APCI+) m/z 461 $(M+H)^+$ and (APCI) m/z 459 (M-H)-, m/z 495 $(M+Cl)^-$.

Example 140

2-(3-Chloro-1-methyl-2E-propenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124, substituting 1,3-dichloro-1-butene in place of 2,4-difluorobenzyl bromide (yield: 55 mg, 30%). mp 152-154 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.71 (dt, J=15 Hz, 7.5 Hz, 2H), 2.28 (d, J=1.5 Hz, 3H), 4.8 (s, 2H), 4.99 (d, J=1 Hz, 1H), 5.02 (d, J=1 Hz, 1H), 5.85 (td, J=4 Hz, 1 Hz, 1H), 6.98 (t, J=9 Hz, 2H), 7.19 (dd, J=9 Hz, 6 Hz, 2H), 7.28 (d, J=9 Hz, 2H), 7.86 (s, 1H), 7.87 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 434 $(M+H)^+$. Anal. calc. for $C_{20}H_{17}ClFN_3O_3S$: C, 55.36; H, 3.94; N, 9.68. Found: C, 54.99; H, 3.83; N, 9.34.

Example 141

2-(2,3,3-Trifluoro-2-propen-1-yl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124 , substituting 1-methylsufonyloxy-2,3,3-trifluoro-2-propene (mesylate), prepared in Example 88, in place of 2,4-difluorobenzyl bromide (yield: 10 mg, 4%). mp 173-175 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.39 (s, 2H), 5.09 (ddd, J=26 Hz, J=3 Hz, J=1 Hz, 2H), 6.98

(t, J=9 Hz, 2H), 7.19 (dd, J=9 Hz. J=6 Hz. 2H), 7.29 (d, J=9 Hz, 2H). 7.78 (s, 1H), 7.78 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 440 $(M+H)^+$, MS (F, high res.) m/z calc. for $C_{19}H_{14}F_4N_3O_3S$: 440.0692 $(M+H)^+$. Found: 440.0695 $(M+H)^+$. (0.7 ppm error).

Example 142

2-(1,1,2-Trifluoro-2-propenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was isolated from the same reaction mixture (Example 141) that was used to prepare 2-(2.3.3-trifluoro-2-propen-1-yl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone (The title product is a result of an SN2' attack.) (yield: 50 mg, 20%). mp 230-232 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 4.7 (s, 2H). 5.28 (dd, J=15 Hz, 4.5 Hz, 1H), 5.39 (dd, J=45 Hz, 4.5 Hz, 1H), 6.98 (t, J=9 Hz, 2H), 7.19 (dd, J=9 Hz, 6 Hz. 2H), 7.31 (d, J=9 Hz. 2H). 7.9 (d, J=9 Hz, 2H), 7.92 (s, 1H),. MS (DCI/NH_3) m/z 440 $(M+H)^+$. Anal. calc. for $C_{19}H_{13}F_4N_3O_3S$: C. 51.93; H. 2.98; N, 9.56. Found: C. 51.88; H, 3.01; N, 9.15.

Example 143

2-(3,3-Difluoro-2-propenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124 , substituting 1,3-dibromo-1,1-difluoropropane in place of 2,4-difluorobenzyl bromide and employing 5 equivalents of potassium carbonate (yield: 220 mg, 65%). mp 191-194 °C. ^1H NMR (300 MHz, DMSO-d_6) δ 4.77 (d, J=7.5 Hz, 2H), 4.95 (dtd, J=24 Hz, 7.5 Hz, 1 Hz. 1H), 7.12 (t, J=9 Hz. 2H). 7.23 (dd, J=9 Hz, 6 Hz, 2H). 7.49 (d. J=9 Hz, 2H). 7.50 (s. 2H), 7.74 (d. J=9 Hz. 2H), 8.1 (s. 1H). MS (DCI/NH_3) m/z 422 $(M+H)^+$. Anal. calc. for $C_{19}H_{14}F_3N_3O_3S$: C. 54.15; H. 3.34; N, 9.97 Found: C. 53.88; H. 3.42; N. 9.76.

Example 144

2-(α-Methyl-3-fluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124 , substituting 3-fluoro-α-methylbenzyl chloride in place of 2,4-difluorobenzyl bromide (yield: 220 mg, 65%). mp 192-194 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.76 (d, 6 Hz, 3H), 6.27 (q, J=7 Hz, 1H), 7.1 (t, J=9 Hz, 2H), 7.22 (dd, J=9 Hz, 6 Hz, 2H), 7.49 (d, J=9 Hz, 2H), 7.51 (s, 2H), 7.72 (d, J=9 Hz, 2H), 8.18 (s, 1H). MS (DCI/NH_3) m/z 468 $(M+H)^+$. Anal. calc. for $C_{24}H_{19}F_2N_3O_3S$: C, 61.66; H, 4.09; N, 8.98 Found: C, 61.36; H, 3.96; N, 8.86.

Example 145

2-(1-Cyclohexenylmethyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124 , substituting 1-bromomethylcyclohexene in place of 2,4-difluorobenzyl bromide (yield: 70 mg, 28%). mp 192-193 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.55 (m, 4H), 1.98 (m, 4H), 4.64 (s, 2H), 5.53 (s, 1H), 7.12 (t, J=9 Hz, 2H), 7.22 (dd, J=9 Hz, 6 Hz, 2H), 7.39 (d, J=9 Hz, 2H), 7.39 (s, 2H), 7.72 (d, J=9 Hz, 2H), 8.07 (s, 1H). MS (DCI/NH_3) m/z 440 $(M+H)^+$. Anal. calc. for $C_{23}H_{22}FN_3O_3S$: C, 62.85; H, 5.04; N, 9.56. Found: C, 62.47; H, 5.23; N, 9.14.

Example 146

2-(α-Methyl-2,3,4-trifluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124 , substituting 2,3,4-trifluoro-α-methylbenzyl chloride in place of 2,4-difluorobenzyl bromide (yield: 70 mg, 50%). mp 192-194 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.84 (d, J=6 Hz, 3H), 4.8 (s, 2H), 6.54 (q, J=7 Hz, 1H), 6.96 (t, J=9 Hz, 2H), 6.99 (m, 1H), 7.18 (dd, J=9 Hz, 6 Hz, 2H), 7.2 (m, 1H), 7.38 (d, J=9 Hz, 2H), 7.86 (d, J=9 Hz, 2H), 7.88 (s,

1H). MS (DCI/NH_3) m/z 504 $(M+H)^+$. Anal. calc. for $C_{24}H_{17}F_4N_3O_3S$: C, 57.25; H, 3.4; N, 8.34. Found: C, 56.84; H, 3.52; N, 7.91.

Example 147

2-(α-Methyl-3,5-difluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124 , substituting 3,5-difluoro-α-methylbenzyl chloride in place of 2,4-difluorobenzyl bromide (yield: 80 mg, 45%). mp 139-141 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.83 (d, J=6 Hz, 3H), 4.79 (s, 2H), 6.32 (q, J=7 Hz, 1H), 6.84 (m, 1H), 6.97 (t, J=9 Hz, 2H), 7.02 (dd, J=6 Hz, 1.5 Hz, 2H), 7.18 (dd, J=9 Hz, 6 Hz, 2H), 7.28 (d, J=9 Hz, 2H), 7.85 (s, 1H), 7.9 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 486 $(M+H)^+$. Anal. calc. for $C_{24}H_{18}F_3N_3O_3S$. C, 59.37; H, 3.73; N, 8.65. Found. C, 59.00; H, 3.70; N, 8.35.

Example 148

2-(α-Methyl-3,4-difluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124, substituting 3,4-difluoro-α-methylbenzyl chloride in place of 2,4-difluorobenzyl bromide (yield: 200 mg, 58%). mp 214-215 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.82 (d, J=6 Hz, 3H), 4.7 (s, 2H), 6.35 (q, J=7 Hz, 1H), 6.96 (t, J=9 Hz, 2H), 7 16 (m, 4H). 7 28 (d, J=9 Hz, 2H), 7.37 (m, 1H), 7.84 (d, J=9 Hz, 2H), 7.90 (s, 1H). MS (DCI/NH_3) m/z 486 $(M+H)^+$. Anal. calc. for $C_{24}H_{18}F_3N_3O_3S$: C, 59.37; H, 3.73; N, 8.65. Found: C, 59.13; H, 3.73; N, 8.54.

Example 149

2-(3-Fluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124 , substituting 3-fluorobenzyl bromide in place of 2,4-difluorobenzyl bromide (yield: 160

mg, 61%). mp 220-222 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.37 (s, 2H), 7.12 (t, J=9 Hz, 2H), 7.22 (m, 5H), 7.39 (m, 5H), 7.73 (d, J=9 Hz, 2H), 8.11 (s, 1H). MS (DCI/NH_3) m/z 454 $(M+H)^+$. Anal. calc. for $C_{23}H_{17}F_2N_3O_3S$: C, 60.92; H, 3.77; N, 9.26. Found: C, 61.06; H, 4.22, N, 8.88.

Example 150

2-(4-Fluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124, substituting 4-fluorobenzyl bromide in place of 2,4-difluorobenzyl bromide (yield: 85 mg, 34%). mp 237-239 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.32 (s, 2H), 7.12 (t, J=9 Hz, 2H), 7.22 (m, 4H), 7.38 (m, 4H), 7.47 (dd, J=9 Hz, 6 Hz, 2H), 7.72 (d, J=9 Hz, 2H), 8.10 (s, 1H). MS (DCI/NH_3) m/z 454 $(M+H)^+$. Anal. calc. for $C_{23}H_{17}F_2N_3O_3S$: C, 60.92; H, 3.77; N, 9.26. Found: C, 60.61; H, 3.96; N, 8.74.

Example 151

2-(2,4,6-Trifluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124, substituting 2,4,6-trifluorobenzyl bromide in place of 2,4-difluorobenzyl bromide (yield: 255 mg, 73%). mp 201-203 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.38 (s, 2H), 7.13 (t, J=9 Hz, 2H), 7.23 (m, 4H), 7.38 (d, J=9 Hz, 2H), 7.42 (s, 2H), 7.70 (d, J=9 Hz, 2H), 8.08 (s, 1H). MS (DCI/NH_3) m/z 490 $(M+H)^+$. Anal. calc. for $C_{23}H_{15}F_4N_3O_3S$: C, 56.44; H, 3.08; N, 8.58. Found: C, 56.31; H, 3.09; N, 8.40.

Example 152

2-(2,4,5-Trifluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124, substituting 2,4,5-trifluorobenzyl bromide in place of 2,4-difluorobenzyl bromide (yield:

180 mg, 49%). mp 236-238 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.35 (s, 2H), 7.13 (t, J=9 Hz, 2H), 7.23 (dd, J=9 Hz, 6 Hz, 2H), 7.39 (d, J=9 Hz, 2H), 7.41 (s, 2H), 7.6 (m, 2H), 7.72 (d, J=9 Hz, 2H), 8.11 (s, 1H). MS (DCI/NH_3) m/z 490 $(M+H)^+$. Anal. calc. for $C_{23}H_{15}F_4N_3O_3S$: C, 56.44; H, 3.08; N, 8.58. Found: C, 56.38; H, 3.28; N, 8.41.

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Example 153

2-(2,3,4-Trifluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124 ,
10 substituting 2,3,4-trifluorobenzyl bromide in place of 2,4-difluorobenzyl bromide (yield, 220 mg, 63%). mp 218-220 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.40 (s, 2H), 7.13 (t, J=9 Hz, 2H), 7.22 (dd, J=9 Hz, 6 Hz, 2H), 7.34 (m, 2H), 7.39 (d, J=9 Hz, 2H), 7.42 (s, 2H), 7.73 (d, J=9 Hz, 2H), 8.12 (s, 1H). MS (DCI/NH_3) m/z 490 $(M+H)^+$. Anal. calc. for $C_{23}H_{15}F_4N_3O_3S$: C, 56.44; H, 3.08; N, 8.58. Found: C, 56.32; H, 3.24; N, 8.31.

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Example 154

2-(4,4,4-Trifluoro-3-methyl-2E-butenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124,
20 substituting 1-bromo-3-methyl-4,4,4-trifluoro-2-butene in place of 2,4-difluorobenzyl bromide (yield: 160 mg, 48%). mp 155-157 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.00 (s, 3H), 4.8 (s, 2H), 4.96 (d, J=7.5 Hz, 2H), 6.33 (m, 1H), 6.99 (t, J=9 Hz, 2H), 7.19 (dd, J=9 Hz, 6 Hz, 2H), 7.29 (d, J=9 Hz, 2H), 7.95 (s, 1H), 7.97 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 468 $(M+H)^+$. Anal. calc. for $C_{21}H_{17}F_4N_3O_3S$: C, 53.96; H, 3.66; N, 8.98. Found: C, 25 53.84; H, 3.51; N, 8.77.

Example 155

2-(4-Biphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 4-bromobiphenyl in place of 4-iodo-1-fluorobenzene (yield. 0.275 g, 100%). mp 249-251 °C. ^{1}H NMR (300 MHz, DMSO d_6) δ 3.24 (s, 3H), 7.16 (m, 2H), 7.30 (m, 2H), 7.42 (m, 1H), 7.48-7.58 (m, 4H), 7.75 (m, 4H), 7.84 (m, 2H), 7.91 (m, 2H), 8.27 (s, 1H). MS (DCI/NH_3) m/z 497 $(M+H)^+$, 514 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{21}FN_2O_3S$: C, 70.15; H, 4.26; N, 5.64. Found: C, 69.81; H, 4.42; N, 5.41.

Example 156

2-(4-Bromophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 1,4-dibromobenzene in place of 4-iodo-1-fluorobenzene (yield: 0.337 g, 93%). ^{1}H NMR (300 MHz, DMSO d_6) δ 3.24 (s, 3H), 7.14 (m, 2H), 7.28 (m, 2H), 7.64 (m, 2H), 7.75 (m, 2H), 7.90 (m, 2H), 8.25 (s, 1H). MS (DCI/NH_3) m/z 499 $(M+H)^+$, 518 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{16}BrFN_2O_3S.0.75\ H_2O$: C, 53.86, H, 3.43; N, 5.46. Found: C, 53.92; H, 3.16; N, 5.34.

Example 157

2-(4-Nitrophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 1-iodo-4-nitrobenzene in place of 4-iodo-1-fluorobenzene (yield: 0 45 g, 100%). mp 110-116 °C. ^{1}H NMR (300 MHz, DMSO d_6) δ 3.24 (s, 3H), 7.17 (m, 2H), 7.32 (m, 2H), 7.53 (m, 2H), 7.91 (m, 2H), 8.03 (m, 2H), 8.34 (s, 1H), 8.40 (m, 2H). MS (DCI/NH_3) m/z 466 $(M+H)^+$, 483 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{16}FN_3O_5S$. C, 59.35; H, 3.46; N, 9.03. Found: C, 59.02; H, 3.62; N, 8.82.

Example 158

2-(4-Phenoxyphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 4-bromodiphenylether in place of 4-iodo-1-fluorobenzene (yield: 0.667 g, 22%). mp 118-125 °C. ^{1}H NMR (300 MHz, DMSO d_6) δ 3.24 (s, 3H), 7.12 (m, 5H), 7.15-7.33 (m, 4H), 7.46 (m, 2H), 7.52 (m, 2H), 765 (m, 2H), 7.90 (m, 2H), 8.23 (s, 1H). MS (DCI/NH_3) m/z 513 $(M-H)^+$. Anal. calc. for $C_{25}H_{21}FN_2O_4S.0.75\ H_2O$: C, 66.21; H, 4.31; N, 5.32. Found: C, 65.98; H, 4.25; N, 5.27.

Example 159

2-(4-t-Butylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 1-bromo-4-t-butyl-benzene in place of 4-iodo-1-fluorobenzene. No product was observed. The solution was concentrated in vacuo. The resulting solid was dissolved in DMF (5 mL) and CuI (13.3 mg, 0.07 mmol) was added. The solution was allowed to reflux overnight. Upon completion, the mixture was poured into 10% citric acid and extracted with ethyl acetate. The organic layer was washed with water, dried over $MgSO_4$ and concentrated in vacuo. The crude solid was purified using flash chromatography (SiO_2), eluting with 5% diethyl ether/CH_2Cl_2 to provide the desired product (yield: 0.292 g, 84%). mp 132-136 °C. ^{1}H NMR (300 MHz, DMSO d_6) δ 1.34 (s, 9H), 3.24 (s, 3H), 7.14 (m, 2H), 7.29 (m, 2H), 7.54 (m, 6H), 7.90 (m, 2H), 8.23 (s, 1H). MS (DCI/NH_3) m/z 477 $(M+H)^+$, 494 $(M+NH_4)^+$. Anal. calc. for $C_{27}H_{25}FN_2O_3S$: C, 68.05; H, 5.29; N, 5.88. Found: C, 67.94; H, 5.31; N, 5.67.

Example 160

2-(4-Chlorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 4-bromo-1-chlorobenzene in place of 4-iodo-1-fluorobenzene (yield: 0.254 g, 83.5%). mp 214-216 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.24 (s, 3H), 7.16 (m, 2H), 7.29 (m, 2H), 7.52 (m, 2H), 7.61 (m, 2H), 7.71 (m, 2H), 7.91 (m, 2H), 8.26 (s, 1H). MS

(DCI/NH_3) m/z 455 $(M+H)^+$, 472 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{16}ClFN_2O_3S$: C, 60.73; H, 3.55; N, 6.16. Found: C, 60.45, H, 3.41; N, 6.05.

Example 161

2-(3-Methylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 3-bromotoluene in place of 4-iodo-1-fluorobenzene (yield: 0.262 g, 83%). mp 213-216 °C. ^1H NMR (300 MHz, DMSO d_6) δ 2.39 (s, 3H), 3.24 (s, 3H), 7.14 (m, 2H), 7.28 (m, 3H), 7.43 (m, 3H), 7.53 (m, 2H), 7.80 (m, 2H), 8.22 (s, 1H). MS (DCI/NH_3) m/z 435 $(M+H)^+$, 452 $(M+NH_4)^+$. Anal. calc. for $C_{24}H_{19}FN_2O_3S$: C, 66.35; H, 4.41; N, 6.45 Found: C, 66.00, H, 4.16; N, 6.23

Example 162

2-(3-Vinylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 3-bromostyrene in place of 4-iodo-1-fluorobenzene (yield: 0.202 g, 62%) mp 182-183 °C. ^1H NMR (300 MHz, DMSO d_6) δ 3.25 (s, 3H), 5.35 (d, J=12 Hz, 1H), 5.92 (d, J=15 Hz, 1H), 6.82 (m, 1H), 7.15 (m, 2H), 7.30 (m, 2H), 7.50-7.60 (m, 4H), 7.74 (m, 1H), 7.91 (m, 2H), 8.24 (s, 1H). MS (DCI/NH_3) m/z 447 $(M+H)^+$, 464 $(M+NH_4)^+$. Anal. calc. for $C_{25}H_{19}FN_2O_3S.0.50\ H_2O$: C, 65.92; H, 4.42; N, 6.14. Found: C, 65.86; H, 4.40; N, 6.07.

Example 163

2-(2-Formylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title was prepared according to the method of Example 62 substituting 2-bromobenzaldehyde in place of 4-iodo-1-fluorobenzene (yield: 0.196 g, 60%). mp 234-236 °C. ^1H NMR (300 MHz, DMSO d_6) δ 3.24 (s, 3H), 7.15 (m, 2H), 7.27 (m, 2H), 7.54 (m, 2H), 7.64-7.75 (m, 2H), 7.86-7.95 (m, 3H), 8.01 (m, 1H), 8.29 (s, 1H), 10.02 (s, 1H).

MS (DCI/NH_3) m/z 449 $(M+H)^+$. Anal. calc. for $C_{24}H_{17}FN_2O_4S.0.50\ H_2O$: C, 63.01; H, 3.96; N, 6.12. Found: 63.04; H, 3.82; N, 5.88.

Example 164

2-(2-Nitrophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 1-bromo-2-nitrobenzene in place of 4-iodo-1-fluorobenzene (yield: 0.307 g, 90.8%). mp 236-239 °C. ^1H NMR (300 MHz, DMSO d_6) δ 3.24 (s, 3H), 7.12-7.27 (m, 4H), 7 56 (m, 2H), 7.7-8.01 (m, 5H), 8.18 (m, 1H), 8.35 (s, 1H). MS (DCI/NH_3) m/z 466 $(M+H)^+$, 483 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{16}FN_3O_5S.0.25\ H_2O$: C, 58.78; H, 3.53; N, 8.94 Found: C, 58.63; H, 3.54, N, 8.88.

Example 165

2-(3-Chlorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 1-bromo-3-chlorobenzene in place of 4-iodo-1-fluorobenzene (yield: 0.255 g, 77%) mp 232-235 °C. ^1H NMR (300 MHz, DMSO d_6) δ 3.23 (s, 3H), 7.14 (m, 2H), 7.29 (m, 2H), 7.49-7.58 (m, 4H), 7.66 (m, 1H), 7.79 (m, 1H), 7.90 (m, 2H), 8.25 (s, 1H). MS (DCI/NH_3) m/z 455 $(M+H)^+$, 472 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{16}ClFN_2O_3S$: C, 60.73; H, 3.55; N, 6.16. Found: C, 60.40; H, 3.43, N, 5.98.

Example 166

2-(3-Bromophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 1,3 dibromobenzene in place of 4-iodo-1-fluorobenzene (yield: 0.216 g, 60%). mp 210-212 °C. ^1H NMR (300 MHz, DMSO d_6) δ 3.23 (s, 3H), 7.15 (m, 2H), 7.29 (m, 2H), 7.48-7.55 (m, 3H), 7.69 (m, 2H), 7.90 (m, 3H), 8.26 (s, 1H). MS (DCI/NH_3) m/z 499 $(M+H)^+$, 519 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{16}BrFN_2O_3S$· C, 55.32; H, 3.23; N, 5.61. Found: C, 55.12; H, 3.12; N, 5.51

Example 167

2-(4-Cyanophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 4-bromobenzonitrile in place of 4-iodo-1-fluorobenzene (yield: 0.349 g, 100%). mp 273-278 °C. ^{1}H NMR (300 MHz, DMSO d_6) δ 3.24 (s, 3H), 7.11-7.21 (m, 2H), 7.25-7.35 (m, 2H), 7.52 (m, 2H), 7.88-7.96 (m, 4H), 8.04 (m, 2H), 8.31 (s, 1H). MS (DCI/NH_3) m/z 445 $(M+H)^+$. Anal. calc. for $C_{24}H_{16}FN_3O_3S$: C, 64.71; H, 3.62; N, 9.43. Found: C, 64.50; H, 3.53; N, 9.35.

Example 168

2-(5-Methyl-2-thienyl))-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 2-bromo-5-methylthiophene in place of 4-iodo-1-fluorobenzene (yield: 0.200 g, 62%). mp 219-224 °C. ^{1}H NMR (300 MHz, DMSO d_6) δ 2.45 (s, 3H), 3.23 (s, 3H), 6.80 (m, 1H), 7.17 (m, 2H), 7.29 (m, 2H), 7.52 (m, 3H), 7.89 (m, 2H), 8.33 (s, 1H). MS (DCI/NH_3) m/z 441 $(M+H)^+$, 458 $(M+NH_4)^+$. Anal. calc. for $C_{22}H_{17}FN_2O_3S_2$: C, 59.99; H, 3.89; N, 6.36. Found: C, 59.90; H, 3.91; N, 6.26.

Example 169

2-(3-Biphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 3-bromobiphenyl in place of 4-iodo-1-fluorobenzene (yield: 0.28 g, 78%). mp 126-134 °C. ^{1}H NMR (300 MHz, DMSO d_6) δ 3.24 (s, 3H), 7.15 (m, 2H), 7.31 (m, 2H), 7.37-7.45 (m, 1H), 7.51 (m, 4H), 7 64 (m, 2H), 7.68-7.79 (m, 3H), 7.92 (m, 3H), 8.27 (s, 1H). MS (DCI/NH_3) m/z 497 $(M+H)^+$, 514 $(M+NH_4)^+$. Anal. calc for $C_{29}H_{21}FN_2O_3S$: C, 70.15; H, 4.26; N, 5.64. Found: C, 69.91; H, 4.33; N, 5.74.

Example 170

2-(3,5-Dimethylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 5-bromo-m-xylene in place of 4-iodo-1-fluorobenzene (yield: 0.152 g, 46.5%). mp 130-134 °C. ^{1}H NMR (300 MHz, DMSO d_6) δ 2.34 (s, 6H), 3.23 (s, 3H), 7.07-7.12 (m, 2H), 7.15 (m, 1H), 7.21-7.32 (m, 4H), 7.52 (m, 2H), 7.90 (m, 2H), 8.29 (s, 1H). MS (DCI/NH_3) m/z 449 $(M+H)^+$, 466 $(M+NH_4)^+$. Anal. calc. for $C_{25}H_{21}FN_2O_3S$: C, 66.95; H, 4.72; N, 6.25. Found: C, 66.81; H, 4.57; N, 6.07.

Example 171

2-(3,4-Difluorophenyl)-4-(4-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

4-(4-Fluorophenylmethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone was prepared according to the method of Example 11, starting with 2-benzyl-4-(4-fluorophenylmethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone in place of 2-benzyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (yield: 0.3319 g, 83%).

The title compound was prepared according to the method of Example 62 substituting 4-(4-fluorophenylmethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone in place of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone and substituting 1-bromo-3,4-difluorobenzene in place of 4-iodo-1-fluorobenzene (yield: 0.085 g, 54%). mp 157-159 °C. ^{1}H NMR (300 MHz, DMSO d_6) δ 3.30 (s, 3H), 3.88 (bs, 2H), 7.04 (m, 4H), 7.49-7.66 (m, 2H), 7.70 (m, 2H), 7.81 (m, 1H), 8.12 (s, 1H). MS (DCI/NH_3) m/z 471 $(M+H)^+$, 488 $(M+NH_4)^+$. Anal. calc. for $C_{24}H_{17}F_3N_2O_3S.0.25\ H_2O$: C, 60.69; H, 3.71; N, 5.84. Found: C, 6.39; H, 3.76; N, 5.81.

Example 172

2-(3-Chloro-4-fluorophenyl)-4-(4-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 4-(4-fluorophenylmethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone in place of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone and substituting 4-bromo-2-chloro-1-fluorobenzene in place of 4-iodo-1-fluorobenzene (yield: 0.110 g, 74%). mp 153-156 °C. ^{1}H NMR (300 MHz, DMSO d_6) δ 3.30 (s, 3H), 3.89 (bs, 2H), 7.02-7.07 (m, 4H), 7.59 (m, 1H), 7.65-7.72 (m, 4H), 8.07 (m, 2H), 8.12 (s, 1H). MS (DCI/NH_3) m/z 487 $(M+H)^+$, 504 $(M+NH_4)^+$. Anal. calc. for $C_{24}H_{17}ClF_2N_2O_3S.0.25\ H_2O$. C, 58.65; H, 3.58; N, 5.64. Found C, 58.41; H, 3.56, N, 5.36..

Example 173

2-(2-Thienyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 2-bromothiophene in place of 1-bromo-4-fluorobenzene (yield: 98 mg, 40%). mp 215-217 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 3H), 7.18 (m, J=9 Hz, 3H), 7.29 (m, 2H), 7.42 (d, 2H), 7.75 (d, 1H), 7.93 (d, J=9 Hz), 8.4 (s, 1H). MS (DCI/NH_3) m/z 427 $(M+H)^+$, 444 $(M+NH_4)^+$. Anal. calc. for $C_{21}H_{15}FN_2O_3S_2$. C, 59.14; H, 3.54, N, 6.57.

Example 174

2-(4-Trifluoromethylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 1-bromo-4-trifluoromethylbenzene in place of 1-bromo-4-fluorobenzene (yield: 185 mg, 64%). mp 171-173 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 3H), 7.18 (t, 2H), 7.29 (m, 2H), 7.52 (d, J=9 Hz 2H), 7.91 (d, J=9 Hz, 2H), 7.93 (s, 4H), 8.32 (s, 1H). MS (DCI/NH_3) m/z 489 $(M+H)^+$, 506 $(M+NH_4)^+$ Anal. calc. for $C_{24}H_{16}F_4N_2O_3S$: C, 59.02; H, 3.3; N, 5.74. Found: C, 58.75; H, 3.35; N, 5.69.

Example 175

2-[4-(1-Pyrrovl)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 1-(4-iodophenyl)pyrrole in place of 1-bromo-4-fluorobenzene (yield: 140 mg, 50%). mp 229-231 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 3H). 6.3 (t, 2H), 7.18 (t, 2H), 7.29 (m, 2H), 7.46 (t, 2H) 7.53 (d. J=9 Hz 2H), 7,75 (s, 4H). 7.91 (d, J=9 Hz, 2H), 8.27 (s, 1H). MS (DCI/NH_3) m/z 486 $(M+H)^+$, 504 $(M+NH_4)^+$. Anal. calc. for $C_{27}H_{20}FN_1O_1S.0.5\ H_2O$: C. 66.79; H. 4.15; N. 8.65. Found· C. 65.21; H. 4.29; N, 8.12.

Example 176

2-(5-Chloro-2-thienyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 2-bromo-5-chlorothiophene in place of 1-bromo-4-fluorobenzene (yield: 225 mg, 93%). mp 190-192 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.38 (s, 3H), δ 3.25 (s, 3H). 7.15 (t, 2H). 7.29 (m, 4H), 7.5 (D, 4H) 7.91 (d, J=9 Hz, 2H), 8.21 (s. 1H). MS (DCI/NH_3) m/z 435 $(M+H)^+$, 452 $(M+NH_4)^+$. Anal. calc. for $C_{21}H_{15}F\ N_2O_3S$: C, 66.35; H, 4.41; N. 6.45. Found: C. 66.15; H. 4.37; N. 6 3.

Example 177

2-(4-Methylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 1-bromo-4-methylbenzene in place of 1-bromo-4-fluorobenzene (yield: 79 mg, 31%). mp 190-192 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.38 (s, 3H), δ 3.25 (s, 3H), 7.15 (t. 2H), 7.29 (m. 4H), 7.5 (D, 4H) 7.91 (d, J=9 Hz. 2H). 8.21 (s, 1H). MS (DCI/NH_3) m/z 435 $(M+H)^+$, 452 $(M+NH_4)^+$ Anal. calc. for $C_{21}H_{19}F\ N_2O_3S$ C. 66.35; H. 4.41; N. 6.45 Found. C, 66.15; H. 4.37; N. 6.3.

Example 178

2-(4-Fluorophenyl)-4-(2-ethyl-1-hexyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

To a solution of 2-ethyl-1-hexanol (65 mg, 0.5 mmol) in THF (15 mL) at room temperature was added NaH (60% oil suspension) (20 mg, 0.5 mmol) and after 10 minutes 2-(4-fluorophenyl)-4-tosyloxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (193 mg, 0.5 mmol) was added. The resulting mixture was stirred at room temperature for the next 2 hours. The mixture was quenched with 10% citric acid and extracted with ethyl acetate. The extract was washed with water, brine, dried with $MgSO_4$, and purified by chromatography (silica gel, 2:1 hexanes-ethyl acetate) to provide the desired product (yield: 140 mg, 60%). mp 120-122 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.75 (m, 6H), 1.1 (m, 6H), 1.20 (quintet, J=7 Hz, 2H), 1.44 (m, 1H), 3.27 (s, 3H), 4.30 (d, J=6 Hz, 2H), 7.37 (t, J=9 Hz, 2H), 7.65 (m, 2H), 7.89 (d, J=9 Hz, 2H), 8.06 (d, J=9 Hz, 2H), 8.18 (s, 1H). MS (APCI+) m/z 473 $(M+H)^+$; (APCI-) m/z 507 $(M+Cl)^-$. Anal. calc. for $C_{25}H_{29}FN_2O_4S.0.5\ H_2O$: C, 62.35; H, 6.27; N, 5 87. Found: C, 62 22; H, 6.14; N, 6.22.

Example 179

2-(3-Thienyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 3-bromothiophene in place of 1-bromo-4-fluorobenzene (yield: 225 mg, 93%). mp 200-202 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 3H), 7.15 (t, 2H), 7.29 (m, 2H), 7.5 (d, J=9 Hz, 2H), 7.6 (M, 1H) 7.66 (dd, 1H), 7.91 (d, J=9 Hz, 2H), 8.13 (dd, 1H), 8.25 (s, 1H). MS (DCI/NH_3) m/z 427 $(M+H)^+$, 444 $(M+NH_4)^+$. Anal. calc. for $C_{21}H_{15}FN_2O_3S_2$: C, 55.07; H, 4.07; N, 6.11. Found. C, 54.63; H, 3.47; N, 6.01.

Example 180

2-(3,5-Difluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 3,5-difluorobromobenzene in place of 1-bromo-4-fluorobenzene (yield: 250 mg, 96%). mp 166-168 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 3H), δ 7.15 (t, 2H), 7.27 (m, 2H), 7.4 (m, 1H). 7.41 (m, 2H). 7.51 (d, J=9 Hz, 4H). 7.9 (d, J=9 Hz, 2H), 8.3 (s, 1H). MS (DCI/NH_3) m/z 457 $(M+H)^+$, 474 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{15}F_3N_2O_3S$: C, 60.13; H, 3.31; N, 6.14. Found: C, 60.49; H, 3.31; N, 6.03.

Example 181

2-(2,4-Difluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 2,4-difluorobromobenzene in place of 1-bromo-4-fluorobenzene (yield: 40 mg, 15%). mp 245-247 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.23 (s, 3H), δ 7.15 (t, 2H), 7.3 (t, 2H), 7.54 (m, 2H), 7.57 (m, 2H), 7.75 (m, 1H), 7.9 (d, J=9 Hz, 2H), 8.27 (s, 1H). MS (DCI/NH_3) m/z 457 $(M+H)^+$, 474 $(M+NH_4)^+$ Anal. calc. for $C_{23}H_{15}F_3N_2O_3S$: C, 60.52; H, 3.31; N, 6.03.

Example 182

2-(3,4-Difluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 3,4-difluorobromobenzene in place of 1-bromo-4-fluorobenzene (yield: 170 mg, 70%). mp 109-110 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.23 (s, 3H), δ 7.15 (t, 2H), 7.3 (t, 2H), 7.25 (m, 2H), 7.59 (m, 4H), 7.83 (m, 1H), 7.9 (d, J=9 Hz, 2H), 8.27 (s, 1H). MS (DCI/NH_3) m/z 457 $(M+H)^+$, 474 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{15}F_3N_2O_3S$: C, 60.52; H, 3.31; N, 6.14. Found 60.60; H, 3.48; N, 5.89

Example 183

2-(3-Furyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 3-bromofuran in place of 1-bromo-4-fluorobenzene (yield: 175 mg, 73%). mp 239-242 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 3H), 7 09 (d, 1H), 7.15 (t, 2H), 7.29 (m, 2H), 7.5 (d, J=9 Hz 2H), 7.8 (t, 1H) 7.91 (d, J=9 Hz, 2H), 8.3 (s 1H), 8.58 (s, 1H). MS (DCI/NH_3) m/z 411 $(M+H)^+$, 428 $(M+NH_4)^+$. Anal. calc. for $C_{21}H_{15}F N_2O_4S.0.5 H_2O$: C, 61.46; H, 3.68; N, 6.83. Found. C, 59.91; H, 3.54; N, 6 54

Example 184

2-(3-Fluoro-4-methoxyphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 3-fluoro-4-methoxybromobenzene in place of 1-bromo-4-fluorobenzene (yield· 230 mg, 85%). mp 97-101 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 3H), 3.9 (s, 3H), 7.16 (d, 1H), 7.29 (m, 3H), 7.5 (m, 4H), 7.91 (d, J=9 Hz, 2H), 8.23 (s 1H). MS (DCI/NH_3) m/z 469 $(M+H)^+$, 491 $(M+NH_4)^+$. Anal. calc. for $C_{24}H_{18}F_2N_2O_4S.0.5 H_2O$: C, 61.53; H, 3.87; N, 5.98. Found: C, 61.18; H, 4.01; N, 5.58.

Example 185

2-(2-Fluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 2-fluorobromobenzene in place of 1-bromo-4-fluorobenzene (yield: 195 mg, 75%). mp 96-103 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.23 (s, 3H), δ 7.15 (t, 2H), 7.3 (m, 3H), 7.55 (m, 5H), 7.9 (d, J=9 Hz, 2H), 8.27 (s, 1H). MS (ESI) m/z 437 $(M-H)^-$). Anal. calc. for $C_{23}H_{16}F_2N_2O_3S$: C, 63.01; H, 3 68; N, 6.39. Found. C, 62.91, H, 4.06; N, 5.99.

Example 186

2-[4-(Aminosulfonyl)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 4-aminosulfonyl-1-bromobenzene in place of 1-bromo-4-fluorobenzene. mp 213-216 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 3H), 7.15 (t, 2H), 7.29 (m, 2H), 7.53 (s, 2H) 7.55 (s, 1H), 7 7 (dd, 2H) 7.91 (t, 4H), 7.98 (d, 2H), 8.3 (s, 1H). MS (DCI/NH_3) m/z 499 $(M+H)^+$, 517 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{18}FN_3O_5S_2$.0.5 H_2O: C, 55.30; H, 3.63; N, 8.41. Found: C. 54.4; H. 3.79; N, 7.78.

Example 187

2-(3-Chloro-4-fluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 3-chloro-4-fluoro-1-bromobenzene in place of 1-bromo-4-fluorobenzene (yield: 320 mg, 78%). mp 155-157 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.23 (s, 3H), δ 7.15 (t, 2H), 7.3 (t, 2H), 7.25 (m, 2H), 7.53 (d, J=9 Hz, 2H), 7.59 (t, 1H), 7.73 (m, 1H), 7.9 (d, J=9 Hz, 2H) 7.96 (m, 1H), 8.27 (s, 1H). MS (DCI/NH_3) m/z 473 $(M+H)^+$, 490 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{15}ClF_2N_2O_3S$. C, 58.42; H, 3.2; N, 5.92. Found 58.23; H, 2.87; N, 5.70

Example 188

2-(3,5-Dichlorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 3,5-dichlorobenzene in place of 1-bromo-4-fluorobenzene (yield: 360 mg, 78%). mp 289-294 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 3H), δ 7.15 (t, 2H), 7.27 (m, 2H), 7.51 (d, J=9 Hz, 4H), 7 75 (t, 1H), 7.83 (d, 2H), 7.9 (d, J=9 Hz, 2H), 8.3 (s, 1H). MS (DCI/NH_3) m/z 490 $(M+H)^+$, 507 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{15}Cl_2FN_2O_3S$ 0.5 H_2O: C, 56.45; H, 3.09, N, 5.72. Found. C, 55.36; H, 3.00; N, 5.50.

Example 189

2-(4-Fluoro-3-methylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 62 substituting 1-bromo-4-fluoro-3-methylbenzene in place of 1-bromo-4-fluorobenzene (yield: 275 mg, 71%). mp 168-170 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.3 (s, 3H), δ 3.25 (s, 3H), 7.15 (t, 2H), 7.3 (m, 3H), 7.56 (m, 4H), 7.9 (d, 2H), 8.23 (s, 2H). MS (DCI/NH_3) m/z 453 $(M+H)^+$, 471 $(M+NH_4)^+$. Anal. calc. for $C_{24}H_{18}F_2N_2O_3S$. C, 63.71; H, 4.01; N, 6.01. Found: C, 63.53; H, 4.06; N, 5.92.

Example 190

2-(4-Chloro-3-fluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone:

The title compound was prepared according to the method of Example 62 substituting 4-bromo-1-chloro-2-fluorobenzene in place of 1-bromo-4-fluorobenzene (yield: 220 mg, 80%). mp 102-110 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.23 (s, 3H), 7.11-7.19 (m, 2H), 7.25-7.32 (m, 2H), 7.51 (d, J=5.6 Hz, 2H), 7.58-7.64 (m, 1H), 7.75-7.87 (m, 2H), 7.91 (d, J=5.6 Hz, 2H), 8.28 (s, 1H). MS (APCI+) m/z 473 $(M+H)^+$.

Example 191

2-(4-Chloro-2-fluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone:

The title compound was prepared according to the method of Example 62 substituting 1-bromo-4-chloro-2-fluorobenzene in place of 1-bromo-4-fluorobenzene (yield: 65 mg 24%). mp 250-260 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.21 (s, 3H), 7.12-7.19 (m, 2H), 7.25-7.32 (m, 2H), 7.49-7.58 (m, 3H), 7.68-7.78 (m, 2H), 7.91 (d, J=8.7 Hz, 2H), 8.29 (s, 1H). MS (APCI+) m/z 473 $(M+H)^+$. Anal. calc. for $C_{23}H_{15}ClF_2N_2O_3S$· C, 58.41; H, 3.19; N, 5.92. Found: C, 58.69; H, 3.45; N, 5.78.

Example 192

2-(1-Adamantyloxycarbonyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

A solution of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone, prepared according to the procedure of Example 11 (200 mg, 0.58 mmol) in CH_2Cl_2 (8 ml) was prepared and stirred. 1-Adamantylfluoroformate (172 mg, 0.87 mmol), dimethylaminopyridine (14 mg, 0.011 mmol) and triethylamine (0.12 ml, 0.87 mmol) were added. The reaction mixture was stirred at room temperature overnight. The reaction mixture was diluted with CH_2Cl_2 (50 ml) and washed with 10% citric acid (50 ml), brine (50 ml) and dried over $MgSO_4$, and concentrated in vacuo. The resulting crude residue was purified using flash chromatography (SiO_2, eluting with 15:1 CH_2Cl_2:diethyl ether) to provide the desired product (yield: 55 mg, 18%). ^1H NMR (300 MHz, DMSO-d_6) δ 1.66 (bs, 6H), 2.25 (bd, 10H), 3.21 (s, 3H), 7.15 (t, 2H), 7.24 (m, 2H), 7.6 (dd, 2H), 7.88 (d, J=9 Hz, 2H), 8.15 (s, 1H). MS (ESI) m/z 521 $(M-H)^-$. Anal. calc. for $C_{21}H_{15}FN_2O_4S_2$: C, 64.35; H, 5.20; N, 5.36.

Example 193

2-(2,2,2-Trifluoroethyl)-4-(4-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

Example 193A

2-(2,2,2-Trifluoroethyl)-4,5-dichloro-3(2H)-pyridazinone

2,2,2-Trifluoroethylhydrazine (70% solution in water, 35.0 g, 0.307 mol) was treated with mucochloric acid (51.88 g, 0.307 mol) in ethanol (300 mL) and refluxed for 5 hours. The solvent was concentrated in vacuo. The crystals obtained were washed with water and air dried (yield: 50 g; 67.5%). ^1H NMR (300 MHz, $CDCl_3$) δ 4.8 (q, J=9 Hz, 2H), 7.85 (s, 1H). MS (DCI-NH_3) m/z 264 $(M+NH4)^+$.

Example 193B

2-(2,2,2-Trifluoroethyl)-4-chloro-5-hydroxy-3(2H)-pyridazinone

2-(2,2,2-Trifluoroethyl)-4,5-dichloro-3(2H)-pyridazinone (15.0 m 60.7 mmol), and potassium carbonate (10 g, 72.4 mmol.) were mixed with water (500 mL) and stirred at reflux for 6 hours. TLC (1:1:2 CH_2Cl_2/hexanes/ethyl acetate) indicated that all starting material was consumed.) The reaction mixture was cooled to room temperature. The pH of the reaction mixture was adjusted to about 4 with hydrochloric acid (15%). The product was extracted with ethyl acetate (700 mL). The organic phase was washed with brine, dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure. The hydroxy compound was obtained as a light brown solid (yield: 13.1 g, 94%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.92 (q, J=9 Hz, 2H). 7.9 (s, 1H) MS (DCI/NH_3) m/z 229 $(M+H)^+$.

Example 193C

2-(2,2,2-Trifluoroethyl)-4-chloro-5-(trifluoromethylsulfonyloxy)-3(2H)-pyridazinone

Anhydrous Na_2CO_3 (9.04 m. 85.32 mmol) was placed in a 500 mL round bottom flask and anhydrous CH_2CL_2 (200 mL) was added. The reaction mixture was cooled to 0 oC under N_2. The halohydroxy pyridazinone prepared in Example 193B was dissolved in CH_2CL_2 (100 mL) and added slowly to the flask and stirred overnight. The reaction slowly warmed to room temperature. (TLC (2: 1 hexanes/ethyl acetate) indicated completion of the reaction.) The reaction was quenched with H_2O. The organic phase containing the product was separated, washed with brine and dried over $MgSO_4$. The resulting filtrate was concentrated under reduced pressure. The crude product was isolated as deep red-brown residue. Purification using a silica gel column (30:70 ethyl acetate/pentanes) provided the title compound as a dark, reddish residue (14.3 m, 70%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.85 (q, J=9 Hz, 2H), 7.9 (s, 1H). MS (DCI/NH_3) m/z 378 $(M+NH_4)^+$.

Example 193D

2-(2,2,2-Trifluoroethyl)-4-chloro-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone

A solution of the triflate prepared in Example 193C (1.56 g 4.3 mmol), 4-(methylthio)phenylboronic acid (870 mg, 5.16 mmol), tetrakis(triphenylphosphine)palladium(0) (250 mg, 5% mmol) and triethylamine (1.44 ml, 10.32 mmol) in toluene was heated at reflux for 1 hour. The mixture was partitioned between ethyl acetate and water. The ethyl acetate layer was washed with water, then brine, followed by drying over $MgSO_4$ and filtration. The filtrate was concentrated in vacuo . The residue was purified by column chromatography (silica gel, 92:8 hexanes/ethyl acetate) to provide the coupled intermediate as a pale, greenish-yellow solid (yield: 500 mg, 35%). mp 130-139 °C ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.55 (s, 3H), 4.87 (q, J=9 Hz, 2H), 7.37 (d, J=9 Hz, 2H), 7.48 (d, J=9 Hz, 2H), 7.82 (s, 1H). MS (DCI/NH_3) m/z 335 $(M+H)^+$.

Example 193E

2-(2,2,2-Trifluoroethyl)-4-chloro-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 10, substituting the coupled intermediate prepared in Example 193D in place of 2-benzyl-4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone (yield: 440 mg, 81%). mp 221-222 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.33 (s, 3H), 5.10 (q, J=9 Hz, 2H), 7.90 (d, J=9 Hz, 2H), 8.12 (d, J=9 Hz, 2H), 8.20 (s, 1H). MS (DCI/NH_3) m/z 367 $(M+H)^+$.

X1E AH

Example 193F

2-(2,2,2-Trifluoroethyl)-4-(4-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

Magnesium turnings (500 mg) were placed in a dry 250 mL round bottom flask. Anhydrous ether (20 mL) was added under N_2 at room temperature then fluorobenzyl bromide (3 mL) was added and stirred. The reaction was heated at 40 °C for 2 hours. All magnesium was consumed resulting in a pale brownish-yellow solution. The 2-(2,2,2-trifluoroethyl)-4-chloro-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone prepared in

Example 193E was dissolved in dry THF (25 mL) and transferred to the Grignard solution. The mixture was heated for 3 hours. TLC (2:1 hexanes/ethyl acetate) indicated that the pyridazinone starting material was consumed.) The reaction was cooled to room temperature then quenched with a saturated NH_4Cl solution. The product was extracted with ethyl acetate (250 mL); and the organic layer was washed with saturated NH_4Cl, and brine. The ethyl acetate solution was dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure. The product was isolated as an orange residue. Purification using a silica gel column (20:80 ethyl acetate/pentanes) provided the title compound as a pale yellow powder (yield: 140 mg, 28%). ^1H NMR (300 MHz, $CDCl_3$) δ 3.13 (s, 3H), 4.85 (m, 2H). 6..93 (m, 4H). 7.49 (d, J=9 Hz, 2H) 7.72 (s, 1H). 8.08 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 441 $(M+H)^+$. Anal. calc. for $C_{20}H_{16}F_4N_2O_3S.0.5$ H_2O: C, 53 45; H, 3.81; N, 6.23. Found C, 53.45; H, 3.81; N, 6.23.

Example 194

2-(4-Fluorophenyl)-4-(4-fluorophenoxymethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

Example 194A

2-(4-Fluorophenyl)-4,5-dibromo-3(2H)-pyridazinone

Mucobromic acid (5.0 g, 19.4 mmol) dissolved in acetic acid (110 mL) was treated with 4-fluorophenyl hydrazine.HCl, and the heterogeneous mixture brought to reflux at a bath temperature of 115 °C for 15 hours. During the course of reaction, the mixture became a homogeneous deep red solution, and upon cooling to 23 °C, a crystalline precipitate formed. The solution was poured into ice water (1000 mL) and stirred for 20 minutes. The yellow/brown crystals were filtered off, washed with additional cold water, and dried in vacuo to provide 5.8 g (86%) of product. (J. Het. Chem.., 1993, 30, 1501, Heterocycles 1985, 23, 2603) ^1H NMR (300 MHz, DMSO-d_6) δ 7.31-7.41 (m, 2H). 7.57-7.64 (m, 2H). 8.29 (s, 1H). MS (DCI+) m/z 347 $(Br_{79}Br_{79}$ $M+H)^+$, m/z 349 $(Br_{79}Br_{81}$ $M+H)^+$, m/z 364 $(Br_{79}Br_{79}$ $M+NH_4)^+$, and m/z 366 $(Br_{79}Br_{81}$ $M+NH_4)^+$.

Example 194B

2-(4-Fluorophenyl)-4-methoxy-5-bromo-3(2H)-pyridazinone

A 23 °C homogeneous solution of 2-(4-fluorophenyl)-4,5-dibromo-3(2H)-pyridazinone (7.18 g, 20.6 mmol) prepared above in tetrahydrofuran (322 mL) was treated with methanol (0.843 mL, 20.8 mmol) and after 5 minutes with NaH (0.833 g, 20.8 mmol, 60% oil dispersion). The reaction exothermed for several minutes and then was continued for 8 hours at 23 °C (Note: several reactions have run to completion at this point). The reaction did not run to completion, and so the temperature was raised to reflux for 4 hours more. The reaction was still not completed. An additional 0.1 equivalent of NaOMe solution was prepared in a separate flask as above with the quantities: 32 mL of tetrahydrofuran, 0.084 mL of methanol, and 83 mg of 60% NaH oil dispersion. This NaOMe solution was added via syringe to the reaction mixture cooled to 23 °C, and then the temperature raised to reflux for 4 hours The reaction was still not complete, and so another 0.1 equivalent NaOMe solution was prepared, added, and the reaction brought to reflux, as above. After this 4 hours, the reaction was completed. The mixture was cooled to 23 °C and diluted to 2000 mL with water. The yellow/white precipitate that formed was filtered off, washed with additional water, and concentrated in vacuo to provide 5.39 g (88%) of product. (J. Het. Chem., 1988, 25, 1757) ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.13 (s, 3H), 7.30-7.40 (m, 2H), 7.56-7.62 (m, 2H), 8.22 (s, 1H). MS (APCI+) m/z 299 (^{79}Br M+H)$^+$ and m/z 301 (^{81}Br M+H)$^+$.

Example 194C

2-(4-Fluorophenyl)-4-methoxy-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 6 starting with 2-(4-fluorophenyl)-4-methoxy-5-bromo-3(2H)-pyridazinone in place of 2-benzyl-4-bromo-5-methoxy-3(2H)-pyridazinone and substituting 4-(methylthio)benzeneboronic acid in place of 4-fluorobenzeneboronic acid (yield: 70 mg, 61%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.54 (s, 3H), 4.02 (s, 3H), 7.35 (dd, J=9.0, 9.0 Hz, 2H), 7.39 (d, J=8.5 Hz,

2H), 7.61 (d, J=8.5 Hz, 2H), 7.65 (dd, J=9.0, 5.0 Hz, 2H), 8.14 (s, 1H). MS (APCI+) m/z 343 $(M+H)^+$.

Example 194D

2-(4-Fluorophenyl)-4-methyl-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 228 substituting methyl magnesium bromide in place of cyclohexylmagnesium chloride (yield: 0.83 g, 87%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.25 (s, 3H), 2.55 (s, 3H), 7.17 (dd, J=8.8, 8.8 Hz, 2H), 7.31 (d, J=8.7 Hz, 2H), 7.38 (d, J=8.7 Hz, 2H), 7.61-7.68 (m, 2H), 7.82 (s, 1H). MS (APCI+) m/z 327 $(M+H)^+$.

Example 194E

2-(4-Fluorophenyl)-4-methyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 10 substituting 2-(4-fluorophenyl)-4-methyl-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone in place of 2-benzyl-4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone (yield: 473 mg, 86%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.24 (s, 3H), 3.14 (s, 3H), 7.19 (dd, J=8.8, 8.8 Hz, 2H), 7.61 (d, J=8.4 Hz, 2H), 7.63-7.69 (m, 2H), 7.80 (s, 1H), 8.12 (d, J=8.4 Hz, 2H). MS (APCI+) m/z 359 $(M+H)^+$ and m/z 376 $(M+NH_4)^+$.

Example 194F

2-(4-Fluorophenyl)-4-bromomethyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

To a heterogeneous, refluxing solution of 2-(4-fluorophenyl)-4-methyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (590 mg, 1.65 mmol) and carbon tetrachloride (24 mL) was quickly added N-bromosuccinimide (yield: 308 mg, 1.73 mmol) followed by benzoyl peroxide (12 mg, 0.05 mmol). After 1 hour the reaction had only run to near 50% completion. Additional benzoyl peroxide (12 mg, 0.05 mmol) was added, and the reaction checked after another 1 hour. The reaction was still not complete, and so more benzoyl peroxide (4 mg, 0.017 mmol) was added. After 30 minutes, the reaction was

completed. The mixture was cooled to 23 °C and diluted with ethyl acetate. The acetate solution was washed with saturated $NaHCO_3$, water, and brine. The solution was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed (flash silica gel, ethyl acetate/hexanes gradient 1:1 to 4:1) to provide the product (yield: 530 mg, 74%). ^1H NMR (300 MHz, $CDCl_3$) δ 3.16 (s, 3H), 4.34 (s, 2H), 7.20 (dd, J=8.8, 8.8 Hz, 2H), 7.67-7.74 (m, 2H), 7.82 (d, J=8.7 Hz, 2H), 7.86 (s, 1H), 8.17 (d, J=8.7 Hz, 2H). MS (APCI+) m/z 437 $(M+H)^+$.

Example 194G

2-(4-Fluorophenyl)-4-(4-fluorophenoxymethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

To a homogeneous solution of 2-(4-fluorophenyl)-4-bromomethyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone, Example 194F, (107 mg, 0.246 mmol) and 4-fluorophenol (30.3 mg, 0.270 mmol) dissolved in acetone (4 mL) was added powdered K_2CO_3 (37.3 mg, 0.270 mmol). The mixture was stirred at 23 °C for 2 hours, filtered through a bed of Celite®, and concentrated in vacuo. The residue was chromatographed (flash silica gel, ethyl acetate/hexanes 3:2) to provide the product (yield, 83 mg, 72%). mp 65-80 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 3.12 (s, 3H), 4.94 (s, 2H), 6.78-6.86 (m, 2H), 6.91-7.00 (m, 2H), 7.15-7.24 (m, 2H), 7.65-7.72 (m, 2H), 7.74 (d, J=8.7 Hz, 2H), 7.93 (s, 1H), 8.08 (d, J=8.7 Hz, 2H). MS (APCI+) m/z 469 $(M+H)^+$. Anal. calc. for $C_{24}H_{18}F_2N_2O_4S$: C, 61.53; H, 3.87; N, 5.97. Found: C, 61.22; H, 3.63; N, 5.64.

Example 195

2-(4-Fluorophenyl)-4-(3-fluorophenoxymethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 194G substituting 3-fluorophenol in place of 4-fluorophenol (yield: 94 mg, 88%). mp 142-144 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 3.12 (s, 3H), 4.98 (s, 2H), 6.49-6.56 (m, 1H), 6.60-6.73 (m, 2H), 7.15-7.25 (m, 3H), 7.65-7.75 (m, 4H), 7.93 (s, 1H), 8.07 (d, J=8.7 Hz, 2H). MS

(APCI+) m/z 469 $(M+H)^+$. Anal. calc. for $C_{24}H_{18}F_2N_2O_4S$: C, 61.53; H, 3.87; N, 5.97. Found: C, 61.20; H, 3.92; N, 5.86.

Example 196

2-(4-Fluorophenyl)-4-phenoxymethyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 294G substituting phenol in place of 4-fluorophenol (yield: 67 g, 93%). mp 42-75 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.28 (s, 3H), 4.92 (s, 2H), 6.83-6.90 (m, 2H), 6.91-6.99 (m, 1H), 7.22-7.30 (m, 2H), 7.35-7.44 (m, 2H), 7.66-7.73 (m, 2H), 7.81-7.88 (m, 2H), 8.02-8.08 (m, 2H), 8.21 (s, 1H). MS (APCI−) m/z 451 $(M+H)^+$.

Example 197

2-(4-Fluorophenyl)-4-(t-butylthiomethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

A 0 °C solution of the 2-(4-fluorophenyl)-4-bromomethyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone prepared in Example 194F (92.5 mg, 0.212 mmol) in acetone (2.5 mL) was treated with NaI (35 mg, 0.233 mmol), and after 5 minutes, the cooling bath was removed and the reaction warmed to 23 °C. After 30 minutes, conversion to the 2-(4-fluorophenyl)-4-iodomethyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone was complete (thin layer chromatography, ethyl acetate/hexanes 4:1). The NaBr and residual NaI were filtered off through a pad of Celite®. Additional acetone (2 mL) was added along with 2-methyl-2-propanethiol (20.5 mg, 0.227 mmol), and the solution cooled to 0 °C before addition of Ag_2CO_3 (63 mg, 0.227 mmol). After 5 minutes, the cooling bath was removed and the solution warmed to 23 °C for 5 hours. The reaction mixture was filtered through Celite® and concentrated in vacuo. The residue was chromatographed (flash silica gel, ethyl acetate/hexanes gradient 1:1 to 3:2) to provide the product (yield: 57 mg, 60%). mp 50-70 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (s, 9H), 3.14 (s, 3H), 3.65 (s, 2H), 7.13-7.21 (m, 2H), 7.63-7.70 (m, 2H), 7.79 (s, 1H), 7.84 (d,

J=8.7 Hz, 2H). 8.13 (d, J=8.7 Hz, 2H). MS (APCI+) m/z 447 $(M+H)^+$. Anal. calc. for $C_{22}H_{23}FN_2O_3S_2$: C, 59.17; H, 5.19; N, 6.27. Found: C, 59.48; H, 5.36; N, 5.90.

Example 198

2-(4-Fluorophenyl)-4-(2-methylpropylthiomethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 197 substituting 2-methyl-1-propanethiol in place of 2-methyl-2-propanethiol (yield: 66 mg, 70%). mp 45-60 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (d, J=6.6 Hz, 6H), 1.67-1.82 (m, 1H), 2.62 (d, J=6.6 Hz, 2H), 3.15 (s, 3H), 3.61 (s, 2H), 7.19 (dd, J=8.2, 8.2 Hz, 2H), 7.62-7.71 (m, 2H), 7.75 (d, J=8.4 Hz, 2H), 7.79 (s, 1H), 8.13 (d, J=8.4 Hz, 2H). MS (APCI+) m/z 447 $(M+H)^+$. Anal. calc. for $C_{22}H_{23}FN_2O_3S_2$: C, 59.17, H, 5.19; N, 6.27. Found: C, 59.35; H, 5.25; N, 6.05.

Example 199

2-(4-Fluorophenyl)-4-(2-propoxy)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone

The title compound was prepared by the following sequence of reactions. Mucobromic acid and 4-fluorophenylhydrazine hydrochloride were reacted to provide 2-(4-fluorophenyl)-4,5-dibromo-3(2H)-pyridazinone following the procedure in Example 194A.

The dibromo intermediate was reacted according to the procedure described in Example 194B, substituting isopropanol in place of methanol, to selectively react at the 4-position and provide 2-(4-fluorophenyl)-4-(2-propoxy)-5-bromo-3(2H)-pyridazinone.

The 5-bromo-compound was coupled to 4-(methylthio)phenylboronic acid according to the method of Example 6 to provide the title compound (yield: 435 mg, 53.9%). mp 135-137 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (d, J=6 Hz, 6H), 2.55 (s, 3H), 5.26 (sept, J=6 Hz, 1H), 7.17 (t, J=9 Hz, 2H), 7.34 (d, J=9 Hz, 2H), 7.57 (d, J=9 Hz, 2H), 7.58-7.66 (m, 2H), 7.95 (s, 1H). MS (DCI/NH_3) m/z 371 $(M+H)^+$.

Example 200

2-(4-Fluorophenyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The methyl sulfide compound prepared in Example 199 was oxidized according to the method of Example 10 to provide the title compound (yield: 240 mg, 92%). mp 160-162 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.30 (d, J=6 Hz, 6H), 3.41 (s, 3H), 5.41 (m, 1H), 7.48 (t, J=9 Hz, 2H), 7.77 (dd, J=9 Hz, 6 Hz, 2H), 8.05 (d, J=9 Hz, 2H), 8.19 (d, J=9 Hz, 2H), 8.31 (s, 1H). MS (DCI/NH_3) m/z 403 $(M+H)^+$, 420 $(M+NH_4)^+$. Anal. calc. for $C_{20}H_{19}FN_2O_4S$: C, 59.70; H, 4.73; N, 6.97. Found: C, 59.40; H, 4.86; N, 6.69.

Example 201

2-(3-Chlorophenyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

2-(3-Chlorophenyl)-4-(2-propoxy)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone was prepared according to the method of Example 199 , substituting 3-chlorophenylhydrazine hydrochloride in place of 4-fluorophenylhydrazine hydrochloride, in the first step. The resulting methyl sulfide was oxidized according to the method of Example 10 to provide the title compound (yield: 260 mg, 80%). mp 134-136 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (d, J=6 Hz, 6H), 3.13 (s, 3H), 5 48 (sept, J=6 Hz, 1H), 7.37-7.48 (m, 2H), 7.59 (dt, J=7 Hz, 1.5 Hz, 1H), 7.70 (br s, 1H), 7.84 (d, J=9 Hz, 2H), 7.93 (s, 1H), 8.06 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 419 $(M+H)^+$, 436 $(M+NH_4)^+$. Anal. calc. for $C_{20}H_{19}ClN_2O_4S$. C, 57.42; H, 4.55; N, 6.70. Found. C, 57.08; H, 4.59; N, 6.44.

Example 202

2-(3-Fluorophenyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The methyl sulfide intermediate was prepared according to the method of Example 199 , substituting 3-fluorophenylhydrazine hydrochloride in place of 4-fluorophenylhydrazine hydrochloride in the first step. The resulting methyl sulfide compound was oxidized according to the method of Example 10 to provide the title compound (yield: 290 mg, 72%). mp 110-112 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (d,

J=6 Hz, 6H), 3.11 (s, 3H), 5.47 (sept, J=6 Hz, 1H), 7.09-7.18 (m, 1H), 7.41-7.52 (m, 3H), 7.83 (d, J=9 Hz, 2H), 7.93 (s, 1H), 8.08 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 403 $(M+H)^+$, 447 $(M+NH_4)^+$. Anal. calc. for $C_{20}H_{19}FN_2O_4S$: C, 59 70; H, 4.73; N, 6.97. Found: C, 59.54; H, 4.87, N, 6.70.

Example 203

2-(3-Bromophenyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The methyl sulfide intermediate was prepared according to the method of Example 199 , substituting 3-bromophenylhydrazine hydrochloride in place of 4-fluorophenylhydrazine hydrochloride. The resulting methyl sulfide compound was oxidized according to the method of Example 10 to provide the title compound (yield: 75 mg, 77.6%). mp 130-132 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (d, J=6 Hz, 6H), 3.15 (s, 3H), 5.48 (sept, J=6 Hz, 1H), 7.38 (t, J=9 Hz, 1H), 7.55 (br d, J=7 Hz, 1H), 7.65 (br d, J=7 Hz, 1H), 7.79-7.87 (m, 1H). 7.83 (d, J=9 Hz, 2H), 8.13 (s, 1H), 8.06 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 465 $(M+H)^+$, 480 $(M+NH_4)^+$. Anal. calc. for $C_{20}H_{19}BrN_2O_4S$: C, 51 84; H, 4.10; N, 6.05. Found: C, 51.95; H, 4.18; N, 5.74.

Example 204

2-(2,5-Difluorophenyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

2-(2,5-Difluorophenyl)-4-(2-propoxy)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone was prepared according to the method of Example 199, substituting 2,5-difluorophenylhydrazine hydrochloride in place of 4-fluorophenylhydrazine hydrochloride.

The resulting methyl sulfide compound was oxidized according to the method of Example 10 to provide the title compound (yield: 390 mg, 90%). mp 161-164 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (d, J=6 Hz, 6H), 3.12 (s, 3H), 5.55 (sept, J=6 Hz, 1H), 7.12-7.29 (m, 3H), 7.82 (d, J=9 Hz, 2H), 7.92 (s, 1H), 8.07 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 421 $(M+H)^+$, 438 $(M+NH_4)^+$. Anal. calc. for $C_{20}H_{18}F_2N_2O_4S.0.5\ H_2O$: C, 55.94; H, 4 31; N, 6.53 Found: C, 55.86; H, 4.19; N, 6.38.

Example 205

2-(3-Chloro-4-fluorophenyl)-4-(2-methylpropoxy)-5-[3-fluoro-4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared by the following sequence of reactions. Mucobromic acid and 3-chloro-4-fluorophenylhydrazine hydrochloride were reacted to provide 2-(3-chloro-4-fluorophenyl)-4,5-dibromo-3(2H)-pyridazinone according to the method of Example 194A.

The intermediate was selectively reacted at the 4-position with isobutanol and base to provide 2-(4-fluorophenyl)-4-[1-(2-methylpropoxy)]-5-bromo-3(2H)-pyridazinone according to the method of Example 194B

The 5-bromo-compound was coupled to 3-fluoro-4-(methylthio)phenylboronic acid prepared in Example 194C according to the method of Example 6 to produce the intermediate methyl sulfide. The sulfide compound was oxidized to the title methyl sulfone according to the method of Example 10 (yield: 810 mg, 83.8%). mp 142-144 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (d, J=6 Hz, 6H), 1.95 (sept, J=6 Hz, 1H), 3.30 (s, 3H), 4.37 (d, J=6 Hz, 2H), 7.26 (t, J=9 Hz, 1H), 7.52-7.61 (m, 3H), 7.75 (dd, J=9 Hz, 3 Hz, 1H), 7.89 (s, 1H), 8.10 (t, J=9 Hz, 1H). MS (DCI/NH_3) m/z 469 $(M+H)^+$, 486 $(M+NH_4)^+$.

Example 206

2-(3,4-Difluorophenyl)-4-(4-fluorophenyl)-5-[3-methyl-4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

Example 206A

2-Methylthioanisole

A solution of 2-bromothioanisole (10.53 g, 52 mmol) in tetrahydrofuran (173 mL) was prepared and cooled to -78 °C. n-BuLi (21.8 mL, 54.5 mmol, 2.5 M solution in hexanes) was slowly added along the interior wall of the reaction vessel. The resultant light yellow solution was stirred for 30 minutes before methyl iodide (8.10 g, 57.1 mmol)

diluted with tetrahydrofuran (6 mL) was slowly added along the interior wall of the reaction vessel. The mixture was stirred for another 30 minutes at -78 °C. The cooling bath was removed, and the mixture stirred for 1 hour. The solution was cooled to 0 °C and a saturated aqueous NH_4Cl solution added. The resultant solution was extracted several times with ethyl acetate, and the combined acetate layers washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed (flash silica gel, ethyl acetate/hexanes 1:19) to provide the product (yield: 6.74 g, 94%). ^1H NMR (300 MHz, $CDCl_3$) δ 2.34 (s, 3H), 2.46 (s, 3H), 7.02-7.09 (m, 1H), 7.12-7.22 (m, 3H).

Example 206B

4-Bromo-2-methylthioanisole.

To a 0 °C solution of 2-methylthioanisole (0.50 g, 3.57 mmol) in methylene chloride (40 mL) was added powdered Fe (20 mg, 0.36 mmol) followed by dropwise addition of bromine (0.58 g, 3.54 mmol). After 30 minutes, the starting material had been consumed (thin layer chromatography, hexanes). The excess bromine was quenched by adding a solution of $NaHSO_3$ and stirring for several minutes. The methylene chloride layer was separated, and the aqueous phase extracted with additional methylene chloride. The combined methylene chloride solution was dried over $MgSO_4$, filtered, and concentrated in vacuo. The resultant oil was chromatographed (flash silica gel, ethyl acetate/hexanes 1:49) to provide the product (yield: 0.74 g, 96%). ^1H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 3H), 2.45 (s, 3H), 7.00 (d, J=8.4 Hz, 1H), 7.27-7.33 (m, 2H).

Example 206C

3-Methyl-4-(methylthio)benzeneboronic acid.

3-Methyl-4-(methylthio)benzeneboronic acid was prepared according to the method of Example 1, substituting 4-bromo-2-(methylthio)anisole in place of 4-bromothioanisole (yield: 5.3 g, 67%). mp 208-210 . ^1H NMR 2.28 (s, 3H), 2.46 (s, 3H), 7.20 (d, J=8.4 Hz, 1H), 7.62 (s, 1H), 7.70 (d, J=8.4 Hz, 1H)

Example 206D

2-(3,4-Difluorophenyl)-4,5-dibromo-3(2H)-pyridazinone.

The title compound was prepared according to the method of Example 194A, substituting 3,4-difluorophenyl hydrazine·HCl in place of 4-fluorophenyl hydrazine·HCl (yield: 39 g, 78%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.45 (m, 1H), 7.61 (m, 1H), 7.75 (m, 1H), 8.30 (s, 1H). MS (DCI/NH_3) m/z 382 $(M+NH_4)^+$.

Example 206E

2-(3,4-Difluorophenyl)-4-methoxy-5-bromo-3(2H)-pyridazinone.

The title compound was prepared according to the method of Example 194B, substituting 2-(3,4-difluorophenyl)-4,5-dibromo-3(2H)-pyridazinone in place of 2-(4-fluorophenyl)-4,5-dibromo-3(2H)-pyridazinone (yield: 15 mg, 88%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.14 (s, 3H), 7.45 (m, 1H), 7.60 (m, 1H), 7.74 (m, 1H), 8.24 (s, 1H). MS (DCI/NH_3) m/z 317 $(M+H)^+$ and m/z 334 $(M+NH_4)^+$.

Example 206F

2-(3,4-Difluorophenyl)-4-methoxy-5-[3-methyl-4-(methylthio)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 6 starting with 2-(3,4-difluorophenyl)-4-methoxy-5-bromo-3(2H)-pyridazinone in place of 2-benzyl-4-bromo-5-methoxy-3(2H)-pyridazinone and substituting 3-methyl-4-(methylthio)benzeneboronic acid in place of 4-fluorobenzeneboronic acid (yield: 2.0 g, 85%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.53 (s, 3H), 4.11 (s, 3H), 7.22-7.32 (m, 2H), 7.34 (s, 1H), 7.42-7.50 (m, 2H), 7.55-7.64 (m, 1H), 7.92 (s, 1H). MS (APCI+) m/z 375 $(M+H)^+$.

Example 206G