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[54] Title: DERIVATIVES OF N-PHENYLPYRAZOLES

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[57] (see abstract next page)

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# SPECIFICATION

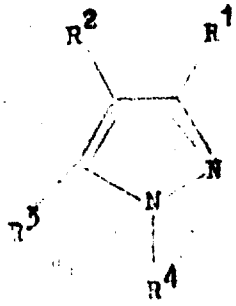
TO ALL WHOM IT MAY CONCERN:

BE IT KNOWN THAT WE, IAN GEORGE BUNTAIN, LESLIE ROY HATTON, DAVID WILLIAM HAWKINS, CHRISTOPHER JOHN PEARSON AND DAVID ALAN ROBERTS, ALL BRITISH SUBJECTS, C/O HAY & BAKER LIMITED, DAGENHAM, ESSEX RM10 7XS, ENGLAND, HAVE INVENTED A CERTAIN NEW AND USEFUL IMPROVEMENT IN "DERIVATIVES OF N-PHENYLPYRAZOLES" OF WHICH THE FOLLOWING IS A SPECIFICATION.

"DERIVATIVES OF N-PHENYLPYRAZOLES"

## ABSTRACT OF THE DISCLOSURE

N-Phenylpyrazole derivatives of the formula:



(I)

wherein $R^1$ represents cyano, nitro, halogen, acetyl, or formyl;

$R^2$ represents $R^5SO_2$, $R^5SO$ or $R^5S$ in which $R^5$ is optionally halogen substituted, alkyl, alkenyl or alkynyl;

$R^3$ represents a hydrogen atom or a group $NR^6R^7$ wherein $R^6$ and $R^7$ each represent hydrogen, alkyl, alkenylalkyl, alkynylalkyl, formyl, optionally halogen substituted alkanoyl, optionally halogen substituted alkoxycarbonyl,

or alkoxymethyleneamino, halogen, or $R^6$ and $R^7$ together form a cyclic imide and $R^4$ represents a substituted phenyl group possess arthropodicidal, plant nematocidal, anthelmintic and anti-protozoal properties; their preparation, compositions containing them and their use are described.

## DERIVATIVES OF N-PHENYLPYRAZOLES

This invention relates to N-phenylpyrazole derivatives, to compositions containing them and to the use of N-phenylpyrazole derivatives against arthropod, plant nemotode, helminth and protozoan pests.

The present invention provides N-phenylpyrazole derivatives of the general formula (I) depicted hereinafter wherein $R^1$ represents a cyano or nitro group, a halogen, i.e. fluorine, chlorine, bromine or iodine, atom, or an acetyl or formyl group; $R^2$

represents a group $R^5SO_2$, $R^5SO$, or $R^5S$ in which $R^5$ represents a straight or branched chain alkyl, alkenyl or alkynyl (preferably 1-(alkynyl)alkyl and more preferably alk-2-ynyl) group containing up to 4 carbon atoms which may be unsubstituted or substituted by one or more halogen atoms which may be the same or different; $R^3$ represents a hydrogen atom, or an amino group $-NR^6R^7$ wherein $R^6$ and $R^7$, which may be the same or different, each represent a hydrogen atom or a straight or brnached chain alkyl, alkenylalkyl or alkynyllkyl group containing up to 5 carbon atoms, a formyl group, a straight or branched chain alkanoyl group (which contains from 2 to 5 carbon atoms and which may be optionally substituted by one or more halogen atoms) or $R^6$ and $R^7$ together with the nitrogen atom to which they are attached form a 5 to 6 membered cyclic imide, or represents a straight or branched-chain alkoxycarbonyl group 9which contains from 2 to 5 carbon atoms and is unsubstituted or substituted by one or more halogen atoms), or

$R^3$ represents a straight or branched-chain alkoxymethyleneamino group containing fromm 2 to 5 carbon atoms which may be unsubstituted or substituted on methylene by a straight or branched-chain alkyl group containing from 1to 4 carbon atoms, or represents a halogen, i.e. fluorine, chlorine, bromine or iodine, atom; and $R^4$ represents a phenyl group substituted in the 2-position by a fluorine, chlorine, bromine or iodine atom; in the 4-position by a straight or branched chain alkyl or alkoxy group containing from 1 to 4 carbon atoms which may be unsubstituted or substituted by one or more halogen atoms which may be the same or different (the trifluoromethyl and trifluoromethoxy groups are preferred), or a chlorine or bromine atom; and optionally in the 6-position by a fluorine, chlorine, bromine or iodine atom, with the exclusion of the compound wherein $R^1$ represents oxano, $R^2$ represents methanesulphenyl, $R^3$ represents amino and $R^4$ represents 2,6-dichloro-4-trifluoromethylphenyl, which have valuable

trifluoromethylthio or trifluoromethylsulphinyl group, $R^3$ represents the hydrogen atom, an amino or methylamino group and $R^1$ represents a halogen atom or preferably the cyano or nitro group.

Compounds of general formula (I) wherein $R^4$ contains the trifluoromethyl or trifluoromethoxy group, and $R^2$ represents an optionally halogenated alkylsulphonyl/sulphinyl/thio group containing from 1 to 4 carbon atoms are preferred. Trifluoromethylthio, trifluoromethylsulphinyl and trifluoromethanesulphonyl are especially preferred for $R^2$.

Preferred compounds of general formula (I) are those with phenyl ($R^4$) substitution which is 2,4,6-trichloro, 2,6-dichloro-4-difluoromethoxy, 2-chloro-4-trifluoromethyl, 2-bromo-6-chloro-4-trifluoromethyl, 2,6-dibromo-4-trifluoromethyl or 2-bromo-4-trifluoromethyl.

Compounds of general formula (I) with 2,6-

dichloro-4-trifluoromethytl or 2,6-dichloro-4-trifluoromethoxy substitution of the phenyl group ($R^4$) are especially preferred.

Compounds of general formula (I) which are of particular interest are:

1. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole.

2. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-trifluoromethylthiopyrazole.

3. 5-Amino-3-cyano-1-(2,6-dichloro-4-difluoromethoxyphenyl)-4-trifluoromethylthiopyrazole.

4. 5-Amino-1-(2-chloro-4-trifluoromethylphenyl)-3-cyano-4-trifluoromethylthiopyrazole.

5. 5-Amino-3-cyano-1-(2,4,6-trichlorophenyl)-4-trifluoromethylthiopyrazole.

6. 5-Amino-3-cyano-1-(2,6-dibromo-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole.

7. 5-Amino-1-(2-bromo-4-trifluoromethylphenyl)-3-cyano-4-

trifluoromethylthiopyrazole.

8. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-difluoromethylthiopyrazole.

9. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-heptafluoropropylthiopyrazole.

10. 5-Amino-1-(2-bromo-6-chloro-4-trifluoromethylphenyl)-3-cyano-4-trifluoromethylthiopyrazole.

11. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trichloromethylthiopyrazole.

12. 5-Amino-3-chloro-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole.

13. 5-Amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole.

14. 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-fluoro-4-trifluoromethylthiopyrazole.

15. 5-Amino-4-chlorodifluoromethylthio-3-cyano-1-(2,6-dichloro-4-

trifluoromethylphenyl)pyrazole.

16. 5-Chloro-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole.

17. 5-Amino-3-chloro-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole.

18. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethyleneamino-4-trifluoromethylthiopyrazole.

19. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxyethylideneamino-4-trifluoromethylthiopyrazole.

20. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethyleneamino-4-methanesulphonylpyrazole.

21. 5-Acetamido-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole.

22. 3-Cyano-1-(2,6-dichloro-4-trilfuoromethylphenyl)-5-bis(propionyl)amino-4-trifluoromethylthiopyrazole.

23. 3-Cyano-1-(2,6-dichloro-4-trifluoromethyl-

phenyl)-5-propionamido-4-trifluoromethylthiopyrazole.

24. 5-Acetamido-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole.

25. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthio-5-trimethylacetamidopyrazole.

26. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-bis(methoxycarbonyl)amino-4-trifluoromethylthiopyrazole.

27. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-bis(ethoxycarbonyl)amino-4-trifluoromethylthiopyrazole.

28. 5-Chloroacetamido-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole.

29. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-bis(ethoxycarbonyl)amino-4-methanesulphonylpyrazole.

30. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonyl-5-

trimethylacetamidopyrazole.

31. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-dimethylamino-4-trifluoromethylthiopyrazole.

32. 3-Vyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-isopropylamino-4-trifluoromethylthiopyrazole.

33. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-propylamino-4-trifluoromethylthiopyrazole.

34. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-dipropylamino-4-trifluoromethylthiopyrazole.

35. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-bis(propargyl)amino-4-trifluoromethylthiopyrazole.

36. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methylamino-4-methanesulphonylpyrazole.

37. 5-Bromo-3-cyano-1-(2,6-dichloro-4-trifluoroethylphenyl)-4-trifluoromethanesulphonylpyrazole.

38. 5-Bromo-3-cyano-1-(2,6-dichloro-4-

trifluoromethylphenyl)-4-trifluoromethylthiopyrazole.

39. 5-Bromo-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole.

40. 5-Amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole.

41. 3-Bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole.

42. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole.

43. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole.

44. 3-Cyano-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-trifluoromethylthiopyrazole.

45. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole.

46. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-iodo-4-trifluoromethylthiopyrazole.

47. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-iodo-4-trifluoromethanesulphonyl-

pyrazole.

48. 5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-iodo-4-methanesulphonylpyrazole.

49. 1-(2,6-Dichloro-4-trifluoromethylphenyl)-3-iodo-4-methanesulphonylpyrazole.

50. 1-(2,6-dichloro-4-trifluoromethylphenyl)-3-iodo-4-trifluoromethylthiopyrazole.

51. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole.

52. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphinylpyrazole.

53. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-trifluoromethanesulphonylpyrazole.

54. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-trifluoromethylsulphonylpyrazole.

55. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphonylpyrazole.

56. 5-Amino-3-cyano-1-92,6-dichloro-4-

trifluoromethylphenyl)-4-(1-methylprop-2-ynylsulphinyl)pyrazole.

57. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylsulphinylpyrazole.

58. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-isopropylsulphinylpyrazole.

59. 5-Amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphinylpyrazole.

60. 5-Amino-4-tert-butanesulphonyl-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole.

61. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-propylamino-4-trifluoromethylsulphonyl)-5-propylamino-4-trifluoromethylsulphonylpyrazole.

62. 5-Acetamido-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole.

63. 1-(2,6-Dichloro-4-trifluoromethylphenyl)-4-methanesulphonyl-3-nitropyrazole.

64. 5-Amino-1-(2,6-dichloro-4-

trifluoromethylphenyl)-4-methanesulphonyl-3-nitropyrazole.

65. 1-(2,6-Dichloro-4-trifluoromethylphenyl)-3-nitro-4-trifluoromethylsulphinylpyrazole.

66. 5-Amino-1-(2-bromo-6-chloro-4-trifluoromethylphenyl)-3-cyano-4-methanesulphonylpyrazole.

67. 5-Amino-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-3-cyano-4-methanesulphonylpyrazole.

68. 3-Acetyl-5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole.

69. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylthiopyrazole.

70. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-ethylthiopyrazole.

71. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-propylthiopyrazole.

72. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-isopropylthiopyrazole.

73 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-(2-

methylpropylthio)pyrazole.

74. 5-Amino-3-cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-4-(1-methylpropylthio)pyrazole.

75. 4-Allylthio-5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole.

76. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-(prop-2-ynylthio)pyrazole.

77. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-(1-methylprop-2-ynylthio)pyrazole.

78. 5-Amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylthiopyrazole.

79. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-tert-butylthiopyrazole.

80. 5-Amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylsulphinylpyrazole.

81. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-ethanesulphonylpyrazole.

82. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methylamino-4-trifluoromethylthiopyrazole.

83. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-(NØethoxycarbonyl-N-methyl)amino-4-trifluoromethylthiopyrazole.

84. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-trifluoroacetamido-4-trifluoromethylthiopyrazole.

85. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-(ethoxycarbonylamino)-4-trifluoromethylthiopyrazole.

86. 3-Acetyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole.

87. 1-(2,6-Dichloro-4-trifluoromethylphenyl)-3-formyl-4-trifluoromethylthiopyrazole.

88. 5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-formyl-4-trifluoromethylthiopyrazole.

89. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-fluoro-4-trifluoromethanesulphonylpyrazole.

90. 5-Amino-3-cyano-4-

dichlorofluoromethylthio-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole.

91 5-Amino-3-chloro-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole.

92. 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-pentafluoroethylthiopyrazole.

93. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-dimethylamino-4-trifluoromethylsulphinylpyrazole.

94. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-iodo-4-trifluoromethylsulphinylpyrazole.

95. 5-Bromo-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphinylpyrazole.

96. 5-Acetamido-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphinylpyrazole.

97 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-bis(ethoxycarbonyl)amino-4-trifluoromethanesulphonylpyrazole.

98. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxycarbonylamino-4-trifluoromethanesulphonylpyrazole.

99. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethyleneamino-4-trifluoromethanesulphonylpyrazole.

100. 5-Amino-4-(2-chloro-1,1,2-trifluoroethylthio)-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-pyrazol.

101. 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-dimethylamino-4-trifluoromethanesulphonylpyrazole.

The numbers 1 to 101 are assigned to the above compounds for identification and reference hereinafter.

According to a feature of the present invention, there is provided a method for the control of arthopod, plant nematode, helminth or portozoan pests at a locus which comprises the treatment of the locus (e.g. by application or administration) with an effective amount of a compound of general formula (I), wherein the various symbols are as hereinbefore defined. The compounds of general formula (I) may, in particular, be used in the field of veterinary medicine and livestock husbandry and in the maintenance of public health against arthopods, helminths or protozoa which are parasitic internally or externally upon vertebrates, particularly warm-blooded vertebrates, for example man and domestic animals, e.g. cattle, sheep, goats, equines, swine, poultry, dogs, cats and fishes, for example Acarina, including ticks (e.g. Ixodes spp., Boophilus spp. e.g. Boophilus microplus, Amblymma spp., Hyalomma spp., Rhipicephalus spp.e.g. Rhipicephalus appendiculatus, Haemaphysalis spp., Dermacentor spp., Ornithodorus spp. (e.g. Ornithodorus

mouhota and mites (e.g. Damalinia spp., Dermahyssus gallinae, Sarcoptes spp. e.g. Sarcoptes scabiei, Psoroptes spp., Choriontes spp., Demodex spp., Eutrombicula spp.); Diptera (e.g. Aedes spp., Anopheles spp., Musca spp., Hypoderma spp., Gasterophilus spp., Simulium spp.); Hemiptera (e.g. Triatoma spp.); Phthiraptera (e.g. Damalinia spp., Linognathus spp.); Siphonaptera (e.g. Ctenocephalides spp.); Dictyoptera (e.g. Periplaneta spp., Blatella spp.); Hymenoptera (e.g. Monomorium pharaonis); for example against infections of the gastro-intestinal tract caused by parasitic nematode worms, for example members of the family Trichostrongylidae, Nematodirus battus, Trichonella spiralis, Haemonchus contortus, Trichostrongylus colubriformis, Haemonchus bedni, Ostertagia circumcincta, Trichostrongylus axei, Cooperiasp and Hymenolepis nana; to the control and treatment of protozoal diseases caused by, for example, Eimeria spp. e.g. Eimeria tenella, Eimeria acervulina, Eimeria brunetti, Eimeria maxima

and Eimeria necatrix, Trypanosoma cruzi, Leishmania spp., Plasmodium spp., Babesia spp., Trichomonadidae spp., Histomonas spp., Giardia spp., Toxoplasma spp., Entamoeba histolytica and Theileria spp., in the protection of stored products, for example cereals, including grain and flour, groundnuts, animal feedstuffs, timber and household goods, e.g. carpets and textiles, against attack by arthropods, more especially beetles, including weevils, moths and mites, for example Ephestia spp. (flour moths), Anthrenus spp. (carpet beetles), Tribolium spp. (flour beetles), Sitophilus spp. (grain weevils) and Acarus spp. (mites), in the control of cockroaches, ants and termites and similar arthropod pests in infested domestic and industrial premises and in the control of mosquito larvae in waterways, wells, reservoirs or other running or standing water; for the treatment of foundations, structure and soil in the prevention of the attack on buildings by termites, for example, Reticulitermes spp., Heterotermes spp., Coptotermes spp.; in

agriculture, against adults, larvae and eggs of Lepidoptera (butterflies and moths) e.g. Heliothis spp. such as Heliothis virescens (tobacco budworm), Heliothis armigera and Heliothis zea, Spodoptera spp. such as S. exempta, S.littoralis (Egyptian cotton worm), S.eridania (southern army worm), Mamestra configurata (bertha army worm); Earias spp. e.g. E. insulana (Egyptian bollworm), Pectinophora spp. e.g. Pectinophora gossypiella (pink bollworm), Ostrinia spp. such as O. nubilalis (European cornborer), Trichoplusia ni (cabbage looper), Plaris spp. (cabbage worms), Laphygma spp. (army worms), Agrotis and Amathes spp. (cutworms), Wiseana spp. (porina moth), Chilo spp. (rice stem borer), Tryporyza spp. and Diatraea spp. (sugar cane borers and rice borers), Sparganothis phillerians (grape berry moth), Cydia pomonella (codling moth), Archips spp. (fruit tree tortrix moths), Plutella xylostella (diamond back moth); against adult and larvae of coleoptera (beetles) e.g. Hypothenemus hampei (coffee berry borer),

Hylesinus spp. (bark beetles), Anthonomus grandis (cotton boll weevil), Acalymma spp. (cucumber beetles), Lema spp., Psylliodes spp., Leptinotarsa decemlineata (Colorado potato beetle), Diabrotica spp. (corn rootworms), Gonocephalum spp. (false wire worms), Agriotes spp. (wireworms), Dermolepida and Heteronychus spp. (white grubs), Phaedon cochleariae (mustard beetle), Lissorhoptrus oryzophilus (rice water weevil), Meligethes spp. (pollen beetles), Ceutorhynchus spp., Rhynchophorus and Cosmopolites spp. (root weevils); against Hemiptera e.g. Psylla spp., Bemisia spp., Trialeurodes spp., Aphis spp., Myzus spp., Megoura viciae, Phylloxera spp., Adelges spp., Phorodon humuli (hop damson aphid), Aeneolamia spp., Nephotettix spp. (rice leaf hoppers), Empoasca spp., Nilaparvata spp., Perkinsiella spp., Pyrilla spp., Aonidiella spp. (red scales), Coccus spp., Pseudococcus spp., Helopeltis spp. (mosquito bugs), Lygus spp., Dysdercus spp., Oxycarenus spp., Nezara spp.; Hymenoptera e.g. Athalia spp. and Cephus spp.

(saw flies), Atta spp. (leaf cutting ants); Diptera e.g. Hylemyia spp. (root flies), Atherigona spp. and Chlorops spp. (shoot flies), Cytomyza spp. (leaf miners), Ceratitis spp. (fruit flies); Thysanoptera such as Thrips tabaci; Orthoptera such as Locusta and Schistocerca spp. (locusts) and crickets e.g. Gryllus spp. and Acheta spp.; Collembola e.g. Sminthurus spp. and Onychiurus spp. (springtails), Isoptera e.g. Odontotermes spp. (termites), Dermaptera e.g. Forficula spp. (earwigs) and also other arthropods of agricultural significance such as Acari (mites) e.g. Tetranychus spp., Panonychus spp. and Bryobia spp. (spider mites), Eriophyes spp. (gall mites), Polyphagotarsonemus spp.; Blaniulus spp. (millipedes), Scutigerella spp. (symphilids), Oniscus spp. (woodlice) and Triops spp. (crustacea); nematodes which attack plants and trees of importance to agriculture, forestry and horticulture either directly or by spreading bacterial, viral, mycoplasma or fungal diseases of the plants, root-knot

nematodes such as Meloidogyne spp. (e.g. M. incognita); cyst nematodes such as Globodera spp. (e.g. G. rostochiensis); Heterodera spp. (e.g. H. avenae); Radopholus spp. (e.g. R. similis); lesion nematodes such as Pratylenchus spp. (e.g. P.pratensis); Belonolaimus spp. (e.g. B. gracilis); Tylenchulus spp. (e.g. T. semipenetrans); Rotylenchulus spp. (e.g. R. reniformis); Rotylenchus spp. (e.g. R. robustus); Helicotylenchus spp. (e.g. H. multicinctus); Hemicycliophora spp. (e.g. H. gracilis); Criconemoides spp. (e.g. C. similis); Trichodorus spp. (e.g. T. primitivus); dagger nematodes such as Xiphinema spp. (e.g. X. diversicaudatum); Longidorus spp. (e.g. L. elongatus); Hoplolaimus spp. (e.g. H. coronatus); Aphelenchoides spp. (e.g. A. ritzema-bosi, A. besseyi); stem and bulb eelworms such as Ditylenchus spp. (e.g. D. dipsaci).

The invention also provides a method for the control of arthropod or nematode pests of plants which comprises the application to the

plants or to the medium in which they grow of an effective amount of a compound of general formula (I).

For the conteol of arthropods and nematodes, the active compound is genrally applied to the locus in which arthropod or nematode infestation is to be controlled at a rate of about 0.1 kg to about 25 kg of active compound per hectare of locus treated. Under ideal conditions, depending on the pest to be controlled, the lower rate may offer adequate protection. On the other hand, adverse weather conditions, resistance of the pest and other factors may require that the active ingredient be used in higher proportions. In foliar application, a rate of 1 g to 1000 g/ha may be used.

When the pest is soil-borne, the formulation containing the active compound is distributed evenly over the area to be treated in any convenient manner. Application may be

made, if desired, to the field or crop-growing area generally or in close proximity to the seed or plant to be protected from attack. The active component can be washed into the soil by spraying with water over the area or can be left to the natural action or rainfall. During or after application, the formulation can, if desired, be distributed mechanically in the soil, for example by ploughing or disking. Application can be prior to planting, at planting, after planting but before sprouting has taken place or after sprouting.

The compounds of general formula (I) may be applied in solid or liquid compositions to the soil principally to control those nematodes dwelling therein but also to the foliage principally to control those nematodes attacking the aerial parts of the plants (e.g. Aphelenchoidan spp. and Ditylenchus spp. listed above).

The compounds of general formula (I) are of

value in controlling pests which feed on parts of the plant remote from the point of application, e.g. leaf feeding insects are killed by the subject compounds applied to roots.

In addition the compounds may reduce attacks on the plant by means of antifeeding or repellent effects.

The compounds of general formula (I) are of particular value in the protection of field, forage, plantation, glasshouse, orchard and vineyard crops, of ornamentals and of plantation and forest trees, for example, cereals (such as maize, wheat, rice, sorghum), cotton, tobacco, vegetables and salads (such as beans, cole crops, cucurbits, lettuce, onions, tomatoes and peppers), field crops (such as potato, sugar beet, ground nuts, soyabea, oil seed rape), sugar cane, grassland and forage (such as maize, sorghum, lucerne), plantations (such as of tea, coffee, cocoa, bean, oil

plam, coconut, rubber, spices), orchards and groves (such as of stone and pip fruit, citrusm kiwifruit, avocado, mango, olives and walnuts), vineyards, ornamental plants, flowers and shrubs under glass and in gardens and parks, forest trees (both deciduous and evergreen) in forests, plantations and nurseries.

They are also valuable in the protection of timber (standing, felled, converted, stored or structural) from attack by sawflies (e.g. Urocerus) or beetles (e.g. scolytids, platypodids, lyctids, bostrychids, cerambycids, anobiids), or termites, for example, Reticulitermes spp., Heterotermes spp., Coptotermes spp.

They have applications in the protection of stored products such as grains, fruits, nuts, spices and tobacco, whether whole, milled or compounded into products, from moth, beetle and mite attack. Also protected are stored animal products such as skins, hair, wool and feathers

in natural or converted form (e.g. an carpets or textiles) from moth and beetle attack, also stored meat and fish from beetle, mite and fly attack.

The compounds of general formula (I) are of particular value in the control of arthropods, helminths or protozoa which are injurious to, or spread or act as vectors of diseases in man and domestic animals, for example those hereinbefore mentioned, and more especially in the control of ticks, mites, lice, fleas, midges and biting, nuisance and pyiagic flies. The compounds of general formula (I) are particularly useful in controlling arthropods, helminths or protozoa which are present inside domestic host animals or which feed in or on the skin or suck the blood of the animal, for which purpose they may be administered orally, parenterally, percutaneously or topically.

Coccidiosis, a disease caused by infections by protozoan parasites of the genus Eimeria, is

an important potential cause of economic loss in domestic animals and birds, particularly those raised or kept under intensive conditions. For example, cattle, sheep, pigs and rabbits may be affected, but the disease is especially important in poultry, in particular chickens.

The poultry disease is generally spread by the birds picking up the infectious organism in droppings on contaminated litter or ground or by way of food or drinking water. The disease is manifested by hemorrhage, accumulation of blood in the ceca, passage of blood to the droppings, weakness and digestive disturbances. The disease often terminates in the death of the animal but the fowl which survive severe infections have had their market value substantially reduced as a result of the infection.

Administration of a small amount of a compound of general formula (I) preferably by

combination with poultry feed is effective in preventing or greatly reducing the incidence of coccidiosis. The compounds are effective against both the cecal form (caused by E. tenella) and the intestinal forms (principally caused by E. acervulina, E. brunetti, E. maxima and E. necatrix).

The compounds of general formula (I) also exert an inhibitory effect on the oocysts by greatly reducing the number and/or the sporulation of those produced.

The compositions hereinafter described for [illegible] topical application to man and animals and in the protection of stored products, household goods, property and areas of the general environment may in general, alternatively be employed for application to growing crops and crop growing soil and as a seed dressing.

Suitable means of applying the compounds of general formula (I) include:

to persons or animals infested by or exposed to infestation by arthropods, helminths or protozoa, by parenteral, oral or topical application of compositions in which the active ingredient exhibits an immediate and/or prolonged action over a period of time against the arthropods, helminths or protozoa, for example by incorporation in feed or suitable orally-ingestible pharmaceutical formulations, edible baits, salt licks, dietary supplements, pour-on formulations, sprays, baths, dips, showers, jets, ducts, greases, shampoos, creams, wax-smears and livestock self-treatment systems; to the environment in general or to specific locations where pests may lurk, including stored products, timber, household goods, and domestic and industrial premises, as sprays, fogs, dusts, smokes, wax-smears, lacquers, granules and baits, and in trickle-feeds to waterways, wells, reservoirs and other running or standing waters; to domestic

animals in feed to control fly larvae feeding in their faeces: to growing crops as foliar sprays, dusts, granules, fogs and foams, also as suspensions of finely divided and encapsulated compounds of general formula (I); as soil and root treatments by liquid drenches, dusts, granules, smokes and foams, and as seed dressings by liquid slurries and dusts.

The compounds of general formula (I) may be applied to control arthropods, helminths or protozoa in compositions of any type known to the art suitable for internal or external administration to vertebrates or application for the control of arthropods in any premises or indoor or outdoor area, containing as active ingredient at least one compound of general formula (I) in association with one or more compatible diluents or adjuvants appropriate for the intended use. All such compositions may be prepared in any manner known to the art.

Compositions suitable for administration to vertebrates or man include preparations suitable for oral, parenteral, percutaneous, e.g. pour-on, or topical administration.

Compositions for oral administration comprise one or more of the compounds of general formula (I) in association with pharmaceutically acceptable carriers or coatings and include, for example, tablets, pills, capsules, pastes, gels, drenches, medicated feeds, medicated drinking water, medicated dietary supplements, slow-release boluses or other slow-release devices intended to be retained within the gastro-intestinal tract. Any of these may incorporate active ingredient contained within microcapsules or coated with acid-labile or alkali-labile or other pharmaceutically acceptable enteric coatings. Feed premixes and concentrates containing compounds of the present invention for use in preparation of medicated diets, drinking water or other materials for

consumption by animals may also be used.

Compositions for parenteral administration include solutions, emulsions or suspensions in any suitable pharmaceutically acceptable vehicle and solid or semisolid subcutaneous implants or pellets designed to release active ingredient over a protected period and may be prepared and made sterile in any appropriate manner known to the art.

Compositions for percutaneous and topical administration include sprays, dusts, baths, dips, showers, jets, greases, shampoos, creams, wax-smears, or pour-on preparations and devices (e.g. ear tags) attached externally to animals in such a way as to provide local or systemic arthropod control.

Solid or liquid baits suitable for controlling arthropods comprise one or more compounds of general formula (I) and a carrier or diluent which may include a food substance

Compositions in the form of aerosols and aqueous or non-aqueous solutions or dispersions suitable for spraying, fogging and low- or ultra-low volume spraying may also be used.

Suitable solid diluents which may be used in the preparation of compositions suitable for applying the compounds of general formula (I) include aluminium silicate, kieselguhr, corn husks, tricalcium phosphate, powdered cork, absorbent carbon black, magnesium silicate, a clay such as kaolin, bentonite or attapulgite, and water soluble polymers and such solid compositions may, if desired, contain one or more compatible wetting, dispersing, emulsifying or colouring agents which, when solid, may also serve as diluent.

Such solid compositions, which may take the form of dusts, granules or wettable powders, are generally prepared by impregnating the solid diluents with solutions of the compound of general formula (I) in volatile solvents, evaporating the solvents and, if necessary,

grinding the products so as to obtain powders and, if desired granulating or compacting the products so as to obtain granules, pellets or briquettes or by encapsulating finely divided active ingredient in natural or synthetic polymers, e.g. gelatin, synthetic resins and polymides.

The wetting, dispersing and emulsifying agents which may be present, particularly, in wettable powders, may be of the ionic or non-ionic types, for example sulphoricinoleates, quaternary ammonium derivatives or products based upon condensates of ethylene oxide with nonyl- and octyl-phenol, or carboxylic acid esters of anhydrosorbitols which have been rendered soluble by etherification of the free hydroxy groups by condensation with ethylene oxide, or mixtures of these types of agents. Wettable powders may be treated with water immediately before use to give suspensions ready for application.

Liquid compositions for the application of the compounds of general formula (I) may take the form of solutions, suspensions and emulsions of the compounds of general formula (I) optionally encapsulated in natural or synthetic polymers, and may, if desired, incorporated wetting, dispersing or emulsifying agents. These emulsions, suspensions and solutions may be prepared using aqueous, organic or aqueous-organic diluents, for example acetophenone, isophorone, toluene, xylene, mineral, animal or vegetable oils, and water soluble polymers (and mixtures of these diluents), which may contain wetting, dispersing or emulsifying agents of the ionic or non-ionic types or mixtures thereof, for example those of the types described above. When desired, the emulsions containing the compounds of general formula (I) may be used in the form of self-emulsifying concentrates containing the active substance dissolved in the emulsifying agents or in solvents containing emulsifying agents compatible with

the active substance, the simple addition of water to such concentrates producing compositions ready for use.

Compositions containing compounds of general formula (I) which may be applied to control arthropod, plant nematodes, helminth or protozoa pests, may also contain synergists (e.g. piperonyl butoxide or sesamex), stabilizing substances, other insecticides, acaricides, plant nematocides, anthelmintics or anticoccidials, fungicides (agricultural or veterinary as apropriate e.g. benomyl, iprodione), bactericides, arthropod or vertebrate attractants or repellents or pheromones, deodorants, flavouring agents, dyes and auxiliary therapeutic agents, e.g. trace elements. These may be designed to improve potency, persistence, safety, uptake where desired, spectrum of pests controlled or to enable the composition to perform other useful functions in the same animal or area treated.

with other substances toxic to arthropods and plant nematodes, anthelmintics, anticoccidials, synergists, trace elements or stabilizers). The actual compositions employed and their rate of application will be selected to achieve the desired effect(s) by the farmer, livestock producer, medical or veterinary practitioner, pest control operator or other person skilled in the art. Solid and liquid compositions for application topically to animals, timber, stored products or household goods usually contain from 0.00005% to 90%, more particularly from 0.001% to 10%, by weight of the fly or moth compounds of general formula (I). For administration to animals orally or parenterally, including percutaneously, solid and liquid compositions normally contain from 0.1% to 90% by weight of one or more compound of general formula (I). Medicated feedstuffs normally contain from 0.001% to 3% by weight of one or more compounds of general formula (I). Concentrates and supplements for mixing with feedstuffs normally contain from 5% to 90%, and

preferably from 5% to 50%, by weight of one or more compounds of general formula (I). Mineral salt licks normally contain from 0.1% to 10% by weight of one or more compounds of general formula (I).

Dusts and liquid compositions for application to livestock, persons, goods, premises or outdoor areas may contain 0.0001% to 15%, and more especially 0.005% to 2.0%, by weight of one or more compounds of general formula (I). Suitable concentrations in treated waters are between 0.0001 ppm and 20 ppm, and more especially 0.001 ppm to 5.0 ppm, of one or more compounds of general formula (I) and may also be used therapeutically in fish farming with appropriate exposure times. Edible baits may contain from 0.01% to 5% and preferably 0.01% to 1.0% by weight of one or more compounds of general formula (I).

When administered to vertebrates parenterally, orally or by percutaneous or

other means, the dosage of compounds of general formula (I) will depend upon the species, age and health of the vertebrate and upon the nature and degree of its actual or potential infestation by arthropod, helminth or protozoa pest. A single dose of 0.1 to 100 mg, preferably 2.0 to 20.0 mg, per kg body weight of the animal or doses of 0.01 to 20.0 mg, preferably 0.1 to 5.0 mg, per kg body weight of the animal per day for sustained medication are generally suitable by oral or parenteral administration. By use of sustained release formulations or devices, the daily doses required over a period of months may be combined and administered to animals on a single occasion.

In experiments on activity against arthropods carried out on representative compounds, the following results (wherein ppm indicates the concentration of the compound in parts per million of the test solution applied) have been obtained:-

Test 1

One or more dilutions of the compounds to be tested were made in 50% aqueous acetone.

(a) Test species: Plutella xylostella (Diamond-back Moth) and Phaedon cochleariae (Mustard beetle)

Turnip leaf discs were set in agr in petri-dishes and infested with 10 larvae (2nd instar Plutella or 3rd instar Phaedon). Four replicate dishes were assigned to each treatment and were sprayed under a Potter Tower with the appropriate test dilution. Four or five days after treatment the dishes were removed from the constant temperature (25°C) room in which they had been held and the mean percentage mortalities of larvae were determined. These data were corrected against the mortalities in dishes treated with 50% aqueous acetone alone which served as controls.

(b) Megoura viciae (Vetch Aphid)

Potted tic bean plants previously infested

with mixed stages of Megoura were sprayed to run-off using a laboratory turntable sprayer. treated plants were held in a greenhouse for 2 days and were assessed for aphid mortality using a scoring system, judging the response in comparison with plants treated with 50% aqueous acetone alone, as controls. Each treatment was replicated 4 times.

| | | |
|---|---|---|
| Score | 3 | all aphids dead |
| | 2 | few aphids alive |
| | 1 | most aphids alive |
| | 0 | no significant mortality |

(c) test species: Spodoptera littoralis.

French bean leaf discs were set in agar in petri-dishes and infected with 5 larvae 92nd instar). Four replicate dishes were assigned to each treatment and were sprayed under a Potter Tower with the appropriate test dilution. After 2 days live larvae were transferred to similar dishes containing untreated leaves set in agar. Two or three

days later the dishes were removed from the constant temperature (25°C) room in which they had been held and the mean percentage mortalities of larvae were determined. These data were corrected against the mortalities in dishes treated with 50% aqueous acetone alone which served as controls.

According to the above method an application of the following compounds was effective against the larvae of Plusiella xylostella producing at least 65% mortality at less than 500 ppm:
1-10, 12-23, 25-27, 31-57, 59-70, 76-79, 81-88, 90-92, 96, 101.

According to the above method an application of the following compounds was effective against all stages of Mamestra brassicae producing a score of 7/12 at 50 ppm:
11, 58, 71, 72, 73, 74, 75

According to the above menthod an application of the following compounds was

effective against the larvae of Phaedon cochleariae producing at least 90% mortality at less than 5 ppm:

21, 29, 80, 89

According to the above method an application of the following compounds was effective against the larvae of Spodoptera littoralis producing at least 70% mortality at less than 500 ppm:

28, 30

The following Composition Examples illustrate compositions for use against arthropod, plant nematode, helminth or protozoa pests which comprise, as active ingredient, compounds of general formula (I). The compositions described in Composition Examples 1 to 6 can each be diluted in water to give a sprayable composition at concentrations suitable for use in the field.

COMPOSITION EXAMPLE 1

A water soluble concentrate was prepared from 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylhenyl)-4-

| | |
|---|---|
| trifluoromethylthiopyrazole | 7% w/v |
| Ethylan BCP | 10% w/v |

and N-methylpyrrolidone to 100% by volume by dissolving the Ethylan BCP in a portion of N-methylpyrrolidone, and then adding the active ingredient with heating and stirring until dissolved. The resulting solution was made up to volume by adding the remainder of the solvent.

COMPOSITION EXAMPLE 2

An emulsifiable concentrate was prepared from 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-

| | |
|---|---|
| trifluoromethylthiopyrazole | 7% w/v |
| Soprophor BSU | 4% w/v |
| Arylan CA | 4% w/v |
| N-methylpyrrolidone | 50% w/v |

and Solvesso 150 to 100% by volume

by dissolving Soprophor BSU, Arylan CA and the active ingredient in N-methylpyrrolidone, and then adding Solvesso 150 to volume.

COMPOSITION EXAMPLE 3

A wettable powder was prepared from

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole 40% w/w

Arylan S 2% w/w

Darvan No. 2 5% w/w

and Celite PF to 100 % by weight

by mixing the ingredients, and grinding the mixture in a hammer-mill to a particle size less than 50 microns.

COMPOSITION TEST 4

An aqueous flowable formulation was prepared from

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-

| | |
|---|---|
| trifluoromethylthiopyrazole | 30% w/v |
| Ethylan BCP | 1% w/v |
| Sopropon T36 | 0.2% w/v |
| Ethylene glycol | 5% w/v |
| Rhodigel 23 | 0.15% w/v |
| and water | to 100% by volume |

by intimately mixing the ingredients and grinding in a bead mill until the median particle size was less than 3 microns.

COMPOSITION EXAMPLE 5

An emulsifiable suspension concentrate was prepared from 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-

| | |
|---|---|
| trifluoromethylthiopyrazole | 30% w/v |
| Ethylan BCP | 10% w/v |
| Bentone 38 | 0.5% w/v |
| and Solvesso 150 | to 100% by volume |

by intimately mixing the ingredients and grinding in a bead mill until the median particle size was less than 3 microns.

COMPOSITION EXAMPLE 6

Water dispersible granules were prepared from 6-Amino-3-cyano-1-(2,6 dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole 30% w/w

Darvan No. 2 15% w/w

Arylan S 8% w/w

and Celite PF to 100% by weight

by mixing the ingredients, micronising in a fluid-energy mill, and then granulating in a rotating pelletiser by spraying on sufficient water (up to 10% w/w). The resulting granules were dried in a fluid-bed drier to remove excess water. Descriptions of commercial ingredients used in the foregoing Composition Examples:-

Ethylan BCP nonylphenol ethylene oxide condensate

Soprophor BSU condensate of tristyrylphenol and ethylene oxide

Arylan CA 70% w/v solution of calcium dodecylbenzenesulphonate

Solvesso 150 light $C_{10}$-aromatic solvent

Arylan S sodium dodecylbenzenesulphonate

Darvan sodium lignosulphonate

Celite PF synthetic magnesium silicate carrier

Sopropon T36 sodium salt of polycarboxylic acid

Rhodigel 23 polysaccharide xanthan gum

Bentone 38 organic derivative of magnesium montmorillonite

COMPOSITION EXAMPLE 7

A dusting powder may be prepared by intimately mixing:-

5-Amino-3-cyano-1-(2,6-dichloro-4-trilfuoromethylphenyl)-4-trifluoromethylthiopyrazole 1 to 10% w/w (weight/weight)

Talc superfine to 100% by weight

This powder may be applied to a locus of arthopod infestation, for example refuse tips or dumps, stored products or household goods or animals infected by, or at risk of infestation by, arthropods to control the arthropods by

oral ingestion. Suitable means for distributing the dusting powder to the locus of arthropod infestation include mechanical blowers, handshakers and livestock self treatment devices.

COMPOSITION EXAMPLE 8

An edible bait may be prepared by intimately mixing:-

| | |
|---|---|
| 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole | Ø.1 to 1.Ø% w/w |
| wheat flour | 8Ø% w/w |
| Molasses | to 1ØØ% w/w |

This edible bait may be distributed at a locus, for example domestic and industrial premises, e.g. kitchens, hospitals or stores, or outdoor areas, infested by arthropods, for example ants, locusts, cockroaches and flies, to control the arthropods by oral ingestion.

COMPOSITION EXAMPLE 9

A solution may be prepared containing:-

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole 15% w/v (weight/volume)

Dimethylsulphoxide to 100% by volume

by dissolving the pyrazole derivative in a portion of the dimethyl-sulphoxide and then adding more dimethylsulphoxide to the desired volume. This solution may be applied to domestic animals infested by arthropods, percutaneously as a pour-on application or, after sterilisation by filtration through a polytetrafluoroethylene membrane (0.22 micrometre pore size), by parenteral injection, at a rate of application of from 1.2 to 12 ml of solution per 100 kg of animal body weight.

COMPOSITION EXAMPLE 10

A wettable powder may be formed from:-

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole 50% w/w

Ethylan BCP (a nonylphenol/ethylene oxide condensate containing 9 moles of ethylene oxide per mol of phenol) 5% w/w

Aerosil (silicon dioxide of microfine-particle size) 5% w/w

Celite PF (synthetic magnesium silicate carrier) 40% w/w

by adsorbing the Ethylan BCP onto the Aerosil, mixing with the other ingredients and grinding the mixture in a hammer-mill to give a wettable powder, which may be diluted with water to a concentration of from 0.001% to2% w/v of the pyrazole compound and applied to a locus of infestation by arthropods, for example dipterous larvae, or plant nematodes by spraying, or to domestic animals infested by, or at risk of infestation by, arthopods, helminths or protozoa, by spraying or dipping, or by oral administration in drinking water, to

control the arthropods, helminths or protozoa.

COMPOSITION EXAMPLE 11

A slow release bolus may be formed from granules containing a density agent, binderm slow-release agent and 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole compound at varying percentage compositions. By compressing the mixture a bolus with a specific gravity of 2 or more can be formed and may be administered orally to ruminant domestic animals for retention within the reticulo-rumen to give a continual slow release of pyrazole compound over an extended period of time to control infestation of the ruminant domestic animals by arthropods, helminths or protozoa.

COMPOSITION EXAMPLE 12

A slow release composition may be prepared from:- 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-

trifluoromethylthiopyrazole

Ø.5 to 25% w/w

polyvinylchloride base to 1ØØ% w/w

by blending the polyvinylchloride base with the pyrazole compound and a suitable plasticiser, e.g. dioctyl phthalate, and melt-extruding or hot-moulding the homogenous composition into suitable shapes, e.g. granules, pellets, brickettes or strips, suitable, for example, for addition to standing water or, in the case of strips, fabrication into collars or ear-tags for attachment to domestic animals, to control insect pests by slow release of the pyrazole compound.

Similar compositions may be prepared by replacing the 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole in the Composition Examples by the appropriate quantity of any other compound of general formula (I).

The compounds of general formula (I) can be prepared by the application or adaptation of

known methods (ie. methods heretofore used or described in the chemical literature), generally pyrazole ring formation followed where necessary by changing substituents.

It is to be understood that in the description of the following processes that the sequences for the introduction of the various groups on the pyrazole ring may be performed in a different order and that suitable protecting groups may be required as will be apparent to those skilled in the art. Compounds of general formula (I) may be converted by known methods into other compounds of general formula (I).

In the following description when symbols appearing in formulae are not specifically defined it is to be understood that they are "as hereinbefore defined" in accordance with the first definition of each symbol in this specification within the process definitions, unless otherwise stated amino refers to the unsubstituted amino group

Compounds of general formula (I) wherein $R^2$ represents an $R^5SO_2$, $R^5SO$ or $R^5S$ group, $R^3$ represents the unsubstituted amino group and $R^1$ represents the cyano or acetyl group may be prepared by a process version "a" in which a compound of general formula (II) wherein $R^8$ represents a cyano or acetyl group is reacted with a compound of general formula $R^2CH_2CN$, preferably a molar equivalent thereof, generally in the presence of an anhydrous inert organic solvent, e.g. ethanol, and a molar equivalent of a base, e.g. sodium ethoxide, and at a temperature from 0° to 50°C.

Compounds of general formula (I) wherein $R^2$ represents an $R^5S$ group and $R^3$ represents an amino group $-NR^6R^7$ wherein $R^6$ and $R^7$ each represent a hydrogen atom or a straight or branched chain alkyl, alkenylalkyl or alkynylalkyl group as hereinbefore defined may be prepared by a process version "b" in which an intermediate corresponding to general formula (I) in which $R^2$ is replaced by the

hydrogen atom is reacted with a compound of general formula:-

$$R^5\text{-SCl} \qquad \text{(III)}$$

(wherein $R^5$ is as hereinbefore defined) in an inert organic solvent, preferably chloroform or dichloromethane, optionally in the presence of a base, preferably pyridine, aobd at temnperature from 0° to 50°C.

Compounds of general formula (I) wherein $R^1$ represents a chlorine or fluorine atom, $R^2$ represents an $R^5SO_2$, $R^5SO$ or $R^5S$ group, and $R^3$ represents an amino group may be prepared by a process version "c" in which a compound of general formula (IV) wherein X and Y both represent chlorine atoms or both represent fluorine atoms, is reacted with a phenylhydrazine of general formula:-

$$R^4NHNH_2 \qquad \text{(V)}$$

(wherein $R^4$ is as hereinbefore defined) or an

acid addition salt thereof, e.g. the hydrochloride, in an inert solvent, preferably ether or tetrahydrofuran, and optionally in the presence of a base, e.g. triethylamine or sodium acetate, and at a temperature from Ø° to the reflux temperature of the solvent. When an acid addition salt of the compound of general formula (V) is used, the reaction with the compound of general formula (IV) is effected in the presence of an alkali metal, e.g. sodium or potassium, acetate, carbonate or bicarbonate.

According to a further process version "d" (1), compounds of general formula (I) wherein $R^2$ represents an $R^5S$ group, $R^1$ represents a chlorine, bromine, iodine or fluorine atom or a cyano or nitro group, and $R^3$ represents an amino group may also be prepared by the reaction of corresponding 4-thiocyanatopyrazoles with an organometallic reagent such as a compound of general formula:-

$$R^5\text{-Mg-}X^1 \qquad \text{(VI)}$$

wherein $R^5$ is as hereinbefore defined and $X^1$ represents a halogen atom in an inert solvent, such as diethyl ether or tetrahydrofuran, and at a temperature from -78°C to the reflux temperature of the reaction mixture, or a compound of general formula:-

$$R^9\text{-}C{\equiv}C^- \quad Li^+ \qquad (IX)$$

wherein $R^9$-C $C^-$ corresponds to $R^5$ in (I), in an inert solvent, such as tetrahydrofuran or diethyl ether, at temperatures from -78°C to ambient.

Alternatively, according to process version "d" 92), compounds of general formula (I) in which $R^2$ represents an $R^5S$ group wherein $R^5S$ is other than a 1-alkenylthio or 1-alkynylthio group may also be prepared by reacting an intermediate corresponding to general formula (I) in which $R^2$ is replaced by a thiocyanato group, with a base preferably sodium hydroxide, or a reducing agent preferably sodium borohydride, in the presence of a reagent of

general formula:-

$$R^{5'} - X^2 \qquad \text{(VII)}$$

wherein $R^{5'}$ is as hereinbefore defined for $R^5$ with the exclusion of 1-alkenyl and 1-alkynyl and $X^2$ represents a halogen, preferably bromine or iodine, for example methyl iodide or poropargyl bromide, or with a base preferably sodium hydroxide, in the presence of a reagent of general formula:-

$$F_2C=C(Z)Z' \qquad \text{(VIIA)}$$

wherein Z represents a fluorine, chlorine or bromine atom and Z' is as hereinbefore defined for Z or represents the trifluoromethyl group in an inert organic or aqueous-organic solvent, such as methanol, ethanol or dioxan or mixtures of these solvents with water, the reaction being performed at a temperature from -40°C to the reflux temperature.

Alternatively, according to process version "d" (3), compounds of general formula (I)

wherein $R^5S$ is other than a 1-alkenylthio or 1-alkynylthio group may be prepared by reductive alkylation of disulphides of general formula (VIII) employing a reducing agent preferably sodium dithionite or sodium borohydride, in the presence of a base, preferably sodium hydroxide or sodium carbonate; and of a halide of general formula (VII), such as methyl iodide, in an inert organic or aqueous-organic solvent such as ethanol or a mixture of alcohol and water, at a temperature from ambient to reflux.

According to a further process version "e", compounds of general formula (I) in which $R^2$ represents an $R^5SO$ or $R^5SO_2$- group may be prepared by oxidation of the sulphur atoms of the corresponding alkylthio, alkenylthio or alkynylthio compounds of formula (I) wherein $R^2$ is a group $R^5S$ as defined above; the oxidation may be effected employing oxidants of the formula:-

$$R^{10}\text{-}Ø\text{-}Ø\text{-}H \qquad (X)$$

wherein $R^{10}$ represents the hydrogen atom, or a trifluoroacetyl or preferably 3-chlorobenzoyl group in a solvent e.g. dichloromethane or chloroform or trifluoroacetic acid and at temperatures from 0°C to 60°C, or with a reagent such as potassium hydrogen persulphate or potassium salt of Caro's acid in a solvent e.g. methanol and water, and at a temperature from -30°C to 50°C.

According to a further process version "f" (1), compounds of general formula (I) wherein $R^1$ represents a chlorine, bromine or iodine atom or a cyano nitro group may be prepared by the diazotisation of an intermediate corresponding to general formula (I) in which $R^1$ is replaced by the amino group and $R^3$ represents a hydrogen atom or the amino group using sodium nitrite in a mineral acid, for example a mixture of concentrated sulphuric acid and acetic acid, at a temperature from 0° to 60°C, and by subsequent reaction with a copper salt and a mineral acid or with an

aqueous solution of potassium iodide (when $R^1$ represents an iodine atom) at a temperature from 0° to 100°C; or with cuprous cyanide, or sodium nitrite in the presence of a copper salt in an inert solvent e.g water at pH from 1 to 7 at 25° to 100°C. The diazotisation may alternatively be performed employing an alkyl nitrite e.g. tert-butyl nitrite in the presence of a suitable halogenating agent preferably bromoform or iodine or anhydrous cupric chloride at temperatures from 0°C to 100°C, and optionally in the presence of an inert solvent, preferably acetonitrile or chloroform.

According to a further process version "f" (2), compounds of general formula (I) wherein $R^1$ represents a fluorine atom and $R^3$ represents a hydrogen atom or the amino group may be prepared by diazotisation of the corresponding amine wherein $R^1$ is replaced by the amino group using for example a solution of sodium nitrite in sulphuric acid and in the presence of fluoroboric acid or its sodium salt and subsequent thermolysis or photolysis of the

diazonium fluoroborate derivative by methods known per se.

According to a further process version "g", compounds of general formula (1Ø wherein $R^1$ represents a fluorine atom or a cyano group, and $R^3$ represents a hydrogen atom or the amino group may be prepared by the reaction of a halide of general (I) wherein $R^1$ represents a chlorine or bromine atom with an alkali metal fluoride, preferably caesium fluoride, or with a metal cyanide preferably KCN under anhydrous conditions in an inert solvent, preferably sulpholane, and at a temperature from ambient to 15Ø°C.

According to a further process version "h", compounds of general formula (I) wherein $R^1$ represents a nitro group, and $R^2$ is a group $R^5SO_2$ or $R^5SO$ may be prepared by the reaction of an intermediate corresponding to general formula (I) in which $R^1$ is replaced by an unsubstituted amino group, and $R^2$ is a group $R^5SO_2$, $R^5SO$ or $R^5S$, and $R^3$ represents a

hydrogen atom or the amino group with an oxidant, preferably trifluoroperacetic acid or m-chloroperbenzoic acid, in an inert solvent, preferably dichloromethane, at a temperature from $0^{o}C$ to the reflux temperature. In this process concomitant oxidation at sulphur may occur when $R^2$ is $R^5S$.

According to a further process version "1", compounds of general formula (I) wherein $R^1$ represents the cyano group and $R^3$ represents a hydrogen atom or the amino group may also be prepared by the dehydration of a compound corresponding to general formula (I) in which $R^1$ is replaced by the carbamoyl groupp. The compound corresponding to general formula (I) in which $R^1$ is replaced by the carbamoyl group may be prepared by the reaction of a compound corresponding to general formula (I) in which $R^1$ is replaced by the carboxy group with a chlorinating agent, preferably thionyl chloride at ambient to reflux temperature, followed by reaction of the intermedaite acid chloride with ammonia to give an intermedaite amide. The

dehydration is generally effected by heating with a dehydrating agent e.g. phosphorus pentoxide or preferably phosphorous oxychloride at a temperature from 50°C to 250°C.

According to a further process version "J", compounds of general formula (I) wherein $R^1$ is the acetyl group, and $R^3$ represents a hydrogen atom or the amino group may be prepared by the reaction of the corresponding nitrile of formula (I) wherein $R^1$ is the cyano group, or of esters wherein $R^1$ is replaced by an alkoxycarbonyl group or of carboxylic acids wherein $R^1$ is replaced by a carboxy group with methyl lithium in an inert solvent, e.g. toluene, and at temperatures from -78°C to ambient. Alternatively the nitrile of formula (I) wherein $R^1$ is the cyano group or ester wherein $R^1$ is replaced by an alkoxycarbonyl group may be reacted with a Grignard reagent $CH_3MgX^3$ wherein $X^3$ represents a halogen, preferably iodine atom, in an inert solvent e.g. diethyl ether or tetrahydrofuran, and at a

temperature from Ø°C to the reflux temperature of the solvent.

According to a further process version "k", compounds of general formula (I) wherein $R^1$ represents the acetyl group and $R^3$ is as defined above may alternatively be prepared by oxidation of alcohols corresponding to general formula (I) wherein $R^1$ is replaced by a 1-hydroxyethyl group, with an oxidant, preferably pyridinium chlorochromate, in an inert solvent, e.g. dichloromethane, and at a temperature from Ø°C to the reflux temperature of the solvent.

According to a further process version "l", compounds of the general formula (I) wherein $R^1$ represents a formyl group and $R^3$ is as defined above may be prepared by the reaction of the corresponding nitriles of general formula (I) wherein $R^1$ represents a cyano group with

(1) a suitable reducing agent preferably diisobutylaluminium hydride in an inert solvent, preferably tetrahydrofuran and at a

temperature from -78°C to the ambient temperature, followed by mild hydrolysis with an acid, e.g. dilute hydrochloric acid, at room temperature; or

(2) Raney nickel in formic acid preferably at the reflux temperature of formic acid.

Derivatives of the 5-amino group form a further feature of the present invention and are collectively referred to as process "m". Compounds of general formula (I) which conform to general formula (IA) wherein $R^6$ represents an $R^{11}C(=O)-$ group, wherein $R^{11}$ represents a straight or branched-chain alkyl or alkoxy group containing from 1 to 4 carbon atoms, and $R^7$ represents a hydrogen atom or an $R^{11}C(=O)-$ group which is identical to the group $R^{11}C(=O)-$ represented by $R^6$ or $-NR^6R^7$ represents a cyclic imide as hereinbefore defined, may be prepared by the reaction of a compound of general formula (I) wherein $R^3$ represents the unsubstituted amino group, or an alkali metal

salt thereof, with a compound of the general formula:-

$$R^{11}\text{-}CO\text{-}X^4 \qquad (XI)$$

wherein $X^4$ represents a chlorine or bromine atom, or with a compound of the general formula:-

$$(R^{11}\text{-}CO)_2O \qquad (XII)$$

or with a dicarboxylic acid derivative. The reaction may be conducted in the absence or presence of an inert organic solvent, for example acetonitrile, tetrahydrofuran, a ketone, e.g. Acetone, an aromatic hydrocarbon, e.g. benzene or toluene, chloroform, dichloromethane or dimethylformamide, and optionally in the presence of an acid-binding agent, for example pyridine, triethylamine or an alkali metal, e.g. sodium or potassium, carbonate or bicarbonate, at a temperature from 0°C to the reflux temperature of the reaction medium, to give a compound of general formula (IA) wherein $R^6$ represents an $R^{11}C(=O)$- group

wherein $R^{11}$ is as hereinbefore defined and $R^7$ represents a hydrogen atom or an $R^{11}C(=O)$- group, depending upon the reaction conditions chosen and/or the use of an excess of the compound of general formula (XI) or (XII), or --$NR^6R^7$ represents a cyclic imide as hereinbefore defined.

Compounds of general formula (IA) wherein $R^6$ represents a formyl group and $R^7$ represents a hydrogen atom or a formyl group, may be prepared by the reaction of a compound of general formula (I), wherein $R^3$ represents the unsubstituted amino group with formylacetic anhydride. Formylacetic anhydride may be prepared from formic acid and acetic anhydride and the reaction with the compound of general formula (I) may be conducted in the absence or presence of an inert organic solvent, for example a ketone, e.g. acetone, or an aromatic hydrocarbon, e.g. benzene or toluene, and optionally in the presence of an acid-binding agent, for example pyridine, triethylamine or

an alkali metal, e.g. sodium or potassium, carbonate or bicarbonate, at a temperature from Ø°C to the reflux temperature of the reaction mixture, to give a compound of general formula (IA) wherein $R^6$ represents a formyl group and $R^7$ represents a hydrogen atom or a formyl group, depending upon the reaction conditions chosen and/or the use of an excess of formylacetic anhydride.

Compounds of general formula (IA) wherein $R^6$ represents a formyl group or a group $R^{11}C(=Ø)$- and $R^7$ represents a hydrogen atom may be prepared by the selective removal by hydrolysis of an $R^{11}C(=Ø)$- group or a formyl group from a compound of general formula (IA) wherein $R^6$ and $R^7$ both represent a $R^{11}C(=Ø)$- group or a formyl group. Hydrolysis is effected under mild conditions, for example by treatment with an aqueous-ethanolic solution or suspension of an alkali metal, e.g. sodium or potassium, bicarbonate, or with aqueous ammonia.

Compounds of general formula (IA) wherein $R^6$ represents a straight or branched-chain alkoxycarbonyl group containing from 2 to 5 carbon atoms which is unsubstituted or substituted by one or more halogen atoms, and $R^7$ represents a hydrogen atom may be prepared by the reaction of a compound of the general formula (IB) wherein $R^{12}$ represents an alkoxycarbonyl group $R^{13}C(=O)$, wherein $R^{13}$ represents a straight or branched-chain alkoxy group containing from 1 to 4 carbon atoms (which is unsubstituted or substituted by one or more halogen atoms) or a phenoxy group, with a compound of the general formula:-

$$R^{13}\text{-}H \qquad \text{(XIII)}$$

(wherein $R^{13}$) is as hereinbefore defined) to replace a first group represented by the symbol $R^{12}$ by a hydrogen atom, and to replace the second group represented by the symbol $R^{12}$ by an alkoxycarbonyl group when $R^{12}$ represents a phenoxycarbonyl group, or, if desired, to replace the second group represented by the

symbol $R^{12}$ by another alkoxycarbonyl group when $R^{12}$ in formula (IB) represents an alkoxycarbonyl group. As will be apparent to those skilled in the art, the desired compound of general formula (IA) is obtained by selection of the appropriate compounds of general formulae (IB) and (XIII). The reaction may be effected in water or an inert aqueous-organic or organic solvent, for example an alkanol containing 1 to 4 carbon atoms, e.g. ethanol, or an aromatic hydrocarbon, e.g. benzene or toluene, or which is preferably an excess of the compound of general formula (XIII), at a temperature from ambient temperature to the reflux temperature of the reaction mixture and, if necessary, at elevated pressure, and optionally in the presence of a base, for example an alkali metal alkoxide, e.g. of the compound of general formula (XIII).

Compounds of general formula (IA) wherein $R^6$ and $R^7$, which may be the same or different, each represents a formyl group or $R^{11}C(=O)$-

group, may be prepared by the reaction of an alakli metal, e.g. sodium or potassium, derivative of a compound of general formula (IA) wherein $R^6$ represents a group $R^{11}(C=O)$- as hereinbefore defined, or a formal group, and $R^7$ represents a hydrogen atom with formylacetic anhydride or a compound of general formula (XI). Reaction may be effected in an inert aprotic solvent, e.g dimethylformamide, at a temprature from laboratory temperature to the reflux temperature of the reaction mixture.

Alkali metal derivatives of compounds of general formula (I) (wherein $R^3$ represents the unsubstituted amino group) or (IA) wherein $R^6$ represents a group $R^{11}CO$ and $R^7$ represents a hydrogen atom may be prepared *in situ* by reaction with an alkali metal, e g. sodium or potassium, hydride, in an inert aprotic solvent, e.g. dimethylformamide, at a temperature from laboratory temperature to the refux temperature of the reaction mixture.

Compounds of general formula (IB) wherein

$R^{12}$ represents a group $R^{13}C(=O)-$, may be prepared as hereinbefore described. Intermediates of general formula (IB) wherein $R^{12}$ represents a phenoxycarbonyl group may be prepared by the reaction of a compound of general formula (I) (wherein $R^3$ represents the unsubstituted amino group), with a compound of general formula:-

$$R^{14}-CO-X^4 \qquad (XIV)$$

(wherein $R^{14}$ represents a phenoxy group and $X^4$ is as hereinbefore defined, e.g. phenyl chloroformate, or with a compound of general formula:-

$$(R^{14}-CO)_2O \qquad (XV)$$

(wherein $R^{14}$ is as hereinbefore defined) using the reaction conditions hereinbefore described for the reaction of a compound of general formula (I) with a compound of formula (XI) or (XII).

Compounds of general formula (IA) wherein $R^6$ represents a group $R^{15}$ which represents a

straight or branched-chain alkyl, alkenylalkyl or alkynylalkyl group containing up to 5 carbon atoms and $R^7$ represents a hydrogen atom may be prepared by the removal of the group $R^{11}C(=O)-$ of a compound of the general formula (IA), wherein $R^6$ represents a group $R^{15}$ and $R^7$ represents a group $R^{11}C(=O)-$. Removal of the group $R^{11}C(=O)-$ may be effected by selective hydrolysis under mild conditions, for example by treatment with an alkali metal, e.g. sodium or potassium, hydroxide in water or an inert organic or aqueous-organic solvent, for example a lower alkanol, e.g. methanol, or a mixture of water and lower alkanol, at a temperature from laboratory temperature up to the reflux temperature of the reaction mixture.

Compounds of general formula (IA), wherein $R^6$ represents a group $R^{15}$ and $R^7$ represents a group $R^{11}C(=O)-$, may be prepared:

(1) by reaction of a compound of general formula (IA) wherein $R^6$ represents a hydrogen atom and $R^7$ represents a group $R^{11}C(=O)$, or an

alkali metal, e.g. sodium or potassium, derivative thereof, with a compound of the general formula:

$$R^{15}X^5 \qquad (XVI)$$

wherein $X^5$ represents a chlorine, bromine or iodine atom; the reaction may be effected in an inert organic solvent, e.g. dichloromethane, tetrahydrofuran, or dimethylformamide, at a temperature from laboratory temperature up to the reflux temperature of the reaction mixture and, when a compound of general formula (IA) is used, in the presence of a base, e.g. Triton B; or

(2) by reaction of a compound of general formula (IA) wherein $R^6$ represents the hydrogen atom and $R^7$ represents a group $R^{15}$ with a compound of general formula (XI) or (XII).

Compounds of general formula (I) wherein $R^3$ represents an N-(alkyl, alkenylalkyl or alkynylalkyl)-N-formylamino group as hereinbefore described may be prepared in a

similar manner to the process just described, where approproate, formylacetic anhydride instead of a compound of general formula (XI) or (XII).

Compounds of general formula (IA) wherein one or both of $R^6$ and $R^7$ represents a straight or branched chain alkyl, alkenylalkyl or alkynylalkyl group containing up to 5 carbon atoms, groups represented by $R^6$ and $R^7$ being identical, may be prepared by reaction of a compound of general formula (I), wherein $R^3$ represents the unsubstituted amino group, or an alkali metal, e.g. sodium or potassium, derivative thereof, with a compound of general formula (XVI), in the absence or presence of an inert organic solvent, for example an aromatic hydricarbon, e.g. benzene or toluene, chloroform, dichloromethane, tetrahydrofuran or dimethylformamide, and optionally in the presence of an acid-binding agent, for example pyridine, triethylamine or an alkali metal, e.g. sodium or potassium, bicarbonate, at a

temperature from 0°C up to the reflux temperature of the reaction mixture.

According to a further process version "n", compounds of general formula (I), wherein $R^3$ represents a straight or branched-chain alkoxymethyleneamino group containing from 2 to 5 carbon atoms which may be unsubstituted or substituted on methylene by a straight or branched-chain alkyl group containing from 1 to 4 carbon atoms may be prepared by the reaction of a compound of general formula (I) (wherein $R^3$ represents the unsubstituted amino group) with a trialkoxyalkane in the presence of an acidic catalyst, e.g. p-toluenesulphonic acid, at a temperature from ambient temperature to the reflux temperature of the reaction mixture.

According to a further process version "o", compounds of general formula (I) wherein $R^3$ represents a group $-NHCH_2R^{16}$ wherein $R^{16}$ represents the hydrogen atom or a straight or branched-chain alkyl group containing from 1 to

4 carbon atoms may be prepared by reaction of a compound of general formula (I) wherein $R^3$ represents $-N=C(OR^{17})R^{16}$ wherein $R^{17}$ represents a straight or branched-chain alkyl group containing from 1 to 4 carbon atoms with a reducing agent, preferably sodium borohydride. The reaction may be effected in an inert organic solvent, ethanol or methanol being preferred, at a temperature from 0°C to the reflux temperature of the reaction mixture.

Compounds of general formula (I), wherein $R^3$ represents a halogen atom, may be prepared by diazotisation of the corresponding compound of general formula (I) wherein $R^3$ represents the amino group, adopting the procedure of process "f" used above to prepare compounds of general formula (I) wherein $R^1$ represents a halogen atom. Fluorides of general formula (I) wherein $R^3$ represents a fluorine atom may also be prepared by a halogen exchange reaction of halides of general formula (I) wherein $R^3$ represents a chlorine or bromine atom, adopting

the procedure of process "g" used above to prepare compounds (I) wherein $R^1$ represents a fluorine atom.

According to a further process version "p", compounds of general formula (I) wherein $R^1$ represents the formyl, acetyl, cyano or nitro group, $R^2$ is as defined, and $R^3$ represents a fluorine atom may be prepared by a halogen exchange reaction with a compound of general formula (I) wherein $R^3$ represents a chlorine or bromine atom by heating with an alkali metal fluoride preferably caesium fluoride in an inert solvent preferably sulpholane and at a temperature from 50°C to 150°C.

According to a further process version "q", compounds of general formula (I) wherein $R^3$ represents a hydrogen atom may be prepared by treatment of a compound of general formula (I) wherein $R^3$ represents an amino group, with a diazotising agent preferably tertiary butyl nitrile in a solvent, preferably

tetrahydrofuran, and at ambient to the reflux temperature.

According to a further process version "r", compounds of general formula (IA) wherein $R^1$ represents a cyano or nitro group, $R^2$ is a group $R^5SO_2$, $R^6$ and $R^7$ each represents a straight or branched chain alkyl, alkenylalkyl or alkynylalkyl group containing up to 5 carbon atoms and $R^7$ may also represents a hydrogen atom may be prepared by the reaction of a compound of general formula (I) wherein $R^3$ represents a halogen, preferably bromine, atom with the corresponding amine within general formula $R^6R^7NH$, or dimethylhydrazine when $R^6$ and $R^7$ are both methyl, in an inert solvent preferably dioxan, tetrahydrofuran, N,N-dimethylformamide, dimethylsulphoxide or sulpholane and at a temperature from 25° to 100°C.

Intermediate compounds of the general formula (II) wherein the $R^8$ group represents a

cyano or acetyl group may be prepared by diazotisation of the aniline $R^4NH_2$ (wherein R4 is as hereinbefore defined) generally with a solution of a molar equivalent of sodium nitrite in a mineral acid, e.g. a mixture of concentrated sulphuric acid and acetic acid, at a temperature from 0° to 60°C, and then reacting with a compound of formula $CH_3COCH(Cl)CN$ [preparation described in J. Org. Chem 43 (20), 3822 (1978)] or a compound of general formula $CH_3COCH(Cl)COCH_3$ in the presence of an inert solvent, e.g. a mixture of water and ethanol, optionally buffered, e.g. with excess sodium acetate and at a temperature from 0° to 50°C.

Intermediates corresponding to general formula (I) in which $R^3$ represents an amino group, $R^2$ is replaced by the hydrogen atom, and $R^1$ represents the cyano group may be prepared by diazotisation of the aniline $R^4NH_2$ (wherein $R^4$ is as hereinbefore defined) generally with a solution of a molar equivalent of sodium

nitrite in a mineral acid, e.g. a mixture of concentrated sulphuric acid and acetic acid, at a temperature from 0° to 60°C, and then reacting with a compound of general formula:-

$$NC-CH_2-CH(CO-R^{18})CN \qquad (XVII)$$

wherein $R^{18}$ represents an alkoxy group containing from 1 to 6 carbon atoms, preferably the ethoxy group, or a hydrogen atom in the presence of an inert solvent, e.g. a mixture of water and ethanol, and optionally buffered, e.g. with sodium acetate, and at a temperature from 0 to 50°C. Subsequent mild hydrolysis with a base such as aqueous sodium hydroxide, sodium carbonate or ammonia may be necessary to effect the cyclisation.

Intermediates of general formula (XVII) used above, in which $R^{18}$ represents the hydrogen atom, may be employed as alkali metal enolate salts which are converted into the aldehydes under the acidic conditions of the above coupling reaction.

Intermediates corresponding to general formula (I) in which $R^1$ is as defined with the exception of the formyl group, $R^2$ is replaced by the hydrogen atom and $R^3$ represents an amino group may be prepared by decarboxylation of a compound corresponding to general formula (I) wherein $R^2$ is replaced by the carboxy group, generally performed by heating at a temperature from 100°C to 250°C optionally in the presence of an inert organic solvent, particularly N,N-dimethylaniline. Alternatively intermediates corresponding to general formula (I) in which $R^2$ is replaced by a hydrogen atom, $R^1$ is as defined with the exception of the formyl group, and $R^3$ represents an amino group may be prepared directly from esters corresponding to general formula (I) wherein $R^2$ represents a group -COOR in which R represents a straight or branched chain alkyl group containing from 1 to 6 carbon atoms, by heating in an inert organic solvent preferably acetic acid at a temperature from 50°C to reflux, in the presence of a strong acid preferably hydrobromic acid. When

the $R^1$ group within the definition of this process is a chlorine or fluorine atom some mild halogen exchange may also occur to give intermediates wherein $R^2$ and $R^3$ are as defined and $R^1$ represents a bromine atom.

Intermediate carboxy compounds corresponding to general formula (I) in which $R^1$ is as defined with the exception of the formyl group, $R^2$ is replaced by the carboxy group and $R^3$ represents an amino group may be prepared by hydrolysis of esters wherein $R^2$ is replaced by a group COOR as defined above, preferably with an alkali metal hydroxide in a solvent such as an aqueous alcohol at a temperature from 0°C to the reflux temperature of the reaction mixture.

Intermediate esters corresponding to general formula (I) in which $R^2$ is replaced by a group -COOR as hereinbefore defined, $R^3$ is the amino group, and $R^1$ represents a cyano or acetyl group may be prepared in a similar manner to process version "a", described

the $R^1$ group within the definition of this process is a chlorine or fluorine atom concomitant halogen exchange may also occur to give intermediates wherein $R^2$ and $R^3$ are as defined and $R^1$ represents a bromine atom.

Intermediate carboxy compounds corresponding to general formula (I) in which $R^1$ is as defined with the exclusion of the formyl group, $R^2$ is repalced by the carboxy group and $R^3$ represents an amino group may be prepared by hydrolysis of esters wherein $R^2$ is replaced by a group -COOR as defined above, preferably with an alkali metal hydroxide in a solvent such as an aqueous alcohol at a temperature from 0°C to the reflux temperature of the reaction mixture.

Intermediate esters corresponding to general formula (I) in which $R^2$ is replaced by a group -COOR as hereinbefore defined, $R^3$ is the amino group, and $R^1$ represents a cyano or acetyl group may be prepared in a similar manner to process version "a", described

hereinbefore, from esters $ROOCCH_2CN$ and intermedaites of general formula (II) wherein $R^8$ represents a cyano or acetyl group.

Intermedaite esters corresponding to general formula (I) in which $R^2$ is replaced by a group -COOR as hereinbefore defined, $R^3$ is the amino group and $R^1$ represents a chlorine or fluorine atom may be prepared by the reaction of a phenylhydrazine (V) with a compound of general formula (XVIII) wherein X, Y and R are as hereinbefore defined, in a similar manner to the procedure of process version "c".

Alternatively intermediates corresponding to general formula (I) in which $R^1$ represents a chlorine or fluorine atom, $R^2$ is replaced by a hydrogen atom, and $R^3$ represents the amino group, may be prepared by reaction of the corresponding aldehydes in which $R^2$ is replaced by the formyl group with an acid, preferably aqueous hydrochloric acid, in a solvent preferably ethanol at a temperature from 50°C

to the reflux temperature.

Intermediates corresponding to general formula (I) in which $R^2$ is replaced by a formyl group may be prepared by reaction of nitriles wherein $R^2$ is replaced by a cyano group with a suitable reducing agent, preferably diisobutyl aluminium hydride in an inert solvent, preferably tetrahydrofuran at a temperature from -78°C to ambient temperature.

Intermediates corresponding to general formula (I) in which $R_2$ is replaced by a cyano group may be prepared by the reactionn of a compound of general formula (XIX) wherein X and Y are as hereinbefore defined (i.e. dichlorodicyannoethylene or difluorodicyanoethylene), with a phenylhydrazine (V) in a similar manner to process version "c".

Intermediates of general formula (XX) wherein $R_{19}$ represents an $R_2$ group or a hydrogen atom and $R_3$ represents a hydrogen atom

or an amino group may be prepared by performing a Curtius rearrangement of the acid azide corresponding to general formula (I) in which $R_1$ is replaced by CON or in which $R_2$ is replaced by the hydrogen atom and $R_1$ is replaced by CON by heating in an inert organic solvent such as toluene at a temperature from $50_oC$ to $150_{op}C$ to give an isocyanate which is then reacted with for example tert-butanol to give a carbamate, which in turn is hydrolysed using dilute acid preferably hydrochloric acid in ethanol at a temperature from ambient to reflux.

Intermediates acid azides may be prepared by reaction of a carboxylic acid corresponding to general formula (I) in which $R^1$ is replaced by a carboxy group and $R^2$ and $R^3$ are as defined above with an azide transfer reagent such as diphenyl phosphoryl azide in the presence of a base, preferably triethylamine and in an inert solvent preferably N,N-dimethylformamide, and at a temperature from $0^o$ to $60^oC$.

Intermediate carboxylic acids in which $R^1$ is replaced by a carboxylic acid group may be prepared by hydrolysis of the corresponding esters in which $R^1$ is replaced by an alkoxycarbonyl group e.g. ethoxycarbonyl, using a base such as sodium hydroxide and a solvent such as aqueous alcohol, and at a temperature fromm Ø°C to the reflux temperature of the solvent.

Intermediates carboxylic esters in which $R^1$ represents an alkoxycarbonyl group and wherein $R^{19}$ represents $R^2$ may be prepared by reaction of an intermedaite (XXI) wherein R and $R^2$ are as hereinbefore defined and $X^6$ is a leaving group, e.g. the chlorine atom, with a phenylhydrazine (VI), in a similar manner to process version "c".

Intermediate carboxylic esters in which $R^1$ is replaced by an alkoxycarbonyl group as defined above, and $R^2$ is replaced by $R^{19}$, may alternatively be prepared in a similar manner

to process version "a" by the reaction of a compound (II) wherein $R^8$ is replaced by a -COOR group in which R is as hereinbefore defined, with a compound of general formula $R^{19}CH_2CN$ wherein $R^{19}$ is as hereinbefore defined.

Intermedaites correponding to general formula (II) in which $R^8$ is replaced by -COOR may be prepared from knownn compounds (e.g. $CH_3COCH(Cl)COOR$) in a similar manner to that described above for compounds of general formula (II) wherein $R^8$ represents a cyano or acetyl group.

Intermedaite halides of general formula (XXI) wherein $X^6$ represents a chloride atom and R and $R^2$ are as hereinbefore defined, may be prepared by the reaction of the sodium or potassium salts (XXI) wherein $X^6$ is $-Ø^-Na^+$ or $-Ø^-K^+$ with a suitable chlorinating agent, preferably phosphorous oxychloride, optionally in the presence of an inert solvent, e.g. tetrahydrofuran, and at a temperature form $Ø^oC$

to the reflux temperature of the solvent.

Intermediate salts (XXI) wherein $X^6$ is $-Ø^-Na^+$ or $-Ø^-K^+$ may be prepared by methods described in the literature, wherein active methylene compounds $R^2CH_2CN$ are reacted with dialkyl oxalates, e.g. diethyl oxalate, in the presence of a metal alkoxide, e.g. sodiumm ethoxide, in an inert solvent, e.g. an alcohol such as ethanol, and at a temperature for 25°C to the reflux temperature of the solvent.

Intermediates corresponding to general formula (I) in which $R^1$ is replaced by a 1-hydroxyethyl group may be prepared by the reaction of aldehydes of general formula (I) wherein $R^1$ represents a formyl group and $R^3$ represents the hydrogen atom or an amino group with a Grignard reagent, preferably methyl magnesium halide, in an inert solvent, e.g. ether or tetrahydrofuran, and at a temperature from ambient to the reflux temperature of the solvent.

Intermediate 4-thiocyanatopyrazoles corresponding to general formula (I) in which $R^2$ is replaced by the thiocyanato group and $R^3$ represents the amino group may be prepared by the reaction of a compound corresponding to general formula (I) in which $R^2$ is replaced by the hydrogen atom with a thiocyanating agent, such as alkali metal or ammonium salts of thiocyanic acid (e.g. NaSCN and bromine, in an inert organic solvent, such as methanol, and at a temperature from 0°C to 100°C.

Intermediates disulphides of general formula (VIII) may be prepared by the hydrolysis of thiocyanates in which $R^2$ is replaced by the thiocyanato group and $R^1$ represents a chlorine, bromine or fluorine atom or the cyano or nitro group using hydrochloric acid in the presence of ethanol or by reduction with sodium borohydride in ethanol, both being at a temperature from ambient to reflux. Alternatively the thiocyanates may be converted into compounds of general formula (VIII) by

treatment with base, preferably aqueous sodium hydroxide and preferably under phase-transfer conditions with chloroform as co-solvent and in the presence of a phase transfer catalyst e.g. triethyl-benzylammonium chloride and at a temperature from ambient to 60°C.

Intermediate diaminoesters corresponding to general formula (I) in which $R^1$ and $R^3$ represent the amino group and $R^2$ is replaced by an ester group -COOR as hereinbefore defined containing from 2to 7 carbon atoms, may be prepared by reaction of an appropriately substituted phenylhydrazine of general formula (V) with an alkali metal salt of an alkyl dicyanoacetate of general formula:-

$$ROOC\text{-}CH(CN)_2 \qquad (XXII)$$

(wherein R is as hereinbefore defined) preferably potassium ethyl dicyanoacetate using hydrochloric acid, at ambient to reflux temperature. Alkyl dicyanoacetate potassium salts may be prepared by reaction of the

appropriate alkyl chloroformate with malononitrile in the presence of potassium hydroxide in tetrahydrofuran at a temperature of 0 to 100°C.

Intermediate diaminosulphonylpyrazoles corresponding to general formula (I) in which $R^1$ and $R^3$ represent the amino group and $R^2$ represents a sulphonyl group $R^5SO_2$ may be prepared in a similar manner to the process just described by reaction of a phenylhydrazine (V) with an alkali metal salt of a suitable alkylsulphonylmalononitrile of general formula:-

$$R^5SO_2\text{-}CH(CN)_2 \qquad \text{(XXIII)}$$

(wherein $R^5$ is as hereinbefore defined).

The preparation of compounds of general formula (XXIII) is described in the literature.

Intermediate esters corresponding to general formula (I) in which $R^1$ represents a

chlorine, bromine or fluorine atom or a nitro group, $R^2$ is replaced by a group -COOR as hereinbefore defined, and $R^3$ is an amino group, may be prepared in a similar manner to process version "f" via diasotisation of compounds corresponding to general formula (I) in which $R^1$ is replaced by an amino group.

Intermediate esters corresponding to general formula (I) in which $R^1$ is replaced by a group -COOR as hereinbefore defined, $R^2$ is replaced by the hydrogen atom, and $R^3$ represents an amino group, may also be prepared from the reaction of a phenylhydrazine of general formula (V) with an alkali metal salt of general formula (XXIV) wherein M is sodium or potassium and R is as hereinbefore defined. The reaction is performed in an acidic medium generally dilute sulphuric acid, optionally in the presence of a co-solvent e.g. ethanol, and at a temperature from ambient to the reflux temperature of the solvent.

According to a further feature of the present invention there are provided intermediates of general formula (XXV), useful in the preparation of compounds of general formula (I), wherein $R^{2'}$ is as defined for $R^2$ or represents the hydrogen atom, a thiocyanato, formyl, cyano or carboxy group, a straight- or branched-chain alkoxycarbonyl group containing from 2 to 7 carbon atoms or the dithio group (which joins two pyrazole rings for example as in formula (VIII)), $R^{3'}$ is as defined for $R^3$ or represents the diphenoxycarbonylamino group, and $R^{1'}$ is as defined for $R^1$ or represents the amino, 1-hydroxyethyl, carboxy or carbamoyl group or a straight- or branched-chain alkoxycarbonyl or alkoxycarbonylamino group containing from 2 to 7 carbon atoms,

with the exclusion of compounds of general formula (I) and of those compounds of general formula (XXV) wherein $R^4$ represents 2,6-dichloro-4-trifluoromethylphenyl, $R^{2'}$ represents the cyano group, $R^{1'}$ represents the cyano group and $R^{3'}$ represents the amino,

acetamido, dichloroacetamido, t.butylcarbonylamino, propionamido, pentanamido, bis(ethoxycarbonyl)amino, ethoxycarbonylamino, methylamino or ethylamino group,

or $R^{1'}$ represents the chlorine atom and $R^{3'}$ represents the amino, t-butylcarbonylamino, bis(ethoxycarbonyl)amino or ethoxycarbonylamino group,

or $R^{1'}$ represents a promine or iodine atom or an amino or ethoxycarbonyl group and $R^{3'}$ represents the amino group,

or $R^{1'}$ represents the fluorine atom and $R^{3'}$ represents the hydrogen atom or the amino group,

or $R^{1'}$ represents a nitro, amino, t.butoxycarbonylamino or ethoxycarbonyl group and $R^{3'}$ represents the hydrogen atom;

$R^4$ represents a 2,4,6-trichlorophenyl, 2-chloro-4-trifluoromethylphenyl or 2,6-dichloro-4-trifluoromethoxyphenyl group, $R^{2'}$ represents

the cyano group, $R^{1'}$ represents the cyano group and $R^{3'}$ represents the amino group;

$R^4$ represents a 2,6-dichloro-4-trifluoromethoxyphenyl group, $R^{2'}$ represents the cyano group, $R^{1'}$ represents the chlorine atom and $R^{3'}$ represents the amino group; and $R^4$ represents the 2,6-dichloro-4-trifluoromethylphenyl group, $R^{2'}$ represents the methanesulphony group, $R^{1'}$ represents a carboxy, carbamoyl or ethoxycarbonyl group and $R^{3'}$ represents the amino group.

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole is a preferred intermediate.

The following Examples and reference Examples illustrate the preparation of compounds of general formula (I) according to the present invention: [Chromatography was effected on a silica column (May & Baker Ltd 40/60 flash silica) at a pressure of $6.8Nm^{-2}$, unless otherwise stated.]

EXAMPLE 1

Compounds Nos.

1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,20.

A solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole (20.0 g) in dichloromethane (100 ml) was stirred magnetically and treated dropwise with a solution of trifluoromethylsulphenyl chloride (10.8 g) in dichloromethane (50 ml) during 1 hour. The solution was stirred overnight at room temperature, then washed with water (100 ml), dried over anhydrous magnesium sulphate, filtered, and evaporated in vacuo to give a solid (26.3 g). This solid was recrystallised from toluene/hexane to give 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole as fawn crystals 924.2 g) m.p. 169-171°C.

By proceeding in a similar manner but replacing the 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole by the hereinafter indicated appropriately substituted

pyrasole there was obtained from trifluoromethylsulphenyl chloride unless otherwise stated:

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-trifluoromethylthiopyrasole, m.p. 125-126°C, in the form of pale yellow crystals, from 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethoxyphenyl)pyrasole.

5-Amino-3-cyano-1-(2,6-dichloro-4-difluoromethoxyphenyl)-4-trifluoromethylthiopyrasole, m.p. 127-128.5°C, in the form of a buff solid, from 5-amino-3-cyano-1-02,6-dichloro-4-difluoromethoxyphenyl)pyrasole.

5-Amino-1-(2-chloro-4-trifluoromethylphenyl)-3-cyano-4-trifluoromethylthiopyrasole, m.p. 142-144°C, in the form of a light brown solid, from 5-amino-1-(2-chloro-4-trifluoromethylphenyl)-3-cyanopyrasole.

5-Amino-3-cyano-1-(2,4,6-trichlorophenyl)-4-trifluoromethylthiopyrasole, m.p. 192-193°C, in

the form of brom crystals, from 5-amino-3-cyano-1-(2,4,6-trichlorophenyl)pyrazole

5-Amino-3-cyano-1-(2,6-dibromo-4-trifluoromethylphenyl-4-trifluoromethylthiopyrazole, m.p. 202-204°C, in the form of orange crystals, from 5-amino-3-cyano-1-(2,6-dibromo-4-trifluoromethylphenyl)pyrazole.

5-Amino-1-(2-bromo-4-trifluoromethylphenyl)-3-cyano-4-trifluoromethylthiopyrazole, m.p 136-138°C, in the form of a pale yellow solid, from 5-amino-1-(2-bromo-4-trifluoromethylphenyl)-3-cyanopyrazole.

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-difluoromethylthiopyrazole, m.p. 159-161°C, in the form of a light brown solid, from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole and difluoromethylsulphenyl chloride.

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-heptafluoropropylthiopyrazole, m.p. 148-150°C,

in the form of a yellow solid, after dry column flash chromatography on silica eluting with dichloromethane and petroleum ether (3:1); from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl) pyrazole and heptafluoropropylsulphenyl chloride.

5-Amino-1-(2-bromo-6-chloro-4-trifluoromethylphenyl)-3-cyano-4-trifluoromethylthiopyrazole, m.p. 183-185°C, in the form of yellow crystals, from 5-Amino-1-(2-bromo-6-chloro-4-trifluoromethylphenyl)-3-cyanopyrazole and employing tetrahydrofuran as solvent.

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trichloromethylthiopyrazole, m.p. 245-247°C, in the form of a white solid after purification by chromatography, starting from 5-amino-3-cyano-1-(2,6-dichloro-4-trilfuoromethylphenyl)pyrazole and trichloromethylsulphenyl chloride.

By proceeding in a similar manner but

replacing the trifluoromethylsulphenyl chloride by dichlorofluoromethylsulphenyl chloride, and by the addition of a molar equivalent of pyradine to the reaction mixture after stirring overnight there was obtained;
5-Amino-3-cyano-4-dichlorofluoromethylthio-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole, m.p. 178-180°C in the form of a white solid, after purification by chromatography eluting with diethyl ether/hexane (1:); from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole.

By proceeding in a similar manner but employing a molar equivalent of pyridine in the reaction solution there was obtained:
5-Amino-3-chloro-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole, m.p. 149-150,5°C, in the form of a white solid, after recrystallisation from hexane fromm 5-amino-3-chloro-1-(2,6-dichloro-4-trilfuoromethylphenyl)pyrazole.

5-Amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole, m.p. 154.6-156°C, in the form of white solid, after recrystallization from hexane/ethyl acetate and then from hexane/cyclohexane, starting from 5-amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole.

5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-fluoro-4-trifluoromethylthiopyrazole, m.p. 122-126°C, in the form of a white solid, starting from 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-fluoropyrazole.

5-Amino-4-chlorodifluoromethylthio-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole, m.p. 167-168°C, in the form of white solid, starting from chlorodifluoromethylsulphenyl chloride. The product was purified by high performance liquid chromatography employing a 8 micron irregular column (21.4 mm x 25 cm) and eluting with acetonitrile/water (3:2).

**Reference Example 1**

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole used in the above Example was prepared as follows:

A suspension of nitrosyl sulphuric acid prepared from sodium nitrile (7.0 g) and concentrated sulphuric acid (27 ml) was diluted with acetic acid (25 ml), cooled to 25°C, and stirred mechanically. To this was added a solution of 2,6-dichloro-4-trifluoromethylaniline (21.2 g) in acetic acid (50 ml) dropwise over 15 minutes at 25-32°C. This mixture was heated to 55°C for 20 minutes and poured onto a stirred solution of ethyl 2,3-dicyanopropionate (14.0 g) in acetic acid (60 ml) and water (125 ml) at 10-20°C. After 15 minutes, water (200 ml) was added, and the oily layer separated. The aqueous solution was then extracted with dichloromethane (3 x 70 ml) and the extracts combined with the oil and washed with ammonia solution ( to pH9). The organic phase was then stirred with ammonia (20

ml) for 2 hours, and the dichloromethane layer then separated. This was washed with water (1 x 100 ml), 1N hydrochloric acid (1 x 100 ml), dried over anhydrous magnesium sulphate, filtered, and evaporated in in vacuo to given an oily solid. Crystallisation from toluene/hexane gave the title compound as brown crystals (20.9 g), m.p. 140-142°C.

By proceeding in a similar manner but replacing the 2,6-dichloro-4-trifluoromethylaniline by the appropriately substituted anilines there was obtained:

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethoxyphenyl)pyrazole in the form of a fawn solid, m.p. 119-120.5°C, from 2,6-dichloro-4-trifluoromethoxyaniline.

5-Amino-3-cyano-1-(2,6-dichloro-4-difluoromethoxyphenyl)pyrazole, after washing the initially formed product as a solution in dichloromethane with saturated sodium carbonate solution. The title compound was obtained as a yellow solid after recrystallisation from

toluene, m.p. 120.5-122.5°C, from 2,6-dichloro-4-difluoromethoxyaniline.

5-Amino-1-(2-chloro-4-trifluoromethylphenyl)-3-cyanopyrazole in the form of an orange crystalline solid, m.p. 133-135°C, from 2-chloro-4-trifluoromethylaniline.

5-Amino-3-cyano-1-(2,4,6-trifluorophenyl)pyrazole in the form of a light brown solid, m.p. 155-158°C, from 2,4,6-trichloroaniline.

5-Amino-3-cyano-1-(2,6-dibromo-4-trifluoromethylphenyl)pyrazole in the form of a yellow crystalline solid, m.p. 142-146°C, from 2,6-dibromo-4-trifluoromethylaniline.

5-Amino-1-(2-bromo-6-chloro-4-trifluoromethylphenyl)-3-cyanopyrazole in the form of a brown crystalline solid, m.p. 146-148°C, from 2-bromo-6-chloro-4-trifluoromethylaniline.

5-Amino-1-(2-bromo-4-trifluoromethylphenyl)-3-cyanopyrazole in the form of a yellow crystalline solid, m.p. 159-162°C, from 2-bromo-4-trifluoromethylaniline.

5-Amino-3-chloro-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole, used in Example 1, was prepared as follows:

A mixture of 5-amino-3-chloro-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-ethoxycarbonylpyrazole (5.0 g) and hydrochloric acid (6N: 75 ml) in glacial acetic acid (75 ml) was heated at reflux for 24 hours. The cooled reaction mixture was evaporated to low bulk and basified to pH 12 with sodium hydroxide (2N) and extracted with diethyl ether (3 x 75 ml). The ether extracts were combined and evaporated in vacuo to give a mixture of 5-amino and 5-acetamido pyrazoles in the form of a yellow gummy solid (3.5 g). This solid was dissolved in a mixture of hydrochloric acid (6N: 30 ml) and dioxan (60 ml) and heated at reflux for 48 hours. The volatiles were removed in vacuo and the residue purified by column chromatography using dichloromethane-hexane (4:1). Evaporation of the eluate containing the major component gave the title compound (1.3 g), m.p. 128-129°C, in the form of an off-white solid.

5-Amino-3-chloro-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-ethoxycarbonylpyrazole, used above, was prepared as follows:

Tertiary-butyl nitrite (15.0 g) was added dropwise to a stirred and cooled (0°C) mixture of 3,5-diamino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-ethoxycarbonylpyrazole (50.0 g) and cupric chloride (21.0 g) in acetonitrile (600 ml) over 10 minutes. The reaction mixture was stirred for 2 hours at 0°C and 2 hours at laboratory temperature then evaporated to low bulk and poured into hydrochloric acid (5N; 1500 ml). The resultant solution was extracted with dichloromethane (3 x 600 ml), washed with hydrochloric acid (2N; 2 x 600 ml), dried over anhydrous magnesium sulphate and evaporated to furnish a brown tar. The tarry material was removed from the product using a dry silica chromatography eluted with dichloromethane-hexane (4:1), further purification by column chromatography using hexane containing increasing proportions of

dichloromethane ( 60 to 80%) gave the title compound (15.8 g), m.p. 143-146.5°C, in the form of an orange solid.

3,5-diamino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-ethoxycarbonylpyrasole, used above, was prepared as follows;

Ethyl dicyanoacetate potassium salt (35.2 g) was added to a stirred suspension of 2,6-dichloro-4-trifluoromethylphenylhydrazine (40 g) in hydrochloric acid (0.9N; 220 ml) and the reaction mixture stirred and heated at reflux for 18 hours. The reaction mixture was then cooled to precipitate a solid which was filtered off, triturated with diethyl ether (250 ml) and dried to give an off-white solid (56 g) which was recrystallised from a mixture of ethyl acetate and hexane to give the title compound (29.2 g), m.p. 196-197°C, in the form of an off-white solid. Ethyl dicyanoacetate potassium salt was prepared as follows:

A solution of ethyl chloroformate (520 g) and malononitrile (330 g) in tetrahydrofuran (550

ml) was added dropwise over one hour to a stirred solution of potassium hydroxide (560 g) and water (2.0l) at a temperature below 40°C (external ice cooling). The reaction mixture was stirred at laboratory temperature for 1 hour then cooled to 0°C to precipitate a solid which was filtered off and dried over phosphorous pentoxide to give the title compound, (334.4 g) in the form of an off-white solid.

5-Amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole, used in the above Example, was prepared as follows:

A mixture of 5-amino-4-carbethoxy-3-chloro-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole (3.3 g) and hydrobromic acid (48%, 30 ml) in glacial acetic acid (50 ml) was heated at reflux for 18 hours. The mixture was evaporated to low bulk, basified with sodium hydroxide solution (1N) and the product filtered off and dried (2.9 g). Recrystallisation from a mixture of ethanol and

water gave the title compound (2.5 g), m.p. 132.5-134°C, in the form of a colourless solid.

5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-fluoropyrazole, used in the above Example was prepared as follows:

A mixture of 5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-fluoro-4-formylpyrazole (1.5 g) in methanol (40 ml) and 2N hydrochloric acid (10 ml) was heated under reflux for 24 hours. After evaporation in vacuo, water (100 ml) was added, and the mixture extracted with ethyl acetate (2 x 100 ml). The extract was washed with saturated sodium bicarbonate solution (60 ml), dried over anhydrous magnesium sulphate, and evaporated in vacuo.

Purification by chromatography eluting with dichloromethane gave the title compound, m.p. 128-129°C, in the form of a white solid.

5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-fluoro-4-formylpyrazole, used above, was prepared as

follows:

A stirred solution of 5-amino-4-cyano-(2,6-dichloro-4-trifluoromethylphenyl)-3-fluoropyrazole (preparation described in PCT Patent Publication WO 8703-781-A) (2.2 g) in dry tetrahydrofuran 940 ml) was treated at -70°C under nitrogen with a solution of diisobutylaluminium hydride (13 ml of a 1M toluene solution). The mixture was allowed to warm to room temperature over 2 hours, left overnight, and poured onto a mixture of 2N hydrochloric acid (50 ml) and ice (50 g). After stirring for 1/2 hour, toluene (25 ml) was added, and the organic layer separated. The aqueous layer was re-extracted with dichloromethane (2 x 100 ml), and the combined organic solution washed with sodium bicarbonate solution 930 ml) and dried over anhydrous magnesium sulphate. Evaporation in vacuo gave a brown solid 91.5 g), which was purified by chromatography eluting with toluene/ethyl acetate (98;2) to give the title compound 91.0

g), m.p. 137-139.5°C, in the form of a pale yellow solid.

EXAMPLE 2

Compounds Nos. 16. 17.

A mixture of anhydrous cypric chloride 91.15 g) in acetonitrile (20 ml) was stirred whilst tert-butyl nitrile (0.73 g) was added at 0°C. After 10 minutes, a solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (3.0 g) in acetonitrile (5 ml) was added at 0°C and the mixture stirred at 0°C for 2 hours, and then at room temperature overnight. After evaporation in vacuo the residue was dissolved in a mixture of dichloromethane (50 ml) and hydrochloric acid (5M; 50 ml). The organic layer was dried over anhydrous magnesium sulphate, evaporated in vacuo and then purified by chromatography, eluting with petroleum ether (b.p. 60-80°C)/dichloromethane (2:1). Recrystallisation of the resultant product from petroleum ether (b.p. 60-80°C) gave 5-chloro-3-cyano-1-(2,6-

dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (0.55 g) as a white crystalline solid, m.p. 131-132°C.

By proceeding in a similar manner but starting from 3,5-diamino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole and performing the reaction at 0°C for 2 hours and then warming to reflux temperature there was obtained:

5-Amino-3-chloro-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole, m.p. 177-179°C, inn the form of a white solid, after purification by chromatography eluting with dichloromethane, and then recrystallising from toluene/hexane.

Reference Example 2

3,5-Diamino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole, used in the above example, was prepared as follows:

Potassium carbonate (11.7 g) was added portionwise to a stirred mixture of methanesulphonylmalononitrile hydrochloride (30.0 g) in water (150 ml).

2,6-Dichloro-4-trifluoromethylphenylhydrazine (41.0 g) was then added and the mixture heated at 100°C overnight. After cooling the yellow solid was filtered, washed with water, and recrystallised from aqueous methanol. This solid was washed thoroughly with ether, yielding the title compound as a white solid (14.6 g) m.p. 224-226°C.

EXAMPLE 3

Compounds Nos. 18, 19, 20, 99.

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (4.0 g) was added to triethyl orthoformate (10.0 ml) and p-toluene/sulphonic acid (0.010 g) added.

The mixture was heated under reflux for 21 hours, cooled, and the triethyl orthoformate

evaporated in vacuo to give a brown oil as residue. This was purified by chromatography eluting with a mixture of dichloromethane and hexane (1:1). Evaporation of the eluates in vacuo gave 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethyleneamino-4-trifluoromethylthiopyrazole as a colourless solid, m.p. 70-71.5°C.

By proceeding in a similar manner but replacing the triethyl orthoformate with triethyl orthoacetate and employing toluene as co-solvent there was obtained:
3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxyethylideneamino-4-trifluoromethylthiopyrazole as a pale yellow solid, m.p. 71-73°C.

By proceeding in a similar manner but replacing the 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole by 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole, and by employing

triethyl orthoformate and toluene, there was obtained:

3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethyleneamino-4-methanesulphonylpyrazole, m.p. 145-147°C, in the form of a cream solid.

By proceeding in a similar manner there was prepared from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphonylpyrazole and triethyl orthoformate and in the absence of toluene as co-solvent:

3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethyleneamino-4-trifluoromethylsulphonylpyrazole, m.p. 118.6-119.8°C, in the form of a white solid, and after recrystallisation from hexane.

EXAMPLE A

Compounds Nos. 21, 22, 23, 24, 96.

To a stirred solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-

trifluoromethylthiopyrasole (4.0 g) and acetyl chloride (2.3 g) in acetonitrile 940 ml) at 0°C was added pyridine 91.3 ml) dropwise. The yellow solution was warmed to room temperature during 45 minutes and then heated under reflux for 24 hours. The cooled solution was evaporated in vacuo and the residue dissolved in dichloromethanbe (100 ml), washed with water (2 x 100 ml), dried over anhydrous magnesium sulphate and evaporated in vacuo to give a buff solid 94.2 g). This was purified by chromatography eluting with dichloromethane to gove 5-acetamido-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrasole (2.0 g) as colourless solid, m.p. 217-218°C, after recrystallisation from toluene.

By proceeding in a similar manner but replacing the acetyl chloride by propionyl chloride there was obtained the following two compounds:
3-Cyanno-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-bis(propionyl)amino-4-trifluoromethylthiopyrasole, m.p. 128-130°C, in

the form of a white crystalline solid, and 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-propionamido-4-trifluoromethylthiopyrazole, m.p. 176.5-182°C, in the form of a pale yellow solid.

By proceeding in a similar manner, but replacing the 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole by 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole, there was obtained: 5-Acetamido-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole, m.p. 220-222°C, in the form of a cream solid.

By proceeding in a similar manner there was obtained -5-acetamido-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphinylpyrazole, m.p. 206-211°C, in the form of a white solid, from 5-amino-3-cyano-1-(2,6-dichloro-4-

trifluoromethylphenyl)-4-trifluoromethylsulphinylpyrazole. The reaction mixture was heated at reflux for 3 hours in this instance.

EXAMPLE 5

Compounds Nos. 25, 26, 27, 28, 29, 30, 97.

To a stirred solution of 5Øamino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (5.Ø g) in dry tetrahydrofuran (6Ø ml) stirred under nitrogen at room temperature, was added sodium hydride (Ø.36 g of an 8Ø% oil dispersion) during 1/2 hour. After a further 1/2 hour, 2 drops of 15-crown-5 followed by trimethylacetyl chloride (1.6 g) was added, and the mixture heated under reflux for 24 hours. After cooling to Ø°C a further addition of sodium hydride (Ø.15 g) followed by trimethylacetyl chloride (Ø.8 g) was made, and the mixture refluxed for another 18 hours. The mixture was cooled, poured onto water (1ØØ ml) and extracted with ether (2 x 8Ø

ml). The ether extracts were dried over anhydrous magnesium sulphate, and evaporated in vacuo to give a yellow oil (6.2 g), which was purified by chromatography eluting with petroleum ether/dichloromethane (3:2) to give 3-cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthio-5-trimethylacetamidopyrazole (0.82 g), m.p. 172.5-173.5°C, in the form of a white solid.

By proceeding in a similar manner but replacing the trimethylacetyl chloride by the appropriate acylating agents there was prepared:

3-Cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-5-bis(methoxycarbonyl)amino-4-trifluoromethylthiopyrazole, m.p. 135-136.5°C, in the form of a white solid, using methyl chloroformate.

3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-bis(ethoxycarbonyl0amino-4-trifluoromethylthiopyrazole, m.p. 83.2-86.5°C,

in the form of a white solid, using ethyl chloroformate and performing the reaction at ambient temperature.

5-Chloroacetamido-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole, m.p. 175-176°C, in the form of a white solid, using chloroacetyl chloride, and after purification by chromatography and recrystallisation from toluene/hexane.

By proceeding in a similar manner but replacing the 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl-4-trifluoromethylthiopyrazole by 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole and by the use of appropriate acylating agents, there was prepared:

3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-bis(ethoxycarbonyl)amino-4-methanesulphonylpyrazole in the form of a white

solid, m.p. 195-198°C, using ethyl chloroformate.

3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonyl-5-trimethylacetamidopyrazole in the form of a white solid, m.p. 245-247°C, using trimethylacetyl chloride.

By proceeding in a similar manner there was prepared form 5-amino-3-cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphonylpyrazole and ethyl chloroformate:-

3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-bis(ethoxycarbonyl)amino-4-trifluoromethylsulphonylpyrazole, m.p. 116-116.9°C, in the form of a white solid, after recrystallisation from toluene/hexane.

EXAMPLE 6

Compounds Nos. 31, 32, 33, 34, 35, 36, 93.

To a mixture of sodium hydride (0.71 g of an

80% oil dispersion) in dry tetrahydrofuran 930 ml) was added 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (4.0 g). After 20 minutes, 3 drips of 15-crown-5 was added and the mixture cooled to 0°C. Methyl iodide (3.4 g) was then added and the mixture stirred at 0°C for 1/2 hour, then at room temperature overnight. The solvent was evaporated in vacuo and the residue partitioned between dichloromethane (60 ml) and water (60 ml). The organic phase was dried over anhydrous magnesium sulphate, and evaporated in vacuo to give a pale yellow solid 94.29 g). Purification by chromatography eluting with dichloromethane/petroleum ether (1:1) gave 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-dimethylamino-4-trifluoromethylthiopyrazole (2.11 g), m.p. 109.5-110.8°C, in the form of a white solid.

By proceeding in a similar manner but replacing the methyl iodide by the appropriate alkyl halides there was prepared:

3-Cayno-1-92,6-dichloro-4-trifluoromethylphenyl)-5-isopropylamino-4-trifluoromethylthiopyrazole, m.p. 173-175°C in the form of a cream solid after purification by chromatography and recrystallisation from toluene/hexane, prepared from isopropyl iodide.

3-Cayno-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-propylamino-4-trilfuoromethylthiopyrazole, m.p. 162-163.5°C, in the form of a white solid, and:

3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-dipropylamino-4-trifluoromethylthiopyrazole, m.p. 72.5-73°C, in the form of a white solid, both compounds prepared using propyl bromide and performing the reaction initially at 0°C and then at 70°C.

3-Cayno-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-bis(propargyl)amino-4-trifluoromethylthiopyrazole, m.p. 86-89°C, in the form of a white solid after recrystallisation from toluene/hexane, prepared from propargyl bromide.

By proceeding in a similar manner but replacing

the 5-amino-3-cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole by 5-amino-3-cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole, and using methyl iodide asalkylating agent, there was prepared: 3-Cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-5-methylamino-4-methanesulphonylpyrazole in the form of a yellow solid, m.p. 169-172°C.

By proceeding in a similar manner but replacing the 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole by 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphinylpyrazole and employing dioxan as solvent and heating under reflux for 6 hours was obtained 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-dimethylamino-4-trifluoromethylsulphinylpyrazole, m.p. 154-161°C, in the form of a white solid.

EXAMPLE 7

Compounds Nos. 37, 38, 39, 40, 41, 95.

A suspension of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole (43.8 g) was stirred in a mixture of bromoform (141 ml) and dry acetonitrile (63 ml). tert-butyl nitrile (29.9 g) was added dropwise during 5 minutes, and the mixture heated at 60-70°C for 2.75 hours. After cooling to 25°C a further addition of tert-butyl nitrile (29.9 g) was made, and the heating resumed for 2 hours. Evaporation in vacuo gave a yellow oily solid which was triturated with hexane and filtered off. Two recrystallisation from toluene/hexane gave 5-bromo-3-cyano-1-(2,6dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole as a yellow solid (34.0 g), m.p. 136-137°C.

By proceeding in a similar manner but replacing the 5-amino-3-cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-4-

trifluoromethanesulphonylpyrazole by the following phenylpyrazoles there was obtained:

5-Bromo-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole, m.p. 161.5-164°C, in the form of a buff solid, from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole. Acetonitrile was not employed as co-solvent for this preparation.

5-Bromo-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole, m.p. 160.5-162°, in the form of a white solid, from 5-amino-3-cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole.

5-Amino-3-bromo-1-92,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole, m.p. 193-195°C, in the form of a white solid, from 3,5-diamino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole (preparation described in Reference Example 2), and by replacing the

bromoform by two equivalents of bromine and by employing chloroform as solvent.

3-Bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole in the form of white crystals, m.p. 178-180°C from 3-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole.

By proceeding in a similar manner there was obtained:-

5-Bromo-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphinylpyrazole, m.p. 147-148°C, in the form of a yellow solid. The reaction was performed at 52°C for 2 hours in this instance.

Reference Example 3

3-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole used in the Example above was prepared as follows:

A solution of 3-tert-butoxycarbonylamino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole (6.4 g) in ethanol (150 ml) was treated with 50% v/v hydrochloric acid (20 ml), and the mixture refluxed for 1 hour. The solvent was evaporated in vacuo and the residue dissolved in dichloromethane, washed with sodium bicarbonate solution, then with water, dried over anhydrous magnesium sulphate and evaporated in vacuo. The product was recrystallised from ethyl acetate/hexane to give the title compound (3.0 g) as white crystals, m.p. 222-223°C.

3-tert-Butoxycarbonylamino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole was prepared as follows:

A mixture of 3-carboxy-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole (9.4 g), and thionyl chloride (70 ml) and N,N-dimethylformamide 93 drops) was heated under reflux for 2 hours.

The solvent was evaporated in vacuo and re-evaporated in vacuo after addition of dry toluene (20 ml). The resultant solid was dissolved in dry acetone 960 ml) and stirred whilst a solution of sodium azide 92.1 g) in water (15 ml) was added during 5 minutes keeping at 10-15°C. After 30 minutes the mixture was poured onto water 9250 ml) and extracted with dichloromethane ( 3 x 80 ml). The combined extract was washed with water, dried over anhydrous magnesium sulphate, and evaporated in vacuo at equal to or below 10°C to give a fawn solid.

The resulting azide was dissolved in dry toluene (80 ml) and heated under reflux for 0.75 hour, with smooth evolution of nitrogen. After cooling, this was treated with tert-butanol (15 g), and the mixture heated under reflux for two hours. After standing overnight at room temperature and evaporation invacuo, the resulting brown semi solid (9.2 g) was purified by chromatography on silica (Merck

230-400 mesh, 6 $8Nm^{-2}$) eluting with dichloromethane and ethyl acetate (98:2) to give the title compound (5.6 g).

3-Carboxy-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole was prepared as follows:

A mixture of 1-(2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-methanesulphonylpyrazole (14.0 g) and 80% sulphuric acid (300 ml) was heated and stirred at 80°C for 4 hours. After standing at room temperature overnight, the solution was poured onto excess ice and the precipitated solid filtered off. This was dissolved in ethyl acetate, washed with water, dried (anhydrous magnesium sulphate) and evaporated to give the title compound as a buff solid (11.1 g), m.p. 215-216°C.

1-(2,6-Dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-methanesulphonylpyrazole, used above, was prepared as follows:

To a solution of 5-amino-1-(2,6-dichloro-4-trifluoroethylphenyl)-3-ethoxycarbonyl-4-methanesulphonylpyrazole (17.1 g) in dry tetrahydrofuran (130 ml) stirred at room temperature, was added during 2 minutes, tert-butyl nitrite (33 ml). The mixture was heated at reflux for 1.5 hours, the solvent evaporated in vacuo, and the residue dissolved in dichloromethane. After washing with water, drying (anhydrous magnesium sulphate), and evaporation a yellow solid was obtained. Recrystallisation from toluene=petorleum ether (b.p. 60-80°C) gave the title compound as yellow crystals (15.2 g), m.p. 183-185°C.

5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-methanesulphonylpyrazole, used above, was prepared as follows:

To absolute ethanol 920 ml) cooled in an ice-water bath was added sodium hydride (0.25 g of an 80% oil dispersion), followed by methanesulphonylacetonitrile (0.99 g) and the mixture stirred for 1/2 hour. a solution of

ethyl chloro(2,6-dichloro-4-trifluoromethylphenyl)hydrazonoacetate (3.Ø g) in absolute ethanol 92Ø ml) was then added, and stirring continued for 5 hours. The yellow solid was filtered off (2.55 g) and recrystallised from ethanol to give the title compound as a colourless solid, m.p. 255°C.

Ethyl chloro(2,6-dichloro-4-trifluoromethylphenyl)hydrazonoacetate was prepared as follows:

Sodium nitrile (3.Ø g) was added during 15 minutes to stirred concentrated sulphuric acid (24 ml) at 3Ø-5Ø°C. The solution was cooled to 2Ø°C, and added dropwise during 15 minutes to a solution of 2,6-dichloro-4-trifluoromethylaniline (9.2 g) in acetic acid (9Ø ml), maintaining at 35-4Ø°C. This solution was then cooled to +1Ø°, and added dropwise to a stirred solution of anhydrous sodium acetate (54 g) and ethyl chloroacetoacetate (7.Ø g) in a mixture of water (72 ml) and ethanol (48 ml) during 45 minutes with cooling such that the temperature was kept at 1Ø°C. After 1 hour at room

temperature the mixture was diluted with water, filtered, and the solid dissolved in dichloromethane. This solution was dried over anhydrous magnesium sulphate, filtered, and evaporated *in vacuo* to give the title compound as a white solid (11.9 g), m.p. 96-98°C.

**EXAMPLE 8**

COMPOUNDS nos. 42, 43, 44, 45.

A solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (4.0 g) in dry tetrahydrofuran (20 ml) was treated with tert-butyl nitrite (5.76 g) at room temperature. The mixture was then heated under reflux for 3 hours and evaporated in vacuo to give a yellow solid. Purification by chromatography eluting with petroleum ether/dichloromethane (2:1) gave 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (3.12 g), m.p.126.5-128°C, in the form of a white solid.

By proceeding in a similar manner but replacing the 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole by the following phenylpyrazoles, there was obtained:

3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole, m.p. 149-151°C, in the form of a white solid, from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole. The product was obtained after 29 hours heating under reflux, followed by purification by chromatography and recrystallisation from toluene/hexane.

3-Cyano-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-trifluoromethylthiopyrazole, m.p. 64-65°C, in the form of a white solid, from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-trifluoromethylthiopyrazole.

3-Cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole, m.p. 147-150°C, in the form of yellow crystals, from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole.

EXAMPLE 9

Compounds Nos. 46, 47, 48, 49, 50, 94.

To a solution of 5-amino-3-cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (8.0 g) in chloroform (50 ml) stirred at room temperature, was added iodine (3.61 g). Tert-butyl nitrite (1.43 g) was then added and after 1/2 hour the mixture was heated under reflux for 2 hours, then left at room temperature overnight. The solid was filtered off, wahed with dichloromethane (50 ml) and the combined filtrate washed with sodium thiosulphate solution (2 x 50 ml) and then with water 950 ml). After drying over anhydrous magnesium sulphate, the solution was evaporated in vacuo

to give a yellow solid (3.8 g), which was purified by chromatography eluting with petroleum ether/dichloromethane (2:1).

Recrystallisation from toluene/hexane gave 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-iodo-4-trifluoromethylthiopyrazole, m.p. 187.3-188.3°C, in the form of a white solid.

By proceeding in a similar manner but replacing the 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole by the following phenylpyrazole, there was obtained:

3-Cayno-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-iodo-4-trifluoromethylsulphonylpyrazole, m.p. 180-181°C, in the form of a white solid; from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole. In this instance the reaction mixture was heated under reflux for 24 hours.

5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-iodo-4-

methanesulphonylpyrazole, m.p. 226-227°C, in the form of a brown solid; from 3,5-diamino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole. The reaction mixture was heated under reflux for 4 1/2 hours in this case.

1-(2,6-Dichloro-4-trifluoromethylphenyl)-3-iodo-4-methanesulphonylpyrazole, in the form of a cream solid, m.p. 150-151°C, prepared from 3-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole (preparation described in Reference Example 3).

1-(2,6-dichloro-4-trifluoromethylphenyl)-3-iodo-4-trifluoromethylthiopyrazole, m.p. 80-81.5°C, in the form of a white solid, prepared from 3-amino-1-92,6-dichloro-4-trifluoromethylphenyl)-4-trilfuoromethylthiopyrazole.

The reaction was performed using dry acetonitrile as solvent and at a temperature of 0-5° initially and then at ambient temperature for 1/2 hour.

By proceeding in a similar manner there was obtained:-

3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-iodo-4-trifluoromethylsulphinylpyrazole, m.p. 165-166°C, in the form of a pale yellow solid; from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphinyl pyrazole.

**Reference Example 4**

3-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole, used in the above Example was prepared as follows:

3-Tert-Butoxycarbonylamino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (3.45 g) dissolved in dry acetonitrile (80 ml) was treated with iodotrimethylsilane (2.6 g) added dropwise under nitrogen. After stirring for 45 minutes, methanol (10 ml) was added, and after a further 15 minutes the solution was concentrated in vacuo to give a dark gum. This was dissolved

in dichloromethane (100 ml), washed with a solution of sodium sulphite 950 ml), then with water (50 ml) and dried over anhydrous magnesium sulphate. Evaporation of the dichloromethane gave the title compound (2.6 g), m.p. 130-135°C, as an off white solid.

3-tert-Butoxycarbonylamino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole used above, was prepared as follows:
1-(2,6-Dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole-3-carboxylic acid (5.6 g) was dissolved in dry N,N-dimethylformamide (50 ml) and triethylamine (1.33 g) added. After cooling to 5°C, a solution of diphenylphosphorylazide (3.63 g) in N,N-dimethylformamide (20 ml) was added. When the solution had reached ambient temperature, it was heated to 35°C for 2 1/2 hours. After evaporation in vacuo at a temperature kept below 40°C, a solution of sodium chloride (5 g) in water (100 ml) was added, and the

suspension extracted with ether (3 x 100 ml). The combined extracts were washed with water (50 ml), dried over anhydrous magnesium sulphate and evaporated to give 1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole-3-carboxylic acid azide (5.4 g). a solution of this in dry toluene (200 ml) was heated under reflux with stirring for 1.5 hours, tert-butanol (35 ml) was added, and reflux continued fro 4 hours. After evaporation in vacuo the residue was purified by chromatography eluting with dichloromethane to give the title compound 93.3 g) as an off-white solid, m.p. 122-125°C.

1-(2,6-Dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole-3-carboxylic acid used above, was prepared as follows:

A solution of sodium hydroxide 91.73 g) in water (50 ml) was added to a suspension of 1-(2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-trifluoromethylthiopyrazole

(6.8 g) in ethanol (70 ml), and the mixture heated under reflux for 1 1/2 hours. The solvent was evaporated in vacuo, water (250 ml) added, followed by concentrated sulphuric acid to pH1. The product was filtered off, washed with water (100 ml) and dried at 120°C in vacuo giving the title compound (5.7 g) as a grey solid, m.p. 175-177°C.

1-(2,6-Dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-trifluoromethylthiopyrazole used above, was prepared by following the procedure of Example 8 by replacing the 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole by 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-trifluoromethylthiopyrazole. The title compound was obtained as an off white solid, m.p. 125.5-126°C.

5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-trifluoromethylthiopyrazole used above, was prepared by the procedure described in Example

1, and obtained in the form of a white solid, m.p. 213-214°C after purification by chromatography; from 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonylpyrazole

5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonylpyrazole was prepared as follows:

A solution of 3-cyano-3-cyan-2-hydroxyprop-2-enoic acid ethyl ester sodium salt (50.0 g) [C.A. 57:16604d N.S. Nelson et al] in cold water (9500 ml) was stirred whilst cold sulphuric acid (2N) was added to pH1. The solution was extracted with ether (2 x 400 ml) and the extract washed with water (200 ml), dried over anhydrous magnesium sulphate, and evaporated in vacuo to give a yellow oil (28.4 g). a solution of this in ethanol (400 ml) was treated with 2,6-dichloro-4-trifluoromethylphenylhydrazine (51.1 g), and the solution heated under reflux overnight. After cooling, the solution was evaporated in

vacuo to give an orange solid. Recrystallisation from toluene/hexane gave the title compound as a fawn solid (40.2 g). m.p. 179-181°C.

EXAMPLE 10

Compounds Nos. 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 91.

A partial solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (48.0 g) in chloroform (600 ml) was stirred mechanically and treated with m-chloroperbenzoic acid (61.4 g). The mixture was stirred and heated under reflux in an atmosphere of nitrogen for 3.5 hours. After cooling, an additional amount of m-chloroperbenzoic acid (12.3 g) was added, and reflux continued for 1 hour. The cooled mixture was diluted with ethyl acetate (600 ml), washed with a solution of sodium metabisulphite (2 x 250 ml), then with sodium hydroxide solution (2 x 250 ml) and finally with water (1 x 500 ml). the organic layer was

dried over anhydrous magnesium sulphatem filtered, and evaporated in vacuo to give a fawn solid.

Recrystallisation from toluene/hexane/ethyll acetate gave 5-amino-3-cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole as white crystals (37.Ø g) m.p. 219-221.5°C.

A stirred solution of 5-amino-1-cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (1Ø.Ø g) in dichloromethane (1ØØ ml) was treated with m-chloroperbenzoic acid (4.6 g). After stirring overnight additional m-chloroperbenzoic acid (1.6 g) was added in 2 portions, and left for 2 days. The reaction product was diluted with ethyl acetate (3Ø ml) and then washed in turn with sodium sulphite solution (5Ø ml), sodium carbonate solution 95Ø ml) and with water 95Ø ml). After drying over magnesium sulphate, this was filtered and evaporated in vacuo. Purification by chromatography on silica

eluting with dichloromethane gave 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphinylpyrazole as a white solid 96.0 g), m.p. 200.5-201°C.

By proceeding in a similar manner and by replacing the abovementioned phenylpyrazoles by the appropriate phenylpyrazoles there was prepared:

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-trifluoromethane-sulphonylpyrazole, m.p. 210-211.5°C, in the formof a white solid, and

5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethoxyphenylØ-4-trifluoromethylsulphinylpyrazole, m.p. 179-180°C, in the form of a white solid.

Both of the above two compounds being prepared from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-trifluoromethylthiopyrazole by the use of an appropriate quantity of m-chloroperbenzoic

acid.

3-Cyano-1-92,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphinylpyrazole, m.p. 142.5-144.2°C, in the form of a white solid, from 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole and by performing the reaction at 40-50°C for 20 hours.

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-91-methylprop-2-ynylsulphinyl)pyrazole, 136.6-137.2°C, in the form of a white solid, from 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-(1-methylprop-2-ynylthio)pyrazole.

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylsulphinylpyrazole, m.p. 176-177°C, in the form of a fawn crystalline solid, prepared from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylthiopyrazole.

5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-

isopropylsulphinylpyrazole, m.p. 187-188°C, in the form of a white solid; prepared from 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-isopropylthiopyrazole.

5-amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphinybdpyrazole, m.p. 179-180°C, in the form of a white solid; prepared from 5-amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole.

5-amino-4-tert-butanesulphonyl-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole, m.p. 183-184°C, in the form of a pale yellow solid; prepared from 5-amino-4-tert-butylthio-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole employing 2 molar equivalents of m-chloroperbenzoic acid in chloroform and at room temperature for 4 hours.

By proceeding in a similar manner there was prepared:-

5-Amino-3-chloro-1-(2,6-dichloro-4-

trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole, m.p. 162-164°C, in the form of a white solid, from 5-amino-3-chloro-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole.

3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-propylamino-4-trifluoromethanesullphonylpyrazole, m.p. 49-65°C in the form of a yellow solid; prepared from 3-cyano-1-(2,6-dichlord-4-trifluoromethylphenyl)-5-propylamino-4-trifluoromethylthuopyrazole at room temperature.

5-Acetamido-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole, m.p. 174-175.9°C, in the form of a white solid; prepared from 5-acetamido-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole employing 2 mols equivalents of m-chloroperbenzoic acid and heating under reflux in chloroform for 20

hours.

EXAMPLE 11

Compounds Nos. 63, 64.

Trifluoroacetic anhydride (6.0 ml) was added dropwise during 15 minutes to a stirred mixture of 85% hydrogen peroxide (0.96 ml) in dichloromethane (20 ml) at 0-10°C. The mixture was warmed to 20°C for 5 minutes, and a suspension of 3-amino-1-92,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole (2.0 g) in dichloromethane (20 ml) was added during 5 minutes. The solution was then heated under reflux for 1 hour and left at room temperature overnight. This was poured onto water (100 ml) and the organic layer washed in turn with sodium metabisulphite solution (30 ml) and sodium bicarbonate solution (30 ml), and then dried over anhydrous magnesium sulphate. Evaporation in vacuo gave, after recrystallisation from dichloromethane/toluene/hexane, 1-(2,6-

dichloro-4-trifluoromethylphenyl)-4-methanesulphonyl-3-nitropyrazole. m.p. 190-192°C, in the form of a white solid.

By proceeding in a similar manner but replacing the 3-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole by 3,5-diamino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole there was prepared: 5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonyl-3-nitropyrazole in the form of a cream solid, m.p. 190-192°C. The oxidation was performed initially at Ø°C and then warmed to room temperature for 1.5 hours. Purification by chromatography eluting with dichloromethane, and recrystallisation from toluene was necessary in this case.

EXAMPLE 12

Compound No. 85.

A stirred mixture of 85% hydrogen peroxide

(Ø.31 g) and dichloromethane (2Ø ml) was treated with trifluoroacetic anhydride (2.1 g) dropwise at -1Ø°C. After 15 minutes the mixture was allowed to reach room temperature, and stirred for a further 15 minutes. After re-cooling to Ø°C, a solution of 3-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (1.Ø g) [preparation described in Reference Example 4] in dichloromethane (2Ø ml) was added, and the solution allowed to warm to room temperature. After 2 hours, an additional quantity of trifluoroperacetic acid [prepared as above using 85% hydrogen peroxide (Ø.31 g); dichloromethane (3Ø ml) and trifluoroacetic anhydride (2.1 g)] was added. The mixture was stirred overnight, then poured onto water 95Ø ml), and the dichloromethane layer washed in turn with 5% sodium sulphite solution (3Ø ml), sodium bicarbonate solution (3Ø ml) and with water (3Ø ml). This soslution was then dried over anhydrous magnesium sulphate, and evaporated <u>in vacuo</u> to gice a green gum (Ø.8

g). Purification by chromatography eluting with dichloromethane/hexane (3:2) gave 1-(2,6-dichloro-4-trifluoromethylphenyl)-3-nitro-4-trifluoromethylsulphinylpyrazole (Ø.3 g), m.p. 124-130°C, in the form of a pale grren solid.

EXAMPLE 13

Compounds Nos. 66, 67.

Phosphorus oxychloride 920 ml) was added to 5-amino-1-(2-bromo-6-chloro 4-trifluoromethylphenyl)-3-carbamoyl-4-methanesulphonylpyrazole (4.Ø g) and the solution heated at 50-60°C for 3.25 hours, and left at room temperature overnight. The mixture was cautiously added to vigorously stirred water (200 ml), and the precipitated solid collected and dried in vacuo. Recrystallisation from toluene/ethanol gave 5-amino-1-(2-bromo-6-chloro-4-trifluoromethylphenyl)-3-cyano-4-methanesulphonylpyrazole as buff crystals, m.p. 235-238°C.

By proceeding in a similar manner to that described above but replacing the 5-amino-1-(2-bromo-6-chloro-4-trifluoromethylphenyl)-3-carbamoyl-4-methylsulphonylpyrazole by 5-amino-3-carbamoyl-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-methanesulphonylpyrazole there was obtained: 5-Amino-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-3-cyano-4-methanesulphonylpyrazole in the form of a white solid, m.p. 202.5-203.5°C.

Reference Example 5

5-Amino-3-carbamoyl-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-methanesulphonylpyrazole, used above, was prepared as follows:
suspension of 5-amino-3-carboxy-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-methanesulphonylpyrazole (40.0 g) in toluene (160 ml) was treated with thionyl chloride (150 ml) and the mixture heated under reflux with stirring for 3 hours. The solution was

evaporated in vacuo and re-evaporated after addition of toluene (100 ml). The resultant acid chloride was dissolved in tetrahydrofuran (200 ml) and this solution added dropwise during 15 minutes to stirred ammonia solution (300 ml), with cooling at 5-10°C throughout. After standing overnight water (250 ml) was added and the solution extracted with ethyl acetate (2 x 100 ml). The combined extract was washed with water (2 x 250 ml), dried over anhydrous magnesium sulphate, and evaporated in vacuo to give a solid (34.9 g). The title compound (19.3 g) was obtained in the form of a white solid, m.p. 219-220°C, after recrystallisation from ethyl acetate/hexane.

By proceeding in a similar manner but replacing the 5-amino-3-carboxy-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-methanesulphonylpyrazole by 5-amino-1-(2-bromo-6-chloro-4-trifluoromethylphenyl)-3-carboxy-4-methanesulphonylpyrazole there was obtained:

5-Amino-1-(2-bromo-6-chloro-4-trifluoromethylphenyl)-3-carbamoyl-4-methanesulphonylpyrazole, m.p. 250-253°C, in the form of a grey-brown powder.

5-Amino-3-carboxy-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-4-methanesulphonylpyrazole, used above, was prepared by using the method employed to prepare 3-carboxy-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole by replacing the 1-(2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-methanesulphonylpyrazole (Reference Example 3) by 5-amino-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-3-ethoxycarbonyl-4-methanesulphonylpyrazole. It was obtained in the form of a white solid, m.p. 195-196°C.

5-Amino-1-(2-bromo-6-chloro-4-trifluoromethylphenyl)-3-carboxy-4-methanesulphonylpyrazole, used above, was prepared as follows:

5-Amino-1-(2-bromo-6-chloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-methanesulphonylpyrazole (8.0 g) was heated under reflux with 48% hydrobromic acid (75 ml) in acetic acid (75 ml) for 3 hours. After cooling overnight, this was evaporated in vacuo, and the residue triturated with aqueous sodium bicarbonate. The title compound was obtained as a grey powder (6.6 g), m.p. 130-133°C, after drying in vacuo.

5-Amino-1-(2,6-dichloro-4-trifluoromethoxyphenyl)-3-ethoxycarbonyl-4-methanesulphonylpyrazole, used above, was prepared by the procedure of Reference Example 3 by replacing ethyl chloro (2,6-dichloro-4-trifluoromethylphenyl)hydrazonoacetate by ethyl chloro (2,6-dichloro-4-trifluoromethoxyphenyl)-hydrazonoacetate. It was obtained in the form of a light brown solid, m.p. 207°C.

5-Amino-1-(2-bromo-6-chloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-methanesulphorylpyrazole, used above, was

prepared similarly from ethyl chloro (2-bromo-6-chloro-4-trifluoromethylphenyl)hydrazonoacetate. It was obtained as a white solid, m.p. 255.5-256.5°C.

Ethyl chloro (2,6-dichloro-4-trifluoromethoxyphenyl)hydrazonoacetate, used above, was prepared by the procedure of Reference Example 3 by replacing 2,6-dichloro-4-trifluoromethylaniline by 2,6-dichloro-4-trifluoromethoxyaniline, and was obtained as a brown solid, m.p. 55-58°C.

Ethyl chloro(2-bromo-6-chloro-4-trifluoromethylphenyl)hydrazonoacetate, used above, was prepared similarly from 2-bromo-6-chloro-4-trifluoromethylaniline, and was obtained as abuff solid, m.p. 116.5-117.5°C.

EXAMPLE 14

Compound No. 68.

A solution of sodium ethoxide prepared from sodium (0.36 g) and absolute ethanol (50 ml) was treated at room temperature with methanesulphonyl acetonitrile (1.88 g) and

stirred for 1 hour. To this was then added dropwise with stirring, a solution of 1-chloro-1-(2,6-dichloro-4-trifluoromethylphenyl)-hydrazonopropen-2-one (5.Ø g) in ether (5Ø ml). After stirring overnight the solution was diluted with water (1ØØml), extracted with ether (3 x 5Ø ml), and the combined ethereal extracts dried over anhydrous magnesium sulphate, and evaporated in vacuo to give a brown solid. Recrystallisation from toluene/hexane gave 3-acetyl-5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole (2.66 g) in the form of a buff solid, m.p. 176.7-178.9°C.

1-Chloro-1-(2,6-dichloro-4-trifluoromethylphenyl)hydrazonopropan-2-one, used above, was prepared by the procedure described in Reference Example 3, but replacing the ethyl chloroacetoacetate by 3-chloropentan-2,4-dione. It waas obtained in the form of a light brown solid, m.p. 77-79°C, after recrystallisation from petroleum ether b.p. 6Ø-8Ø°C.

EXAMPLE 15

Compounds Nos. 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 100.

A solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-thiocyanatopyrazole (3.1 g) in methanol (50 ml) was stirred under nitrogen nitrogen at 7°C and methyl iodide (5.25 ml) added. A solution of potassium hydroxide (0.92 g) in water (15 ml) was then added dropwise during 10 minutes, keeping the mixture below 8°C. After stirring at room temperature for 3 hours, the mixture was neutralised by the addition of carbon dioxide pellets, followed by water (150 ml). The precipitated solid was filtered off, and recrystallised from toluene/hexane (2:1). 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylthiopyrazole was obtained as a brown crystalline solid 91.84 g), m.p. 170-172°C.

By proceeding in a similar manner but replacing the methyl iodide by the following alkyl

halides there was obtained:

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-ethylthiopyrazole in the form of a yellow solid, m.p. 158-160°C, by using ethyl iodide and aqueous ethanol as solvent.

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-propylthiopyrazole in the form of a pale brown solid, m.p. 123-124°C, by using propyl bromide and aqueous dioxan as solvent.

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-isopropylthiopyrazole in the form of a pale brown solid, m.p. 168-169°C by using isopropyl bromide and aqueous isopropyl alcohol as solvent.

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-(2-methylpropylthio)pyrazole in the form of a pale brown solid, m.p. 134-137°C, by using 1-iodo-2-methylpropane and aqueous dioxan as solvent.

5-Amino-3-cyano-1-(2,6-dichloro-4-

trifluoromethylphenyl)-4-(1-methylpropylthio_pyrazole in the form of a pale brown solid, m.p. 152.5-154°C, by using 2-iodobutane and aqueous dioxan as solvent. The product was purified by dry column chromatography on silica eluting with hexane/diethylether (1:1).

4-Allylthio-5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole in the form of a pale brown solid, m.p. 140-141°C, by using allyl bromide and aqueous dioxan as solvent. The product was purified by chromatography eluting with hexane/diethyl ether (1:1), followed by recrystallisation from toluene.

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-(prop-2-ynylthio)pyrazole in the form of a brown solid, m.p. 162-263°C, by using propargyl bromide and aqueous methanol as solvent.

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-(1-methylprop-2-ynylthio)pyrazole in the form of a white solid,

m.p. 134-135.6°C, by using 3-bromobut-1-yne and aqueous meethanol as solvent. The product was purified by chromatography eluting with diethyl ether/hexane (1:1), followed by recrystallisation from toluene/hexane.

5-Amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylthiopyrazole in the form of a white solid, m.p. 117-119°C, by using methyl iodide and aqueous methanol as solvent. The product was purified by chromatography eluting with dichloromethane.

By proceeding in a similar manner there was prepared:

5-Amino-4-(2-chloro-1,1,2-trifluoroethylthio)-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole, m.p. 116-118°C, in the form of a white solid, by using chlorotrifluoroethylene and aqueous dioxan as solvent. The product was purified by chromatography eluting with dichloromethane, and subsequent recrystallisation from toluene/hexane (3:10).

Reference Example 6

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-thiocyanatopyrazole

used above was prepared as follows:

A suspension of potassium thiocyanate (4.09 g) in methanol (75 ml) was stirred at -78°C. Bromine (0.8 ml) dissolved in methanol (10 ml) was then added dropwise during 25 minutes. After a further 20 minutes, a solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole (5.0 g) in methanol (50 ml) was then added over 30 minutes. The mixture was stirred at -78°C and then allowed to warm to room temperature for 3 hours, before pouring onto water (250 ml). The precipitated solid was filtered off, washed with water, and recrystallised from toluene/hexane to give the title compound (3.1 g) as a white solid, m.p. 179-182°C.

proceeding in a similar manner but replacing the 5-amino-3-cyano-1-(2,6-dichloro-4-

trifluoromethylphenyl)pyrazole in the above Reference Example by 5-amino-3-bromo-1-92,6-dichloro-4-trifluoromethylphenyl)pyrazole, there was obtained

5-Amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl) 4-thiocyanatopyrazole in the form of a white solid, m.p. 162-163.5°C, after purification by chromatography, eluting with dichloromethane. The preparation of 5-amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole, used above, is described in Reference Example 1.

EXAMPLE 18

Compound No. 479

To a stirred solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-thiocyanatopyrazole (5.0 g) in dry diethyl ether (70 ml) at 0°C under an atmosphere of nitrogen, was added dropwise a solution of tert-butylmagnesium chloride (7.92 ml of a 2M solution in dry ether). The solution was then

allowed to reach room temperature, and the stirring continued for 3 hours. Water (40 ml) was then added and the mixture stirred for 15 minutes. The ethereal layer was separated, washed with water (50 ml), dried over anhydrous magnesium sulphate, and evaporated in vacuo to give a brown solid. Purification by chromatography eluting with dichloromethane:diethyl ether (3:1) gave 5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-tert-butylthiopyrazole (2.62 g), m.p. 195-198.5°C, in the form of a pale yellow solid.

EXAMPLE 17

Compounds Nos. 30, 81.

A solution of 5-amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylthiopyrazole (2.8 g) [preparation described in Example 15] in methanol (45 ml) at -25°C was treated with a rapidly added solution of potassium hydrogen persulphate (1.66 g), followed immediately by

the addition of water (2% ml). The mixture was stirred for 30 minutes at 0°C, and potassium hydrogen persulphate (0.4 g) added. After 2 1/2 hours stirring at room temperature, the mixture was poured onto water (300 ml) and saturated sodium bisulphite solution (35 ml) added. This was extracted with dichloromethane (2 x 150 ml) and the extract washed with water (2 x 50 ml), dried over anhydrous magnesium sulphate, and evaporated in vacuo. The crude product was purified by chromatography eluting with dichloromethane/ethyl acetate (4:1) to give 5-amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylsulphinylpyrazole (0.9 g) as a white solid, m.p. 135-136°C.

By proceeding in a similar manner but replacing the 5-Amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylthiopyrazole by 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-ethylthiopyrazole and by utilising an appropriate quantity of potassium hydrogen persulphate there was

obtained:

5-Amino-3-cyano-1-(2,6-dichloro-4-triflouromethylphenyl)-4-ethanesulphonylpyrazole in the form of a yellow solid, m.p. 180-183°C. In this case the reaction mixture was kept at room temperature for 20 hours, and gave the title compound without chromatographic purification.

EXAMPLE 18

Compound No. 82.

A solution of 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethyleneamino-4-trifluoromethylthiopyrazole (1.7 g) in methanol (30 ml) was stirred, and sodium borohydride (1.08 g) added portionwise. The solution was allowed to reach room temperature, and after a further 7 hours was poured onto water (200 ml). This was extracted with dichloromethane (3 x 50 ml), dried over anhydrous magnesium sulphate, and evaporated in vacuo to give a white solid (1.4 g).

Purification by chromatography eluting with dichloromethane/petroleum ether (4:1) gave 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methylamino-4-trifluoromethylthiopyrazole (Ø.42 g) in the form of a white solid, m.p. 2Ø8.5-2Ø9.5°C.

EXAMPLE 19

Compound No. 83.

To a solution of 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxycarbonylamino-4-trifluoromethylthiopyrazole (1.Ø g) in dry tetrahydrofuran (2Ø ml) was added sodium hydride (Ø.Ø95 g) with stirring at Ø-1Ø°C. After stirring at room temperature for 2 1/2 hours, methyl iodide (Ø.6 g) was added dropwise with cooling at Ø-1Ø°C, and the mixture stirred overnight. Additional methyl iodide (Ø,6 g) was added and stirring continued for 8 1/2 hours. The solution was poured onto water (1ØØ ml) and extracted with dichloromethane (2 x 5Ø ml). The extracts were dried over anhydrous magnesium sulphate and evaporated <u>in vacuo</u> to

give 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-(N-ethoxycarbonyl-N-methyl)amino-4-trifluoromethylthiopyrazole (0.61 g), m.p. 86.2-86.5°C, in the form of a white solid.

EXAMPLE 20

Compound No. 84.

A mixture of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (3.0 g) and trifluoroacetic anhydride (15.0 g) in tetrahydrofuran (25 ml) was heated under reflux for 6 hours. After standing overnight the mixture was evaporated in vacuo, dissolved in dichloromethane (50 ml) and washed with sodiumbicarbonate solution (50 ml) and with water 950 ml). The solution was dried over anhydrous magnesium sulphate and evaporated in vacuo to give a brown oil (2.9 g). Trituration with hexane then gave 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-trifluoroacetamido-4-trifluoromethylthiopyrazole (1.86 g), m.p.

138.2-139.8°C, in the form of a white solid.

EXAMPLE 21

Compounds Nos. 85, 98.

A solution of 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-bisethoxycarbonyl)amino-4-trifluoromethylthiopyrazole (1.8 g) in ethanol (20 ml) was treated with a saturated solution of sodium bicarbonate (20 ml), and the mixture heated under reflux for 1 1/2 hours. After evaporation in vacuo the yellow oil was distributed between dichloromethane (70 ml) and water (70 ml). The aqueous layer was re-extracted with dichloromethane (50 ml) and the combined organicsolution dried over anhydrous magnesium sulphate, and evaporated in vacuo. Trituration with hexane then gave 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxycarbonylamino-4-trifluoromethylthiopyrazole (1.23 g), m.p. 108.7-109.7°C, in the form of a white solid.

By proceeding in a similar manner there was prepared from 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-bis(ethoxycarbonyl)amino-4-trifluoromethylsulphonylpyrazole:

3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxycarbonylamino-4-trifluoromethylsulphonylpyrazole, m.p. 112.4-113°C, in the form of a white solid, and after purification by chromatography eluting with dichloromethane/hexane (1:1).

EXAMPLE 22

Compound No. 86

To a solution of 1-(2,6-dichloro-4-trifluoromethylphenyl)-3-(1-hydroxyethyl)-4-trifluoromethylthiopyrazole (1.1 g) in dichloromethane (40 ml) was added pyridinium chlorochromate (0.62 g), and the mixture stirred at room temperature overnight. Ether (50 ml) was added and the mixture filtered diatomaceous earth. Evaporation of the filtrate in vacuo gave a brown solid, which was

triturated with hexane and filtered. The filtrate was evaporated in vacuo to give a yellow solid, which recrystallised from cyclohexane to give 3-acetyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (Ø.4 g) in the form of a yellow solid, m.p. 89-91°C.

Reference Example 7

1-(2,6-Dichloro-4-trifluoromethylphenyl)-3-(1-hydroxyethyl)-4-trifluoromethylthiopyrazole used in the above Example was prepared as follows:

A stirred solution of 1-(2,6-dichloro-4-trifluoromethylphenyl)-3-formyl-4-trifluoromethylthiopyrazole (1.64 g) in dry ether (2Ø ml) was treated with a solution of methyl magnesium iodide (1.35 ml of a 3M solution in ether) added dropwise during 5 minutes under nitrogen. The solution was then heated under reflux for 1 1/2 hours, after which time it was cooled and treated with an additional portion of methyl magnesium iodide

solution (0.2 ml) in the same manner as before. After another 1 hour of reflux, the mixture was poured onto excess ice and dilute hydrochloric acid (100 ml) and extracted with ether (2 x 50 ml). The extract was washed with sodium bicarbonate solution (50 ml), and with water (50 ml) and dried over anhydrous magnesium sulphate. Evaporation in vacuo gave the title compound (1.46 g), in the form of a yellow oil.

EXAMPLE 23

Compound No. 87

A stirred solution of 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (2.03 g) in dry tetrahydrofuran (20 ml) was treated with a solution of diisobutyl aluminium hydride (10 ml of a 1.0M solution in toluene) which was added dropwise under nitrogen at -60 to 70°C during 10 minutes. The solution was allowed to warm to room temperature for 3 hours and then at -10°C overnight. After pouring onto ice and 2N sulphuric acid (100 ml) and stirring for 1/2

hour, the mixture was extracted into dichloromethane (3 x 25 ml). The extract was washed with water (50 ml), dried over anhydrous magnesium sulphate, and evaporated *in vacuo* to give a yellow oil 1.8 g). Purification by chromatography eluting with dichloromethane/hexane (1:1) gave 1-(2,6-dichloro-4-trifluoromethylphenyl)-3-formyl-4-trifluoromethylthiopyrazole 91.5 g) in the formm of a white solid, m.p. 79-81°C.

EXAMPLE 24

Compound No. 88

A solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (2.0 g) in formic acid (90%, 50 ml) was heated under reflux with Raney nickel (2.0 g), cooled and heating continued for 5 hours after a further addition of Raney nickel (2.0 g). The filtered mixture was diluted with water (250 ml) and extracted with dichloromethane (4 x 50 ml). The extract was washed with sodium bicarbonate solution (2

x 50 ml), dried over anhydrous magnesium sulphate, and evaporated in vacuo to give a solid (1.0 g). Purification by chromatography eluting with dichloromethane gave 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-formyl-4-trifluoromethylthiopyrazole (0.05 g), m.p. 140-143°C, in the form of yellow crystals, after recrystallisation from toluene/hexane.

EXAMPLE 25

Compound No. 82

A mixture of dry sulpholane 915 ml) and 4A molecular sieve (3.0 g) was stirred under nitrogen with caesium fluoride 92.4 g) at 60°C for 1/2 hour. To this was added 5-bromo-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulphonylpyrazole (2.0 g) and the mixture stirred at 60°C for 2 hours, and left overnight at room temperature. This was diluted with ether 950 ml), filtered, and washed with water (100 ml). The aqueous layer was re-extracted with ether (3 x 50 ml) and the combined organic solution re-washed with water

(4 x 50 ml), dried over anhydrous magnesium sulphate, and evaporated in vacuo to give an oil. Purification by chromatography, eluting with ether/hexane (1:4) gave 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-fluoro-4-trifluoromethanesulphonylpyrazole (0.17 g), m.p. 95-98°C, in the form of a white solid, after recrystallisation from hexane.

EXAMPLE 28

Compound No. 92

A solution of pentafluoroethyl iodide (5.0 g) in dry ether 930 ml) was stirred at -78°C, whilst a solution of phenylmagnesium bromide (0.02 mol) in dry ether (20 ml) and a separate solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-thiocyanatopyrazole (7.6 g) in dry ether (75 ml) were added simultaneously dropwise during 2.5 hours. The mixture was allowed to reach room temperature, and after a further 0.5 hour, was treated with a solution of hydrochloric acid 92M, 15 ml) at 0°C. The ethereal layer was dried over

anhydrous magnesium sulphate, and evaporated in vacuo to give a brown gum (8.8 g). Purification by dry column flash chromatography eluting with dichloromethane/petroleum ether (1:1) gave 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-pentafluoroethylthiopyrazole, m.p. 134.5-136.5°C, in the form of a yellow solid.

EXAMPLE 27

Compound No. 101

To a solution of 5-bromo-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulphonylpyrazole (1.5 g) in dioxan (20 ml) there was added 1,1-dimethylhydrazine (0.62 g) and the mixture heated to 60°C for 4.25 hours. After pouring onto water (20 ml) the aqueous layer was extracted with dichloromethane (2 x 50 ml) and this extract combined with the dioxan layer, washed with water (1 x 50 ml) dried over anhydrous magnesium sulphate, and evaporated

in vacuo to give a solid 31.4 g). Purification by chromatography eluting with dichloromethane/hexane (1:1) gave 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-dimethylamino-4-trifluoromethylsulphonylpyrazole (0.35 g), m.p. 178-179°C, in the form of a white solid.

EXAMPLE 28

Compounds Nos. 1, 13 and Intermediate in Reference Example 4

To a stirred solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole (2.23 g) and pyridine (0.6 g) in chloroform (50 ml) was added dropwise at 0°C, a solution of trifluoromethylsulphenyl chloride (1.24 g) in chloroform (10 ml) during 20 minutes. The mixture was stirred at 0°C for 3 hours, and the solvent evaporated in vacuo to give a yellow solid (3.1 g). This was purified by chromatography on silica (Merck, 230-400 mesh,

Ø.7 $kgcm^{-2}$) eluting with dichloromethane and petroleum ether b. 4Ø-6Ø°C (3:1) to give 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-cyano-4-trifluoromethylthiopyrazole in the form of a white solid 92.33 g), m.p. 169.5-17Ø.5°C.

By proceeding in a similar manner to thatdescribed above but replacing the' 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-cyanopyrazole by the following phenylpyrazoles there was obtained:-

5-Amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole in the form of a colourless solid, m.p. 154.5-156°C, from 5-amino-3-bromo-1-(2,6-dichloro-4-trifluoromethylphenyl)pyrazole.

5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole-3-carboxylic acid ethyl ester in the form of a white solid, m.p. 213-215°C from 5-amino-1-92,6-dichloro-4-

trifluoromethylphenyl)-3-ethoxycarbonylpyrazole.

5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonylpyrazole used in the above example was prepared as follows:-

A solution of 3-cyano-1-hydroxyprop-2-enoic acid ethyl ester sodium salt (50.0 g) in cold water (500 ml) was stirred and acidified to pH 1 with cold dilute sulphuric acid. Sodium chloride (50 g) was added and the solution extracted with ether (2 x 200 ml). This extract was washed with water (250 ml), dried (anhydrous magnesium sulphate), and evaporated to give a yellow liquid (30.2 g). This was dissolved in ethanol (400 ml) and stirred whilst 2,6-dichloro-4-trifluoromethylphenylhydrazine (52.5 g) was quickly added. The solution was then heated under reflux overnight, cooled, and evaporated in vacuo to give an orange solid. After trituration with hexane (300 ml), the filtered

solid was recrystallised from toluene-hexane with charcoaling to give the title compound (43.4 g), m.p. 177-179°C as buff crystals.

REFERENCE EXAMPLE 8

A solution of 2,6-dichloro-4-trifluoromethylphenylhydrazine (10.1 g) in tetrahydrofuran (50 ml) was stirred at room temperature, and potassium carbonate (anhydrous, 8.5 g) added. To this was added, dropwise at 0°C, a solution of 2-chloro-3-cyano-3-(1-methyl)ethylsulphonylprop-2-enoic acid ethyl ester (11.0 g) in tetrahydrofuran (100 ml). After stirring for 2 hours, the mixture was filtered, and the filtrate evaporated in vacuo to give a brown oil. After trituration with hexane (100 ml) this gave an off white solid (11.7 g). After refluxing this in ethanol and cooling there was obtained 5-amino-1 (2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-(1-methyl)ethylsulphonyl pyrazole (8.5 g), m.p. 255.5-256.5°C as white crystals.

REFERENCE EXAMPLE 9

2-Chloro-3-cyano-3-(1-methylØethylsulphonylprop-2-enoic acid ethyl ester used above was prepared as follows:-

3-Cyano-2-hydroxy-3-(1-methyl)ethylsulphonylprop-2-enoic acid ethylester sodium salt (1Ø.Ø g) was added to the stirred phosphorous oxychloride (28.5 g) at room temperature. After 3 hours the mixture was heated at 5Ø°C for 1 hours, and then evaporated in vacuo. The residue was re-evaporated after addition of toluene to give the title compound as a brown oil.

3-Cyano-2-hydroxy-3-(1-methyl)ethylsulphonylprop-2-enoic acid ethyl ester sodium salt was prepared as follows:-

A solution of sodium ethoxide, prepared from sodium (4.Ø g) and ethanol (8Ø ml) was treated with propane-2-sulphonylacetonitrile (24.5 g) with stirring. After complete dissolution diethyl oxalate (21.8 g) was added

dropwise over 10 minutes giving a heavy precipitate. After heating under reflux for 1 hour, the yellow solid was filtered, washed with hexane, and dried in a vacuum dessicator (41.3 g). This was the title compound, m.p. 195-197.6°C.

EXAMPLE 28

Compounds Nos. 58 and 62 and an Intermediate for No. 62

By proceeding in a similar manner to that described below but replacing [illegible] 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylthio-3-trifluoromethylpyrazole by the following phenylpyrazoles, there was obtained:-

5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-trifluoromethylsulphinylpyrazole as an off white solid, m.p. 210-214°C from 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-

trifluoromethylthiopyrazole.

5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-bromo-4-trifluoromethylsulphinylpyrazole in the form of an white solid, m.p. 179-180°C from 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-bromo-4-trifluoromethylthiopyrazole.

5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-cyano-4-trifluoromethylsulphinylpyrazole in the form of white solid, m.p. 203-203.5°C from 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-cyano-4-trifluoromethylthiopyrazole.

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A stirred solution of 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylthio-3-trifluoromethylpyrazole (1.0 g) in chloroform (40 ml) was treated with m-chloroperbenzoic acid (0.42 g), portionwise at room temperature.

After stirring for 6 hours, the solution was diluted with dichloromethane and washed in turn with sodium sulphite solution, sodium hydroxide solution, and water. The solution was dried over anhydrous magnesium sulphate, and evaporated in vacuo to give a yellow oil. Purification by chromatography on silica (Merck, 230-400 mesh, 0.7 kg $cm^{-2}$) eluting with dichloromethane-ethylacetate (4:1) gave 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methylsulphinyl-3-trifluoromethylpyrazole in the form of a white solid, m.p. 142-145°C with decomposition.

**REFERENCE EXAMPLE 10**

5-Carbamoyl-4-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-trifluoromethylpyrazole (3.57 g) was heated to 200°C with phosphorus pentoxide (2.82 g) with stirring. After 3 hours, the cooled product was treated with ice, and extracted with dichloromethane (3 x 50 ml). The organic solutin was washed with water, dried over

anhydrous magnesium sulphate, and evaporated in vacuo to give a solid. Recrystallisation from hexane gave 1-(2,6-dichloro-4-trifluoromethylphenyl)-4,5-dicyano-3-trifluoromethylpyrazole in the form of white crystals 91.8 g), m.p. 80°C.

By proceeding in a similar manner to that described above but replacing the 5-carbamoyl-4-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-trifluoromethylpyrazole by 5-amino-3-carbamoyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole there was prepared:-

5-Amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole in the form of a white solid, m.p. 214°C.

**REFERENCE EXAMPLE 11**

5-Carbamoyl-4-cyano-1-(2,6-dichloro-4-

trifluoromethylphenyl)-3-trifluoromethylpyrazole used in the above Reference Example 10, was prepared as follows:-

5-Carboxy-4-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-trifluoromethylpyrazole (6.0 g) was added to thionyl chloride (30 ml) and the stirred solution heated to reflux for 4 hours. The solvent was evaporated <u>in vacuo</u>, and re-evaporated after addition of dry toluene 930 ml). The resultant orange oil was dissolved in dry ether (10 ml) and added dropwise to a stirred solution of ammonia (0.88, 20 ml) cooled by an ice bath. After stirring overnight, water 9150 mml) was added, and the mixture extracted with dichloromethane (3 x 50 ml). The combined extract was washed with water, dried over anhydrous magnesium sulphate, and evaporated <u>in vacuo</u> to give a white solid (7.0 g). Recrystallisation from a mixture of ethyl acetate and petroleum ether gave the title compound (4.3 g), in the form of white

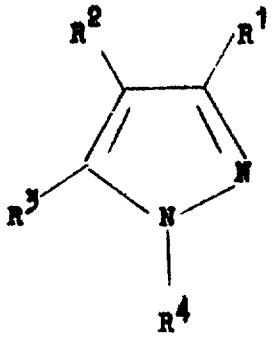
crystals, m.p. 180-181°C.

5-Amino-3-carbamoyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole used in the above Reference Example 10 was prepared by the same procedure, but by replacing the 5-carboxy-4-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-trifluoromethylpyrazole by 5-amino-3-carboxy-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyraole. The title compound was obtained in the form of an off-white solid, m.p. 223-224°C.

5-Amino-3-carboxy-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-methanesulphonylpyrazole used above was prepared as follows:-

5-Amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-ethoxycarbonyl-4-methanesulphonylpyrazole (8.15 g; Reference Example 3) was added to stirred 80% sulphuric acid (80 ml), and heated at 100°C for 5 hours.

After cooling, the solution was poured onto ice, the solid filtered off and dried over phosphorus pentoxide in a vacuum dessicator. Recrystallisation from a mixture of methanol and petroleum ether gave the title compound as a white solid, m.p. 203-205°C.



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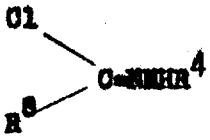

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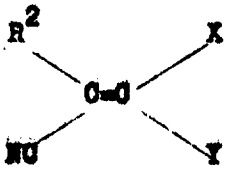

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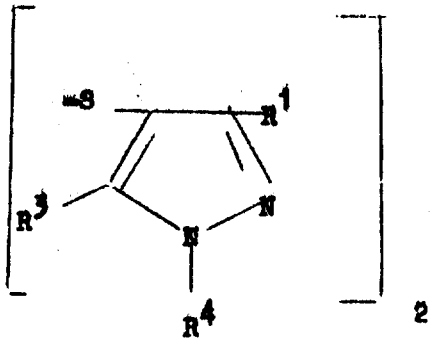

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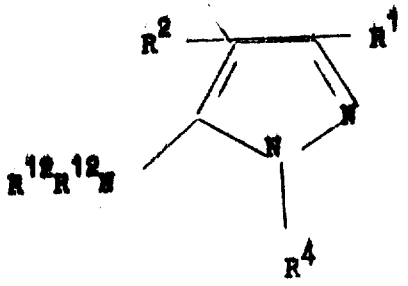

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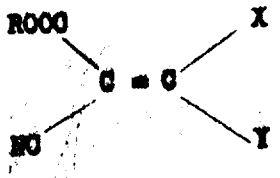

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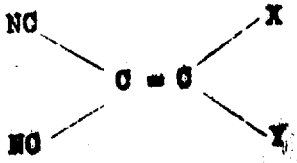

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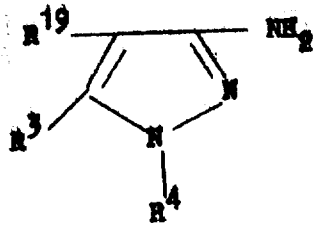

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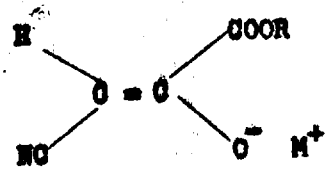

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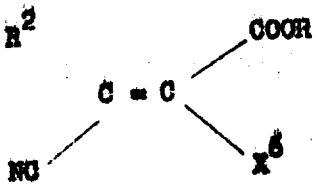

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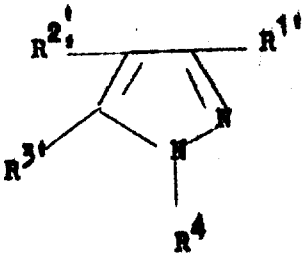

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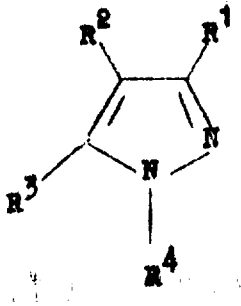
WE CLAIM

1. An N-phenylpyrazole derivative of the formula:



(I)

wherein $R^1$ represents a cyano or nitro group, a halogen atom, or an acyl or formyl group;

$R^2$ represents a group $R^5SO_2$, $R^5SO$, or $R^5S$ in which $R^5$ represents a straight- or branched-chain alkyl, alkenyl or alkynyl group of up to 4 carbon atoms which may be unsubstituted or substituted by one or more halogen atoms which may be the same or different;

$R^3$ represents a hydrogen atom or an amino group $-NR^6R^7$ wherein $R^6$ and $R^7$, which may be the same or different, each represent a hydrogen atom or an straight- or branched-chain alkyl, alkenylalkyl or alkynylalkyl group of up

to 6 carbon atoms, a formyl group, a straight- or branched-chain alkanoyl group (which is of 2 to 6 carbon atoms and which may be optionally substituted by one or more halogen atoms) or $R^6$ and $R^7$ together with the nitrogen atom to which they are attached form a 5 to 6 membered cyclic imide, or represents a straight- or branched-chain alkoxycarbonyl group (which is of 2 to 5 carbons atoms and is unsubstituted or substituted by one or more halogen atoms), or $R^3$ represents a straight or branched-chain alkoxymethyleneamino group of 2 to 6 carbon atoms which may be unsubstituted or substituted on methylene by a straight or branched-chain alkyl group of 1 to 4 carbon atoms or represents a halogen atom; and $R^4$ represents a phenyl group substituted in the 2-position by a fluorine, chlorine, bromine or iodine atom; in the 4-position by a straight- or branched-chain alkyl or alkoxy group of 1 to 4 carbon atoms, which may be unsubstituted or substituted by one or more halogen atoms which may be the same or different, or a chlorine or bromine atom;

and optionally in the 6-position by a flourine, chlorine, bromine or iodine atom, with the exclusion of the compound wherein $R^1$ represents cyano, $R^2$ represents methanesulphonyl, $R^3$ represents amino and $R^4$ represents 2,6-dichloro-4-trifluoromethylphenyl.

2. A compound according to claim 1 wherein $R^1$ is other than a formyl group and $R^6$ and $R^7$ are not alkenylalkyl or alkynylalkyl group.

3. A compound according to claim 1 wherein $R^2$ represents an alkylsulphonyl/sulphinyl/thio group which is optionally halogen substituted and of 1 to 4 carbon atoms, or an alkenyl- or alkynyl-sulphonyl/-sulphinyl/thio group which is optionally halogen substituted and of up to 4 carbon atoms, $R^3$ represents the hydrogen atom, an amino or methylamino group and $R^1$ represents a halogen atom or a cyano or nitro group.

4. a compound according to claim 3 wherein $R^1$

represents a cyano or nitro group.

5. compound according to claim 1 wherein $R^4$ contains a trifluoromethyl or trifluoromethoxy group and $R^2$ represents an optionally halogenated alkylsulphonyl/sulphinyl/thio group of 1 to 4 carbon atoms.

6. A compound according to claim 5 wherein $R^2$ represents a trifluoromethylthio, trifluoromethylsulphinyl or trifluoromethylsulphonyl group.

7. a compound according to claim 1 wherein $R^4$ represents a 2,4,6-trichloro-2,6-dichloro-4-difluoromethoxy-2-chloro-4-trifluoromethyl-, 2-bromo-6-chloro-4-trifluoromethyl-, 2,6-dibromo-4-trifluoromethyl- or 2-bromo-4-trifluoromethyl-phenyl group.

8. A compound according to claim 1 wherein $R^4$ represents a 2,6-dichloro-4-trifluoromethyl- or 2,6-dichloro-4-trifluoromethoxy-phenyl group.

9. An arthropodicidal, plant nematocidal, anthelmintic or anti-protozoal composition which comprises an effective amount of a compound according to claim 1 in association with one or more compatible diluents or carriers.

10. A method for the control of arthropod, plant nematode, helminth or protozoal pests at a locus which comprises treatment of the locus with an effective amount of a compound according to claim 1.