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Some Diazinon Analogues Containing the 4-Trifluoromethyl Group

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Summary. Diazinon analogues were prepared containing trifluoromethyl in place of the 4-methyl group and methylthio (**2a**), amino (**2b**), dimethylamino (**2c**), methylphenylamino (**2d**), or isopropyl (**2e**) in position 2 of the pyrimidine ring. The most active analogue (**2b**) was less than half as insecticidal as Diazinon.

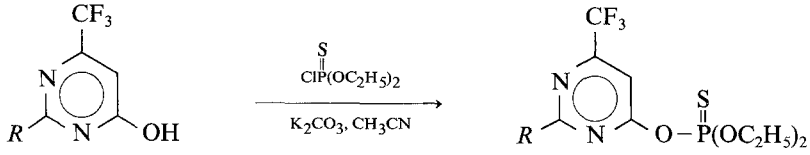
Keywords. Diazinon analogues; 4-Trifluoromethylpyrimidines; O,O-Diethyl phosphorothiolate esters; Insecticides.

Einige Diazinon-Analoga mit einer 4-Trifluormethylgruppe

Zusammenfassung. Es wurden Diazinon-Analoga hergestellt, die anstelle der 4-Methylgruppe die Trifluormethylgruppe und in 2-Position des Pyrimidin-Rings verschiedene Substituenten enthielten. **2a**: 2-Methylthio-; **2b**: 2-Amino; **2c**: 2-Dimethylamino-; **2d**: 2-Methylphenylamino-; **2e**: 2-Isopropyl-. Das aktivste Analogon war **2b**, das allerdings auch weniger als die Hälfte der insektiziden Wirkung des Diazinon aufwies.

Diazinon [O,O-diethyl O-(2-isopropyl-4-methyl-6-pyrimidyl)-phosphorothiolate] is a broad spectrum pesticide [1]. Since we were involved in the preparation of 4-trifluoromethylpyrimidines for another study [2–4], it became apparent that intermediates could become easily available for the preparation of a number of Diazinon analogues containing the trifluoromethyl substituent in place of the methyl group along with variations of the functionality in the 2 position: methylthio, amino, dimethylamino, methylphenylamino, or isopropyl. The five analogues of Diazinon were prepared by condensing the respective pyrimidinol with ethyl chlorothiophosphate in acetonitrile in the presence of potassium carbonate (Scheme 1).

The analogues were tested for insecticidal activity against bean aphid (*Aphis fabae* Scopoli), Mexican bean beetle (*Epilachna varivestis* Mulsant), southern armyworm (*Spodoptera eridania* Cramer), and southern corn rootworm (*Diabrotica undecimpunctata howardi* Barber). The compounds can be ranked in the following order with respect to overall activity as compared with Diazinon



1 **2** **Scheme 1**

1a and **2a**, $R=CH_3S$; **1b** and **2b**, $R=NH_2$; **1c** and **2c**, $R=(CH_3)_2N$; **1d** and **2d**, $R=CH_3NC_6H_5$; **1e** and **2e**, $R=CH(CH_3)_2$

(100) > **2b** (45) > **2c** (43) > **2d** (10) > **2e** (4) > **2a** (0). The trifluoromethyl analogue of Diazinon (**2e**) was nearly devoid of insecticidal activity, and it seems that either the increased size of the trifluoromethyl group as compared with the methyl and/or the increased electronegativity due to the fluorine atoms caused this marked loss of activity.

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Experimental Part

Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. The purity of samples was established by gas chromatography which was performed on a Varian Aerograph Model 1400 gas chromatograph with a flame ionization detector to which was attached a Varian Model 20 recorder. The column employed was 5 feet × 1/8 inch o.d., packed with 3% Dexsil 400 in Anachrom A (90–100 mesh) purchased from Analabs, New Haven, CT. Nitrogen was used as the carrier gas. NMR spectra were obtained with a Varian XL-100 spectrometer using *DMSO-d_6* as the solvent and tetramethyl silane as the internal standard for ^{1}H-NMR spectra and trichlorofluoromethane for ^{19}F-NMR spectra.

2-Methylthio-4-trifluoromethyl-6-pyrimidinol (**1a**)

Compound **1a** was prepared previously [2].

^{1}H-NMR: δ = 13.5 (broad s, 6-OH), 6.68 (s, 5-H), 2.60 (s, CH_3S); ^{19}F-NMR: 70.7 (s, CF_3).

2-Amino-4-trifluoromethyl-6-pyrimidinol (**1b**)

The title compound was known [5].

^{1}H-NMR: δ = 9.50 (broad s, 2-NH_2), 6.06 (s, 5-H); ^{19}F-NMR: 70.4 (s, CF_3).

2-Dimethylamino-4-trifluoromethyl-6-pyrimidinol (**1c**)

To sodium (5.1 g, 0.22 g atm) dissolved in 200 ml of anhydrous ethanol was added 1,1-dimethylguanidine hydrochloride (24.6 g, 0.2 mol) and ethyl trifluoroacetoacetate (36.5 g, 0.2 mol). The mixture was heated under reflux for 1 h with stirring and allowed to stir at room temperature overnight. The alcohol was removed in a rotary evaporator, and water was added until most of the residue went

into solution. It was acidified with acetic acid and refrigerated overnight. The product was obtained by filtration, washing (water), and drying at 80 °C overnight. The yield of product was 13.4 g (32%), m.p. 172–173°C. An additional yield was obtained by evaporation of the combined filtrate and washings, cooling overnight (1.4 g, 3.4%), m.p. 171–172°C. An analytical sample was prepared by crystallization from water, m.p. 173°C.

Anal. calcd. for $C_7H_8F_3N_3O$: C 40.58, H 3.89, N 20.29. Found: C 40.50, H 4.18, N 20.59. ^{1}H-NMR: δ = 6.05 (s, 5-H), 3.14 [s, $(CH_3)_2N$]; ^{19}F-NMR: 70.4 (s, CF_3).

2-Methylphenylamino-4-trifluoromethyl-6-pyrimidinol (**1 d**)

The preparation of **1 d** was reported previously [3].

^{1}H-NMR: δ = 11.7 (broad s, 6-OH), 7.50 (broad s, C_6H_5), 6.27 (s, 5-H), 3.47 (s, CH_3N); ^{19}F-NMR: 70.1 (s, CF_3).

2-Isopropyl-4-trifluoromethyl-6-pyrimidinol (**1 e**)

Compound **1 e** was prepared from isobutyramidine hydrochloride and ethyl trifluoroacetoacetate in the same manner as **1 d**. The yield of product was 26%, m.p. 135–136°C. The analytical sample was prepared by crystallization from dilute aqueous alcohol, m.p. 136°C.

Anal. calcd. for $C_8H_9F_3N_2O$: C 46.60, H 4.34, N 13.59. Found: C 46.30, H 4.56, N 13.70. ^{1}H-NMR: δ = 13.1 (broad s, 6-OH), 6.76 (s, 5-H), 2.99 [m, H, $(CH_3)_2CH$], 1.27 [d, CH_3, $(CH_3)_2CH$, $J_{CH_3, H}$ = 7 Hz]; ^{19}F-NMR: 70.3 (s, CF_3).

O,O-Diethyl O-(2-methylthio-4-trifluoromethyl-6-pyrimidyl)phosphorothiolate (**2 a**)

A mixture of **1 a** (4.0 g, 0.02 mol), diethyl chlorothiophosphate (3.8 g, 0.02 mol), and anhydrous potassium carbonate (2.8 g, 0.02 mol) in 50 ml of acetonitrile was heated under reflux with stirring for 2 h. The solids were removed by filtration, and the solvent was evaporated under vacuum. The residue was distilled, and the fraction boiling at 112–118°C/0.06 mm was collected. The yield of product was 13.5 g (93%). An analytical sample was obtained at b.p. 116°C/0.06 mm, n_D^{25} 1.4969.

Anal. calcd. for $C_{10}H_{14}F_3N_2O_3PS_2$: C 33.14, H 3.89, N 7.73, P 8.55. Found: C 33.02, H 4.10, N 7.67, P 8.81. ^{1}H-NMR: δ = 7.60 (s, 5-H), 4.27 (dq, CH_3CH_2, J_{CH_3, CH_2} = 7 Hz, $J_{CH_2, P}$ = 3 Hz), 2.64 (s, CH_3S), 1.37 (t, CH_3CH_2); ^{19}F-NMR: 69.5 (s, CF_3).

O,O-Diethyl O-(2-amino-4-trifluoromethyl-6-pyrimidyl)phosphorothiolate (**2 b**)

Compound **2 b** was prepared from **1 b** and diethyl chlorothiophosphate in nearly quantitative yield in the same manner as **2 a**, m.p. 85–86°C. An analytical sample was crystallized from a mixture of ethanol and hexane, m.p. 86–87°C.

Anal. calcd. for $C_9H_{13}F_3N_3O_3PS$: C 32.63, H 3.93, N 12.69, P 9.35. Found: C 32.70, H 4.11, N 12.72, P 9.05. ^{1}H-NMR: δ = 9.80 (broad s, 2-NH_2), 6.87 (s, 5-H), 4.14 (dq, CH_3CH_2, J_{CH_3, CH_2} = 7 Hz, $J_{CH_2, P}$ = 3 Hz), 1.36 (t, CH_3CH_2); ^{19}F-NMR: 69.7 (s, CF_3).

O,O-Diethyl O-(2-dimethylamino-4-trifluoromethyl-6-pyrimidyl)phosphorothiolate (**2 c**)

Compound **2 c** was prepared from **1 c** and diethylchlorothiophosphate in 98% yield, b.p. 110–116°C/0.02 mm, in the same manner as **2 a**. The analytical sample was collected at 114–116°C/0.02 mm, n_D^{25} 1.4839.

Anal. calcd. for $C_{11}H_{17}F_3N_3O_3PS$: C 36.77, H 4.77, N 11.69, P 8.62. Found: C 36.54, H 4.77, N 11.80, P 8.71. ^{1}H-NMR: δ = 6.67 (s, 5-H), 4.41 (dq, CH_3CH_2, J_{CH_3, CH_2} = 7 Hz, $J_{CH_2, P}$ = 3 Hz), 3.25 [s, $(CH_3)_2N$], 1.40 (t, CH_3CH_2); ^{19}F-NMR: 70.0 (s, CF_3).

O,O-Diethyl O-(2-methylphenylamino-4-trifluoromethyl-6-pyrimidyl)phosphorothiolate (**2 d**)

Compound **2 d** was prepared from **1 d** and diethyl chlorothiophosphate in 96% yield, b.p. 156–158°C/0.07 mm in the same manner as **2 a**. The analytical sample was taken at b.p. 158°C/0.07 mm, n_D^{25} 1.5260.

Anal. calcd. for $C_{16}H_{19}F_3N_3O_3PS$: C 45.61, H 4.54, N 9.97, P 7.35. Found: C 45.72, H 4.65, N 10.13, P 7.09. ^{1}H-NMR: δ = 7.52 (s, C_6H_5), 6.89 (s, 5-H), 4.06 (dq, CH_3CH_2, J_{CH_3, CH_2} = 7 Hz, $J_{CH_2, P}$ = 3 Hz), 3.56 (s, CH_3), 1.21 (t, CH_3CH_2); ^{19}F-NMR: 69.7 (s, CF_3).

O,O-Diethyl O-(2-isopropyl-4-trifluoromethyl-6-pyrimidyl)phosphorothiolate (**2 e**)

Compound **2 e** was prepared from **1 e** and diethyl chlorothiophosphate in 98% yield, b.p. 90–92°C/0.04 mm in the same manner as **2 a**. The analytical sample was taken at b.p. 92°C/0.04 mm, n_D^{25} 1.4545. Anal. calcd. for $C_{12}H_{18}F_3N_2O_3PS$: C 40.22, H 5.06, N 7.82, P 8.64. Found: C 40.50, H 5.28, N 7.73, P 8.86. ^{1}H-NMR: δ = 7.75 (s, 5-H), 4.12 (dq, CH_3CH_2, J_{CH_3, CH_2} = 7 Hz, $J_{CH_2, P}$ = 3 Hz), 2.85 [m, H, $(CH_3)_2CH$], 1.37 (t, CH_3CH_2), 1.35 [dq, CH_3, $(CH_3)_2CH$, J_{CH_3, CH_2} = 7 Hz, $J_{CH_2, P}$ = 3 Hz]; ^{19}F-NMR: 69.4 (s, CF_3).

References

[1] Gasser R. (1953) Z. Naturforsch. **8 B**: 225
[2] Gershon H., Grefig A. T., Scala A. A. (1983) J. Heterocycl. Chem. **20**: 219
[3] Gershon H., Grefig A. T. (1984) J. Heterocycl. Chem. **21**: 1161
[4] Gershon H., Grefig A. T., Clarke D. D. (1987) J. Heterocycl. Chem. **24**: 1243
[5] Giner-Sorolla A., Bendich A. (1958) J. Am. Chem. Soc. **80**: 5744

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