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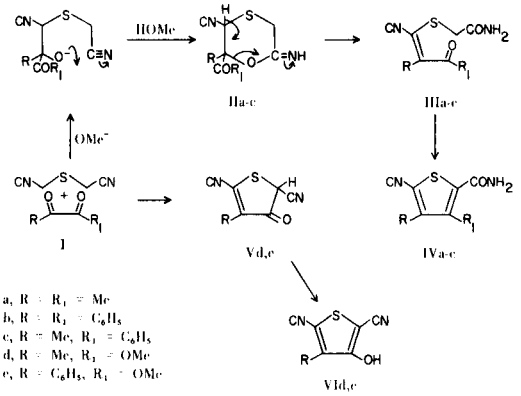
Received July 17, 1978

Thiodiacetonitrile reacted with α-diketones to form 5-cyano-2-thiophenecarboxamides and with α-keto esters to give 3-hydroxy-2,5-thiophenedicarbonitriles. Sulphonyldiacetonitrile condensed with α,β-unsaturated ketones to give 6-cyano-3,4-dihydro-1,1-dioxo-2*H*-thiopyran-2-carboxamides.

J. Heterocyclic Chem., 16, 381 (1979).

Thiodiacetonitrile and its sulphone are easily available (1) and appear to be useful starting materials for sulphur heterocycles.

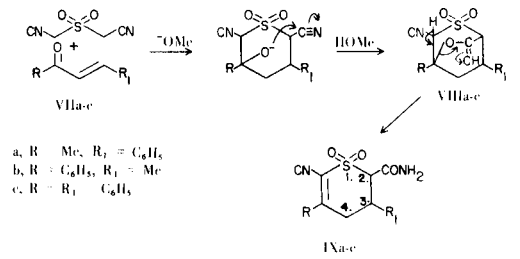
Thiodiacetonitrile reacted with the α-diketones Ia-c in methanol in the presence of sodium methoxide to give the thiophene derivatives IVa-c. This method offers a useful alternative to the well established thiophene ring synthesis in which thiodiacetate esters are condensed with α-diketones (2). The reaction appears to follow a course similar to that established for the condensations of the esters (3) and involve condensation of the anion from thiodiacetonitrile with the diketones followed by ring closure and proton abstraction from the solvent to give the iminolactone intermediates IIa-c which open to the unsaturated amides IIIa-c. Knoevenagel condensation, with formation of the stable aromatic system as the driving force, produces the amides IVa-c. These crystallised directly from the reaction mixture, unlike the acid-esters obtained from dialkyl thiodiacetates which usually require extraction or hydrolysis before isolation.



a, R = R_1 = Me
b, R = R_1 = C_6H_5
c, R = Me, R_1 = C_6H_5
d, R = Me, R_1 = OMe
e, R = C_6H_5, R_1 = OMe

Thiodiacetonitrile condensed under similar conditions with the α-keto esters Id,e to give the hydroxythiophenes VId,e. These reactions clearly proceed by successive Knoevenagel and Dieckmann condensations *via* the intermediates Vd,e again following a course similar to that established for the corresponding condensations of dialkyl thiodiacetates (4).

Sulphonyldiacetonitrile did not condense with α-diketones possibly due to the lack of aromatic stability in the thiophene 1,1-dioxide system (5). Unlike the sulphide however it did condense, in methanol in the presence of sodium methoxide, with the αβ-unsaturated ketones VIIa-c to give the 3,4-dihydro-2*H*-thiopyran derivatives IXa-c, produced presumably by Michael reaction and ring closure proceeding in this case *via* the bicyclic imino-lactone intermediates VIIIa-c.



a, R = Me, R_1 = C_6H_5
b, R = C_6H_5, R_1 = Me
c, R = R_1 = C_6H_5

The structures of the compounds IV, VI and IX were consistent with their spectral and analytical data (see Table I).

The large coupling (J = 12-13 Hz) observed in the signal of the C-2 proton in the nmr spectrum of each of the compounds IXa-c indicated a *trans* configuration between C-2 and C-3 in each case (6).

EXPERIMENTAL

Melting points were determined on a Kofler hot stage apparatus. Microanalyses were carried out by Dr. F. B. Strauss, Microanalytical Laboratories, Carlton Road, Oxford. Nmr spectra were determined on a Varian A60A spectrometer. Mass spectra were recorded by the Physico-chemical Measurement Unit, Harwell. Crotonophenone was prepared by the method of Tuson (7).

5-Cyano-3,4-dimethyl-2-thiophenecarboxamide (IVa).

Thiodiacetonitrile (1.12 g., 0.01 mole) and diacetyl (0.86 g., 0.01 mole) were dissolved in dry methanol (10 ml.) and cooled in ice. A solution of sodium (0.3 g.) in dry methanol (16 ml.) was added dropwise. The dark brown solution was kept at 0° for 2 days. The product (IVa) was filtered, washed with ether and recrystallised from acetic acid to give 1.16 g. (65%) m.p. 192°; ir (nujol): 3350, 3150 cm^{-1} (NH_2) 2220 (CN) 1690 (C=O); nmr (trifluoroacetic acid): δ 2.40 (S, 3H, Me) 2.51 (S, 3H, Me) 6.00-8.02 (broad S, 2H, NH_2); M^+ 180.

The compounds IVb and IVc were prepared in a similar manner except that the reaction mixture for IVb was shaken at

0022-152X/79/020381-02$02.25

Table I

Compound No.	M.p. °C	Yield %	Molecular Formula	Analyses: Calcd. (Found) C	H	N	S
IVa	192	65	$C_8H_8N_2OS$	53.2 (53.2)	4.4 (4.5)	15.6 (15.7)	17.8 (17.5)
IVb	264-265	85	$C_{18}H_{12}N_2OS$	71.1 (70.8)	4.0 (4.1)	9.2 (9.0)	10.5 (10.7)
IVc	185	65	$C_{13}H_{10}N_2OS$	64.5 (64.3)	4.1 (4.3)	11.6 (11.4)	13.2 (13.4)
VId	180-183	67	$C_7H_4N_2OS$	51.2 (50.9)	2.4 (2.5)	17.1 (16.9)	19.5 (19.2)
VIe	195-199	68	$C_{12}H_6N_2OS$	63.7 (63.5)	2.7 (2.7)	12.4 (12.2)	14.2 (13.9)
IXa	180	40	$C_{14}H_{14}N_2O_3S$	57.9 (57.5)	4.8 (5.1)	9.7 (9.4)	11.0 (11.1)
IXb	247-249	40	$C_{14}H_{14}N_2O_3S$	57.9 (57.8)	4.8 (5.1)	9.7 (9.5)	11.0 (11.0)
IXc	242-244	35	$C_{19}H_{16}N_2O_3S$	64.8 (64.6)	4.6 (4.8)	8.0 (7.8)	9.1 (9.3)

room temperature for 2 days and the product recrystallised from a mixture of acetic acid and dimethylformamide.

Compound IVb.

This compound had ir: 3360, 3210 cm^{-1} (NH_2) 2200 (CN) 1670 (C=O); nmr (DMSO): δ 3.2-3.7 (broad S, 2H, NH_2) 7.1-7.5 (m, 10H, ArH).

Compound IVc.

This compound had ir: 3350, 3220 cm^{-1} (NH_2) 2730 (CN) 1670 (C=O); nmr (trifluoroacetic acid): 2.54 (S, 3H, Me) 5.50-6.51 (broad S, 2H, NH_2) 6.9-7.3 (m, 5H, ArH).

3-Hydroxy-4-methyl-2,5-thiophenedicarbonitrile (VId).

Thiodiacetonitrile (1.12 g., 0.01 mole) and methyl pyruvate (1.02 g., 0.01 mole) were dissolved in dry methanol (5 ml.) and cooled in ice. A solution of sodium (0.3 g.) in dry methanol (8 ml.) was added gradually. The mixture was kept at 0° for 24 hours, acidified with hydrochloric acid and concentrated to half its volume. The product (VId) was filtered and recrystallised from acetic acid to give 1.10 g. (67%) m.p. 180-183°; ir (nujol): 3200 cm^{-1} (OH) 2210 (CN); nmr (trifluoroacetic acid): δ 2.41-2.52 (S, 3H, Me); ms; M^+ 164.

Compound VIe was prepared in a similar manner; ir: 3220 cm^{-1} (OH) 2210 (CN); nmr (acetone): δ 5.2-6.5 (broad S, 1H, OH) 7.6-8.0 (m, 5H, ArH).

6-Cyano-3,4-dihydro-5-methyl-3-phenyl-1,1-dioxo-2*H*-thiopyran-2-carboxamide (IXa).

Sulphonyldiacetonitrile (1.44 g., 0.01 mole) and benzylideneacetone (2.08 g., 0.01 mole) were dissolved in a solution of sodium (0.3 g.) in dry methanol (10 ml.). The reaction mixture was shaken for 24 hours and acidified to give IXa which recrystallised from acetic acid to give 1.16 g. (40%) m.p. 242-244°; ir (nujol): 3350, 3190 cm^{-1} (NH_2) 2220 cm^{-1} (CN) 1690 (C=O) 1310, 1145 (SO_2); nmr (trifluoroacetic acid): δ 2.41 (S, 3H, Me) 2.90-3.35 (m, 2H, C-4 methylene) 3.71-4.2 (m, 1H, C-3 methine) 5.0 (d, 1H, J ≃ 13.0 Hz, C-2 methine) 7.41 (S, 5H, ArH); M^+ 290.

Compounds IXb and IXc were prepared in a similar manner.

Compound IXb.

This compound had ir: 3390, 3200 cm^{-1} (NH_2) 2250 (CN) 1680 (C=O) 1310, 1140 (SO_2); nmr (DMSO-d_6): δ 1.11 (d, 3H, Me) 2.8-3.1 (m, 2H, C-4 methylene) 3.40-3.8 (m, 1H, C-3 methine) 4.4 (d, 1H, J ≃ 12 Hz, C-2 methine) 7.51 (m, 5H, ArH) 7.7-7.8 (m, 2H, NH_2).

Compound IXc.

This compound had ir: 3350, 3200 cm^{-1} (NH_2) 2250 (CN) 1690 (C=O) 1300, 1140 (SO_2); nmr (trifluoroacetic acid): 3.32-3.56 (m, 2H, C-4 methylene) 4.0-4.4 (m, 1H, C-3 methine) 5.00 (d, 1H, J≃ 12 Hz, C-2 methine) 7.45 (S, 5H, ArH) 7.60 (S, 5H, ArH).

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