Condensed Thiophen Ring Systems. Part 20.[1] Synthesis of 5-Arylthieno-[3,2-b]pyrroles and 5-Arylthieno[3,2-*c*]pyrazoles

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Reductive cyclisation of the alkenes (5)—(8) (prepared by condensation of methyl 2-methyl-3-nitrothiophen-5-carboxylate with an aromatic aldehyde) with triethyl phosphite gave thieno[3,2-*b*]pyrroles (1)—(4). Thieno[3,2-*c*]pyrazoles (12)—(14) were prepared similarly from the anils (15)—(18) or the nitrones (22) and (23). Condensations between alkyl 2-methyl-3-nitrothiophen-5-carboxylates or 2-methyl-3-nitrobenzo[*b*]thiophen and *NN*-dimethyl-4-nitrosoaniline have been shown to give mixtures of nitrones [(22), (23), and (27) (major products), respectively] and the corresponding anils [(16), (17), and (26)]. A procedure is given for alkylation of 2-formyl-3-nitrothiophen-5-carboxylic acid (19) which avoids deformylation and involves formation of its sodium or potassium salt with an alkali metal hydrogen carbonate in hexamethylphosphoramide followed by addition of an alkyl iodide.

2-ARYL-1H-[1]BENZOTHIENO[2,3-*b*](AND [3,2-*b*])PYRROLES,[2] and 2-aryl[1]benzothieno[2,3-*c*](and [3,2-*c*])-pyrazoles,[3] have been prepared previously by reductive cyclisation with triethyl phosphite of a 2- or 3-nitrobenzo[*b*]thiophen substituted in the adjacent position with a styryl or an azomethine moiety, respectively. In a parallel investigation we have prepared the title compounds (1)—(4) and (12)—(14) similarly from the corresponding alkenes (5)—(8) or anils (15)—(18), respectively. Since we began our studies Srinivasan *et al.*[4] and Gronowitz and his co-workers [5] have reported similar preparations of thieno[3,2-*b*]pyrroles.

The alkenes (5)—(11) were prepared from methyl 2-methyl-3-nitrothiophen-5-carboxylate by condensation with the appropriate aromatic aldehyde in a procedure similar to that reported by Srinivasan *et al.*[4] The *trans*-stereochemistry of the alkenes (5)—(11) was indicated by a coupling constant of 16.0 Hz between the two alkene protons. The absence of *cis*-isomers parallels our results in the benzo[*b*]thiophen series and can be rationalised similarly.[2] Reductive cyclisation of the alkenes (5)—(8) with triethyl phosphite gave the corresponding methyl 5-arylthieno[3,2-*b*]pyrrole-2-carboxylates (1)—(4). Electron-donating groups in the 4-position of the aryl ring afford the highest yields of products (*cf.* ref. 3). When these groups are present in the 2-position, however, yields are lower, presumably because of steric hindrance (see Table 2).

Condensation of methyl 2-methyl-3-nitrothiophen-5-carboxylate with *NN*-dimethyl-4-nitrosoaniline gave a mixture of two products (t.l.c.), one red and one purple. N.m.r. analysis of this mixture suggested that the two components were the anil (16) and the nitrone (22) (ratio 1 : 6). That the anil was the minor component was shown by a comparison of its R_F and ^1H n.m.r. chemical shift values and its mass spectrum with those of an authentic sample prepared as described later. The major component, the nitrone (22), could be separated from the anil by several recrystallisations from toluene. A more convenient method, however, involves selective

[1] Part 19, R. V. Davies, B. Iddon, T. McC. Paterson, M. W. Pickering, H. Suschitzky, and M. W. Gittos, *J.C.S. Perkin I*, 1976, 138.

[2] K. E. Chippendale, B. Iddon, and H. Suschitzky, *J.C.S. Perkin I*, 1973, 125.

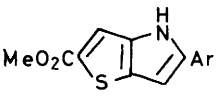
[3] K. E. Chippendale, B. Iddon, and H. Suschitzky, *J.C.S. Perkin I*, 1973, 129.

[4] K. Srinivasan, K. G. Srinivasan, K. K. Balbasubramanian, and S. Swaminathan, *Synthesis*, 1973, 313.

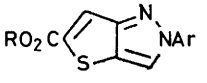
[5] S. Gronowitz and I. Ander, *Acta Chem. Scand.*, 1975, **29B**, 513; S. Gronowitz, C. Westerlund, and A.-B. Hörnfeldt, *ibid.*, 1976, **30B**, 391.

hydrolysis of the anil (16) with 2M-sulphuric acid at ambient temperature for 15 min. The resulting mixture of the nitrone (22) and methyl 2-formyl-3-nitrothiophen-5-carboxylate (20) is separated readily by fractional crystallisation from toluene.

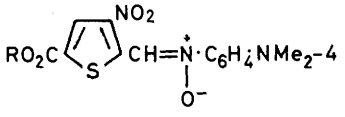
Condensation of ethyl 2-methyl-3-nitrothiophen-5-carboxylate with *NN*-dimethyl-4-nitrosoaniline similary gave a mixture containing the nitrone (23) (red) (major component) and the anil (17) (purple), not separable by classical liquid column chromatographic techniques but



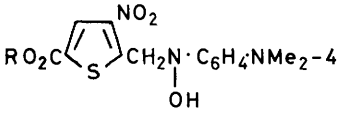
(1) Ar = 2-ClC$_6$H$_4$
(2) Ar = 2-MeO·C$_6$H$_4$
(3) Ar = 4-Me$_2$N·C$_6$H$_4$
(4) Ar = 2,4,6-(MeO)$_3$C$_6$H$_2$



(12) Ar = Ph, R = Me
(13) Ar = 4-Me$_2$N·C$_6$H$_4$, R = Me
(14) Ar = 4-Me$_2$N·C$_6$H$_4$, R = Et



(22) R = Me
(23) R = Et



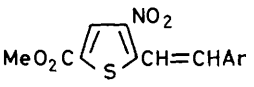
(24)

separable by high performance liquid chromatography. A third component (yellow) was shown by t.l.c. to be present in trace amount.

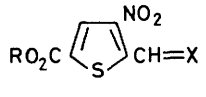
Formation of the nitrones (22) and (23) presumably proceeds *via* intermediates (24; R = Me or Et) which are oxidised by the excess (50%) of *NN*-dimethyl-4-nitrosoaniline present. The intermediate 4-dimethylaminophenylhydroxylamine presumably reacts further with the nitroso-compound to give the azoxy-compound (25).[6] This azoxy-compound, which is reported[7,8] to be orange, is possibly the third component present in the mixture obtained by condensation of ethyl 2-methyl-3-nitrothiophen-5-carboxylate with *NN*-dimethyl-4-nitrosoaniline. An authentic sample of the azoxy-compound (25) had the same R_F value (t.l.c.) as this third component.

[6] F. Barrow and F. J. Thorneycroft, *J. Chem. Soc.*, 1939, 769.
[7] J. F. Corbett, *Chem. Comm.*, 1968, 1257.

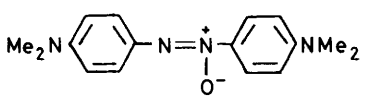
Previously we[2] reported that condensation of 2-methyl-3-nitrobenzo[*b*]thiophen with *NN*-dimethyl-4-nitrosoaniline gives the anil (26). In the light of the results reported in the preceding paragraphs we have repeated this reaction and discovered that the product is largely the corresponding nitrone (27), containing small amounts of the anil (26). The nitrone (27) was obtained by selective hydrolysis of the anil (26) followed by fractional crystallisation of the resulting mixture, as described before for separation of the nitrone (23). The



(5) Ar = 2-ClC$_6$H$_4$
(6) Ar = 2-MeO·C$_6$H$_4$
(7) Ar = 4-Me$_2$N·C$_6$H$_4$
(8) Ar = 2,4,6-(MeO)$_3$C$_6$H$_2$
(9) Ar = 4-MeC$_6$H$_4$
(10) Ar = 3-MeO·C$_6$H$_4$
(11) Ar = 4-pyridyl

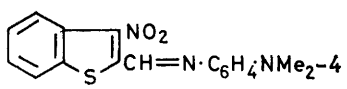


(15) X = NPh, R = Me
(16) X = 4-Me$_2$N·C$_6$H$_4$N, R = Me
(17) X = 4-Me$_2$N·C$_6$H$_4$N, R = Et
(18) X = 4-Me$_2$N·C$_6$H$_4$N, R = H
(19) X = O, R = H
(20) X = O, R = Me
(21) X = O, R = Et

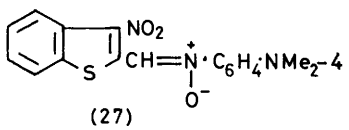


(25)

^{1}H n.m.r. chemical shift values of the anil present in the mixture were identical with those obtained from a sample prepared unambiguously by condensation of



(26)



(27)

3-nitrobenzo[*b*]thiophen-2-carbaldehyde with 4-dimethylaminoaniline.

[8] M. Sekiya and S. Takayama, *Chem. and Pharm. Bull. (Japan)*, 1970, **18**, 2146.

Attempts to reduce the nitrone (23) to the corresponding anil (17) with sulphur dioxide in 1,4-dioxan [9] proved abortive. Hydrolysis of a mixture of this nitrone (23) and the anil (17), obtained as described before, with concentrated hydrochloric acid heated under reflux gave an almost quantitative yield of 2-formyl-3-nitrothiophen-5-carboxylic acid (19). This acid was converted into its methyl ester (20) in high yield only by alkylation of its sodium or potassium salt with methyl iodide or dimethyl sulphate in hexamethylphosphoramide. A similar reaction with dimethyl sulphate in acetone resulted in a low conversion (33%). Alkylation with ethyl iodide yielded the ethyl ester (21). It is essential to prepare the alkali metal salts of the acid (19) with sodium or potassium hydrogen carbonate (monitored by carbon dioxide evolution). The use of sodium hydroxide or potassium carbonate according to literature procedures [10] resulted in partial deformylation with the formation of 4-nitrothiophen-2-carboxylic acid (isolated as its ethyl ester following esterification of its potassium salt with ethyl iodide). More recent procedures [11,12] for esterification of acids involving salt formation of the acid with potassium or sodium hydroxide in hexamethylphosphoramide resulted in our case in total deformylation to give only 4-nitrothiophen-2-carboxylic acid.

The methyl ester (20) was prepared also by hydrolysis of a mixture of the anil (16) and the nitrone (22) with 3M-sulphuric acid for 2.2 h at ambient temperature (see before). Ethyl 2-formyl-3-nitrothiophen-5-carboxylate (21) was prepared similarly.

Condensation of methyl 2-formyl-3-nitrothiophen-5-carboxylate (20) with aniline or 4-dimethylaminoaniline gave the anil (15) or (16), respectively, in high yield. Reductive cyclisation of these anils to the novel 5-arylthieno[3,2-*c*]pyrazoles (12) and (13) was achieved by use of triethyl phosphite (ratio 1 : 3) in t-butylbenzene. The formylcarboxylic acid (19) also condensed with 4-dimethylaminoaniline and the resulting anil (18) cyclised in triethyl phosphite to give the thieno[3,2-*c*]pyrazole (14) together with a mixture of other products (this mixture was not separable by classical liquid chromatographic techniques). Triethyl phosphite is known to alkylate at positions carrying acidic hydrogen. We prepared the thieno[3,2-*c*]pyrazole (13) also by reductive cyclisation of the nitrone (22) with triethyl phosphite (ratio 1 : 3.5) in t-butylbenzene. Compound (14) was prepared similarly from the nitrone (23). Although cyclisation of these nitrones gives lower yields than those obtained by cyclisation of the corresponding anils, it is more convenient. The thieno[3,2-*c*]pyrazoles (12)—(14) were readily obtained from the crude products by column chromatography and identified on the column by strong fluorescence under u.v. illumination. As far as we are aware, the nitrones (22) and (23) are the first to be deoxygenated and reductively cyclised in this way.

Cadogan and his co-workers [13] have shown recently that the availability and cheapness of triethyl phosphite makes it the tervalent phosphorus reagent of choice for reactions such as those described in this paper. They also cast further light on the mechanism of these reactions, but whether or not a nitrene is involved as an intermediate is still not clear.

The lanthanoid shift reagent $Eu(fod)_3$ was useful in the assignment of chemical shifts in some of our compounds. With the alkenes (5)—(11), for example, it complexed with the methoxycarbonyl group, as evidenced by a significant downfield shift of ester methyl proton signals, and this allowed us to identify the 4-H signal by its downfield shift, whereas the two *trans*-olefinic proton signals were unaffected. In a similar fashion the 3- and 6-protons of the 5-arylthieno[3,2-*c*]-pyrazoles were distinguished.

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded with a Varian A60, HA100, or EM360 instrument (Me_4Si as internal standard),* and i.r. spectra with a Perkin-Elmer 257 spectrometer. Molecular weights were determined by mass spectrometry (A.E.I.–G.E.C. MS902S or MS12 spectrometer). High performance liquid chromatography (h.p.l.c.) was carried out with a Waters LC (6000A solvent delivery system) instrument fitted with a 183 cm × 2 mm i.d. Corasil II (37—50 μ) normal phase column and a differential u.v. detector.

Reactions involving air- or moisture-sensitive reagents (*e.g.* n-butyl-lithium and triethyl phosphite) were carried out under dry, oxygen-free nitrogen (B.O.C. ' white spot ' grade) in solvents dried by standard procedures.

Light petroleum had b.p. 60—80 °C unless stated otherwise.

The following compounds were prepared by literature procedures, in some cases with the modifications indicated, which increased the reported yields: 5-methylthiophen-2-carboxylic acid (99%), m.p. 140—141 °C (from water) (lit.,[14] 139—140°) [n-butyl-lithium in hexane (commercial) was added to 2-methylthiophen in tetrahydrofuran at −70 °C; then dry carbon dioxide was bubbled through the solution while it was allowed to warm from −50 °C to ambient temperature]; 2-methyl-3-nitrothiophen-5-carboxylic acid (51%) (this moderate yield was due to unchanged starting material rather than formation of 2-methyl-3,5-dinitrothiophen [15]), m.p. 181 °C (from ethanol–light petroleum) (lit.,[15] 178—180°); ethyl 2-methyl-3-nitrothiophen-5-carboxylate (80%), b.p. 93—99 °C at 0.005 mmHg (lit.,[16] 122° at 1.6 mmHg); and methyl 2-methyl-3-nitrothiophen-5-carboxylate (99%) (prepared in the same

* N.m.r. data are available as Supplementary Publication No. SUP 22103 (5 pp.). For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin I*, 1976, Index issue.

[9] O. M. Stashkevich, G. T. Pilyugin, and A. A. Malakhova, *Zhur. Vsesoyuz. Khim. obshch. im. D.T. Mendeleeva*, 1970, **15**, 598 (*Chem. Abs.*, 1971, **74**, 42262).

[10] W. T. Moreland, *J. Org. Chem.*, 1956, **21**, 820; F. H. Stodola, *ibid.*, 1964, **29**, 2490; A. J. Parker, *Adv. Org. Chem.*, 1965, **5**, 37.

[11] J. E. Shaw, D. C. Kunerth, and J. J. Sherry, *Tetrahedron Letters*, 1973, 689.

[12] P. E. Pffefer, T. A. Foglia, P. A. Barr, I. Schmeltz, and L. S. Silbert, *Tetrahedron Letters*, 1972, 4063.

[13] M.-A. Armour, J. I. G. Cadogan, and D. S. B. Grace, *J.C.S. Perkin II*, 1975, 1185.

[14] S. Gronowitz and B. Gestblom, *Arkiv Kemi*, 1962, **18**, 513.

[15] H. R. Snyder, L. A. Carpino, J. F. Zack, and J. F. Mills, *J. Amer. Chem. Soc.*, 1957, **79**, 2556.

way as the ethyl ester [16]), b.p. 25—30 °C at 0.09 mmHg (lit.,[14] 96—97° at 12 mmHg).

trans-1-*Aryl*-2-(5-*methoxycarbonyl*-3-*nitro*-2-*thienyl*)*ethenes* (5)—(11).—*General method.* A stirred mixture of methyl 2-methyl-3-nitrothiophen-5-carboxylate (10 mmol), an aromatic aldehyde (15 mmol), and methanol (25 ml) was heated until a solution was obtained, then 2 drops of pyrrolidine were added and the mixture was heated under reflux. Removal of the solvent and the excess of reagents by distillation left the product. Details are given in Table 1.

5-*Arylthieno*[3,2-b]*pyrroles* (1)—(4).—*General method.* A mixture of the alkene (Table 1) (5 mmol) and triethyl phosphite (30 mmol) was stirred and heated under reflux. Then the excess of triethyl phosphite and the triethyl phosphate produced were distilled off at 10^{-3} mmHg and 120 °C to leave a solid, which was triturated with cold (0 °C) carbon tetrachloride and recrystallised to give the product. Details are given in Table 2.

Condensation of Ethyl 2-*Methyl*-3-*nitrothiophen*-5-*carboxylate with* NN-*Dimethyl*-4-*nitrosoaniline*.—A solution of the nitroso-compound (20.0 g, 133.0 mmol) in ethanol (100 ml) was added dropwise to a stirred solution of the ester (19.1 g, 88.8 mmol) in ethanol (50 ml) heated under reflux. When pyrrolidine (2 drops) was added to the resulting green solution the latter turned red. The mixture was heated under reflux for a further 5 h, then cooled to 0 °C, and the precipitate (25.1 g) was filtered off, washed with cold (0 °C) ethanol, and dried. The product was shown by t.l.c. to be a mixture of three components (see main text). The mass spectrum of the mixture indicated the presence of the anil (17) (M^+, 347.0936. $C_{16}H_{17}N_3O_4S$) and the nitrone (23) (M^+, 363.0917. Calc. for $C_{16}H_{17}N_3O_5S$: M, 363.0916). The absence of a metastable peak at 331.71 suggests that the peak at m/e 347 does not arise by loss of oxygen from the nitrone, m/e 363 (*cf.* pyridine 1-oxides) (source temp. 200 °C).

The two major components were separated in a sample of the mixture by h.p.l.c. Chloroform–iso-octane (3 : 7) eluted (i) *N*-(5-ethoxycarbonyl-3-nitrothiophen-2-ylidene)-4-dimethylaminoaniline (17) (Found: M^+, 347.0936. Calc. for $C_{16}H_{17}N_3O_4S$: M, 347.0940), identical (m.p. and ^{1}H n.m.r. spectrum) with an authentic sample prepared as described later, as the minor component; and (ii) N-(5-*ethoxy carbonyl*-3-*nitrothiophen*-2-*ylidene*)-4-*dimethylaminoaniline* N-*oxide* (23), m.p. 209 °C (with decomp.) (from toluene), $\nu_{max.}$ (Nujol) 1 720 cm^{-1} (C:O) (Found: C, 52.9; H, 5.0; N, 11.7%; M^+, 363. $C_{16}H_{17}N_3O_5S$ requires C, 52.9; H, 4.7; N, 11.6%; M, 363).

TABLE 1

trans-1-Aryl-2-(5-methoxycarbonyl-3-nitro-2-thienyl)ethenes

Compound no.	Reaction time (h)	M.p. (°C)	Yield (%)	Found (%) C	H	N	Formula	Required (%) C	H	N
(5)	26	175—176 [a]	72	51.75	3.6	4.1	$C_{14}H_{10}ClNO_4S$	51.9	3.1	4.3
(6)	24	166—168 [a]	72	56.0	4.3	4.1	$C_{15}H_{13}NO_5S$	56.4	4.1	4.4
(7)	24	175—176 [b]	66	57.6	5.0	8.6	$C_{16}H_{16}N_2O_4S$	57.8	4.85	8.4
(8)	24	224—225 [c]	70	53.9	4.9	3.6	$C_{17}H_{17}NO_7S$	53.8	4.5	3.7
(9)	72	146—147 [d]	37	59.3	4.45	4.6	$C_{15}H_{13}NO_4S$	59.4	4.3	4.6
(10)	24	118—119 [e]	67	56.2	4.2	4.2	$C_{15}H_{13}NO_5S$	56.4	4.1	4.4
(11)	72	168—170 [f]	30	53.55	3.5	9.6	$C_{13}H_{10}N_2O_4S$	53.8	3.5	9.6

[a] From ethanol–ethyl acetate. [b] From ethyl acetate. [c] From ethanol. [d] From ether–light petroleum. [e] From light petroleum. [f] From ethanol–light petroleum.

TABLE 2

Methyl 5-arylthieno[3,2-*b*]pyrrole-2-carboxylates [a]

Compound no.	Reaction time (h)	M.p. (°C)	Yield (%)	Found (%) C	H	N	Formula	Required (% C	H	N
(1)	2.0	148—150 [b]	25	57.1	3.6	4.9	$C_{14}H_{10}ClNO_2S$	57.6	3.45	4.8
(2)	2.5	166—167 [b,c]	35				$C_{15}H_{13}NO_2S$			
(3)	2.0	266 (decomp.) [d,e]	59	63.6	5.5	9.1	$C_{16}H_{16}N_2O_2S$	64.0	5.4	9.3
(4)	3.25	273—275 (decomp.) [d,f]	70	58.8	5.0	3.9	$C_{17}H_{17}NO_5S$	58.8	4.9	4.0

[a] Mass spectra were consistent with structures assigned. [b] From toluene. [c] Found: M^+, 287.0611. $C_{15}H_{13}NO_3S$ requires M, 287.0616; $\nu_{max.}$(Nujol) 1 690 (C:O) and 3 310 cm^{-1} (NH). [d] From chloroform–dichloromethane. [e] $\nu_{max.}$(Nujol) 1 700 (C:O) and 3 419 cm^{-1} (NH). [f] $\nu_{max.}$(Nujol) 1 700 (C:O) and 3 438 cm^{-1} (NH).

Condensation of Methyl 2-*Methyl*-3-*nitrothiophen*-5-*carboxylate with* NN-*Dimethyl*-4-*nitrosoaniline*.—This reaction, carried out in a manner similar to that described in the preceding paragraph, yielded a mixture (t.l.c. and ^{1}H n.m.r. and mass spectroscopy) (see main text) of *N*-(5-methoxycarbonyl-3-nitrothiophen-2-ylidene)-4-dimethylaminoaniline (16) (14 mol %) and its *N*-oxide (22) (86 mol %). The relative proportions of these two compounds were determined by ^{1}H n.m.r. spectroscopy; the chemical shifts of the anil (16) were the same as those of an authentic sample (see later). Five recrystallisations of the mixture from toluene gave the N-*oxide* (22), m.p. 230 °C (with decomp.), $\nu_{max.}$ (Nujol) 1 725 cm^{-1} (C:O) (Found: C, 51.6; H, 4.3; N, 12.1%; M^+, 349. $C_{15}H_{15}N_3O_5S$ requires C, 51.6; H, 4.3; N, 12.0%; M, 349).

Selective Hydrolysis of the Nitrone (22)–*Anil* (16) *Mixture*.—A sample (1.0 g) of the mixture, prepared as described in the preceding paragraph, was hydrolysed by stirring with 2M-sulphuric acid (20 ml) for 15 min at ambient temperature. Extraction with chloroform, distillation of the solution, and recrystallisation of the residue from toluene gave the nitrone (22) (0.5 g), identical (m.p., t.l.c., and ^{1}H

[16] W. W. Gale, A. N. Scott, and H. R. Snyder, *J. Org. Chem.*, 1964, **29**, 2160.

n.m.r. spectrum) with the sample obtained as described in the preceding paragraph.

Condensation of 2-Methyl-3-nitrobenzo[b]*thiophen with* NN-*Dimethyl-4-nitrosoaniline*.—A mixture of the benzo[*b*]-thiophen (1.93 g, 10.0 mmol) and *NN*-dimethyl-4-nitroso-aniline (2.25 g, 15.0 mmol) in methanol (12 ml) was heated under reflux for 5 h, then cooled. The dark-red precipitate was filtered off and shown by t.l.c. and ^{1}H n.m.r. spectroscopy to be a mixture (2.81 g) of the anil (26) (14 mol %) and the nitrone (27) (86 mol %). A sample (1.0 g) of this mixture was hydrolysed by stirring with 2M-sulphuric acid for 15 min at ambient temperature. Extraction with chloroform gave N-(3-*nitro*-2-*benzo*[b]*thenylidene*)-4-*dimethylaminoaniline* N-*oxide* (27) (0.30 g), m.p. 239—240 °C (from toluene) (Found: C, 59.7; H, 4.4; N, 12.2%; M^+, 341. $C_{17}H_{15}N_3O_3S$ requires C, 59.8; H, 4.4; N, 12.3%; *M*, 341).

N-(3-*Nitrobenzo*[b]*thiophen*-2-*ylidene*)-4-*dimethylamino-aniline* (26).—4-Dimethylaminoaniline (0.14 g, 1.0 mmol) in methanol (2.5 ml) was added to a stirred solution of 3-nitrobenzo[*b*]thiophen-2-carbaldehyde (0.21 g, 1.0 mmol) in methanol (2.5 ml) and the resulting purple mixture was heated under reflux for 10 min. The mixture was cooled and the dark-red precipitate filtered off and recrystallised from toluene to yield the *anil* (26) (0.25 g, 76%), m.p. 224—225 °C (Found: C, 62.6; H, 4.6; N, 12.6%; M^+, 325. $C_{17}H_{15}N_3O_2S$ requires C, 62.75; H, 4.65; N, 12.9%; *M*, 325) (*cf.* ref. 3).

2-*Formyl*-3-*nitrothiophen*-5-*carboxylic Acid* (19).—A mixture (5.0 g) of the anil (16) and the nitrone (22), prepared as described before, was added to concentrated hydrochloric acid (100 ml), and the resulting mixture was heated under reflux for 1 h. Then it was cooled, and extraction with ether gave the *acid* (19) (2.7 g, 98%), yellow crystals, m.p. 172—174 °C (sublimed at 138 °C and 0.002 mmHg), $\nu_{max.}$ (Nujol) 1 687 and 1 705 cm^{-1} (C:O) (Found: C, 35.3; H, 1.7; N, 6.9%; M^+, 201. $C_6H_3NO_5S$ requires C, 35.8; H, 1.5; N, 7.0%; *M*, 201).

Similar hydrolysis of a mixture (5.0 g) of the anil (17) and the nitrone (23) also gave the acid (19) (2.52 g, 90%).

Methyl 2-*Formyl*-3-*nitrothiophen*-5-*carboxylate* (20).—(*a*) A stirred mixture of 2-formyl-3-nitrothiophen-5-carboxylic acid (19) (5.02 g, 25.0 mmol), sodium hydrogen carbonate (3.20 g, 38.0 mmol), and hexamethylphosphoramide (20 ml) was heated at 100 °C for 15 min while carbon dioxide evolution was monitored. Dimethyl sulphate (6.30 g, 50.0 mmol) was added and the mixture was heated at 100 °C for a further 1 h. Then it was cooled and poured into water, and extraction with ether gave a red oil (5.38 g). Distillation gave the *formyl ester* (20) (4.89 g, 91%), b.p. 110 °C at 10^{-3} mmHg (Kugelrohr apparatus), m.p. 47—49 °C (from light petroleum), $\nu_{max.}$ (Nujol) 1 695 (CHO) and 1 735 cm^{-1} (ester C:O) (Found: C, 38.5; H, 2.5; N, 6.4%; M^+, 215. $C_7H_5NO_5S$ requires C, 39.1; H, 2.3; N, 6.5%; *M*, 215).

(*b*) A reaction carried out in acetone according to the procedure described in (*a*) gave the same product in only 33% yield.

(*c*) Esterification of the acid (19) with methyl iodide in hexamethylphosphoramide for 15 h at ambient temperature and work-up as described in (*a*) gave the formyl ester (20) (70%), identical (m.p. and i.r. and ^{1}H n.m.r. spectra) with the other samples.

(*d*) A mixture (1.0 g) of the anil (16) and the nitrone (22) was stirred with 3M-sulphuric acid for 2.2 h at ambient temperature. Extraction with ether gave a red oil (0.45 g) which was distilled at 110 °C and 10^{-3} mmHg (Kugelrohr apparatus) to give the ester (20), m.p. 47—48 °C (from light petroleum).

Ethyl 2-*Formyl*-3-*nitrothiophen*-5-*carboxylate* (21).—(*a*) A mixture (2.0 g) of the anil (17) and the nitrone (23) was stirred with 6M-sulphuric acid for 5 min at ambient temperature, then the sulphuric acid was diluted to 3M and the mixture was stirred at the same temperature for a further 2.5 h. Extraction with ether gave a red oil (0.85 g), which was distilled at 90 °C and 0.01 mmHg (Kugelrohr apparatus) to give *ethyl* 2-*formyl*-3-*nitrothiophen*-5-*carboxylate* (21) (0.70 g, 56% based on nitrone), m.p. 35—36 °C (from light petroleum), $\nu_{max.}$ (Nujol) 1 682 (CHO) and 1 732 cm^{-1} (ester C:O) (Found: C, 41.7; H, 3.0; N, 6.05%; M^+, 229. $C_8H_7NO_5S$ requires C, 41.9; H, 3.1; N, 6.1%; *M*, 229).

(*b*) To a solution of 2-formyl-3-nitrothiophen-5-carboxylic acid (0.201 g, 1.0 mmol) in hexamethylphosphoramide (2.5 ml) was added sodium hydroxide (0.06 g, 1.5 mmol) in water (2 ml) and the solution was shaken for 30 min at ambient temperature. Ethyl iodide (0.62 g, 4.0 mmol) was added and shaking was continued for a further 30 min. Addition of 5% hydrochloric acid (5 ml) followed by extraction with ether gave a red oil (0.30 g) which was chromatographed on alumina. Chloroform eluted (i) ethyl 2-formyl-3-nitrothiophen-5-carboxylate (0.106 g, 46%), b.p. 90 °C at 10^{-2} mmHg (Kugelrohr apparatus), yellow solid, m.p. 35—36 °C (from light petroleum), identical (i.r. and ^{1}H n.m.r. spectrum) with the sample prepared as described in (*a*); and (ii) *ethyl* 3-*nitrothiophen*-5-*carboxylate* (0.1 g, 50%), m.p. 60—62 °C (from light petroleum), b.p. 75 °C at 0.05 mmHg (Kugelrohr apparatus), $\nu_{max.}$ (Nujol) 1 710 cm^{-1} (C:O) (Found: C, 42.1; H, 3.7; N, 6.7%; M^+, 201. $C_7H_7NO_4S$ requires C, 41.8; H, 3.5; N, 7.0%; *M*, 201).

N-(5-*Methoxycarbonyl*-3-*nitrothiophen*-2-*ylidene*)-4-*dimethylaminoaniline* (16).—4-Dimethylaminoaniline (0.75 g, 5.5 mmol) in methanol (6 ml) was added to a stirred solution of methyl 2-formyl-3-nitrothiophen-5-carboxylate (20) (1.08 g, 5.0 mmol) in methanol (4 ml). The resulting purple mixture was heated under reflux for 10 min, then kept overnight at ambient temperature. The precipitate was filtered off, washed with methanol (8 ml), and dried *in vacuo* (10^{-2} mmHg) to give the *anil* (16) (1.47 g, 88%), m.p. 175—176 °C (from toluene), $\nu_{max.}$ (Nujol) 1 740 cm^{-1} (C:O) (Found: C, 53.5; H, 4.6; N, 12.45%; M^+, 333. $C_{15}H_{15}N_3O_4S$ requires C, 54.0; H, 4.5; N, 12.6%; *M*, 333).

The following anils were prepared similarly: N-(5-*methoxycarbonyl*-3-*nitrothiophen*-2-*ylidene*)*aniline* (15) (85%), m.p. 129—130 °C (from light petroleum), $\nu_{max.}$ (Nujol) 1 740 cm^{-1} (C:O) (Found: C, 53.3; H, 3.4; N, 9.6%; M^+, 290. $C_{13}H_{10}N_2O_4S$ requires C, 53.8; H, 3.5; N, 9.65%; *M*, 290); and N-(5-*carboxy*-3-*nitrothiophen*-2-*ylidene*)-4-*dimethylaminoaniline* (18) (70%), m.p. 186—187 °C (with decomp.) (from ethyl acetate), $\nu_{max.}$ (Nujol) 1 680 cm^{-1} (C:O) (Found: C, 52.4; H, 4.2; N, 13.0%; M^+, 319. $C_{14}H_{13}N_3O_4S$ requires C, 52.7; H, 4.1; N, 13.2%; *M*, 319).

Methyl 5-(4-*Dimethylaminophenyl*)*thieno*[3,2-c]*pyrazole*-2-*carboxylate* (13).—(*a*) A mixture of the anil (16) (0.50 g, 1.50 mmol), triethyl phosphite (0.77 g, 4.60 mmol), and t-butylbenzene (5 ml) was heated under reflux for 14 h. The excess of reagent, the solvent, and the triethyl phosphate produced were distilled off at 10^{-3} mmHg, and the

residue was chromatographed on alumina. Ether eluted the *thienopyrazole* * (13) (0.17 g, 37%), m.p. 195—197 °C (from carbon tetrachloride), $\nu_{max.}$ (Nujol) 1 705 and 1 725 cm^{-1} (C:O) (Found: C, 59.8; H, 5.0; N, 14.0%; M^+, 301. $C_{15}H_{15}N_3O_2S$ requires C, 59.8; H, 5.0; N, 13.9%; *M*, 301).

Methyl 5-phenylthieno[3,2-c]*pyrazole-2-carboxylate* (12) (21%), m.p. 159—160 °C (from carbon tetrachloride), $\nu_{max.}$ (Nujol) 1 705 and 1 725 cm^{-1} (C:O) (Found: C, 60.2; H, 4.0; N, 11.0%; M^+, 258. $C_{13}H_{10}N_2O_2S$ requires C, 60.45; H, 3.9; N, 10.85%; *M*, 258), was prepared similarly from the anil (15). Reductive cyclisation of the anil (18) with triethyl phosphite resulted in simultaneous esterification of the acid group to give *ethyl 5-(4-dimethylaminophenyl)thieno*[3,2-c]*pyrazole-2-carboxylate* (14) (after work-up as described before the crude product was chromatographed on a silica thick-layer with chloroform as eluant; a band which fluoresced bright yellow under u.v. light was collected and washed several times with chloroform); yield 11%; m.p. 174—175 °C (from toluene), $\nu_{max.}$ (Nujol) 1 710 and 1 725 cm^{-1} (C:O) (Found: C, 60.5; H, 5.5; N, 12.9%; M^+, 315. $C_{16}H_{17}N_3O_2S$ requires C, 60.9; H, 5.4; N, 13.3%; *M*, 315).

(*b*) A mixture of the nitrone (22) (0.17 g, 0.5 mmol), triethyl phosphite (0.29 g, 1.75 mmol), and t-butylbenzene (5 ml) was heated under reflux for 14 h. Work-up as described in (*a*) gave, after chromatography on alumina, the thienopyrazole * (13) (0.02 g, 12%), m.p. 195—196 °C (from carbon tetrachloride), identical in other respects (i.r. and ^1H n.m.r. spectra) with the sample prepared as described in (*a*).

Ethyl 5-(4-dimethylaminophenyl)thieno[3,2-*c*]pyrazole-2-carboxylate * (14) (11%), m.p. 174—175 °C (from toluene), identical in other respects (i.r. and ^1H n.m.r. spectra) with the sample prepared as described before, was prepared similarly from the nitrone (23).

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* The thienopyrazoles (12)—(14) are readily detected on the column by their fluorescence under u.v. illumination.