1,2-Benzisothiazoles. Part III.[1] 3-Substituted Derivatives

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Ethyl (1,2-benzisothiazol-3-yl)cyanoacetate exists as a mixture of two tautomers which decomposes to (1,2-benzisothiazol-3-yl)acetonitrile (85%) when heated in dimethyl sulphoxide. Treatment of diethyl (1,2-benzisothiazol-3-yl)malonate with ethanolic sodium ethoxide gives ethyl (1,2-benzisothiazol-3-yl)acetate, which affords 3-methyl-1,2-benzisothiazole on successive hydrolysis and decarboxylation. The methyl group in 3-methyl-1,2-benzisothiazole is resistant to oxidation. Attempted Vilsmeier–Haack formylation of 3-methyl-1,2-benzisothiazole with dimethylformamide and phosphoryl chloride gives a mixture of N^2-(3-benzo[*b*]thienyl)-N^1N^1-dimethylformamidine and N^2-(2-formyl-3-benzo[*b*]thienyl)-N^1N^1-dimethylformamidine. In contrast, 2-methylbenzothiazole gives (benzothiazol-2-yl)malonaldehyde or a related enamine.

We have shown[1] that 3-chloro-1,2-benzisothiazole, when treated with ethyl cyano(sodio)acetate or diethyl sodiomalonate, can either rearrange to give benzo[*b*]-thiophen derivatives or can undergo normal nucleophilic substitution to give the expected products, (1) and (3) respectively. We hoped to use these products as starting materials for the preparation of a range of 3-substituted 1,2-benzisothiazoles which, by analogy with certain 3-substituted indoles[2] and benzo[*b*]thiophens,[3] might be expected to possess useful biological activity.

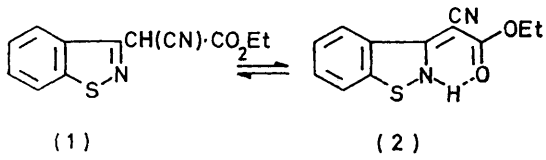
Spectroscopic evidence suggested that the product from the reaction with ethyl cyano(sodio)acetate exists as a mixture of the tautomers (1) and (2). The i.r. spectrum of the mixture (in KCl) showed strong NH absorption at 3190, strong absorption at 1625 (chelated C=O), and relatively weak absorption at 1745 (normal ester C=O) cm^{-1}, indicating the predominance of tautomer (2) in the solid phase. The relative intensities of the two carbonyl absorptions were reversed in the spectrum of a solution in chloroform, showing that tautomer (1)

[1] Part II, D. E. L. Carrington, K. Clarke, and R. M. Scrowston, *J. Chem. Soc.* (*C*), 1971, 3903.

[2] *E.g.*, V. Erspamer, *Drug. Res.*, 1961, **3**, 151.

[3] E. Campaigne, D. R. Knapp, E. S. Neiss, and T. R. Bosin, *Adv. Drug. Res.*, 1970. **5**. 1.

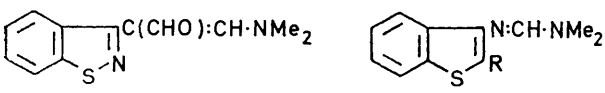
predominates under these conditions. The n.m.r. spectrum [$CDCl_3$ or $(CD_3)_2SO$] confirmed the latter observation by showing a broad, weak signal at low field [δ 12·18 p.p.m.; exchangeable by D_2O(NH)], a singlet at δ 6·64 p.p.m. (CH·CN), and two closely related sets of ethyl proton signals, which became coincident when the solution in [$^2H_6$]dimethyl sulphoxide was



(1) (2)

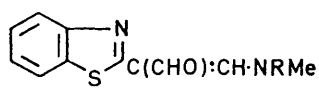
(3)

(4) X = CN
(5) X = CO_2Et
(6) X = CO_2H



(7)

(8) R = H
(9) R = CHO



(10) R = Me
(11) R = Ph

heated to *ca.* 80°. Above this temperature the solute decomposed unexpectedly into ethanol and a single product with the spectral characteristics expected for (1,2-benzisothiazol-3-yl)acetonitrile (4). On a preparative scale the decomposition in dimethyl sulphoxide was accomplished in high yield (85%), confirming that the two components of the original mixture were indeed the tautomers (1) and (2), even though attempts to separate them were unsuccessful. The decomposition of certain substituted ethyl cyanoacetates, $R_2C(CN)\cdot CO_2Et$, into the corresponding nitriles, $R_2CH\cdot CN$, and diethyl carbonate by base-catalysed ethanolysis is known.[4] The ready decomposition observed in the present case is probably due to the hydrolysis of the reactive carbonyl group by water present in the solvent, followed by the decarboxylation of the resulting acid.

We next used diethyl (1,2-benzisothiazol-3-yl)malonate (3), for which we could find no evidence for tautomerism of the type just described, as the starting material for an independent synthesis of the nitrile (4). The preparation was facilitated when we found that the substituted diethyl malonate (3) did not react with urea in the presence of sodium ethoxide to give a pyrimidine derivative, but gave instead ethyl (1,2-benzisothiazol-3-yl)acetate (5) (67%) and diethyl carbonate. Similar reverse Claisen reactions have been observed [5] for other substituted diethyl malonate derivatives. When urea was omitted from the reaction the same product (5) was formed, but in lower yield (<50%). The ester (5) was converted by standard procedures (see Experimental section) into the cyanomethyl compound (4), identical with that just described.

Hydrolysis of the ester (5) gave the corresponding carboxylic acid (6) which readily lost CO_2 at its m.p. to give 3-methyl-1,2-benzisothiazole. Crawford and Woo [6] have obtained 3-methyl-1,2-benzisothiazole (60%) by heating *o*-(methylthio)acetophenone oxime *O*-*p*-nitrobenzoate in tetrachloroethane. We heated *o*-(benzylthio)acetophenone oxime *O*-*p*-nitrobenzoate in diethylene glycol (to facilitate work-up) and obtained 3-methyl-1,2-benzisothiazole (66%), identical with that obtained by decarboxylation of the acid (6).

Next we hoped to use 3-methyl-1,2-benzisothiazole to prepare some 3-substituted 1,2-benzisothiazoles. Treatment with selenium dioxide, which readily converts 2-methylbenzothiazole into the 2-carbaldehyde [7] gave back starting material. Attempted oxidation to the 3-carbaldehyde (with CrO_3–Ac_2O–H_2SO_4) gave 3-methyl-1,2-benzisothiazole 1,1-dioxide (19%) as the only identifiable product. The same 1,1-dioxide was obtained more readily by the use of hydrogen peroxide in acetic acid. Unlike 2-methylbenzothiazole [8] and other compounds with 'reactive' methyl groups, 3-methyl-1,2-benzisothiazole did not react with benzaldehyde or chloral, even under forcing conditions.

Attempted Vilsmeier–Haack formylation of 3-methyl-1,2-benzisothiazole with dimethylformamide and phosphoryl chloride at 100° gave a mixture of two products, which were separated with difficulty. The major (85%) component, $C_{12}H_{12}N_2OS$ (mass spectrum), was first believed to be the enamine (7), by analogy with the product of Vilsmeier–Haack formylation of 4-methylpyridine.[9] Structure (7) was apparently supported by the n.m.r. spectrum, which showed a typical ABCD pattern for the four aromatic proton signals, and singlets at δ 9·82 (CHO), 7·65 (=C*H*·NMe_2), and 3·17 (6H, NMe_2) p.p.m. However, the fact that acidic or alkaline hydrolysis of the supposed enamine (7) failed to produce any of the expected dialdehyde prompted us to seek an alternative structure.

The major compound was identified correctly during

[4] R. Ya. Levina and F. K. Velichko, *Russ. Chem. Rev.*, 1960, **29**, 437.
[5] A. C. Cope and S. M. McElvain, *J. Amer. Chem. Soc.*, 1932, **54**, 4319.
[6] R. J. Crawford and C. Woo, *J. Org. Chem.*, 1966, **31**, 1655.
[7] Methoden der Organischen Chemie (Houben-Weyl), 1954, **7/1**, 149.
[8] A. I. Kiprianov and A. Ya. Il'chenko, *Zhur. obshchei Khim.*, 1965, **35**, 498.
[9] Z. Arnold, *Coll. Czech. Chem. Comm.*, 1963, **28**, 863.

experiments on the minor (15%) component from the formylation reaction. The latter had the formula, $C_{11}H_{12}N_2S$ (mass spectrum), and its n.m.r. spectrum showed the presence of four aromatic protons, two *uncoupled* vinylic proton signals (δ 7·69 and 6·51 p.p.m.), and a dimethylamino-group (δ 3·02 p.p.m.). These data were inconsistent with any structure based upon the 1,2-benzisothiazole nucleus, but were consistent with the formamidine structure (8). Further, the mass spectrum showed peaks at *m/e* values corresponding to $M - 1$, $M -$ Me, $M -$ Me $-$ HCN, $M - CH_2N$, and $\overset{+}{N}Me_2$, and was thus closely similar to that [10] of N^1N^1-dimethyl-N^2-phenylformamidine ($PhN{=}CH{\cdot}NMe_2$). The structure was confirmed by heating the minor component with acetic anhydride in the presence of either sodium hydroxide or acetic acid; in either case successive hydrolysis and acetylation occurred to give the known 3-acetamidobenzo[*b*]thiophen. We attempted to prepare [11] N^2-(3-benzo[*b*]thienyl)-N^1N^1-dimethylformamidine (8) by treating 3-aminobenzo[*b*]thiophen (prepared *in situ* by the decarboxylation of the corresponding 2-carboxylic acid) with dimethylformamide and phosphoryl chloride, but it was obtained in only low yield; the major product was identical with the major product from the formylation reaction of 3-methyl-1,2-benzisothiazole. It became apparent that N^2-(3-benzo[*b*]-thienyl)-N^1N^1-dimethylformamidine (8) was the first product of the formylation of both 3-methyl-1,2-benzisothiazole and 3-aminobenzo[*b*]thiophen and was formylated further to give the aldehyde (9). In support of this suggestion the minor formylation product (8) gave the aldehyde (9) under the Vilsmeier–Haack conditions used previously. Further, when the formylation of 3-methyl-1,2-benzisothiazole was carried out at room temperature, the formamidine (8) became the major product. Structure (7) is therefore incorrect and must be amended to (9).

These results suggest that the attempted formylation of 3-methyl-1,2-benzisothiazole may proceed *via* the isomeric 3-aminobenzo[*b*]thiophen, but further work on the mechanism of the reaction is in progress. There are several [1,12] known examples of the conversion of 1,2-benzisothiazole derivatives into benzo[*b*]thiophens, but the type of ring-opening reaction described here appears to be novel.

We confirmed that 2-methylbenzothiazole behaves similarly to 4-methylpyridine [9] on Vilsmeier–Haack formylation. With dimethylformamide and phosphoryl chloride the expected enamine (10) was hydrolysed during work-up to give (benzothiazol-2-yl)malonaldehyde, which was characterised by its reactions with hydroxylamine and hydrazine to give an isoxazole and a pyrazole derivative, respectively. With *N*-methylformanilide and phosphoryl chloride, the crystalline enamine (11) was isolated; it was readily hydrolysed to the malonaldehyde derivative just described.

EXPERIMENTAL

General experimental directions are given in Part I.[13]

(1,2-*Benzisothiazol*-3-*yl*)*acetonitrile* (4).—A mixture of ethyl (1,2-benzisothiazol-3-yl)cyanoacetate [1] (2·17 g, 0·09 mol), water (0·3 ml), and dimethyl sulphoxide (10 ml) was kept at 100° for 24 h, then cooled and poured into water. The resulting precipitate (1·3 g, 85%) was washed with water, dried in air, and crystallised from ethanol–light petroleum (b.p. 40—60°) (charcoal) to give (1,2-*benzisothiazol*-3-*yl*)-*acetonitrile* as needles, m.p. 57—59° (Found: C, 61·8; H, 3·4; N, 16·1%; *M*, 174. $C_9H_6N_2S$ requires C, 62·05; H, 3·5; N, 16·1%; *M*, 174), $\nu_{max.}$ 2260 cm^{-1} (C≡N), δ 8·2—7·4 (m, ArH) and 4·24 p.p.m. (s, $CH_2{\cdot}CN$).

Ethyl (1,2-*Benzisothiazol*-3-*yl*)*acetate* (5).—Diethyl (1,2-benzisothiazol-3-yl)malonate [1] (4·0 g, 0·014 mol) and a solution of urea (0·82 g, 0·014 mol) in hot ethanol (10 ml) were added successively to a solution of sodium (0·315 g, 0·014 g atom) in ethanol (8 ml), then the resulting mixture was boiled under reflux for 90 min, cooled, and poured into water. The resulting oil was extracted with ether, and the extracts were washed, dried, and evaporated. The residue crystallised from light petroleum (b.p. 40—60°) (charcoal) to give needles (2·0 g, 67%), m.p. 48—50° (lit.,[14] 49—50°),* $\nu_{max.}$ 1737 cm^{-1} (C=O), δ 8·0—7·3 (m, ArH), 4·19 (q, CH_2Me), 4·17 (s, $CH_2{\cdot}CO$), and 1·21 p.p.m. (t, $CH_2\mathit{Me}$).

(1,2-*Benzisothiazol*-3-*yl*)*acetic Acid* (6).—A mixture of ethyl (1,2-benzisothiazol-3-yl)acetate (1·0 g), ethanol (5 ml), and aqueous sodium hydroxide (1·35 ml; 15% w/v) was boiled under reflux for 45 min, cooled, and poured into water. The solution was treated with charcoal and filtered, and the filtrate was acidified with ice-cold dilute hydrochloric acid. The crystalline precipitate was collected, washed with water, and dried in air; it crystallised from ethanol as *prisms* (0·72 g, 82%), m.p. 148—149° (decomp.) [lit.,[14] 153—155° (decomp.)]], $\nu_{max.}$ 3200—2500 (OH) and 1720 cm^{-1} (C=O), δ [$(CD_3)_2SO$] 4·19 p.p.m. (s, CH_2).

(1,2-*Benzisothiazol*-3-*yl*)*acetamide*.—Aqueous ammonia (50 ml; *d* 0·88) was added to a solution of ethyl (1,2-benzisothiazol-3-yl)acetate (1·0 g) in ethanol (20 ml). The mixture was stirred overnight at room temperature and poured into water, and the resulting precipitate was filtered off and dried; it crystallised from ethanol as *prisms* (0·52 g, 60%), m.p. 187—189° (lit.,[14] 188—190°), $\nu_{max.}$ 3400, 3210 (NH_2), and 1665 (C=O) cm^{-1}.

A mixture of the amide (0·5 g) and phosphoryl chloride (2 ml) was boiled under reflux for 30 min, then cooled and poured on crushed ice. The resulting solid was filtered off, washed with water, dried, and crystallised from ethanol–light petroleum (b.p. 40—60°) to give (1,2-benzisothiazol-3-yl)acetonitrile (0·315 g, 70%), identical with that obtained before.

3-*Methyl*-1,2-*benzisothiazole*.— (1,2-Benzisothiazol-3-yl)-

* An alternative synthesis [14] of (1,2-benzisothiazol-3-yl)acetic acid and some of its derivatives from 4-hydroxy-1-thiocoumarin was reported after the present work had been completed.

[10] A. K. Bose, I. Kugajevsky, P. T. Funke, and K. G. Das, *Tetrahedron Letters*, 1965, 3065.

[11] *Cf.* H. Bredereck, R. Gompper, K. Klemm, and H. Rempfer, *Chem. Ber.*, 1959, **92**, 837.

[12] L. L. Bambas, ' Five-membered Heterocyclic Compounds with Nitrogen and Sulphur or Nitrogen, Sulphur, and Oxygen,' Interscience, New York, 1952, pp. 227 ff.

[13] D. E. L. Carrington, K. Clarke, and R. M. Scrowston, *J. Chem. Soc.* (*C*), 1971, 3262.

[14] M. Giannella, F. Gualtieri, and C. Melchiorre, *Phytochem.*, 1971, **10**, 539.

acetic acid (6) (33 g, 0·17 mol) was kept at 165° until the evolution of carbon dioxide had ceased. The resulting oil was distilled to give 3-methyl-1,2-benzisothiazole (23·4 g, 95%), b.p. 87—89° at 2·75 mmHg (Found: *M*, 149·029. Calc. for C_8H_7NS: *M*, 149·029), δ 8·0—7·3 (m, ArH) and 2·72 p.p.m. (s, Me).

o-(*Benzylthio*)*acetophenone* (*with* M. S. El Shanta).—*o*-(Benzylthio)benzoyl chloride [15] reacted in the usual [16] way with diethyl ethoxy(magnesio)malonate to give the *ketone* (75%) as plates, m.p. 143° (Found: C, 74·2; H, 6·0%; *M*, 242. $C_{15}H_{14}OS$ requires C, 74·35; H, 5·8%; *M*, 242), $\nu_{max.}$ 1670 cm^{-1} (C=O). The *oxime* had m.p. 178—180° (from benzene) (Found: C, 70·15; H, 5·8; N, 5·35. $C_{15}H_{15}NOS$ requires C, 70·1; H, 5·85; N, 5·45%).

3-*Methyl*-1,2-*benzisothiazole*.—Sodium amide (6 g) was added in portions to a rapidly stirred solution of *o*-(benzylthio)acetophenone oxime (26·0 g, 0·097 mol) in dry ether (500 ml) under nitrogen. The mixture was stirred overnight, a solution of *p*-nitrobenzoyl chloride (19·0 g, 0·102 mol) in dry ether (200 ml) was then added, and stirring was continued for a further 2 h. The mixture was filtered and the solid residue was washed with chloroform. The combined filtrates were then evaporated to dryness to give the oxime *O*-ester as a yellow solid which was used without further purification. The *O*-ester was boiled in diethylene glycol (200 ml) for 2 h, and the cooled solution was poured into water and shaken with ether (3 × 200 ml). The combined extracts were washed with water, dried, evaporated, and the gummy residue was extracted with boiling light petroleum (b.p. 60—80°). The petroleum extracts were distilled to give 3-methyl-1,2-benzisothiazole (10 g, 66%), b.p. 66—70° at 0·2 mmHg. The i.r. spectrum was identical with that of the product already described; the hydrochloride had m.p. 126—127° (lit.,[6] 116°).

Oxidation of 3-*Methyl*-1,2-*benzisothiazole*.—(a) *With hydrogen peroxide*. A mixture of 3-methyl-1,2-benzisothiazole (1·0 g), glacial acetic acid (10 ml), and hydrogen peroxide (1 ml; 28% w/v) was kept at 100° for 2 h, then cooled and diluted with water. The solid was collected, washed with water, and crystallised from ethanol to give 3-*methyl*-1,2-*benzisothiazole* 1,1-*dioxide* (0·5 g, 41%), m.p. 208—210° (Found: C, 52·8; H, 3·6; N, 7·6%; *M*, 181. $C_8H_7NO_2S$ requires C, 53·1; H, 3·9; N, 7·7%; *M*, 181), $\nu_{max.}$ 1325 and 1175 cm^{-1} (SO_2), δ 8·05—7·60 (m, ArH), and 2·65 p.p.m. (s, Me).

(b) *With chromium trioxide*. Concentrated sulphuric acid (4·4 ml) was added slowly to a stirred solution of 3-methyl-1,2-benzisothiazole (3·0 g, 0·02 mol) in acetic anhydride (25 ml). The mixture was cooled to 5° and a solution of chromium trioxide (5·5 g, 0·055 mol) in acetic anhydride (25 ml) was added dropwise so that the temperature did not exceed 10°. The mixture was then stirred for a further 15 min, and poured on crushed ice. The resulting solid was collected, washed with water, then suspended in a mixture of water (7 ml), ethanol (7 ml), and concentrated sulphuric acid (1·0 ml). The mixture was boiled under reflux for 30 min, cooled, and diluted with water. The resulting solid was collected, washed with water, and crystallised from ethanol, to give 3-methyl-1,2-benzisothiazole 1,1-dioxide (0·7 g, 19%), m.p. 208—210°, identical with that obtained in (a).

Attempted Vilsmeier–Haack Formylation of 3-*Methyl*-1,2-*benzisothiazole*.—3-Methyl-1,2-benzisothiazole (5·0 g, 0·033 mol) was added dropwise during 10 min to a stirred ice-cold mixture of dimethylformamide (5·0 g, 0·07 mol) and phosphoryl chloride (5·0 g, 0·033 mol). The mixture was kept at 100° for 5 h, cooled, and treated with an excess of aqueous 20% sodium carbonate. The resulting bright yellow solid (4·8 g) was collected and crystallised (×3) from light petroleum (b.p. 40—60°) to give N^2-(2-*formyl*-3-*benzo*[b]*thienyl*)-N^1N^1-*dimethylformamidine* (9) (component A), as needles, m.p. 115—116° (Found: C, 62·15; H, 5·25; N, 12·25%; *M*, 232·065. $C_{12}H_{12}N_2OS$ requires C, 62·05; H, 5·2; N, 12·15%; *M*, 232·066), $\lambda_{max.}$ 265 nm (ε 24,800), $\nu_{max.}$ 1650 [CO (*cf.* ref. 17)] and 1625 cm^{-1} (C=N), *m/e* 217 (*M* − Me), 204 (*M* − CH_2N, *m** 179), 190 (*M* − Me − HCN), and 162 (190 − CO, *m** 138).

A portion (0·15 g) of the solid remaining after evaporation of the mother liquor was dissolved in benzene and chromatographed on silica gel. Elution with ether gave N^2-(3-*benzo*[b]*thienyl*)-N^1N^1-*dimethylformamidine* (8) (component B) (50 mg). This formed needles, m.p. 70—71·5° [from light petroleum (b.p. 40—60°)] (Found: C, 64·8; H, 5·9; N, 13·65%; *M*, 204·072. $C_{11}H_{12}N_2S$ requires C, 64·8; H, 5·9; N, 13·7%; *M*, 204·072), $\lambda_{max.}$ 247 nm (ε 27,000), $\nu_{max.}$ 1630 cm^{-1} (C=N), *m/e* 203 (*M* − 1), 189·0477 (*M* − Me), 176·0523 (*M* − CH_2N, *m** 152), 162·0390 (*M* − Me − HCN, *m** 139), and 44 (Me_2N^+).

When the foregoing reactants were mixed and kept at room temperature overnight, the resulting mixture contained a greater proportion of component B [B : A ≡ 60 : 40 (t.l.c.)]. A single crystallisation from ethanol gave pure component A.

Identification of the Products from the Attempted Formylation Reaction. N^2-(3-*Benzo*[b]*thienyl*)-N^1N^1-*dimethylformamidine* (8).—(*a*) Acetic anhydride (1·0 ml) was added to a stirred, ice-cold solution of component B (0·2 g) in aqueous 10% sodium hydroxide (5 ml). The mixture was heated on a water-bath for 30 min, then cooled. The product was collected and crystallised from benzene–light petroleum (b.p. 60—80°) to give 3-acetamidobenzo[*b*]thiophen (0·10 g), m.p. 167—168° (lit.,[18] 169°), identical with authentic material.[17]

(*b*) A mixture of glacial acetic acid (10 ml), acetic anhydride (1·0 ml), and component B (0·2 g) was boiled for 2 h, then poured into ice–water. The product was extracted with chloroform, washed successively with aqueous sodium hydrogen carbonate and water, and dried. Evaporation of the solvent gave 3-acetamidobenzo[*b*]thiophen, m.p. 166—168°, identical with that prepared in (*a*).

Formylation of Component B.—A mixture of component B (0·2 g), dimethylformamide (0·2 g), and phosphoryl chloride (0·2 g) was kept at 70° for 2 h, then cooled and treated with an excess of aqueous 20% sodium carbonate. The product was collected and crystallised from ethanol to give N^2-(2-formyl-3-benzo[*b*]thienyl)-N^1N^1-dimethylformamidine (9) (component A), m.p. 114—115°, identical with that obtained before.

Vilsmeier–Haack Formylation of 3-*Aminobenzo*[b]*thiophen*.—3-Aminobenzo[*b*]thiophen-2-carboxylic acid [1] (1·0 g) and cumene (25 ml) were stirred and boiled under reflux for 90 min, after which time no starting material remained

[15] F. Gialdi, R. Ponci, and A. Baruffini, *Farmaco* (*Pavia*), *Ed. Sci.*, 1960, **15**, 856 (*Chem. Abs.*, 1961, **55**, 21,040).
[16] *Cf.* G. A. Reynolds and C. R. Hauser, *Org. Synth.*, 1950, **30**, 70.
[17] M. S. El Shanta and R. M. Scrowston, *J. Chem. Soc.* (*C*), 1967, 2084.
[18] M. S. El Shanta, R. M. Scrowston, and M. V. Twigg, *J. Chem. Soc.* (*C*), 1967, 2364.

(t.l.c.). The solution was cooled and shaken with 2M-hydrochloric acid (2 × 50 ml). The acid layer was washed with ether and basified with 2M-sodium hydroxide, and the resulting amine was extracted into ether. The ether was evaporated off and the residue was dissolved in dimethylformamide (5 ml) and added to an ice-cooled, stirred solution of phosphoryl chloride (2 ml) in dimethylformamide (4 ml). The mixture was allowed to attain room temperature and was then kept at 70—80° for 2 h, cooled, and treated with an excess of aqueous 20% sodium carbonate. The resulting solid was collected, washed, and dried. T.l.c. revealed the presence of two components with the same R_F values as components A and B (see before). Crystallisation from ethanol gave N^2-(2-formyl-3-benzo[*b*]thienyl)-N^1N^1-dimethylformamidine (0·25 g), m.p. 113·5—114·5°, identical with the major product (component A) from the attempted formylation of 3-methyl-1,2-benzisothiazole, and with the product obtained by formylation of component B under the conditions described earlier.

Vilsmeier–Haack Formylation of 2-Methylbenzothiazole (*with* M. S. El Shanta *and* R. M. Thompson).—2-Methylbenzothiazole (2·5 g) was added to a stirred mixture of *N*-methylformanilide (3·2 g) and phosphoryl chloride (3·2 g). The mixture was stirred at 70—80° for 5 h, cooled, treated with aqueous 40% sodium carbonate, and set aside overnight. The precipitate was collected, washed with water, and crystallised from ethanol, to give *benzothiazol-2-yl-*(N-*methylanilinomethylene*)*acetaldehyde* (11) (2·8 g, 60%) as yellow needles, m.p. 140—142° (Found: C, 69·45; H, 4·5; N, 9·55%; *M*, 294·0827. $C_{17}H_{14}N_2OS$ requires C, 69·45; H, 4·8; N, 9·55%; *M*, 294·0827), $\lambda_{max.}$ 269 and 382 nm (ε 27,800 and 10,500), $\nu_{max.}$ 1648 cm^{-1} (C=O), δ 9·94 (s, CHO), 8·17 (s, =CH), and 3·6 p.p.m. (s, NMe), *m/e* 266 (*M* − CO), 265 (*M* − CHO), and 188 (*M* − PhNMe, *m** 120).

Hydrolysis of the Enamine (11).—A suspension of the enamine (1·0 g) in aqueous 50% sodium hydroxide (10 ml) was stirred at 70—80° for 2 h, then cooled, diluted with water, and acidified with hydrochloric acid. The precipitate was collected, washed with water, and crystallised from ethanol, to give (*benzothiazol-2-yl*)*malonaldehyde* (0·45 g, 70%), m.p. 227—230° (decomp.) (Found: C, 58·35; H, 3·3; N, 6·75%; *M*, 205·0193. $C_{10}H_7NO_2S$ requires C, 58·6; H, 3·45; N, 6·8%; *M*, 205·0196), $\lambda_{max.}$ 261 and 352 nm (ε 15,400 and 23,400), $\nu_{max.}$ 2815 and 2745 cm^{-1} (CH of CHO), δ 9·55 (s, CHO) and 9·52 p.p.m. (s, CHO), *m/e* 177 (*M* − CO, *m** 152·8), 176 (*M* − CO − H, *m** 175), 148 (176 − CO, *m** 124·3), and 29 (HC≡O$^+$).

The same malonaldehyde derivative was formed (70%) when the formylation of 2-methylbenzothiazole was carried out as already described, by using dimethylformamide in place of *N*-methylformanilide.

4-(*Benzothiazol-2-yl*)*isoxazole*.—A mixture of (benzothiazol-2-yl)malonaldehyde (0·5 g), hydroxylamine hydrochloride (0·21 g), and sodium acetate (2·5 g) in ethanol (30 ml) was heated under reflux for 30 min, evaporated to 10 ml under reduced pressure, and diluted with water. The precipitate was collected, washed with water, and crystallised from benzene as brownish *needles* (0·33 g), m.p. 208—210° (Found: C, 59·3; H, 2·85; N, 13·6. $C_{10}H_6N_2OS$ requires C, 59·4; H, 3·0; N, 13·85%), δ 7·15 (d, CH=N) and 7·33 p.p.m. (d, *J* 1·75 Hz, =CH–O), *m/e* 202 (*M*$^+$), 174 (*M* − CO, *m** 149·6), and 147 (*M* − CO − HCN, *m** 124·0).

4-(*Benzothiazol-2-yl*)*pyrazole*.—An ethanolic solution of (benzothiazol-2-yl)malonaldehyde (0·5 g) and hydrazine hydrate (98% w/v; 2 ml) was kept at room temperature for 3 h. The solvent was removed under reduced pressure, and the residue crystallised from benzene as brown *plates* (0·25 g), m.p. 213—214° (Found: C, 59·5; H, 3·3; N, 20·65. $C_{10}H_7N_3S$ requires C, 59·7; H, 3·5; N, 20·9%), $\lambda_{max.}$ 226 and 290 nm (ε 19,700 and 16,500), *m/e* 201 (*M*$^+$), 174 (*M* − HCN, *m** 150·6), 173 (*M* − HCN − H), and 146 (173 − HCN, *m** 123·2).

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