

Condensed Thiophen Ring Systems. Part IX.¹ Synthesis and Some Reactions of [1]Benzothieno[3,2-*c*]cinnolines

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[1]Benzothieno[3,2-*c*]cinnoline (1) and some of its derivatives are obtained (55—75% yields) when aqueous solutions of the diazonium chlorides derived from 2-(*o*-aminophenyl)benzo[*b*]thiophens are kept at room temperature. A number of reactions of compound (1) are reported.

IN Part VIII¹ we reported the synthesis of 2-(*o*-azidophenyl)benzo[*b*]thiophen through diazotisation of 2-(*o*-aminophenyl)benzo[*b*]thiophen and treatment of the diazonium compound with sodium azide at 0°. A by-product of this reaction was the hitherto unknown heterocycle, [1]benzothieno[3,2-*c*]cinnoline (1), which arises by a Widman-Stoermer-type cyclisation of the diazonium compound.² We have found that a high yield (75%) of compound (1) is obtained when an aqueous solution of the diazonium compound is kept at room temperature. Ring-closure on to the thiophen ring is due to the resonance contributor (4), and is analogous to the recently reported³ synthesis of 2-

methoxybenzo[*c*]cinnoline (5), where the methoxy-group provides the necessary activation for cyclisation. The reaction which we now report can be extended, for example to prepare 8-methyl- (2) and 8-chloro-[1]benzothieno[3,2-*c*]cinnoline (3).

[1]Benzothieno[3,2-*c*]cinnoline (1) undergoes the expected reactions; for example it is oxidised by peroxyacetic acid² to a trioxide. The i.r. spectrum of this compound confirms the presence of a sulphone group (ν_{\max} 1155 and 1310 cm^{-1}), but its spectroscopic properties do not indicate the position of *N*-oxidation. Oxidation with alkaline potassium permanganate at 90—95°⁴ gave [1]benzothieno[3,2-*c*]pyridazine-3,4-dicarboxylic acid (6), a derivative of a new heterocyclic system. (Benzo[*b*]thiophen is readily oxidised by this reagent

¹ Part VIII, K. E. Chippendale, B. Iddon, and H. Suschitzky, preceding paper.

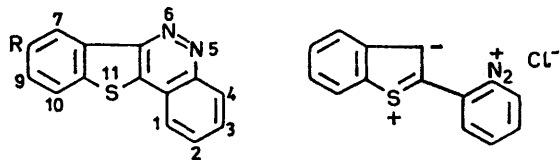
² J. C. E. Simpson, 'Condensed Pyridazine and Pyrazine Rings,' ed. A. Weissberger, Interscience, New York, 1953, Part I, pp. 3—65.

³ J. S. Swenton, T. J. Ikeler, and B. H. Williams, *J. Amer. Chem. Soc.*, 1970, **92**, 3103.

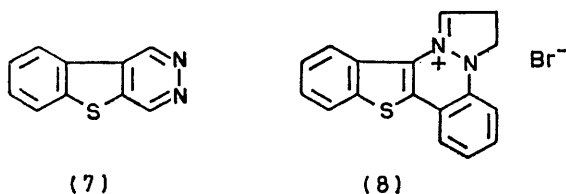
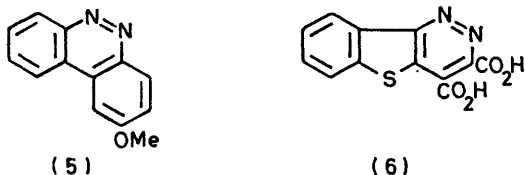
⁴ E. Täuber, *Ber.*, 1895, **28**, 451.

system to give *o*-carboxybenzenesulphonic acid.⁵) The isomeric [1]benzothieno[2,3-*d*]pyridazine (7) and a number of its derivatives have been reported recently.⁶

When cinnolines are treated with sodium ethoxide in boiling ethanol, ring contraction occurs to give indoles.^{2,7}



- (1) R = H
(2) R = Me
(3) R = Cl



[1]Benzothieno[3,2-*c*]cinnoline (1) similarly gives a low yield of 10*H*-[1]benzothieno[3,2-*b*]indole¹ together with an intractable tar.

As expected,⁸ its reaction with ethanolic 1,3-dibromopropane yields 2,3-dihydro[1]benzothieno[3,2-*c*]pyrazolo[1,2-*a*]cinnolinium bromide (8), also a new heterocyclic system.

[1]Benzothieno[3,2-*c*]cinnoline (1) dissolves in 20% sulphuric acid to give a red-orange solution. Addition of zinc dust decolorises this solution and yields a precipitate of 5,6-dihydro[1]benzothieno[3,2-*c*]cinnoline sulphate.² Attempts to isolate this salt failed, however, because it is rapidly aromatised back to (1) in air.

Attempts to prepare 3-phenylcinnoline by desulphurisation of compound (1) with W-7 Raney nickel in ethanol, propan-2-ol, or butanol^{9,10} were abortive.

EXPERIMENTAL

The spectroscopic instruments used are described in Part VIII.¹ Molecular weights were determined by mass spectrometry.

5-Methyl-2-(*o*-nitrophenyl)benzo[*b*]thiophen and 2-(*o*-aminophenyl)-5-methylbenzo[*b*]thiophen were prepared as described in the preceding paper.¹

5-Chloro-2-(*o*-nitrophenyl)benzo[*b*]thiophen (40%) was prepared from 5-chloro-2-benzo[*b*]thienyl-lithium¹¹ in a

⁵ F. B. Erickson, U.S.P. 2,642,458/1953 (*Chem. Abs.*, 1954, 48, 5219).

⁶ M. Robba, G. Doré, and M. Bonhomme, *Compt. rend.*, 1969, 268C, 256; 1969, 269C, 245; 1970, 271C, 1328; *Tetrahedron*, 1972, 28, 2553 (see also O. Tsuge, S. Iwanami, and S. Hagio, *Bull. Chem. Soc. Japan*, 1972, 45, 237).

⁷ C. M. Atkinson and J. C. E. Simpson, *J. Chem. Soc.*, 1947, 1649.

manner similar to that used¹ for 2-(*o*-nitrophenyl)benzo[*b*]thiophen. It had m.p. 111–112° (from ethanol), τ (CDCl₃) 1.95–2.70 (m, aromatic) [Found: C, 58.0; H, 2.8; N, 4.5%; *M*, 289; *M* + 2, 291 (ratio 3 : 1). C₁₄H₈ClNO₂S requires C, 58.0; H, 2.8; N, 4.8%; *M*, 289; *M* + 2, 291 (ratio 3 : 1)].

2-(*o*-Aminophenyl)-5-chlorobenzo[*b*]thiophen hydrochloride (82%), prepared by reduction¹ of 5-chloro-2-(*o*-nitrophenyl)benzo[*b*]thiophen, had m.p. 213–218° (from ethanol), τ (Me₂SO) 1.75–2.63 (m, aromatic) and 3.80 (exchangeable, NH₃); ν_{\max} (Nujol) 2560br cm⁻¹ (NH₃) (Found: C, 56.5; H, 3.6; N, 4.4. C₁₄H₁₁Cl₂NS requires C, 56.75; H, 3.75; N, 4.7%).

[1]Benzothieno[3,2-*c*]cinnoline.—A solution of sodium nitrite (0.56 g, 8.1 mmol) in water (4 ml) was added dropwise to a stirred mixture of 2-(*o*-aminophenyl)benzo[*b*]thiophen hydrochloride¹ (2.1 g, 7.75 mmol), concentrated hydrochloric acid (5 ml), and water (25 ml) at 0°, and the resulting mixture was stirred at 0° for a further 30 min. It was then filtered; the filtrate was allowed to warm to room temperature, and stirred at this temperature for 90 min. The precipitate was filtered off and crystallised from ethanol to give the product (1.4 g, 75%), m.p. 212–214°, identical with the sample prepared as described previously;¹ τ (CDCl₃) 0.95–1.32 (m, 4-H and 7-H) and 1.80–2.45 (m, aromatic); λ_{\max} (EtOH) 205 (ϵ 18,780), 237 (35,000), 256 (33,560), and 271 nm (21,600); *m/e* 236 (*M*⁺, 100%) and 208 (*M* – N₂; *m*^{*}, 187.6).

The following compounds were prepared similarly: 8-methyl[1]benzothieno[3,2-*c*]cinnoline (56%), m.p. 222–224° (from ethanol), τ (CDCl₃) 1.05–1.34 (m, 4-H and 7-H), 1.85–2.73 (m, aromatic), and 7.38 (CH₃) (Found: C, 71.7; H, 4.1; N, 11.2%; *M*, 250. C₁₅H₁₀N₂S requires C, 72.0; H, 4.0; N, 11.2%; *M*, 250); 8-chloro[1]benzothieno[3,2-*c*]cinnoline (55%), m.p. 261–263° (from ethyl acetate), τ (CF₃·CO₂D) 1.08–2.00 (m, aromatic) [Found: C, 61.9; H, 2.7; N, 10.4%; *M*, 270; *M* + 2, 272 (ratio 3 : 1). C₁₄H₇ClN₂S requires C, 62.1; H, 2.6; N, 10.3%; *M*, 270; *M* + 2, 272 (ratio 3 : 1)].

Reactions of [1]Benzothieno[3,2-*c*]cinnoline.—(a) Oxidation. (i) Hydrogen peroxide (100 vols; 8 ml) was added dropwise to a stirred mixture of [1]benzothieno[3,2-*c*]cinnoline (0.8 g, 3.39 mmol) in acetic acid (8 ml) at room temperature, and the resulting mixture was then heated at 90–95° for 2 h. It was cooled and the precipitate was filtered off to give [1]benzothieno[3,2-*c*]cinnoline 5(6),11,11-trioxide (0.8 g, 84%), m.p. 264–266° (from ethanol), ν_{\max} (Nujol) 1155s and 1310s cm⁻¹ (SO₂); τ (Me₂SO) 0.84–1.18 (q, *J*_o 8.0, *J*_m 2.0 Hz, 4-H or 7-H) and 1.20–2.00 (m, aromatic) (Found: C, 58.6; H, 3.1; N, 9.5. C₁₄H₈N₂O₃S requires C, 59.15; H, 2.8; N, 9.8%).

(ii) A solution of potassium permanganate (8.0 g, 50.6 mmol) and potassium hydroxide (0.5 g, 9.0 mmol) in water (100 ml) was added slowly to a stirred mixture of [1]benzothieno[3,2-*c*]cinnoline (1.0 g, 4.24 mmol) and water (25 ml) heated on a steam-bath, and the resulting mixture was heated on the steam-bath for a further 3 h. It was then filtered and the volume of the filtrate was reduced to 50 ml. Acidification of the residual solution with concentrated

⁸ D. G. Farnum, R. J. Alaimo, and J. M. Dunston, *J. Org. Chem.*, 1967, 32, 1130.

⁹ D. E. Boswell, J. A. Brennan, P. S. Landis, and P. G. Rodewald, *J. Heterocyclic Chem.*, 1968, 5, 69.

¹⁰ B. Iddon and R. M. Scrowston, *Adv. Heterocyclic Chem.*, 1970, 11, 375.

¹¹ R. P. Dickinson and B. Iddon, *J. Chem. Soc. (C)*, 1971, 182.

hydrochloric acid gave [1]benzothieno[3,2-*c*]pyridazine-3,4-dicarboxylic acid (0.4 g, 35.5%), m.p. 263—265° (from aqueous ethanol), ν_{\max} (Nujol) 3300br (OH) and 1700s cm^{-1} (C=O) (Found: C, 52.95; H, 2.5; N, 10.2%; *M*, 274. $\text{C}_{12}\text{H}_8\text{N}_2\text{O}_4\text{S}$ requires C, 52.5; H, 2.2; N, 10.2%; *M*, 274).

(b) *Ring contraction*. To a solution of [1]benzothieno[3,2-*c*]cinnoline (1.0 g, 4.24 mmol) in ethanol (40 ml) heated under reflux sodium (3.5 g, 0.15 g atom) was added piece by piece (0.2—0.4 g). The resulting mixture was heated under reflux for a further 3 h, then cooled and poured into water (10 ml). Continuous extraction of the resulting aqueous solution for 24 h with chloroform gave a tar which was chromatographed on alumina. Ether eluted starting material (0.5 g, 50%), m.p. 212—214° (from ethanol), and chloroform eluted 10*H*-[1]benzothieno[3,2-*b*]indole (0.1 g, 21% based on conversion), m.p. 250—252° (from benzene), identical with an authentic sample.¹

(c) *With 1,3-dibromopropane*. A solution of [1]benzothieno[3,2-*c*]cinnoline (1.0 g, 4.24 mmol) and 1,3-dibromopropane (4.6 g, 22.8 mmol) in ethanol (60 ml) was heated under reflux for 100 h. Distillation of the solvent under reduced pressure gave a residue which was crystallised from ethanol, to give 2,3-dihydro[1]benzothieno[3,2-*c*]pyrazolo[1,2-*a*]cinnolinium bromide (0.4 g, 26.5%), m.p. 223—229° (decomp.) (Found: C, 56.65; H, 3.6. $\text{C}_{17}\text{H}_{13}\text{BrN}_2\text{S}$ requires C, 57.1; H, 3.7%).

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