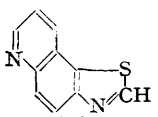
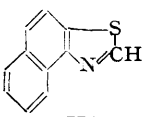
133. *Some Naphthothiazoles.*

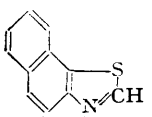
By W. A. Boggust, Wesley Cocker, J. C. P. Schwarz, and E. R. Stuart.

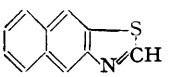
Naphtho(1′ : 2′-4 : 5)thiazole and *naphtho*(2′ : 1′-4 : 5)*thiazole* have been prepared and their light-absorption characteristics compared with those of pyridino(2′ : 3′-6 : 7)benzthiazole. Attempts to prepare naphtho(2′ : 3′-4 : 5)thiazole are described.

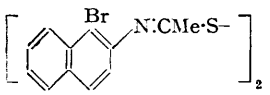
Recently Cocker and Boggust (*J.*, 1949, 355) described a new quinthiazole which was assumed to be the angular compound, pyridino(2′ : 3′-6 : 7)benzthiazole (I). Two angular naphthothiazoles have now been prepared for comparison of their light-absorption properties with those of the quinthiazole. These compounds, naphtho(1′ : 2′-4 : 5)thiazole (II) and *naphtho*(2′ : 1′-4 : 5)*thiazole* (III), were obtained by the route used by Mercury, Vincent, and Sherrill (*J. Amer. Chem. Soc.*, 1946, **68**, 1594) which involves oxidative ring closure of the appropriate naphthylthio-oxamic acid to the corresponding naphthothiazole-2-carboxylic acid which is then decarboxylated. The naphthothiazole (II) had previously been obtained by Hofmann (*Ber.*, 1887, **20**, 1798, 2265) from formo-α-naphthylamide and sulphur. The compound (III) was also obtained by an alternative method described below.

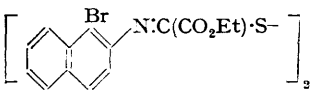

(I.)

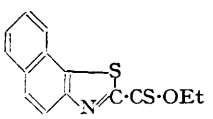

(II.)

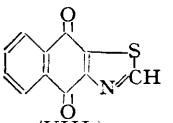

(III.)


(IV.)


(V.)


(VI.)


(VII.)


(VIII.)

All attempts to prepare naphtho(2′ : 3′-4 : 5)thiazole (IV) were unsuccessful. Attempted cyclisation of 1-*bromo*-2-*naphthylthio-oxamic acid* or its *ethyl* ester, obtained by thionation of *ethyl* 1-*bromo*-2-*naphthyloxamate* in toluene, yielded a product which on heating with mineral acid gave 1-bromo-2-naphthylamine. A similar experience was recorded by Levkoev and Baskirova (*Chem. Abstr.*, 1947, **41**, 447) who showed that 1-bromo-2-thioacetamidonaphthalene on oxidation yielded the disulphide (V), which gave 1-bromo-2-naphthylamine when heated with mineral acid. These workers also showed that the " linear naphthothiazole " of Fries and Buchler (*Annalen*, 1927, **454**, 260) prepared by oxidation of 1-bromo-2-thiobenzamidonaphthalene is, in reality, a similar disulphide. When ethyl 1-bromo-2-naphthyloxamate was thionated in boiling xylene it yielded a mixture of an unidentified, sparingly soluble compound which may be the *disulphide* (VI) and *ethyl naphtho*(2′ : 1′-4 : 5)*thiazole*-2-*thioncarboxylate* (VII) (the latter being produced with elimination of bromine). (VII) was hydrolysed to *sodium naphtho*(2′ : 1′-4 : 5)*thiazole*-2-*carboxylate*, and this gave the parent thiazole (III) when boiled with acid.

Naphtho(2′ : 3′-4 : 5)*thiazole*-1′ : 4′-*quinone* (VIII) was prepared by condensation of 2-amino-1 : 4-naphthaquinone-3-thiol with formaldehyde in weakly acid solution (cf. B.P. 262,141/1926), the resulting thiazoline being spontaneously oxidised during isolation as shown by the fact that the product is unaffected by hydrogen peroxide. All attempts to reduce the quinone to the naphthothiazole were unsuccessful.

We were unable to obtain 2-methylnaphtho(2′ : 3′-4 : 5)thiazole by the method of B.P. 445,538, as in our hands the preparation of 2-aminonaphthalene-3 : 6-disulphonyl chloride recorded there failed. Further attempted deamination of 1-bromo-2-aminonaphtho(2′ : 3′-4 : 5)thiazole (Hunter and Jones, *J.*, 1930, 941) gave unpromising results.

Ultra-violet light absorption data are as follows :

Compound :	(I).		(II).		(III).	
	$\lambda_{max.}$, A.	log ε.	$\lambda_{max.}$, A.	log ε.	$\lambda_{max.}$, A.	log ε.
	2500	4·35	2310	4·80	2300	4·35
					2500	4·60
	(2900	3·7)	2900	3·93	2800	3·75
					2900	3·73
	3320	3·31	3250	3·09	3200	2·79
					3350	2·81

The higher degree of resolution apparent in (III) is in accordance with previous experimental evidence that addition of an auxochrome or chromophore in the 2-position in naphthalene produces a more complex spectrum than does substitution in the 1-position (Ewing and Steck, *J. Amer. Chem. Soc.*, 1946, **68**, 2181; A.P.I. Research Project 44 Nat. Bur. Stand. Catalog of U.V. Spectral Data, Serial Nos. 244—247, 1- and 2-naphthols, contributed by U.O.P. Co., Riverside, Illinois; Cocker *et al.*, to be published).

Naphtho(2′ : 3′-4 : 5)thiazole-1′ : 4′-quinone shows maxima at 2450 A. (log ε 4·45), 2800 A. (log ε 4·20), and 3400 A. (log ε 3·52), characteristic of tricyclic quinones (Spruit, *Rec. Trav. chim.*, 1949, **68**, 325).

All light-absorption measurements were made in alcoholic solution using the Beckman model DU quartz spectrophotometer.

Experimental.

(Analyses are by Drs. Weiler and Strauss.)

Naphtho(1′ : 2′-4 : 5)*thiazole* (II).—Ethyl 1-naphthyloxamate was obtained substantially as described by Ballo (*Ber.*, 1873, **6**, 247).

1-*Naphthylthio-oxamic acid.* The above oxamic ester (11 g.) in boiling anhydrous xylene (220 c.c.) was slowly treated with phosphorus pentasulphide (6·9 g.), and refluxing was continued for 1 hour. The hot xylene was decanted from some tarry material and was distilled in steam, leaving an oily residue consisting of the thio-ester, which was shaken with an excess of cold 10% sodium hydroxide solution until a clear solution was obtained. After filtration, the solution was acidified and the *thio-oxamic acid* (10 g.; m. p. 117°) was crystallised from light petroleum (b. p. 60—80°) as yellow needles, m. p. 124—125° (Found : C, 62·4; H, 4·2. $C_{12}H_9O_2NS$ requires C, 62·4; H, 3·9%).

Naphtho(1′ : 2′-4 : 5)*thiazole.* A filtered solution of the crude thio-oxamic acid (10 g.) in 10% sodium hydroxide solution (330 c.c.) was stirred and slowly treated with a solution of potassium ferricyanide (75 g.) in water (180 c.c.). The yellowish-brown precipitate which formed was collected and immediately refluxed with 8% hydrochloric acid (150 c.c.) for 1 hour. The hot solution was filtered from Prussian blue, boiled with charcoal, and filtered. On cooling, the hydrochloride of the required thiazole was obtained (5·5 g.). It readily dissociated when heated or in water, but crystallised satisfactorily from concentrated hydrochloric acid as pale yellow needles, m. p. 185°. The hydrochloride (5·0 g.), basified with aqueous ammonia, yielded the thiazole (2·9 g.) which crystallised from light petroleum (b. p. 40—60°) as large, pale yellow prisms, m. p. 53—54° (cf. Hofmann, *loc. cit.*, who gives m. p. 45—**46°**) (Found : C, 71·0; H, 4·0. Calc. for $C_{11}H_7NS$: C, 71·3; H, 3·8%).

Naphtho(2′ : 1′-4 : 5)*thiazole* (III).—Ethyl 2-naphthyloxamate was obtained as described by Meyer and Muller (*Ber.*, 1897, **30**, 770).

2-*Naphthylthio-oxamic acid.* This was prepared from ethyl 2-naphthyloxamate (11 g.) as described for the 1-isomer. A small sample crystallised from water as yellow, glistening plates, m. p. 269—271°, but a satisfactory analysis was not obtained.

Naphtho(2′ : 1′-4 : 5)*thiazole.* The foregoing crude thio-oxamic acid was treated as in the preparation of (II). The hydrochloride of the required thiazole was not isolated, but its clarified solution (charcoal) in 10% hydrochloric acid was basified with aqueous ammonia, and the *product* (3·4 g.; m. p. 60°) crystallised from dilute alcohol as colourless plates or needles, m. p. 65° (Found : C, 70·8; H, 3·6%).

Ethyl 1-*Bromo*-2-*naphthyloxamate.*—Ethyl 2-naphthyloxamate (24·5 g.) was brominated in the minimum quantity of cold chloroform with bromine (5·5 c.c.) in chloroform (15 c.c.). After 1 hour, the chloroform was removed in a vacuum, and the crude ester was washed with aqueous sodium carbonate and crystallised from alcohol as colourless needles (27·5 g.), m. p. 98—99° (Found : C, 52·2; H, 3·7. $C_{14}H_{12}O_3NBr$ requires C, 52·2; H, 3·7%). The compound was also obtained when 1-bromo-2-naphthylamine was refluxed for 1 hour with ethyl oxalate.

Thionation, in Xylene, of Ethyl 1-*Bromo*-2-*naphthyloxamate.*—The compound (16·6 g.) in boiling anhydrous xylene (350 c.c.) was slowly treated with phosphorus pentasulphide (11·5 g.), and refluxing was continued for 45 minutes. Hydrogen bromide was evolved, especially during the later stages of the reaction. The hot xylene was decanted and cooled, yielding a yellow solid (*A*; 4·5 g.), m. p. 100—230°. On extraction with ether, (*A*) left a residue (*B*; 3·3 g.), m. p. 250—275° (according to the rate of heating) which crystallised from xylene as red needles. After melting, it resolidified and then gave m. p. 328—331°. We were unable to identify (*B*), but it may be the *disulphide* (VI) (Found : C, 49·6; H, 2·7. $C_{28}H_{22}O_4N_2S_2Br_2$ requires C, 49·8; H, 3·3%), since it is sparingly soluble in organic solvents, *e.g.*, ethanol, ethyl acetate, and benzene, requiring boiling xylene for recrystallisation, and thus probably has a relatively high molecular weight. The mother-liquor from (*A*) was evaporated in a vacuum to 50 c.c. and cooled, whereupon yellow crystals (*C*) were deposited. The mother-liquor from (*C*) was evaporated to dryness in a vacuum, and the resulting tarry solid crystallised from dilute alcohol as yellow needles

(2·9 g.), m. p. 100—110° (according to rate of heating), consisting of *ethyl naphtho*(2′ : 1′-4 : 5)*thiazole*-2-*thioncarboxylate* (VII) (Found: C, 61·4; H, 4·1; S, 21·1. $C_{14}H_{11}ONS_2$ requires C, 61·5; H, 4·0; S, 23·4%). Extraction of (*C*) with ether gave a further 1 g. of the thion-ester. The ester (VII) (0·5 g.) was heated for 10 minutes with 10% aqueous sodium hydroxide (2·0 c.c.) in water (100 c.c.), and the hot solution was filtered and cooled, yielding *sodium naphtho*(2′ : 1′-4 : 5)*thiazole*-2-*carboxylate* as colourless plates, m. p. 350—355° (Found: S, 11·6. $C_{12}H_6O_2NSNa,H_2O$ requires S, 11·9%). The salt was boiled for 90 minutes with 15% hydrochloric acid, and the hot solution was filtered, cooled, and basified with aqueous ammonia, giving naphtho(2′ : 1′-4 : 5)thiazole (0·2 g.), identical with that prepared by the previous method.

Ethyl 1-*Bromo*-2-*naphthylthio-oxamate*.—Ethyl 1-bromo-2-naphthyloxamate (22·5 g.) in boiling anhydrous toluene (550 c.c.) was stirred with phosphorus pentasulphide (18 g.) under reflux for 90 minutes and then filtered. On cooling, the filtrate deposited yellow crystals, m. p. 275°, identical with (*B*). The mother-liquor was evaporated to dryness in a vacuum, leaving a yellow solid (23 g.), m. p. 75—78°, which was crystallised several times from alcohol, to give the required *thio*-ester as yellow needles, m. p. 88° (Found: C, 49·6; H, 4·5. $C_{14}H_{12}O_2NSBr$ requires C, 49·7; H, 3·6%).

1-*Bromo*-2-*naphthylthio-oxamic Acid*.—Ethyl 1-bromo-2-naphthylthio-oxamate (1 g.) was shaken with cold 10% potassium hydroxide solution (10 c.c.) for 2 hours. The salt was collected and shaken for 30 minutes with dilute hydrochloric acid, and the precipitated *acid* (0·8 g.) crystallised from dilute alcohol as golden needles, m. p. 123° (decomp.) (Found: C, 45·3; H, 3·3. $C_{12}H_8O_2NSBr$ requires C, 46·5; H, 2·6%).

Naphtho(2′ : 3′-4 : 5)*thiazole*-1′ : 4′-*quinone* (VIII).—2-Chloro-3-amino-1 : 4-naphthaquinone (36 g.) was refluxed with sodium sulphide (45 g.) in water (330 c.c.) for 25 minutes. To the resultant deep-blue solution, formaldehyde (40%; 72 c.c.) was added, followed by glacial acetic acid (36 c.c.) diluted with water (72 c.c.). The mixture was refluxed for 1 hour and filtered. The black residue was extracted several times with boiling alcohol (500 c.c.). On cooling, *naphtho*(2′ : 3′-4 : 5)*thiazole*-1′ : 4′-*quinone* (13 g.), m. p. 245—252°, was deposited. The m. p. was not raised above 245—252° by repeated crystallisation (Found: C, 61·3; H, 2·4; N, 6·5. $C_{11}H_5O_2NS$ requires C, 61·4; H, 2·3; N, 6·5%).

Attempts to reduce this quinone to the parent naphthothiazole by zinc dust distillation in hydrogen, zinc dust fusion (Clar, *Ber.*, 1939, **72**, 1645), stannous chloride in acetic acid (Fries and Kerkow, *Annalen*, 1922, **427**, 281), or hydrogen iodide and phosphorus were unsuccessful.

The authors thank Imperial Chemical Industries Ltd. and the Medical Research Council of Ireland for financial support. One of them (J. C. P. S.) is grateful for a grant from the Sarah Purser Fund of Trinity College, Dublin.

UNIVERSITY CHEMICAL LABORATORY,
TRINITY COLLEGE, DUBLIN.

[*Received, November 22nd*, 1949.]