395. *Cyclization Products from Amino-substituted Bunte Salts.*

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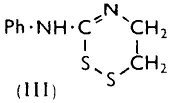
WE have shown[1] that reaction of thiourea with Bunte salts (salts of *S*-alkyl or *S*-aryl hydrogen thiosulphates) in acid solution gives the corresponding disulphides through intermediates of type (I). Therefore acid treatment of a Bunte salt containing a thioureido-group might be expected to give a cyclic disulphide in addition to polymeric material. Indeed treatment of sodium *S*-2-[*N'*-phenyl(thioureido)]ethyl thiosulphate (II) with cold 5N-hydrochloric acid gave a crude product from which 3-anilino-5,6-dihydro-1,2,4-dithiazine (III) was isolated as its picrate; attempts to isolate the free base were unsuccessful.

$$\mathrm{RS{\cdot}SO_3^- + SC(NH_2)_2 \longrightarrow [RS{\cdot}S{\cdot}C(=NH_2^+){\cdot}NH_2]\ (I) + SO_3^{2-}}$$

$$\mathrm{(I) + RS{\cdot}SO_3^- + H_2O \longrightarrow RS{\cdot}SR + H_2SO_4 + SC(NH_2)_2}$$

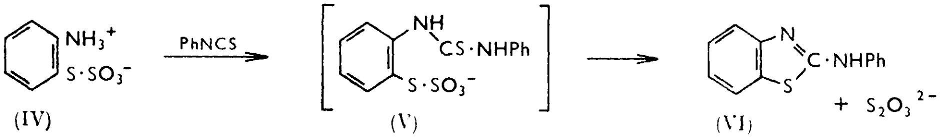
$\mathrm{Ph{\cdot}NH{\cdot}CS{\cdot}NH{\cdot}CH_2{\cdot}CH_2{\cdot}S{\cdot}SO_3Na}$

(II)



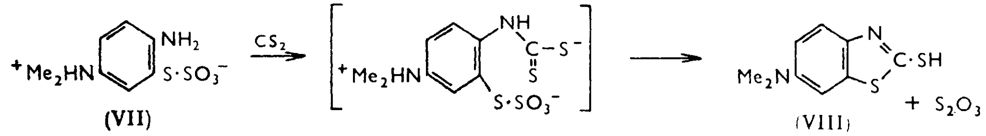
(III)

Similar products were expected from corresponding aryl hydrogen thiosulphates, but *S*-*o*-aminophenyl hydrogen thiosulphate (IV) and phenyl isothiocyanate in pyridine and aqueous sodium carbonate gave a 97% yield of 2-anilinobenzothiazole (VI) and not the expected phenylthioureido-derivative (V); thiosulphate ion was also a major product.



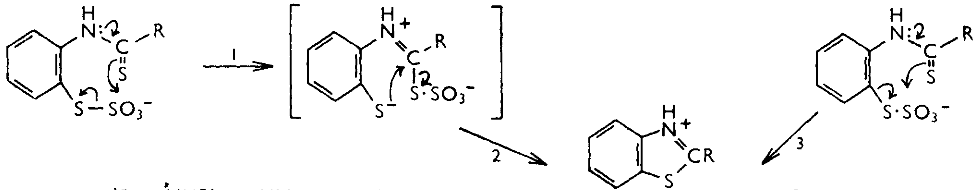
(IV) (V) (VI)

The acid (IV) and its 5-dimethylamino-derivative with methyl isothiocyanate also gave benzothiazoles, but no benzothiazole derivative was isolated after reaction of phenyl isothiocyanate with *SS'*-(2,5-diamino-1,4-phenylene) di(hydrogen thiosulphate).



(VII) (VIII)

Heller[2] has shown that *S*-(2-amino-5-dimethylaminophenyl) hydrogen thiosulphate (VII) reacts with carbon disulphide in aqueous ammonia, giving 6-dimethylaminobenzothiazole-2-thiol (VIII). We find that improved yields are obtained by using pyridine–aqueous sodium carbonate as the reaction medium. By this variation, benzothiazole-2-thiol and thiosulphate were obtained in 80% and 84% yield, respectively, from *S*-*o*-aminophenyl hydrogen thiosulphate. *S*-2-Aminoethyl thiosulphate and carbon disulphide react similarly, giving 2-thiazoline-2-thiol together with polymeric material.



(R = NHPh, NHMe or S⁻)

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[1] Milligan and Swan, *J.*, 1962, 2172.

[2] Heller, *J. prakt. Chem.*, 1924, **108**, 257.

No benzothiazole derivatives were isolated after reaction of *S*-*o*-aminophenyl hydrogen thiosulphate with *O*-ethyl *S*-methyl xanthate or methyl *N*-acetyldithiocarbamate.

Possible mechanisms for these syntheses of benzothiazoles are as annexed. Migration of the SO_3^- group to the thione sulphur (step 1) would produce a new $-S{\cdot}SO_3^-$ group attached to an electrophilic carbon from which it could readily be displaced by the thiol anion (step 2). The alternative direct displacement of the thiosulphate group from the aromatic ring by the thione sulphur atom (step 3) is perhaps less likely but may be favoured by the high aromatic stability of the benzothiazole and the high anionic stability of the thiosulphate ion.

Experimental.—Sodium S-N′-[*phenyl*(*thioureido*)]*ethyl thiosulphate* (II). Phenyl isothiocyanate (14 g.) and *S*-*p*-2-aminoethyl hydrogen thiosulphate [3] (8·0 g.) in 50% aqueous pyridine (100 ml.) was stirred vigorously, the pH being maintained at 9 by addition of 10% sodium hydroxide solution. After 1·5 hr. the solvent was evaporated under reduced pressure and the residue extracted with boiling ethanol (150 ml.). The *Bunte salt* (9·0 g., 56%) separated as prisms, m. p. 177° (decomp.) (Found: C, 34·4; H, 3·8; S, 31·0. $C_9H_{11}N_2NaO_3S$ requires C, 34·4; H, 3·5; S, 30·6%).

3-*Anilino*-5,6-*dihydro*-1,2,4-*dithiazine* (III). 10N-Hydrochloric acid (25 ml.) was added dropwise with stirring to a solution of the salt (II) (2·75 g.) in water (25 ml.) at 0°, sulphur dioxide being expelled by a stream of nitrogen. After 1 hr. the pH of the mixture was adjusted to 7, while the temperature was kept below 5°. The crude product (2·2 g.) was then filtered off and dissolved in warm acetic acid (75 ml.) to which was added a solution of picric acid (3·3 g.) in acetic acid (75 ml.). On cooling, a *picrate* (1·9 g.) separated as yellow prisms, m. p. 195—199° (decomp.) (Found: C, 41·7; H, 3·5; N, 16·2; O, 25·7. $C_{15}H_{13}N_5O_7S_2$ requires C, 41·0; H, 3·0; N, 15·9; O, 25·5%).

2-*Anilinobenzothiazole* (VI). A solution of *S*-*o*-aminophenyl hydrogen thiosulphate [4] (1·50 g.) and phenyl isothiocyanate (1·10 g.) in pyridine (15 ml.) and 5% aqueous sodium carbonate (15 ml.) was set aside for 30 min., then heated on a steam-bath for 30 min. The mixture was evaporated under reduced pressure, and the residue partitioned between ethyl acetate and water. Evaporation of the ethyl acetate layer gave 2-anilinobenzothiazole (1·61 g., 97%), which crystallised from benzene as needles (1·27 g., 76%), m. p. 160°, undepressed on admixture with an authentic sample.[5] Iodometric analysis of the aqueous phase (cf. Mitchell and Ward [6]) showed the presence of thiosulphate (85%).

2-*Anilino*-6-*dimethylaminobenzothiazole*. *S*-(2-Amino-5-dimethylaminophenyl) hydrogen thiosulphate [2] (0·5 g.) and phenyl isothiocyanate (0·27 g.) were allowed to react in 1 : 1 pyridine–5% aqueous sodium carbonate (10 ml.) at room temperature for 1 hr. Crystallisation of the crude product (0·48 g.) from light petroleum (b. p. 60—90°) gave 2-*anilino*-6-*dimethylaminobenzothiazole* (0·28 g., 51%) as needles, m. p. 173° (Found: C, 67·0; H, 5·9; N, 15·3; S, 11·7. $C_{15}H_{15}N_3S$ requires C, 66·9; H, 5·6; N, 15·6; S, 11·9%).

When pyridine alone was used as the reaction medium the yield of recrystallised product was 46%.

2-*Methylaminobenzothiazole*. Equimolar amounts of *S*-*o*-aminophenyl hydrogen thiosulphate and methyl isothiocyanate in 1 : 1 pyridine–5% aqueous sodium carbonate were heated at 100° for 30 min. Crystallisation of the crude product (87%) from carbon tetrachloride gave 2-methylaminobenzothiazole (56%), m. p. 139—140° (lit.,[7] 138°) (Found: N, 16·8; S, 19·5. Calc. for $C_8H_8N_2S$: N, 17·1; S, 19·5%).

6-*Dimethylamino*-2-*methylaminobenzothiazole*.—Reaction of *S*-(2-amino-5-dimethylaminophenyl) hydrogen thiosulphate and methyl isothiocyanate gave a crude product (65%) from which the *benzothiazole* was obtained as yellow granules, m. p. 148—150° (from light petroleum) (Found: C, 57·8; H, 6·2; S, 15·4. $C_{10}H_{13}N_3S$ requires C, 57·9; H, 6·3; S, 15·1%).

Benzothiazole-2-*thiol*. *S*-*o*-Aminophenyl hydrogen thiosulphate (1·0 g.) and carbon

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[3] Bretschneider, *Oest. Akad. Wiss. Mathnaturw. Klasse Sitzber. Abt. IIB*, 1950, **159**, 372; *Chem. Abs.*, 1953, **47**, 6860.

[4] Lecher and Hardy, *J. Org. Chem.*, 1955, **20**, 475.

[5] Hugershoff, *Ber.*, 1903, **36**, 3121.

[6] Mitchell and Ward, "Modern Methods in Quantitative Chemical Analysis," Longmans, Green and Co., London, 1932, p. 138.

[7] Hunter, *J.*, 1926, 1385.

disulphide (5 ml.) were heated under reflux in 1 : 1 pyridine–5% aqueous sodium carbonate (20 ml.) for 30 min., and the mixture was worked up in the usual way, giving benzothiazole-2-thiol (0·65 g., 80%), m. p. and mixed m. p. 181° (from aqueous ethanol). The aqueous layer contained thiosulphate (84%), but negligible amounts of sulphite and sulphide.

6-*Dimethylaminobenzothiazole*-2-*thiol* (VIII). Reaction of *S*-(2-amino-5-dimethylaminophenyl) hydrogen thiosulphate and carbon disulphide in the same way gave 6-dimethylaminobenzothiazole-2-thiol (90%), m. p. 234° (from ethanol) (lit.,[2] 230°).

2-*Thiazoline*-2-*thiol*. *S*-2-Aminoethyl hydrogen thiosulphate acid (1·0 g.) and carbon disulphide (5 ml.) were heated under reflux in 1 : 1 pyridine–5% aqueous sodium carbonate for 1 hr., and the mixture was then evaporated under reduced pressure. Water (15 ml.) was added to the residue, and the crude product (0·48 g.) was filtered off. Crystallisation from benzene–light petroleum gave 2-thiazoline-2-thiol (0·20 g.) as prisms, m. p. and mixed m. p. 105—106° (lit.,[8] m. p. 106—107°).

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[8] Gabriel, *Ber.*, 1889, **22**, 1139.