43. *Heterocyclic Compounds from Urea Derivatives. Part III.* Synthesis and Cyclisation of Isothioureas Derived from* o-*Aminothiophenol and Diarylcarbodi-imides.*

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The addition of diarylcarbodi-imides to *o*-aminothiophenol yields successively *S*-*o*-aminophenyl-*NN'*-diarylisothioureas and *NN'*-diaryl-*S*-*o*-(*NN'*-diarylguanidino)phenylisothioureas. The nature and proportions of the carbodi-imide determine whether one or two moles are added to one mole of *o*-aminothiophenol.

The resulting isothioureas are readily cyclised to 2-arylaminobenzothiazoles under various conditions. The rapid conversion of *o*-mercaptophenylurea into 2-hydroxybenzothiazole is a comparable cyclisation.

Amongst general syntheses of benzothiazoles,[1] a group of reactions involving the cyclisation of suitable *o*-aminothiophenol derivatives provides one of the most important routes. The present paper describes an additional variant of this type of synthesis and illustrates further the ease with which the benzothiazole molecule is formed.

o-Aminothiophenol reacted additively with 1 mol. of various diarylcarbodi-imides to afford high yields of products which are formulated, on the basis of their mode of formation, composition, molecular weight, and chemical properties, as *S*-*o*-aminophenyl-*NN'*-diarylisothioureas (I). It is well known that carbodi-imides condense with ammonia or amines to yield substituted guanidines;[2] they also react with thiols, affording for example *SNN'*-triphenylisothiourea with thiophenol.[2,3] The formulation of the present series of compounds as isothioureas (I), and not as guanidines (Ia), implying a more rapid attack of carbodi-imides at the thiol than at the amino-group in *o*-aminothiophenol, is based on the chemical behaviour of the products.

Thus, the presence of amino- and absence of thiol groups in the addition products were suggested by the following observations: the parent compound (I; R = Ph) dissolved readily in cold dilute acids, was insoluble in alkalis, failed to decolorise bromine rapidly [with formation of the corresponding disulphide or thiadiazine (V)], and did not yield an *S*-benzyl derivative under conditions that converted *o*-aminothiophenol into *o*-benzylthioaniline almost quantitatively.[4] Alkaline hydrolysis of the isothiourea (I; R = Ph) gave *o*-aminothiophenol and carbanilide; since *NN'N''*-triphenylguanidine was unaffected by alkalis under identical conditions, a compound (Ia) of comparable guanidine structure was unlikely to have undergone this cleavage, while the fission of the sulphur–carbon link in isothioureas (I) is well known.[3,5] Similar indirect evidence in favour of structure (I) was provided by aminolysis: boiling aniline cleaved the product into *o*-aminothiophenol and triphenylguanidine, a reaction typical of the isothiourea (I)[6] rather than of the guanidine (Ia).

Unequivocal direct confirmation for the presence of an amino-group (in I) was nevertheless difficult to obtain. Attempts to isolate an anil with benzaldehyde were unsuccessful, and the diazo-test was inconclusive, but the compound (I; R = Ph) gave a carbylamine reaction. Since the di-addition product (II; R = Ph, in which the amino-group is certain to be blocked identically) gave at most a faint reaction, it is unlikely that the positive

* Part II, Godfrey and Kurzer, *J.*, 1961, 5137.

[1] Sprague and Land, in Elderfield's "Heterocyclic Compounds," Vol. V, Wiley, New York, 1957, pp. 506 *et seq.*

[2] Khorana, *Chem. Rev.*, 1953, **53**, 145, 160.

[3] Busch, Blume, and Pungs, *J. prakt. Chem.*, 1909, **79**, 513.

[4] Lantz, Mingasson, and Delarue, *Bull. Soc. chim. France*, 1957, 1201.

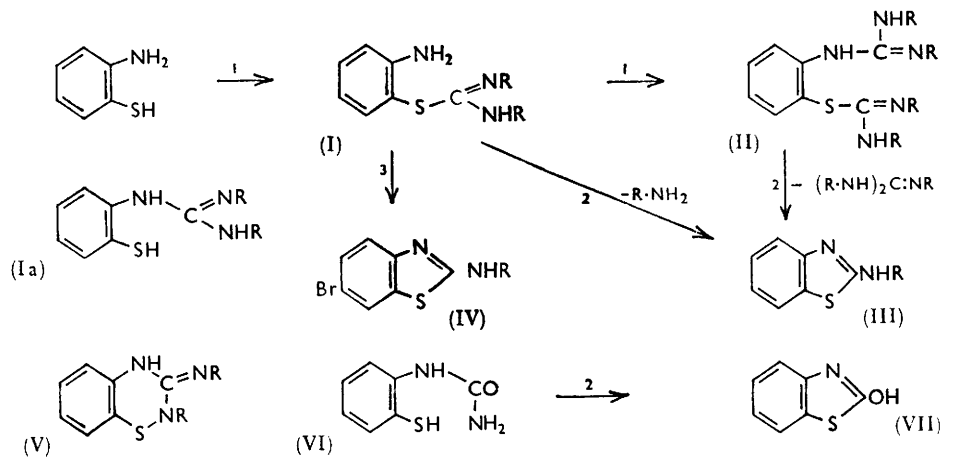
[5] Arndt, *Ber.*, 1921, **54**, 2238.

[6] Schering-Kahlbaum A.G., G.P. 509,264/1927; Smith, *J. Amer. Chem. Soc.*, 1929, **51**, 476.

carbylamine reaction of the monoaddition product depended on the preliminary liberation of free amino-groups (in Ia) by hydrolysis.

The most striking property of *S*-*o*-aminophenyl-*NN'*-diarylisothioureas (I) was the ease of cyclisation, with loss of arylamine, to 2-arylaminobenzothiazoles (III). Reaction occurred readily in acid media, or simply on fusion of the reactants: thus, brief treatment with boiling glacial acetic acid, or dilute ethanolic hydrochloric acid converted the parent compound (I; R = Ph) into 2-anilinobenzothiazole (III; R = Ph) in 75—90% yield, aniline being eliminated. This conversion occurred in fact partially on rapid dissolution of the isothiourea in cold 3N-hydrochloric acid, and 2-anilinobenzothiazole or its derivatives resulted in attempts to prepare simple derivatives of the isothiourea (I; R = Ph) under the usual conditions (cf. Experimental section).

In agreement with its assigned structure, *S*-*o*-aminophenyl-*NN'*-diphenylisothiourea failed to decolorise bromine rapidly, but prolonged reaction at room temperature resulted in a non-homogeneous halogenated product from which very small yields of 2-anilino-6-



Reagents: 1, RN:C:NR. 2, HCl. 3, Br_2.

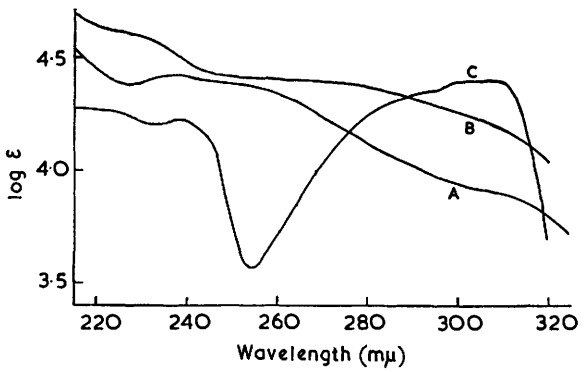
bromobenzothiazole (IV) were isolated, presumably by cyclisation in the acid medium before halogenation in the position *para* to the ring-nitrogen,[7] also established in the comparable conversion of 2-amino- into 2-amino-6-bromobenzothiazole.[8]

An excess of diphenylcarbodi-imide reacted with *o*-aminothiophenol at both the thiol and the amino-group. *S*-*o*-(*NN'*-Diphenylguanidino)phenyl-*NN'*-diphenylisothiourea (II; R = Ph) thus obtained was also accessible, in better yields, from the monoaddition product (I; R = Ph) by treatment with a further mol. of diphenylcarbodi-imide. The nature of the diarylcarbodi-imide employed appears to control the ease with which the further addition occurs at the amino-group. Thus, the di-addition product (II; R = *p*-C_6H_4Me) was isolated exclusively after reaction of *o*-aminothiophenol with only one mol. of di-*p*-tolylcarbodi-imide, but the monoaddition products (I; R = *o*-C_6H_4·OMe, *p*-C_6H_4Br) only resulted when an excess of the corresponding carbodi-imides was used. *NN'*-Diaryl-*S*-*o*-(*NN'*-diarylguanidino)phenylisothioureas (II), having both thiol and amino-groups blocked, were insoluble in acids and alkalis. Like their monoaddition analogues (I), they were rapidly cyclised in acid media to 2-arylaminobenzothiazoles (III) in excellent yields, a triarylguanidine being eliminated.

[7] Dyson, Hunter, and Soyka, *J.*, 1929, 462.
[8] Hunter, *J.*, 1925, **127**, 2270; *J.*, 1930, 125; Chaudri, Desai, and Hunter, *J. Indian Chem. Soc.*, 1934, **11**, 249.

The experiments now described demonstrate the considerably faster addition of diarylcarbodi-imides to aromatic thiol than amino-groups; in no case was the alternative isomer (Ia) obtained. Since in *o*-aminophenol, on the other hand, it is the amino-group that reacts preferentially with diphenylcarbodi-imide, yielding *N*-*o*-hydroxyphenyl-*N'N''*-diphenylguanidine,[3] the reactivity of the groups concerned in the addition appears to decrease in the order SH > NH_2 > OH.

Although neither the mono- (I) nor the di-addition products (II) of *o*-aminothiophenol exhibited pronounced absorption bands in the near-ultraviolet region, each series of compounds gave characteristic absorption curves (cf. Figure). The common features of those of *S*-*o*-aminophenyl-*NN'*-diarylisothioureas (I), having a shallow maximum in the region of 240 mμ, may be taken as additional indication that all relevant compounds were members of the same series (I). 2-Arylaminobenzothiazoles (III) had substantially identical spectra, irrespective of the substituent in the anilino-group; these spectra, resembling those of 2-mercapto-[9] and 2-guanidino-benzothiazole,[10] are characterised by a wide absorption maximum in the region 300—320 mμ. Conjugation between the thiazole ring and one of the benzene nuclei in both the 2-arylaminobenzothiazole and 2-arylimino-benzothiazoline tautomers, retaining the chromophoric system (·C:C·N:C·) in both forms, may contribute largely to the wide intense *K*-band.[11]



Ultraviolet absorption spectrum of:
(A) *S*-*o*-Aminophenyl-*NN'*-diphenylisothiourea.
(B) *S*-*o*-(*NN'*-diphenylguanidino)-phenyl-*NN'*-diphenylisothiourea.
(C) 2-anilinobenzothiazole.

Cyclisation of *o*-mercaptophenylurea, a simple analogue of the condensation products (I and II), was finally examined for comparison. Its formation by Wöhler's synthesis was accompanied by the production of smaller proportions of a compound which, from its composition and positive biuret reaction, is formulated as *o*-mercaptophenylbiuret. The occasional formation of arylbiurets in the interaction of amines and cyanic acid has previously been noted.[12] In acid media, *o*-mercaptophenylurea was rapidly cyclised to 2-hydroxybenzothiazole in excellent yield. This synthesis, comparable with that of 2-hydroxybenzoxazole by the pyrolytic cyclisation of *o*-hydroxyphenylurea,[13] illustrates again the ready formation of the benzothiazole ring-system, in preference to possible alternative cyclisations to 2-substituted benzoxazoles or benzimidazoles.

Experimental

Acetone was dried over calcium sulphate hemihydrate. Light petroleum was of boiling range 60—80°.

Ultraviolet absorption measurements were made with a Unicam S.P. 500 spectrophotometer and 0·00005M-ethanolic solutions.

Preparation of S-o-*Aminophenyl*-NN'-*diphenylisothiourea*.—A solution of *o*-aminothiophenol

[9] Morton and Stubbs, *J.*, 1939, 1321; Koch, *J.*, 1949, 401.
[10] Kurzer and Sanderson, *J.*, 1960, 3240.
[11] Gillam and Stern, "Electronic Absorption Spectroscopy," Arnold, London, 1957, p. 73, 126.
[12] Kurzer, *Chem. Rev.*, 1956, **56**, 95, 125.
[13] Kalkhoff, *Ber.*, 1883, **16**, 1828; Sandmeyer, *Ber.*, 1886, **19**, 2655.

(12·5 g., 0·1 mole) in anhydrous acetone (80 ml.) was slowly treated (exothermic action) with diphenylcarbodi-imide (19·4 g., 0·1 mole) and then refluxed during ½ hr. The solvent was removed almost completely in a vacuum, and the residual yellow oil dissolved in warm ethanol (15—20 ml.). The separated product was collected at 0° [m. p. 110—112° (decomp.); 20·7—23·9 g., 65—75%] (filtrate F) and crystallised from ethanol (3 ml. per g., recovery 70%), giving prisms of S-o-*aminophenyl*-NN′-*diphenylisothiourea*, m. p. 110—112° (decomp.) [Found: C, 71·6; H, 5·1; N, 13·4; S, 10·1%; *M* (cryoscopic, in thymol), 330. $C_{19}H_{17}N_3S$ requires C, 71·5; H, 5·3; N, 13·2; S, 10·0%; *M*, 319], $\lambda_{min.}$ 225 mμ (log ε 4·40), $\lambda_{max.}$ 240 mμ (log ε 4·47).

Filtrate F gave (in some, but not all, experiments), on storage and later partial evaporation, prisms (m. p. 138—142°; up to 2·5 g., 10%), which consisted, after purification (see below), of *S-o*-(*NN′*-diphenylguanidino)phenyl-*NN′*-diphenylisothiourea, m. p. and mixed m. p. (see below) 143—145° (Found: C, 74·9; H, 5·3; N, 13·85%). The final filtrates therefrom gave, on complete evaporation, only resins.

S-o-Aminophenyl-*NN′*-diphenylisothiourea was readily soluble in cold 3N-hydrochloric acid, but insoluble in 3N-ammonia or sodium hydroxide.

Carbylamine resulted when the compound was briefly boiled with 0·5N-ethanolic potassium hydroxide and a few drops of chloroform. The isothiourea (0·005 mole) was recovered after treatment with benzaldehyde (0·005 mole) at 100° during 1 hr. in the absence or presence of ethanol (10 ml.). A picrate was not obtained, interaction of the reactant and picric acid (0·001 mole each) in ethanol (10 ml.) giving an immediate precipitate (65%) of 2-anilinobenzothiazole picrate, m. p. and mixed m. p. (see below) 225—226° (decomp.) (Found: C, 50·0; H, 2·8. Calc. for $C_{13}H_{10}N_2S,C_6H_3N_3O_7$: C, 50·1; H, 2·9%). The isothiourea and toluene-*p*-sulphonyl chloride (1·25 mole) in pyridine at 100° during 20 min. gave 2-anilinobenzothiazole, m. p. and mixed m. p. 158—159° (50%; after crystallisation from ethanol).

Reactions of S-o-*Aminophenyl*-NN′-*diphenylisothiourea.*—(a) *With hydrochloric acid.* The thiourea (3·2 g., 0·01 mole) was refluxed in ethanol (20 ml.) and concentrated hydrochloric acid (1·5 ml.) during 10 min. and then stirred into ice-water (150 ml.) containing 3N-ammonia (10 ml.). The resulting precipitate gave, on crystallisation from chloroform–light petroleum, prismatic needles (1·63 g., 72%) of 2-anilinobenzothiazole, m. p. 157—159° (lit.,[14,15] m. p. 157—159°) [Found: C, 69·1; H, 4·2; N, 12·3; S, 14·25%; *M* (cryoscopic, in thymol), 220. Calc. for $C_{13}H_{10}N_2S$: C, 69·0; H, 4·4; N, 12·4; S, 14·2%; *M*, 226], $\lambda_{max.}$ 238 mμ (log ε 4·23), $\lambda_{min.}$ 255 mμ (log ε 3·56), shoulder 298—310 mμ (log ε 4·40).

In a separate experiment the reaction mixture was quickly evaporated almost completely in a vacuum, and the residue treated with 20% aqueous sodium hydroxide (30 ml.) and steam-distilled. The non-volatile solid was, as before, 2-anilinobenzothiazole (60%). The distillate (~50 ml.) gave, on treatment with 40% aqueous sodium hydroxide (10 ml.) and benzoyl chloride (2 ml.), benzanilide (56%; from ethanol), m. p. and mixed m. p. 161—163°.

Powdered *S-o*-aminophenyl-*NN′*-diphenylisothiourea (0·005 mole) dissolved almost instantly in N-hydrochloric acid (30 ml.). The liquid, when immediately basified with 3N-ammonia at 0° (addition of ice), gave a granular precipitate, which was collected, dried at room temperature, and dissolved in ethanol (6 ml.). The yellow liquid deposited two forms of crystal (total 0·9 g., ~50% each; easily separated mechanically). The massive pale yellow prisms were starting material, m. p. and mixed m. p. 110—112°; the silky felted needles were 2-anilinobenzothiazole, m. p. and mixed m. p. 157—159°.

(b) *With acetic acid.* A solution of the isothiourea (0·005 mole) in glacial acetic acid (10 ml.) was refluxed during 15 min., stirred into ice-water (100 ml.), and basified with ammonia (*d* 0·88). The precipitate was 2-anilinobenzothiazole (90%), m. p. and mixed m. p. 157—159° (from chloroform–light petroleum).

(c) *Pyrolysis.* The fused isothiourea (0·005 mole) was kept at 165—170° during 30 min. The cooled solidified melt, crystallised as above, was 2-anilinobenzothiazole, m. p. and mixed m. p. 156—158° (74%).

2-Anilinobenzothiazole, obtained as above, was identified further as follows: The picrate formed needles, m. p. 224—226° (from acetone containing 5% of water) (lit.,[16] m. p. 222°). The acetyl derivative (obtained in 80% yield in boiling acetic anhydride) formed needles, m. p. 162—163° (from ethanol) (Found: C, 66·8; H, 4·8; N, 10·3. Calc. for $C_{15}H_{12}N_2OS$:

[14] Hofmann, *Ber.*, 1880, **13**, 12; Rassow, Döhle, and Reim, *J. prakt. Chem.*, 1916, **93**, 197.
[15] Fromm, *Annalen*, 1912, **394**, 289.
[16] Jacobson and Frankenbacher, *Ber.*, 1891, **24**, 1410.

C, 67·2; H, 4·5; N, 10·45%) (lit., m. p. 162—163° [17] or 167° [16]). The benzoyl derivative (obtained in 85% yield by pyridine and an excess of benzoyl chloride at 100°) formed needles, m. p. 154—156° (from ethanol) (Found: C, 72·3; H, 4·3; N, 8·3. Calc. for $C_{20}H_{14}N_2OS$: C, 72·7; H, 4·2; N, 8·5%) (lit.,[15] m. p. 156°). The *toluene-p-sulphonyl derivative* (obtained in 65% yield by pyridine–toluene-*p*-sulphonyl chloride at 100°) formed needles, m. p. 125—127° (from ethanol) (Found: C, 63·7; H, 4·5; N, 7·3; S, 16·2. $C_{20}H_{16}N_2O_2S_2$ requires C, 63·1; H, 4·2; N, 7·4; S, 16·8%).

(d) *Alkaline hydrolysis.* A solution of the reactant (1·60 g., 0·005 mole) in ethanol (18 ml.) and 3N-sodium hydroxide (3·3 ml., 0·01 mole) was refluxed during 1 hr., then distilled to dryness in a vacuum. The residue was extracted with warm 3N-hydrochloric acid (3 × 5 ml.; extracts E). The undissolved material was *NN'*-diphenylurea, m. p. and mixed m. p. 236—238° (from ethanol, 0·65 g., 62%). The combined extracts E, when treated with 40% aqueous sodium hydroxide and shaken with benzoyl chloride (5 ml.; added in one portion), precipitated *NNS*-tribenzoyl-*o*-aminothiophenol, m. p. and mixed [10] m. p. 136—137° (from ethanol) (1·1 g., 50%).

A solution of *NN'N''*-triphenylguanidine (2·87 g., 0·01 mole) in ethanol (35 ml.) and 3N-sodium hydroxide (6·7 ml.; 0·02 mole) was refluxed during 1 hr., then distilled to half-bulk in a vacuum, and the resulting suspension was diluted with water (40 ml.). The precipitate, collected at 0° (m. p. 144—145°; 2·65 g., 92%), was the starting material, m. p. and mixed m. p. 144—145° (from acetone–ethanol).

(e) *With aniline.* A solution of the isothiourea (3·20 g., 0·01 mole) in aniline (12 ml.) was refluxed during 15 min., treated with water (40 ml.) and 3N-sodium hydroxide (2 ml.), and steam-distilled until all the aniline had been removed (steam-distillate S). The oily droplets in the residual suspension rapidly solidified and were collected at 0° (2·5 g.) (filtrate U). Two crystallisations from acetone–ethanol gave massive prisms of *NN'N''*-triphenylguanidine, m. p. and mixed m. p. 144—145° (1·5 g., 52%).

The steam-distillate S was treated with 3N-sodium hydroxide (10 ml.) and again distilled (to remove all the aniline), leaving a clear aqueous alkaline solution T (~40 ml.). Solution T and filtrate U were each separately benzoylated (in each case, 15 ml. of 40% sodium hydroxide, and 5 ml. of benzoyl chloride, added in one portion [10]); the resulting crude product (0·75 and 1·55 g., respectively) gave, on crystallisation from ethanol, *NNS*-tribenzoyl-*o*-aminothiophenol, m. p. and mixed m. p. 136—137° [10] (1·75 g., 40%).

(f) *With bromine.* A stirred solution of the reactant (3·20 g., 0·01 mole) in chloroform (20 ml.) was treated dropwise with M-bromine (in chloroform, 10 ml., 0·01 mole). The liquid became purple, and a precipitate appeared when half the halogen had been added. After 2 hours' storage at room temperature, the solvent was removed *in vacuo*, and the residue dissolved in ethanol (10 ml.) and stirred into ice-water containing 3N-ammonia (10 ml.). The precipitate was covered with cold ethanol (10 ml.), and the undissolved white solid (1·25—1·75 g.) (filtrate F) crystallised three times from chloroform–light petroleum (10 ml. each, per g.), needles of 2-anilino-6-bromobenzothiazole, m. p. 186—188°, being obtained (0·25—0·46 g., 8—15%) (lit., m. p. 194°,[18] 188° [19]) [picrate had m. p. 245—246° (decomp.) (Hunter and Wali [18] give m. p. 246—247°)] (Found: C, 52·0; H, 3·0; N, 9·3; S, 10·55; Br, 25·25. Calc. for $C_{13}H_9BrN_2S$: C, 51·2; H, 2·95; N, 9·2; S, 10·5; Br, 26·2%). The mother liquors therefrom, as well as filtrates F, each gave separately successive crops of bromine-containing non-homogeneous unidentified fractions, having unsharp m. p.s between 140° and 180°.

2-*Benzylthioaniline.*—A solution of *o*-aminothiophenol (12·5 g., 0·1 mole) in ethanol (100 ml.) and benzyl chloride (12·65 g., 0·1 mole) was treated with 3N-sodium hydroxide (33·3 ml., 0·1 mole) and kept at 60° during 1 hr. After being distilled to half-bulk at 50° in a vacuum, the liquid was stirred into ice-water, and the solidified oil air-dried at room temperature. Dissolution in light petroleum (250 ml.), filtration (carbon), and slow evaporation gave successive crops (15—17·2 g., 70—80%) of large, pale yellow, flat prisms of 2-benzylthioaniline, m. p. 44—45°. The method is essentially that of Lantz, Mingasson, and Delarue,[4] who give m. p. 42—43°.

S-o-Aminophenyl-*NN'*-diphenylisothiourea, treated identically, failed to yield an *S*-benzyl derivative.

[17] Hugershoff, *Ber.*, 1903, **36**, 3128.
[18] Hunter and Wali, *J.*, 1937, 1513.
[19] Brewster and Dains, *J. Amer. Chem. Soc.*, 1936, **58**, 1364.

S-o-(NN′-*Diphenylguanidino*)*phenyl*-NN′-*diphenylisothiourea*.—(*a*) A solution of *o*-aminothiophenol (3·75 g., 0·03 mole) and diphenylcarbodi-imide (12·2 g., 0·063 mole) in acetone (50 ml.) was refluxed during 30 min., the solvent removed in a vacuum, and the residual syrup redissolved in chloroform (15 ml.)–light petroleum (15 ml.). The crystals, collected after several days' storage (finally at 0°) (m. p. 144—146°; 2·75—3·85 g., 18—25%), gave, after further crystallisation from the same solvents, needles of the substituted *isothiourea*, m. p. 144—145° (Found: C, 75·0; H, 4·8; N, 13·85; S, 5·8. $C_{32}H_{27}N_5S$ requires C, 74·85; H, 5·3; N, 13·6; S, 6·2%). It gave an ultraviolet absorption curve of negative slope, defined by the following points: λ 215, 230, 250, 275, 310 mμ (log ε 4,70, 4·60, 4·41, 4·40, 4·20; plateau between λ 250 and 275 mμ). No further crystals were isolated from the viscous filtrate from the crude product.

The product was insoluble in 3N-hydrochloric acid and 3N-sodium hydroxide. At most a trace of carbylamine resulted with boiling ethanolic potassium hydroxide–chloroform.

A solution of the isothiourea and picric acid (0·0005 mole each) in ethanol (25 ml.) slowly deposited 2-anilinobenzothiazole picrate, m. p. and mixed m. p. 224—225° (decomp.) (0·12 g., 53%).

(*b*) A solution of *S-o*-aminophenyl-*NN′*-diphenylisothiourea (3·2 g., 0·01 mole) and diphenylcarbodi-imide (1·95 g., 0·01 mole) in acetone (50 ml.) was refluxed during 1 hr. Isolation and crystallisation of the product (total, crude: m. p. 139—143°; 2·82—3·1 g., 55—60%) as before gave the above isothiourea, m. p. and mixed m. p. (with material from *a*) 142—144° (Found: C, 74·6; H, 5·1%). Its ultraviolet absorption curve was coincident with that of a specimen prepared by method (*a*). The filtrates from the crude product gave no further crystals.

Action of Hydrochloric Acid on S-o-(NN′-*Diphenylguanidino*)*phenyl*-NN′-*diphenylisothiourea*.—The isothiourea (1·54 g., 0·003 mole) was refluxed in ethanol (20 ml.) and concentrated hydrochloric acid (2 ml.) during 20 min., poured into ice-water (100 ml.), and basified (to litmus) with 3N-ammonia. The precipitated dried solid (1·5 g.) was crystallised fractionally from chloroform–light petroleum (b. p. 40—60°). The initial fractions, after further crystallisation, were 2-anilinobenzothiazole, m. p. and mixed m. p. 156—158° (total, 0·55 g., 80%). The most soluble fractions consisted, after crystallisation from the same solvents, of *NN′N″*-triphenylguanidine, m. p. and mixed m. p. 142—144° (total, 0·65 g., 75%) (Found: C, 78·9; H, 5·7. Calc. for $C_{19}H_{17}N_3$: C, 79·4; H, 5·9%).

S-(o-NN′-*Di*-p-*tolylguanidino*)*phenyl*-NN′-*di*-p-*tolylisothiourea*.—*o*-Aminothiophenol (2·50 g., 0·02 mole) and freshly distilled di-*p*-tolylcarbodi-imide [20] (8·9 g., 0·04 mole) in acetone (50 ml.) were refluxed during 1 hr., the solvent removed in a vacuum, and the oily residue dissolved in ethanol (20 ml.). On storage and partial evaporation, two crops of a crude product were obtained (m. p. 140—144°; total, 2·85 g., 25%), which consisted after crystallisation from acetone–ethanol (20 and 5 ml. per g. respectively; recovery 70—80%) of ivory prisms of the substituted *isothiourea*, m. p. 146—150° (subject to the rate of heating) (Found: C, 76·2; H, 6·2; N, 11·9; S, 5·5. $C_{36}H_{35}N_5S$ requires C, 75·9; H, 6·15; N, 12·3; S, 5·6%), giving an ultraviolet absorption curve of negative slope, defined by the following points: λ 215, 230, 250, 275, 310 mμ (log ε 4·73, 4·60, 4·48, 4·42, 4·24). The final filtrates gave only oils.

In equimolar proportions the reactants during 30 min. gave, by the same procedure, the above isothiourea in 30—35% yield (based on the carbodi-imide) (Found: C, 75·6; H, 6·2%).

2-p-*Toluidinobenzothiazole*.—The foregoing isothiourea (1·14 g., 0·002 mole) in ethanol (10 ml.) and concentrated hydrochloric acid (1 ml.) was refluxed during 15 min., then stirred into water (50 ml.) and basified with 3N-ammonia. The precipitate, crystallised from chloroform–light petroleum (10 ml. each, per g.), gave needles (0·38 g., 80%) of 2-p-*toluidinobenzothiazole*, m. p. 178—180° (Found: C, 69·9; H, 4·7; N, 12·0; S, 13·3. $C_{14}H_{12}N_2S$ requires C, 70·0; H, 5·0; N, 11·7; S, 13·3%), shoulder at 230—240 mμ (log ε 4·23), $\lambda_{min.}$ 255 mμ (log ε 3·62), $\lambda_{max.}$ (shallow) 302 mμ (log ε 4·40). The final filtrates contained tri-*p*-tolylguanidine, m. p. 122°.

S-o-*Aminophenyl*-NN′-*di*-(o-*methoxyphenyl*)*isothiourea*.—*o*-Aminothiophenol (1·88 g.,0·015 mole) and di-*o*-methoxyphenylcarbodi-imide [20] (3·2 g., 0·0125 mole) in acetone (20 ml.) were refluxed during 30 min., the solvent removed in a vacuum, and the residual oil dissolved in ethanol (6 ml.). The crystals were collected at 0° (m. p. 132—135°, after sintering at 129°; 3·9 g., 82%); they crystallised from chloroform–light petroleum (4 ml. each, per g., recovery 70%) yielding plates of the *isothiourea*, m. p. 132—134° (decomp.) [Found: C, 66·3; H, 5·5; N, 11·8; S, 9·2%; *M* (cryoscopic in thymol), 362. $C_{21}H_{21}N_3O_2S$ requires C, 66·5; H, 5·5;

[20] Hünig, Lehmann, and Grimmer, *Annalen*, 1953, **579**, 77.

N, 11·1; S, 8·4%; *M*, 379], $\lambda_{min.}$ 231 mμ (log ε 4·35), $\lambda_{max.}$ 242 mμ (4·42) (shoulder), $\lambda_{min.}$ 277 mμ (4·14), $\lambda_{max.}$ 294 mμ (4·26). The product was soluble in cold 3N-hydrochloric acid.

o-Aminothiophenol with an excess of the carbodi-imide (2·5 mol.) gave merely the same isothiourea, m. p. and mixed m. p. 133—135° (decomp.), in diminished yields (20—30%). The more soluble fraction, isolated by partial evaporation of the mother liquors, consisted, after crystallisation from chloroform–light petroleum (b. p. 40—60°), of prisms (25%) of NN′N″-*tri*-o-*methoxyphenylguanidine*, m. p. 142—144° (Found: C, 70·3; H, 5·9; N, 11·6%; *M*, 400. $C_{22}H_{23}N_3O_3$ requires C, 70·0; H, 6·1; N, 11·1%; *M*, 377); its chloroplatinate has been described [21] but the base was not obtained crystalline.

2-o-*Methoxyanilinobenzothiazole*.—The foregoing isothiourea (0·95 g., 0·0025 mole) was refluxed in ethanol (10 ml.) and concentrated hydrochloric acid (0·5 ml.) during 15 min. and stirred into ice-water and ammonia. The solidified oil, collected at 0°, crystallised from chloroform–light petroleum (8 ml. each, per g.) to yield prisms (0·55 g., 85%) of 2-o-*methoxyanilinobenzothiazole*, m. p. 154—156° (Found: C, 65·4; H, 4·8; N, 10·9; S, 12·5. $C_{14}H_{12}N_2OS$ requires C, 65·6; H, 4·7; N, 10·9; S, 12·5%), $\lambda_{max.}$ 222, 281, 310 mμ (log ε 4·38, 4·18, 4·35), $\lambda_{min.}$ 255, 287 mμ (log ε 3·68, 4·11).

S-o-*Aminophenyl*-NN′-*di*-p-*bromophenylisothiourea*.—Interaction of *o*-aminothiophenol and di-(*p*-bromophenyl)carbodi-imide [20] (0·005 mole each) in boiling acetone (15 ml.) during 30 min., removal of the solvent, and crystallisation of the residue from acetone (5 ml.)–ethanol (5 ml.) gave the crude product (m. p. 134—136°; 1·72 g., 72%). Further crystallisation from the same solvents gave needles of the *isothiourea*, m. p. 137—139° (Found: C, 47·8; H, 3·1; N, 8·4; S, 6·6. $C_{19}H_{15}Br_2N_3S$ requires C, 47·8; H, 3·1; N, 8·8; S, 6·7%), $\lambda_{min.}$ 227 mμ (log ε 4·37), plateau 240—255 mμ (4·43), $\lambda_{max.}$ 264 mμ (4·46). It dissolved in cold 3N-hydrochloric acid.

Interaction of the above reactants in the molar ratio 1 : 2 in boiling acetone during 45 min. gave the same isothiourea (m. p. and mixed m. p. 138—140°) in 60—65% yield.

2-p-*Bromoanilinobenzothiazole*.—The foregoing isothiourea, on the usual treatment with hydrochloric acid, gave 2-*p*-bromoanilinobenzothiazole, m. p. 213—215° (from acetone–ethanol) (85%) (lit.,[7] 214—215°), plateau at 230—240 mμ (log ε 4·22), $\lambda_{min.}$ 255 mμ (3·60), shoulder 290—295 mμ (log ε 4·40—4·42), $\lambda_{max.}$ 304 mμ (4·52).

2-*Mercaptophenylurea*.—A freshly prepared cold stirred solution of *o*-aminothiophenol (2·5 g., 0·02 mole) in 2N-hydrochloric acid (25 ml., 0·05 mole) was treated with ice (15—20 g.), followed immediately by 80% potassium cyanate (5 g., 0·05 mole) in water (10 + 5 ml.). The pale yellow precipitate was collected at 0° [m. p. 148—150° (decomp.); 3 g.] and crystallised by addition to boiling ethanol (15 ml. per g.), undissolved material M being filtered off. The resulting o-*mercaptophenylurea* (1·5—1·85 g., 45—55%) formed colourless plates, m. p. 152—154° (decomp., somewhat subject to the rate of heating) (Found: C, 50·0; H, 4·5; N, 17·0; S, 19·4. $C_7H_8N_2OS$ requires C, 50·0; H, 4·8; N, 16·7; S, 19·05%). The sparingly soluble fraction M (0·35—0·5 g., 8—12%) (which increased in quantity the longer the crude material was boiled with ethanol, or more particularly with 90% aqueous ethanol) gave, after crystallisation from ethanol (100 ml. per g., recovery 50%), needles of o-*mercaptophenylbiuret*, m. p. 169—170° (decomp.) (Found: C, 45·4; H, 4·0; N, 19·85; S, 15·4. $C_8H_9N_3O_2S$ requires C, 45·5; H, 4·3; N, 19·9; S, 15·2%). This compound was soluble in aqueous sodium hydroxide, and was reprecipitated by hydrochloric or acetic acid. On addition of a little very dilute copper sulphate, the alkaline solution became deep reddish-purple.

2-*Hydroxybenzothiazole*.—*o*-Mercaptophenylurea (1·68 g., 0·01 mole) dissolved rapidly when its suspension in ethanol (15 ml.) and concentrated hydrochloric acid (3 ml.) was kept at 100°. The product began to separate after 6—8 min.; after 10 min. the suspension was stirred into ice-water (50 ml.), then basified with 3N-ammonia, and the crystalline precipitate collected after storage at 0° overnight. Crystallisation from methanol (5 ml. per g.) gave prisms (1·2 g., 80%) of 2-hydroxybenzothiazole, m. p. 135—137° (lit.,[22] 136—138°) (Found: C, 55·6; H, 3·1. Calc. for C_7H_5NOS: C, 55·6; H, 3·3%); its absorption curve is given by λ 215, 225, 235, 245 mμ (log ε 4·56, 4·05, 3·76, 3·76), then $\lambda_{min.}$ 265 mμ (3·05), $\lambda_{max.}$ 282 mμ (3·47), $\lambda_{min.}$ 286 mμ (3·42), $\lambda_{max.}$ 290 mμ (3·46).

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[21] Foerster, *Ber.*, 1888, **21**, 1862.
[22] Hofmann, *Ber.*, 1879, **12**, 1128; 1880, **13**, 10; Claasz, *Ber.*, 1912, **45**, 1030; Hunter, *J.*, 1930, 135.