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1170. *Triazines. Part II.*[1] *The Interaction of Diguanide with Isothiocyanate Esters*

By Frederick Kurzer and Ernest D. Pitchfork

The interaction of diguanide and isothiocyanate esters in dimethylformamide under controlled conditions gives excellent yields of 1-substituted hexahydro-4,6-di-imino-*s*-triazine-2-thiones, together with small quantities of monosubstituted melamines and thioammeline. Under more severe conditions, the melamine derivatives become the main products. The production of these triazines is accounted for by a mechanism involving the primary formation of simple addition products, followed by their cyclisation, with loss of either ammonia, hydrogen sulphide, or primary amine.

The results of the condensation of *N*-cyano-*N'*-phenylguanidine and thiocyanic acid (also yielding hexahydro-4,6-di-imino-1-phenyl-*s*-triazine-2-thione), and of that of *N*-amidino-*N'*-phenylthiourea and cyanamide (yielding phenylmelamine) are correlated with the above mechanism.

The formulation of the triazinethiones is supported indirectly by the fact that authentic 4-amino-6-anilino-*s*-triazine-2-thiol, synthesised from cyanuric chloride, is different from hexahydro-4,6-di-imino-1-phenyl-*s*-triazine-2-thione. Certain chemical properties of the triazinethiones are described: they are convertible into the corresponding *S*-methyl derivatives, and thence into substituted melamines by aminolysis.

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In continuation of our investigation of the addition of systems containing twinned double bonds to diguanide and its homologues, we have examined the behaviour of isothiocyanate esters in this reaction. Previous work [1] has shown that addition of carbodi-imides to diguanides is followed by immediate cyclisation of the intermediates to triazines. However, while ring-closure of the adducts of diguanides and carbodi-imides is necessarily limited to the production of melamine derivatives,[1] that of analogues derived from isothiocyanates should be more versatile; thus, retention or elimination of sulphur in the cyclisation would result in the formation of thioammelines or melamines, respectively. By a proper choice of reactants and conditions, representatives of both these series have now been obtained.

The principal products of the interaction of diguanide (I) and isothiocyanate esters under mild conditions are 1-substituted hexahydro-4,6-di-imino-*s*-triazine-2-thiones (VIII), subsequently referred to more concisely as 1-substituted 2-thioammelines. Thus, equimolar quantities of phenyl isothiocyanate and diguanide reacted at 40—50° in pyridine, or preferably dimethylformamide, giving 1-phenyl-2-thioammeline (VIII; R = Ph) rapidly in 85—90% yield, together with very small quantities of thioammeline (VI) and phenylmelamine (VII; R = Ph). Other aromatic isothiocyanates gave similar results; the less reactive [2] alkyl isothiocyanates afforded comparable yields on more prolonged reaction at 100°.

The assigned structure (VIII) of the 1-substituted 2-thioammelines is based on their composition, mode of formation, and certain of their properties. The initial addition of the isothiocyanate ester to diguanide may occur theoretically at the central or at the equivalent terminal nitrogen atoms (of I), giving adducts (IVa) or (IV), respectively, of which only the latter are capable of yielding triazines on cyclisation. A mechanism involving the elimination (from IV) of ammonia, arylamine, or hydrogen sulphide, resulting in 1-substituted 2-thioammelines (VIII), thioammeline (VI), and monosubstituted melamines (VII), respectively, accounts satisfactorily for the experimental observations. Loss of ammonia (from IV), with formation of a triazine can occur in one way only,

[1] Part I, F. Kurzer and E. D. Pitchfork, *J.*, 1964, 3459.
[2] K. H. Slotta, R. Tschesche, and H. Dressler, *Ber.*, 1930, **63**, 208; L. E. A. Godfrey and F. Kurzer, *J.*, 1961, 5137.

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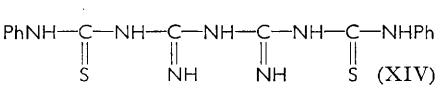
involving necessarily the alkyl(or aryl)amino-grouping of the adduct (IV); in the absence of rearrangement, the final main products are therefore 1-substituted 2-thioammelines (VIII) and not the isomeric 4-alkyl(or aryl)amino-6-amino-*s*-triazine-2-thiols (XII).

Evidence for the absence of such isomerisation, and consequent support for the proposed formulation (VIII) was provided by the observation that 4-amino-6-anilino-*s*-triazine-2-thiol (XII; R = Ph), synthesised unequivocally from the preformed triazine system, was not identical with 1-phenyl-2-thioammeline (VIII; R = Ph). In this synthesis, the chlorine atoms in cyanuric chloride were successively replaced by an amino-, an anilino-, and a mercapto-group. 2-Amino-4,6-dichloro-*s*-triazine,[3] obtained in the first stage, was convertible in excellent yield into 2-amino-4-anilino-6-chloro-*s*-triazine (XIII; R = Ph) in acetone by the action of one mole of aniline in presence of one equivalent of sodium carbonate. The familiar use of two moles of amine for performing this replacement, recommended for this specific example by Thurston *et al.*,[3] was not found suitable, giving in our hands good yields of 2,4-diphenylmelamine (hydrochloride). Substitution of the final chlorine atom of chlorotriazines by amines normally requires fairly high temperatures;[4,5] the replacement under the present mild conditions is therefore noteworthy. In the final stage, the general method of converting chloro- into mercapto-derivatives by the successive action of thiourea and alkali[6] was applied to the 6-chloro-*s*-triazine (XIII; R = Ph). The resulting 4-amino-6-anilino-*s*-triazine-2-thiol (XII; R = Ph) was characterised further as the picrate and by its absorption properties. The distinctness of the two series (VIII) and (XII) was also established for aliphatic isomers, by a comparison of the n-butyl homologues (VIII, XII; R = Bu^n), 4-amino-6-n-butylamino-*s*-triazine-2-thiol being synthesised unequivocally from cyanuric chloride.

The postulated intermediates (IV) of the present reaction were generally not stable enough to be isolated and characterised. Except in one single case,* attempts to prepare such primary addition products were not successful. However mild the conditions of the condensation, and the method of isolating the products, the cyclic end-products (mostly VIII) were invariably obtained.

Action of two moles of phenyl isothiocyanate on diguanide also gave 1-phenyl-2-thioammeline (VIII; R = Ph) (75—80%). The absence of the di-addition product (XIV), or a thioureido-thioammeline, *e.g.*, (XV), derived therefrom, may be ascribed to the difficulty of building up extended "urea-chains." Thus, in the simplest parallel case, the existence of triurets [corresponding to (IV)] is well established, but tetrauret [corresponding to (XIV)] and higher "amidologues" do not exist.[7]



(XIV)

Like their parent compound (VI),[8] 1-substituted 2-thioammelines (VIII) are amphoteric. They are sufficiently acidic to dissolve in strong caustic alkalis, but are of predominantly basic character: thus, 1-phenyl-2-thioammeline formed stable salts (*e.g.*, hydrochloride and picrate) and acyl derivatives (including diacetyl and dibenzoyl compounds). The presence of a (potential) exocyclic mercapto-group was confirmed by the near-quantitative

* The preparation of 1-(isopropylthioamido)diguanide (IV; R = Pr^i) appears to be the only exception so far, and will be reported in another connexion.

[3] J. T. Thurston, J. R. Dudley, D. W. Kaiser, I. Hechenbleickner, F. C. Schaefer, and D. Holm-Hansen, *J. Amer. Chem. Soc.*, 1951, **73**, 2981.

[4] E. J. Modest in "Heterocyclic Compounds," ed. R. C. Elderfield, Wiley, New York and London, 1961, vol. VII, pp. 627, 670.

[5] W. W. Cuthbertson and J. S. Moffatt, *J.*, 1948, 561; E. A. H. Friedheim, *J. Amer. Chem. Soc.* 1944, **66**, 1775; O. Diels and M. Liebermann, *Ber.*, 1903, **36**, 3191; H. H. Fries, *Ber.*, 1886, **19**, 242, 2055. See also American Cyanamid Co., New Product Bulletin, Coll. Vol. I, 1952, pp. 27, 36.

[6] T. B. Johnson and J. M. Sprague, *J. Amer. Chem. Soc.*, 1936, **58**, 1348; 1937, **59**, 1837; G. G. Urquart, J. W. Gates, jun., and R. Connor, *Org. Synth.*, Coll. Vol. III, 1955, p. 363; A. T. Speciale, *Org. Synth.*, Coll. Vol. IV, 1963, p. 401.

[7] F. Kurzer, *Chem. Rev.*, 1956, **56**, 95, 170, 177.

[8] R. P. Welcher, D. W. Kaiser, and V. P. Wystrach, *J. Amer. Chem. Soc.*, 1959, **81**, 5665.

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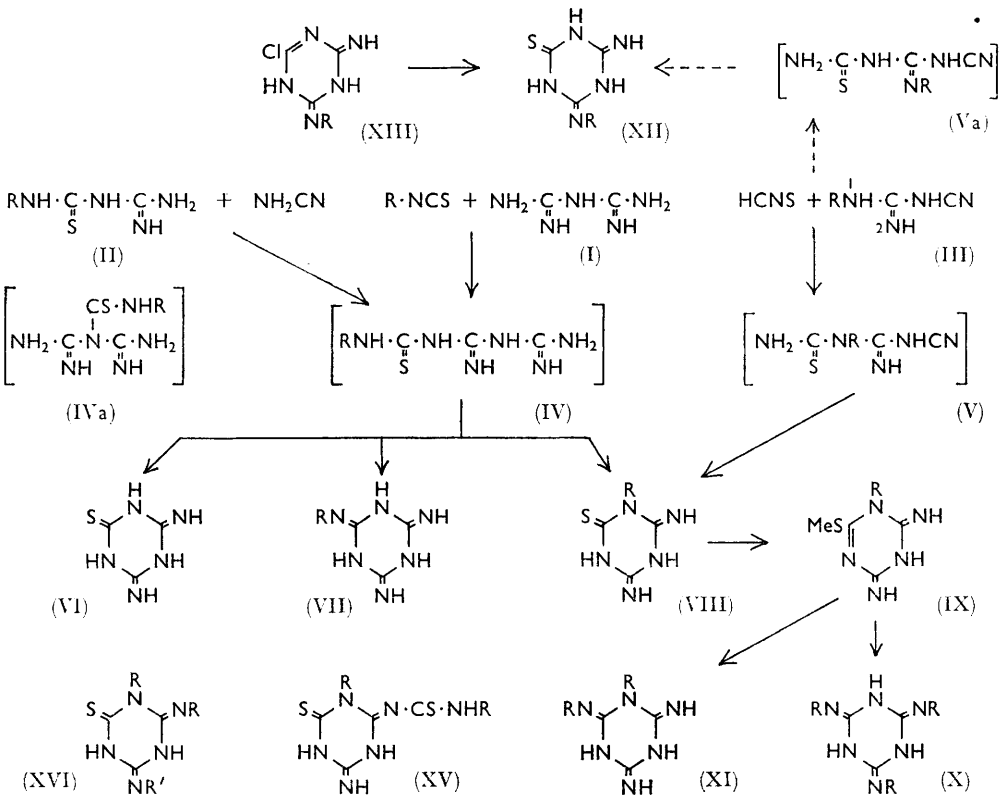
conversion of 1-phenyl-2-thioammeline into the methyl thioether (IX; R = Ph). This evolved methanethiol on treatment with aniline yielding 1,2-diphenylisomelamine (XI; R = Ph) at 100°, or *s*-triphenylmelamine (X; R = Ph) at 185°. The production of the former involves the expected aminolysis of the methylthio-grouping.[9] Formation of *s*-triphenylmelamine (X; R = Ph) necessitates the migration of a phenyl group [possibly by a temporary ring-opening at N(1)–C(2), the N(1)-phenyl group assuming the exocyclic position], and the replacement of an amino- by an anilino-group, reactions that are both well-authenticated [10,11] in the triazine field.

1-Aryl-2-thioammelines were unaffected by ethanolic ammonia–mercuric oxide,[12] but rapidly deposited lead sulphide on treatment with boiling 3N-sodium hydroxide containing sodium plumbite; their acyl derivatives were similarly desulphurised, as were aliphatic analogues (VIII; R = Alk), though generally somewhat more slowly. Since the parent



For the purpose of uniformity, all triazines are represented as their " iso " structures, all other possible tautomeric forms being understood.

compound, thioammeline (VI), was stable under these conditions, the ready desulphurisation of 1-substituted 2-thioammelines (VIII) is ascribed to the presence of the ring substituent, and consequent " isoammeline " structure of the resulting *s*-triazines.

[9] A. Hofmann, *Ber.*, 1885, **18**, 2755; G. D'Alelio and J. Pyle, U.S.P. 2,361,823/1944; S. Birtwell, F. H. S. Curd, J. A. Hendry, and F. L. Rose, *J.*, 1948, 1645.

[10] B. Rathke, *Ber.*, 1888, **21**, 867; J. T. Thurston, U.S.P. 2,482,076/1949 (*Chem. Abs.*, 1950, **44**, 5926).

[11] A. Grün, U.S.P. 2,437,691/1948 (*Chem. Abs.*, 1948, **42**, 5475); J. T. Thurston, U.S.P. 2,385,766 1945; J. T. Thurston, U.S.P. 2,474,194/1949 (*Chem. Abs.*, 1949, **43**, 7053); W. Zerweck and K. Keller U.S.P. 2,228,161 (*Chem. Abs.*, 1941, **35**, 2531); I. Honda and Y. Oshima, *J. Soc. Org. Synth. Chem. Japan*, 1962, **20**, 756 (*Chem. Abs.*, 1963, **58**, 5687).

[12] B. Rathke, *Ber.*, 1887, **20**, 1065.

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The ultraviolet absorption spectra of all 1-substituted 2-thioammelines examined showed a high-intensity peak in the 280—290-mμ region. They resembled that [8] of the parent thioammeline (VI), and were very similar to each other, regardless of the 1-substituent being aromatic or aliphatic; the absorption is thus almost exclusively a function of the thioammeline nucleus.

Information concerning thioammelines of the type now described is very sparse. A more highly substituted analogue, hexahydro-1-phenyl-4,6-bisphenylimino-*s*-triazine-2-thione (XVI; R = R′ = Ph) has been prepared by other routes by Rathke;[12] it resembles the present series of compounds in being amphoteric, in resisting the action of ammoniacal silver nitrate, and in undergoing *S*-alkylation. Two other examples, formulated as (XVI; R = *p*-C_6H_4Cl; R′ = Me or Bu^n) have been obtained in small yields as by-products of the interaction of *p*-chlorophenyl isothiocyanate and methyl- or n-butyl-guanidine.[13]

In a higher temperature range, the hypothetical intermediates (IV) lost hydrogen sulphide preferentially, so that substituted melamines (VII) tended to become the main products, their yields increasing with time (Table 1). The use of aliphatic isothiocyanates under these conditions was not attended by evolution of hydrogen sulphide, except in the case of the cyclohexyl homologue, which afforded cyclohexylmelamine (VII; R = C_6H_{11}) and thioammeline (VI) (32 and 15%, respectively, after 6 hr.). The fact that melamine formation in the present reaction is slow is not without bearing on the interpretation of the

TABLE 1

Interaction of diguanide and phenyl isothiocyanate

			Products (%)		
Temp.	Time (min.)	Solvent	(VI)	(VII)	(VIII)
45°	15	DMF	5	2	85
100	20	DMF	—	32	54
100	180	DMF	—	65	20
50	30	Pyridine	—	—	85

alternative thioammeline (VIII) formation in the aromatic series. This slowness of the hydrogen sulphide elimination suggests that the primary addition products (IV) must be appreciably stable in dimethylformamide even at 100°. Since, on the other hand, excellent yields of 1-phenyl-2-thioammeline (VIII; R = Ph) are obtained from the same reaction mixtures at 40—50° after short periods only, there are strong grounds for the view that this alternative and more ready cyclisation to substituted thioammelines (VIII) may in fact occur during the isolation procedure, the intermediate being present in solution in the anhydrous dimethylformamide or pyridine, but being sensitive to hydrogen or hydroxyl ions in aqueous media.

The condensation of cyanoguanidine and thiocyanic acid, an established synthesis of thioammeline (VI),[14,15] has recently been extended to 1-cyano-3-substituted guanidines (III) by Kaiser and his co-workers.[8,16] They obtained from the phenyl homologue (III; R = Ph) a product, m. p. 287—288° (69%) which was formulated as 4-amino-6-anilino-*s*-triazine-2-thiol (XII; R = Ph). We have confirmed their experimental results, but have found their compound to be identical with our 1-phenyl-2-thioammeline (VIII; R = Ph). Since cyanic acid and its analogues react additively at the amidino-moiety of cyanoguanidine,[15,17] 1-phenyl-2-thioammeline produced in Kaiser's experiment may be

[13] A. F. Crowther, F. H. S. Curd, D. N. Richardson, and F. L. Rose, *J.*, 1948, 1636.
[14] B. Rathke, *Ber.*, 1885, **18**, 3102; E. A. Werner and J. Bell, *J.*, 1920, **117**, 1133.
[15] T. L. Davis and H. W. Underwood, *J. Amer. Chem. Soc.*, 1922, **44**, 2595.
[16] D. W. Kaiser and R. P. Welcher (to American Cyanamid Co.), U.S.P. 2,820,033 (*Chem. Abs.*, 1958, **52**, 9229).
[17] A. Smolka and A. Friedreich, *Monatsh.*, 1888, **9**, 201.

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visualised to arise by addition of the elements of thiocyanic acid to the 1-anilino-group of the cyanoguanidine (III; R = Ph), followed by cyclisation of the resulting intermediate (V) to (VIII) by a prototropic change. The alternative addition of thiocyanic acid to the 2-imino-group (of IV; R = Ph) and cyclisation would give the isomer (XII) postulated by Kaiser.[8] In this condensation, *N*-(phenylamidino)urea was also formed as a by-product (up to 15%) and was isolated as the picrate; it obviously arose by the direct hydrolysis of the reactant (III; R = Ph) under the influence of the mineral acid, as has previously been observed.[18]

Another approach to intermediates of type (IV) appeared to be the condensation of *N*-amidino-*N'*-substituted thioureas (II) with cyanamide, guanidines being convertible into substituted diguanides by this reaction,[19] particularly in high-boiling solvents. Accordingly, *N*-amidino-N'-phenylthiourea was found to react with cyanamide in boiling toluene–n-butanol, to yield phenylmelamine (52%): at the relatively high temperature employed, the intermediate (IV; R = Ph) thus cyclised with loss of hydrogen sulphide as expected.

The reactions now described fit satisfactorily into the framework of the group of related additions of reactive compounds containing twinned double bonds to guanidino- and related structures,[20] and supplement the existing knowledge of the use of diguanides as a source of amino-*s*-triazines.[4,21]

Experimental

Light petroleum had b. p. 60—80°. Dimethylformamide was redistilled, and the water-containing fore-run rejected.

Treatment of compounds with boiling 3N-sodium hydroxide containing a few drops of 3N-lead acetate is referred to as the " plumbite test."

Ultraviolet absorption measurements were made with a Unicam S.P. 500 spectrophotometer and 0·00005M-ethanolic solutions. Qualitative infrared measurements were made with a Perkin-Elmer " Infracord " instrument, using potassium bromide discs.

1-*Phenyl*-2-*thioammeline and Derivatives*

Hexahydro-4,6-*di*-*imino*-1-*phenyl*-s-*triazine*-2-*thione*.—(*a*) *In dimethylformamide*. A solution of diguanide (2·0 g., 0·02 mole) (freshly prepared [22] from its sulphate) in dimethylformamide (25 ml.) at room temperature was treated with phenyl isothiocyanate (2·7 g., 0·02 mole). The hot (~50°) liquid (transient colour change to deep green) was kept at 40—50° for 15—20 min., then stirred into ice–water (200 ml.), and the white precipitate, m. p. 280—282° (4·05 g., 85%), collected at 0° (filtrate F). Crystallisation from 50% aqueous ethanol (100—120 ml./g., recovery 70—80%) gave lustrous platelets of *hexahydro*-4,6-*di*-*imino*-1-*phenyl*-s-*triazine*-2-*thione monohydrate*, m. p. 286—288° (decomp., somewhat rate-dependent) (Found: C, 45·8, 46·0; H, 4·7, 4·7; N, 30·2, 30·0; S, 13·0, 13·9. $C_9H_9N_5S,H_2O$ requires C, 45·6; H, 4·6; N, 29·5; S, 13·5%). It was converted by 4 hours' heating at 150° into the *anhydrous thione*, m. p. 286—288° (decomp.) (Found: C, 48·8; H, 4·0; N, 32·5. $C_9H_9N_5S$ requires C, 49·3; H, 4·1; N, 32·0%). It had $\lambda_{min.}$ 260 mμ (log ε 3·72); $\lambda_{max.}$ 290 (4·31); $\nu_{max.}$ (KBr) (from 1700): 1600s,

[18] R. von Walther and W. Griesshammer, *J. prakt. Chem.*, 1915, **92**, 209, 241, 249; see also N. Kundu and P. Ray, *J. Indian Chem. Soc.*, 1952, **29**, 811, 816.

[19] B. Rathke, *Ber.*, 1879, **12**, 776; K. H. Slotta and R. Tschesche, *Ber.*, 1929, **62**, 1390; H. Schotte, H. Priewe, and H. Roescheisen, *Z. physiol. Chem.*, 1928, **174**, 119; A. D. Ainley, F. H. S. Curd, and F. L. Rose, *J.*, 1949, 98.

[20] L. E. A. Godfrey and F. Kurzer, *J.*, 1960, 3437, and subsequent Papers.

[21] E. M. Smolin and L. Rapoport, " s-Triazines and Derivatives," Interscience, London, 1959, pp. 225, 239, 258, 282, 311, and 354.

[22] K. H. Slotta and R. Tschesche, *Ber.*, 1929, **62**, 1396; see also American Cyanamid Co., U.S.P. 2,330,376/1941.

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1550s, 1480s, 1320s, 1180m, 940m, 773m, 762m, 695m cm.$^{-1}$. The compound was not sufficiently soluble in naphthalene or thymol for its molecular weight to be determined cryoscopically in these solvents.

Filtrate F was acidified with 3N-hydrochloric acid, and the finely divided precipitate collected at 0° (filtrate G). After being successively extracted with boiling dimethylformamide and ethanol, it formed a white crystalline powder of thioammeline (0·14 g., 5%) (infusible) (Found: C, 25·9; H, 3·6; N, 49·5; S, 21·5. Calc. for $C_3H_5N_5S$: C, 25·2; H, 3·5; N, 48·95; S, 22·4%). Its identity was further confirmed by its ultraviolet [in water: λ_{infl} 242 (log ε 3·75); $\lambda_{min.}$ 252 (3·64); $\lambda_{max.}$ 279 mμ (4·33)] [lit.,[8] $\lambda_{max.}$ 282 (4·38)] and infrared (compare ref. 8) absorption spectra.

Addition of 0·05M-picric acid (0·0075 mole) to filtrate G precipitated a yellow powder which gave diguanide dipicrate, m. p. and mixed m. p.[1,23] 216—218° (decomp.) (1·35 g., 12%) (from 50% aqueous ethanol) (Found: C, 30·5; H, 2·5; N, 27·95. Calc. for $C_2H_7N_5,2C_6H_3N_3O_7$: C, 30·05; H, 2·3; N, 27·55%). The small ethanol-insoluble residue was phenylmelamine picrate, m. p. and mixed m. p.[1] 292—293° (decomp.) (0·18 g., 2%).

(*b*) Interaction of the above reactants at 100° for 3 hr. gave a deep reddish-brown liquid (evolving ammonia and hydrogen sulphide, the latter particularly in the later stages), which was stirred into water (200 ml.), and the very pale yellow precipitate collected at 0° (filtrate H). Extraction of the dried solid with boiling ethanol (60 ml.) gave a residue (0·95 g., 20%) of the thione monohydrate, m. p. 288—289° (decomp.) (from 50% ethanol) (Found: C, 45·5; H, 4·6; N, 28·9%). The ethanol extracts deposited, after evaporation to small volume and storage at 0°, a white amorphous solid, m. p. 203—205° (1·4 g., 35%), which gave, on crystallisation from acetone–light petroleum (b. p. 40—60°), prisms of phenylmelamine, m. p. and mixed m. p.[24] 197—198° (decomp.) (Found: C, 52·9; H, 4·75. Calc. for $C_9H_{10}N_6$: C, 53·5; H, 4·95). Addition of 0·05M-picric acid (0·01 mole) to filtrate H gave phenylmelamine picrate (2·6 g., 30%), m. p. and mixed m. p.[1] 292—293° (decomp.) (from nitrobenzene) (Found: C, 42·1; H, 3·1. Calc. for $C_9H_{10}N_6,C_6H_3N_3O_7$: C, 41·8; H, 3·0%).

In experiments carried out at 100° for 20 min., the following were isolated as above: the triazinethione (54%), phenylmelamine (12%), phenylmelamine picrate (20%), and diguanide dipicrate (4%).

(*c*) *In pyridine.* Diguanide (0·022 mole), suspended in pyridine (25 ml.), dissolved gradually when phenyl isothiocyanate (0·02 mole) was added, and the spontaneously warmed mixture (40—50°) was stirred for 20—30 min. The liquid was added to ice–water containing concentrated hydrochloric acid (25 ml.), giving a crystalline precipitate (84—90%) of the triazinethione, m. p. 289—290° (decomp.) (from 50% ethanol) (Found: C, 45·3; H, 4·6; N, 30·5; S, 13·9%), $\lambda_{min.}$ 260 (3·72); $\lambda_{max.}$ 289 (4·32). The use of 2 moles of phenyl isothiocyanate per mole of diguanide gave the same product in 75—80% yield.

Diguanide sulphate monohydrate did not dissolve and was recovered (90%) after being treated with phenyl isothiocyante (1 mole) in pyridine at 100° for 30 min.

Hexahydro-4,6-di-imino-1-phenyl-s-triazine-2-thione.—Properties. The compound was not appreciably soluble in hot ammonia, sparingly to moderately soluble in boiling acetic and hydrochloric acid, soluble in warm sodium hydroxide and cold sulphuric acid, being reprecipitated crystalline by acetic acid and ammonia, respectively (all 3N).

The compound was recovered (95%) after 1 hour's refluxing in 3N-hydrochloric acid–ethanol (2 : 1). Its boiling solution in 0·5N-hydrochloric acid, treated with 6% hydrogen peroxide (3 moles), deposited first colloidal and later globular sulphur.

It rapidly gave a positive " plumbite test " on boiling, but was not desulphurised by ethanolic ammonia–mercuric oxide,[12] or ammoniacal silver nitrate.

The compound was recovered (75%) after its 5% solution in dimethyl sulphoxide had been kept at 100° for 6 hr. (a procedure that has been used to convert mercapto-compounds into their disulphides by oxidation).[25]

Salts and derivatives. A solution of the reactant (0·47 g., 0·002 mole) in 0·2N-hydrochloric acid (0·003 mole), added to 0·05M-picric acid (0·002 mole) gave the *hydrated picrate*, m. p. 226—

[23] The m. p. of this salt has been given [1] erroneously as 230—232°.

[24] D. W. Kaiser, J. T. Thurston, J. R. Dudley, F. C. Schaefer, I. Hechenbleickner, and D. Holm-Hansen, *J. Amer. Chem. Soc.*, 1951, **73**, 2984.

[25] *E.g.*, C. N. Yiannios and J. V. Karabinos, *J. Org. Chem.*, 1963, **28**, 3246; T. J. Wallace, *J. Amer. Chem. Soc.*, 1964, **86**, 2018.

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228° (decomp.) as granular prisms (90%) (from 60% aqueous ethanol) (Found: C, 39·1; H, 3·0; N, 23·4. $C_9H_9N_5S,C_6H_3N_3O_7,H_2O$ requires C, 38·6; H, 3·0; N, 24·0%).

The *hydrated hydrochloride* separated (85%) on cooling from solutions of the base in boiling 0·5N-hydrochloric acid, forming lustrous ivory prisms, m. p. 280—282° (decomp.) (Found: C, 39·3; H, 4·4; Cl, 12·75; N, 26·1. $C_9H_9N_5S,HCl,H_2O$ requires C, 39·5; H, 4·4; Cl, 13·0; N, 25·6%).

The reactant (0·002 mole) was heated in pyridine–acetic anhydride (5 ml. each) at 100° during 1 hr., solution being complete after 20 min. The liquid was stirred into ice–water (containing 5 ml. of concentrated hydrochloric acid); the precipitate (85%) gave pale yellow needles of the *diacetyl derivative*, m. p. 208—210° (decomp. to a bright red melt; somewhat rate-dependent) (from acetone–methanol) (Found: C, 52·1; H, 4·4; N, 22·4; S, 10·4. $C_{13}H_{13}N_5O_2S$ requires C, 51·5; H, 4·3; N, 23·1; S, 10·6%). The compound slowly gave a positive "plumbite test."

The reactant (0·002 mole) in pyridine (5 ml.) was treated with benzoyl chloride (0·84 g., 0·006 mole), and the solution kept at 100° during 15 min., then stirred into ice–water–hydrochloric acid. The precipitate was extracted with hot water and gave after three crystallisations from ethanol (75 ml./g.), pale yellow needles (total, 0·62 g., 66%) of the *solvated dibenzoyl derivative*, m. p. 156—158° (solidifying and re-melting at 210°) (Found: C, 62·8; H, 4·6; N, 15·2; S, 7·0. $C_{23}H_{17}N_5O_2S,C_2H_5OH$ requires C, 63·4; H, 4·9; N, 14·8; S, 6·8%). After being kept at 120—140° for 4 hr., the *dibenzoyl derivative* had m. p. 212—214° (Found: C, 64·6; H, 4·2; S, 7·9. $C_{23}H_{17}N_5O_2S$ requires C, 64·6; H, 4·0; S, 7·5%). It slowly gave a positive "plumbite test."

Hexahydro-4,6-di-imino-1-phenyl-s-triazine-2-thione. Enol 2-S-*Methyl Derivative.*—(*a*) *Preparation.* The triazine-2-thione (2·37 g., 0·01 mole) dissolved rapidly on being boiled in methanol (15 ml.)–methyl iodide (21·3 g., 0·15 mole). After 1 hr. under reflux, the liquid was distilled to small volume (10 ml.) and gradually diluted with ether. Storage at 0° gave a white solid, m. p. 244—248° (decomp.) (3·4 g., 94%). Crystallisation from ethanol (10 ml./g., recovery *ca.* 70%) gave cubes of the *hydriodide*, m. p. 252—254° (decomp., with evolution of methanethiol; somewhat rate-dependent) (Found: C, 33·2; H, 3·3; I, 35·7; N, 19·6; S, 8·3. $C_{10}H_{11}N_5S,HI$ requires C, 33·25; H, 3·3; I, 35·2; N, 19·4; S, 8·9%). The base remained in solution when the hydriodide (0·001 mole) was dissolved in 3N-ammonia (0·006 mole).

(*b*) *Aminolysis.* (i) The foregoing hydriodide (0·72 g., 0·002 mole) was heated in aniline (12 ml.) at 100° for 6 hr., solution occurring within 30 min. and methanethiol being evolved. The liquid was treated with 3N-sodium hydroxide, and steam-distilled to remove the aniline. The residual suspended powder was collected at 0° and crystallised from 80% ethanol, yielding white opaque microprisms of 1,2-diphenylisomelamine, m. p. 250—252° (decomp.) (0·18 g., 32%), identical (mixed m. p. and ultraviolet spectrum) with authentic material.[26]

(ii) The above mixture was refluxed for 8 hr. and the crude product isolated as before. Crystallisation of the resulting brown granules from ethanol gave felted needles of *s*-triphenylmelamine, m. p. and mixed m. p.[24,27] 226—228° (total, 0·46 g., 65%) (Found: C, 70·6; H, 5·2; N, 24·3. Calc. for $C_{21}H_{18}N_6$: C, 71·2; H, 5·1; N, 23·7%). It had $\lambda_{min.}$ 229 mμ (log ε 3·96); $\lambda_{max.}$ 273 (4·86), identical with those of authentic material (see below). After 3 hr. under reflux, the yield of the same product was 52%.

Interaction of N-*Cyano*-N′-*phenylguanidine and Thiocyanic Acid.*[8]—To a stirred refluxing suspension of *N*-cyano-*N*′-phenylguanidine [28] (4·0 g., 0·025 mole) in water (12 ml.) containing potassium thiocyanate (2·72 g., 0·028 mole) and an emulsifying agent (Teepol, 1 ml.), 3N-hydrochloric acid (13·3 ml., 0·04 mole) was added dropwise during 1 hr., and the resulting solution refluxed for 5 hr. The cooled liquid was basified with 3N-ammonia, and the precipitate collected at 0° (filtrate F). It consisted, after reprecipitation from 3N-sulphuric acid solution with ammonia, and crystallisation from 50% ethanol, of platelets of hexahydro-4,6-di-imino-1-phenyl-*s*-triazine-2-thione monohydrate, m. p. and mixed m. p. 283—285° (decomp.) (3·7 g., 62%) (Found: C, 45·1; H, 4·6. Calc. for $C_9H_9N_5S,H_2O$: C, 45·6; H, 4·6%). Its identity was confirmed by its ultraviolet and infrared spectra (see above), and by its conversion (80%) into the hydrated picrate, m. p. and mixed m. p. 226—228° (decomp.) (Found: C, 38·9; H, 3·2%).

Filtrate F was treated with 0·05M-picric acid (0·005 mole), the yellow curdy precipitate

[26] F. Kurzer and E. D. Pitchfork, unpublished results.
[27] C. Grundmann and A. Kreutzberger, *J. Amer. Chem. Soc.*, 1955, **77**, 44.
[28] F. H. S. Curd and F. L. Rose, *J.*, 1946, 733.

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collected after storage at 0°, and boiled with ethanol (10 ml.). The undissolved material was again collected at 0° [m. p. 179—182° (decomp.), 1·53 g., 15%] and consisted of *N*-(phenylamidino)urea picrate, m. p. and mixed m. p. (see below) 187—189° (decomp.) (from 80% ethanol) (Found: C, 41·8; H, 3·5; N, 23·2. Calc. for $C_8H_{10}N_4O,C_6H_3N_3O_7$: C, 41·3; H, 3·2; N, 24·1%).

Authentic *N*-(phenylamidino)urea hydrochloride was obtained from *N*-cyano-*N'*-phenylguanidine [28] by the method of Walther and Griesshammer [18] and gave the picrate, m. p. 187—188° (decomp.) (from 80% ethanol) [lit.,[18] 181—182° (from water)] (Found: C, 41·2; H, 3·3%).

Interaction of N-*Amidino*-N'-*phenylthiourea and Cyanamide.*—A solution of *N*-amidino-*N'*-phenylthiourea [2] (2·91 g., 0·015 mole) and cyanamide (1·05 g., 0·025 mole) in anhydrous toluene (30 ml.)–n-butanol (10 ml.) was heated under reflux for 1 hr., distilled to small volume *in vacuo*, and the residue treated with ethanol (20 ml.). A trace of solid which separated on storage at 0° was filtered off, and the filtrate treated with two successive portions of 0·05M-picric acid (120 and 150 ml.) giving two fractions of picrate. The first was phenylmelamine picrate (3·35 g., 52%), m. p. and mixed m. p.[1] 292—293° (decomp.) (from nitrobenzene). The second (1·81 g., 42%) was guanidine monopicrate, m. p. and mixed m. p.[29] 318—320° (decomp.) (from 50% ethanol).

Other 1-*Substituted* 2-*Thioammelines*

Hexahydro-4,6-*di-imino*-1-p-*tolyl*-s-*triazine*-2-*thione.*—A suspension of diguanide (1·52 g., 0·015 mole) in pyridine (15 ml.) was treated with *p*-tolyl isothiocyanate (2·23 g., 0·015 mole). The mixture was kept at 45—50° for 30 min. while complete solution occurred. Addition of the liquid to 3M-hydrochloric acid (35 ml.) and storage at 0° gave a white solid, which was collected and boiled with 50% ethanol (120 ml.). The residue, m. p. 290—294° (decomp.) (2·95 g., 84%), was crystallised from boiling dimethylformamide (60 ml./g., recovery 90%); the resulting lustrous needles, on being washed with ethanol, changed to a white opaque powder of the p-*tolyl*-s-*triazinethione*, m. p. 299—300° (decomp.) (Found: C, 51·3; H, 4·4; N, 31·0. $C_{10}H_{11}N_5S$ requires C, 51·5; H, 4·7; N, 30·0%). It had $\lambda_{min.}$ 259 (log ε 3·68); $\lambda_{max.}$ 286 mμ (4·33) (in 50% aqueous ethanol).

The *picrate*, obtained from equimolar quantities (0·001 mole) of the components in boiling dimethylformamide (12 ml.), and precipitated by the addition of water, formed a yellow powder (80%), m. p. 243—244° (decomp., rate-dependent) (from 50% ethanol) (Found: C, 40·85; H 3·7; N, 23·7. $C_{10}H_{11}N_5S,C_6H_3N_3O_7$ requires C, 41·6; H, 3·0; N, 24·2%).

Hexahydro-4,6-*di-imino*-1-p-*methoxyphenyl*-s-*triazine*-2-*thione.*—Interaction of diguanide and *p*-methoxyphenyl isothiocyanate (0·015 mole each) in dimethylformamide (15 ml.) at 100° during 30 min., and addition of the mixture to water (60 ml.) gave a pale yellow precipitate. This was collected, heated under reflux with ethanol (80 ml.), and the white powder filtered off while hot, m. p. 294—296° (decomp.) (3·18 g., 85%). A portion was crystallised from boiling dimethylformamide (80 ml./g., recovery 50%), and washed copiously with ethanol, affording the p-*methoxyphenyltriazine* as a white powder, m. p. 301—302° (decomp.) (Found: C, 48·2; H, 4·4; N, 27·95; S, 12·7. $C_{10}H_{11}N_5OS$ requires C, 48·2; H, 4·4; N, 28·1; S, 12·85%). It had $\lambda_{min.}$ 259 (log ε 3·76); $\lambda_{max.}$ 285 (4·37) (in 50% aqueous ethanol). The compound was practically insoluble in the common organic solvents, including 2-ethoxyethanol.

The *picrate*, prepared in boiling dimethylformamide (as above), formed a powder (56%), m. p. 246—248° (decomp.) (from 50% ethanol) (Found: C, 40·5; H, 3·4. $C_{10}H_{11}N_5OS,C_6H_3N_3O_7$ requires C, 40·2; H, 2·9%).

1-p-*Bromophenylhexahydro*-4,6-*di-imino*-s-*triazine*-2-*thione.*—Interaction of diguanide and *p*-bromophenyl isothiocyanate (0·01 mole each) in pyridine (12 ml.) gave, by the usual procedure, a white product. Reprecipitation from 3N-hydrochloric acid by 3N-ammonia, followed by crystallisation from 50% ethanol gave the p-*bromophenyltriazine* as a white solid, m. p. 298—300° (decomp.) (total, 1·80 g., 60%) (Found: C, 36·4; H, 2·7; Br, 27·1; N, 24·2; S, 10·9. $C_9H_8BrN_5S$ requires C, 36·25; H, 2·7; Br, 26·8; N, 23·5; S, 10·7%). It had $\lambda_{min.}$ 262 (log ε 3·82), $\lambda_{max.}$ 286 (4·33), plateau 216—220 mμ (4·51) (in 50% aqueous ethanol, the compound being insoluble in ethanol). Sodium plumbite test positive on brief boiling.

The *picrate*, prepared in 50% ethanol with addition of a little 3N-hydrochloric aid, formed prisms (75%), m. p. 240—242° (decomp.) (from 60% aqueous ethanol) (Found: C, 34·15; H, 2·9; N, 21·6. $C_9H_8BrN_5S,C_6H_3N_3O_7$ requires C, 34·2; H, 2·1; N, 21·3%).

Hexahydro-4,6-*di-imino*-1-*methyl*-s-*triazine*-2-*thione.*—Diguanide and methyl isothiocyanate

[29] Beilstein's Handbuch, 4th edn., vol. 6, 279, and supplements.

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(0·015 mole each) in dimethylformamide (12 ml.) were kept at 100° for 30 min. A white solid separated rapidly while ammonia was evolved. The mixture was stirred into ice–water (50 ml.), the precipitate collected at 0°, and extracted with boiling 50% ethanol (25 ml.). Crystallisation of the residue, m. p. 295—297° (decomp.) (2·0 g., 76%), from a large volume of the same solvent gave needles of the *solvated triazine*, m. p. 294—295° (decomp.) (Found: C, 27·7; H, 5·05; N, 39·8; S, 18·4. $C_4H_7N_5S,H_2O$ requires C, 27·4; H, 5·1; N, 40·0; S, 18·3%). It had $\lambda_{min.}$ 243 (log ε 3·70), $\lambda_{max.}$ 282 mμ (4·28). It gave a strongly positive "plumbite" test. The aqueous filtrate, on treatment with 0·05M-picric acid (100 ml., 0·005 mole), gave diguanide dipicrate (1·5 g., 18%), m. p. and mixed m. p.[1,23] 216—218° (decomp.) (from 50% aqueous ethanol).

The *picrate*, prepared in 40% ethanol nearly quantitatively, formed microprisms m. p. 260—262° (decomp.) (from 50% ethanol) (Found: C, 31·4; H, 3·0; N, 29·05. $C_4H_7N_5S,C_6H_3N_3O_7$ requires C, 31·1; H, 2·6; N, 29·0%).

1-*n-Butylhexahydro*-4,6-*di-imino*-s-*triazine*-2-*thione*.—Interaction of diguanide and n-butyl isothiocyanate (0·015 mole each) in dimethylformamide (15 ml.) at 100° for 4 hr. gave a colourless liquid slowly depositing a white precipitate. Addition of the suspension to water (60 ml.) gave the *n-butyltriazine*, m. p. 282—283° (decomp.) (2·7 g., 90%) (from 66% aqueous ethanol; 200 ml./g., recovery 70%) (Found: C, 42·1; H, 6·5; N, 35·2; S, 15·9. $C_7H_{13}N_5S$ requires C, 42·2; H, 6·5; N, 35·2; S, 16·1%). It had λ_{infl} 240 (log ε 3·79); $\lambda_{min.}$ 257 (3·61); $\lambda_{max.}$ 286 mμ (4·35). It slowly gave a positive "plumbite test" on prolonged boiling.

The *picrate*, obtained on dropwise dilution of a solution of the components (0·001 mole each) in warm dimethylformamide (3 ml.) with water, formed felted needles (77%), m. p. 202—203° (decomp.) (from water) (Found: C, 36·7; H, 3·9. $C_7H_{13}N_5S,C_6H_3N_3O_7$ requires C, 36·45; H, 3·7%). The triazine (0·4 g., 0·002 mole) was dissolved in pyridine–acetic anhydride (5 ml. each) by brief gentle boiling, the solution kept at 100° for 1 hr., then stirred into ice–concentrated hydrochloric acid (5 ml.). The precipitate gave opaque felted needles (0·33 g., 68%) of the *monoacetyl derivative*, m. p. 222—224° (decomp.) (from methanol) (Found: C, 44·1; H, 6·1; N, 28·3; S, 12·8. $C_9H_{15}N_5OS$ requires C, 44·8; H, 6·2; N, 29·0; S, 13·3%).

Cyclohexylmelamine.—Diguanide and cyclohexyl isothiocyanate (0·02 mole each) in dimethylformamide (24 ml.) were kept at 100° for 6 hr.: a small precipitate appeared gradually and an orange sublimate (of ammonium polysulphide) collected in the air-condenser. Addition of the mixture to water (50 ml.) gave a little orange gum, from which the aqueous phase was decanted; addition of excess of 3N-sodium hydroxide (50 ml.) gave a white precipitate which was collected after storage at 0° (filtrate P) and crystallised from water, giving needles (total, 1·39 g., 32%) of cyclohexylmelamine hemihydrate, m. p. and mixed m. p.[1] 144—146° (after sintering at 138°) (Found: C, 49·7; H, 7·9; N, 39·2. Calc. for $C_9H_{16}N_6,\frac{1}{2}H_2O$: C, 49·8; H, 7·8; N, 38·7%).

Filtrate P, on acidification with concentrated hydrochloric acid, slowly deposited a finely divided white solid, which was collected (filtrate Q), dried, and successively extracted with boiling dimethylformamide (8 ml.) and ethanol, leaving thioammeline (0·43 g., 15%) as an infusible white powder (Found: C, 25·7; H, 3·8; N, 49·3; S, 21·5. Calc. for $C_3H_5N_5S$: C, 25·2; H, 3·5; N, 48·95; S, 22·4%). Filtrate Q, on treatment with 0·05M-picric acid (0·005 mole) gave a flocculent precipitate, which afforded cyclohexylmelamine picrate (1·3 g., 15%), m. p. and mixed m. p.[1] 269—271° (decomp.) (from nitrobenzene) (Found: N, 28·6. Calc. for $C_9H_{16}N_6,C_6H_3N_3O_7$: N, 28·8%).

s-*Triazines from Cyanuric Chloride*

2-*Amino*-4-*anilino*-6-*chloro*-s-*triazine*.—A stirred solution of freshly prepared 2-amino-4,6-dichloro-*s*-triazine[3] (8·25 g., 0·05 mole) in acetone (120 ml.) was treated dropwise at room temperature with aniline (4·65 g., 0·05 mole) and simultaneously with 3N-aqueous sodium carbonate (16·7 ml., 0·025 mole), keeping the mixture just acid (to Phenolphthalein) throughout. Stirring was continued at room temperature for 30 min., and at 40° for 1 hr. The suspension was distilled to about half-bulk under reduced pressure, stirred into water (200 ml.), the precipitate collected after 1 hr., washed with water, and air-dried. The resulting crude substituted *s*-triazine, m. p. 204—206° (decomp.) (7·75—8·85 g., 70—80%) was suitable for further syntheses (lit. m. p. 205—206°,[30] 213—214°[3,31]).

[30] Ciba A.G., G.P. 433,100.
[31] M. Goi, *J. Soc. Org. Synth. Chem. Japan*, 1960, **18**, 332 (*Chem. Abs.*, 1960, **54**, 19,703).

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A refluxing solution of 2-amino-4,6-dichloro-*s*-triazine [3] (4·13 g., 0·025 mole) in dry acetone was treated dropwise with aniline (4·65 g., 0·05 mole) during 30 min., and the resulting stirred suspension refluxed for 3 hr. It was distilled to third-bulk, stirred into ice–water (120 ml.), the white precipitate collected at once, pressed between filter papers, and air-dried, m. p. 252—254° (decomp.) (5·1—5·9 g., 65—75%). It formed opaque granular *2,4-diphenylmelamine hydrochloride*, m. p. 253—254° (decomp.) (from ethanol) (Found: C, 56·8; H, 5·0; N, 27·0. $C_{15}H_{14}N_6$,HCl requires C, 57·2; H, 4·8; N, 26·7%). It was further identified by its near-quantitative conversion into the base, m. p. and mixed m. p.[1,24] 216—217°.

The same hydrochloride was obtained on treating cyanuric chloride in acetone successively with 2 moles of ammonia (*d* 0·88) at 5°, and with 2 moles of aniline under reflux, and isolating the product as above (overall yield of the two-stage process, 72%).

4-*Amino*-6-*anilino*-s-*triazine*-2-*thiol*.—A stirred solution of 2-amino-4-anilino-6-chloro-*s*-triazine (2·22 g., 0·01 mole) and thiourea (0·95 g., 0·0125 mole) in dioxan (12 ml.) was refluxed for 2 hr.; a small amount of solid separated after 15 min. Treatment with 3N-sodium hydroxide (6·66 ml., 0·02 mole) gave a solution which was stirred and refluxed for 45 min., then added to ice–3N-acetic acid (10 ml., 0·03 mole). The precipitate, collected and air-dried, was refluxed with successive portions of ethanol (20 ml. each). The solid residue (1·23 g., 56%) formed an ivory-white powder of the *thiol*, m. p. 263—265° (decomp.) (Found: C, 49·6; H, 4·1; N, 32·6; S, 13·5. $C_9H_9N_5S$ requires C, 49·3; H, 4·1; N, 32·0; S, 14·6%). It had $\lambda_{min.}$ 232 (log ε 3·89), $\lambda_{max.}$ (shallow) 268 (4·29), $\lambda_{min.}$ (shallow) 287 (4·22), $\lambda_{max.}$ (shallow) 303 mμ (4·25).

A solution of the foregoing triazine and picric acid (0·001 mole each) in dimethylformamide (2 ml.), on being slowly diluted with water, deposited a granular precipitate, which gave the *picrate*, m. p. 206—207° (decomp.) as a yellow microcrystalline powder (72%) (from 75% ethanol; 10 ml./g.) (Found: C, 40·4; H, 3·4; N, 24·4. $C_9H_9N_5S$,$C_6H_3N_3O_7$ requires C, 40·2; H, 2·7; N, 25·0%).

4-*Amino*-6-*n-butylamino*-s-*triazine*-2-*thiol*.—A stirred solution of 2-amino-4-n-butylamino-6-chloro-*s*-triazine [3] (1·61 g., 0·008 mole) and thiourea (0·91 g., 0·012 mole) in dioxan (15 ml.) was refluxed for 2 hr., a little solid appearing after 1 hr. After addition of 3N-sodium hydroxide (6·7 ml., 0·02 mole), the stirred two-phase system was heated under reflux for 1 hr., added to water (150 ml.), and adjusted to pH 8 with 3N-acetic acid. The precipitate, m. p. 195—196° (decomp.) (1·38 g., 86%), gave, on crystallisation from acetone–light petroleum, pale buff granules of the *thiol*, m. p. 200—201° (decomp.) (Found: C, 42·0; H, 6·85. $C_7H_{13}N_5S$ requires C, 42·2; H, 6·5%). It had $\lambda_{min.}$ 262 (log ε 3·80), $\lambda_{max.}$ 286 mμ (4·30).

2,4,6-*Triphenylmelamine*.—2,4-Dianilino-6-chloro-*s*-triazine, obtained by the method of Grundmann and Kreutzberger [27] was converted in excess of boiling aniline into *s*-triphenylmelamine (82%), m. p. 226—228° (decomp.). It had $\lambda_{min.}$ 228 (log ε 3·93), $\lambda_{max.}$ 274 mμ (4·86).

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