Heterocyclic Compounds from Urea Derivatives. Part XIV.[1] The Interaction of Thiocarbohydrazide and Diarylcarbodi-imides

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Thiocarbohydrazide reacts with two molar proportions of diarylcarbodi-imides in dimethylformamide or methanol to yield 5-arylamino-4-(*NN'*-diarylguanidino)-3-mercapto-1,2,4-triazoles, together with some 4-aryl-3-arylamino-5-mercapto- and 4-aryl-3,5-di(arylamino)-1,2,4-triazoles. The structure of the main-products follows from the identity of their 3-*S*-alkylthio-derivatives with compounds synthesised unequivocally from equimolecular quantities of diarylcarbodi-imides and 3-alkylthio-4-amino-5-arylamino-1,2,4-triazoles. The structure of the latter is confirmed by the deamination of a selected member of this series to 3-anilino-5-methylthio-1,2,4-triazole.

The 4-amino-3-arylamino-5-mercapto-1,2,4-triazoles required in this synthesis are accessible (side by side with their 4-aryl-3-hydrazino-5-mercapto-isomers) from 2-arylamino-1,3,4-thiadiazol-5-yl alkyl sulphones by the action of hydrazine which replaces the alkylsulphonyl moiety and effects the ring-conversion simultaneously. The ring-fission in this reaction may proceed by way of intermediates of the type $H_2N{\cdot}NH{\cdot}C(:NR){\cdot}NH{\cdot}NH{\cdot}CS{\cdot}SO_2R$; this mechanism is supported by the observation that interaction of 1,2-diamino-3-phenylguanidine and carbon disulphide gives the same two *s*-triazoles.

3-Alkylthio-5-arylamino-4-(*NN'*-diarylguanidino)-1,2,4-triazoles are further cyclised thermally, with loss of alkanethiol, to 7-aryl-3,6-di(arylamino)-*s*-triazolo[4,3-*b*]-*s*-triazoles.

In continuation of our investigation of the interaction of heterocumulenes [2,3] with compounds related to urea, we have extended our study to thiocarbohydrazide (I) and carbohydrazide, and their derivatives. This paper reports the action of diarylcarbodi-imides on the parent thiocarbohydrazide, and correlates the observed reactions with those [4,5] of its structural analogues, particularly thiosemicarbazide and diaminoguanidine.

That thiocarbohydrazide reacts with heterocumulenes such as isothiocyanate esters has previously been

[1] Part XIII, F. Kurzer and D. Hanks, *J. Chem. Soc.* (*C*), 1968, 1375.

[2] F. Kurzer and K. Douraghi-Zadeh, *Chem. Rev.*, 1967, **67**, 107.

[3] H. Ulrich, 'Cycloaddition Reactions of Heterocumulenes,' Academic Press, New York and London, 1967.

[4] L. E. A. Godfrey and F. Kurzer, *J. Chem. Soc.*, 1962, 3561.

[5] F. Kurzer and K. Douraghi-Zadeh, *J. Chem. Soc.*, 1965, 3912.

established. Action of isothiocyanates [6-10] or isocyanates [7] rapidly yields di-addition products of the type $(RNH{\cdot}CX{\cdot}NH{\cdot}NH)_2CS$ (X = O, S), even when the reactants are employed in equimolar quantities.[10] The di-adducts can be cyclised to various 1,2,4-triazole derivatives, their nature depending on the reagents used.[9,11] With cyanic or thiocyanic acid, thiocarbohydrazide yields, according to the conditions, either mono- [7,13,14] or di-addition [12] compounds.

The interaction of thiocarbohydrazide (I) and 2 mol. of diarylcarbodi-imides gave principally 5-arylamino-4-(*NN'*-diarylguanidino)-3-mercapto-1,2,4-triazoles (X), together with varying quantities of 4-aryl-3-arylamino-5-mercapto- (III) and 4-aryl-3,5-diarylamino-1,2,4-triazoles (XV). The formulation of the new main products is based on their composition, chemical behaviour, and alternative unequivocal synthesis described below. The by-products were identified by comparison with authentic compounds.

Thus, treatment of thiocarbohydrazide, dissolved in a large volume of methanol, with 2 mol. of diphenylcarbodi-imide gave a complex reaction mixture; this was separated with some difficulty into 3-anilino-4-(*NN'*-diphenylguanidino)-5-mercapto-1,2,4-triazole (X; R = Ph) (*ca.* 20%), 3,5-di(anilino)-4-phenyl- (XV; R = Ph) (*ca.* 15%), and 3-anilino-5-mercapto-4-phenyl-1,2,4-triazole (III; R = Ph) (12%). The last product (III), forming the most soluble fraction, was readily removed; the mixture of the former two could be separated by the special chromatographic technique recently described by Loev and Snader.[15] The use of dimethylformamide as solvent increased the yield of the substituted 4-guanidino-1,2,4-triazole (X) to 42—48%, and reduced those of the by-products sufficiently to permit the main product to be directly isolated. Dimethyl sulphoxide,[16] used in conjunction with di-*p*-tolylcarbodi-imide afforded 4-(*NN'*-di-*p*-tolylguanidino)-3-mercapto-5-*p*-toluidino-1,2,4-triazole (X; R = *p*-C_6H_4Me) in 55% yield; in methanol, however, formation of the by-products (III) and, especially, (XV) was again favoured.

The interaction of equimolar proportions of thiocarbohydrazide and diphenylcarbodi-imide under various conditions did not terminate with the production of the possible mono-adduct (II), but gave the usual three triazoles, in diminished yields.

The 3-arylamino-4-(*NN'*-diarylguanidino)-5-mercapto-1,2,4-triazoles (X) were predominantly basic and gave picrates. Their *S*-alkylthio-derivatives (XXIV; R = Ph, *p*-C_6H_4Me; Alk = Me, CH_2Ph) were converted, on thermolysis, by intramolecular loss of alkanethiols, into products formulated as 3,6-di(arylamino)-7-aryl-*s*-triazolo[4,3-*b*]-*s*-triazoles (XXV; R = Ph, *p*-C_6H_4Me). The parent mercapto-compounds (X; R = Ph, *p*-C_6H_4Me), on the other hand, did not undergo the comparable ring-closure with loss of hydrogen sulphide under identical conditions to the same bicyclic system (XXV), the reactants being recovered nearly quantitatively. This observation supports the view that the cyclisation of the *S*-alkyl-derivatives (XXIV) is unlikely to be attended by rearrangement; it is thus visualised to proceed by the intramolecular nucleophilic replacement of the alkylthio-group by the anilino-moiety of the substituted guanidino-grouping [both in (XXIV)]. This ready aminolysis differs strikingly from the behaviour of the closely related 5-alkylthio-3-phenyl-1,2,4-triazoles, which do not react with amines,[17] or of 3-aryl (or anilino)-1,2,4-triazol-5-yl alkyl sulphones,[5,17] which, notwithstanding their better 5-leaving group, fail to undergo aminolysis [17] or even hydrazinolysis.[5]

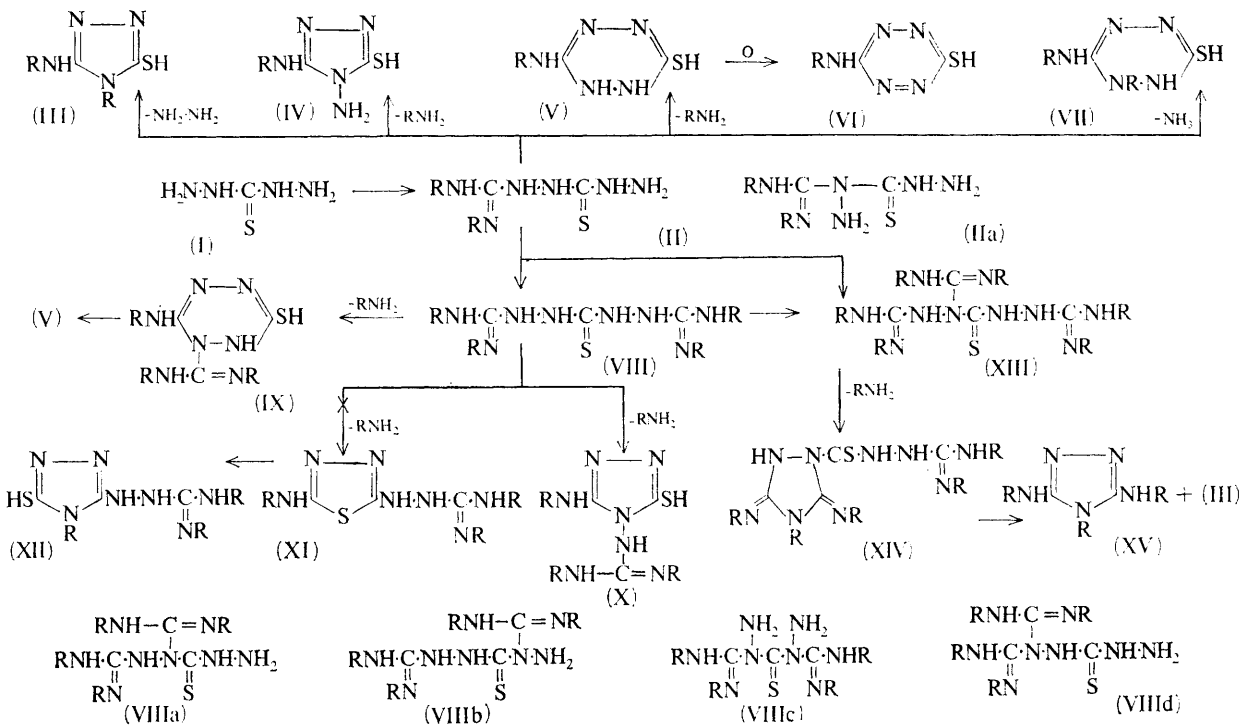
The interaction of thiocarbohydrazide and carbodi-imides proceeds most probably by the usual addition–cyclisation mechanism that has previously been advanced to account for comparable condensations.[4,5,18] Although the reactants can yield, theoretically, two intermediate mono- [(II), (IIa)] and thence five di-addition products [(VIII), (VIIIa—d)], the simplest and most likely course of the reaction is believed to be as follows. Addition of carbodi-imide at the terminal 1- and 5-nitrogen atoms of thiocarbohydrazide (I) yields successively the monoadduct (II) and the symmetrical di-adduct (VIII). The latter can be directly converted, by loss of aniline, into the observed main product (X). Introduction of a third molecule of carbodi-imide into (VIII), proceeding in competition with its ring-closure (VIII) ⟶ (X), generates the triadduct (XIII); its cyclisation with loss of aniline [to (XIV)], followed by prototropic fission and simultaneous ring-closure of the eliminated side-chain, would yield the observed by-products (XV) and (III).

The postulated formation of limited quantities of a triadduct (XIII), and its role in the reaction mechanism, is supported by the parallel behaviour of *N*-amino- [4] and *NN'*-diamino-guanidine.[5] Once the terminal amino-nitrogens of their hydrazino-groups have attached 1 mol. of carbodi-imide, their penultimate NH-group displays an enhanced reactivity towards this heterocumulene, resulting, as in the present case, in the formation of 4-aryl-3,5-di(arylamino)-1,2,4-triazoles (XV). In order to suppress this triaddition and consequent production of the by-products (XV) and (III) as far as possible, the carbodi-imide was introduced slowly, and the reaction mixtures were kept dilute in the present reactions of thiocarbohydrazide.

[6] P. C. Guha and S. C. De, *J. Chem. Soc.*, 1924, **125**, 1215.
[7] P. C. Guha and S. C. De, *J. Indian Chem. Soc.*, 1924, **1**, 141.
[8] N. P. Buu-Hoï, T. B. Loc, and N. D. Xuong, *Bull. Soc. chim. France*, 1955, 694.
[9] A. Dornow and H. Paucksch, *Chem. Ber.*, 1966, **99**, 81.
[10] R. S. McElhinney, *J. Chem. Soc.* (*C*), 1966, 1256.
[11] A. Dornow and H. Paucksch, *Chem. Ber.*, 1966, **99**, 85.
[12] H. Beyer and C. F. Kröger, *Annalen*, 1960, **637**, 126.
[13] E. S. Scott and L. F. Audrieth, *J. Org. Chem.*, 1954, **19**, 742.
[14] A. W. Lutz, *J. Org. Chem.*, 1964, **29**, 1174.
[15] B. Loev and K. M. Snader, *Chem. and Ind.*, 1965, 15; B. Loev and M. M. Goodman, *ibid.*, 1967, 2026.
[16] D. Martin, A. Weise, and H. J. Niclas, *Angew. Chem. Internat. Edn.*, 1967, **6**, 318.
[17] E. Hoggarth, *J. Chem. Soc.*, 1949, 1160.
[18] F. Kurzer and K. Douraghi-Zadeh, *J. Chem. Soc.* (*C*), 1967, 742.

Although the scheme outlined above is believed to explain the experimental facts most plausibly, the reaction may proceed, at least partly, by other pathways. In particular, immediate cyclisation of the primary monoadduct (II) might yield 4-aryl-3-arylamino-5-mercapto-1,2,4-triazoles (III) directly, the eliminated hydrazine reacting with an excess of carbodiimide to produce the 4-aryl-3,5-di(arylamino)-1,2,4-triazole (XV).[19] The latter could also be formed analogously from the diadduct (VIIIa). Further, that 1,2,4,5-tetrazines [*e.g.* (VI)]; they could arise from the intermediate adducts (II) and (VIII) by loss of amine, followed by dehydrogenation of the resulting dihydro-1,2,4,5-tetrazines [*e.g.*, (V) and (IX), but not (VII)] by atmospheric oxygen. It is well known that dihydro-1,2,4,5-tetrazines are readily oxidised to the deep reddish-purple 1,2,4,5-tetrazines,[20,21] and that thiocarbohydrazide is a suitable precursor from which the 1,2,4,5-tetrazine structure may be built up.[22]

The formulation of the main products of the present



SCHEME 1

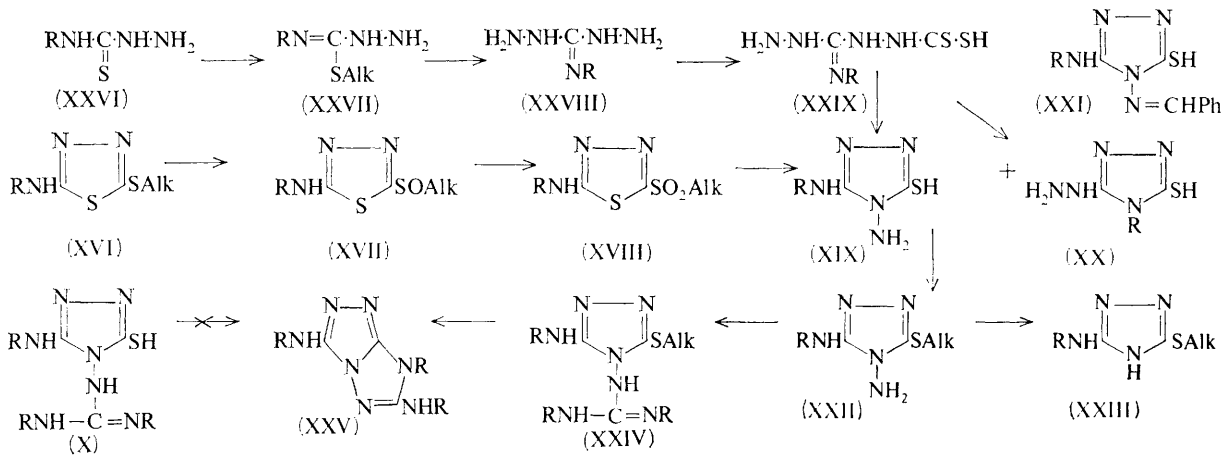
4-amino-3-arylamino-5-mercapto-1,2,4-triazoles (IV), arising directly from the monoadducts (II), were *not* the precursors of the main products (X), was established by separate experiments, which showed that 4-amino-3-anilino-5-mercapto-1,2,4-triazole (IV; R = Ph) failed to yield (X; R = Ph) on treatment with diphenylcarbodi-imide under the usual conditions. The participation of the alternative monoadduct (IIa) and of the diadducts (VIIIb—d) as intermediates in the overall reaction may be discounted; there was no evidence for the formation of significant quantities of the appropriate 1,2,4-triazoles, including 4-amino-derivatives, that might have arisen from them by the usual cyclisation process.

The condensation of thiocarbohydrazide and carbodiimides was in each case attended by the appearance of intense purple to blue colours, persisting in the initial crude products, but readily extracted therefrom by cold ethanol. These intensely coloured by-products, which were not obtained pure, were probably substituted reaction as (X) was confirmed by the identity of their *S*-alkyl-derivatives (XXIV; R = Ph; Alk = Me, CH_2Ph) with authentic specimens. In the unequivocal synthesis of these compounds, 3-alkylthio-4-amino-5-arylamino-1,2,4-triazoles (XXII), obtained from the parent 3-mercapto-compounds (XIX) by *S*-alkylation, were condensed with diarylcarbodi-imides in dimethylformamide, the desired 4-(*NN'*-diarylguanidino)-1,2,4-triazoles (XXIV) being formed in fair yield (total, *ca.* 55%). However, since the addition reaction proceeded only slowly even at elevated temperatures, the greater part of this primary product (XXIV) was further converted into the substituted *s*-triazolo[4,3-*b*]-*s*-triazole (XXV) by the cyclisation described above.

The 4-amino-3-arylamino-5-mercapto-1,2,4-triazoles (XIX) required in this synthesis were obtained by the

[19] M. Busch and T. Ulmer, *Ber.*, 1902, **35**, 1721.
[20] T. Curtius and E. Rimele, *Ber.*, 1908, **41**, 3108.
[21] P. F. Wiley, in A. Weissberger, ' The Chemistry of Heterocyclic Compounds: The Triazines, Tetrazines, and Pentazines,' Interscience, New York, 1956, p. 179; V. P. Wystrach, in R. C. Elderfield, ' Heterocyclic Compounds,' vol. 8, Wiley, New York, 1967, p. 110.
[22] J. Sandström, *Acta Chem. Scand.*, 1961, **15**, 1575.

hydrazinolysis of 2-arylamino-1,3,4-thiadiazol-5-yl alkyl sulphones (XVIII); hydrazinolysis has previously been observed to convert 2-halogeno-1,3,4-thiadiazoles successively into 3-hydrazino-1,3,4-thiadiazoles and 4-amino-3-mercapto-1,2,4-triazoles.[23,24] In the present case, two isomeric 1,2,4-triazoles were obtained side by side: treatment of 2-anilino-1,3,4-thiadiazol-5-yl benzyl- (or methyl) sulphone (XVIII; R = Ph; Alk = Me or CH_2Ph) with hydrazine hydrate at 150° for 0·5—1 hour gave 4-amino-3-anilino-5-mercapto-1,2,4-triazole (XIX; R = Ph) (40—45%) and 3-hydrazino-5-mercapto-4-phenyl-1,2,4-triazole [25] (XX; R = Ph) (14—18%); their separation posed no problem owing to the virtual

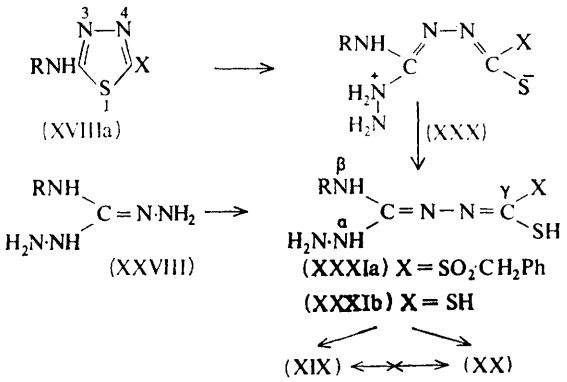


SCHEME 2

insolubility of the latter triazole in the usual solvents. The corresponding *p*-tolyl homologues (XIX, XX; R = *p*-C_6H_4Me) (35 and 40% respectively) were similarly produced. The alkylsulphonyl residues eliminated in the course of the hydrazinolysis gave the appropriate alkyl alkylthiosulphonates ($RSO_2·SR$), by the familiar disproportionation of the sulphinic acid thus liberated. The use of ethanolic hydrazine [26] gave less favourable results, affording the usual triazoles, (XIX) and (XX), in diminished yields, in spite of greatly prolonged reaction times. Since (XIX) and (XX) could not be converted into each other under the conditions of the hydrazinolysis, the triazoles were obviously formed in parallel cyclisations, independently of one another (cf. mechanism shown).

The production of the triazoles (XIX) and (XX) by the hydrazinolysis of 1,3,4-thiadiazol-5-yl sulphones (XVIIIa; R = Ph, *p*-C_6H_4Me; X = SO_2Me, $SO_2·CH_2Ph$) involves a transient ring-opening. A possible mechanism requiring only *one* mode of ring-cleavage [of (XVIIIa)] visualises the nucleophilic attack of the hydrazine at C-2 of the 1,3,4-thiadiazole (XVIIIa), and concomitant formation of the open-chain intermediate (XXX) and thence (XXXIa). Intramolecular nucleophilic attack of the α- or β-nitrogen atoms on the γ-carbon, with elimination of HX (X = $PhCH_2·SO_2$), would result in the formation of the observed triazoles, (XIX) and (XX), respectively.

The postulated mechanism is supported by the production of the *same* triazole pair, (XIX) and (XX), by an alternative reaction, in which the formation of an intermediate (XXXIb) very closely related to the postulated species (XXXIa) is highly probable. Thus, 1,2-diamino-3-phenylguanidine (XXVIII; R = Ph) [prepared [18] from 4-phenylthiosemicarbazide (XXVI) as shown in Scheme 2] reacted with equimolar quantities of carbon disulphide and potassium hydroxide to afford the triazoles (XIX and XX; R = Ph) in moderate yield, hydrogen sulphide being eliminated. Since the addition



of carbon disulphide to hydrazines to yield dithiocarbazoic acid derivatives is a standard reaction,[27,28] the formation of the intermediate (XXXIb) in the present instance can hardly be doubted. In view of the close structural resemblance of (XXXIa) and (XXXIb), the former intermediate may reasonably be considered to be

[23] M. Kanaoka, *J. Pharm. Soc. Japan*, 1955, **75**, 1149; *Pharm. Bull. (Japan)*, 1957, **5**, 385.
[24] K. T. Potts and R. M. Huseby, *J. Org. Chem.*, 1966, **31**, 3528.
[25] F. Kurzer and K. Douraghi-Zadeh, *J. Chem. Soc.* (*C*), 1966, 1.
[26] K. Fujii, H. Yoshikawa, and M. Yuasa, *J. Pharm. Soc. Japan*, 1954, **74**, 1056.
[27] M. Busch, *Ber.*, 1895, **28**, 2635.
[28] U. Anthoni, *Acta Chem. Scand.*, 1966, **20**, 2742.

concerned in the mechanism of the hydrazinolysis of the 1,3,4-thiadiazol-5-yl sulphones (XVIII). The two reactions under consideration would thus give the *same* products (XVIII) or (XXVIII) ⟶ (XIX) + (XX) from a common type of intermediate by loss of alkyl sulphinate, or hydrogen sulphide, respectively.

The 4-amino-3-arylamino-5-mercapto-1,2,4-triazoles (XIX) gave 4-benzylidene derivatives (XXI; R = Ph, *p*-C_6H_4Me) with benzaldehyde, and were readily *S*-alkylated, to (XXII; R = Ph, *p*-C_6H_4Me; Alk = Me, CH_2Ph), by the usual procedures. Their assigned structure was confirmed by the deamination of 4-amino-3-anilino-5-methylthio-1,2,4-triazole (XXII; R = Ph; Alk = Me) by nitrous acid [14,29,30] to the known [5] 3-anilino-5-methylthio-1,2,4-triazole (XXIII; R = Ph, Alk = Me). 4-Amino-3-anilino-5-mercapto-1,2,4-triazole has recently been found [9] to be one of four products of the cyclisation of 1,5-di(phenylthiocarbamoyl)thiocarbohydrazide by pyridine. The physical properties of the compound (and those of its 4-benzylidene and 5-methyl derivatives) prepared by both methods are in satisfactory agreement.

The 2-arylamino-1,3,4-thiadiazol-5-yl alkyl sulphones (XVIII) required in this work were obtained by the oxidation of the corresponding alkylthiols (XVI) with hydrogen peroxide.[31] As previously observed with 5-alkylthio-3-anilino-1,2,4-triazoles,[5] this oxidation requires carefully controlled conditions: it gave the desired products in good yields most consistently when carried out in two distinct stages, with isolation of the intermediate sulphoxides (XVII). The attempted direct oxidation of the alkylthiols (XVI) to the sulphones (XVIII) by an excess of peroxide resulted in considerable destruction of the reactant in some experiments, or the production of mixtures of sulphoxide and sulphone in others. The alleged '2-anilino-1,3,4-thiadiazol-5-yl methyl(and benzyl) sulphones' previously reported [32] differ widely in their physical constants from our specimens that were carefully characterised by analysis and i.r. spectra, and they were therefore probably mixtures.

The reaction between thiocarbohydrazide and carbodi-imides now described clearly resembles those of structurally related compounds previously studied.[4,5] In particular, *NN'*-diaminoguanidine [5] yields principally 4-aryl-3,5-di(arylamino)- (XV) and 3-amino-4-aryl-5-arylamino-1,2,4-triazoles [*i.e.*, the amino-analogue of (III)], presumably by an analogous mechanism. Although the postulated intermediate adducts were not isolated in either of these reactions, symmetrical di-addition compounds of this type derived from thiocarbohydrazide and isothiocyanate esters are known to be stable.[6-10] Further, the formation, from thiosemicarbazide [4] and carbodi-imides, of definite monoadducts [cyclisable to (III) and their 3-amino-analogues by alkalis], or of (XV) directly under the influence of 2 mol. of carbodi-imide, lends support to the reaction mechanism now suggested. Amongst the numerous 4-amino-1,2,4-triazoles that are accessible by a variety of condensation and cyclisation reactions,[33,34] the substituted 4-guanidino-1,2,4-triazoles (X) appear to be the first examples of their kind.

EXPERIMENTAL

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

Thin-layer chromatography of the 1,2,4-triazoles was performed on plates coated (0·25 mm.) with Merck Silica Gel G (after Stahl), using ethyl acetate–benzene (3 : 2) as solvent, and 5% iodine in chloroform for developing the spots.

Infrared spectra were measured with a Unicam SP 200 instrument, employing potassium bromide discs, except where stated. Ultraviolet spectra were measured with a Unicam SP 800A spectrophotometer, using 10^{-5}M-solutions in ethanol.

Interaction of Thiocarbohydrazide and Diphenylcarbodi-imide.—(a) *In methanol.* Finely powdered thiocarbohydrazide (2·12 g., 0·02 mole) was refluxed in anhydrous methanol (85 ml.); the stirred suspension was then treated dropwise at 45° during 20 min. with a solution of diphenylcarbodi-imide (7·76 g., 0·04 mole) in anhydrous methanol (20 ml.) and refluxed for 2·5 hr. (colour change deep purple to dark blue). The liquid was decanted from a trace of undissolved solid, set aside at 0° for 24 hr., and the separated crystals were collected (solid S; 4 g.) and rinsed with methanol. The filtrate deposited, on evaporation under reduced pressure to quarter bulk and storage, more solid which gave (0·64 g., 12% based on thiocarbohydrazide) 3-anilino-5-mercapto-4-phenyl-1,2,4-triazole, m.p. 204—206° (needles from ethanol), identified [4] by t.l.c. and its i.r. spectrum, $\nu_{max.}$ 3320m and 3140m (NH), 1610s and 1585s (C=N), 1600s, 1500s, 755s, and 700s (Ph), and 1440s, 1450s, 1330m, and 1215s cm.$^{-1}$.

Solid S was partially separated into its two constituents by the 'dry-column' chromatography technique of Loev and Snader.[15] A solution of the solid (1 g.) in ethyl acetate (50 ml.)–benzene (20 ml.) was trickled during 1 hr. on to a dry column (18 × 3 cm.) of silica gel (Merck G, after Stahl), so as to be completely absorbed. The column was then eluted with ethyl acetate–benzene (3 : 2), eight fractions (of approximately 25—30 ml. each) being collected (employing slight suction), and the identity of their contents was ascertained by t.l.c. The combined fractions 1—3 gave, on vacuum-evaporation and crystallisation from acetone–ethanol (12 and 6 ml. per g., recovery 70%), opaque needles of *3-anilino-4-(NN'-diphenylguanidino)-5-mercapto-1,2,4-triazole*, m.p. 235—237° (0·40 g., 20%) (Found: C, 62·7; H, 4·7; N, 24·7; S, 7·8. $C_{21}H_{19}N_7S$ requires C, 62·8; H, 4·7; N, 24·4; S, 8·0%), $\nu_{max.}$ 3410m and 3210m,br (NH), 1630s and 1590s (C=N), 1600s, 1500s, 750s, and 690s (Ph), and 1540s, 1455s, and 1300m cm.$^{-1}$.

Fractions 4 and 5 contained an approximately 1 : 1 mixture of the foregoing triazole and 3,5-dianilino-4-phenyl-1,2,4-triazole (by t.l.c.).

Fractions 6—8 gave, on distillation to dryness, opaque

[29] C. G. Overberger and B. S. Marks, *J. Amer. Chem. Soc.*, 1955, **77**, 4097; H. Beyer, W. Lässig, and U. Schultz, *Chem. Ber.*, 1954, **87**, 1401.
[30] J. Sandström, *Acta Chem. Scand.*, 1961, **15**, 1295.
[31] J. Goerdeler and H. Rachwalski, *Chem. Ber.*, 1960, **93**, 2190.
[32] S. Giri and H. Singh, *J. Indian Chem. Soc.*, 1967, **44**, 145.
[33] K. T. Potts, *Chem. Rev.*, 1961, **61**, 87.
[34] J. H. Boyer, in R. C. Elderfield, 'Heterocyclic Compounds, Wiley, New York, 1961, p. 425 *et seq.*

platelets of 3,5-dianilino-4-phenyl-1,2,4-triazole, m.p. 228—234° (lit.,[4] 236—237°) (0·23 g., 14% based on the thiocarbohydrazide), identified by t.l.c. and i.r. spectrum.[1]

Attempts to effect the above separation on alumina (Spence H; 100—200 mesh) were unsuccessful.

(b) *In dimethylformamide.* Thiocarbohydrazide (1·59 g., 0·015 mole) was dissolved in dimethylformamide (50 ml.) with warming; the liquid was cooled to room temperature, and treated while being cooled externally with ice–water, dropwise during 20 min. with diphenylcarbodi-imide (5·82 g., 0·03 mole), dissolved in dimethylformamide (30 ml.) (reaction exothermic). The deep-purple liquid was next stirred at 100° for 30 min., cooled to room temperature, and stirred into ice–water (200 ml.). The resulting precipitate was collected at 0°, thoroughly washed with water, and air-dried at room temperature. It was covered with methanol, set aside for several hours, collected, and washed with more methanol (3 × 15 ml.). The solid (3·5—4 g.) was finally dissolved in acetone (60 ml.), and reprecipitated by the addition of water (60 ml.), giving a white or faintly purple precipitate (m.p. 233—236°; 2·55—2·9 g., 42—48%) of 3-anilino-4-(*NN'*-diphenylguanidino)-5-mercapto-1,2,4-triazole; according to t.l.c. this was nearly pure, and gave white powdery solid, m.p. 240—242°, from acetone–water (30 and 20 ml., respectively, per g., recovery 50%) (Found: C, 62·8; H, 4·8; N, 23·8; S, 7·8%).

Interaction of equimolar quantities of the reactants (0·01 mole each) in dimethylformamide (50 ml.) as above gave again the foregoing triazole in 36% yields, together with 3-anilino-5-mercapto-4-phenyl-1,2,4-triazole (*ca.* 10%). By performing the reaction in smaller volumes of solvent, and at slightly higher temperatures, the formation of the by-products, *viz.*, 3,5-dianilino-4-phenyl- and 3-anilino-5-mercapto-4-phenyl-1,2,4-triazole, appeared to be favoured.

3-Anilino-4-(*NN'*-diphenylguanidino)-5-mercapto-1,2,4-triazole was very soluble in dimethylformamide, soluble in acetone, and sparingly soluble in methanol and ethanol. It dissolved in both 3N-alkali and 3N-hydrochloric acid on warming.

The *picrate*, prepared (from 0·0005 mole of the components) in ethanol (12 ml.) formed a powder, m.p. 226—227° (from acetone) (75%) (Found: C, 51·5; H, 3·8; N, 22·5. $C_{27}H_{22}N_{10}O_7S$ requires C, 51·4; H, 3·5; N, 22·2%).

3-*Anilino*-4-(NN'-*diphenylguanidino*)-5-*methylthio*-1,2,4-*triazole*.—A solution of the 5-mercapto-compound (0·4 g., 0·001 mole) in N-sodium methoxide (1 ml., 0·001 mole)–methanol (5 ml.), treated with methyl iodide (2·85 g., 0·02 mole), was refluxed for 30 min., distilled to half-bulk, and diluted with water (5 ml.). The solid gave the *5-methylthio-derivative* as a microcrystalline powder, m.p. 230—231° (decomp.) (from methanol, 100 ml. per g.) (0·27 g., 65%) (Found: C, 63·3; H, 5·2; N, 23·6; S, 7·95. $C_{22}H_{21}N_7S$ requires C, 63·6; H, 5·1; N, 23·6; S, 7·7%), $\nu_{max.}$ 3380m and 3260m,br (NH), 1625s and 1570s (C=N), 1600s, 1500s, 750s, and 690s (Ph), and 1540s and 1230m cm.$^{-1}$.

3-*Anilino*-5-*benzylthio*-4-(NN'-*diphenylguanidino*)-1,2,4-*triazole*.—The 5-mercapto-compound (0·4 g., 0·001 mole), suspended in ethanol (10 ml.)–benzyl chloride (0·127 g., 0·001 mole), dissolved on addition of N-sodium hydroxide (1 ml., 0·001 mole). The solution rapidly deposited crystalline solid on being boiled; the mixture was refluxed for 30 min., distilled to half-bulk (reduced pressure), and the solid crystallised from methanol (100 ml. per g., recovery 60%), giving a microcrystalline powder (0·32 g., 65%) of the *benzylthiol*, m.p. 196—197° (Found: C, 66·0; H, 5·2; N, 19·6; S, 6·4. $C_{28}H_{25}N_7S,H_2O$ requires C, 66·0; H, 5·3; N, 19·25; S, 6·3%), $\nu_{max.}$ 3400m and 3190m (NH), 1635s and 1570s (C=N), 1600s, 1500s, 750s, and 690s (Ph), and 1250m and 1030m cm.$^{-1}$.

3,6-*Dianilino*-7-*phenyl*-s-*triazolo*[4,3-b]-s-*triazole*.—(a) A solution of 3-anilino-4-(*NN'*-diphenylguanidino)-5-methylthio-1,2,4-triazole (0·42 g., 0·001 mole) in dimethylformamide (5 ml.) was slowly heated to 150° during 30 min., kept at this temperature for 2 hr., and finally refluxed for 30 min. The liquid was allowed to cool somewhat and diluted with water (0·5 ml.). The pale yellow precipitate, which separated on 24 hr. storage at 0° was collected [m.p. 253—255° (decomp.); 0·26 g., 70%], extracted with boiling ethanol (10 ml.), and crystallised from dimethylformamide containing a few drops of water (10 ml., and 15 drops, respectively, per g., recovery 70%), yielding opaque white microneedles of 3,6-*dianilino*-7-*phenyl*-s-*triazolo*[4,3-b]-s-*triazole*, m.p. 256—258° (decomp. to deep-blue mass) (Found: C, 68·2; H, 4·6; N, 27·1. $C_{21}H_{17}N_7$ requires C, 68·7; H, 4·6; N, 26·7%), $\nu_{max.}$ 3250m and 3210m (NH), 1635m and 1580s (C=N), 1600s, 1500s, 745s, and 690s (Ph), and 1570s, 1270m, and 1035mw cm.$^{-1}$.

(*b*) Thermolysis of 3-anilino-5-benzylthio-4-(*NN'*-diphenylguanidino)-1,2,4-triazole (0·49 g., 0·001 mole) in boiling dimethylformamide (5 ml.) for 2 hr. gave the above substituted *s*-triazolo[4,3-*b*]-*s*-triazole in 67% yield.

(*c*) 3-Anilino-4-(*NN'*-diphenylguanidino)-5-mercapto-1,2,4-triazole was substantially recovered (70%) after 3 hr. refluxing in dimethylformamide as above.

2-*Anilino*-5-*mercapto*-1,3,4-*thiadiazole*.[35]— $\nu_{max.}$ 3220m, 3180m, and 3125m (NH), 1570s (C=N), 1600s, 1500s, 775s, and 690s (Ph), and 1475m, 1360s, and 1055s cm.$^{-1}$.

2-*Anilino*-5-*methylthio*-1,3,4-*thiadiazole*.[36]— $\nu_{max.}$ 3260mw and 3200mw (NH), 1620m and 1575s (C=N), 1600s, 1500s, 750s, and 685m (Ph), and 1460s, 1210m, and 1100ms cm.$^{-1}$.

2-*Anilino*-5-*benzylthio*-1,3,4-*thiadiazole*.[37]— $\nu_{max.}$ (Nujol) 3240m and 3190m (NH), 1625s and 1570s (C=N), 1605s, 1510s, 760s, and 690s (Ph), and 1460s and 1220m cm.$^{-1}$.

2-*Anilino*-1,3,4-*thiadiazol*-5-*yl Benzyl Sulphoxide*.—A stirred suspension of finely powdered 2-anilino-5-benzylthio-1,3,4-thiadiazole (3·0 g., 0·01 mole) in glacial acetic acid (12 ml.) was treated at room temperature with 30% hydrogen peroxide (9·1 ml., 0·08 mole) during 2 min., and then stirred at 55—60° during 1½ hr. Complete solution did not occur, but the suspended material changed in appearance. It was collected at 0°, rinsed with ether and water, and the remaining white solid (m.p. 173—176°; 2·35—2·65 g., 75—85%) crystallised from ethanol (25 ml. per g., recovery 80%), giving needles of the *sulphoxide*, m.p. 178—180° (Found: C, 57·4; H, 4·3; N, 13·3; S, 20·1. $C_{15}H_{13}N_3OS_2$ requires C, 57·1; H, 4·1; N, 13·3; S, 20·3%), $\nu_{max.}$ 1055s (S=O) cm.$^{-1}$, and all peaks of the foregoing 5-benzylthio-analogue.

In some experiments, using conditions (*e.g.*, 12 molar excess of hydrogen peroxide at 70° for 60 min.) intermediate for the production of the sulphoxide and sulphone (see below), mixtures (m.p. 170—180°) of these two compounds were obtained in satisfactory yield. These were separable into their components by fractional crystallisation from

[35] J. R. Vaughan, jun., K. H. Wood, and R. W. Young, U.S.P. 2,783,240/1957 (*Chem. Abs.*, 1958, **52**, 2084).

[36] M. Busch and F. Biehler, *J. prakt. Chem.*, 1916, **93**, 339; M. Busch and W. Schmidt, *Ber.*, 1913, **46**, 2240.

[37] E. Fromm, E. Layer, and K. Nerz, *Annalen*, 1923, **433**, 1.

ethanol (the sulphone being the less soluble fraction) or were with advantage oxidised further to the pure sulphone.

2-Anilino-1,3,4-thiadiazol-5-yl Benzyl Sulphone.—(a) *From the benzylthiol.* A stirred suspension of finely powdered 2-anilino-5-benzylthio-1,3,4-thiadiazole (3·0 g., 0·01 mole) in glacial acetic acid (30 ml.)–30% hydrogen peroxide (13·6 ml., 0·12 mole) was kept at 100° for 30 min. (or at 75—80° for 1 hr., using 0·18 mole of peroxide). Solution first occurred slowly, and finely divided solid reappeared. This was collected at 0° (m.p. 188—192°; 1·16—1·5 g., 35—45%), rinsed with ethanol, and crystallised from the same solvent (40 ml. per g., recovery 75%), giving pale yellow needles of *2-anilino-1,3,4-thiadiazol-5-yl benzyl sulphone*, m.p. 194—196° (Found: C, 53·9; H, 4·2; N, 13·0; S, 18·8. $C_{15}H_{13}N_3O_2S_2$ requires C, 54·4; H, 3·9; N, 12·7; S, 19·3%), $\nu_{max.}$ 1335s and 1115s (SO_2) cm.$^{-1}$ and all peaks of the foregoing 5-benzylthio-analogue.

(b) *From the sulphoxide.* A suspension of the sulphoxide (3·15 g., 0·01 mole) in glacial acetic acid (30 ml.)–30% hydrogen peroxide (9·1 ml., 0·08 mole) was stirred at 70—75° for 1·5 hr. Complete solution did not occur. The solid was collected at 0° and washed with a little cold ethanol (crude: m.p. 189—192°; 2·7—3·0 g., 82—90%); it was the sulphone, m.p. and mixed m.p. with (a) 194—196° (from ethanol) (Found: C, 54·3; H, 4·1%).

2-Anilino-1,3,4-thiadiazol-5-yl Methyl Sulphone.—A stirred suspension of 2-anilino-5-methylthio-1,3,4-thiadiazole (2·23 g., 0·01 mole) in glacial acetic acid (20 ml.)–30% hydrogen peroxide (11·3 ml., 0·1 mole) was slowly heated to 60—65° (30 min.) and kept at this temperature for 1·5 hr. A pale yellow solution was first formed and deposited crystalline solid after 30 min. This was collected at 0°, rinsed with ether (solid: m.p. 185—188°; 1·65—1·9 g., 65—75%), and crystallised from ethanol (25 ml. per g., recovery 85%), giving pale yellow needles of the *sulphone*, m.p. 188—190° (Found: C, 42·2; H, 3·65; N, 16·55; S, 24·8. $C_9H_9N_3O_2S_2$ requires C, 42·35; H, 3·5; N, 16·5; S, 25·1%), $\nu_{max.}$ 1330s and 1125s (SO_2) cm.$^{-1}$ and all peaks of the foregoing 5-methylthio-analogue.

2-Anilino-1,3,4-thiadiazol-5-yl Methyl Sulphoxide.—In a similar experiment, the quantity of hydrogen peroxide was reduced to a 3-molar excess, the temperature to 55°, and the time of reaction to 1 hr. Dilution of the reaction mixture with water precipitated a crude product which gave, on crystallisation from ethanol (18 ml. per g., recovery 70%), needles (65%) of the *sulphoxide*, m.p. 147—149° (Found: C, 45·1; H, 3·8; N, 17·8; S, 26·9. $C_9H_9N_3OS_2$ requires C, 45·2; H, 3·8; N, 17·6; S, 26·8%), $\nu_{max.}$ 1060s (S=O) cm.$^{-1}$ and all peaks of the foregoing 5-methylthio-analogue.

Hydrazinolysis of 2-Anilino-1,3,4-thiadiazol-5-yl Benzyl Sulphone.—(*a*) A suspension of 2-anilino-1,3,4-thiadiazol-5-yl benzyl sulphone (6·62 g., 0·02 mole) in hydrazine hydrate (30 ml.) was gradually heated to boiling (*ca.* 150°) during 30 min., the solution refluxed for 30 min., and the whole allowed to cool to room temperature during 1 hr. The colourless liquid was stirred into ice–water; addition of concentrated hydrochloric acid (to pH 8) precipitated a white solid (3—3·5 g.) which was collected at 0° and air-dried. Its extraction with boiling ethanol (40 ml.) gave a residue of 3-hydrazino-5-mercapto-4-phenyl-1,2,4-triazole, m.p. and mixed m.p.[25] 243—244° (0·6—0·75 g., 14—18%) (also characterised by its i.r. spectrum, and by its conversion, by means of acetylacetone, into its pyrazolyl derivative, m.p. and mixed m.p.[25] 229—231°), $\nu_{max.}$ 3250s, 3200s,br, and 1657m (NH), 1519s (C=N), 1610s, 1500s, and 695s (Ph), and 1330s, 1250ms, 1160s, and 1100s cm.$^{-1}$.

The ethanol filtrate therefrom rapidly deposited needles (1·65—1·85 g., 40—45%) of 4-amino-3-anilino-5-mercapto-1,2,4-triazole, m.p. 203—205° (from ethanol, 30 ml. per g., recovery 60%) (lit.,[9] 208°) (Found: C, 46·5; H, 4·4; N, 34·4; S, 15·6. Calc. for $C_8H_9N_5S$: C, 46·4; H, 4·35; N, 33·8; S, 15·5%), $\nu_{max.}$ 3360m and 3260m,br (NH), 1645s,br (NH_2 deform.), 1590s (C=N), 1600s, 1500m, 765s, and 695s (Ph), and 1480s, 1195ms, and 870ms cm.$^{-1}$.

A solution of 3-hydrazino-5-mercapto-4-phenyl-1,2,4-triazole (0·41 g., 0·002 mole) in hydrazine hydrate (6 ml.) was refluxed for 3 hr. Dilution with water, and addition of hydrochloric acid (to pH 8) reprecipitated the starting material (80%) (identified by its i.r. spectrum). Similarly, 4-amino-3-anilino-5-mercapto-1,2,4-triazole was recovered (90%) after 3 hr. refluxing in hydrazine hydrate, showing that appreciable interconversion of (XX) and (XIX) did not occur in the above hydrazinolysis.

(*b*) A solution of 2-anilino-1,3,4-thiadiazol-5-yl benzyl sulphone (4·95 g., 0·015 mole) in ethanol (40 ml.)–hydrazine hydrate (15 g., 0·3 mole) was refluxed during 96 hr. The nearly insoluble 3-hydrazino-5-mercapto-4-phenyl-1,2,4-triazole which had begun to separate after *ca.* 10 hr. was filtered off at room temperature (8—12%), and the filtrate was stirred into ice–water (100 ml., containing a few drops of glacial acetic acid); the precipitate was 4-amino-3-anilino-5-mercapto-1,2,4-triazole, m.p. 198—200° (prisms from ethanol) (Found: C, 46·3; H, 4·3; N, 34·3; S, 15·3%) (1·2—1·5 g., 38—48%).

The aqueous filtrate therefrom deposited, on spontaneous evaporation to half-bulk at room temperature, a white solid which gave (1·25 g., 60%) benzyl benzylthiosulphonate, m.p. 104—107° (needles from ethanol) (lit.,[38] 108°) (Found: C, 60·2; H, 5·0. Calc. for $C_{14}H_{14}O_2S_2$: C, 60·4; H, 5·0%).

Hydrazinolysis of 2-Anilino-1,3,4-thiadiazol-5-yl Methyl Sulphone.—A solution of the sulphone (1·27 g., 0·005 mole) in ethanol (12 ml.)–hydrazine hydrate (4 ml., 0·08 mole) was refluxed for 12 hr. (smell of methanethiol). The following were isolated as described in the corresponding experiment employing the benzyl sulphone [procedure (*b*)], and identified by mixed m.p. and their i.r. spectra: 3-hydrazino-5-mercapto-4-phenyl-1,2,4-triazole (5%) and 4-amino-3-anilino-5-mercapto-1,2,4-triazole (18%). The use of a smaller excess (3 moles) of hydrazine hydrate resulted substantially in the recovery of the starting material.

Interaction of 1,2-Diamino-3-phenylguanidine and Carbon Disulphide.—A solution of 1,2-diamino-3-phenylguanidine hydriodide [18] (2·93 g., 0·01 mole) in 90% ethanol (35 ml.) was treated with carbon disulphide (0·84 g., 0·011 mole) and 85% potassium hydroxide (1·65 g., 0·025 mole) in water (6 ml.). The liquid was refluxed for 6 hr. (evolution of hydrogen sulphide), distilled to nearly dryness, diluted with water (8 ml.), and the solution acidified with 3N-hydrochloric acid. The white resinous precipitate solidified on storage at 0°; it was collected and extracted with boiling ethanol. The residue was 3-hydrazino-5-mercapto-4-phenyl-1,2,4-triazole (0·23 g., 11%). The filtrate deposited needles (total, 0·37 g., 18%) of 4-amino-3-anilino-5-mercapto-1,2,4-triazole. Both products were identified by mixed m.p., and by their i.r. spectra. The final ethanol filtrates gave only intractable red gums.

3-Anilino-4-benzylideneamino-5-mercapto-1,2,4-triazole.—A suspension of 4-amino-3-anilino-5-mercapto-1,2,4-triazole

[38] E. Fromm and J. de Seixas Palma, *Ber.*, 1906, **39**, 3308.

(0·41 g., 0·002 mole) in ethanol (8 ml.)–benzaldehyde (0·32 g., 0·003 mole), containing concentrated hydrochloric acid (8 drops), was refluxed for 3 hr. Complete solution did not occur, but yellow solid was formed. This gave yellow needles of the 4-benzylideneamino-derivative, m.p. 215—216° (from ethanol, 50 ml. per g., recovery 70%) (lit.,[9] 216°) (0·41 g., 70%) (Found: C, 61·05; H, 4·4; N, 23·6; S, 10·55. Calc. for $C_{15}H_{13}N_5S$: C, 61·0; H, 4·4; N, 23·7; S, 10·85%), $\nu_{max.}$ 3350m and 3170m,br (NH), 1640s (PhCH=N), 1555s (C=N), 1600s, 1500ms, 750s, and 690s(Ph), and 1490s, 1270s, 1165m, and 865m cm.$^{-1}$.

4-*Amino*-3-*anilino*-5-*methylthio*-1,2,4-*triazole*.—A solution of the 5-mercapto-compound (1·04 g., 0·005 mole) in N-sodium hydroxide (5 ml., 0·005 mole) was treated with methyl iodide (0·85 g., 0·006 mole) and shaken at room temperature for 3 hr. The separated solid was collected, washed with ether, and crystallised from methanol–water (3 : 1; 10 ml. per g., recovery 80%), giving needles of the 5-methylthiol, m.p. 167—169° (lit.,[9] 173—174°) (0·88 g., 80%) (Found: C, 48·8; H, 4·8; N, 31·9; S, 14·4. Calc. for $C_9H_{11}N_5S$: C, 48·9; H, 5·0; N, 31·7; S, 14·5%), $\nu_{max.}$ 3340m and 3170m,br (NH), 1640m (NH_2 deform.), 1570s (C=N), 1605s, 1500m, 750s, and 695s (Ph), and 1450s and 1240m.

4-*Amino*-3-*anilino*-5-*benzylthio*-1,2,4-*triazole*.—A solution of the 5-mercapto-compound (0·41 g., 0·002 mole) in ethanol (10 ml.)–benzyl chloride (0·38 g., 0·003 mole)–3N-sodium hydroxide (1 ml., 0·003 mole) was refluxed for 20 min., set aside at room temperature, slowly diluted with water (10 ml.), and the solid collected. Crystallisation from ethanol (20 ml. per g., recovery 60%) gave platelets (0·42 g., 70%) of the *benzylthiol*, m.p. 188—190° (Found: C, 60·5; H, 5·4; N, 23·6; S, 11·4. $C_{15}H_{15}N_5S$ requires C, 60·6; H, 5·05; N, 23·6; S, 10·8%), $\nu_{max.}$ 3330m, 3230m, 3190m, and 3120m (NH), 1640m (NH_2 deform.), 1625s and 1585s (C=N), 1600s, 1500s, 750s, and 700s (Ph), and 1460s and 1250m cm.$^{-1}$.

4-*Amino*-3-*anilino*-5-*methylthio*-1,2,4-*triazole*.— *Deamination*. The reactant (1·1 g., 0·005 mole) was dissolved in N-hydrochloric acid (20 ml., 0·02 mole) with warming; the stirred liquid was allowed to cool to *ca.* 10°, and was treated, during 15 min., with sodium nitrite (0·69 g., 0·01 mole) in water (10 ml.). The solution rapidly deposited a dark gum; the mixture was allowed to attain room temperature, then shaken for 1 hr., and the supernatant aqueous phase (A) decanted. The gum (consisting according to t.l.c. mostly of the required product and some unchanged starting material) was rinsed with water, air-dried, and then dissolved in chloroform (20 ml.). The solution was absorbed on an alumina column (17 × 2·5 cm.; Spence H grade, 100—200 mesh, previously saturated with benzene), and successively eluted with chloroform (3 × 200 ml.), ethyl acetate (200 ml.), and ethanol (3 × 200 ml.). The chloroform removed the orange-brown constituents, and deposited a minute quantity of unidentified bright orange needles (possibly nitroso-compounds). The ethyl acetate eluate contained traces of gums. The ethanol eluates (first 400 ml.) deposited, on evaporation to small volume (10 ml.) and storage, successive crops (m.p. 176—182°; 0·27 g., 26%), which gave faintly yellow granular 3-anilino-5-methylthio-1,2,4-triazole, m.p. 182—184° (from ethanol). Its identity with authentic material (lit.,[5] m.p. 187—188°) was shown by its i.r. spectrum [$\nu_{max.}$ 3380m, 3320m, and 3140m,br (NH), 1610s and 1570s (C=N), 1510s, 750s, and 695m (Ph), and 1555s, 1460s, and 1040ms cm.$^{-1}$] and by t.l.c.

Evaporation of the aqueous phase A to dryness in a vacuum, extraction of the residual gum with hot ethanol (5 ml.), filtering, and storage gave crystalline needles; dissolution of this hydrochloride in water, and basification, gave up to 20% recovered starting material (confirmed by i.r. spectra).

Interaction of 4-*Amino*-3-*anilino*-5-*methylthio*-1,2,4-*triazole and Diphenylcarbodi-imide*.—A solution of the reactants (0·44 and 0·39 g., 0·002 mole each) in dimethylformamide (5 ml.) was gradually heated to 130° during 1 hr., kept at this temperature for 5 hr., and the cooled liquid slowly stirred into ice–water (30 ml.). The resulting resinous precipitate solidified on storage; it was extracted with boiling methanol (5 ml.). The undissolved residue (0·25 g., 34%) was 3,6-dianilino-7-phenyl-*s*-triazolo[4,3-*b*]-*s*-triazole, m.p. 256—258° (from dimethylformamide–water) (Found: C, 68·8; H, 5·2; N, 26·3. Calc. for $C_{21}H_{17}N_7$: C, 68·7; H, 4·6; N, 26·7%).

The methanol filtrate deposited 3-anilino-4-(*NN'*-diphenylguanidino)-5-methylthio-1,2,4-triazole, m.p. 230—231° (decomp.) (from methanol) (total, 0·15 g., 18%). Both triazoles were characterised by comparison with authentic samples, by mixed m.p., i.r. spectra, and t.l.c. The final methanol filtrates contained only intractable resin.

Interaction of Thiocarbohydrazide and Di-p-*tolylcarbodi-imide*.—(*a*) A solution of thiocarbohydrazide (0·53 g., 0·005 mole) in dimethyl sulphoxide (15 ml.) was treated at room temperature with di-*p*-tolylcarbodi-imide (2·22 g., 0·01 mole) in portions (colour change green to pale yellow), and the liquid then kept at 100° for 1 hr. Its addition to ice–water (100 ml.) gave a finely divided precipitate. The collected air-dried brown solid was crystallised by dissolution in acetone (30 ml. per g.) and dilution of the filtered liquid with an equal volume of 50% ethanol, giving lustrous felted needles (1·22 g., 55%) of 3-*mercapto*-4-(NN'-*di*-p-*tolylguanidino*)-5-p-*toluidino*-1,2,4-*triazole*, m.p. 241—242° (decomp.) (Found: C, 64·7; H, 6·2; N, 21·4; S, 7·5. $C_{24}H_{25}N_7S$ requires C, 65·0; H, 5·6; N, 22·1; S, 7·2%), $\nu_{max.}$ 3370m, 3285m,br, and 3125m,br (NH), 1620s,br and 1590ms (C=N), 1600s and 1500s (aryl), 815s (split) (1,4-disubst. aryl), and 1550s, 1310m, 1235m, and 1020m cm.$^{-1}$.

(*b*) Slow addition of the carbodi-imide (0·01 mole) in dimethylformamide (15 ml.) to the thiocarbohydrazide (0·005 mole) in the same solvent (25 ml.) at room temperature, followed by heating at 100° during 1 hr., and isolation as before, gave the same substituted 1,2,4-triazole in 35—55% yield.

(*c*) The use of methanol as solvent tended to favour the production of 3,5-di-*p*-toluidino-4-*p*-tolyl-1,2,4-triazole as by-product, and was not examined more closely.

4-(NN'-*Di*-p-*tolylguanidino*)-3-*methylthio*-5-p-*toluidino*-1,2,4-*triazole*.—A solution of the 3-mercapto-compound (0·44 g., 0·001 mole) in 0·33M-sodium methoxide (3 ml., 0·001 mole) was treated with methyl iodide (1 ml., 0·015 mole), refluxed for 30 min., distilled to half bulk, and diluted with water. The precipitate was crystallised from acetone–ethanol (1 : 2), giving microprisms (0·29 g., 64%) of the *methylthiol*, m.p. 227—228° (Found: C, 65·4; H, 5·9; N, 21·2; S, 7·2. $C_{25}H_{27}N_7S$ requires C, 65·6; H, 5·9; N, 21·4; S, 7·0%), $\nu_{max.}$ (Nujol) 3400m, 3250m,br, and 3200m,br (NH), 1620m and 1570s (C=N), 1595s (aryl), 815s (1,4-disubst. aryl), and 1490s, 1340m, and 1200m cm.$^{-1}$.

3-*Benzylthio*-4-(NN'-*di*-p-*tolylguanidino*)-5-*p*-*toluidino*-1,2,4-*triazole*.—A refluxing solution of the 3-mercapto-compound (0·88 g., 0·002 mole) in ethanol (20 ml.)–benzyl chloride (0·38 g., 0·003 mole)–3N-sodium hydroxide (1 ml., 0·003 mole) rapidly deposited white solid. Refluxing was

continued for 20 min., and the cooled mixture diluted with water (10 ml.). The solid gave, on crystallisation from acetone–ethanol, ivory prisms (0·68 g., 64%) of the *benzylthiol*, m.p. 216—217° (Found: C, 69·3; H, 5·8; N, 17·95; S, 6·7. $C_{31}H_{31}N_7S$ requires C, 69·8; H, 5·8; N, 18·4; S, 6·0%).

3,6-*Di*-p-*toluidino*-7-p-*tolyl*-s-*triazolo*[4,3,-b]-s-*triazole*.—A solution of 4-(*NN'*-di-*p*-tolylguanidino)-3-methylthio-5-*p*-toluidino-1,2,4-triazole (0·46 g., 0·001 mole) in dimethylformamide (4 ml.) was kept at 160° and 145° for successive periods of 1 hr., then cooled and diluted with a few drops of water. The resulting pale yellow crystalline solid (m.p. 224—226°; 0·28 g., 68%) gave, on crystallisation from ethanol (60 ml. per g., recovery 50%), minute needles of 3,6,-*di*-p-*toluidino*-7-p-*tolyl*-s-*triazolo*[4,3,-b]-s-*triazole*, m.p. 229—230° (decomp. to deep-blue mass) (Found: C, 70·0; H, 5·8; N, 24·3. $C_{24}H_{23}N_7$ requires C, 70·4; H, 5·6; N, 24·0%), $\nu_{max.}$ 3270m and 3220m (NH), 1620s and 1570s (C=N), 820s (split) (1,4-disubst. aryl), and 1600s and 1520s $cm.^{-1}$.

2-*Mercapto*-5-p-*toluidino*-1,3,4-*thiadiazole*.[39]—$\nu_{max.}$ 3240m, 3190m, and 3125m (NH), 1605s and 1570s,br (C=N), 815s (1,4-disubst. aryl), and 1330s, 1055s, and 1040s.

2-*Benzylthio*-5-p-*toluidino*-1,3,4-*thiadiazole*.—To 2-mercapto-5-*p*-toluidino-1,3,4-thiadiazole (17·8 g., 0·08 mole), dissolved in nearly boiling ethanol (110 ml.), was added benzyl chloride (11·4 g., 0·09 mole), and the stirred liquid treated at 60° with 3N-sodium hydroxide (30 ml., 0·09 mole) within 5 min. The mixture set almost immediately to a mass of suspended crystals; this was broken up by shaking (15 min.) and set aside for 2 hr. The crystals (m.p. 136—139°; 16·6 g., 66%) were collected and washed with very little 60% ethanol, followed by water. Crystallisation from ethanol (10 ml., per g., recovery 85%) gave silky felted needles of the benzylthiol, m.p. 138—140° (lit.,[40] 173° for a specimen prepared by a different route) (Found: C, 61·0; H, 4·9; N, 13·0; S, 20·1. Calc. for $C_{16}H_{15}N_3S_2$: C, 61·3; H, 4·8; N, 13·4; S, 20·45%), $\nu_{max.}$ 3270mw and 3190mw (NH), 1620s and 1570s (C=N), 835ms (1,4-disubst. aryl), 775ms and 705ms (aryl), and 1520s, 1455s, and 1050m $cm.^{-1}$.

5-p-*Toluidino*-1,3,4-*thiadiazol*-2-*yl Benzyl Sulphoxide*.—2-Benzylthio-5-*p*-toluidino-1,3,4-thiadiazole (3·13 g., 0·01 mole), suspended in glacial acetic acid (15 ml.)–30% hydrogen peroxide (9·1 ml., 0·08 mole), was stirred at 55—60° for 3 hr., and the solid collected at 0° and washed with water and ether. The crude product (m.p. 152—155°; 2·95 g., 90%) gave, on crystallisation from ethanol (30 ml. per g., recovery 80%), lustrous flakes of the *solvated sulphoxide*, m.p. 159—162° (Found: C, 57·2; H, 5·65; N, 11·7. $C_{16}H_{15}N_3OS_2,C_2H_5OH$ requires C, 57·6; H, 5·6; N, 11·2%). The material was not desolvated on being kept at 110° in a vacuum for 4 hr.; $\nu_{max.}$ 3270m (OH?), 3190m (NH), 1605s and 1550s (C=N), 1040s (S=O), 810s (1,4-disubst. aryl), and 765s and 695s (aryl) $cm.^{-1}$.

5-p-*Toluidino*-1,3,4-*thiadiazol*-2-*yl Benzyl Sulphone*.—A stirred suspension of the foregoing solvated sulphoxide (3·75 g., 0·01 mole) in glacial acetic acid (18 ml.)–30% hydrogen peroxide (11·3 ml., 0·1 mole) was kept at 65—75° for 5 hr. The solid was collected at 0° (m.p. 180—186°; 2·75—2·9 g., 80—85%) and crystallised from ethanol (50 ml. per g., recovery 70%), giving needles of the *sulphone*, m.p. 183—186° (Found: C, 55·4; H, 4·35; N, 12·1; S, 18·2. $C_{16}H_{15}N_3O_2S_2$ requires C, 55·65; H, 4·35; N, 12·2; S, 18·55%), $\nu_{max.}$ 1335s and 1120s (SO_2) and all peaks of the foregoing 2-benzylthio-5-*p*-toluidino-1,3,4-thiadiazole.

Hydrazinolysis of 2-p-*Toluidino*-1,3,4-*thiadiazol*-5-*yl Benzyl Sulphone*.—Treatment of the sulphone (3·45 g., 0·01 mole) with hydrazine hydrate (12·5 g., 0·25 mole) as described for the 2-anilino-analogue gave, after acidification, a crude product (1·8 g.) which was extracted with two successive portions of boiling ethanol (20 and 15 ml.). The residue was 3-hydrazino-5-mercapto-4-*p*-tolyl-1,2,4-triazole (0·89 g., 40%), m.p. and mixed m.p.[25] 240—242° (decomp.), also identified by its i.r. spectrum. The ethanol extracts deposited solid (total, 0·77 g., 35%), which gave, on crystallisation from ethanol, needles of 4-*amino*-3-*mercapto*-5-p-*toluidino*-1,2,4-*triazole*, m.p. 229—231° (Found: C, 48·9; H, 5·2; N, 31·6. $C_9H_{11}N_5S$ requires C, 48·9; H, 5·0; N, 31·7%), $\nu_{max.}$ 3390m, 3330m, 3190m,br (NH), 1635s (NH_2 deform.), 1610s and 1590m (C=N), 815m (1,4-disubst. aryl), and 1490s, 1200m, and 950m $cm.^{-1}$.

4-*Benzylideneamino*-3-*mercapto*-5-p-*toluidino*-1,2,4-*triazole*.—This was prepared as the corresponding anilino-analogue (see above). It formed pale yellow opaque granules (75%), m.p. 220—221° (from 80% methanol) (Found: C, 61·9; H, 4·9; N, 21·1; S, 10·9. $C_{16}H_{15}N_5S$ requires C, 62·1; H, 4·85; N, 22·65; S, 10·4%), $\nu_{max.}$ (Nujol) 3400m and 3100m (NH), 1640s (PhCH=N), 1615s (C=N), 810m (1,4-disubst. aryl), 755m and 690m (Ph), and 1550s and 1275s $cm.^{-1}$.

4-*Amino*-3-*methylthio*-5-p-*toluidino*-1,2,4-*triazole*.— The corresponding 3-mercapto-compound (2·21 g., 0·01 mole), nearly dissolved in N-sodium hydroxide (10 ml., 0·01 mole), was shaken with methyl iodide (1·7 g., 0·012 mole) for 1 hr. The separated solid (m.p. 168—170°; 2·1 g., 90%) was the *methylthiol*, forming minute flakes, m.p. 167—169° (from water containing a few drops of ethanol; 50 ml. per g.) (Found: C, 51·1; H, 5·7; N, 29·4; S, 13·7. $C_{10}H_{13}N_5S$ requires C, 51·1; H, 5·5; N, 29·8; S, 13·6%), $\nu_{max.}$ 3400m, 3280m,br, and 3150m (NH), 1630s (NH_2 deform.), 1620s and 1570s (C=N), and 815s (1,4-disubst. aryl) $cm.^{-1}$.

Interaction of 4-*Amino*-3-*methylthio*-5-p-*toluidino*-1,2,4-*triazole and Di*-p-*tolylcarbodi-imide*.—The reactants (0·0025 mole each) in dimethylformamide (4 ml.) were heated at 125—130° for 8 hr. (or at 165° for 1·5 hr.), then stirred into water. The coagulated precipitate was collected, washed with water, and air-dried (1 g.). T.l.c. (using alumina-coated plates, and chloroform as solvent) showed the presence of three constituents (R_F 0·21, 0·39, and 0·68). 4-(*NN'*-Di-*p*-tolylguanidino)-3-methylthio-5-*p*-toluidino-1,2,4-triazole was absent; the main product (R_F 0·39) was 3,6-di-*p*-toluidino-7-*p*-tolyl-*s*-triazolo[4,3-*b*]-*s*-triazole, but attempts to isolate it from the mixture by chromatography were not successful.

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