Heterocyclic Compounds from Urea Derivatives. Part XXII.[1] Thiobenzoylated Carbonohydrazides and their Cyclisation

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Thioaroylthioacetic acids convert carbonohydrazide successively into 1-thioaroyl- and 1,5-bis(thioaroyl)-carbonohydrazides. 1-Phenyl- and 1-benzylidene-carbonohydrazide similarly yield 5-monothioaroyl compounds. All are readily cyclised by mineral acids to 2-aryl-5-hydroxy-1,3,4-thiadiazoles, with loss of hydrazine or its appropriate derivative, but are unaffected by alkali. The thioaroyl adducts and their stable *S*-alkyl derivatives undergo ring closure when treated with hydrazine to give 4-(substituted amino)-3-aryl-5-hydroxy-1,2,4-triazoles.

CARBONOHYDRAZIDE and its thio-analogue are convertible into derivatives that are useful precursors of five-membered heteroaromatic systems, particularly pyrazoles, 1,2,4-triazoles, and 1,3,4-thiadiazoles.[1-5] The production and ring closure of acyl(thio)carbonohydrazides (A; X = O or S) [2,6,7] is one of the simplest examples of this general route. We now report the comparable behaviour of the corresponding thioacyl compounds (B; X = O or S).

$$R^1CO\cdot NH\cdot NH\cdot CX\cdot NH\ NHR^2$$
(A)

$$R^1CS\cdot NH\cdot NH\cdot CX\cdot NH\cdot NHR^2$$
(B)

The thioacylation of carbonohydrazide (V; R = H) afforded the mono- (VI; R = H) or di-thioaroyl derivative (II), depending on the proportions of reactants employed. Treatment of carbonohydrazide with thioaroylthioacetic acids [8,9] under the usual conditions [9] in an excess of alkali afforded solutions of 1-thiobenzoylcarbonohydrazides (VI; R = H), but their isolation therefrom was uncertain because of their pronounced sensitivity to acid (see below): they were therefore directly converted *in situ* into stable derivatives, such as the *S*-benzyl (IX; R = H, Alk = CH_2Ph) or alkylidene compounds (XIII; *e.g.* X = Y = Me). The parent compounds (VI; R = H, Ar = Ph, *p*-ClC_6H_4) were isolable in good yield when the thiobenzoylation was performed in such a way that the final reaction mixture was exactly neutral.

1,5-Bis(thioaroyl)carbonohydrazides (II; Ar = Ph or *p*-ClC_6H_4) were produced by the action of 2 mol. equiv. of thioaroylthioacetic acid on carbonohydrazide (I) in dimethyl sulphoxide or alkali. Yields of (II; Ar = Ph) were moderate, because 2,5-diphenyl-1,3,4-thiadiazole (IV) arose in a side reaction, evidently by attack of the second molecule of the reagent at the vicinal N(2) instead of the ultimate N(5) atom of the intermediate 1-thiobenzoylcarbonohydrazide (VI; R = H); hydrolysis and cyclisation of the resulting unsymmetrical diadduct (III) during work-up accounts for the observed product (IV). Comparable cyclisations have been explained similarly; [10] the existence of a diadduct of ethyl carbazate [11] of structure $RNH(RN{:})C\cdot NH\cdot N(CO_2Et)\cdot C(:NR)\cdot NHR$ supports this interpretation.

Competing side reactions are avoided in the monothioacylation of carbonohydrazides having one hydrazine group suitably blocked. 1-Phenyl- (V; R = Ph) or benzylidene- (X; X = H, Y = Ph) carbonohydrazide,

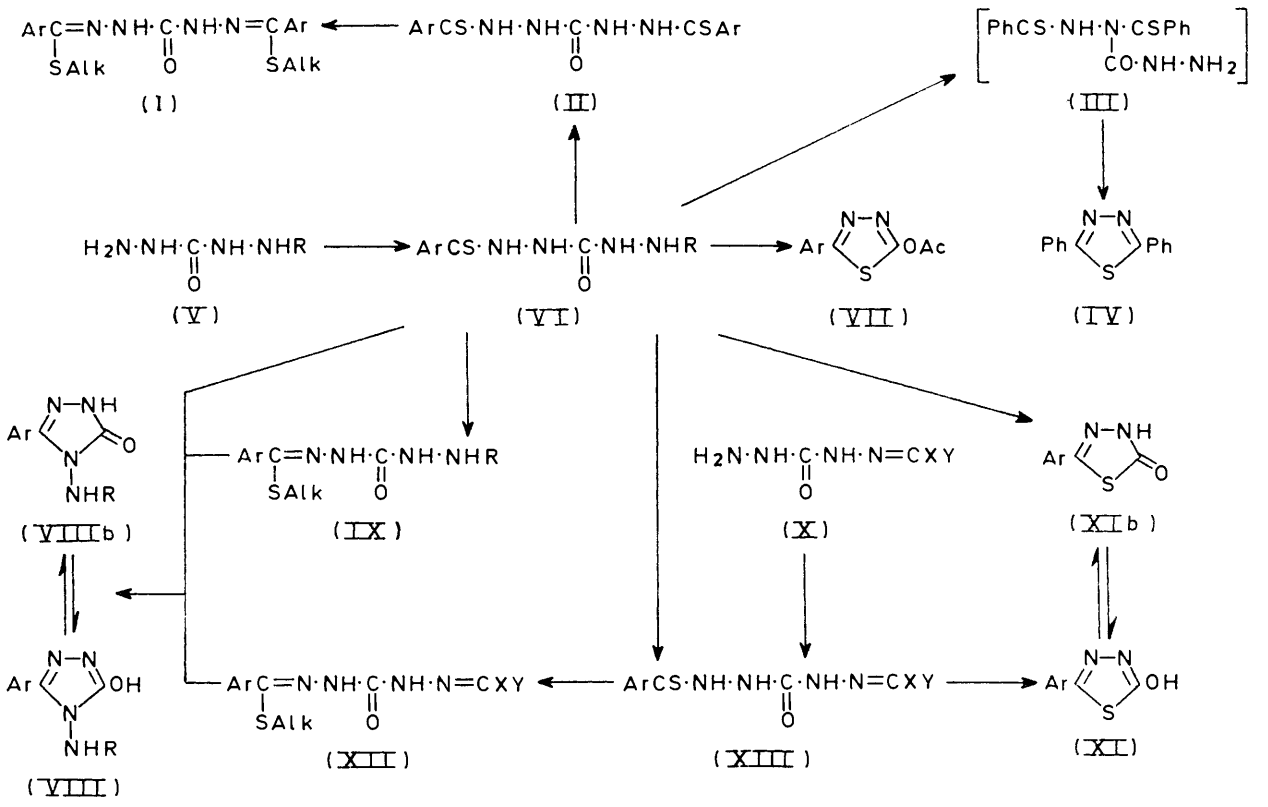
[1] Part XXI, F. Kurzer, *J. Chem. Soc.* (*C*), 1971, 2932.
[2] F. Kurzer and M. Wilkinson, *Chem. Rev.*, 1970, **70**, (*a*) p. 111; (*b*) pp. 128, 138.
[3] F. Kurzer and M. Wilkinson, *J. Chem. Soc.* (*C*), 1968, 2099.
[4] F. Kurzer and M. Wilkinson, *J. Chem. Soc.* (*C*), 1970, 19, 26.
[5] F. Kurzer, *J. Chem. Soc.* (*C*), 1971, 2927.
[6] R. Stollé, *J. prakt. Chem.*, 1907, **75**, 416, 423; R. Stollé and K. O. Leverkus, *Ber.*, 1913, **46**, 4076; R. Stollé and K. Krauch, *ibid.*, 1914, **47**, 724.
[7] H. Beyer and C. F. Kröger, *Annalen*, 1960, **637**, 135; C. F. Kröger, L. Hummel, M. Mutscher, and H. Beyer, *Chem. Ber.* 1965, **98**, 3025.
[8] B. Holmberg, *Arkiv Kemi*, 1944, **17***A*, No. 23; F. Kurzer and A. Lawson, *Org. Synth.*, 1962, **42**, 100.
[9] F. Kurzer, *Chem. and Ind.*, 1961, 1333; K. M. Doyle and F. Kurzer, *ibid.*, 1974, 803.
[10] L. E. A. Godfrey and F. Kurzer, *J. Chem. Soc.*, 1962, 3561; F. Kurzer and K. Douraghi-Zadeh, *ibid.*, 1965, 3912; 1967, 742.
[11] F. Kurzer and D. H. Hanks, *J. Chem. Soc.*, 1968, 1375.

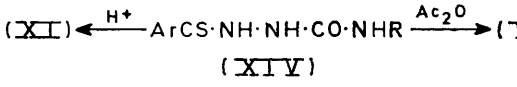
for example, readily gave good yields of 5-thiobenzoyl compounds (VI or XIII; Ar = Ph or *p*-ClC_6H_4, R = Ph, X = H, Y = Ph); they were convertible into *S*-benzyl derivatives, (IX) and (XII), as expected.

The i.r. spectra of the thioaroylcarbonohydrazides and their *S*-alkyl derivatives display intense absorption at 1 660—1 705 cm^{-1} characteristic of their amide carbonyl groups. A prominent absorption centred at 1 500—1 550 cm^{-1}, indicative of C–N–H vibration,[12,13] is regarded as a combination band due to NH deformation and C–N stretching vibration,[4,12,13] and the weaker maxima at *ca.* 3 100 cm^{-1} are considered as overtones resulting therefrom. Absorption due to NH stretching vibration occurs in the 3 000—3 300 cm^{-1} range, with a peak at 3 400 cm^{-1} for compounds containing a free terminal amino-group.[13] The parent carbonohydrazide produces similar though broader and blunter peaks.[14] However, the spectra exhibit no obvious regularity that could be attributed to the thioamide CS group; the uncertainties that surround such assignments are well known.[15]

The action of mineral acids on 1-thiobenzoylcarbonohydrazide (VI; R = H) and its 5-phenyl (VI; R = Ph) and 5-benzylidene derivative (XIII) gave, in each case, an excellent yield of 2-hydroxy-5-phenyl-1,3,4-thiadiazole (XI), with elimination of hydrazine, phenylhydrazine, or benzylidenehydrazine, respectively. Treatment with acetic anhydride furnished 2-acetoxy-5-phenyl-1,3,4-thiadiazole (VII) directly in one stage. Since these reagents cyclise the closely related 1-thiobenzoylsemicarbazides (XIV; Ar = Ph, R = H or Ph) to the same products [(XI), (VII)],[16] the corresponding structural patterns are seen to eliminate ammonia, amines, or hydrazines with comparable and pronounced readiness. The ring closures are examples of a general cyclisation of which the early synthesis[17] of 2-amino-5-hydroxy-1,3,4-thiadiazole (XVI; R = NH_2) from 2-thiobiurea (XV; R = NH_2, X = Y = H) may be regarded as the prototype. A possible mechanism common to them all is shown in the Scheme.

According to their i.r. spectra, the 2-aryl-5-hydroxy-1,3,4-thiadiazoles exist in the keto-form (XIb), their intense absorption at *ca.* 1 670 cm^{-1} being assigned to the ring CO group. The acetyl derivative (VII; Ar =

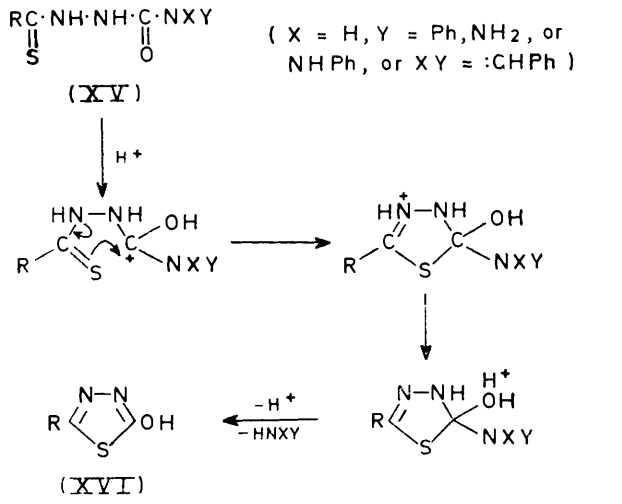




[12] D. M. Wiles and T. Suprunchuk, *Canad. J. Chem.*, 1968, **46**, 701.
[13] C. M. Kraebel, S. M. Davis, and M. J. Landon, *Spectrochim. Acta*, 1967, **23A**, 2541.
[14] Sadtler's Standard Spectra Catalogue, Spectrum No. 5701, Sadtler Research Laboratories Inc., Philadelphia.
[15] W. Walter and H. P. Kubersky, *Annalen*, 1966, **694**, 56, and numerous references given therein.
[16] F. Kurzer, *J. Chem. Soc.*, 1961, 1617.
[17] M. Freund and A. Schander, *Ber.*, 1896, **29**, 2506; M. Busch and H. Lotz, *J. prakt. Chem.*, 1914, **90**, 257; F. Arndt, E. Milde, and F. Tschenscher, *Ber.*, 1922, **55**, 341.

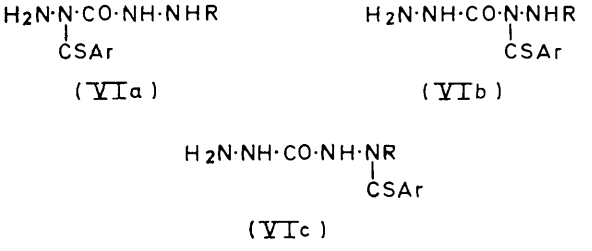
Ph), derived from the enolic form, produces a strong peak at 1 765 cm^{-1}, attributable to the acetoxy CO group, and one at 1 210 cm^{-1} [absent in the parent compound (XIb)] characteristic of the ester C–O–C grouping.[18]

The conversion of the thiobenzoylated carbonohydrazides into 2-aryl-5-hydroxy-1,3,4-thiadiazoles confirms, incidentally, their formulation as linear adducts



SCHEME

[(VI; R = H or Ph), (XIII)] since their branched isomers [*e.g.* (VIa—c)] cannot cyclise in the observed manner. This evidence is useful, since thiobenzoylation of monoalkyl- or aryl-hydrazines is known to occur either at the free or at the substituted amino-group, depending on steric and other structural factors.[19]

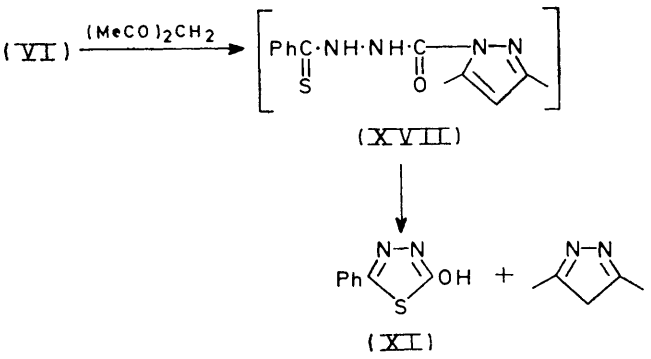


2-Hydroxy-5-phenyl-1,3,4-thiadiazole arose also nearly quantitatively from 1-thiobenzoylcarbonohydrazide (VI; Ar = Ph, R = H) by the action of acetylacetone, even in the absence of acid. In this reaction, the expected pyrazolyl derivative (XVII) is evidently cyclised and cleaved spontaneously to 3,5-dimethylpyrazole and the thiadiazole (XI).

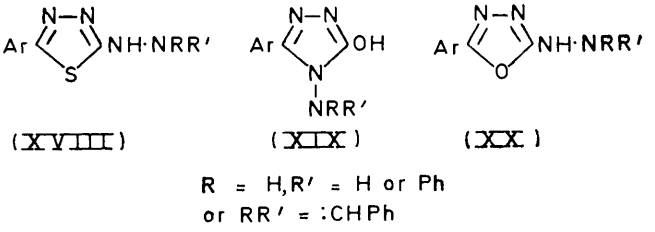
Other possible ring closures of thiobenzoylcarbonohydrazides include their conversion into 2-aryl-5-hydrazino-1,3,4-thiadiazoles (XVIII) by loss of water, or into 4-amino-3-aryl-5-hydroxy-1,2,4-triazoles (XIX) or 2-aryl-5-hydrazino-1,3,4-oxadiazoles (XX) by alternative modes of loss of hydrogen sulphide. With the exception of the last, these reactions have been realised.

[18] R. T. Conlan, 'Infrared Spectroscopy,' Allyn and Bacon, Boston, 1966, p. 145.

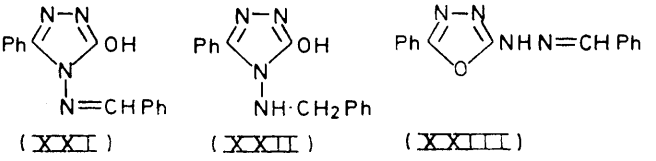
Thiobenzoylcarbonohydrazides were stable towards alkali and therefore not convertible into substituted



1,2,4-triazoles [*e.g.* (XIX)] by these reagents. They are thought to be stabilised, like the analogous thiobenzoylsemicarbazides and -guanidines,[16] by alkali-metal salt formation involving their acidic thiobenzoyl grouping. The action of boiling dimethylformamide on 1-benzylidene-5-thiobenzoylcarbonohydrazide (XIII; Ar = Y = Ph, X = H) gave, in addition to 2,5-diphenyl-1,3,4-thiadiazole (35%), small yields of a product formulated as 4-benzylamino-3-hydroxy-5-phenyl-1,2,4-triazole (XXII) on the basis of its composition, molecular weight



(266), and its non-identity with the authentic 4-benzylideneamino-analogue (XXI). The latter is presumably the primary cyclisation product but is reduced by the nascent hydrogen sulphide. The suggested reduction of the side-chain rather than the heteronucleus is supported by the n.m.r. spectrum [of (XXII)], which includes a strong signal attributable to the CH_2 group (see Experimental section). The carbonyl i.r. absorption confirms the absence of the possible isomeric 1,3,4-oxadiazole structure (XXIII). However, it is

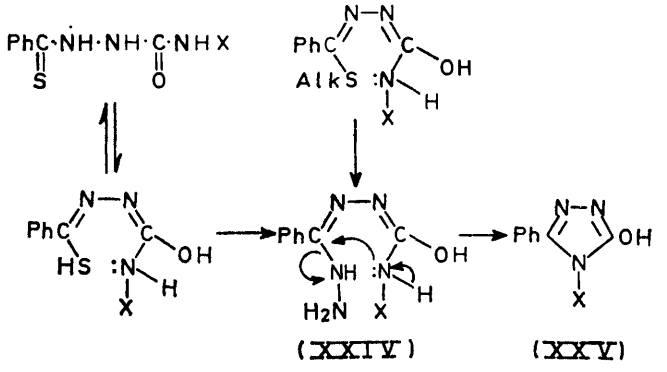


doubtful whether the reaction is a general one, since 1-phenyl-5-thiobenzoylcarbonohydrazide was converted in boiling dimethylformamide merely into 2-hydroxy-5-phenyl-1,3,4-thiadiazole.

[19] B. Holmberg, *Arkiv Kemi*, 1955, **9**, 47; K. A. Jensen and J. F. Miquel, *Acta Chem. Scand.*, 1952, **6**, 189; K. A. Jensen, H. R. Baccaro, O. Burchardt, G. E. Olsen, C. Pedersen, and J. Toft, *ibid.*, 1961, **15**, 1109.

The action of hydrazine finally provided a reliable method for abstracting the elements of hydrogen sulphide from thioaroylcarbonohydrazides, or of alkanethiols from their *S*-alkyl derivatives, affording good yields of products formulated as hydroxy-1,2,4-triazoles. Boiling hydrazine hydrate converted 1-thiobenzoylcarbonohydrazide (VI; R = H), its *S*-benzyl (IX; R = H, Alk = CH_2Ph), and their benzylidene derivatives [(XII), (XIII)] into 4-amino-3-hydroxy-5-phenyl-1,2,4-triazole (VIII; R = H). 1-Phenyl-5-thiobenzoylcarbonohydrazides (VI and IX; R = Ph) gave the corresponding 4-anilinotriazole (VIII; R = Ph). The action of phenylhydrazine on 1-thiobenzoylcarbonohydrazide gave low yields of the 4-aminotriazole (VIII; R = H). The i.r. spectra of the products feature a prominent absorption near 1 720 cm^{-1} and are consistent with their expected occurrence as triazolinones (VIIIb). Their possible formulation as hydrazino-1,3,4-oxadiazoles (XX) is thus excluded by the spectral data, and by the non-identity of the benzylidene derivative of (VIII; R = H, Ar = Ph) and authentic [20] 2-benzylidenehydrazino-5-phenyl-1,3,4-oxadiazole.

Since the cyclisation is brought about by hydrazine, but not by alkali, its mechanism is believed to involve the initial nucleophilic replacement of the sulphur function of the adducts by hydrazine. The resulting intermediate base (XXIV) may cyclise to (XXV) by extrusion of either of its hydrazino-groups. It appears that the hydrazino-group first introduced into the thiobenzoyl residue is also the one that is preferentially eliminated from (XXIV). This is established by the formation of the 4-anilinotriazole (XXV; X = NHPh) from (VI and IX; R = Ph) and of the 4-aminotriazole (XXV; X = NH_2) from thiobenzoylcarbonohydrazide and phenylhydrazine. The cyclisation is therefore thought to occur in the same sense in the other examples.



(XXIV) (XXV)

An isolated example of a cyclodehydration occurred spontaneously in some but not all experiments when 1-benzylidenecarbonohydrazide was treated with *p*-chlorothiobenzoylthioacetic acid. Instead of the expected adduct (XIII), 2-benzylidenehydrazino-5-*p*-hydroxyphenyl-1,3,4-thiadiazole was the sole product. The factors controlling this anomalous cyclodehydration are at present unknown.

Attempts to find reproducible conditions for the cyclodehydration of thioaroylcarbonohydrazides [(VI; R = H or Ph), (XIII)] to hydrazino-1,3,4-thiadiazoles (XVIII) have so far not been successful. Acidic dehydrating agents, including polyphosphoric or concentrated sulphuric acid gave 2-hydroxy-5-phenyl-1,3,4-thiadiazole nearly quantitatively. Evidently, their power of abstracting hydrazine operates before any dehydration can occur. The action of boiling toluene on 1-benzylidene-5-thiobenzoylcarbonohydrazide (XIII) in a Dean–Stark apparatus, ensuring neutral dehydrating conditions, was without effect.

EXPERIMENTAL

Compounds are named in this and the subsequent paper as hydroxy- or mercapto-triazoles and thiadiazoles, although their true structures approach the corresponding oxo- and thioxo-forms.

The usual general remarks [4] regarding reagents and apparatus are applicable. Simple triazole derivatives, and a series of analogues derived from *p*-chlorothiobenzoylthioacetic acid are described in Supplementary Publication No. SUP 21423 (3 pp.).*

Carbonohydrazide

1-*Thiobenzoylcarbonohydrazide*.—A stirred solution of carbonohydrazide (4.50 g, 0.05 mol) in N-hydrochloric acid (50 ml, 0.05 mol) was treated dropwise at room temperature *without cooling* with a solution of thiobenzoylthioacetic acid (5.3 g, 0.025 mol) in 3N-sodium hydroxide (25 ml, 0.075 mol). After 2 h stirring at room temperature, the solid was collected and washed with water (filtrate F) (crude: m.p. 128—132°; 4.2—4.5 g, 80—86%). Rapid crystallisation from methanol (slight smell of hydrogen sulphide; recovery 75%) gave pale greenish-yellow flat prisms of 1-*thiobenzoylcarbonohydrazide*, m.p. 134—135° (Found: C, 45.9; H, 4.8; N, 26.6; S, 14.8. $C_8H_{10}N_4OS$ requires C, 45.7; H, 4.8; N, 26.7; S, 15.2%), $\nu_{max.}$ 3 400s, 1 630m (NH_2), 3 300s, 3 240s (NH), 3 050s (aryl C=C), 1 660vs,br (CO), 1 530vs,br (NH/CN), 780s, and 700s cm^{-1} (Ph). The compound was soluble in alkali and reprecipitated by acid. It was substantially unaffected after 30 min boiling in 1.5N-sodium hydroxide. It did not yield a picrate.

Filtrate F, on being treated with acetone (30 ml), and acidified with 3N-hydrochloric acid, deposited a little (5—8%) 1-isopropylidene-5-thiobenzoylcarbonohydrazide, m.p. 170—172° (see below).

Reactions of 1-*Thiobenzoylcarbonohydrazide*.—(a) *Action of hydrochloric acid.* A boiling solution of the reactant (2.10 g, 0.01 mol) in ethanol (50 ml), treated with concentrated hydrochloric acid (20 ml), was refluxed for 10 min; lustrous platelets then began to separate. They were collected at 0 °C (filtrate F), and identified as 2-hydroxy-5-phenyl-1,3,4-thiadiazole, m.p. 145—147° (from chloroform–light petroleum; 1.20 g, 67%) (lit.,[16,21] m.p. 146—148°) (Found: C, 53.9; H, 3.2. Calc. for $C_8H_6N_2OS$: C, 53.9; H, 3.4%), $\nu_{max.}$ 3 150s, 3 050s, 2 830m, 1 535m (NH),

* For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1974, Index issue.

[20] R. Stollé and K. Fehrenbach, *J. prakt. Chem.*, 1929, **122**, 289, 315; S. C. De, *J. Indian Chem. Soc.*, 1930, **7**, 651; R. N. Butler, T. Lambe and F. L. Scott, *Chem. and Ind.*, 1970, 628.

[21] K. Fuji, H. Yoshikawa, and M. Yuasa, *J. Pharm. Soc. Japan*, 1954, **74**, 1056; T. Sato and M. Ohta, *ibid.*, 1955, **75**, 1535.

1 665vs,vbr (CO and C=N), 1 495m (aryl C=C), 765s (doublet), and 680s cm^{-1} (Ph).

Filtrate F was treated with 0.05M-picric acid (0.01 mol); it slowly deposited (45%) hydrazine picrate hemihydrate, m.p. 194—196° (lit.,[10] 196°; lit.,[22] 201°) (Found: C, 26.9; H, 3.3; N, 26.1. Calc. for $N_2H_4,C_6H_3N_3O_7,0.5H_2O$: C, 26.7; H, 3.0; N, 25.9%).

(b) *Action of sulphuric acid.* The reactant (0.005 mol) was added during 10 min to stirred concentrated sulphuric acid (10 ml) at room temperature and dissolved gradually. The liquid was set aside for 3 h, then added to ice–water. The white precipitate was 2-hydroxy-5-phenyl-1,3,4-thiadiazole (82%).

(c) *Action of orthophosphoric acid.* The reactant (0.005 mol) dissolved when added to melted 100% orthophosphoric acid (25 g), which was then kept at 140 °C (external bath) for 30 min. Addition of the cooled liquid to water gave 2-hydroxy-5-phenyl-1,3,4-thiadiazole (90%).

(d) *Action of acetic anhydride.* A solution of the reactant (0.005 mol) in acetic anhydride (12 ml) was kept at 100 °C for 2 h, then stirred into ice–water, giving 2-acetoxy-5-phenyl-1,3,4-thiadiazole, m.p. 116—117° (from ethanol) (lit.,[16,23] 117—119°) (Found: C, 54.7; H, 3.7; N, 13.2. Calc. for $C_{10}H_8N_2O_2S$: C, 54.5; H, 3.6; N, 12.7%), $\nu_{max.}$ 1 765s,br (CO of Ac), 1 210vs,br (C–O–C, ester), 775s, 710, and 690s cm^{-1} (Ph).

(e) *Action of acetylacetone.* A solution of the reactant (0.005 mol) in ethanol (20 ml), acetylacetone (3 ml), and glacial acetic acid (1 drop) was refluxed for 1 h, then stirred into water. The precipitate (0.84 g, 95%) was 2-hydroxy-5-phenyl-1,3,4-thiadiazole. Identical results were observed in the absence of acetic acid.

(f) *Action of hydrazine.* A solution of the reactant (0.005 mol) in hydrazine hydrate (10 ml) was boiled under reflux for 2 h, diluted with water (5 ml), and partly neutralised with concentrated hydrochloric acid until no further precipitate appeared. The solid gave minute opaque prisms (total 0.66 g, 75%) of *4-amino-3-hydroxy-5-phenyl-1,2,4-triazole*, m.p. 238—240° (from ethanol) (Found: C, 54.8; H, 4.6; N, 31.5. $C_8H_8N_4O$ requires C, 54.5; H, 4.5; N, 31.8%), $\nu_{max.}$ 3 380m (NH_2), 3 250s,br, 3 120m, 2 950w (NH), 1 725—1 700vs,br (CO and C=N), 1 635s (C=N or C=C), 1 510m, 775s, and 690s cm^{-1} (Ph). The compound did not form a picrate in ethanol under the usual conditions.

(g) *Action of phenylhydrazine.* A solution of the reactant (0.005 mol) and phenylhydrazine (0.81 g, 0.0075 mol) in anhydrous benzene (30 ml) was boiled under reflux for 3 h, then distilled to half volume. The yellow gum was washed with ether and dissolved in ethanol (8 ml). The solution deposited 4-amino-3-hydroxy-5-phenyl-1,2,4-triazole, m.p. 236—238° (0.16 g, 18%). The use of boiling phenylhydrazine (1 h) caused extensive decomposition, and gave no isolable products.

1-*Isopropylidene-5-thiobenzoylcarbonohydrazide.*—A stirred solution of carbonohydrazide (0.022 mol) in N-sodium hydroxide (0.022 mol) was treated dropwise during 5 min with thiobenzoylthioacetic acid (0.02 mol) in the same solvent (0.025 mol), and stirring at room temperature was continued for 20 min. A small precipitate was filtered off and the filtrate was treated with acetone (30 ml) and acidified at 0 °C with 3N-acetic acid. The resulting yellow crystalline precipitate was collected after storage in an open beaker (product: m.p. 144—145°, but having the correct i.r. spectrum, see below; 2.8—3.5 g, 56—70%). Crystallisation from acetone–ethanol (1 : 1) gave pale yellow felted needles of *1-isopropylidene-5-thiobenzoylcarbonohydrazide*, m.p. 170—172° (Found: C, 52.7; H, 5.4; N, 22.1; S, 12.9. $C_{11}H_{14}N_4OS$ requires C, 52.8; H, 5.6; N, 22.4; S, 12.8%), $\nu_{max.}$ 3 250s, 2 950m (NH), 3 080m (C–N–H overtone), 1 670vs (CO), 1 495vs,br (NH/CN), 765m, and 700m cm^{-1} (Ph). The compound was recovered nearly quantitatively after being refluxed in N-sodium hydroxide for 30 min.

1-(*α-Benzylthiobenzylidene*)*carbonohydrazide.*— 1-Thiobenzoylcarbonohydrazide was prepared *in situ* as in the foregoing paragraph (0.02 mol scale); the filtered solution was treated with ethanol (30 ml) and benzyl chloride (3.2 g, 0.025 mol) and stirred at 60 °C for 45 min. The suspension was stirred into water and the solidified resinous precipitate crystallised from chloroform–light petroleum, giving the opaque microcrystalline *S-benzyl derivative*, m.p. 152—154° (2.52 g, 42%) (Found: C, 59.4; H, 5.4; N, 18.8; S, 9.9. $C_{15}H_{16}N_4OS$ requires C, 60.0; H, 5.3; N, 18.7; S, 10.7%), $\nu_{max.}$ 3 300s, 2 820m (NH), 3 050m (doublet, CH_2?), 1 660—1 680vs (doublet, CO), 1 510vs (triplet, NH/CN), 760s, and 700s (doublet) cm^{-1} (Ph).

The action of hydrazine on the product [procedure (f)] gave 4-amino-3-hydroxy-5-phenyl-1,2,4-triazole (60%).

1,5-*Bis*(*thiobenzoyl*)*carbonohydrazide.*—To a solution of carbonohydrazide (0.45 g, 0.005 mol) in dimethyl sulphoxide (20 ml), a solution of thiobenzoylthioacetic acid (0.01 mol) in the same solvent (20 ml) was added during 10 min. The red liquid was stirred at room temperature for 1 h, then added to ice–water (100 ml) and set aside; the resulting finely divided precipitate coagulated on storage. Crystallisation from ethanol (8 ml; with addition of a few drops of water) gave a first crop (filtrate F) (m.p. 138—140°; 0.3—0.58 g, 18—35%) of *1,5-bis(thiobenzoyl)carbonohydrazide*, forming faintly yellow opaque microplatelets, m.p. 142—144° (from the same solvents) (Found: C, 54.4; H, 4.4; N, 17.3; S, 19.0. $C_{15}H_{14}N_4OS_2$ requires C, 54.5; H, 4.2; N, 17.0; S, 19.4%), $\nu_{max.}$ 3 300s, 3 200s (NH), 1 660vs (CO), 1 535s (NH/CN), 770s (doublet), and 690s cm^{-1} (Ph).

On partial evaporation, filtrate F slowly deposited lustrous platelets of 2,5-diphenyl-1,3,4-thiadiazole, m.p. and mixed m.p.[16,24] 138—140° (0.42—0.54 g, 35—45%), $\nu_{max.}$ 760vs, 695vs (Ph), 1 460s, 1 430s, 1 240m, 1 065m, 1 005, 990m (doublet), and 920m cm^{-1}. The use of aqueous alkali as reaction medium gave the same products in diminished yields.

1,5-*Bis*-(*α-benzylthiobenzylidene*)*carbonohydrazide*, obtained by the standard procedure from the foregoing compound, formed lustrous needles, m.p. 124—125° (from chloroform–light petroleum) (70%) (Found: C, 67.5; H, 5.2; N, 10.9; S, 12.3. $C_{29}H_{26}N_4OS_2$ requires C, 68.2; H, 5.1; N, 11.0; S, 12.55%), $\nu_{max.}$ 3 300m, 3 200s (NH), 3 100s (doublet, C–N–H overtone), 1 705vs (CO), 1 510, 1 490vs (doublet, NH/CN), 760m, and 710—700s,br cm^{-1} (Ph).

1-*Phenylcarbonohydrazide*

1-*Phenyl-5-thiobenzoylcarbonohydrazide.*—A solution of 1-phenylcarbonohydrazide (5.0 g, 0.03 mol) in dimethylformamide (75 ml) was treated with one of thiobenzoylthioacetic acid (6.35 g, 0.03 mol) in the same solvent (45 ml) during 3—5 min. The liquid was kept at room temperature for 3 h, then stirred into ice–water (500 ml). The precipitated viscid deep-red oil solidified after several

[22] E. C. Gilbert, *J. Phys. Chem.*, 1929, **33**, 1236.
[23] A. Lawson and C. E. Searle, *J. Chem. Soc.*, 1957, 1556.
[24] R. Stollé, *Ber.*, 1899, **32**, 797; *J. prakt. Chem.*, 1904, **69**, 366.

hours. Crystallisation from chloroform (40 ml)–light petroleum (10 ml) gave the *5-thiobenzoyl compound*, m.p. 136—138° (4.5—5.5 g, 52—64%) (Found, for a specimen crystallised from ethanol: C, 58.4; H, 5.0; N, 20.1; S, 10.7. $C_{14}H_{14}N_4OS$ requires C, 58.7; H, 4.9; N, 19.6; S, 11.2%), $\nu_{max.}$ 3 250s, 3 180s (NH), 3 000s (aryl C=C), 1 690vs,br (CO), 1 505s, 1 490s,br (NH/CN), 770—750s,br, and 690s cm^{-1} (Ph). It was recovered (75%) after 30 min refluxing in 1.5N-sodium hydroxide.

Reactions of 1-*Phenyl-5-thiobenzoylcarbonohydrazide*.—(a)—(d) *Cyclisation by acids*. The action of hydrochloric, sulphuric, and phosphoric acid, as described for 1-thiobenzoylcarbonohydrazide [procedures (a)—(c)], gave 2-hydroxy-5-phenyl-1,3,4-thiadiazole in 82, 86, and 95% yield, respectively. Acetic anhydride [procedure (d), above] gave 2-acetoxy-5-phenyl-1,3,4-thiadiazole (75%).

(e) *Action of hydrazine*. A solution of the reactant (0.005 mol) in hydrazine hydrate (15 ml) was boiled under reflux for 3 h and diluted with water (20 ml), and the precipitated solid was collected at 0 °C (m.p. 240°; 0.95 g, 75%). Crystallisation from ethanol (40 ml per g; recovery 60%) gave small opaque prisms of *4-anilino-3-hydroxy-5-phenyl-1,2,4-triazole*, m.p. 245—246° (Found: C, 66.7; H, 4.9; N, 21.8. $C_{14}H_{12}N_4O$ requires C, 66.7; H, 4.8; N, 22.2%), $\nu_{max.}$ 3 230s, 3 180s, 3 080s, 2 950m (NH), 1 720vs,br (CO and C=N), 1 605m (C=N or C=C), 1 505s, 755s, and 695s cm^{-1} (Ph).

1-(α-*Ethylthiobenzylidene*)-*5-phenylcarbonohydrazide*.— To a solution of sodium (0.115 g, 0.005 g atom) in ethanol (15 ml), the 5-thiobenzoyl compound (1.43 g, 0.005 mol) was added, followed by ethyl bromide (3.3 g, 0.03 mol) The deep-red solution was stirred at room temperature for 1 h, then added to water (75 ml). The precipitated resin solidified; crystallisation from chloroform–light petroleum (3 : 1) gave prisms (1.02 g, 65%) of the S-*ethyl derivative*, m.p. 151—153° (Found: C, 60.65; H, 5.65; N, 17.6; S, 10.8. $C_{16}H_{18}N_4OS$ requires C, 61.15; H, 5.7; N, 17.8; S, 10.2%), $\nu_{max.}$ 3 400s, 3 300s, 2 950m (NH), 3 100m (C–N–H overtone), 3 050—3 000m (CH_2?), 1 680vs (CO), 1 490s,br (NH/CN), 775s, and 690s cm^{-1} (Ph).

Hydrazinolysis [see 1-thiobenzoylcarbonohydrazide, procedure (f)] gave 4-anilino-3-hydroxy-5-phenyl-1,2,4-triazole (48%), identified by its i.r. spectrum (see above).

1-(α-*Benzylthiobenzylidene*)-*5-phenylcarbonohydrazide*, prepared by the standard procedure and crystallised from chloroform–light petroleum (4 and 1 ml per g), formed an opaque ivory crystalline powder (65—72%), m.p. 132—133° (Found: C, 66.6; H, 5.3; N, 14.8; S, 8.8. $C_{21}H_{20}N_4OS$ requires C, 67.0; H, 5.3; N, 14.9; S, 8.5%), $\nu_{max.}$ 3 220s (NH), 3 000, 2 950m (multiplet, CH_2?), 1 675s,br (CO), 1 500, 1 485s,br (doublet) (NH/CN), 760s, and 690s cm^{-1} (Ph).

Hydrazinolysis of this compound (but including a steam-distillation) gave 4-anilino-3-hydroxy-5-phenyl-1,2,4-triazole (56%).

1-*Benzylidenecarbonohydrazide*

1-*Benzylidene-5-thiobenzoylcarbonohydrazide*.—This was prepared from 1-benzylidenecarbonohydrazide (0.02 mol) by the procedure described for the 5-phenyl analogue (see above). The resulting resinous precipitate solidified, and was broken up, washed with water, and air-dried. Crystallisation from ethanol–acetone (20 and 10 ml per g; recovery 50%) gave pale-yellow felted *needles* (3.6—4.3 g, 60—72%), m.p. 170—172° (Found: C, 60.3; H, 4.8; N, 18.6; S, 10.5. $C_{15}H_{14}N_4OS$ requires C, 60.4; H, 4.7; N, 18.8; S, 10.7%), $\nu_{max.}$ 3 200s, 2 980m (NH), 3 080s (C–N–H overtone), 1 665vs,br (CO), 1 485, 1 455s,br (doublet) (NH/CN), 755s,br, 695, and 685s cm^{-1} (doublet, Ph).

Reactions of 1-*Benzylidene-5-thiobenzoylcarbonohydrazide*. —(*a*) The material was recovered (80%) after being refluxed (0.003 mol) in 1.5N-sodium hydroxide (15 ml) for 30 min. (*b*) It was recovered (60%) after its solution in anhydrous toluene was refluxed in a Dean–Stark apparatus for 1 h.

(c) *Action of hydrochloric acid*. A solution of the reactant (1.50 g, 0.005 mol) in ethanol (40 ml)–5N-hydrochloric acid (10 ml) was refluxed for 15 min and distilled to *ca.* 15 ml (odour of benzaldehyde), and the resulting suspension was diluted with water (10 ml). Crystallisation from ethanol–water (4 and 1 ml) gave pale yellow opaque prisms (0.63 g, 65%) of the 1 : 1 *addition compound* of 2-hydroxy-5-phenyl-1,3,4-thiadiazole and dibenzylidenehydrazine, m.p. 115—120° (after softening at 80°) (Found: C, 68.3; H, 4.5; N, 14.65; S, 9.1. $C_8H_6N_2OS$,$C_{14}H_{12}N_2$ requires C, 68.4; H, 4.7; N, 14.5; S, 8.3%). It was partially soluble in 3N-sodium hydroxide, leaving undissolved dibenzylidenehydrazine as a yellow solid, m.p. 89—92°.

Alternatively, crystallisation of the crude product from chloroform–light petroleum gave 2-hydroxy-5-phenyl-1,3,4-thiadiazole (0.32 g, 36%).

(d) *Action of hydrazine*. Hydrazinolysis as described for 1-thiobenzoylcarbonohydrazide [procedure (f)] gave 4-amino-3-hydroxy-5-phenyl-1,2,4-triazole (75%).

(e) *Action of dimethylformamide*. A solution of the reactant (0.005 mol) in dimethylformamide (30 ml) was boiled under reflux for 1 h (some evolution of hydrogen sulphide), then stirred into ice–water. The resulting emulsion slowly gave a white solid (*ca.* 0.8 g); this was dissolved in ethanol (12 ml), producing successive crops of crystals. The first was 2,5-diphenyl-1,3,4-thiadiazole (0.21 g, 35%), identified by mixed m.p. and i.r. spectrum (see above).

Subsequent crops (0.33 g, 25%) gave, on crystallisation from ethanol, faintly yellow prismatic needles of *4-benzylamino-3-hydroxy-5-phenyl-1,2,4-triazole*, m.p. 190—191° (Found: C, 68.2; H, 5.1; N, 20.4%; M^+, 266. $C_{15}H_{14}N_4O$ requires C, 67.7; H, 5.3; N, 21.05%; *M*, 266), $\nu_{max.}$ 3 350m, 3 200m, 3 100s, 2 950s (NH), 1 690vs (CO and C=N), 1 495m, 760s, and 690s cm^{-1} (Ph), δ [$(CD_3)_2SO$] 3.40 (2 H, s, CH_2), 7.4 and 7.75 (10 H, m, 2 × Ph), and 8.2 (1 H, m, NH).[25] The product was insoluble in 1.5N-sodium hydroxide, even on warming.

1-*Benzylidene-5-*(α-*ethylthiobenzylidene*)*carbonohydrazide*, prepared by the standard procedure (see 1-phenyl analogue, above), formed lustrous prisms (90%), m.p. 156—157° (from chloroform–light petroleum) (Found, for a specimen desolvated at 110° and 3 mmHg for 4 h: C, 63.0; H, 5.5; N, 17.35; S, 9.4. $C_{17}H_{18}N_4OS$ requires C, 62.6; H, 5.5; N, 17.2; S, 9.8%), $\nu_{max.}$ 3 200m (NH), 3 100s (C–N–H overtone), 3 000, 2 950s (doublet, CH_2?), 1 680vs (CO), 1 520, 1 510, 1 495s (triplet, NH/CN), 750s,br, and 695s cm^{-1} (doublet, Ph). Hydrazinolysis of this compound (as described for the parent compound) gave 4-amino-3-hydroxy-5-phenyl-1,2,4-triazole (72%).

1-*Benzylidene-5-*(α-*benzylthiobenzylidene*)*carbonohydrazide*, formed massive plates (67—80%), m.p. 191—192° (from chloroform–light petroleum) (Found: C, 67.4; H, 5.0;

[25] For assignments, see J. A. Elvidge in ' Nuclear Magnetic Resonance,' ed. D. W. Mathieson, Academic Press, London 1967, pp. 179 *et seq.*

N, 13.8; S, 8.0. $C_{22}H_{20}N_4OS$ requires C, 68.0; H, 5.15; N, 14.4; S, 8.25%), $\nu_{max.}$ 3 300m, 3 200m, 2 880s (NH), 3 100s (C–N–H overtone), 2 950s (CH_2?), 1 690vs (CO), 1 520, 1 510, 1 490s (triplet, NH/CN), 765s, and 700s cm^{-1} (doublet, Ph).

1-*Benzylidene*-5-p-*chlorothiobenzoylcarbonohydrazide*.—Interaction of 1-benzylidenecarbonohydrazide (1.78 g, 0.01 mol) and *p*-chlorothiobenzoylthioacetic acid (2.45 g, 0.01 mol) in dimethylformamide (30 ml) for 2 h at room temperature and addition to water precipitated a solid (2.65—3.0 g, 80—90%). This gave, on crystallisation from acetone–ethanol (10 and 30 ml per g; recovery 60%), pale yellow silky needles of the *adduct*, m.p. 181—182° (Found: C, 53.7; H, 4.1; Cl, 11.0; N, 17.0. $C_{15}H_{13}ClN_4OS$ requires C, 54.1; H, 3.9; Cl, 10.7; N, 16.8%), $\nu_{max.}$ 3 200s, 2 950m (doublet) (NH), 3 100m (C–N–H overtone), 1 680vs,br (CO and C=N), 1 485—1 470vs,br (NH/CN), 840s (*p*-disubst. aryl), 755s, and 690s cm^{-1} (Ph).

An identical experiment gave, in two cases, a crude product (3 g), which on crystallisation from ethanol (75 ml) slowly formed faintly yellow needles (1.42 g, 48%), of 2-*benzylidenehydrazino*-5-p-*hydroxyphenyl*-1,3,4-*thiadiazole*, m.p. 173—174° (Found: C, 60.4; H, 4.2; N, 18.7; S, 10.4%; M^+, 296. $C_{15}H_{12}N_4OS$ requires C, 60.8; H, 4.05; N, 18.9; S, 10.8%; *M*, 296), $\nu_{max.}$ 3 200s, 3 000m (NH), 3 100m (C–N–H overtone), 1 680—1 660vs,br (C=N), 750s, and 690s (doublet) cm^{-1} (Ph). The compound was soluble in 1.5N-sodium hydroxide, and reprecipitated by dilute acetic or hydrochloric acid.

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