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CHEMISTRY OF AMIDRAZONES—II

SYNTHESIS AND CYCLISATION OF 1-THIOACYLAMIDRAZONES

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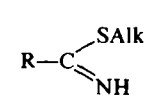
Abstract—1-Thioaroylamidrazones are formed by the action of carboxymethyl dithioates on unsubstituted amidrazones; they are cyclised by acids to 2,5-disubstituted 1,3,4-thiadiazoles. 1-(Ethoxythiocarbonyl)amidrazones are similarly accessible by the use of ethoxythiocarbonylthioacetic acid. They yield 3-ethoxy (or hydroxy)-5-substituted-1,3,4-thiadiazoles under the influence of acids, but are cleaved into smaller fragments by alkalis.

Amidrazones (**1**, **2**)[1] participate in reactions leading to a variety of ring-closures; their versatility in heterocyclic synthesis has long been recognised[1,2] as their chief interest. Although they have remained less familiar than their well-known analogues such as aminoguanidines (**1**, **2**; $R = NH_2$)[3] or amidines,[4] interest in amidrazones has recently greatly intensified.[1]

Substituted amidrazones (**2**) are more readily accessible than the parent compounds (**1**), and most of the knowledge concerning the chemistry of amidrazones has therefore been gained using variously substituted examples.[1] The study of the unsubstituted amidrazones (**1**) is more instructive, however, revealing differences in the reactivities of the hydrazino- and imidoyl-moieties of the amidrazone-group, and providing direct comparisons with analogous structural types, especially amino-(**1**, $R = NH_2$) and diaminoguanidines[3] (**3**, $R = NH_2$), and iso(thio)semicarbazides (**6**).[1]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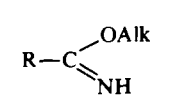
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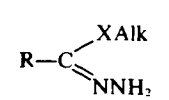
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4

5

6: X = O, S

To provide unsubstituted amidrazones (**1**) for the present work, we developed a simple synthesis based on the hydrazinolysis of the appropriate S-thioethers (**4**), which furnished benzamidrazone and phenylacetamidrazone (**1**; R = Ph, CH_2Ph) in high yield.[5] Acetamidrazone (**1**; R = Me)[6-9] was best obtained from acetamidine.[9] The hydrazinolysis of O-ethyl acetimidate[6] (**5**; R = Me, Alk = Et) was less satisfactory, giving low yields (15–22%), and suffered from the marked sensitivity of most amidrazone syntheses[1] to minor changes in the conditions (see especially, Ref. 6). Thus, treatment of the acetimidate (**5**) with hydrazine hydrate in place of the anhydrous reagent produced the hydrazidine (**3**; R = Me) instead of the amidrazone (**1**; R = Me).

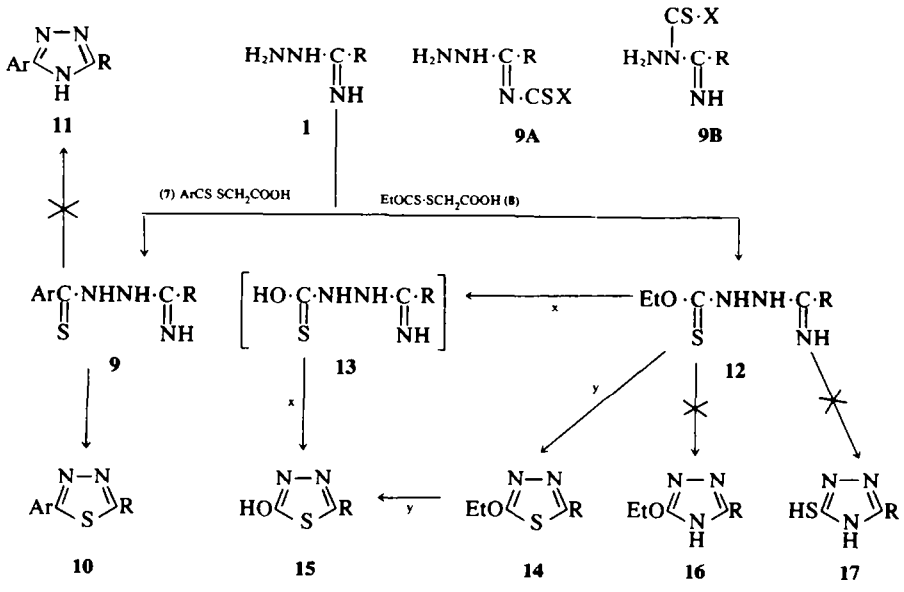
The amidrazones were converted into derivatives and adducts suitable as precursors of heterocyclics. This paper describes the production and cyclisation of thioacylated amidrazones. Three types of thioacylating agents were employed, viz. carboxymethyl dithioates (**7**; Ar = Ph, p-ClC_6H_4),[10,11] ethoxythiocarbonylthioacetic acid ("ethylxanthogenacetic acid") (**8**)[11,12] and a carboxymethyl dithiocarbamate ($Et_2N{\cdot}CS{\cdot}SCH_2COOH$).[11] Amongst comparable carbodithioate esters,[11,13,14] these are known to be particularly serviceable in thioacylating basic centres.

The action of aromatic carboxymethyl dithioates (**7**) on amidrazones (**1**) in slightly alkaline media gave good yields of 1-thioaroylamidrazones (N - imidoyl - N′ - thioaroylhydrazines) (**9**). Their formulation, suggested by the known preference of the thioacylating agents (**7**) to attack the ultimate hydrazino-nitrogen rather than an imino-nitrogen in aminoguanidine,[15,16] is confirmed by their properties, especially their mode of cyclisation (see below). In contrast to the acidic nature of simple thioamides,[13,14,17,18] thioaroylamidrazones (**9**) are essentially basic, undoubtedly owing to the predominating basic strength of their amidino-moiety: they were not appreciably soluble in alkalis, but because of their proneness to cyclisation in acid media, failed to yield isolable picrates.

The IR spectra of the 1-thioaroylamidrazones (**9**) feature several common characteristic peaks. The bands at *ca.* 3400, 3275 and 3070 cm^{-1} are assigned to the amino groups, the latter two being associated with asymmetric and symmetric stretching vibration, respectively. The broad intense band at *ca.* 1650 cm^{-1} and the sharp peak at 1470 cm^{-1} are attributed to C–N stretching vibration combined with NH-deformation. Comparable maxima in the spectra of substituted amidrazones[19,20] on the one hand, and thioamides[21,22] on the other, have been thus interpreted. The aromatic moieties (in **9**) produce the appropriate absorption bands, which require no comment.

Information concerning the IR spectra of thiohydrazides is sparse,[14] but detailed studies of those of thioamides,[13] involving both systematic measurement[21,22] and theoretical calculation[23] have aimed at overcoming the long-standing difficulty of assigning absorption peaks to thiocarbonyl groups linked to nitrogen. In the light of this new information it is suggested that, in the present series of compounds, the N–C–S-stretching (combined with NH_2-rocking) vibration is associated with the band at either 960 or 1080 cm^{-1}, and the CS-vibration with the medium peak below 835 cm^{-1}[21-24] (i.e. corresponding to the D and G thioamide bands of Jensen and Nielsen[22]).

The outstanding chemical property of 1-thioaroylamidrazones (**9**) is their ready cyclisation, with loss of ammonia, to 2-alkyl (or aryl) - 5 - aryl - 1,3,4 - thiadiazoles (**10**). The reaction occurs slowly in neutral media, such as boiling solvents, and proceeds rapidly and completely in acids, providing a facile route to 1,3,4-thiadiazoles that are not accessible by substitution in the

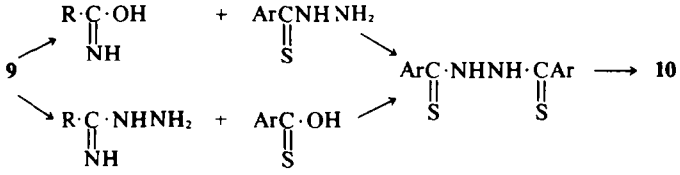


9a,10a: Ar = Ph R = Me
9b,10b: Ar = p-ClC$_6$H$_4$ R = Me
9c,10c: Ar = Ph R = Ph
9d,10d: Ar = p-ClC$_6$H$_4$ R = Ph
9e,10e: Ar = Ph R = CH_2Ph

12a: R = Me
12b,14b,15b: R = Ph
12c,15c: R = CH_2Ph

preformed heterocyclic ring. The nature of the cyclisation products, established by the identity of the 2,5 - diphenyl - compound (**10**; Ar=R=Ph) with authentic material,[16,25] excludes at the same time the possible formulation of the precursors as "branched" isomers (**9A** or **9B**; X = Ar or OEt). The cyclisation thus clearly resembles that of the closely related thioacylsemicarbazides[26] and thioacyl-aminoguanidines,[16] which yield 1,3,4 - thiadiazoles (**10**; R=OH, NHR) under these conditions.

The alternative cyclisation of 1-thioaroylamidrazones (**9**) to 1,2,4-triazoles (**11**) in alkaline media, with loss of hydrogen sulphide, was not observed. The action of boiling 3 N NaOH on **9a** slowly gave low yields of 2,5 - diphenyl - 1,3,4 - thiadiazole (**10c**, 20%), arising presumably from fragments of the cleaved reactant; one possible scheme is suggested in outline:



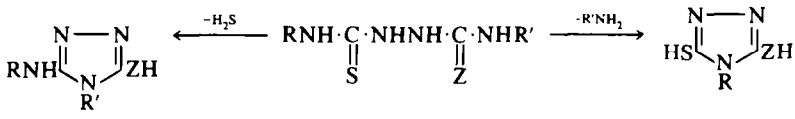
The bulk of the linear reactant (**9a**) appeared to remain unchanged, being converted into 2 - methyl - 5 - phenyl - 1,3,4 - thiadiazole (**10a**) only after acidification. By prolonging the action of the alkali on **9a**, the proportion of **10c** was increased, and that of **10a** diminished, as expected.

The resistance to cyclisation of **9** in alkali is ascribed, as in the case of the analogous thioacylated aminoguanidines,[16] semicarbazides,[16] and carbonohydrazides,[27] to the stabilisation of the thioacyl-group by alkali-salt formation, consistent with the production of the most stable anion in the process.

This interpretation does not conflict with the ready conversion, by alkalis, of comparable substituted thiosemicarbazides (**18**) into 1,2,4-triazoles,[28,29] where cyclisation proceeds predominantly with loss of ammonia or amines, the stabilised thiono-function reappearing in the resultant mercapto - 1,2,4 - triazoles (**20**).[29] However, the degree of stabilisation by alkali of the CS-group is likely to be lower in the thiocarbamoyl-moiety (RNHCS., e.g. in **18**), than in the more acidic RCS-function (in **9**, **12**, etc.): this permits the elimination of hydrogen sulphide from suitable thiosemicarbazides (**18**), resulting in amino - 1,2,4 - triazoles (**19**).[30] In such cases, the alternative more favoured cyclisation (**18**→**20**) may still occur to some extent, so that both types of triazoles are formed side by side (e.g. **19**, **20** from **18**; R = H, R′ = Ph, Z = PhN).[31]

Ethoxythiocarbonylamidrazones (**12**) resembled the foregoing thioacyl-compounds (**9**) both in their mode of formation and cyclisation. They were readily obtained in high yield by the interaction, in aqueous media, of sodium ethoxythiocarbonylthioacetate (**8**)[11,12] and amidrazones (**1**), electrophilic attack occurring at the ultimate hydrazino-nitrogen of (**1**). Their IR spectra resembled in all essentials those of the thioacylamidrazones (**9**) and may no doubt be similarly interpreted (see above).

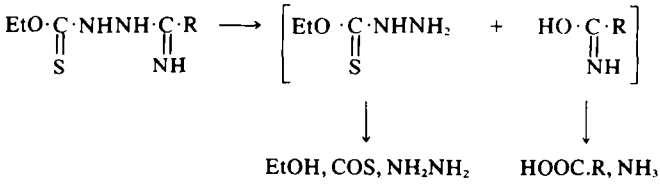
The acidic cyclisation of the ethoxythiocarbonylamidrazones (**12**), proceeding with loss of ammonia, gave 5-substituted 2-hydroxy- (**15**) instead of the expected 2 - ethoxy - 1,3,4 - thiadiazoles (**14**) as principal products. The simultaneous hydrolytic replacement of the ethoxy-group may occur in the initial linear reactant (**12**) (pathway x) or in the 2 - ethoxy - 1,3,4 - thiadiazole (**14**) (pathway y). The feasibility of the latter sequence was shown by the conversion, in good yield, of the 2-ethoxy- into 2 - hydroxy - 5 - phenyl - 1,3,4 - thiadiazole (**14**→**15**) by



19 18 20

hydrochloric acid under the conditions of the ring-closure. Although this does not rule out the alternative route, pathway y is favoured in view of the known speedy formation of the 1,3,4-thiadiazole ring-system, and the isolation of the 2-ethoxy-compound (**14**; R = Ph) as the minor product when (**12**; R = Ph) was employed.

Like their thioacyl-analogues (**9**), ethoxythiocarbonylamidrazones (**12**) were not convertible into 1,2,4-triazoles (e.g. **16**, **17**) by alkalis, but were cleaved into small fragments, as shown by the isolation of phenylacetic acid from **12c**.



A third type of thioacylating agent, carboxymethyl N,N - diethyl - dithiocarbamate ($Et_2N{\cdot}CS{\cdot}SCH_2COOH$),[11] failed to react with amidrazones, being recovered almost quantitatively after interaction with benzamidrazone under various conditions. Semicarbazide which is readily thiobenzoylated,[15,16] likewise failed to react. These observations are in accord with the reported[32,33] lower reactivity of the reagents concerned, and may be ascribed to the effect of the strongly electron-releasing dialkylamino-group, rendering the thiono-carbon a less suitable site for nucleophilic attack than that of the more effective thioacylating agents (**7**, **8**).

EXPERIMENTAL

General. M.ps are uncorrected. The IR spectra were measured on a Unicam SP 200 instrument, using KBr discs. Absorption peaks reported over a range are multiplets.

Starting materials. Benzamidrazone and phenylacetamidrazone hydriodides were prepared as previously described.[5]

Acetamidrazone hydrochloride was prepared (i) By the action of anhyd hydrazine on O-ethyl acetimidate hydrochloride[6] (17–22%). The use of hydrazine hydrate gave acethydrazidine hydrochloride (see below). (ii) By the hydrazinolysis of acetamidine hydrochloride (80–86%).[9] It formed minute prisms, m.p. 118–120° (dec.). Lit. m.p. 131–132°,[6] 130°.[9] (Found: C, 21.55; H, 7.0; N, 39.7; Cl, 32.0. Calc. for $C_2H_7N_3{\cdot}HCl$: C, 21.9; H, 7.3; N, 38.4; Cl, 32.4%). IR: 3380s, 3250–3130s, 1660m (NH); 1705s (C=N); 1450–1390w, 1355m, 1205s, 1150m, 1050s, 960s, 740–690s cm^{-1}.

The *picrate* formed flat needles (80%), m.p. 158–162° (dec.) (from EtOH). (Found: C, 32.2; H, 3.6; N, 27.2. $C_2H_7N_3{\cdot}C_6H_3N_3O_7$ requires: C, 31.8; H, 3.3; N, 27.8%).

Acethydrazidine. A stirred soln of hydrazine hydrate (12.5 g., 0.25 mole) in EtOH (150 ml) was treated at −25° to −20° during 10–12 min with finely powdered O-ethyl acetimidate hydrochloride (31 g, 0.25 mole) (max temp. −10°). Stirring at 0° was continued for 45 min and the collected solid extracted with portions of near-boiling EtOH (4 × 60 ml). Partial vacuum evaporation of the extract gave a solid consisting, after crystallisation from EtOH, of white needles (*ca.* 5.0 g, 32%) of acethydrazidine hydrochloride, m.p. 147–149° (dec. rate-dependent). Lit.[6] m.p. 140–150°. (Found: C, 19.9; H, 6.8; N, 44.5; Cl, 28.7. Calc. for $C_2H_8N_4{\cdot}HCl$: C, 19.3; H, 7.2; N, 45.0; Cl, 28.5%). IR: 3350m, 3300s, 3170s, 3050s, 2980s, 2920s, 1640m (NH); 1700–1680s (C=N); 1560m, 1425m, 1400m, 1340ms, 1140s, 1040m, 960vs br, 850m, 795m, 710m cm^{-1}.

Carboxymethyl p-chlorodithiobenzoate. One half of the volume of a soln of 85% KOH (59.3 g, 0.9 mole) in EtOH (400 ml) was saturated with H_2S, recombined with the other half, and treated with stirring under N_2 at 45–50° with *p*-chlorobenzotrichloride (57.5 g, 0.25 mole) at a rate to keep the temp at 50–60° (1–1.5 hr). The deep-red liquid was refluxed for 30 min, then treated with a soln of chloroacetic acid (33.1 g, 0.35 mole) in H_2O (200 ml) containing $NaHCO_3$ (29.4 g, 0.35 mole), the whole reheated rapidly and refluxed for 5 min. The resulting deep brownish-red liquid was decanted from a stickly resin (8–10 ml) and acidified with conc HCl (to Congo red). The orange ppt (35–40 g) gave, on crystallisation from $CHCl_3$–light petroleum (200 ml each), reddish-orange plates (22.3–28 g, 36–45%) of the product, m.p. 118–120°. (Found: C, 44.2; H, 3.3. Calc. for $C_9H_7ClO_2S_2$: C, 43.8; H, 2.8%). IR: 3100–2500s br (COOH); 1680s br (CO); 1045s (?CS); 825s (p-disub. aryl); 1570s, 1470ms, 1405ms, 1390ms, 1315ms, 1230ms, 1195s, 1080s, 1000s, 875ms, 660ms cm^{-1}.

In this instance, the foregoing procedure[10] is more effective than the methods[11] employing the appropriate thiopiperidide (*p*-$ClC_6H_4CSNC_5H_{10}$)[34] or Grignard reagent (*p*-ClC_6H_4MgX)[34–36] as starting materials.

THIOBENZOYLATION

N-Acetimidoyl-N′-thiobenzoylhydrazine (**9a**)

(a) *Preparation.* A stirred soln of acetamidrazone hydrochloride (10.95 g, 0.01 mole) in N NaOH (100 ml, 0.01 mole) was treated at room temp during 3–5 min with carboxymethyl dithiobenzoate (15.9 g, 0.075 mole) dissolved in N NaOH (100 ml, 0.01 mole). The turbid liquid slowly deposited a yellow ppt, which was collected after 3 hr (filtrate: F). Rapid crystallisation from MeOH (50 ml) gave **9a**, m.p. 136–138° as lustrous prisms (opaque on storage) (8.1–9.3 g, 56–64%). (Found: C, 55.4; H, 5.3; N, 21.3; S, 16.7. $C_9H_{11}N_3S$ requires C, 56.0; H, 5.7; N, 21.8; S, 16.6%). IR: 3450s, 3280m, 3050s br, 2710m (NH); 1655s br (C=N); 1090s or 1070s, 960s (N–C–S?); 780s, 700s (Ph); 1600, 1590s, 1475s, 1430m br, 1235s br, 915s, 725s cm^{-1}. The compound was not appreciably soluble in 2N NaOH, even on warming (when decomposition set in).

The aqueous filtrate F gave, on acidification with AcOH and prolonged storage, lustrous pale yellow crystals (0.5–1.05 g, 4–8%), identified as **10a** by mixed m.p. and IR spectrum (see b, below).

(b) *Cyclisation by acid.* A soln of **9a** (1.93 g, 0.01 mole) in EtOH (15 ml)–3N HCl (12 ml) was refluxed for 30 min. The crystalline product which separated after partial evaporation and storage (24 hr) (0.75 g, 85%) was **10a**, m.p. 103–105°. Lit. m.p. 105–107°, 107–108°[37,38] (Found: C, 60.9; H, 4.7; N, 15.7; S, 18.3. Calc. for $C_9H_8N_2S$: C, 61.4; H, 4.5; N, 15.9; S, 18.2%). IR: 3020w (CH arom.); 2880w (CH_2); 1500w (C=C); 765s, 685s (Ph); 1455s, 1420s, 1230s, 1200, 1185, 1175m, 1060s, 990, 985, 975m, 920m, 845w cm^{-1}.

(c) *Cyclisation by alkali.* A soln of **9a** (0.01 mole) in EtOH (15 ml)–3N NaOH (12 ml) was boiled for 10 min (evolution of NH_3) and set aside at room temp for 24 hr. The separated crystalline product (filtrate: F) was 2,5 - diphenyl - 1,3,4 - thiadiazole (0.24 g, 20%). Filtrate F gave, on acidification at 0°, a crystalline solid identified as 2 - methyl - 5 - phenyl - 1,3,4 - thiadiazole (1.15 g; 65%)

by mixed m.p. and IR spectrum (see above). The IR spectra of **10a** and **10c** (see below) are barely distinguishable except for the presence in the former of the additional medium strong triplet centred at 1185, and the weak peak at 845 cm^{-1}.

The following substituted hydrazines (**9b–e**) were obtained by the general method (a) (crystallised from EtOH):

N - *Acetimidoyl* - N' - (p - *chlorothiobenzoyl)hydrazine* (**9b**), (65%), platelets, m.p. 164–167° (dec.). (Found: C, 47.7; H, 4.7; Cl, 15.65; N, 17.8; S, 13.9. $C_9H_{10}ClN_3S$ requires: C, 47.5; H, 4.4; Cl, 15.6; N, 18.5; S, 14.1%). IR: 3370s, 3270m, 3070s br (NH); 1660s br (C=N); 845s (*p*-disub. aryl); 745m, 720m (aryl); 1085s br, 960, 950ms (N–C–S ?); 1605s br, 1470, 1460s, 1245, 1230s, 1010s, 910s cm^{-1}.

N - *Benzimidoyl* - N' - *thiobenzoylhydrazine* (**9c**), (rapid separation, collected after 2 hr, filtrate: F), pale yellow platelets (1.28 g, 50%), m.p. 154–156° (dec.). (Found: C, 66.2; H, 4.9; N, 16.9; S, 12.7. $C_{14}H_{13}N_3S$ requires: C, 65.9; H, 5.1; N, 16.5; S, 12, 55%). IR: 3270m, 3070s br (NH); 1640s br (C=N); 785, 775s, 690s (Ph); 1070ms, 945s (N–C–S ?); 835m (CS ?), 1605m, 1570s, 1460s, 1430m, 1305m, 1230s br cm^{-1}. Acidification of filtrate F gave 2,5 - diphenyl - 1,3,4 - thiadiazole (12–15%).

N - *Benzimidoyl* - N' - p - *chlorothiobenzoylhydrazine* (**9d**), (80%), platelets, m.p. 177–179°. (Found: C, 58.2; H, 4.7; Cl, 12.3; N, 14.3. $C_{14}H_{12}ClN_3S$ requires C, 58.0; H, 4.1; Cl, 12.25; N, 14.5%). IR: 3280m, 3080s br (NH); 1645s br (C=N); 845s (*p*-disub. aryl); 695s (aryl); 1090, 1075ms, 945s (N–C–S ?), 780m (CS ?); 1460s br, 1245s br, 1020ms cm^{-1}.

N - *Phenylacetimidoyl* - N' - *thiobenzoylhydrazine* (**9e**), (72%), platelets, m.p. 184–187° (from a large volume of acetone–EtOH). (Found: C, 66.5; H, 5.4; N, 16.25; S, 11.9. $C_{15}H_{15}N_3S$ requires C, 66.9; H, 5.6; N, 15.6; S, 11.9%). IR: 3450s, 3080s br (NH); 1655s br (C=N); 760s, 700s (Ph); 1090m, 1070m, 965m (N–C–S ?); 725m (CS ?); 1600m, 1470, 1480s, 1240s, 915m cm^{-1}.

The following 2,5-disubstituted 1,3,4-thiadiazoles (**10b–10e**) were obtained by the cyclisation in acid media of **9b–9e** by method (b):

2 - p - *Chlorophenyl* - 5 - *methyl* - 1,3,4 - *thiadiazole* (**10b**), (70%), minute platelets, m.p. 133–135° (from EtOH). (Found: C, 51.5; H, 3.5; Cl, 17.4; N, 12.65. $C_9H_7ClN_2S$ requires C, 51.3; H, 3.3; Cl, 16.85; N, 13.3%). IR 3080w (CH arom.); 2900w (CH_2); 855s (*p*-disub. aryl); 705m (aryl); 1585s, 1440–1420s, 1400m, 1260m, 1230m, 1195, 1180m, 1090s, 980m, 825s, 780m cm^{-1}.

2,5 - *Diphenyl* - 1,3,4 - *thiadiazole* (**10c**), (70%), m.p. 138–140°. IR: 3020w (CH arom.); 1500w (C=C); 760vs, 690vs (Ph); 1460s, 1430s, 1240ms, 1065m, 1005, 990m, 920m cm^{-1}.

2 - p - *Chlorophenyl* - 5 - *phenyl* - 1,3,4 - *thiadiazole* (**10d**), (nearly 100%), microplatelets, m.p. 181–183° (from acetone). Lit[39,40] m.p. 181–182° (Found: C, 61.3; H, 3.9; Cl, 13.1; N, 10.6; S, 12.0. Calc. for $C_{14}H_9ClN_2S$: C, 61.7; H, 3.3; Cl, 13.0; N, 10.3; S, 11.7%). IR: 3050w (CH arom.); 840s (*p*-disub. aryl); 690s (aryl); 1600m, 1505m, 1460, 1445, 1425m, 1240m, 1095s, 760s cm^{-1}.

2 - *Benzyl* - 5 - *phenyl* - 1,3,4 - *thiadiazole* (**10e**), (64%), minute prisms, m.p. 71–73° (from MeOH). (Found: C, 71.45; H, 4.6; N, 11.65. $C_{15}H_{12}N_2S$ requires C, 71.4; H, 4.8; N, 11.1%). IR: 3050w (CH arom.); 2930w (CH_2); 775s, 690s (Ph); 1500m, 1460s, 1430m, 1060m, 985m cm^{-1}.

N - *Benzimidoyl* - N' - *ethoxythiocarbonylhydrazine* (**12b**)

(d) *Preparation.* A stirred soln of benzamidrazone hydriodide[5] (3.15 g, 0.012 mole) in 0.5N NaOH (24 ml, 0.012 mole) was treated at room temp during 5 min with a soln of ethoxythiocarbonylthioacetic acid[11,12] (1.80 g, 0.01 mole) in 0.5N NaOH (3.3 ml, 0.01 mole), and stirring continued for 2 hr. The crystalline solid, which had begun to separate after 10 min was collected at 0°, and a second crop after more prolonged storage (m.p. 158–160°; total 1.4–1.6 g, 64–72%). Crystallisation from v. little EtOH (recovery only 30%) gave **12b** as prisms, m.p. 155–156°. (Found: C, 53.5; H, 6.2; N, 19.3; S, 14.2. $C_{10}H_{13}N_3OS$ requires: C, 53.8; H, 5.8; N, 18.3; S, 14.35%). IR: 3400s, 3300s, 3180m, 3080s, 1615s (NH); 2990w (CH arom.); 2890w (CH_3); 1660s (C=N); 1065ms (N–C–S ?); 855m (CS ?); 780s, 695s (Ph); 1495, 1460, 1440vs; 1225–1200s, 1025m, 660m cm^{-1}. The compound was soluble in cold 2N NaOH and reprecipitated by 2N AcOH, but only transiently by 3N HCl.

(e) *Cyclisation by acid.* (**14b**, **15b**). The reactant (1.12 g, 0.005 mole), suspended in water (10 ml), was dissolved by the addition of 3N HCl (5 ml.) and the liquid boiled under reflux for 30 min. The deposited oil solidified on storage at 0°, and was extracted with N NaOH (10 ml).

The undissolved residue (0.33 g, 32%) was **14b**, m.p. 64–66° (from EtOH). Lit m.p. 69–70°,[37] 68°,[41] but also 26–27°,[42] and 45–46°[43] (Found: C, 57.9; H, 4.8; N, 13.3. Calc. for $C_{10}H_{10}N_2OS$: C, 58.25; H, 4.85; N, 13.6%). IR: 2980m (CH arom); 2800m (CH_3); 1500s; 770, 760s, 685s (Ph); 1465s, 1395ms, 1260s, 1020ms, 885ms cm^{-1}.

Acidification of the alkaline extracts gave crystalline **15b** (0.55 g, 62%) as platelets, m.p. 147–148° (from EtOH). Lit.[27] m.p. 146–148° (identified by mixed m.p. and IR spectrum[27]).

The following substituted hydrazines (**12a**, **12c**) were prepared by method (d):

N - *Acetimidoyl* - N' - *ethoxythiocarbonylhydrazine* (**12a**), (isolated by neutralisation of the clear reaction mixture with 3N HCl and evaporation to small bulk in a vacuum), (52%); minute needles, m.p. 137–139° (from very little EtOH). (Found: C, 37.5; H, 6.45; N, 25.4; S, 19.3. $C_5H_{11}N_3OS$ requires: C, 37.3; H, 6.8; N, 26.1; S, 19.9%). IR: 3380ms, 3140s br, 1620m br (NH); 2980w (CH_3); 1675s br (C=N); 825 m (CS ?); 1520s br, 1470, 1460s, 1385m, 1195s br, 940–920m, 680w br cm^{-1}.

N - *Ethoxythiocarbonyl* - N' - *phenylacetimidoylhydrazine* (**12c**), (90%), m.p. 167–168° (from EtOH). (Found: C, 55.15; H, 6.2; N, 17.3. $C_{11}H_{15}N_3OS$ requires C, 55.7; H, 6.3; N. 17.7%). IR: 3360s, 3180m, 3090m, 1615m (NH); 2980w (CH arom); 2900w (CH_3); 1665s (C=N); 705m (Ph); 1070m (N–C–S ?); 1490m, 1465s, 1420m, 1190s br, 665m br cm^{-1}.

Cyclisation of **12c** by method (e) gave 2 - *benzyl* - 5 - *hydroxy* - 1,3,4 - *thiadiazole* (**15c**), forming needles, m.p. 95–96° (from MeOH) (78%). (Found: C, 56.1; H, 4.25; N, 15, 1; S, 16.8. $C_9H_8N_2OS$ requires: C, 56.25; H, 4.2; N, 14.6; S, 16.7%). IR: 3200s br (NH); 2950w (CH arom.); 2850w (CH_2); 1655vs br (CO/C=N); 760s (Ph); 1555s, 1500m, 1460m, 1425m, 1195s, 800s, 680m br cm^{-1}.

Action of sodium hydroxide on **12c**. A soln of **12c** (0.005 mole) in N NaOH (12 ml) was boiled under reflux for 3 hr then acidified with conc HCl. The precipitated oil which solidified on storage was phenylacetic acid (0.31 g, 46%).

Action of hydrochloric acid on **14b**. A soln of the reactant (0.21 g, 0.001 mole) in EtOH (5 ml)–3N HCl (5 ml) was boiled under reflux for 1 hr. The needles (70%) that separated on storage were **15b**, identified by mixed m.p. and IR spectra.

Carboxymethyl N,N - *diethyldithiocarbamate*, obtained (above 90%) from sodium diethyldithiocarbamate trihydrate (1 mole) and chloroacetic acid (0.8 mole) in boiling aq 0.5M $NaHCO_3$ (1 mole) (20 min) (compare Refs 32, 33), had IR 3000, 2950s, 2700ms, 2600ms, 1705vs, 1495s, 1425s, 1350s, 1315s, 1210, 1195s, 1140ms, 1065ms, 980ms, 920ms br, 830ms, 665ms cm^{-1}.

The reagent (1 mole) was recovered (by precipitation with 3N HCl) (i) after a soln containing it (1 mole) and benzamidrazone hydriodide (1.5 mole) in N NaOH (3.5 mole) was kept at room temp for 15 hr (recovery, 75%).

(ii) After being treated with semicarbazide HCl (1.5 mole) in N NaOH (3 mole) for 1 hr at room temp, or at the b.p. (recovery 80 and 70%, respectively).

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