

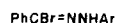
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Benzohydrazides, benzothiohydrazides, and benzamidrazones have been converted to 1,3,4(2*H*)-oxadiazolenones, 1,3,4(2*H*)-thiadiazolenones, and 1,2,4(5*H*)-triazolenones respectively by reaction with ethyl chloroformate, with ethyl thiolchloroformate, and with phenyl isocyanate. In some reactions, a carbamate or urea has been isolated as intermediate.

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Our studies in the 1,3,4-oxadiazole and 4,1,2(1*H*)-benzoxadiazine series and in the 1,3,4-thiadiazole and 4,1,2(1*H*)-benzthiadiazine series [1] have involved a number of hydrazonyl halides **1**, hydrazides **2**, and thiohydrazides **3** as intermediates. Hydrazides, thiohydrazides, and related amidrazones **4** are also reasonable choices as precursors of 1,3,4(2*H*)-oxadiazolenones **5** (X, Y = O), 1,3,4(2*H*)-thiadiazolenones **5** (X = S, Y = O), and 1,2,4(5*H*)-triazolenones **5** (X = NH, Y = O) respectively. Heterocycles of structural types **5** were of potential interest for 1,3-dipolar addition studies [2], while 1,3,4(2*H*)-thiadiazolenones are useful in our continuing work in the 1,3,4-thiadiazole series [1]. We have accordingly examined the reactions of representative hydrazides, thiohydrazides, and amidrazones with ethyl chloroformate, ethyl thiolchloroformate, and phenyl isocyanate.



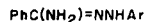
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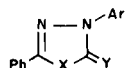
2



3



4



5

a: Ar = Ph
b: Ar = C₆H₃Br₂ (2, 4)

Reaction of *N*'-phenylacetylhydrazide with ethyl chloroformate is known to give the *N*'-ethoxycarbonyl derivative (carbamate) and hence by thermolysis the corresponding oxadiazolenone [3]. We found that **2a** and **b**, similarly treated in benzene or in acetonitrile with added triethylamine, also gave carbamates which could be thermolysed

to oxadiazolenones **5a** and **b** (X, Y = O) respectively. Compound **2a** and ethyl thiolchloroformate in benzene, however, gave a mixture (tlc) of two compounds (probably the thiolcarbamate and oxadiazolenone) which on heating gave **5a** (X, Y = O), albeit in indifferent yield. The corresponding **5b** (X, Y = O) was obtained directly from a similar reaction conducted in ethanol with added triethylamine.

Reaction of **2b** with phenyl isocyanate, sluggish in benzene, occurred readily when the two ingredients were heated directly together. This procedure gave oxadiazolenone **5b** (X, Y = O), a small amount of its anil **5b** (X = O, Y = NPh) (ms: m/e 469), and *N,N'*-diphenylurea [4]. The first two products arise from alternative thermolytic pathways (elimination of either aniline or water); both aniline and water react with excess phenyl isocyanate to give *N,N'*-diphenylurea.

Thiohydrazide **3b**, prepared by treating **2b** with phosphorus pentasulfide or better by treating **1b** with sodium hydrosulfide, reacted smoothly both with ethyl chloroformate and with ethyl thiolchloroformate in ethanol with added triethylamine to give **5b** (X = S, Y = O). Reaction of **3b** with phenyl isocyanate under reflux gave the same thiadiazolenone, a small amount of its anil **5b** (X = S, Y = NPh) (mass spectrum m/e 485), and *N,N'*-diphenylurea. This thiadiazolenone has previously been prepared indirectly *via* the imine **4b** (X = S, Y = NH) [5]. Interestingly, treatment of **3b** with cyanogen bromide in ethanol with added triethylamine gave the *bis*-hydrazonyl disulfide, not the imine, a reaction which finds precedent in the oxidation of thiohydrazides by iodine [6].

In the triazolenone series, **5a** (X = NH, Y = O) has been synthesized by condensing ethyl *N*-benzoylcarbamate with phenylhydrazine and then thermolysing the intermediate carbamate [7]. The same intermediate may be transiently involved in a more recent synthesis from ethyl

carbamate and 2,5-diphenyltetrazole [4]. We found that **4b** reacted readily both with ethyl chloroformate and with ethyl thiolchloroformate and that crystallization gave **5b** (X = NH, Y = 0) directly in each case. We also noted that **4b** reacted smoothly with phenyl isocyanate in hot toluene to give a urea derivative which cyclized to **5b** (X = NH, Y = 0) at higher temperature [8].

The reactions of compounds **2-4** with ethyl chloroformate and with ethyl thiolchloroformate provide reasonably convenient sources of heterocycles **5**, and are alternatives to reactions involving phosgene [9]. The mass spectra of our heterocycles **5** are characterized by a main breakdown of the molecular ion to the diarylnitrilimine ion ($M^+ - CXY$). However, unlike the 2-oxazolen-5-ones and the oxazolium 5-oxides [10], these heterocycles **5** are relatively quite stable to heat. The 2,5-diaryltetrazoles and especially the hydrazonoyl halides [2,11] remain preferred sources of diarylnitrilimines in 1,3-dipolar addition reactions.

EXPERIMENTAL

Instrumental techniques were as noted previously [1]. Criteria for identity were mp and mixture mp, tlc, and ir and mass spectral correlation, with authentic samples when available. Prepared for reference purposes by the literature method, **5b** (X = NH, Y = 0) had mp 275.5-277° (lit [5], mp 274°); ms: m/e 393 (M^+) and 350 ($M^+ - NHCO$).

N'-(2,4-Dibromophenyl)benzothiohydrazide (**3b**).

(a) A suspension of sodium hydrosulfide (2.76 g, 0.03 mole) (predried at 100° *in vacuo* for 20 minutes) and **1b** (Caution: possibility of allergic reaction) [12] (4.33 g, 0.01 mole) in ethanol (100 ml) was refluxed for 24 hours, cooled, diluted with water, acidified with acetic acid, and the solid was collected. Crystallization from light petroleum (bp 60-90°) gave **3b** (2.5 g, 65%), mp 114-115°, identical with an authentic sample (lit [6], mp 118-119°).

(b) A mixture of **2b** [13] (1.0 g), phosphorus pentasulfide (0.7 g), and toluene (50 ml) was refluxed for 4 hours and then ethanol (50 ml) was added. After, several days, the solution was evaporated *in vacuo*. Trituration of the residue with light petroleum (bp 60-90°) and crystallization from cyclohexane gave **3b** (0.54 g, 52%), mp 115-116°.

Reactions Involving Ethyl Chloroformate and Ethyl Thiolchloroformate.

(a) A mixture of **2a** (10.0 g), ethyl chloroformate (5.1 g), and dry benzene (100 ml) was refluxed for 4 hours, and then evaporated. *N'*-Ethoxycarbonyl-*N'*-phenylbenzohydrazide (10.4 g, 78%) crystallized from light petroleum (bp 100-120°) as prisms mp 132-133°; ir (potassium bromide): 1725 and 1655 (CO) cm^{-1} .

Anal. Calcd. for $C_{16}H_{16}N_2O_3$: C, 67.61; H, 5.63; N, 9.86. Found: C, 67.6; H, 5.9; N, 9.9.

N'-Ethoxycarbonyl-*N'*-phenylbenzohydrazide (9.2 g) was heated under reflux (bath temperature 190-200°) for 1 hour. On cooling, **5a** (X, Y = 0) (5.7 g, 74%) crystallized as prisms, mp 112-113° (Lit [9], mp 113-114°).

Anal. Calcd. for $C_{14}H_{10}N_2O_2$: C, 70.59; H, 4.20; N, 11.76. Found: C, 70.6; H, 4.2; N, 11.9.

A mixture of **2b** (1.0 g), ethyl chloroformate (0.45 g), acetonitrile (20 ml), and triethylamine (0.75 g), similarly treated for 2 hours, gave *N'*-ethoxycarbonyl-*N'*-(2,4-dibromophenyl)benzohydrazide (0.5 g, 42%), mp 104-106° (from light petroleum, bp 80-100°).

Anal. Calcd. for $C_{12}H_8Br_2N_2O_3$: C, 43.43; H, 3.17; N, 6.33. Found: C, 43.48; H, 3.15; N, 6.44.

N'-Ethoxycarbonyl-*N'*-(2,4-dibromophenyl)benzohydrazide (0.45 g),

heated as above for 3 hours gave **5b** (X, Y = 0) (0.2 g, 50%), mp 121° (from light petroleum, bp 80-100°).

Anal. Calcd. for $C_{14}H_8Br_2N_2O_2$: μ , 411.8703. Found: μ (ms) 411.8922.

A mixture of **2b** (100 mg), ethyl thiochloroformate (32 mg), ethanol (15 ml), and triethylamine (75 mg) was refluxed for 2 hours and then evaporated. Crystallization from light petroleum (bp 110-115°) gave **5b** (X, Y = 0) (64 mg, 60%), mp 121°; ms: m/e 394 (M^+) and 350.

(b) A mixture of **3b** (400 mg), ethyl chloroformate (150 mg), ethanol (25 ml), and triethylamine (300 mg) was refluxed for 30 minutes and then evaporated *in vacuo*. Crystallization from light petroleum (bp 100-115°) gave **5b** (Y = S, Y = 0) (350 mg, 82%), mp 145-146° (lit [5], mp 148-150°).

A similar experiment using **3b** (386 mg) and ethyl thiolchloroformate (124 mg) in place of ethyl chloroformate gave **5b** (X = S, Y = 0) (335 mg, 82%), mp 145-146°; ms: m/e 410 (M^+) and 350.

(c) A solution of **4b** [12] (0.7 g) and ethyl chloroformate (0.5 g) in acetone (30 ml) was stirred for 15 minutes. Crystallization of the precipitated solid from isoamyl alcohol gave **5b** (X = NH, Y = 0) (0.3 g, 40%), mp 270-272°.

A similar experiment using ethyl thiolchloroformate (0.5 g) in place of ethyl chloroformate also gave **5b** (X = NH, Y = 0) (0.4 g, 53%), mp 270-272°.

Reactions Involving Phenyl Isocyanate.

(a) A solution of **2b** (185 mg) in a few ml of phenyl isocyanate was refluxed under dry nitrogen for 1.5 hours. The solution was evaporated *in vacuo* and residual phenyl isocyanate was then removed by co-evaporation with dry benzene. Three successive crystallizations from light petroleum (bp 100-120°) gave **5b** (X, Y = 0) (110 mg, 56%), mp 120-121°.

Similarly treated, **3b** (386 mg) gave **5b** (X = S, Y = 0) (140 mg, 34%), mp 145-147° (after three crystallizations).

(b) A solution of **4b** (1.0 g) and phenyl isocyanate (323 mg, 1 equivalent) in dry toluene (30 ml) was heated under nitrogen for 3 hours. A solid separated. Crystallization from 1,4-dioxan gave the derived urea (820 mg, 62%) as silky needles, transformed during mp determination to **5b** (X = NH, Y = 0), mp 274-276.5°; ms: m/e 486 (M^+), 393, 367 ($M^+ - PhNCO$), and 350.

Anal. Calcd. for $C_{20}H_{16}Br_2N_4O$: C, 49.18; H, 3.28; Br, 32.79. Found: C, 48.84; H, 3.38. Br, 32.50.

Bis-[α -(2,4-dibromophenylhydrazono)benzyl] Disulfide.

A solution of **3b** (386 mg), cyanogen bromide (106 mg), and triethylamine (200 mg) in ethanol (20 ml) was refluxed for 2 hours. The solution was concentrated *in vacuo* to approximately half-bulk and the solid was collected. Crystallization from light petroleum (bp 100-115°) gave the disulfide (260 mg, 68%), mp 169°, identical with an authentic specimen (lit [14], mp 168-169°).

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