REACTION OF 1-BROMO-2-ACYLACETYLENES WITH THIOBENZHYDRAZIDE

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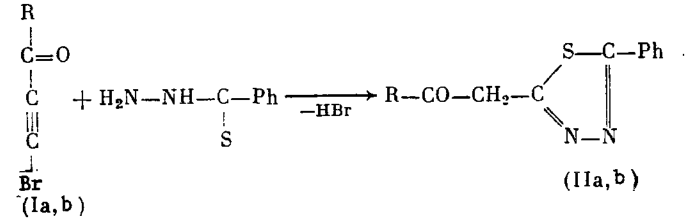
Aromatic thiohydrazides react with the dimethyl ester of acetylenedicarboxylic acid and methyl propiolate in methanol at reflux to give 2-methoxycarbonyl-2-methoxycarbonylmethyl- and 2-methoxycarbonylmethyl-5-aryl-2,3-dihydro-1,3,4-thiadiazoles in 50-65% yield [1].

We have found that the reaction of 1-bromo-2-acylacetylenes (Ia) and (Ib) with an equivalent amount of thiobenzhydrazide in a protic solvent (methanol) at from −10 to −30°C gives 2-acylmethyl-5-phenyl-1,3,4-thiadiazoles (IIa) and (IIb) in 64-75% yield. In the presence of equivalent amounts of Et_3N, the product yields are increased to 73-90%.


(Ia,b)
(IIa,b)

R = Ph (a), 2-thienyl (b).

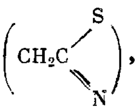
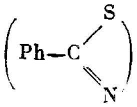
The reaction of 1-bromo-2-acylacetylenes (Ia) and (Ib) with an equivalent amount of thiobenzhydrazide in absolute ether at from −10 to −30°C proceeds with the formation of the hydrobromide salts of 2-acylmethyl-5-phenyl-1,3,4-thiadiazoles (IIa) and (IIb) in 65-74% yield.

2-Acylmethyl-5-phenyl-1,3,4-thiadiazoles (IIa) and (IIb) are readily formed from the corresponding hydrobromide salts upon their recrystallization from acetone, methanol, ethanol, or aqueous ethanol.

The reaction of 1-bromo-2-acylacetylenes (Ia) and (Ib) with thiobenzhydrazide proceeds apparently by nucleophilic substitution of the bromine atom at the ethynyl carbon atom [2, 3].

EXPERIMENTAL

The IR spectra were taken on a UR-75 spectrophotometer in KBr pellets. The PMR spectra were taken on a Tesla BS-487C spectrometer at 80 MHz. The ^{13}C NMR spectrum was taken on a Jeol FX-90Q spectrometer at 22.49 MHz. The mass spectra were taken on an MKh-1303 mass spectrometer with direct sample inlet into the ion source. The ionizing voltage was 30 eV.

2-Benzoylmethyl-5-phenyl-1,3,4-thiadiazole (IIa). A solution of 1.05 g (5 mmoles) 1-bromo-2-benzoylacetylene (Ia) in 20 ml methanol was added slowly to a solution of 0.76 g (5 mmoles) thiobenzhydrazide in 10 ml methanol at −30°C. The mixture was slowly warmed to 0°C. The precipitate formed was filtered off, washed with cold methanol, and dried in vacuum to give 1.05 g (75%) yellow crystalline (IIa), mp 175-177°C (from ethanol). IR spectrum (ν, cm^{-1}): 670 (C−S), 1400-1470 (ring vibrations), 1580-1605 (arom. C=C), 1680 (C=O), 3090 (C−H). PMR spectrum in $CDCl_3$ (δ, ppm): 4.90 s (2H, CH_2), 7.52-8.04 m (10H, Ph). ^{13}C NMR spectrum in $CDCl_3$ (δ, ppm): 193.68 (C=O), 170.06 , 161.88 , 40.0 (CH_2), 127.86-134.19 (benzene ring CH). Mass spectrum: 280 (20) $[M]^+$, 175 (50) $[M-PhCO]^+$, 119 (30) $[M-CH_2COPh]^+$, 105 (100) $[PhCO]^+$, 77 (40) $[Ph]^+$. Found: C, 68.80; H, 4.40; N, 10.02; S, 11.45%. Calculated for $C_{16}H_{12}N_2OS$: C, 68.57; H, 4.29; N, 10.00; S, 11.42%.

The yield of 1,3,4-thiadiazole (IIa) under analogous conditions in the presence of an equimolar amount of triethylamine was 1.26 g (90%). When the ketone/thiobenzhydrazide ratio

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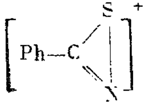
was 1:2, we obtained 0.99 g (71%) 1,3,4-thiadiazole (IIa) and 0.12 g (20%) 2,5-diphenyl-1,3,4-thiadiazole as colorless crystals with mp 140-142°C (141-142°C [4]).

2-(Theno-2-yl)methyl-5-phenyl-1,3,4-thiadiazole (IIb). This was obtained by analogy to (IIa) from 0.76 g (5 mmoles) thiobenzhydrazide and 1.08 g (5 mmoles) 1-bromo-2-thenoylacetylene (Ib). The yield of (IIb) was 0.92 g (64%) as dark yellow crystals, mp 150-153°C (from ethanol). Under analogous conditions, 1.04 g (73%) (IIb) was obtained in the presence of triethylamine. IR spectrum (ν, cm^{-1}): 695 (C−S), 1410-1455 (ring vibrations), 1580-1620 (arom. C=C), 1660 (C=O), 3100 (C−H). PMR spectrum in $CDCl_3$ (δ, ppm): 4.80 s (2H, CH_2), 7.46-7.94 m (8H, Ph, C_4H_3S). Mass spectrum: 286 (25) $[M]^+$, 135 (50)  , 111 (100) $[C_4H_3S-CO]^+$, 77 (60) $[Ph]^+$. Found: C, 58.93; H, 3.46; N, 9.90; S, 22.60%. Calculated for $C_{14}H_{10}N_2OS_2$: C, 58.74; H, 3.50; N, 9.79; S, 22.38%.

Hydrobromide Salt of 2-Benzoylmethyl-5-phenyl-1,3,4-thiadiazole. A solution of 1.05 g (5 mmoles) 1-bromo-2-benzoylacetylene (Ia) in 20 ml absolute ether was slowly added to a solution of 0.76 g (5 mmoles) thiobenzhydrazide in 30 ml absolute ether at −30°C. The mixture was slowly warmed to 20°C. The precipitate formed was filtered off, washed with absolute ether, and dried in vacuum to give 1.33 g (74%) of a yellow crystalline product, 114-116°C. IR spectrum (ν, cm^{-1}): 675 (C−S), 1405-1480 (ring vibrations), 1580-1605 (arom. C=C), 1675 (C=O), 2550-3130 (N^+H). Found: C, 53.34; H, 3.42; Br, 22.56; N, 7.94; S, 8.61%. Calculated for $C_{16}H_{12}N_2OS \cdot HBr$: C, 59.19; H, 3.60; Br, 22.16; N, 7.76; S, 8.86%.

The yield of this hydrobromide salt was 1.26 g (70%) under analogous conditions at −10°C.

In acetonitrile, 0.53 g (30%) hydrobromide salt and 0.31 g (24%) 2-benzoylmethyl-5-phenyl-1,3,4-thiadiazole (IIa) were obtained at −30°C.

Hydrobromide Salt of 2-(Theno-2-yl)methyl-5-phenyl-1,3,4-thiadiazole. This was obtained analogously from 1.08 g (5 mmoles) 1-bromo-2-thenoylacetylene (Ib) and 0.76 g (5 mmoles) thiobenzhydrazide. The product yield was 1.2 g (65%) as dark yellow crystals, mp 99-102°C. IR spectrum (ν, cm^{-1}): 680 (C−S), 1400-1470 (ring vibrations), 1570-1590 (arom. C=C), 1655 (C=O), 2560-3150 (N^+H). Found: C, 45.90; H, 2.85; Br, 21.44; N, 7.63; S, 17.44%. Calculated for $C_{14}H_{10}N_2OS_2 \cdot HBR$: C, 45.78; H, 3.00; Br, 21.80; N, 7.63; S, 17.44%.

Under analogous conditions, the product yield was 1.14 g (62%) at −10°C.

CONCLUSIONS

The reactions of 1-bromo-2-acylacetylenes with thiobenzhydrazide at from −10 to −30°C in ether, acetonitrile, methanol without catalyst, or methanol in the presence of triethylamine gave 2-acylmethyl-5-phenyl-1,3,4-thiadiazoles and their hydrobromide salts.

LITERATURE CITED

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