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LETTERS TO THE EDITOR

Thiobenzohydrazides and Dithiocarbazates in the Synthesis of New 1,3,4-Thiadiazine and 1,3,4-Thiadiazole Derivatives

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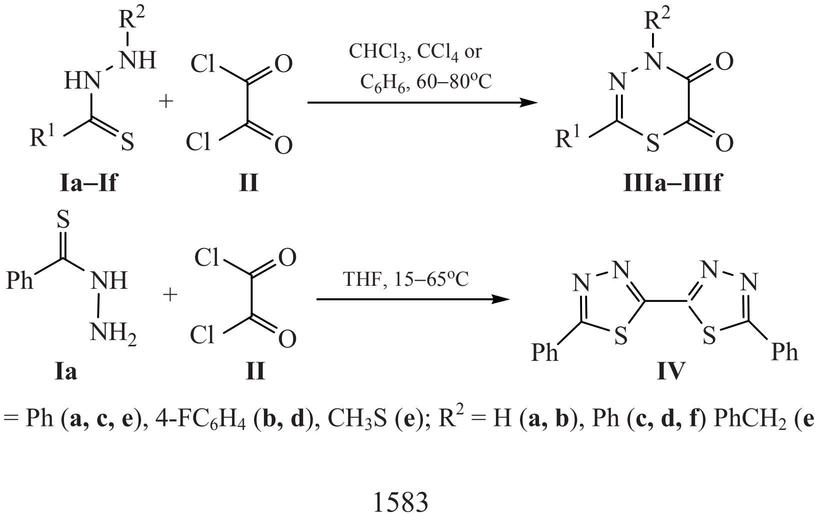
We previously reported on reactions of aromatic and heteroaromatic acid hydrazides with oxalyl chloride in boiling benzene, which afforded 80–90% of the corresponding 2-aryl(hetaryl)-4*H*-1,3,4-oxadiazine-5,6-diones [1]. Analogous 4*H*-1,3,4-thiadiazine-5,6-diones **IIIa**–**IIIf** were synthesized by reaction of carbothiohydrazides **Ia**–**Ie** and *S*-methyl-3-phenyldithiocarbazate (**If**) with 10–15% excess of oxalyl chloride (**II**) in anhydrous inert solvents (benzene, chloroform, carbon tetrachloride). The yields of thiadiazines **IIIa**–**IIIf** were 80–94%.

However, the reaction of thiobenzohydrazide (**Ia**) with oxalyl chloride (**II**) in tetrahydrofuran in the temperature range from 15–65°C gave 72% of 5,5'-diphenyl-2,2'-bi-1,3,4-thiadiazole (**IV**). The reaction temperature strongly affected the reaction rate. The reaction in boiling THF was complete in 2 h, and it took 8 h at 15°C. Thus thiobenzohydrazides **Ia**–**Ie** and *S*-methyl-3-phenyldithiocarbazate (**If**) react with oxalyl chloride in weakly polar solvents (benzene, chloroform, etc.), following the [4+2]-cyclo-condensation pattern with formation of 1,3,4-thiadiazine ring, whereas the reaction in fairly polar coordinating medium (THF) at different temperatures occurs as [4+1]-condensation with formation of five-membered 1,3,4-thiadiazole derivatives.

The structure of compounds **IIIa**–**IIIf** and **IV** was confirmed by ^{1}H and ^{13}C NMR, IR, UV, and mass spectra.

2-Phenyl-4*H*-1,3,4-thiadiazine-5,6-dione (IIIa). A solution of 2.92 g of oxalyl chloride (**II**) in 50 ml of anhydrous chloroform was cooled to 0°C, 3.04 g of thiobenzohydrazide (**Ia**) was added under stirring, and the mixture was heated for 3 h under reflux. The mixture was cooled, and the precipitate was filtered off and recrystallized twice from acetonitrile. Yield 3.38 g (82%), mp 225–227°C (decomp.). UV spectrum, λ_{max}, nm: 207, 233, 270. IR spectrum, ν, cm^{-1}: 3190, 1695, 1675, 1450. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.51–7.68 m (5H), 12.90 s (1H). ^{13}C NMR spectrum (DMSO-d_6): δ_C, ppm: 125.8, 129.2, 130.9, 133.7, 141.6, 148.6, 176.4. Mass spectrum: *m*/*z* 206 [*M*]$^+$.



R^1 = Ph (**a, c, e**), 4-FC_6H_4 (**b, d**), CH_3S (**e**); R^2 = H (**a, b**), Ph (**c, d, f**) $PhCH_2$ (**e**).

2-(4-Fluorophenyl)-4*H*-1,3,4-thiadiazine-5,6-dione (IIIb) was synthesized in a similar way. Yield 4.13 g (92%), mp 232–234°C (decomp.). UV spectrum, λ_{max}, nm: 207, 233, 270. IR spectrum, ν, cm^{-1}: 3120, 1685, 1655, 1595. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.51 t (2H), 7.71 d.d (2H), 12.96 s (1H). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 114.5, 114.9, 129.5, 129.7, 135.1, 143.2, 148.7, 160.8, 170.4, 176.5. Mass spectrum: *m*/*z* 224 $[M]^+$.

2,4-Diphenyl-4*H*-1,3,4-thiadiazine-5,6-dione (IIIc). A solution of 2.79 g of oxalyl chloride (**II**) in 5 ml of anhydrous benzene was added under stirring to a solution of 4.56 g of thiohydrazide **Ic** in 30 ml of anhydrous benzene. The mixture was heated for 4 h under reflux and cooled, and the mixture was filtered off and recrystallized from benzene–acetonitrile (2:1). Yield 5.25 g (93%), mp 212–214°C. UV spectrum, λ_{max}, nm: 208.0, 242.5, 337.5. IR spectrum, ν, cm^{-1}: 3150, 1680, 1660, 1610. ^{1}H NMR spectrum (DMSO-d_6): δ 7.34–7.72 ppm, m (10H). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 125.1, 126.0, 128.0, 128.3, 128.8, 131.2, 133.3, 140.9, 141.1, 147.8, 175.4. Mass spectrum: *m*/*z* 282 $[M]^+$.

2-(4-Fluorophenyl)-4-phenyl-4*H*-1,3,4-thiadiazine-5,6-dione (IIId) was synthesized in a similar way. Yield 5.11 g (85%), mp 181–183°C. UV spectrum, λ_{max}, nm: 208.0, 243.0, 334.0. IR spectrum, ν, cm^{-1}: 3065, 1695, 1665, 1595, 1510. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.35 t (2H), 7.41–7.60 m (5H), 7.77 d.d (2H). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 115.4, 116.6, 123.8, 126.4, 129.2, 132.3, 135.3, 140.2, 148.7, 160.8, 170.2, 177.3. Mass spectrum: *m*/*z* 300 $[M]^+$.

4-Benzyl-2-phenyl-4*H*-1,3,4-thiadiazine-5,6-dione (IIIe). A solution of 2.79 g of oxalyl chloride (**II**) in 5 ml of anhydrous benzene was added under stirring to a suspension of 4.84 g of thiohydrazide **Ie** in 30 ml of anhydrous benzene. The mixture was heated for 3.5 h under reflux and cooled, the solvent was removed under reduced pressure, and the precipitate was filtered off and recrystallized twice from benzene–hexane (2:3). Yield 5.57 g (85%), mp 134–136°C. UV spectrum, λ_{max}, nm: 206.5, 244.0, 285.0. IR spectrum, ν, cm^{-1}: 3065, 2960, 1690, 1660, 1490. ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 5.23 s (2H), 7.30–7.65 m (10H). ^{13}C NMR spectrum (CDCl$_3$), δ_C, ppm: 56.6, 126.2, 128.4, 128.7, 129.1, 129.2, 131.4, 133.6, 135.2, 141.5, 148.1, 175.0. Mass spectrum: *m*/*z* 296 $[M]^+$.

2-Methylsulfanyl-4-phenyl-4*H*-1,3,4-thiadiazine-5,6-dione (IIIf). A suspension of 8.34 g of methyl 2-phenylhydrazinecarbodithioate (**If**) in 75 ml of anhydrous carbon tetrachloride was cooled to 0°C, a solution of 5.88 g of oxalyl chloride (**II**) in 15 ml of the same solvent was added under stirring, and the mixture was heated for 4 h under reflux, cooled, and evaporated to dryness under reduced pressure. The residue was treated with ~30 ml of *n*-heptane–carbon tetrachloride (3:1), the mixture was heated to the boiling point and kept boiling for 3 min, and the yellow solution was separated by decanting from the undissolved material. This procedure was repeated 3–4 times. The extracts were combined and cooled to 0°C, and the precipitate was filtered off, washed with cold hexane, and dried. Yield 1.79 g (87%), mp 80–82°C. UV spectrum, λ_{max}, nm: 208.0, 247.0, 281.0. IR spectrum, ν, cm^{-1}: 3060, 2930, 1695, 1670, 1550. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.51 s (3H), 7.39–7.54 m (5H). ^{13}C NMR spectrum (CDCl$_3$), δ_C, ppm: 15.19, 125.5, 128.2, 128.9, 140.6, 141.7, 148.0, 175.6. Mass spectrum: *m*/*z* 252 $[M]^+$.

5,5′-Diphenyl-2,2′-bi-1,3,4-thiadiazole (IV). A solution of 2.02 g of thiobenzohydrazide (**Ia**) in 11.0 ml of anhydrous THF was cooled to 0°C, a solution of 1.85 g of oxalyl chloride in 5.5 ml of the same solvent was added, and the mixture was heated for 2 h under reflux. The precipitate was filtered off and washed with cold methylene chloride, and the filtrate was concentrated under reduced pressure to isolate an additional amount of the product. Recrystallization from dimethylformamide gave pure compound **IV** as fine needles. Yield 1.54 g (72%), mp 256–258°C. UV spectrum, λ_{max}, nm: 205.0, 231.5, 337.0. IR spectrum, ν, cm^{-1}: 3065, 1620, 1455, 1415. ^{1}H NMR spectrum (CF$_3$COOD): δ 7.47–7.89 ppm, m (10H). ^{13}C NMR spectrum (CF$_3$COOD), δ_C, ppm: 126.3, 131.2, 132.7, 138.3, 160.1, 180.0. Mass spectrum: *m*/*z* 322 $[M]^+$.

The ^{1}H and ^{13}C NMR spectra were recorded from solutions in DMSO-d_6, CDCl$_3$, or CF$_3$COOD on Bruker WM-400 (^{1}H, 400 MHz) and Bruker AC-200 spectrometers (^{13}C, 50 MHz) using hexamethyldisiloxane as internal reference. The UV spectra were measured from solutions in 96% ethanol on an SF-2000 spectrophotometer. The IR spectra were recorded in KBr on an FSM-1201 spectrometer with Fourier transform. The mass spectra (electron impact, 70 eV) were obtained on an MKh-1321 instrument (direct sample admission into the ion source heated to 200°C).

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