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SHORT COMMUNICATIONS

Reaction of 1,3-Dihalopropan-2-ones with 2-Sulfanylbenzoic Acid Mono- and Disodium Salts

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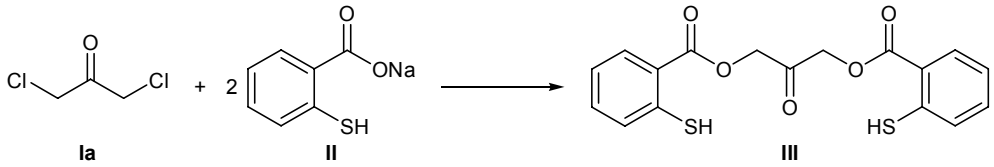
Well known biological activity of benzoic acid derivatives [1] prompted us to examine the possibility for building up novel heterocyclic systems by reactions of 2-sulfanylbenzoic acid mono- and disodium salts with α,α′-dihalo ketones of the general formula $XCH_2C(=O)CH_2X$ (**Ia**–**Ic**, X = Cl, Br, I). Initial sodium 2-sulfanylbenzoate (**II**) was prepared *in situ* according to the procedure described in [2] and was brought into reaction with 1,3-dichloropropan-2-one (**Ia**) in aqueous acetone at room temperature. The reaction occurred as intermolecular O-alkylation of sodium 2-sulfanylbenzoate (**II**) (Williamson reaction [3]) and led to the formation of 76% of previously unknown 2-oxo-3-(2-sulfanylbenzoyloxy)propyl 2-sulfanylbenzoate (**III**) (Scheme 1). The structure of compound **III** was confirmed by its elemental composition and IR and NMR spectra. The IR spectrum of **III** contained absorption bands belonging to stretching vibrations of S–H (2567 cm^{-1}), ester carbonyl (1690 cm^{-1}), and ketone carbonyl groups (1723 cm^{-1}). Two methylene units in molecule **III** gave rise to signals at δ 5.38 ppm in the ^1H NMR spectrum and at δ_C 67.58 ppm in the ^{13}C NMR spectrum.

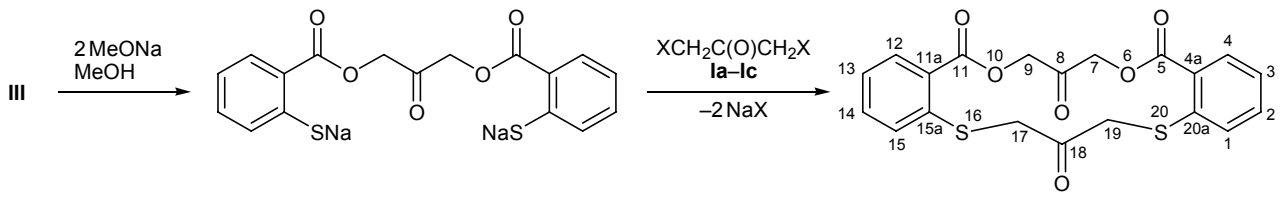
In order to construct a heterocyclic system, bisbenzoate **III** was treated with 1,3-dihalopropan-2-ones **Ia**–**Ic** with a view to obtain S-alkylation products. However, these reactions resulted in the formation of sulfur-containing oligomers which were insoluble in organic solvents. We succeeded in synthesizing the desired monomeric cyclization product, compound **V**, only by reaction of disodium salt **IV** with dihalo ketones **Ia**–**Ic** (Scheme 2). Macrocyclic 5*H*,7*H*,11*H*,17*H*-dibenzo[*g*,*n*][1,5,9,13]dioxadithiacyclohexadecine-5,8,11,18(9*H*,19*H*)-tetraone (**V**) was formed in 63%

Scheme 1.



Ia **II** **III**

Scheme 2.



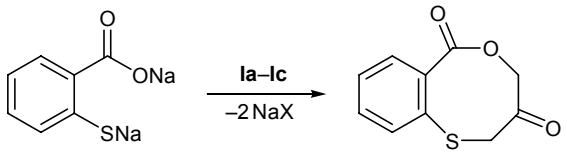
IV **V**

X = Cl (**a**), Br (**b**), I (**c**).

yield, and the reactivity of dihalo ketones **Ia**–**Ic** decreased in the series I > Br > Cl.

The reaction of 2-sulfanylbenzoic acid disodium salt (**VI**) with dihalo ketones **Ia**–**Ic** gave 5,1-benzoxathiocine-3,6-dione (**VII**) (Scheme 3). The structure of heterocyclic compounds **V** and **VII** was confirmed by the data of elemental analysis, mass spectrometry, and IR and ^{1}H and ^{13}C NMR spectroscopy. In the IR spectra of compounds **V** and **VII** we observed strong absorption bands due to stretching vibrations of ester (lactone, 1690 and 1712 cm^{-1}) and ketone carbonyl groups (1714 and 1748 cm^{-1}), respectively. The ^{13}C NMR spectrum of benzoxathiocinedione **VII** contained a signal at δ_C 198.26 ppm, which was assigned to the lactone carbonyl carbon atom. Its chemical shift was approximately equal to the average chemical shift of two carbonyl carbon atoms, SC–**C**(=O)C–S and OC–**C**(=O)C–O (δ_C 196.41 and 200.21 ppm, respectively) in the spectrum of compound (**V**).

Scheme 3.



VI **VII**

According to the results of B3LYP/6-31G(*d*,*p*) quantum-chemical calculations, the most stable conformer of **V** is characterized by almost planar arrangement (within 0.2°) of the heteroatoms in the central heteroring. Each *cis*-oriented phenyl ring forms with that plane a dihedral angle of 128.3°.

2-Oxo-3-(2-sulfanylbenzoyloxy)propyl 2-sulfanylbenzoate (III). An aqueous solution of 0.4 g (0.01 mol) of sodium hydroxide was added dropwise to a solution of 2 g (0.01 mol) of 2-sulfanylbenzoic acid in aqueous acetone until the mixture became neutral. A solution of 0.7 g (0.006 mol) of 1,3-dichloropropan-2-one (**Ia**) in acetone was added to the resulting solution of salt **II** at room temperature, and the mixture was stirred for 2 h until a solid separated. The precipitate was filtered off, washed with water and acetone, and dried under reduced pressure. Yield 1.8 g (76%), white powder, mp 245°C. IR spectrum, ν, cm^{-1}: 2567 (S–H), 1723 (C=O, ketone), 1690 (C=O, ester). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.88 s (2H, SH), 5.38 s (4H, CH_2), 7.27–8.03 m (8H, H_{arom}). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 67.58 (CH_2), 124.80–137.10 (C_{arom}), 161.48 (C=O, ester), 201.15 (C=O, ketone). Found, %: C 56.55; H 3.45; S 17.76. $C_{17}H_{14}O_5S_2$. Calculated, %: C 56.35; H 3.86; S 17.67.

2-Oxo-3-(2-sulfanylbenzoyloxy)propyl 2-sulfanylbenzoate disodium salt (IV). A solution of 0.26 g (0.004 mol) of sodium methoxide in methanol was added dropwise to a solution of 0.9 g of compound **III** in methanol until neutral reaction. The solvent was removed under reduced pressure. Yield 0.9 g (90%), white powder, decomposes above 350°C. IR spectrum, ν, cm^{-1}: 1706 (C=O, ketone), 1680 (C=O, ester). Found, %: C 49.46; H 3.30; Na 10.50; S 15.21. $C_{17}H_{12}Na_2O_5S_2$. Calculated, %: C 50.24; H 2.95; Na 11.33; S 15.76.

5*H*,7*H*,11*H*,17*H*-Dibenzo[*g*,*n*][1,5,9,13]dioxadithiacyclohexadecine-5,8,11,18(9*H*,19*H*)-tetraone (V). A solution of 0.28 g (0.002 mol) of 1,3-dichloropropan-2-one (**Ia**) in 0.5 ml of dimethyl sulfoxide was added to a solution of 0.9 g (0.002 mol) of disodium salt **IV** in 5 ml of DMSO. The mixture turned yellow–orange and was stirred for 1.5 h (until the initial ketone disappeared according to the TLC data) and poured onto finely crushed ice. The precipitate was filtered off, dried under reduced pressure, and purified by reprecipitation from chloroform with hexane. Yield 0.58 g (63%), white powder, mp 185–186°C. IR spectrum, ν, cm^{-1}: 1714 (C=O, ketone), 1690 (C=O, ester). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.25 s (4H, CH_2S), 5.15 s (4H, CH_2O), 7.17–8.00 m (8H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 46.57 (CH_2S), 66.18 (CH_2O), 123.49–140.83 (C_{arom}), 167.58 (C=O, ester), 196.41 (C^{18}=O), 200.21 (C^8=O). Found, %: C 57.55; H 3.65; S 15.86. *M* 392 (by cryoscopy in benzene). $C_{20}H_{16}O_6S_2$. Calculated, %: C 57.69; H 3.85; S 15.38. *M* 416.

2-Sulfanylbenzoic acid disodium salt (VI). Metallic sodium, 0.9 g (0.038 mol), was added in small pieces under stirring to a solution of 3.0 g (0.019 mol) of 2-sulfanylbenzoic acid in 30 ml of anhydrous ethanol. The mixture was heated for 7 h under reflux and cooled, and the precipitate was filtered off, washed with a small amount of cold ethanol, and dried under reduced pressure. Yield 2.8 g (72%), light yellow powder, decomposes above 350°C. IR spectrum: ν 1591 cm^{-1} (C=O). ^{1}H NMR spectrum (D_2O), δ, ppm: 7.15–7.83 m (4H, H_{arom}). ^{13}C NMR spectrum (D_2O), δ_C, ppm: 121.49–144.23 (C_{arom}), 168.51 (C=O). Found, %: C 42.69; H 2.38; Na 22.76. $C_7H_4Na_2O_2S$. Calculated, %: C 42.42; H 2.02; Na 23.23.

5,1-Benzoxathiocine-3,6-dione (VII). A solution of 0.23 g (1.2 mmol) of 2-sulfanylbenzoic acid disodium salt (**VI**) in 5 ml of DMSO was slowly added to

a solution of 0.15 g (1.2 mmol) of 1,3-dichloropropan-2-one (**Ia**) in 3 ml of DMSO. The mixture was kept for 24 h at room temperature (TLC) and poured onto finely crushed ice, and the precipitate was filtered off, dried under reduced pressure, and purified by reprecipitation from chloroform with hexane. Yield 0.15 g (62%), off-white powder, mp 105°C. IR spectrum, ν, cm^{-1}: 1748 (C=O, ketone), 1712 (C=O, lactone). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 5.24 s (2H, CH_2S), 5.36 s (4H, CH_2O), 7.17–8.00 m (4H, H_{arom}). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 41.35 (CH_2S), 67.75 (CH_2O), 125.36–139.86 (C_{arom}), 165.15 (C^6=O), 198.26 (C^3=O). Mass spectrum: *m*/*z* 208 $[M]^+$. Found, %: C 58.10; H 3.65; S 14.95. $C_{10}H_8O_3S$. Calculated, %: C 57.69; H 3.85; S 15.38. *M* 208 (for ^{32}S).

The ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 instrument at 400 and 100 MHz, respectively. The IR spectra were measured in KBr on a Bruker IFS-25 spectrometer. The mass spectra (electron impact, 70 eV) were obtained on a GCMS-QP5050A quadrupole instrument with direct sample admission into the ion source. The purity of the isolated compounds was checked by thin-layer chromatography on Silufol UV-254 plates using chloroform as eluent.

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