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Synthesis of Heterocycles on the Basis of Arylation Products of Unsaturated Compounds: XX.* Reaction of 2-Aryl-1,4-benzoquinones with Potassium *O*-Butyl Carbonodithioate

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Abstract—Reactions of 2-aryl-1,4-benzoquinones with potassium *O*-butyl carbonodithioate gave the corresponding 7-aryl-5-hydroxy-1,3-benzoxathiole-2-thiones. In some cases, 7-aryl-5-hydroxy-1,3-benzoxathiol-2-ones were also formed.

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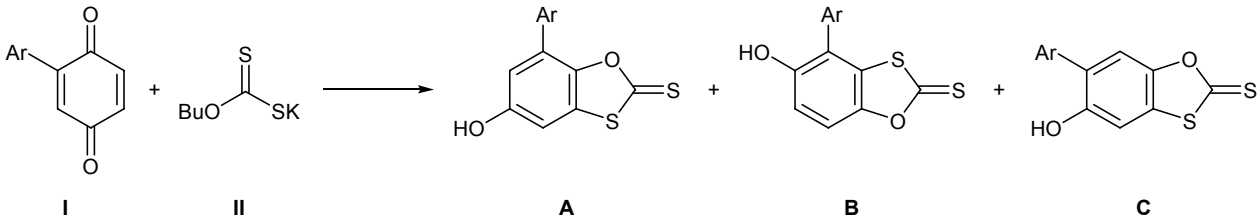
Reactions of 1,4-quinones with nucleophilic reagents, in particular with nitrogen-, sulfur-, oxygen-, and carbon-centered nucleophiles, play an important role in the chemistry of these compounds [2–5]. Such reactions generally follow 1,4-addition pattern, leading to the formation of hydroquinone or 1,4-benzoquinone derivatives which may be used in practice or as reagents in organic synthesis. If a nucleophile possesses two or more functional groups, its reactions with 1,4-quinones do not stop at the addition step but involve subsequent intramolecular cyclization leading to benzo-fused heterocyclic compounds [3]. Just that pattern is typical of quinone reactions with difunctional sulfur-centered nucleophiles [3, 6–9]. However, only reactions with unsubstituted 1,4-benzoquinone were studied in detail. Analogous reactions with monosubstituted quinones may be complicated due to possible formation of different regioisomers. For example, halogen-substituted quinones were reported to react with thiourea to produce mixtures of three isomeric halogen-substituted 5-hydroxy-1,3-benzoxathiol-2-ones [10]. Reactions of alkylquinones with thiourea were also nonselective [10, 11]. On the whole, the regioselectivity of reactions of monosubstituted 1,4-benzoquinones with sulfur-centered nucleophiles was studied poorly [3, 4]. Also, a few published data are available on reactions of nucleophiles with 2-aryl-1,4-benzoquinones, though the latter can readily be obtained by arylation of 1,4-benzoquinone with arenediazonium chlorides [12, 13] or other reagents [14–16]. We previously showed that reactions of 2-aryl-1,4-benzoquinones with thiourea in acid medium are selective [17]: nucleophilic attack is directed at position *6* of the quinone ring. Intermediate thiuronium salt thus formed undergoes intramolecular cyclization with formation of 7-aryl-5-hydroxy-1,3-benzoxathiol-2-ones. The reactions of 2-aryl-1,4-benzoquinones with dithiols gave 1,3-benzodithiole or 1,3-benzoxathiole derivatives, depending on the substituent in the aromatic ring [18]. In the present work we examined reactions of 2-aryl-1,4-benzoquinones with potassium *O*-butyl carbonodithioate.

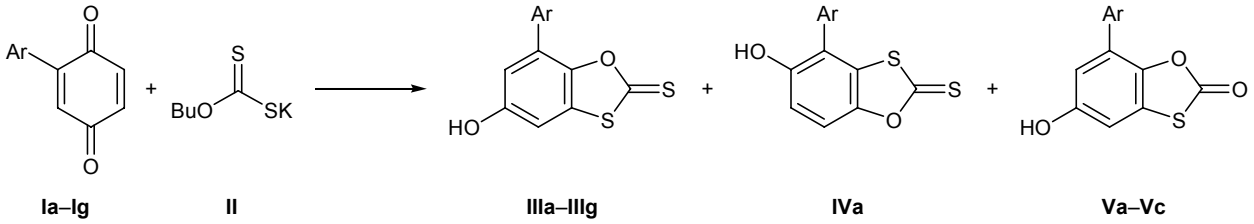
Scheme 1.



I II A B C

* For communication XIX, see [1].

Scheme 2.

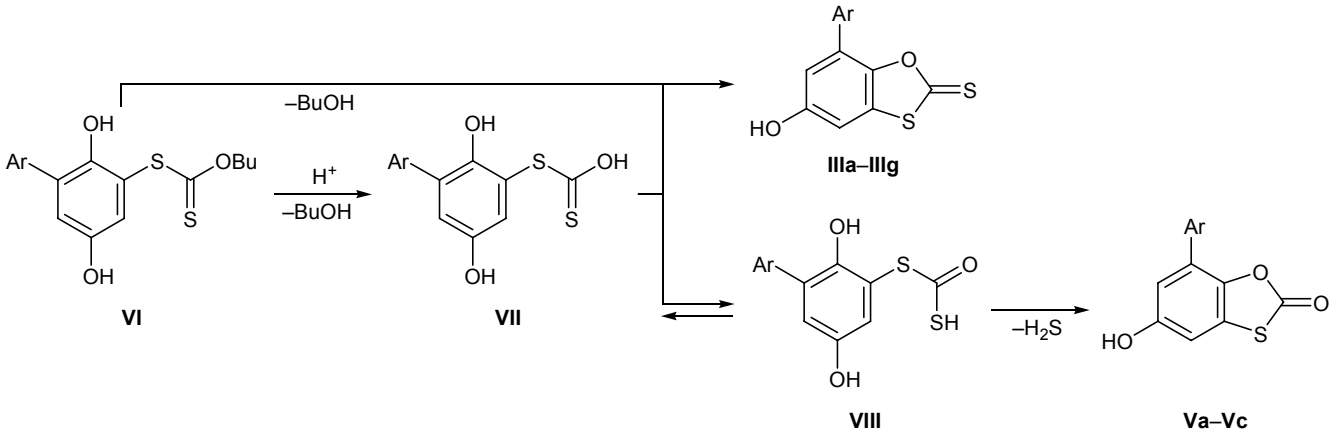


I, **III**, Ar = 4-BrC_6H_4 (**a**), 4-ClC_6H_4 (**b**), 3,5-$Cl_2C_6H_3$ (**c**), 4-$O_2NC_6H_4$ (**d**), 4-MeC_6H_4 (**e**), 4-$MeOC_6H_4$ (**f**), 3-$F_3CC_6H_4$ (**g**); **IVa**, Ar = 4-$O_2NC_6H_4$; **V**, Ar = 4-MeC_6H_4 (**a**), 4-$MeOC_6H_4$ (**b**), 3-$F_3CC_6H_4$ (**c**).

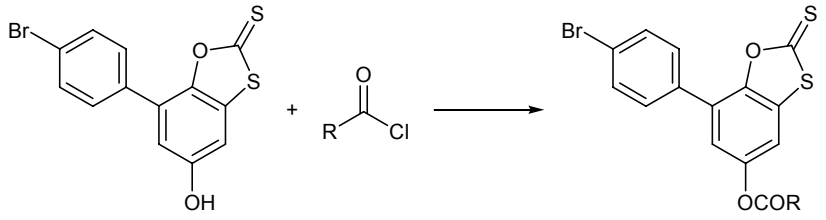
We have found that reactions of 2-aryl-1,4-benzoquinones **Ia**–**Ig** with potassium *O*-butyl carbonodithioate (**II**) on heating in acetic acid for a short time lead to the formation of 1,3-benzoxathiole-2-thiones. Theoretically, three isomeric compounds **A**–**C** (Scheme 1) could be formed, depending on the regioselectivity of primary addition of nucleophile **II** to quinones **I**. The reactions of arylquinones with thiourea gave 7-aryl-5-hydroxy-1,3-benzoxathiol-2-ones as analogs of isomer **A** [17]. Analysis of the ^{1}H NMR and mass spectra of the products showed that 2-aryl-1,4-benzoquinones **Ia**–**Ig** reacted with potassium *O*-butyl carbonodithioate less selectively than with thiourea. In all cases, 7-aryl-5-hydroxy-1,3-benzoxathiole-2-thiones **IIIa**–**IIIg** (isomer **A**) were the major products (Scheme 2). In the reactions of arylquinones **Ia**–**Ic** with KSC(=S)OBu, other cyclization products were also formed in insignificant amounts, and compounds **IIIa**–**IIIc** were readily isolated by recrystallization. The reactions of arylquinones **Id**–**Ig** with potassium *O*-butyl carbonodithioate (**II**) gave two products in comparable amounts. For example, the major product in the reaction of 2-(4-nitrophenyl)-1,4-benzoquinone (**Id**) with nucleophile **II** was compound **IVa** (isomer **B**; $J_{6,7}$ = 7.6 Hz). Arylquinones **Ie**–**Ig** reacted with **II** to form compounds **IIIe**–**IIIg** as the major products and significant amounts of 7-aryl-5-hydroxy-1,3-benzoxathiol-2-ones **Va**–**Vc**. 1,3-Benzoxathiol-2-ones **V** were also formed in the reactions with quinones **Ia**–**Ic**, but their yields were very poor (2–3%). The product ratios in the reactions of **Id**–**Ig** with **II** are listed below: **Id** (R = 4-O_2N), **IIId**:**IVa** = 30:70; **Ie** (R = 4-Me), **IIIe**:**Va** = 50:50; **If** (R = 4-MeO), **IIIf**:**Vb** = 75:25; **Ig** (R = 3-F_3C), **IIIg**:**Vc** = 65:35.

Thus the main reaction direction is nucleophilic attack by the anionic sulfur atom of potassium *O*-butyl carbonodithioate at position *6* of the quinone ring. This is confirmed by the long-range coupling constant for the 4-H and 6-H protons (J = 2.0–2.4 Hz) appearing in the ^{1}H NMR spectrum as two doublets. Obviously, compound **IVa** is formed as a result of primary nucleophile addition at C^3 (*ortho* position with respect to the aryl substituent), which is likely to be favored by electron-withdrawing effect of the nitro group. Scheme 3 shows a probable mechanism of formation of cyclization products **III** and **V**. Addition product of potassium *O*-butyl carbonodithioate (**II**) to arylquinone **I**, substituted hydroquinone **VI**, undergoes cyclization to thiones **III** via intramolecular transesterification. Unexpected formation of benzoxathiol-2-ones **Va**–**Vc**

Scheme 3.



Scheme 4.



IIIa **IXa–IXc** **Xa–Xc**

R = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4CH{=}CH$ (**c**).

may be rationalized assuming hydrolysis of butyl ester **VI** to carbonodothioic *O*-acid **VII**, followed by thione–thiol isomerization **VII** → **VIII** and intramolecular cyclization. Thiones **IIIa**–**IIIg** can also be formed through intermediate **VII**.

Compounds **IIIa**–**IIIg** readily undergo acylation with carboxylic acid chlorides in the presence of a base. The reaction of **IIIa** with acid chlorides **IXa**–**IXc** gave the corresponding *O*-acyl derivatives **Xa**–**Xc** (Scheme 4).

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on Bruker WP-300 (300 MHz; **IIIb**, **IIId**–**IIIg**, **IVa**, **Va**–**Vc**) and Bruker DRX-500 spectrometers (500 MHz; **IIIa**, **IIIc**, **Xa**–**Xc**) using DMSO-d_6 as solvent and tetramethylsilane as internal reference. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT Incos-50 GC–MS system.

Initial 2-aryl-1,4-benzoquinones **Ia**–**Ig** were synthesized as described in [12, 13, 18–20].

Reaction of 2-aryl-1,4-benzoquinones Ia–Ig with potassium *O*-butyl carbonodithioate (II) (*general procedure*). A suspension of 10 mmol of 2-aryl-1,4-benzoquinone **Ia**–**Ig** in 20 ml of glacial acetic acid was added under stirring to a solution of 2.1 g (11 mmol) of potassium *O*-butyl carbonodithioate (**II**) in 10 ml of water. The mixture was heated for 30 min at the boiling point under stirring and cooled, and the precipitate was filtered off, washed with several portions of water and with alcohol, and dried. The crude product was analyzed by gas chromatography–mass spectrometry and ^{1}H NMR to identify particular isomers and determine their ratio.

7-(4-Bromophenyl)-5-hydroxy-1,3-benzoxathiole-2-thione (IIIa). Yield 61%, mp 215–216°C (from EtOH–H_2O, 1:1). ^{1}H NMR spectrum, δ, ppm: 6.95 d (1H, 4-H, $J_{4,6}$ = 2.0 Hz), 7.19 d (1H, 6-H, $J_{4,6}$ = 2.0 Hz), 7.61 d (2H, C_6H_4, J = 8.1 Hz), 7.74 d (2H, C_6H_4, J = 8.1 Hz), 10.14 s (1H, OH). Mass spectrum, m/z (I_{rel}, %): 340/338 (100) $[M]^+$, 199 (27), 183 (70), 171 (48), 155 (36), 127 (55), 115 (20), 101 (30). Found, %: C 45.84; H 2.01; S 19.12. $C_{13}H_7BrO_2S_2$. Calculated, %: C 46.03; H 2.08; S 18.90. M 339.23.

7-(4-Chlorophenyl)-5-hydroxy-1,3-benzoxathiole-2-thione (IIIb). Yield 51%, mp 211–212°C (from MeOH–H_2O, 1:1). ^{1}H NMR spectrum, δ, ppm: 6.95 d (1H, 4-H, $J_{4,6}$ = 2.3 Hz), 7.19 d (1H, 6-H, $J_{4,6}$ = 2.3 Hz), 7.60 d (2H, C_6H_4, J = 8.4 Hz), 7.68 d (2H, C_6H_4, J = 8.4 Hz), 10.15 s (1H, OH). Mass spectrum, m/z (I_{rel}, %): 296 (44), 294 (100) $[M]^+$, 183 (30), 171 (25), 162 (18), 115 (10). Found, %: C 53.21; H 2.48; S 21.91. $C_{13}H_7ClO_2S_2$. Calculated, %: C 52.97; H 2.39; S 21.75. M 294.78.

7-(3,5-Dichlorophenyl)-5-hydroxy-1,3-benzoxathiole-2-thione (IIIc, 1:1 solvate with DMF). Yield 69%, mp 238–239°C (from EtOH–DMF, 3:1). ^{1}H NMR spectrum, δ, ppm: 7.09 d (1H, 4-H, $J_{4,6}$ = 2.4 Hz), 7.44–7.50 m (3H, 6-H, C_6H_3), 7.58 s (1H, C_6H_3), 10.24 s (1H, OH); DMF signals: 2.75 s (3H, CH_3), 2.92 s (3H, CH_3), 7.94 s (1H, CHO). Mass spectrum, m/z (I_{rel}, %): 332 (15), 330 (65), 328 (100) $[M]^+$, 233 (38), 205 (36), 198 (13), 170 (12), 126 (14). Found, %: C 47.45; H 3.11; S 16.12. $C_{13}H_6Cl_2O_2S_2 \cdot C_3H_7NO$. Calculated, %: C 47.77; H 3.26; S 15.94. M 329.23.

5-Hydroxy-7-(4-nitrophenyl)-1,3-benzoxathiole-2-thione (IIId). Yield 26%. ^{1}H NMR spectrum, δ, ppm: 7.03 d (1H, 4-H, $J_{4,6}$ = 2.1 Hz), 7.28 d (1H, 6-H, $J_{4,6}$ = 2.1 Hz), 7.97 d (2H, C_6H_4, J = 7.8 Hz), 8.39 d (2H, C_6H_4, J = 7.8 Hz), 10.25 s (1H, OH).

5-Hydroxy-4-(4-nitrophenyl)-1,3-benzoxathiole-2-thione (IVa). Yield 58%. ^{1}H NMR spectrum, δ, ppm: 7.15 d (1H, 6-H, $J_{6,7}$ = 7.6 Hz), 7.59 d (1H, 7-H, $J_{6,7}$ = 7.6 Hz), 7.80 d (2H, C_6H_4, J = 7.8 Hz), 8.33 d (2H, C_6H_4, J = 7.8 Hz), 10.48 s (1H, OH); Mass spectrum of mixture **IIId**/**IVa**, m/z (I_{rel}, %): 305 (100) $[M]^+$, 258 (11), 198 (13), 171 (22), 155 (18), 126 (25), 115

(16). Found, %: C 51.10; H 2.23; N 4.70; S 21.21. $C_{13}H_7NO_4S_2$. Calculated, %: C 51.14; H 2.31; N 4.59; S 21.00. *M* 305.33.

5-Hydroxy-7-(4-methylphenyl)-1,3-benzoxathiole-2-thione (IIIe) and 5-hydroxy-7-(4-methylphenyl)-1,3-benzoxathiol-2-one (Va) (1:1 mixture**).** Yield 56%. ^{1}H NMR spectrum, δ, ppm: 2.36 s (1.5H, Me), 2.37 s (1.5H, Me), 6.85 d (0.5H, 4-H, $J_{4,6}$ = 2.4 Hz), 6.93 d (0.5H, 4-H, $J_{4,6}$ = 2.1 Hz), 7.13 m (1H, 6-H), 7.25–7.39 m (2H, C_6H_4), 7.47–7.58 m (2H, C_6H_4), 9.89 s (0.5H, OH), 10.11 s (0.5H, OH). Mass spectrum, *m*/*z* (I_{rel}, %): 274 (100) $[M]^+$ (**IIIe**), 258 (90) $[M]^+$ (**Va**), 214 (17), 202 (45), 171 (12), 142 (15), 115 (27). Found, %: C 63.33; H 3.90; S 17.89. Calculated for **IIIe**/**Va** (1:1), %: C 63.14; H 3.78; S 18.06. *M* 274.36 (**IIIe**), 258.30 (**Va**).

5-Hydroxy-7-(4-methoxyphenyl)-1,3-benzoxathiole-2-thione (IIIf) and 5-hydroxy-7-(4-methoxyphenyl)-1,3-benzoxathiol-2-one (Vb) (3:1 mixture**).** Yield 35 and 12% respectively. ^{1}H NMR spectrum, δ, ppm: 3.82 s (0.75H, MeO), 3.83 s (2.25H, MeO), 6.83 d (0.25H, 4-H, $J_{4,6}$ = 2.4 Hz), 6.92 d (0.75H, 4-H, $J_{4,6}$ = 2.5 Hz), 7.04–7.15 m (3H, 6-H, C_6H_4), 7.53–7.64 m (2H, C_6H_4), 9.87 s (0.25H, OH), 10.08 s (0.75H, OH). Mass spectrum, *m*/*z* (I_{rel}, %): 290 (100) $[M]^+$ (**IIIf**), 274 (45) $[M]^+$ (**Vb**), 246 (15), 218 (37), 203 (40), 187 (13), 158 (14), 143 (15), 115 (33). Found, %: C 58.97; H 3.67; S 19.35. Calculated for **IIIf**/**Vb** (3:1), %: C 58.72; H 3.52; S 19.59. *M* 290.36 (**IIIf**), 274.30 (**Vb**).

5-Hydroxy-7-(3-trifluoromethylphenyl)-1,3-benzoxathiole-2-thione (IIIg) and 5-hydroxy-7-(3-trifluoromethylphenyl)-1,3-benzoxathiol-2-one (Vc) (65:35 mixture**).** Yield 39 and 21%, respectively. ^{1}H NMR spectrum, δ, ppm: 6.93 d (0.35H, 4-H, $J_{4,6}$ = 2.1 Hz), 7.02 d (0.65H, 4-H, $J_{4,6}$ = 2.1 Hz), 7.20 m (1H, 6-H), 7.72–7.88 m (2H, C_6H_4), 7.90–8.04 m (2H, C_6H_4), 9.99 s (0.35H, OH), 10.19 s (0.65H, OH). Mass spectrum, *m*/*z* (I_{rel}, %): 328 (100) $[M]^+$ (**IIIg**), 312 (30) $[M]^+$ (**Vc**), 268 (14), 256 (48), 196 (20), 171 (23), 151 (20), 85 (30). Found, %: C 52.32; H 2.28; S 16.53. Calculated for **IIIg**/**Vc** (65:35), %: C 52.11; H 2.19; S 16.39. *M* 328.33 (**IIIg**), 312.27 (**Vc**).

Reaction of 7-(4-bromophenyl)-5-hydroxy-1,3-benzoxatiole-2-thione (IIIa) with carboxylic acid chlorides IXa–IXc (*general procedure***).** Compound **IIIa**, 3.4 g (10 mmol), was dissolved in 30 ml of anhydrous benzene, 1 g (10 mmol) of *N*-methylmorpholine and 10 mmol of acid chloride **IXa**–**IXc** were added, and the mixture was heated for 1 h with stirring under reflux. The mixture was cooled, the precipitate was filtered off, the filtrate was evaporated, and the residue was washed several times with water and purified by recrystallization.

7-(4-Bromophenyl)-2-thioxo-1,3-benzoxathiol-5-yl benzoate (Xa). Yield 53%, mp 175–176°C (from EtOH–DMF, 2:1). ^{1}H NMR spectrum, δ, ppm: 7.45 d (1H, 4-H, $J_{4,6}$ = 2.1 Hz), 7.58 t (2H, C_6H_4, J = 8.0 Hz), 7.62–7.72 m (5H, C_6H_5), 7.66 d (1H, 6-H, $J_{4,6}$ = 2.1 Hz), 8.17 d (2H, C_6H_4, J = 7.8 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 444/442 (67) $[M]^+$, 428/426 (12), 105 (100), 77 (37). Found, %: C 54.02; H 2.45; S 14.28. $C_{20}H_{11}BrO_3S_2$. Calculated, %: C 54.18; H 2.50; S 14.46. *M* 443.34.

7-(4-Bromophenyl)-2-thioxo-1,3-benzoxathiol-5-yl 4-methylbenzoate (Xb). Yield 66%, mp 182–183°C (from EtOH–DMF, 2:1). ^{1}H NMR spectrum, δ, ppm: 7.36 d (2H, C_6H_4, J = 7.7 Hz), 7.43 d (1H, 4-H, $J_{4,6}$ = 2.1 Hz), 7.64 d (1H, 6-H, $J_{4,6}$ = 2.1 Hz), 7.68 s (4H, C_6H_4), 8.05 d (2H, C_6H_4, J = 7.8 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 458/456 (46) $[M]^+$, 442/440 (10), 119 (100), 91 (28). Found, %: C 55.34; H 2.96; S 13.88. $C_{21}H_{13}BrO_3S_2$. Calculated, %: C 55.15; H 2.87; S 14.02. *M* 457.37.

7-(4-Bromophenyl)-2-thioxo-1,3-benzoxathiol-5-yl (2*E*)-3-(4-methoxyphenyl)prop-2-enoate (Xc). Yield 59%, mp 226–227°C (from EtOH–DMF, 2:1). ^{1}H NMR spectrum, δ, ppm: 3.83 s (3H, MeO), 6.72 d (1H, 3′-H, J = 15.0 Hz), 6.96 d (2H, C_6H_4, J = 7.6 Hz), 7.42 d (1H, 4-H, $J_{4,6}$ = 2.0 Hz), 7.54 d (2H, C_6H_4, J = 7.6 Hz), 7.62 d (1H, 6-H, $J_{4,6}$ = 2.0 Hz), 7.63 d (1H, 2′-H, J 15.0 Hz), 7.66–7.70 m (4H, C_6H_4). Mass spectrum, *m*/*z* (I_{rel}, %): 500/498 (25) $[M]^+$, 161 (100), 133 (16), 119 (15). Found, %: C 55.45; H 2.97; S 12.73. $C_{23}H_{15}BrO_4S_2$. Calculated, %: C 55.32; H 3.03; S 12.84. *M* 499.41.

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