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CONVENIENT PREPARATIONS OF THE THREE 2,3-DIHALO-1,4-BENZOQUINONES

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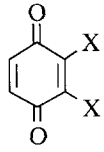
Abstract: Efficient preparations of 2,3-dichloro-1,4-benzoquinone (**1**) and 2,3-dibromo-1,4-benzoquinone (**2**) from 1,4-benzoquinone are reported, as is the synthesis of the previously unknown 2,3-diiodo-1,4-benzoquinone (**3**) from **2**.

2,3-Dichloro-1,4-benzoquinone (**1**) is widely used as a dienophile in the Diels Alder reaction, reacting at the unhalogenated double bond.[1] It also serves as a precursor for diaminated quinones and other derivatives with nucleophiles substituted onto the quinone ring.[2] We wished to use Diels Alder chemistry to incorporate quinones into structures that could then exploit their electron-acceptor nature. At the same time we needed halogen substituents on the quinones to provide additional synthetic handles. To provide those quinones, we developed an efficient preparation of **1**, and a cognate preparation of 2,3-dibromo-1,4-benzoquinone (**2**). To further extend our range of reactivity of the halogen substituents, we also devised a preparation of the previously unknown 2,3-diiodo-1,4-benzoquinone (**3**).



1 X = Cl
2 X = Br
3 X = I
4 X = H

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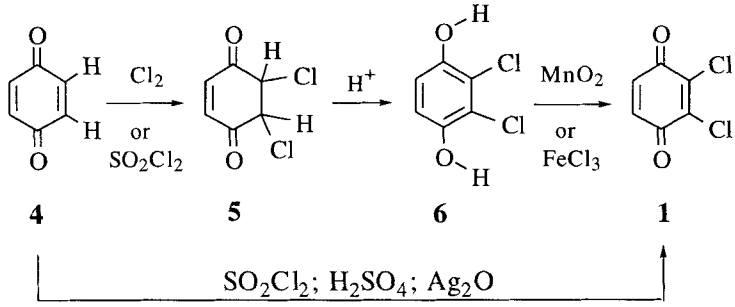
Literature methods for the preparation of **1** proceed in three steps. Benzoquinone (**4**) is chlorinated with SO_2Cl_2[3,4] or Cl_2[3,5] to give 5,6-dichloro-2-cyclohexen-1,4-dione (**5**), which is isolated and then tautomerized to 2,3-dichloro-hydroquinone (**6**).[3,5] After purification, **6** is oxidized with MnO_2[6] or $FeCl_3$[3,7] to give **1**. Overall yields range from 26%[6] to 73%.[3]

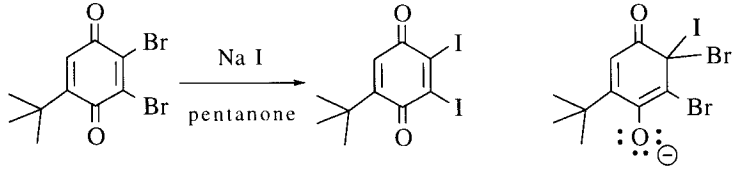


Our procedure avoids the isolation of intermediates. Chlorination of **4** was performed with SO_2Cl_2. After acidic workup, the ether extract of the reaction mixture was treated directly with Ag_2O.[8] Purification of the crude product gave **1** in 81% yield. The isomeric product 2,5-dichloro-1,4-benzoquinone could be isolated chromatographically in 5% yield.

An analogous convenient procedure involving bromination with Br_2 gave **2** in 68% crystallized yield. The 2,5-dibromo isomer could be isolated chromatographically from the mother liquor in 8% yield.

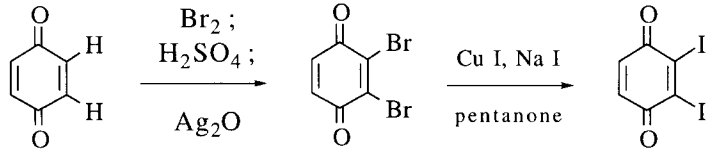
We hoped to make the diiodo analog by straightforward application of an existing method: 2,3-diiodo-5-*t*-butyl-1,4-benzoquinone (**8**) can be prepared by treatment of the dibromo compound **7** with excess iodide in boiling 3-pentanone in 96% yield.[9] A reasonable mechanism for this halide exchange is conjugate addition of iodide with subsequent β elimination of bromide from the resulting enolate (e.g., **9**). This reaction, like the nucleophilic substitution reaction that exchanges iodide

for the bromide of an bromoalkane in acetone, presumably relies on the insolubility of NaBr to shift the reaction equilibrium towards products.



7 **8** **9**

This exchange was unsuccessful on the parent compound **2**. No **3** was observed following treatment with 6.3 equivalents of NaI in hot 3-pentanone. However, pretreatment of **2** with 6 equivalents of CuI[10] for 2 hours, followed by 6.3 equivalents of NaI overnight, resulted in a 36% purified yield of **3**. Lower yields were observed if the CuI and NaI were added together, or if the pretreatment lasted 4 hours instead of 2. The mechanism is likely to involve copper in an oxidative addition / reductive elimination process.



4 **2** **3**

Experimental

2,3-Dichloro-1,4-benzoquinone (1). 1,4-Benzoquinone (Acros, 2.01 g, 18.6 mmol) was dissolved in 50 mL of dry Et_2O and 20 mL of $CHCl_3$ under N_2. Sulfuryl chloride (Acros, 5.01 g, 37 mmol) was then added dropwise over 15 min while the reaction mixture was stirred on an ice bath. After 30 min the mixture was warmed to room temperature, stirred for another 30 min, returned to the ice bath, and treated with 25 mL of Et_2O and 30 mL of concd H_2SO_4. After 45 min, the mixture was poured onto ice water and extracted 3 times with Et_2O. Ag_2O (10 g, 43 mmol) was

added to the combined ether layers, which were stirred for 1 hr, then filtered; the residue was rinsed with Et_2O and $CHCl_3$. Evaporation of the filtrate gave 3.1 g (94% crude yield); crystallization from 20% ethyl acetate / hexane gave 2.21 g (67%) of pale yellow crystals; mp 100-101 °C (lit.[3] mp 100-101 °C); ^1H NMR (300 MHz, $CDCl_3$): δ 6.97 (s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.4 (CO), 141.2 (CCl), 136.1 (CH). Silica gel chromatography of the mother liquor (10% ethyl acetate in hexane) gave an additional 0.45 g (14%). Chromatography also afforded a 5% yield of 2,5-dichloro-1,4-benzoquinone; mp 158-159 °C (lit.[8] mp 162 °C); ^1H NMR ($CDCl_3$): δ 7.35 (s); ^{13}C NMR ($CDCl_3$): δ 177.2 (CO), 144.6 (CCl), 133.0 (CH).

2,3-Dibromo-1,4-benzoquinone (**2**). 1,4-Benzoquinone (1.05 g, 10 mmol) was dissolved in 45 mL of dry Et_2O under N_2. The solution was cooled in an ice bath, and bromine (MCB, 1.55 g, 19 mmol) in 20 mL of $CHCl_3$ and 5 mL of dry Et_2O was added over 10 min. The mixture was stirred at room temperature for 15 min, returned to the ice bath, and treated with 25 mL of concd H_2SO_4. After 35 min, the mixture was treated as above for **1** (using 6.0 g, 26 mmol of Ag_2O), giving a crude yield of 2.55 g (96%); crystallization from hexane afforded 1.82 g of yellow **2** (68%); mp 126-127 °C (lit.[7] mp 124-125 °C); ^1H NMR ($CDCl_3$): δ 7.02 (s); ^{13}C NMR ($CDCl_3$): δ 177.0 (CO), 137.8 (CBr), 137.0 (CH). Chromatography of the mother liquor as above gave an additional 0.02 g (1%). Chromatography also afforded an 8% yield of 2,5-dibromo-1,4-benzoquinone; mp 189-191 °C (lit.[8] mp 193-194 °C); ^1H NMR ($CDCl_3$): δ 7.48 (s); ^{13}C NMR ($CDCl_3$): δ 177.0 (CO), 137.8 (CBr), 137.0 (CH).

2,3-Diiodo-1,4-benzoquinone (**3**). Compound **2** (0.10 g, 0.38 mmol) and copper(I) iodide (0.43 g, 2.3 mmol) were refluxed in 10 mL of 3-pentanone under N_2 for 2 h. Finely powdered sodium iodide (0.36 g, 2.4 mmol) was added and the resulting red mixture was refluxed overnight. The solvent was removed by rotary evaporation and 20 mL of water was added. The mixture was extracted several times with Et_2O. The organic layers were dried over $MgSO_4$ and evaporated to afford a dark

red oil which was purified by column chromatography (silica gel, 20% ethyl acetate in hexane) to give 50 mg (36%) of an orange-red solid; mp 138-140 °C; ^{1}H NMR ($CDCl_3$): δ 7.12 (s); ^{13}C NMR ($CDCl_3$): δ 177.8 (CO), 135.4 (CH), 133.9 (CI). The analytical sample was recrystallized from hexane. Anal. Calcd for $C_6H_2I_2O_2$: C, 20.02; H, 0.56; I, 70.52. Found: C, 19.91; H, 0.63; I, 70.57.

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