A Mild Silver Salt-induced Oxidation of Dibromo-5-hydroxytropolones to Dibromo-*p*-tropoquinones

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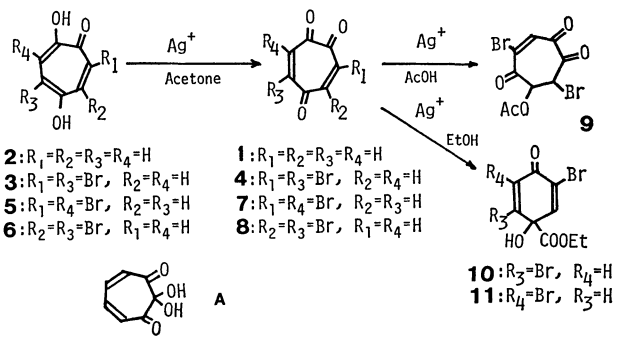
Synopsis. The treatment of 3,6-dibromo-, 3,7-dibromo, 4,6-dibromo-, and unsubstituted 5-hydroxytropolones with silver acetate in acetone gave the corresponding *p*-tropoquinones in good yields. When this reaction was carried out in protic solvents, some of these tropoquinones underwent further attack by solvent nucleophiles to give Michael-adducts or ring-contracted cyclohexadienones.

Some years ago, Itô *et al.* reported the first synthesis of *p*-tropoquinone, 3,6-cycloheptadiene-1,2,5-trione (**1**), from 5-hydroxytropolone (**2**),[1] and a hydrated *o*-tropoquinone, 2,2-dihydroxy-4,6-cycloheptadiene-1,3-dione (**A**),[2] and subsequent papers described the remarkable physical and chemical properties of these basic nonbenzenoid quinones.[3,4] We will herein describe an alternative synthesis of **1** and its bromo derivatives.

When an acetone solution of 3,6-dibromo-5-hydroxytropolone (**3**) and silver acetate was kept at room temperature, metallic silver was precipitated after 15 min. From the supernatant organic layer, pale yellow crystals (**4**) were obtained by means of brief silica-gel chromatography. The **4** retained two bromine atoms intact, and the NMR data were in accord with 3,6-dibromo-*p*-tropoquinone [δ:[5] 7.59 (1H, s) and 7.72 (1H, s)]. Similarly, 3,7-dibromo-5-hydroxytropolone (**5**), 4,6-dibromo-5-hydroxytropolone (**6**), and the bromine-free **2** gave the *p*-tropoquinones, 3,7-dibromo-*p*-tropoquinone (**7**), 4,6-dibromo-*p*-tropoquinone (**8**), and **1**, respectively in good yields.

On the other hand, silver salt-induced oxidation in a protic solvent gave no tropoquinone derivative; the oxidation of **3** in acetic acid gave a Michael-type adduct of **4**, 3-acetoxy-4,7-dibromo-6-cycloheptene-1,2,5-trione (**9**), while the oxidation of **3** in ethanol gave a ring-contraction product, 2,5-dibromo-4-ethoxycarbonyl-4-hydroxy-2,5-cyclohexadien-1-one (**10**). The Michael addition must be catalyzed by the silver ion exemplified in the case of authentic **4**, changing to **9**. As expected, one 4,6-disubstituted quinone, **8**, gave no Michael adduct. Furthermore, **5** in ethanol gave 3,5-dibromo-4-ethoxycarbonyl-4-hydroxy-2,5-cyclohexadien-1-one (**11**), and the ring-contraction occurred only with the 3-bromo-*p*-tropoquinones; from the parent compound (**2**) or **6**, no cyclohexadienone was isolated.



2: $R_1=R_2=R_3=R_4=H$
3: $R_1=R_3=Br$, $R_2=R_4=H$
5: $R_1=R_4=Br$, $R_2=R_3=H$
6: $R_2=R_3=Br$, $R_1=R_4=H$

1: $R_1=R_2=R_3=R_4=H$
4: $R_1=R_3=Br$, $R_2=R_4=H$
7: $R_1=R_4=Br$, $R_2=R_3=H$
8: $R_2=R_3=Br$, $R_1=R_4=H$

9

10: $R_3=Br$, $R_4=H$
11: $R_4=Br$, $R_3=H$

A

The results of an early attempt at synthesizing **1** by an iron(III) chloride or silver nitrate oxidation of **2**,[6] should be, in view of the present results, explained in terms of the protic solvents used in the reaction.

Experimental

Preparation of the Dibromo Derivatives of 2. To a refluxing AcOH solution (300 cm³) containing **2** (5.42 g), an AcOH solution (200 cm³) of Br_2 (13.7 g, 2.2 mol equiv.) was added, drop by drop. After the evaporation of the solvent, the residue was separated by fractional recrystallizations; from the least soluble fractions, **5** was obtained as pale yellow needles (mp 166—167 °C (from MeOH); 356 mg (3%) [Found: C, 28.30; H, 1.64%. Calcd for $C_7H_4O_3Br_2$: C, 28.41; H, 1.36%. δ^{MeOD}: 7.68 (2H, s). δ(C): 128.1(2C), 130.3(2C), 154.3, 162.8(2C). ν: 1605, 1570, 920, 870 cm^{-1}. λ_{max}^{MeOH}: 261 nm (ε=25000), 350 (7400), 412 (7600)]), followed by other pale yellow needles, **6** (mp 146—147 °C (from MeOH); 2420 mg (21%) [Found: C, 28.61; H, 1.54%. δ^{MeOD}: 8.20 (2H, s). δ(C): 131.0(2C), 134.6(2C), 151.3, 168.7(2C). ν: 1605, 1530, 960, 930 cm^{-1}. λ_{max}^{MeOH}: 263 nm (ε=14000), 386 (6300), 406 (6900)]). From the most soluble fractions, **3** was obtained as pale yellow needles; mp 166—168 °C (from EtOAc–CCl_4); 700 mg (6%) [Found: C, 28.90; H, 1.62%. δ^{MeOD}: 7.76 (1H, s), 8.08 (1H, s). δ(C): 120.6, 126.5, 131.5, 132.0, 153.6, 158.4, 169.5. ν: 1590, 1520, 990, 920 cm^{-1}. λ_{max}^{MeOH}: 251 nm (ε=13000), 334 (4300), 400 (550)].

AgOAc-oxidation of 3 in Acetone. To an acetone solution (6 cm³) of **3** (44 mg), AgOAc (50 mg) was added all at once. After magnetical stirring for 10 h at room temperature, the deposited Ag was filtered off; the filtrate was evaporated *in vacuo* and chromatographed on a short silica-gel column with benzene to give yellow crystals (**4**) (35 mg, 80%), which after recrystallizations from benzene showed a mp of 146—150 °C [Found: C, 28.74; H, 0.93; Br, 53.80%. Calcd for $C_7H_2O_3Br_2$: C, 28.60; H, 0.69; Br, 54.37%.[7] δ: 7.72 (1H, s), 7.59 (1H, s). δ(C): 135.5, 136.1, 139.3, 140.8, 178.1, 179.6, and 181.8. ν: 1700, 1680, 1640, 1600 cm^{-1}].

Catalytic Hydrogenation of 4. An EtOAc solution of **4** (50 mg) was hydrogenated with 5%-Pd-on-carbon (50 mg) at room temperature under an H_2-atmosphere for 10 min. After the filtration of the catalyst, the yellow needles obtained by the removal of the solvent were identical with **3** (45 mg, 89.4%).

AgOAc-oxidation of 5 in Acetone. Similarly, an acetone solution (4 cm³) of **5** (99 mg) was treated with AgOAc (51 mg) for 1 h at room temperature to give yellow needles (**7**); mp 96—97 °C (from benzene); 79 mg (81%) [Found: C, 28.64; H, 1.02%. δ: 7.51 (2H, s). δ(C): 134.9(2C), 140.6(2C), 181.8(2C), 181.9. ν: 1695, 1685 cm^{-1}].

AgOAc-oxidation of 6 in Acetone. Similarly, an acetone

solution (10 cm³) of **6** (550 mg) was oxidized with AgOAc (630 mg) at room temperature. The yellow needles obtained from the benzene fraction by silica-gel-column chromatography consisted of 480 mg (87%) of **8**; mp 146—150 °C [Found: C, 28.66; H, 0.94%. δ: 7.58 (2H, s). δ(C): 136.1(2C), 138.5(2C), 176.1(2C), and 180.7. ν: 1660, 1595 cm^{-1}].

*AgOAc-oxidation of **2** in Acetone.* An acetone solution (3 cm³) of **2** (100 mg) was similarly oxidized by AgOAc (245 mg) for 1.5 h. The yellow needles, 45 mg (46%), obtained by a similar work-up were identical with the authentic **1**[1] in every respect.

*AgOAc-oxidation of **3** in Acetic Acid.* To an AcOH solution (2 cm³) of **3** (95 mg), AgOAc (108 mg) was added at room temperature, after which the mixture was stirred for 1.5 h. The mixture was then heated *in vacuo* (below 60 °C) to remove the AcOH, and the residue was fractionated by preparative thin-layer chromatography (PTLC) to give a colorless oil (**9**); 12.6 mg (13.3%) [Found: *m/e*, 352, 353.8579 (M^+, Calcd for $C_9H_6O_5{}^{79}Br^{81}Br$: 353.8562), 356. δ: 2.18 (3H, s), 4.16 (1H, d, J=3 Hz), 5.22 (1H, d, J=3 Hz), and 6.70 (1H, s) for *cis*-**9**; 2.13 (3H, s), 4.48 (1H, d, J=9 Hz), 5.17 (1H, d, J=9 Hz), and 6.72 (1H, s) for *trans*-**9**. *cis*/*trans*=1/2. ν: 1750, 1700 cm^{-1}].

*Treatment of **4** with Acetic Acid.* An AcOH solution (4 cm³) of **4** (42 mg) was kept under magnetical stirring at room temperature until all of the starting **4** had been consumed (for 20 h). By PTLC fractionation, 11 mg (21%) of a colorless oil was then obtained from the mixture; it was identical with respect to the NMR spectroscopy with the **9** prepared from **3**. The rest of the material was insoluble to most ordinary organic solvents, and no further attempt at its fractionation was made.

*AgOAc-treatment of **1** in Acetic Acid.* To an AcOH solution (0.5 cm³) of **1** (44.4 mg), AgOAc (54.5 mg) was added all at once, after which the mixture was stirred at room temperature for 24 h. The PTLC of the reaction mixture afforded only the recovered **1** (23.9 mg, 54%), although some minor spots due to other products were detectable.

*AgOAc-treatment of **8** in Acetic Acid.* To an AcOH solution of **8** (34 mg), AgOAc (19 mg) was added all at once, after which the mixture was stirred at room temperature for 24 h. The PTLC resulted in the recovery of **8** (22.4 mg, 66%); no other compound was isolable.

*AgOAc-oxidation of **3** in Ethanol.* An EtOH solution (2 cm³) of **3** (11 mg) was stirred at room temperature with AgOAc (15 mg) for 10 h. After the filtration of the deposited Ag, the mixture was heated *in vacuo* to remove the solvent and separated by PTLC to give a colorless oil (**10**); 5.3 mg (42%) [Found: C, 32.07; H, 2.59%. Calcd for $C_9H_8O_4Br_2$: C, 31.80; H, 2.37%. δ: 1.28 (3H, t), 4.36 and 4.33 (2H, AB-part of ABX_3), 6.84 (1H, s), and 7.18 1H, s)].

*AgOAc-treatment of **4** in Ethanol.* An EtOH solution (4 cm³) of **4** (23.7 mg) was treated with AgOAc (14 mg) at room temperature for 20 h. The reaction mixture was then separated on PTLC to give **10** (17.3 mg, 64%).

*AgOAc-oxidation of **5** in Ethanol.* To an EtOH solution (1.5 cm³) of **5** (32 mg), AgOAc (37 mg) in EtOH (1.5 cm³) was added at room temperature, after which the mixture was kept for 10 h. After the filtration of metallic Ag, the mixture was separated by PTLC to give colorless crystals, mp 104—105 °C (from $CHCl_3$); 14.2 mg (38%) of **11** [Found: C, 31.91; H, 2.48%. δ: 1.33 (3H, t), 4.47 (2H, q), 6.96 (2H, s). δ(C): 13.8, 65.2, 132.8, 142.8, 167.8, 180.8. ν: 1760, 1740 cm^{-1}].

*An Attempted Ring Contraction of **6**.* An EtOH solution (4 cm³) of **6** (50 mg) was treated with AgOAc (85 mg) for 24 h. The PTLC of the reaction mixture revealed the very slow development of a new spot, but no product was isolable other than the quinone, **8** (31 mg, 63%).

*AgOAc-treatment of **1** in Ethanol.* An ethanol solution (2 cm³) of **1** (80.1 mg) was similarly treated with AgOAc (97.5 mg) for 24 h. The recovered **1** (52.1 mg, 65%) was the sole isolable compound in the PTLC fractionation.

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7) The determination of the bromine content has been carried out by The Kyoto University Station of Elemental Analyses. We thank Dr. T. Otsuki, Kyoto University, for his arrangement of this measurement.