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NUCLEOPHILIC REACTIONS OF p-TROPOQUINONE

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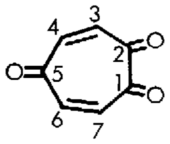
In the previous paper (1), we have reported the synthesis of the title compound, namely cyclohepta-3,6-diene-1,2,5-trione 1. Because of its lower symmetry compared with p-benzoquinone, its behavior toward various reagents is in principle more complicated than those of the latter. In order to evaluate the reactivities of each position and compare them with those of benzoquinones (2), we have carried out some chemical reactions of this interesting compound. The result is described herein.

Reactions at carbonyl groups o-Phenylenediamine gave quinoxalotropone 2 (3) quantitatively. m-Chloroperbenzoic acid afforded the eight-membered acid anhydride 3, colorless needles, m.p. 102-103°, in 23% yield. 3 was also obtained in 46% yield with anhydrous acetaldehyde. Peracetic acid formed from acetaldehyde and aerial oxygen is probably the reacting species (4). p-Toluenesulfonylhydrazone in CH_2Cl_2 afforded, after treatment with basic alumina (5), the diazoketone 4, yellow granules, m.p. 77-81° (dec.), in 58% yield (6). 4 is stable at 0° in dark, but decomposes easily by light. Photolysis ($\lambda > 340$ nm, methanol) as well as thermolysis (110°, toluene-methanol) of 4 yielded methyl 4-hydroxybenzoate quantitatively, probably via ketene intermediate 5 (7). These reactions implies the o-quinone character in 1.

Conjugate addition reactions HMO calculations (8) as well as CMR spectrum of 1 predict such an addition should occur at C-4 (C-6) rather than C-3 (C-7) as shown in Table.

Table. CMR and HMO-Calculation (8)

positions	1,2	5	3,7	4,6
π-electron density	0.7009	0.6774	0.8917	0.8698
Superdelocalizability ($S_r(N)$)	2.1371	2.1543	1.3589	1.3711
CMR (in $CDCl_3$, ppm from TMS)	186.0	187.4	134.6	138.8



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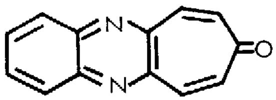

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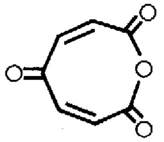

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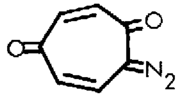

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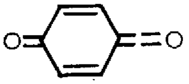

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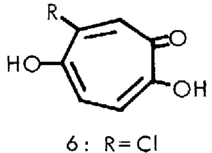
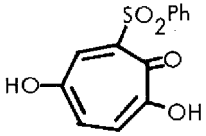


6: R=Cl

7: R=SO_2Ph



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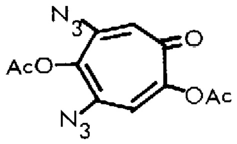

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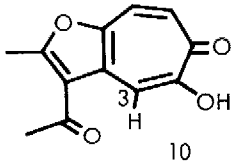

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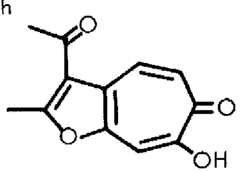

10a

In agreement with the prediction, most of the nucleophiles were found to attack at C-4 position under a standard condition (9). Thus, hydrogen chloride yielded 4-chloro-5-hydroxytropolone 6, yellow prisms, m.p. 170° (dec.), exclusively. Concentration (0.09N-12N), solvent ($CHCl_3$, THF, H_2O) and temperature (r.t. or 80°) affected the yield (25-73%) of 6 but not regioselectivity.

Sodium benzenesulfinate added to 1 in acetic acid in the same way to give the 4-phenylsulfonyl derivative 7, yellow plates, m.p. 166-168° (dec.) (35% yield) (10). However, when the reaction was carried out using aqueous solution of 1, the isomeric 3-phenylsulfonyl derivative 8, yellow needles, m.p. 223-226° (dec.), was formed in 40% yield in addition to 7 (10). The formation of p-tropoquinone hydrate in water (1) may be responsible for the reduction of regioselectivity.

Sodium azide reacted with 1 in acetic acid (0°, 15 min.) to give unstable solid, which, after acetylation and chromatographic separation, produced the 3,6-diazido compound 9, yellow needles, m.p. 90-93° (dec.), (34% yield) along with 5-hydroxytropolone diacetate (11) (22% yield). The formation of the disubstituted derivative and the reduction product is rationalized by the cross-oxidation of the initially formed monosubstituted 5-hydroxytropolone by 1; nitrogen-substituted quinone has lower redox potential than the unsubstituted quinones (2).

Carbanion reagent also adds to 1: acetyl acetone afforded the adduct 10, yellow prisms, m.p. 258-260° (dec.), in the presence of sodium acetate. Structure 10 is prefered to 10a because in PMR spectrum of this compound only H-3 is abnormally deshielded, probably due to the anisotropy of neighboring carbonyl group.

Structure assignment of all products rests on the spectra listed below. The coupling (2.0-2.6 Hz) observed between H_4 and H_6 in tropolone derivatives has a diagnostic value. The position of azido groups in 9 was further confirmed by the reaction starting from p-tropoquinone-3,7-d_2 (1).

Other reactions on 1 as well as o-tropoquinone (12) will be published elsewhere.

Spectral data (5)

3 : δ 6.37 (2H, d, 5.6), 7.19 (2H, d, 5.6); ν 3110, 1802, 1781, 1610, 1338, 1224, 1073, 1019, 888 cm^{-1}; λmax ~250 sh nm (log ε 2.08); m/e 152 (M^+), 108, 82 (b.p.), 80, 54.

4 : δ 6.08 (1H, dt, 12.4, 1.1), 6.82 (2H, d, 1.1), 6.85 (1H, d, 12.4); ν 2206, 2145, 1621, 1572, 1375, 1161, 863 cm^{-1}; λmax (CH_2Cl_2) 244.5 (log ε 4.20), 302 (2.64), 311 (2.62), 375 nm (3.85).

6 : δ 7.31 (1H, d, 12.5), 7.38 (1H, d, 12.5), 7.52 (1H, s); ν 3094, 2600, 1609, 1412, 1403, 1272, 1240 cm^{-1}; λmax 228 sh (log ε 4.24), 245 (4.39), 267 sh (3.74), 320 sh (3.73), 340 (3.94), 380 sh (3.98), 391 (3.99), 422 sh nm (3.48); m/e 174, 172 (M^+, 1:3 (b.p.)), 146, 144 (1:3), 108, 80, 52.

7 : δ (DMSO) 7.18 (1H, d, 12.9), 7.36 (1H, d, 12.9), 7.4-8.1 (5H, m), 8.13 (1H, s); ν 3300, 3025, 2500, 1591, 1538, 1415, 1318, 1310, 1291, 1275, 1251, 1148, 1079, 597 cm^{-1}; λ max 235 sh (log ε 4.35), 247 (4.36), 342 sh (3.95), 357 (4.01), 415 (3.94), 444 sh nm (3.78).

8 : δ (DMSO-d_6) 7.12 (1H, dd, 11.4, 2.5), 7.23 (1H, d, 11.4), 7.4-8.1 (5H, m), 8.43 (1H, d, 2.5); ν 3390, 3225, 1538, 1400, 1382, 1287, 1239, 1198, 1146, 592 cm^{-1}; λmax 230 (log ε 4.30), 250 (4.29), 344 (3.91), 360 sh (3.83), 404 sh (3.80), 427 (3.89), 454 sh nm (3.71).

9 : δ 2.27 (6H, s), 7.00 (2H, s); ν 2165 sh, 2127, 1770, 1757, 1571, 1366, 1330, 1190, 1170 cm^{-1}; λmax (CH_2Cl_2) 267 (log ε 4.29), 292 (4.56), 376 sh (3.97), 399 (4.03), 420 nm (3.94); m/e 304 (M^+), 276, 250, 234, 208, 206, 166 (b.p.).

10: δ 2.61 (3H, s), 2.78 (3H, s), 7.24 (1H, d, 12.2), 7.70 (1H, d, 12.2), 8.37 (1H, s); ν 3240, 1666, 1619, 1593, 1551, 1514, 1461, 1393, 1265, 1244, 862, 808 cm^{-1}; λmax 266 (log ϵ 4.57), 320 sh (3.65), 331 sh (3.71), 346 sh (3.83), 362 (4.00), 376 (4.04), 402 sh nm (3.09); m/e 218 (M$^+$, b.p.), 203, 190, 175, 147, 119, 91.

References and Notes

1) S. Itô, Y. Shoji, H. Takeshita, M. Hirama and K. Takahashi, *Tetrahedron Letters,* 1075 (1975).

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6) All new compounds described gave correct elemental analyses. Spectral data collected at the end of the text refer to the following conditions unless otherwise stated: UV; MeOH solution, IR; KBr disk for solid, film for liquid, NMR; CDCl$_3$ solution.

7) M. Yagihara, Y. Kitahara and T. Asao, *Chemistry Letters,* 1015 (1974); R. Clinging, F.M. Dean and G.H. Mitchell, *Tetrahedron*, **30**, 4065 (1974); J. Griffiths and M. Lockwood, *Tetrahedron Letters,* 683 (1975).

8) The parameters used for HMO calculations are as follows. Coulomb integrals: $\alpha_1=\alpha+0.3\beta$, $\alpha_5=\alpha+0.2\beta$, $\alpha_8=\alpha+1.2\beta$, $\alpha_{10}=\alpha+1.3\beta$, $\alpha_3=\alpha_4=\alpha$; exchange integrals: $\beta_{1,8}=0.9\beta$, $\beta_{5,10}=\beta$, $\beta_{1,2}=\beta_{2,3}=\beta_{4,5}=0.8\beta$, $\beta_{3,4}=1.1\beta$. Cf. A. Kuboyama, *Bull. Chem. Soc. Japan,* **31**, 752 (1958); *Idem, ibid.*, **32**, 1226 (1959).

9) Unless otherwise stated reaction was performed by adding a solution of excess reagent to the quinone solution at once at 0°C and stirred at room temperature overnight in dark.

10) Although the reaction proceeded nearly quantitatively, the great solubility of **7** reduced the isolated yield. **7** and **8** are formed in the 6:4 ratio in the reaction using aqueous solution of **1**.

11) T. Nozoe, S. Seto, S. Itô and T. Katôno, *Sci. Repts. Tohoku Univ.*, Ser. I, **37**, 191 (1953).

12) M. Hirama and S. Itô, *Tetrahedron Letters,* 1071 (1975).