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CYCLOADDITION REACTION OF p-TROPOQUINONE AND ITS UTILIZATION TO THE SYNTHESIS OF 1,2,5-BENZOTROPOQUINONE

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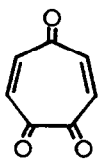
p-Tropoquinone 1 is a quinone unique in nonbenzenoid series in that, like in benzenoids, the corresponding hydroquinone, 5-hydroxytropolone, is a stable compound. Since its synthesis[1], we have been investigating its chemical behavior[2] for the comparison with benzenoids[3]. This communication describes the selectivities disclosed in its cycloaddition reaction with dienes and the successful synthesis of 1,2,5-benzotropoquinone 2, a seven-membered analog of naphthoquinone, utilizing the reaction. The synthesis completes the benzolog triads of 1, 2 and 1,2,4,5-dibenzocyclohepta-1,4-diene-3,6,7-trione 3[4].



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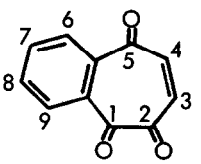

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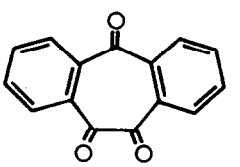

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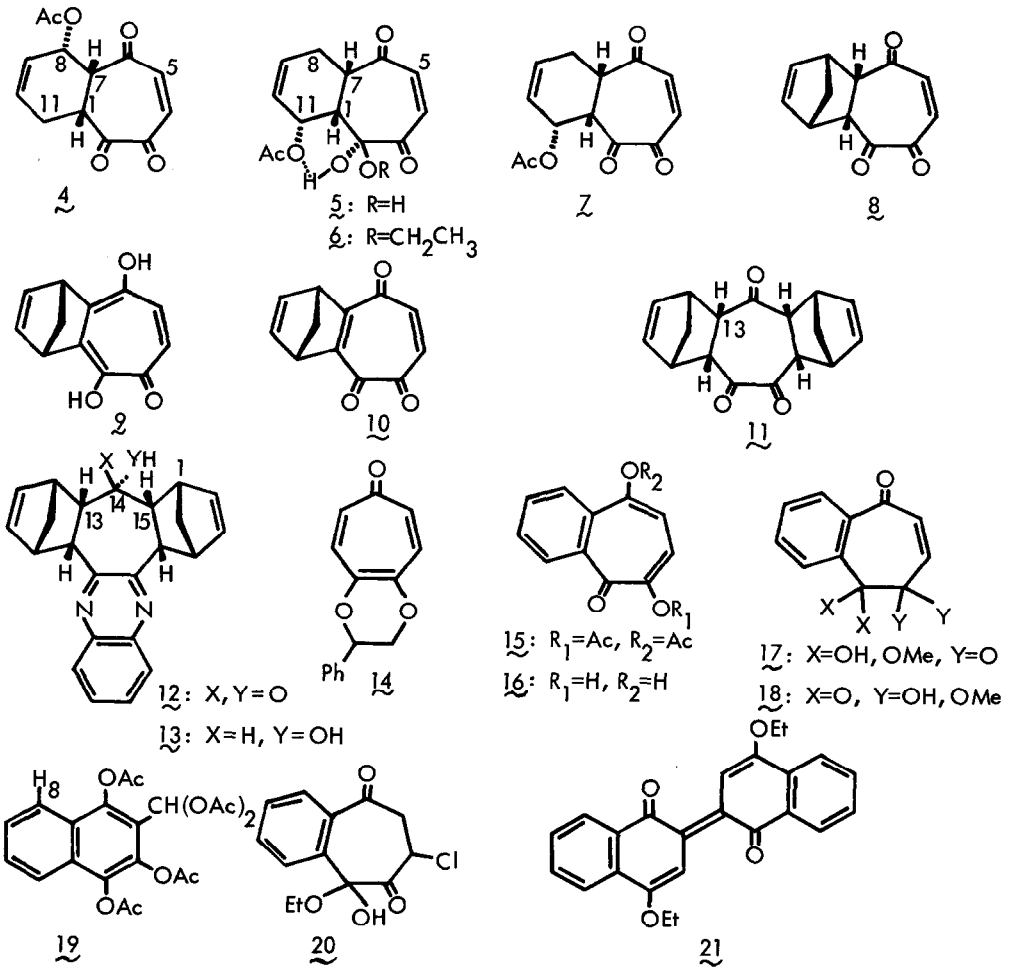
Cycloaddition Reactions of 1 By the reaction with 1-acetoxybutadiene (benzene, room temp., 16 hr) 1 yielded two regioisomeric 1:1 cycloadducts, 4 and 5, in 18% and 51% yield, respectively, after recrystallization from benzene [4, yellow needles, m.p. 118-119° (dec.), 5, colorless granules, m.p. 98-99° (dec.)]. 5 can be converted quantitatively to the ethyl acetal 6, m.p. 104-107° (dec.) with ethanol[5]. The structures of 4 and 6 were determined by detailed PMR analyses: The position of the acetoxyl group and stereochemistry in 6 were derived from the coupling constants ($J_{1,7}$=4.3, $J_{1,11}$=3.4, $J_{7,8\beta}$=5.5, $J_{7,8\alpha}$=1.0, $J_{5,7}$=0.5 Hz) and the presence of intramolecular hydrogen-bonding (ν (CCl_4) 3458 cm^{-1}, concentration independent), while those in 4 rest on the coupling constants ($J_{1,7}$=4.0, $J_{1,11\beta}$=5.0, $J_{1,11\alpha}$=1.5, $J_{7,8}$=3.5, $J_{5,7}$=0.7 Hz)[6].

For the quantitative determination of the regioselectivity of the reaction, the solvent was replaced by acetone-d_6 after the reaction and PMR spectrum was measured. The spectrum exhibited a methyl signal at δ 1.80 in addition to those due to 4 and 5 at δ 1.67 and 1.63, respectively, in the ratio of 48:29:23, and, upon addition of D_2O, the first signal disappeared and the ratio of the other two changed to 27:73.



This established that the orientation leading to the primary product 7 is favored to that leading to 4 in the transition state, the result being in accord with the prediction based on the CMR spectrum and HMO calculation[2].

With cyclopentadiene (benzene, room temp.) 1 yielded the endo 1:1 adduct 8 which was characterized as a quinoxaline derivative, red needles, m.p. 109-111° (dec.). 8 is very sensitive to acid and on SiO_2 chromatography enolized to the tricyclic tropolone 9 (80% yield from 1), yellow needles, m.p. 251-254° (dec.); δ (DMSO-d_6) 2.00 (t, J=2.0 Hz, 2H), 4.34 (m, 2H), 6.83 (t, 2.0, 2H), 7.05, 7.13 (d, 12.0, each 1H); λmax 244 (log ε 4.45), 262 (4.22 sh), 295 (3.80 sh), 331 (4.03), 342 (3.97 sh), 376 (4.05 sh), 393 (4.12), 424 nm (3.24 sh). DDQ oxidation of 9 afforded the stable tricyclic p-tropoquinone 10 (91% yield), orange needles, m.p. 102-103°; δ 2.25 (t, J=1.5 Hz, 2H), 4.37 (m, 2H), 6.82 (s, 2H), 6.94 (t, 2.0, 2H); ν 1675, 1642, 1600 cm^{-1}; λmax (CH_2Cl_2) 268 (log ε 3.96), 323 (3.13), 383 (3.00), 520 nm (1.46 sh)[7].

When the reaction with cyclopentadiene was carried out at 60°C, the 1:2 adduct 11, m.p. 159-160°, was obtained in 60% yield. For the determination of the relative stereochemistry of the two cyclopentene moieties, 11 was converted to its quinoxaline derivative 12, m.p. 210-213° (dec.) and then by LAH reduction to the alcohol 13, m.p. 217-219° (dec.). While the coupling pattern of H_{13} (H_{15}) [δ 3.85, dd, J=11.8, 2.9 Hz] and H_8 (H_5) [δ 4.18, dd, J=11.8, 3.5 Hz] in PMR spectrum of 12 revealed the endo configuration of both cyclopentene moieties, that of H_{14} in 13 [δ 4.41, br.s, $J \leq 1$ Hz] disclosed syn configuration. Thus 11 has the endo-syn-endo configuration. This stereochemistry is different from that of the benzoquinone-cyclopentadiene 1:2 adduct which has endo-anti-endo configuration[8]. The difference probably originates from the smaller steric hindrance in the syn attack of cyclopentadiene to 8, compared to the benzoquinone cyclopentadiene 1:1 adduct. The most stable conformation of 8 has more open face in syn side compared with anti side because of the bridgehead hydrogens.

1 underwent photochemical cycloaddition with styrene under N_2 and UV irradiation (~340 nm) to afford (9% yield) the dioxene derivative 14, m.p. 133-135°; λmax 237 (log ε 4.32), 352.5 (4.25), ca. 363 nm (4.13 sh), although unreactive with diphenylacetylene and 2-methyl-2-butene.

Synthesis of 2 Acetylation of 4 (Ac_2O, NaOAc) or 5 (Ac_2O, H_2SO_4) gave the diacetoxybenzotropone 15, m.p. 124-125°, acid hydrolysis of which afforded after sublimation (at 130°/0.04 torr), 5-hydroxybenzo[c]tropolone 16 (55% yield), yellow needles, m.p. 166.5-169° (dec.); δ (acetone-d_6) 6.72 (br.d, J=10.5 Hz, 1H), 7.09 (d, 10.5, 1H), 7.7-8.0 (m, 2H), 8.64 (m, 1H), 8.94 (m, 1H); λmax 242 (log ε 4.34), 261 (3.96 sh), 287 (3.51 sh), 300 (3.35 sh), 362 (3.41), 408 (3.48), 486 nm (2.79). Oxidation of 16 with excess silver carbonate-celite[9] (dichloromethane, room temp., dark, 4 hr) provided a yellow liquid which after drying was sublimed at 60°/0.04 torr to give 2 as yellow needles, m.p. 83-84°, in 50% yield.

The structure of 2 is based on its spectra. Mass spectrum shows a strong molecular ion peak (m/e 186), and the fragmentation pattern is very similar to that of 1,4-naphthoquinone[3]. While its carbonyl frequencies, ν 1678, 1656, 1630-1620 (sh) cm^{-1}, resemble those of 1, PMR signals due to the seven-membered ring, appearing as AB type (J=12.8 Hz) at δ 6.89 and 7.14, differ from those of 1 (δ 6.88, s)[1]. The small downfield shift due to benzene annelation has a precedence in benzoquinone-naphthoquinone series (Δδ 0.25 ppm)[3]. CMR signals, δ 130.7 (C_8), 130.9 (C_7), 132.7 (C_6), 133.8 (C_9), 134.0 (C_3), 141.5 (C_4), 189.1 (C_5), 190.3 (C_2), 191.3 (C_1) can be assigned on the basis of HMO calculation[10]. UV spectrum [λmax (CH_2Cl_2) 249 (log ε 4.16), 318 (3.47), ca. 450 nm (1.7, sh)] is similar with 1,4-naphthoquinone. Polarogram (1mM in acetonitrile, at 25°, supporting electrolyte: 0.05M-Et_4NClO_4) shows one-electron half-wave potential at E_1=-0.42 volt, more negative than that of 1, E_1=0.28[1], and more positive than those of p-benzoquinone and 1,4-naphthoquinone[11].

2 is stable under anhydrous conditions in the dark but is hygroscopic, forming a hydrate, yellow liquid, which reverts to 2 when dried in vacuo. Its tendency of hydration lied between that of 1 and 3. Upon the addition of methanol, 2 reversibly forms methylacetals 17 and 18 in 1:3 ratio. 2 gives a quinoxaline derivative, pale orange needles, m.p. 172.5-174° with o-phenylenediamine and is catalytically

reduced (5% Pd-C, in ethyl acetate) to 16. Thiele acetylation (Ac_2O, H_2SO_4, room temp.) afforded the naphthaldehyde derivative 19, m.p. 141-143.5°[12] in 11% yield; the similar behavior to 1[2b]. Hydrogen chloride also adds to 2 (chloroform-ethanol) but the adduct 20 obtained in 74% yield exists in the keto form[13]. 20, colorless plates, m.p. 117° (dec.); δ 1.30 (t, J=7.0 Hz, 3H), 2.23 (dd, 14.2, 3.3, 1H), 3.09 (dd, 14.2, 11.2, 1H), 3.72 (q, 6.7, 1H), 3.75 (q, 7.1, 1H), 4.53 (dd, 11.2, 3.3, 1H), 5.17 (br, 1H), 7.4-7.85 (m, 3H), 8.05-8.3 (m, 1H); ν 3470, 1700, 1602 cm^{-1}. Upon oxidation with silver carbonate-celite, 20 yielded in 30% yield the indigoid 21, dark violet powder, m.p. 227-229° (dec.); m/e 372 (M^+, 90%), 343 (100%); δ 1.57 (t, J=7 Hz, 6H), 4.31 (q, 7, 4H), 7.44 (td, 8, 2, 2H), 7.58 (td, 8, 2, 2H), 7.80 (dd, 8, 2, 2H), 8.14 (dd, 8, 2, 2H), 8.37 (s, 2H); ν 1605, 1590, 1558 cm^{-1}; λmax (CH_2Cl_2) 281 (log ε 4.28), 320 (4.03), 640 nm (4.15).

Thus, 2 was shown to be a genuine quinone similar to 1,4-naphthoquinone and 1[14].

References and Notes

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

2) a. M. Hirama and S. Itô, ibid., 2339 (1976). b. Idem, Chemistry Letters, 627 (1977).

3) Cf. "The Chemistry of the Quinonoid Compounds", Parts 1 and 2, S. Patai Ed., John Wiley, London (1974).

4) J. Rigaudy and L. Nèdèlec, Bull. Soc. Chim. France, 655 (1959).

5) The acetal 6 can be obtained directly from the reaction mixture by recrystallization with ethanol.

6) All new compounds gave correct elemental analyses and/or correct parent ion peaks on Mass spectra. Spectra were measured under the following conditions unless otherwise stated. MS (m/e) at 70eV, NMR (δ) in $CDCl_3$, IR (ν) in KBr and UV (λmax) in MeOH.

7) UV spectrum of 10 disclosed a non-bonded π-π* interaction between the quinone system and the isolated double bond, when compared with the corresponding dihydro-quinone, m.p. 64.5-66°, λmax (CH_2Cl_2) 267 (log ε 3.95), 343 (3.38), ~500 (1.57 sh), obtained by catalytic reaction (Pd-C) of 9 and subsequent DDQ oxidation.

8) R.C. Cookson, R.R. Hill and J. Hudec, J. Chem. Soc., 3043 (1964).

9) V. Balogh, M. Fétizon and M. Golfier, J. Org. Chem., 36, 1339 (1971).

10) Parameters adopted are those used in the calculation of α- and β-naphthoquinones. Cf. A. Kuboyama, Bull. Chem. Soc. Japan, 31, 752 (1958), 32, 1226 (1959).

11) M.E. Peover, J. Chem. Soc., 4540 (1962).

12) Compound 19 is hitherto unknown. The structure assignment rests on its spectral properties and its conversion to the corresponding naphthaldehyde, pale yellow prisms, m.p. 175-176°, with the spectra similar to 1-hydroxy-2-naphthaldehyde [I.M. Hunsberger, J. Amer. Chem. Soc., 72, 5626 (1950)].

13) The tendency of ketonization in hydroxybenzotropones are already known. Cf. V.H. Fernholz, E. Hartwig and J.-C. Salfeld, Ann., 576, 131 (1952), M. Hoshino and S. Ebine, Bull. Chem. Soc. Japan, 41, 2949 (1968), Idem, ibid., 43, 1778 (1970).

14) We are grateful to Professor M. Suzuki, Meijo University, for MS measurements and helpful discussion on the structure of 21, and to Professors S. Ebine and J. Tsunetsugu, Saitama University, for their helpful information on benzotropolones. We are also grateful to Professor N. Tanaka, Drs. Y. Kato and T. Ogata, Tohoku University, for their polarographic measurements of tropoquinone series.