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A NOVEL CYCLOADDITION REACTION OF p-BENZOQUINONES. TRANSANNULAR CYCLOADDITION IN p-C_8-BRIDGED p-BENZOQUINONES BY WAY OF AN OXYALLYL INTERMEDIATE

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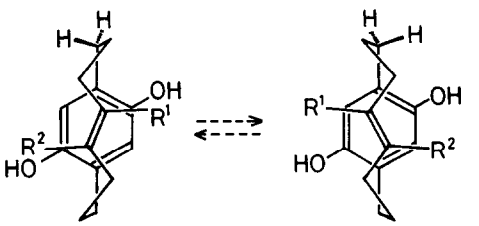
Summary: The transannular cycloaddition between the double bond on the side chain and the p-benzoquinone ring in p-C_8-bridged p-benzoquinones by way of an oxyallyl intermediate is described.

In the preceding paper,[1] we reported the preparation of p-C_8-bridged p-benzoquinones possessing a double bond on the side chain. During the course of the study, it was noted that their stabilities were highly dependent on the electronic property of the substituent on the olefinic carbon and also on the orientation of the unsaturated bond to the p-benzoquinone moiety. Indeed, some of the derivatives underwent facile secondary reactions under the conditions of preparation, thus defying the isolation. The structural elucidation of the secondary reaction products revealed a novel transannular [π2s+π4s] cycloaddition between the double bond on the side chain and the p-benzoquinone ring, which would presumably proceed by way of an oxyallyl intermediate.

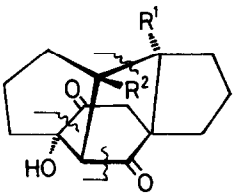
The monomethyl derivative, 1b, was treated with $Ce(NO_3)_4 \cdot 2NH_4NO_3$ in 80% aqueous CH_3CN in the dark[2] and, after stirring overnight at room temperature,[3] the products were extracted with $CHCl_3$. Preparative GLC separation of the products and subsequent purification by crystallization from benzene-hexane gave two isomeric, colorless products in 50% and 15% isolated yields, respectively. The elemental analysis and their



1A ⇌ 1B

a. $R^1=R^2=H$
b. $R^1=CH_3$, $R^2=H$
c. $R^1=R^2=OEt$

R^2=H m/e 97
$R^2=CH_3$ 111
R^2=OEt 141



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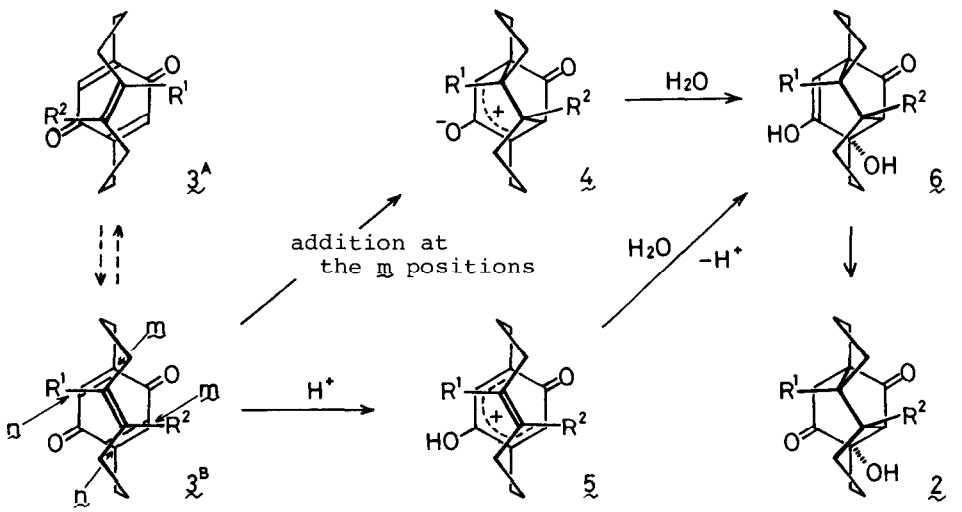
a. $R^1=R^2=H$
b. $R^1=CH_3$, $R^2=H$
b'. $R^1=H$, $R^2=CH_3$
c. $R^1=R^2=OEt$

mass spectra showed that both the compounds had a molecular formular of $C_{15}H_{20}O_3$ indicating the incorporation of one molecule of water into the expected quinone. Analysis of the PMR spectra with the aid of shift reagent and of CMR, IR, and mass spectra allowed us to assign the structures represented by 2b and 2b' to the major and minor products, respectively.[4] Observation of an AB quartet (J=18.6 Hz, 2H) at δ 2.81 and a doublet (J=6.8 Hz, 1H) at δ 2.53 in the PMR spectrum of 2b, as the fast moving signals on addition of shift reagent, was compatible with the proposed structure. Moreover, The base peaks in the mass spectra of 2b and 2b' were the fragment ions presumably formed by the fragmentations shown in the figure, i.e. m/e 97 for 2b and m/e 111 for 2b', which were also consistent with the assignments.[5]

Of the two isomeric diethoxy-substituted bridged hydroquinones, $1c^A$ and $1c^B$,[1] the former afforded the corresponding p-benzoquinone in good yield when treated with $Ce(NO_3)_4 \cdot 2NH_4NO_3$ in 80% aqueous CH_3CN at room temperature. In a marked contrast, the oxidation of the latter under the same conditions produced none of the p-benzoquinone.[1] From the reaction mixture, a colorless crystalline product, for which the structure represented by 2c was assigned on the basis of the spectroscopic property,[6] was isolated in 35% yield. The parent p-benzoquinone, 3a, underwent the analogous transannular reaction giving 2a[7] in 33% yield when heated in 80% aqueous THF for 20 h at 100°.

The present reaction may be rationalized by the addition of the double bond on the side chain to the cross conjugated dienone moiety of the p-benzoquinone in a [π2s+π4s] manner giving an oxyallyl intermediate,[8] 4, to which water adds

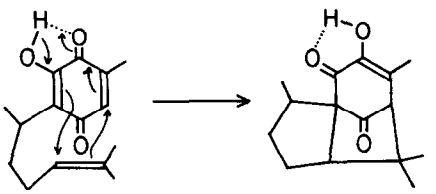
Scheme 1.



a. $R^1=R^2=H$; b. $R^1=CH_3$, $R^2=H$; c, $R^1=R^2=OEt$.

to give 6 which in turn tautomerizes to 2. Protonation on the carbonyl oxygen may precede the cycloaddition.[9] The observation that the more electron donating the substituent on the double bond is, the more labile the bridged p-benzoquinone is ($3\underset{\sim}{c}^{B} > 3\underset{\sim}{b} > 3\underset{\sim}{a}$), is consistent with the above mechanism. The formation of two isomeric products from 1b is also reasonably explained by the concurrent additions to the two available reaction sites, m and n (Scheme 1). The intramolecular cycloaddition in 3 is apparently feasible only in the B conformer since the analogous reaction in the A conformer should lead to a highly strained product.[10] Such a orientational requirement for the reaction is undoubtedly responsible for the remarkable difference in the reactivity between the isomeric diethoxy derivatives, $3\underset{\sim}{c}^{A}$ and $3\underset{\sim}{c}^{B}$. It seems the difference in the lability of 3a and 3b is too large even if the electronic effect of the methyl substituent in 3b is taken into account. However, it is probably also related to the conformational equilibration. The NMR spectral analysis on 1a with the aid of shift reagent indicates that the equilibrium is displaced in favor of $1\underset{\sim}{a}^{A}$, probably due to the more pronounced repulsion between the hydroxyl groups and the benzylic protons in $1\underset{\sim}{a}^{B}$. The same displaced equilibrium may be assumed for 3a, allowing to conclude that $3\underset{\sim}{a}^{A}$, non-reacting conformer, is predominating. Substitution of the olefinic proton with a methyl group, however, would cause a shift of the equilibrium to the opposite direction, i.e. in favor of the reacting conformer, $3\underset{\sim}{b}^{B}$, to relieve the steric hindrance between the methyl substituent and the carbonyl group.[11]

An analogous reaction has been reported for 7 which is transformed into 8 on heating.[12] In 7, however, the α-hydroxyl group would greatly activate the quinone ring by forming the hydrogen bond to the adjacent carbonyl oxygen. It might also enable the reaction, formally at least, to proceed without formation of an ionic intermediate. It is to be noted that the present cycloaddition of p-benzoquinones by way of the oxyallyl intermediate lacks such an activating group. Further work is in progress to study if such cycloaddition is feasible in p-benzoquinone not possessing a cyclophane structure.



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REFERENCES AND NOTES

1) Y. Hienuki, T. Tsuji, S. Nishida, Tetrahedron Lett., submitted for publication.

2) The p-C8-bridged p-benzoquinones are photo-labile.

3) GLC analysis of the reaction mixture after 20 min from the addition of oxidizing agent showed the formation of three products, one of which had been consumed after stirring overnight and would presumably be 3b.

4) Satisfactory elemental analysis was obtained for each new compound. 2b: mp 106.5-107.5°; PMR($CDCl_3$, 200 MHz), δ 1.05 (s, 3H), 1.1-1.9 (m, 11H), 2.3-2.5 (m, 3H), 2.53 (d, J=6.8 Hz, 1H), 2.71 (d, J=18.6 Hz, 1H), 2.91 (d, J=18.6 Hz, 1H); CMR($CDCl_3$), δ_c 215.21 (>CO), 208.00 (>CO), 80.31 (>C<), 59.33 (>C<), 56.60 (≡CH), 48.28 (>C<), 47.63 ($>CH_2$), 46.33 ($>CH_2$), 40.87 (≡CH), 32.68 ($>CH_2$), 28.00 ($>CH_2$), 22.94 ($>CH_2$), 21.96 ($>CH_2$), 20.99 ($>CH_2$), 17.09 ($-CH_3$); Mass (70 eV), m/e(rel intensity) 248 (M^+, 2.5), 220 (15), 206 (24), 202 (17), 97 (100); IR(KBr), 3430, 1735, 1705 cm^{-1}; UV(EtOH), λmax(ε) 304 nm (63). 2b' : mp 129.5-130.5°; NMR($CDCl_3$, 200 MHz), δ 0.91 (s, 3H), 1.0-1.8 (m, 11H), 2.12 (s, 1H), 2.2-2.4 (m, 3H), 2.69 (d, J=17.6 Hz, 1H), 3.06 (d, J=17.6 Hz, 1H); Mass(70 eV), m/e(rel intensity) 248 (M^+, 1.5), 206 (30), 187 (33), 111 (100); IR(KBr), 3475, 1745, 1705 cm^{-1}; UV(EtOH), λmax(ε) 304 nm (63).

5) Fragment ion expected from the analogous fragmentation was also the most abundant in the mass spectra of 2a and 2c.[6,7]

6) 2c: mp 123.5-124.5°; NMR($CDCl_3$, 200 MHz), δ 1.0-1.4 (m, 9H), 1.6-2.0 (m, 7H), 2.2-2.4 (m, 3H), 2.62 (s, 1H), 2.70 (d, J=17 Hz, 1H), 2.87 (d, J=17 Hz, 1H), 3.2-3.7 (m, 4H); Mass(70 eV), m/e(rel intensity) 322 (M^+, 2), 247 (3), 156 (6), 141 (100), 126 (45), 113 (24); IR(KBr), 3390, 1735 cm^{-1}; UV(EtOH), λmax(ε) 294 nm (87).

7) 2a: NMR($CDCl_3$, 200 MHz), δ 1.0-2.0 (m, 12H), 2.2-2.4 (m, 3H), 2.43 (d, J=5.4 Hz, 1H), 2.67 (d, J=17.6 Hz, 1H), 3.07 (d, J=17.6 Hz, 1H); Mass(70 eV), m/e(rel intensity) 234 (M^+, 2.5), 206 (16), 192 (27), 188 (17), 97 (100); IR(neat), 3400, 1745, 1715 cm^{-1}.

8) R. Hoffmann, J. Am. Chem. Soc., 90, 1475 (1968); D. I. Rawson, B. K. Carpenter, H. M. R. Hoffmann, ibid., 101, 1786 (1979).

9) The reaction of 3a proceeded in a neutral aqueous solution. Addition of acid, however, accelerated the reaction.

10) As to the prefered conformation of [8]paracyclophane, see: M. G. Newton, T. J. Walter, N. L. Allinger, J. Am. Chem. Soc., 95, 5650 (1973).

11) The interconversion between the two conformers would be facile compared to the reaction rate. See the preceding paper.[1]

12) F. Walls, J. Padilla, P. Joseph-Nathan, F. Giral, J. Romo, Tetrahedron Lett., 1577 (1965).

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