Communications

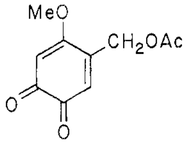
Diels–Alder Reactions of *o*-Benzoquinones

Summary: Dienophilic properties of 4-methoxy-*o*-benzoquinones with 1,3-butadiene have been demonstrated.

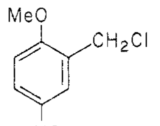
Sir: The *p*-benzoquinones are powerful dienophiles in the Diels–Alder reaction.[1] This tendency has been exploited in a variety of classical total synthesis projects.[2] In contrast, the *o*-benzoquinones have both dienic and dienophilic potentialities. This duality is no doubt responsible for their ready involvement in dimerization reactions.[3]

The greater dienophilicity of any alkyl enedione [O═C—C═C(R)C═O] relative to an alkoxy enedione [O═C—C═C(OR)C═O] in the *p*-benzoquinone series results in a strong directing influence in Diels–Alder reactions.[2a] This effect is no doubt due to the resonance stabilization, available to the methoxyenedione, which is forfeited (in the transition state) were this grouping to undergo cycloaddition. By analogy, we reasoned, that a 4-methoxy-*o*-benzoquinone should exhibit reduced dienic tendencies in the Diels–Alder reaction.[4,5] Furthermore, the 5,6 double bond of the 4-methoxy-*o*-benzoquinone would be expected to be the dominant site of dienophilicity relative to the 3,4 double bond. These suppositions have been nicely corroborated in the excellent dienophilic properties of *o*-quinone **1.** However, in the case of *o*-quinone **2,** an unexpected reaction takes place which provides a ready access to the spiroundecane [5.5] series in a highly functionalized state.

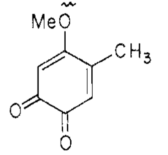
The known[6] 2-chloromethyl-4-nitroanisole (**3**) served as a starting material for both quinones. Acetolysis by known methodology[6] gave the acetoxymethyl compound **4.** Reduction of the nitro group (zinc–dilute HCl) gave the anilino compound **5**[7] (mp 58–59°) in 77% yield. Diazotization and hydrolysis of **5** afforded the phenol **6** (mp 92–93°[7]) in 76% yield. Oxidation of **6** with Fremy's salt[8] gave *o*-quinone **1**[7] (mp 128–130°) in quantitative yield.



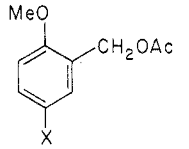
1



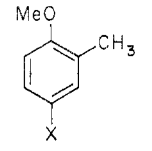
3



2



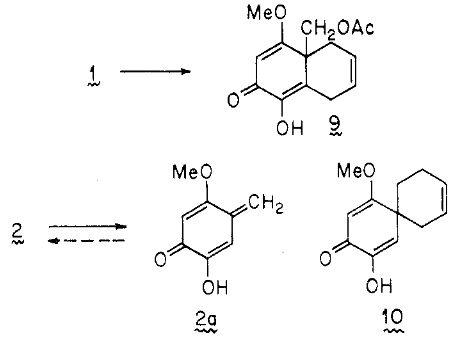
4 X = NO$_2$
5 X = NH$_2$
6 X = OH



7 X = NH$_2$
8 X = OH

Compound **3** was also converted by overall hydrogenation–hydrogenolysis to the known aniline derivative **7**[9] and thence (diazotization–hydrolysis) to the phenol **8.**[10] Fremy's salt oxidation of **8** afforded 89% *o*-quinone **2**[7] (mp 110–120° dec).

Compound **1** was heated with excess 1,3-butadiene in benzene in a sealed tube at 105° for 5 hr. A 63% yield of a crystalline product, mp 150–151°, was obtained. On the basis of its combustion analysis,[7] ir [$\bar{\nu}$ (CHCl$_3$) 3430, 1740, 1625 cm^{-1}], nmr [δ (CDCl$_3$) 1.9 (s, 3), 2.2–2.4 (m, 4), 3.8 (s, 3), 4.3 (d, J = 17Hz, 1), 4.4 (d, J = 17 Hz, 1), 5.4–6.0 (m, containing s at δ 5.7, 3), 6.7 (s, 1 exchange with D$_2$O)], and mass (*m/e* 264 – parent) spectra, this compound is defined as structure **9.** Clearly **9** is the result of Diels–Alder reaction of **1** with 1,3-butadiene followed by enolization of the α diketone, so produced, to the tautomeric diosphenol. *To our knowledge this represents the first successful Diels–Alder reaction where a nonactivated o-benzoquinone*[11] *has been successfully condensed with 1,3-butadiene itself.*



Reaction of *o*-benzoquinone **2** with 1,3-butadiene under identical reaction conditions produced a crystalline product (mp 185–187°) in 48% yield. The combustion analysis (Found: C, 69.72; H, 6.72) and mass spectra (*m/e* parent 206) are consistent with its being a 1:1 adduct. However, even a cursory examination of its pmr spectrum indicates that this compound can not be formulated as the analog of **9** bearing an angular methyl group. In fact, the only 3 H singlet in the spectrum appears at δ 3.80, clearly ascribable to a methoxy group. On the basis of the analysis of the proton chemical shifts (see Figure 1) structure **10**[7] was assigned to this compound.

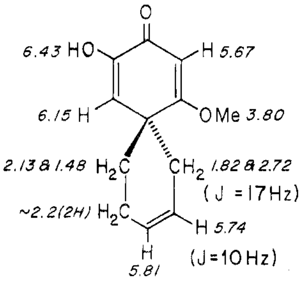


Figure 1.

The presence of a 2-hydroxy 4,4-disubstituted 5-methoxycyclohexadienone system is supported by a strong ferric chloride test, the presence of an exchangeable proton at δ 6.43, and two singlets at 5.67 and 6.15, which are characteristic of vinylic protons. The remaining protons were assigned with the aid of double resonance at 250 MHz (Figure 1).

Corroboration of the structure was obtained by examination of its cmr spectrum at 62.5 MHz in which the spiro carbon atoms was found at 41.3 ppm (CDCl$_3$ containing TMS). The assignments for the eight hydrogen-bearing carbons are shown in Figure 2.

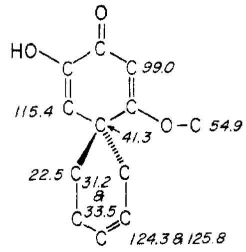


Figure 2.

The formation of **10**, though not predicted, can be rationalized in terms of cycloaddition of **2a** with 1,3-butadiene. Intermediate **2a** must arise by tautomerization of **2**. The tautomerization of an *o*-benzoquinone to a 2-hydroxy-4-methylenecyclohexadienone, followed by cycloaddition of the latter at the exocyclic methylene group, is to our knowledge a new route to spiro systems.

Some rather subtle structural features are exercising strong control over the choice of the options of conventional cycloadditon (*cf.* **1** → **9**) *vs.* enolization–cycloaddition (*cf.* **2** → **10**).[12] These factors have not, at this point, been defined.

Synthetic applications of Diels–Alder reactions of o-benzoquinones will be described in due course.

Acknowledgments. This research was supported by PHS Grant C.A. 12107-09. Nmr spectra were measured on facilities supported by PHS Grant RR-00292-03.

Supplementary Material Available. The experimental procedures for the reactions described in this investigation will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JOC-74-3610.

References and Notes

(1) A. S. Onischenko, "Diene Synthesis," Israel Program of Scientific Translations, Daniel Davy, New York, N.Y., 1964.

(2) (a) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. M. MeLamore, *J. Amer. Chem. Soc.*, **74**, 4223 (1952); (b) L. H. Sarett, R. M. Lukes, G. I. Poos, J. M. Robinson, R. E. Beyler, J. M. Vandergrift, and G. E. Arth, *ibid.*, **74**, 1393 (1952); (c) J. E. Cole, W. S. Johnson, P. A. Robins, and J. Walker, *J. Chem. Soc.*, 244 (1962); (d) R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey, and R. W. Kierstead, *Tetrahedron*, **2**, 1 (1958); (e) E. E. Van Tamelen, M. Shamma, A. Burgstahler, J. Wolinsky, R. Tam, and P. Aldrich, *J. Amer. Chem. Soc.*, **91**, 7135 (1969); (f) S. Sallay, *ibid*, **89**, 6767 (1967); (g) R. A. Dickinson, R. Kubela, G. A. MacAlpine, Z. Stojanac, and Z. Valenta, *Can. J. Chem.*, **50**, 2377 (1972). (h) Y. Kishi, M. Aratani, T. Fukuyama, F. Nakatsubo, T. Goto, S. Inoue, H. Tanino, S. Sugurra, and H. Kakoi, *J. Amer. Chem. Soc.*, **94**, 9217 (1972).

(3) J. M. Bruce, "Rodd's Chemistry of Carbon Compounds," Vol IIIB, S. M. Coffey, Ed., American Elsevier, New York, N.Y., 1974, Chapter 1.

(4) To our knowledge there are only two examples of a 4-methoxy-*o*-benzoquinone acting in a dienophilic capacity. These were reported on the parent 4-methoxy-*o*-benzoquinone with cyclopentadiene[5a] and with 2,3-dimethyl-1,3-butadiene.[5b] Neither case is necessarily suggestive of the deactivating effect of the 4-methoxyl group on the dienophilicity of the 3,4 double bond since the cycloaddition at the 5,6 double bond may be rationalized in purely steric terms. The case of quinone **1**, described here, is the first one involving a 5-substituted 4-methoxy system. The exclusive dienophilicity of the 5,6 double bond and the stability required to allow for cycloaddition with 1,3-butadiene are most readily rationalized on the basis of the effects of the 4-methoxy group on both the diene and dienophilic properties postulated above.

(5) (a) M. F. Ansell, A. F. Gosden, V. J. Leslie, and R. A. Murray, *J. Chem. Soc. C*, 1401 (1971); (b) M. F. Ansell, A. J. Bignold, A. F. Gosden V. J. Leslie, and R. A. Murray, *ibid.*, 1414 (1971).

(6) R. Quelet and H. Coudanne, *Bull. Soc. Chim. Fr.*, 2445 (1963).

(7) C, H, and N combustion analyses within 0.4% of theory were obtained for this compound. Confirmatory ir, nmr, and mass spectra were also obtained. They are reported in the Experimental Section which follows these pages in the microfilm edition.

(8) H. Zimmer, D. Clankin, and S. W. Horgan, *Chem. Rev.*, **71**, 229 (1971).

(9) E. Bamberger, *Ann. Chim. (Paris)*, **443**, 201 (1925).

(10) N. Kharasch, S. Kalfayan, and D. Arlerberry, *J. Org. Chem.*, **21**, 925 (1956).

(11) The only two previous examples of the condensation of the relatively nonreactive 1,3-butadiene with *o*-benzoquinones were cases involving a 4-carbomethoxyl[5b] or a 4-cyano group.[5b] Such groups are known[3] to enhance dienophilicity.

(12) Although we do not have a full accounting of the material in either the reaction of **1** or **2** with butadiene, we believe that there is very little, if any, spiro product in the case of **1** of fused product in the case of **2**. Tlc analysis of the mother liquors in the reaction of **1**, where a 63% yield of crystalline **9** was obtained, shows additional **9** and variety of other spots. While these have not been identified, it is not likely that any one is present to the extent of more than a few per cent. In the case of **2**, where a 48% yield of crystalline **8** was obtained, the major loss, 20-25%, arises from a red, intractible substance. The mother liquors after separation of crystalline **10**, show (tlc analysis) additional amounts of **10** and several other unidentified spots. The nmr spectrum of these mother liquors does not show any methyl resonance in the region δ 1-1.5 where it would be expected from the direct cycloaddition of **2** with 1,3-butadiene.

Department of Chemistry
University of Pittsburgh
Pittsburgh, Pennsylvania
15260
S. Mazza
S. Danishefsky*

Department of Chemistry
Carnegie-Mellon University
Pittsburgh, Pennsylvania
15213
P. McCurry

Received September 30, 1974

"Nucleophilic" Replacement of Two Halogens in Dihalobenzenes without the Intermediacy of Monosubstitution Products[1]

Summary: The fact that several dihalobenzenes react with thiophenoxide ion in ammonia under irradiation to form disubstitution products without substantial intermediacy of monosubstitution products constitutes unique evidence of mechanism, serving to exclude numerous possibilities, but straightforwardly accommodated by the SRN1 mechanism.

Sir: Aryl iodides react readily with thiophenoxide ion in liquid ammonia, under irradiation, to form diaryl sulfides in high yield[2] (eq 1). We now report that under the same conditions many dihalobenzenes afford disubstitution products. Typically, little if any monosubstitution product is formed. Moreover, we have evidence that for the most part *the monosubstitution product is not an intermediate in the production of disubstitution product.*

$$\mathrm{ArI} + \mathrm{PhS}^- \xrightarrow{h\nu} \mathrm{Ar{-}S{-}Ph} + \mathrm{I}^- \qquad (1)$$

A representative reaction is that of *m*-chloroiodobenzene with thiophenoxide ion during 2.5-hr irradiation with Pyrex-filtered light to form the bis sulfide, *m*-di(thiophenoxy)benzene, in 91% yield accompanied by a mere trace of *m*-chlorophenyl phenyl sulfide. Even at short reaction times, at which the dihalobenzene is but partially reacted, only a trace of monosubstitution is observable alongside predominant disubstitution.

The results of numerous experiments are summarized in Table I. It is noteworthy that *m*-fluoroiodobenzene (run 8) underwent only replacement of iodine, yielding 96% of *m*-fluorophenyl phenyl sulfide. However, in *p*-iodophenyltrimethylammonium ion (run 6) both the iodine and the trimethylammonio group were replaced, forming the bis sulfide in 95% yield. Replacement of the trimethylammonio substituent in aromatic SRN1 reactions is a familiar phenomenon.[3-5]