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Nucleophilic Alkenes. V*
Formation of a Naphthalenic System by Addition of 1,1-Dimethoxyethene to 2-Acetyl-1,4-benzoquinone and Subsequent Transformation

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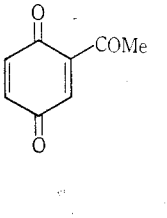
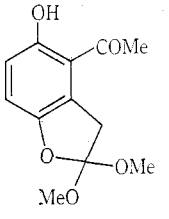
Abstract

2-Acetyl-1,4-benzoquinone underwent rapid 1 : 1-addition of 1,1-dimethoxyethene at position 3 to give a 2,3-dihydro-2,2-dimethoxybenzofuran derivative (2). Ring opening of this cyclic orthoester and subsequent ring closure onto the acetyl group gave a naphthalene derivative incorporating the 1,3-dioxygenation pattern found in many polyketides.

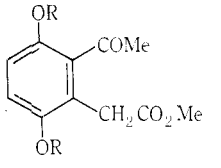
In an extensive investigation[1–3] Eugster and his coworkers have demonstrated the strong influence of the acetyl substituent of 2-acetyl-1,4-benzoquinone (1) in facilitating nucleophilic attack at position 3. In particular, enol ethers react with subsequent cyclization to yield cyclic acetals.[2] In Parts III[4] and IV[5] it has been shown that 1,1-dialkoxyethenes are highly effective nucleophiles towards unsubstituted 1,4-benzoquinone and 1,4-naphthoquinone. It was therefore expected that reaction between the quinone (1) and 1,1-dimethoxyethene would occur readily.



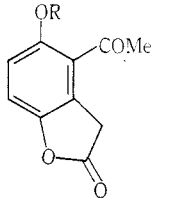
(1)



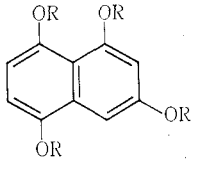
(2)



(3) R = H
(4) R = Ac



(5) R = H
(6) R = Ac



(7) R = H
(8) R = Ac

This expectation has been borne out, a mixture of the two reactants in dimethyl sulfoxide rapidly forming a new product (65%), formulated as the cyclic orthoester (2). Its proton magnetic resonance spectrum contained singlet resonances of appropriate intensity (δ 3·45, 3·37, 2·49) corresponding to methylene, methoxy and acetyl protons

* Part IV, *Aust. J. Chem.*, 1978, **31**, 1353.

[1] Fumagalli, S. E., and Eugster, C. H., *Helv. Chim. Acta*, 1971, **54**, 959.
[2] Kuser, P., Frauenfelder, E. F., and Eugster, C. H., *Helv. Chim. Acta*, 1971, **54**, 969.
[3] Kuser, P., Inderbitzin, M., Brauchli, J., and Eugster, C. H., *Helv. Chim. Acta*, 1971, **54**, 980.
[4] Cameron, D. W., Crossley, M. J., Feutrill, G. I., and Griffiths, P. G., *Aust. J. Chem.*, 1978, **31**, 1335.
[5] Cameron, D. W., and Crossley, M. J., *Aust. J. Chem.*, 1978, **31**, 1353.

respectively. Its structure is analogous to those of other stoichiometric 1 : 1 adducts reported earlier.[5]

On mild treatment with sodium methoxide in methanol compound (2) efficiently underwent ring opening to give the phenylacetate derivative (3) after workup. It showed two carbonyl absorption bands in the infrared while its p.m.r. spectrum was consistent with replacement of the two methoxy groups of (2) by a single methyl ester (δ 3·60). It readily gave a diacetate (4).

Whilst the phenylacetate (3) was stable in the solid phase, it was converted into a new product during preparative thin-layer chromatography. This was formulated as the lactone (5) on the basis of a new carbonyl absorption band at 1799 cm^{-1} and the absence of any methoxy resonance from its p.m.r. spectrum. The corresponding acetate (6) was formed from the diacetate (4) by treatment with acetic anhydride and sulfuric acid. The lactone (5) has been reported previously[1] as a by-product which was acetylated to (6).

The ester grouping in the ring-opened compound (3) was suitably positioned for intramolecular cyclization onto the adjacent acetyl.[6] This was achieved by contact with sodium methoxide in boiling methanol. The presumed product (7) was not isolated as such but was converted directly into the known tetraacetate (8).[7,8] The yield was limited (18%), exclusion of air being necessary in view of the susceptibility of the tetraol (7) and of the derived 5,7-dihydroxy-1,4-naphthoquinone to base-catalysed oxidation. However, the overall sequence (1) → (8) has generated a new benzenoid ring having the 1,3-dioxygenated pattern of substitution found in many polyketides. Development of this approach to the synthesis of significantly more complicated natural polyketides is being investigated.

Experimental

Unless otherwise stated infrared spectra were measured as KBr discs, electronic spectra in ethanol (95%) and p.m.r. spectra in $CDCl_3$. Chemical shifts are quoted on the δ scale from $SiMe_4$ as internal reference.

Addition of 1,1-Dimethoxyethene to 2-Acetyl-1,4-benzoquinone

A solution of 2-acetyl-1,4-benzoquinone (4 g) in dry dimethyl sulfoxide was treated with 1,1-dimethoxyethene[4] (6 g). The mixture, which rapidly became hot, was allowed to stand for 10 min and then poured into ethyl acetate (300 cm^3). The resulting solution was washed with water (6 × 300 cm^3) and dried; the solvent was evaporated under vacuum to give *orthoester* (2), yellow crystals (3·39 g), m.p. 108–110°, from ethyl acetate (Found: C, 60·6; H, 5·8. $C_{12}H_{14}O_5$ requires C, 60·5; H, 5·9%). λ_{max} (log ε) 220sh, 234, 256, 357 nm (4·07, 4·10, 3·90, 3·54). ν_{max} 1630 cm^{-1}. δ 2·49, s, $COCH_3$; 3·37, s, 2 × OCH_3; 3·45, s, CH_2; 6·75, 6·90, d, d, J 8·5 Hz, 2 × ArH. *m/e* 238 (M, 70%).

Ring Opening of Orthoester (2)

A solution of the orthoester (100 mg) in methanol (50 cm^3) was stirred at room temperature for 1 h with a solution of sodium (4 g) in methanol (50 cm^3) under nitrogen. The mixture was then cooled to 0° and acidified with chilled dilute hydrochloric acid. It was diluted with water (500 cm^3) and then extracted with ethyl acetate (6 × 100 cm^3). After removal of the solvent under vacuum the residue (80 mg) was recrystallized from ethyl acetate to give the *methyl ester* (3) as pale yellow plates, m.p. 188–189°. This value is close to that of the lactone (5) and there was a pronounced phase change during melting, suggesting the possibility of lactonization during the process (Found:

[6] Bycroft, B. W., Roberts, J. C., and Baker, P. M., *J. Chem. Soc.*, 1964, 2289.
[7] Garden, J. F., and Thomson, R. H., *J. Chem. Soc.*, 1957, 2483.
[8] Cameron, D. W., and Sidell, M. D., *J. Chem. Soc., Chem. Commun.*, 1976, 252.

C, 58·9; H, 5·4. $C_{11}H_{12}O_5$ requires C, 58·9; H, 5·7%). λ_{max} (log ε) 328 nm (3·48). ν_{max} 1718, 1662, 1615 cm^{-1}. δ ($(CD_3)_2CO$) 2·50, s, $COCH_3$; 3·60, s, CO_2CH_3; 3·71, s, CH_2; 6·73, 6·78, d, d, J 8·5 Hz, 2 × ArH. m/e 224 (M, 20%).

Treatment of this product with acetic anhydride and pyridine gave the *diacetate* (4), colourless needles, m.p. 72–73°, from benzene/petroleum (Found: C, 58·6; H, 5·2. $C_{15}H_{16}O_7$ requires C, 58·4; H, 5·2%). λ_{max} (log ε) 280 nm (3·19). ν_{max} 1765, 1736, 1692 cm^{-1}. δ 2·26, 2·28, s, s, 2 × O_2CCH_3; 2·50, s, $COCH_3$; 3·62, s, CO_2CH_3 and CH_2; 7·12, s, 2 × ArH. m/e 308 (M, 25%).

Lactonization of Ester (3)

On attempted preparative t.l.c. on silica gel GF the ester (3) (45 mg) was converted into the lactone (5) (30 mg), yellow plates, m.p. 190–191°, from ethyl acetate (lit.[1] 186–187°) (Found: C, 62·5; H, 4·2. Calc. for $C_{10}H_8O_4$: C, 62·5; H, 4·2%). λ_{max} (log ε) 234, 250sh, 345 nm (4·16, 3·97, 3·58). ν_{max} 1799, 1634 cm^{-1}. δ 2·50, s, $COCH_3$; 3·91, s, CH_2; 6·91, 7·19, d, d, J 9 Hz, 2 × ArH. m/e 192 (M, 65%). [These electronic, infrared and p.m.r. data do not agree with the literature.[1] However, the literature data are themselves incompatible with the assigned structure in lacking, for example, a high frequency carbonyl band in the infrared and in containing two methyl p.m.r. resonances. These literature data are actually consistent with a second structure described in the same section of the Experimental. Transposition of the two sets of literature values would lead to compatibility with the assigned structures and to reasonable agreement with the values quoted here.]

Lactonization of Ester (4)

A solution of ester (4) (45 mg) in a mixture of acetic acid (1 cm^3), acetic anhydride (1 cm^3) and sulfuric acid (1 drop) was boiled for 1 h. Workup in the usual way gave the lactone acetate (6), yellow needles, m.p. 129–130°, from benzene/petroleum (lit.[1] 126–127°).

Naphthalene-1,3,5,8-tetrayl Tetraacetate (8)

A solution of ester (3) (95 mg) in methanol (1 cm^3) was flushed with dry nitrogen, added dropwise to a boiling solution of sodium (500 mg) in methanol (10 cm^3) under nitrogen and the mixture boiled for a further 7 min. Most of the solvent was removed under vacuum. Chilled acetic anhydride (5 cm^3), freshly flushed with nitrogen, was then added. The mixture was shaken for 5 min, cooled and poured into ethyl acetate (50 cm^3). This was then washed with water (3 × 50 cm^3), dried and solvent evaporated. The residue (91 mg) was subjected to preparative t.l.c. in chloroform. The major band (27 mg) gave naphthalene-1,3,5,8-tetrayl tetraacetate (8), as colourless needles, m.p. 185–186°, from ethyl acetate. It was undepressed in admixture with an authentic sample (lit.[7] 181°) and had identical infrared absorption, p.m.r. spectrum and chromatographic behaviour. λ_{max} (log ε) 228, 291, 327 nm (4·82, 3·85, 3·23). ν_{max} 1768 cm^{-1}. δ 2·30, s, O_2CCH_3; 2·35, s, 2 × O_2CCH_3; 2·41, s, O_2CCH_3; 6·96–7·58, m, 4 × ArH.

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