Generation of Heterocyclic Quinone Methides from *ortho*-Hydroxy Methyl Derivatives and a Study of Their Cycloaddition Reactions

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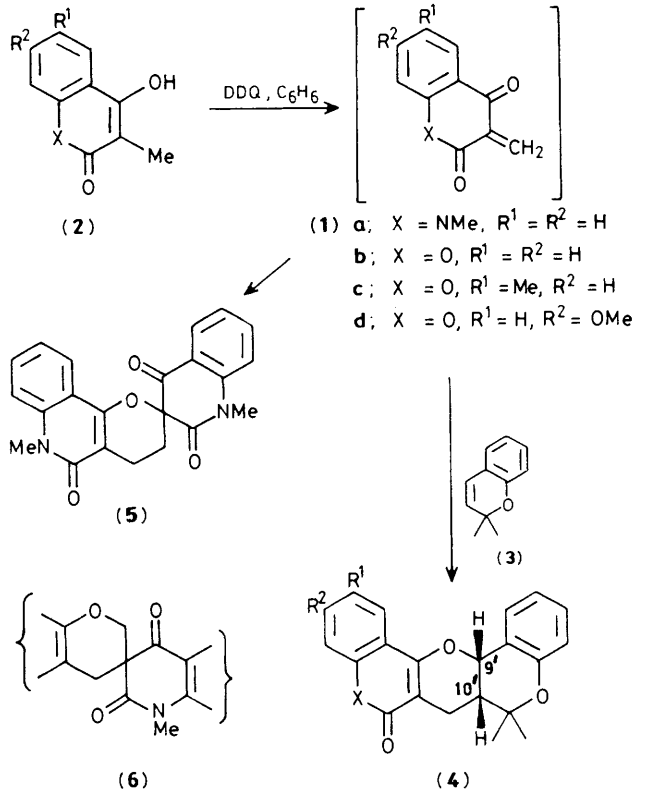
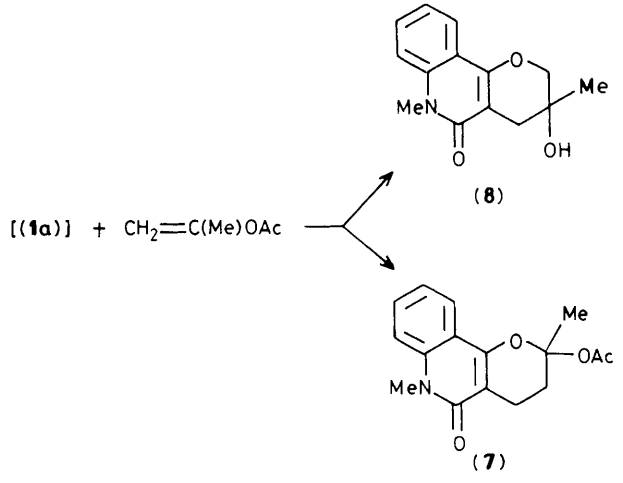
Quinolinone quinone methide (**1a**), prepared from 1,3-dimethyl-4-hydroxyquinolin-2-one and 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), gives a dimer (**5**) and reacts *in situ* with 2,2-dimethyl-2*H*-1-benzopyran, and with isopropenyl acetate, to give Diels–Alder cycloaddition products; coumarin quinone methides behave similarly with 2,2-dimethylbenzopyran, but with isopropenyl acetate and with 2,3-benzofuran give adducts that probably result from [2 + 2] cycloaddition reactions.

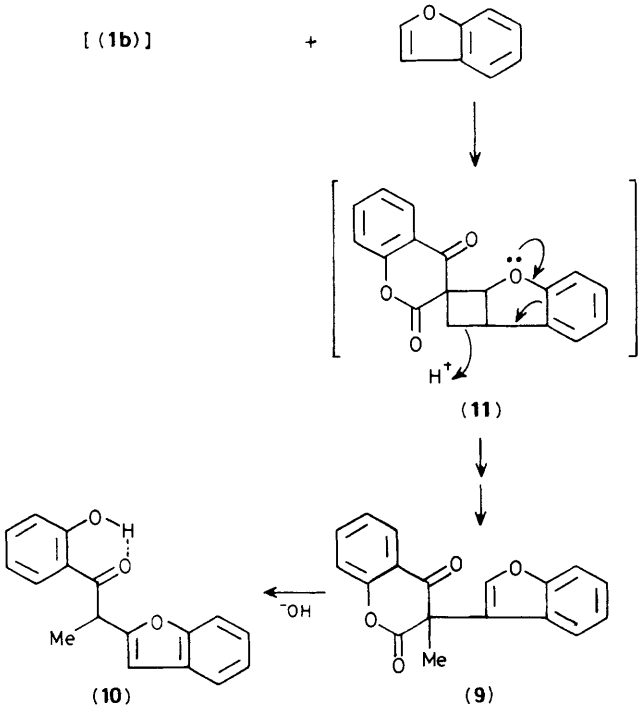
Heterocyclic quinone methides, which can act as reactive intermediates in cycloaddition reactions,[1] have been prepared *in situ* by a number of methods. For example, pyrolysis of 3-dimethylaminomethyl-4-hydroxyquinolinones in the presence of aromatic amines gives dibenzonaphthyridinone derivatives, apparently *via* quinone methides of type (**1**; X = NH or NMe);[2] reaction of 4-hydroxypyran-2-ones with aldehydes also yields quinone methides that can be trapped with thiols.[3] Prenyl derivatives are converted by oxidation[4] or strong base[5] into heterocyclic quinone methides (leading to intramolecular cycloaddition) and pyrolysis results in non-specific dimerization.[6] Following an interest in dimeric coumarins and quinolinone alkaloids,[7] we generated the quinolinone quinone methide (**1a**) by refluxing a solution of 1,3-dimethyl-4-hydroxyquinolin-2-one (**2a**) and 2,3-dichloro-5,6-dicyanbenzoquinone (DDQ) in benzene; in the presence of the pyranoquinolinone alkaloid, *N*-methylflindersine, a cycloaddition product was formed in good yield.[8] We now



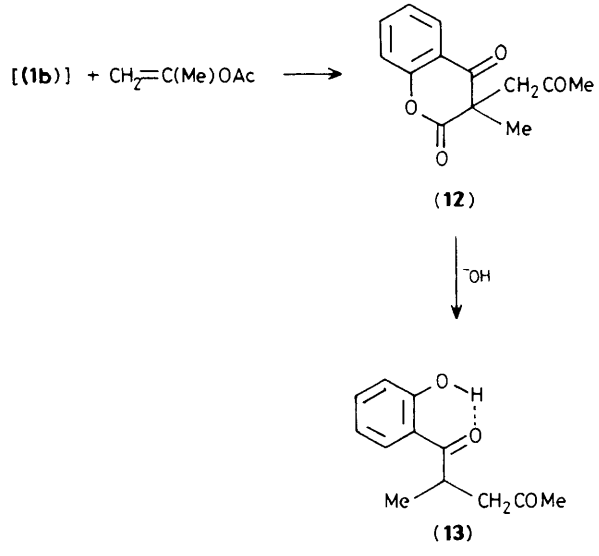
Scheme 1



Scheme 2



Scheme 3



Scheme 4

report a study of this convenient method of preparing methides (**1**) and describe their reactivity.

Methide (**1a**) was reacted with 2,2-dimethyl-2*H*-1-benzopyran (**3**) to give a Diels–Alder cyclo-adduct (14%), which was shown by its ^1H and ^{13}C n.m.r. spectra, and by mass spectrometry, to have structure (**4a**); catalysis with the shift reagent Eu(fod)$_3$ (fod = 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionato) raised the yield to 30%. In the absence of the dienophile, dimerization of the methide occurred to give compound (**5**) (66%); its structure was distinguished from that of the alternative (**6**) by the presence of two-proton multiplets in the ^1H n.m.r. spectrum at δ 2.61 and 2.34, which were attributed to adjacent methylene groups, see Scheme 1. This type of dimerization is analogous to that of 2,6-dibenzylidenecyclohexanone[9] and of the quinone methides derived from *ortho*-alkyl phenols.[10] The quinone methide (**1a**) can be regarded as an electron-deficient enone and in the presence of the electron-rich benzopyran (**3**) it preferentially undergoes an inverse electron demand cycloaddition reaction; with the electron-deficient dienophiles maleic anhydride and dimethyl acetylenedicarboxylate, however, only the dimer (**5**) is isolated. This interpretation accords with theoretical calculations on related cycloaddition reactions and dimerization of quinone methides.[11] We also

studied the formation of methide (**1a**) in the presence of the electron-rich olefin, isopropenyl acetate. In this case, two cyclo-adducts were formed and were shown by spectroscopy to be the hemiketal acetate (**7**) (20%) and the tertiary alcohol (**8**) (18%), see Scheme 2.

Reaction of the 4-hydroxy-3-methylcoumarins (**2b**)—(**2d**) with DDQ and 2,2-dimethyl-2*H*-1-benzopyran in refluxing benzene gave the pentacyclic derivatives (**4b**)—(**4d**) in 34—35% yield. That these compounds are the oxygen analogues of the quinolinone (**4a**) was shown by spectroscopic studies; the *cis*-relationship of the hydrogen atoms at C-9[1] and C-10[1] as shown by the ^{1}H n.m.r. spectra (J 4.2—4.4 Hz) indicates that the intermediate quinone methides (**1b**)—(**1d**) undergo Diels–Alder cycloaddition reactions with the benzopyran.

Reaction of the coumarin (**1b**) with 2,3-benzofuran produced compound (**9**) (62%), which showed i.r. absorption at 1750 (lactone carbonyl) and 1690 cm^{-1} (ketone carbonyl). Treatment of the keto-lactone (**9**) with aqueous sodium hydroxide resulted in hydrolysis of the lactone ring, followed by decarboxylation, to give the hydroxyketone (**10**); its structure was apparent from the ^{1}H n.m.r. spectrum which showed resonances at δ 12.15 (1H, s, OH), 6.55 (1H, s, –CH=C–O–), 4.95 (1H, q, C*H*Me), and 1.70 (3H, d, CH*Me*). Simple acid-catalysed addition of benzofuran to methide (**1b**) would be expected to occur at the methylene group and a plausible mechanism for formation of isomer (**9**) involves [2 + 2] cycloaddition of the benzofuran to the carbon–carbon double bond of methide (**1b**) followed by acid-catalysed ring fission of the cyclobutane intermediate (**11**), see Scheme 3. In contrast to its behaviour with quinolinone methide (**1a**), isopropenyl acetate reacts with the coumarin methide (**1b**) to give the diketo lactone (**12**), which with base is converted into the hydroxy diketone (**13**): mechanisms similar to those for benzofuran addition are proposed, see Scheme 4.

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References

1 G. Desimoni and G. Tacconi, *Chem. Rev.*, 1975, **75**, 651.
2 J. L. Asherson and D. W. Young, *J. Chem. Soc., Perkin Trans. 1*, 1980, 512 and 522.
3 P. de March, M. Moreno-Manãs, R. Pi, and A. Trius, *J. Heterocycl. Chem.*, 1982, **19**, 335.
4 F. Piozzi, P. Venturella, and A. Bellino, *Gazz. Chim. Ital.*, 1969, **99**, 711.
5 R. M. Bowman, M. F. Grundon, and K. J. James, *J. Chem. Soc., Perkin Trans. 1*, 1973, 1055.
6 J. F. Ayafor, B. L. Sondengam, J. D. Connolly, and D. S. Rycroft, *Tetrahedron Lett.*, 1985, **26**, 4529.
7 *Cf.*, M. F. Grundon in 'Chemistry and Chemical Taxonomy of the Rutales,' ed. P. G. Waterman and M. F. Grundon, Academic Press, London, 1983, p. 21.
8 M. F. Grundon, V. N. Ramachandran, and B. M. Sloan, *Tetrahedron Lett.*, 1981, **22**, 3105.
9 H. O. House and A. G. Hortmann, *J. Org. Chem.*, 1961, **26**, 2190.
10 A. Merijan, B. A. Shoulders, and P. D. Gardner, *J. Org. Chem.*, 1963, **28**, 2148.
11 P. Lanteri, R. Longeray, and J. Royer, *J. Chem. Res. (S)*, 1981, 168.