Tetrahedron Letters,Vol.24,No.24,pp 2453-2456,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

REGIOSPECIFIC ADDITIONS OF SOME SIMPLE DIENES TO HALOQUINONES

Louise Boisvert and Paul Brassard*
Département de chimie, Université Laval
Québec, Canada, G1K 7P4

Abstract - Some simple dienes have been shown to react regiospecifically with haloquinones; the adducts can be oxidized without loss of the oxygenated function or aromatized to a variety of natural products and useful intermediates.

In our continuing study of efficient methods for the synthesis of naturally occurring quinones, we have already established that ketene acetals[1], vinylketene acetals[2a-g] and vinylogous ketene acetals[3a-c] give regiospecific products with a variety of halogenated quinones. These essentially convergent[2c,d] methods are doubly advantageous in that the regiochemistry depends only on the position of the halogen[1,2c,g,3c] and that the latter is eliminated in the overall process.

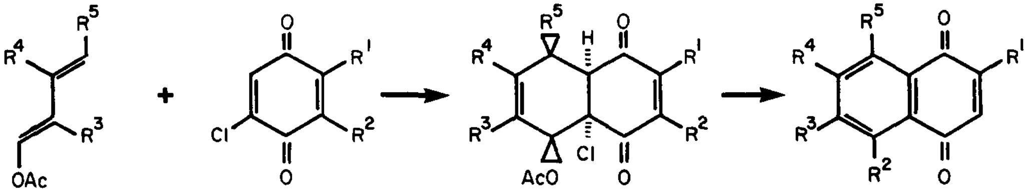
Cycloadditions of dienes bearing a lone oxygen function (or less polar groups) to unsymmetrical quinones, mainly juglones and methylquinones are notorious for their lack of regiospecificity[4]. However this unfavorable result can be overcome in some cases by applying Lewis acid catalysis[5], specific dienes[6] and dienophiles[7] or substrates with functions having complementary effects[8]. These conditions restrict the usefulness of the process which generally serves only particular purposes. Moreover attempts to reverse the regiochemical outcome through catalysis[5a,9] or functional modifications[4c,8] usually are either somewhat unpredictable or give mixtures of isomers. (TABLE I)

TABLE I - THE ADDITIONS OF SOME SIMPLE DIENES TO QUINONES

Quinone	1,3-Diene	Conditions	Regioselectivity,A:B[§]
2,6-Dimethylbenzo-	1-Acetoxy-4-methylbuta-	C_6H_6,150°	4:1[4a]
5-Hydroxynaphtho-	1-Acetoxybuta-	C_6H_6,80°	~3:1[4b]
5-Hydroxynaphtho-	2-Methoxybuta-	C_6H_6, Δ	2.7:1[4e]
5-Hydroxynaphtho-	1-Acetoxybuta-	BF_3,55°	>50:1[5b,c]
2-Methoxybenzo-	1-Methoxycyclohexa-	C_6H_6,80°	A[6b]
5-Ethoxy-8-hydroxynaphtho-	1-Methoxycyclohexa-	CH_2Cl_2,r.t.	A[8b]
5-Hydroxynaphtho-	1-Methoxycyclohexa-	MgI_2,25°	1:17[5a]
5-Methoxynaphtho-	2-Methoxybuta-	EtOH,100°	~4:1[4c]

[§] A is the expected regioisomer based on the polarization of reactants.

The reactions of a number of 1-acetoxybutadienes[10] (1 a-d) with 2,5- or 2,6- dichlorobenzoquinones (2a or 2b) as well as other halogenated quinones[11] have now been carried out and been found to give only one detectable adduct (3a-j) in each case[12] (SCHEME I). In a typical procedure, a benzene solution (20 mL) of the quinone (2.0 mmols) and the diene (2.2 mmols) was refluxed for 36-40 hours. The corresponding aromatized product (4 a-g) then could readily be obtained by rapidly passing the reaction mixture several times through a column of silica gel[13]. In particular, reactions with 2-chloro-5- or 6-methoxy-benzoquinones (2c-d) also demonstrated independence of electronic effects due to certain other substituents (TABLE II).



1a $R^3=R^4=R^5=H$
b $R^3=CH_3, R^4=R^5=H$
c $R^3=R^5=H, R^4=CH_3$
d $R^3=R^4=H, R^5=CH_3$

2a $R^1=Cl, R^2=H$
b $R^1=H, R^2=Cl$
c $R^1=OCH_3, R^2=H$
d $R^1=H, R^2=OCH_3$

3a-j

4a $R^1=Cl, R^2=R^3=R^4=R^5=H$
b $R^1=Cl, R^2=R^4=R^5=H, R^3=CH_3$
c $R^1=Cl, R^2=R^3=R^5=H, R^4=CH_3$
d $R^1=Cl, R^2=R^3=R^4=H, R^5=CH_3$
e $R^1=Cl, R^2=CH_3, R^3=R^4=R^5=H$
f $R^1=OCH_3, R^2=R^3=R^5=H, R^4=CH_3$
g $R^1=OCH_3, R^2=R^4=R^5=H, R^3=CH_3$

Scheme I

TABLE II

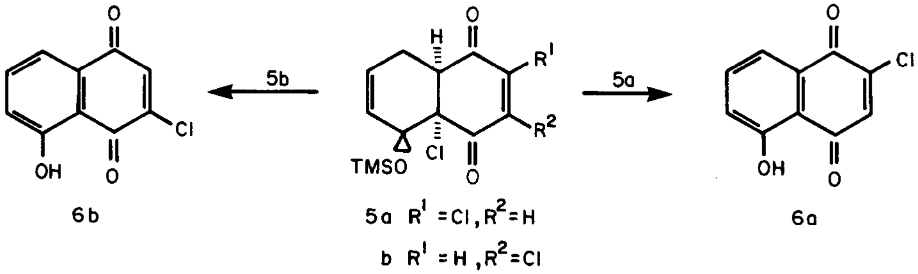
PREPARATION OF NAPHTHOQUINONES BY AROMATIZATION OF ADDUCTS

Diene	Benzoquinone	Naphthoquinone	m.p.	Yield (%)
1a	2b	4a	112-113°	92
1b	2a	4b	134.5-135.5°	79
1b	2b	4c	122-123°	65
1c	2a	4c	122-123°	88
1c	2b	4b	134.5-135.5°	80
1d	2a	4d	116-117°	80
1d	2b	4e	110-111°	90
1c	2c	4f	187-188°	96
1c	2d	4g	165°	79

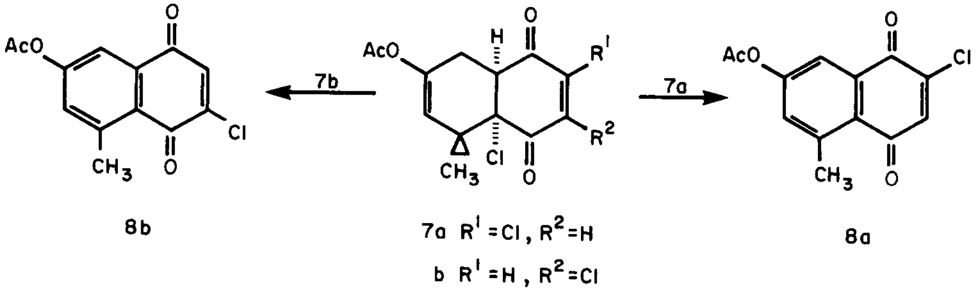
The samples of quinones obtained either from 1b and 2a or 1c and 2b are indistinguishable as are those from 1b and 2b or 1c and 2a. All adducts and naphthoquinones give n.m.r. spectra consistent with their structure. The structures of intermediates are tentatively ascribed by analogy with well established cycloaddition products[14]. However the 2- and 3-chloro-6-methylnaphthoquinones (and a bromo analog) exhibit m.p.'s markedly different from those recorded in the literature[15]. Repetition of the earlier procedure provided a sample of "3-bromo-6-methylnaphthoquinone" comparable to the original but which, according to the n.m.r. data was obviously a mixture of the two possible isomers[16].

The acetylated adducts (3a-j) could not be oxidized directly without loss of the oxygenated function. On the other hand, the corresponding trimethylsiloxy derivatives[17] (5 a-j) were readily converted to the desired naphthoquinones. Thus, the important 2- and 3-chlorojuglones (6a and 6b) in particular were produced in 58% and 49% yields respectively by refluxing the crude adduct (from 2.0 mmols of 2a or 2b) with chromium trioxide (1.0 g) in acetic acid (1.5 h) (SCHEME II).

2-Oxygenated butadienes such as 2-acetoxypentadiene add to haloquinones (e.g. 2a or 2b) under the same conditions and also lead to regiospecific products[18] (7a or 7b). The latter could then be oxidized to the corresponding naphthoquinones 8a (m.p. 142-143°C) and 8b (m.p. 121-122°C) as above in 43% and 45% yields (SCHEME III).



Scheme II



Scheme III

REFERENCES AND NOTES

1. J. Banville, J.-L. Grandmaison, G. Lang, and P. Brassard, Can. J. Chem., 1974, 52, 80.

2.a) J. Banville and P. Brassard, J. Chem. Soc. Perkin I, 1976, 1852; b) J. Banville and P. Brassard, J. Org. Chem., 1976, 41, 3018; c) J.-L. Grandmaison and P. Brassard, Tetrahedron, 1977, 33, 2047; d) J.-L. Grandmaison and P. Brassard, J. Org. Chem., 1978, 43, 1435; e) J.

Savard and P. Brassard, Tetrahedron Letters, 1979, 4911; f) G. Roberge and P. Brassard, Synthesis, 1981, 381; g) G. Roberge and P. Brassard, J. Org. Chem., 1981, 46, 4161.

3. a) G. Roberge and P. Brassard, J. Chem. Soc. Perkin I, 1978, 1041; b) G. Roberge and P. Brassard, Synthesis, 1979, 148; c) C. Brisson and P. Brassard, J. Org. Chem., 1981, 46, 1810.

4. For some pertinent examples among many others see: a) C. Schmidt, J. Org. Chem., 1970, 35, 1324; b) H.H. Inhoffen, H. Muxfeldt, H. Schaefer, and H. Kramer, Croat. Chem. Acta, 1957, 29, 329; c) M.M. Shemyakin, M.N. Kulosov, Yu. A. Arbusov, M.G. Karapetyan, E.S. Chaman, and A.A. Onishchenko, Zh. Obshch. Khim., 1959, 29, 1831; d) T.R. Kelly, J.W. Gillard, and R.N. Goerner, Jr., Tetrahedron Letters, 1976, 3873; e) R.K. Boeckman, Jr., T.M. Dolak, and K.O. Culos, J. Am. Chem. Soc., 1978, 100, 7098.

5. a) T.R. Kelly and M. Montury, Tetrahedron Letters, 1978, 4311; b) G. Stork and A.A. Hagedorn III, J. Am. Chem. Soc., 1978, 100, 3609; c) B.M. Trost, W.C. Vladuchick, and A.J. Bridges, J. Am. Chem. Soc., 1980, 102, 3554; d) J.S. Tou and W. Reusch, J. Org. Chem., 1980, 45, 5012.

6. a) A.J. Birch and V.H. Powell, Tetrahedron Letters, 1970, 3467; b) R.G.F. Giles and G.H.P. Roos, J. Chem. Soc. Perkin I, 1976, 1632, 2057.

7. a) R.A. Russell, G.J. Collin, M. Sterns, and R. N. Warrener, Tetrahedron Letters, 1979, 4229; b) R.C. Gupta, D.A. Jackson, and R.J. Stoodley, J. Chem. Soc. Chem. Commun., 1982, 929.

8. a) T.R. Kelly, J.W. Gillard, R.N. Goerner, Jr., and J.M. Lyding, J. Am. Chem. Soc., 1977, 99, 5513; b) K. Tolkiehn and K. Krohn, Chem. Ber., 1980, 113, 1575; c) I.-M. Tegmo-Larsson, M.D. Rozeboom, and K.N. Houk, Tetrahedron Letters, 1981, 22, 2043.

9. R.A. Dickinson, R. Kubela, G.A. MacAlpine, Z. Stojanac, and Z. Valenta, Can. J. Chem., 1972, 50, 2377.

10. a) H.J. Hagemeyer, Jr. and D.C. Hull, Ind. Eng. Chem., 1949, 41, 2920; b) R.E. Banks, J.A. Miller, M.J. Nunn, P. Stanley, T.J.R. Weakley, and Z. Ullah, J. Chem. Soc. Perkin I, 1981, 1096.

11. Diene 1b and 2-chloronaphthoquinone gave tectoquinone (2-methylanthraquinone) (93%) while diene 1c afforded chimaphilin (2,7-dimethylnaphthoquinone) (71%) with 2-chloro-5-methylbenzoquinone and 6-methylxanthopurpurin 3-methyl ether (95%) with 3-chloro-7-methoxyjuglone.

12. A somewhat similar result was obtained earlier[3c] with 1-methoxy-2,4- bistrimethylsiloxypentadiene in which the effects of two polar groups effectively cancel one another.

13. Some adducts produced from the analogous 1-trimethylsiloxybutadienes were aromatized by simple crystallization from aqueous methanol containing a drop of conc. HCl.

14. Y.-M. Ngan, S.J. Rettig, J.R. Scheffer, and J. Trotter, Can. J. Chem., 1975, 53, 2068; S. Danishefsky, P.F. Schuda, S. Mazza, and K. Kato, J. Org. Chem., 1976, 41, 3468; D. Rutolo, S. Lee, R. Sheldon, and H.W. Moore, J. Org. Chem., 1978, 43, 2304; etc.

15. J.M. Lyons and R.H. Thomson, J. Chem. Soc., 1953, 2910.

16. The pure compounds prepared according to the present method have the following characteristics: 2-bromo-6-methylnaphthoquinone, m.p. 138-9°; the 3,6-isomer, m.p. 123-4°.

17. A. Ishida and T. Mukaiyama, Bull. Chem. Soc. Jpn, 1977, 50, 1161.

18. While this paper was in preparation a similar reaction appeared in print: Y. Tamura, A. Wada, M. Sasho, K. Fukunaga, H. Maeda, and Y. Kita, J. Org. Chem., 1982, 45, 4376.

(Received in USA 3 January 1983)