Tetrahedron Vol 33, pp 2047 to 2053 Pergamon Press 1977 Printed in Great Britain

REACTIONS OF KETENE ACETALS—IX[1]

THE SYNTHESIS OF NAPHTHOQUINONES FROM BENZOQUINONES

JEAN-LOUIS GRANDMAISON and PAUL BRASSARD*
Département de Chimie, Université Laval, Québec G1K 7P4, Canada

(*Received in USA 4 August 1976; Received in UK for publication 16 February 1977*)

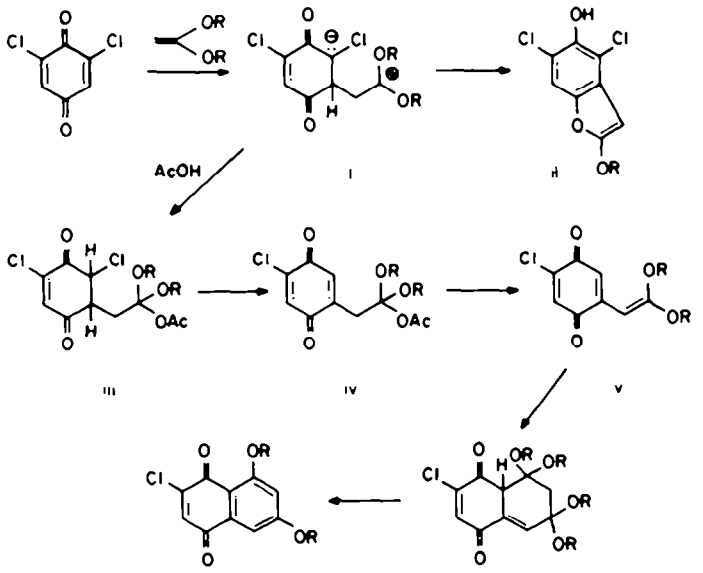
Résumé—La réaction d'halogénobenzoquinones avec les acétals de cétènes n'a donné auparavant que des benzofurannes. Toutefois, par addition d'acide acétique au milieu réactionnel, on a obtenu pour la première fois des naphtoquinones. Plusieurs aspects de la transformation ont été étudiés et la méthode a servi à la préparation d'intermédiaires utiles et de dérivés de produits naturels tels la tri-*O*-méthylflavioline **20** et le tétra-*O*-méthylspinochrome B **23**. Les benzoquinones réagissent par ailleurs avec les acétals de cétènes conjugués sans catalyse acide et fournissent en particulier des synthèses pratiques de la ramentacéone **43**, de la *O*-méthylstypandrone **45** et de la tétraméthoxy-1,3,6,8 anthraquinone **34**.

Abstract—Halogenobenzoquinones react with ketene acetals and give benzofurans, but in the presence of acetic acid, naphthoquinones are produced in variable yields. Some aspects of the reaction have been studied and the method has been applied to the synthesis of useful intermediates and of derivatives of some naturally occurring naphthoquinones such as tri-*O*-methylflaviolin **20** and tetra-*O*-methylspinochrome B **23**. Benzoquinones also react with conjugated ketene acetals without acid catalysis, providing convenient syntheses of ramentaceone **43**, *O*-methylstypandrone **45** and 1,3,6,8-tetramethoxyanthraquinone **34**.

Bromonaphthoquinone has been known for some time to react with ketene diethyl acetal and to yield 1,3-diethoxyanthraquinone.[2] Among halonaphthoquinones, a wide range of reactivity has been encountered; *peri*-hydroxyl groups, as in juglones and naphthazarins, increase the yields quite spectacularly[3] whereas the corresponding ethers generally have an unfavorable effect. In the latter case, addition of acetic acid to the reaction medium raises the efficiency to the level encountered with the hydroxylated compounds.[4]

Under similar conditions, halobenzoquinones give only benzofurans.[2] Modifying the structure of the substrate did not alter this result, however carrying out the reaction with benzoquinone dihalides did produce small amounts of the desired products. This course was assumed to have been taken following elimination of hydrogen chloride and acid catalyzed condensation of ketene acetals with the resulting benzoquinones.[5] Like juglone ethers, halobenzoquinones have now been found to react with ketene acetals in the presence of acetic acid and to form quinonic products. In the case of the most useful substrate, 2,6-dichlorobenzoquinone **8**, some attempts have been made to optimize the process and yields of up to 76% of 2-chloro-6,8-diethoxynaphthoquinone **16** have been attained.

It therefore appears that when applied to benzoquinones, the uncatalyzed reaction involves an initial nucleophilic attack by the ketene acetal, gives the zwitterion **i**, and is followed by rapid enolisation, cyclisation and elimination of alcohol forming the benzofuran **ii**. In



Scheme 1.

the case of naphthoquinones, the added stability of the intermediate provided by the aromatic ring permits the reaction with a second molecule of ketene acetal and thence cyclisation and aromatisation to the anthraquinone. Appropriately placed hydroxyl groups repress enolisation of the zwitterion even more effectively (than for example in the diketo tautomer of apionol)[6] and thus facilitate the desired conversion. Although no clear-cut reaction mechanism results from this study, nevertheless a consistent picture does emerge for the acid-catalyzed processes and a number of possibilities can be rejected. It is now proposed that intervention of the weak acid stabilizes the intermediate by formation of the more difficultly enolisable cyclohexenedione iii. This type of compound is known to eliminate hydrogen halide under extremely mild conditions (the mere presence of an hydroxylated solvent)[7] and can give rise successively to the intermediates iv and v.

Cyclobutane derivatives are formed from quinones and ketene acetals in certain instances, however it has been shown that they do not lead to significant amounts of quinonic products under a variety of conditions and therefore do not constitute a determining step in the over-all process.[4] A mechanism involving the prior dimerisation of ketene acetals, possibly to 1,1,3-trialkoxybutadienes, can also readily be discounted although substances like acetic acid have been found to catalyse their condensation to 3-alkoxycrotonic esters.[8] Indeed the optimum yields of naphthoquinones were obtained according to method A when the reactants were cooled, mixed and allowed to reach room temperature very slowly. The formation of dienes from polyalkoxybutanes by elimination are known to require high temperatures[9] and experiments in which the substrates were permitted to react spontaneously and consequently at higher temperatures invariably gave lower yields.

As in preceding studies,[3,4] 5 equivalents of ketene acetal per equivalent of quinone was found to give the best results. In view of this large proportion, the fact that 2–2.5 equivalents of acetic acid was found to be the optimal amount is perhaps not significant. Ketene acetals undoubtedly react with acetic acid even at very low temperatures to form a sort of orthoester which seems to be unstable. One possible result is that ketene acetals are slowly regenerated in the reaction medium and react further with very reactive intermediates. One unusual aspect of the reaction was found to be the clear dependence of yield on the scale of the preparation; an occurrence which seem to confirm that a very reactive intermediate is formed and that its capture or evolution depends largely on surface effects. This was implicit in an earlier observation when it was ascertained that reactions of this type proceed better without solvent.[3]

In order to facilitate the interpretation of the NMR spectra of crude reaction mixtures which are often complex, use of the methyl acetals are usually preferred in exploratory work. In this particular case, the more readily prepared ethyl compound was also found to have produced higher yields of the required naphthoquinones. This effect is probably due to the fact that acetic acid is eliminated with significantly greater ease from the intermediate iv when the R groups are bulkier. However it seems likely that competitive processes also occur at other steps. There are increasingly numerous indications that homogentisic esters are not produced exclusively by fortuitous hydrolysis of benzofurans but arise by another route possibly by nucleophilic attack on the intermediate i. In this eventuality ethyl groups would also be less susceptible to attack and produce better yields of quinone. Use of less than the optimal amount of acetic acid led to the unexpected formation of small amounts of anthraquinones. Under these conditions, the acid-catalyzed formation of naphthoquinone seems to have reached its limit before the total expenditure of the ketene acetals. Since this particular naphthoquinone has been shown not to require acid catalysis in order to react with excess reagent,[3] the reaction proceeds further albeit with reduced yields than when larger amounts of acetic acid are used.

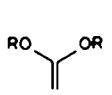
The reactivity of various halogenated benzoquinones showed marked dependence on structure. From the point of view of the synthesis of natural products it was fortunate that of the substrates examined, 2,6-dichlorobenzoquinone gave the best yield (up to 76%), an occurrence which can be attributed to the cross-conjugation of this system since the more highly resonance-stabilized 2,5-isomer gave only very poor results. This moreover accounts for the absence of a product derived from this isomer in earlier work on chlorobenzoquinone dichloride.[3] On the other hand, brominated benzoquinones inexplicably gave bad results whereas the fact that an unsubstituted substrate did give naphthoquinones but in very low yield indicates that a somewhat different mechanism can intervene involving an oxidative step.

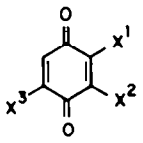
Other substrates can also provide convenient syntheses of a number of natural products. 2-Chloro-5-methoxybenzoquinone **11** readily gives flaviolin trimethyl ether **20** which can also be obtained less effectively from 2,5-dichlorobenzoquinone **10** after nucleophilic displacement of the remaining halogen. Trichlorobenzoquinone **13** gave the corresponding naphthoquinone **21** which could only be converted into spinochrome B tetramethyl ether **23** in low yield, the main product being the unreactive monochloro compound **22**. It was also hoped that the method could be extended to dibenzoquinones and thus afford simple syntheses of some naturally occurring dinaphthoquinones. The synthesis of mamegakinone and dianellinone using conjugated ketene acetals[1,3] requires 3,3'-dichloro-2,5,2',5'-dibenzoquinone which is unknown and could not be prepared. On the other hand, the isomeric 4,4'-dichloro compound is readily accessible but did not give encouraging results. The partially reduced analog 2 - chloro - 5 - (4 - chloro - 2,5 - dimethoxyphenyl) benzoquinone **14** did give a 34% yield of the corresponding naphthoquinone **24**.

The reaction of benzoquinones with conjugated ketene acetals (1,1-dialkoxybutadienes) was expected to assume the advantages both of ketene acetals (regiospecificity) and of dienes (high yields) and therefore to facilitate the preparation of a number of useful intermediates and natural products.

The reactions were indeed found to be regiospecific, as indicated in particular by the NMR spectrum of the intermediate adduct in the preparation of the naphthoquinone **39**, but with most dienes the yields were considerably lower with benzoquinones than with naphthoquinones and thus indicated that towards the former at least the reagents behave largely as ketene acetals (i.e. by a dipolar process). Nonetheless, attempts to counteract this effect by addition of acetic acid to the reaction medium did not provide the expected improvement.

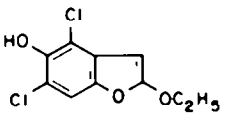
Some of the most useful results obtained by this method were acquired with the use of 1,1-dimethoxy-3-



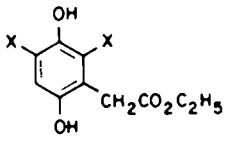


1 $R = CH_3$
2 $R = C_2H_5$
3 $R = C_2H_4OCH_3$

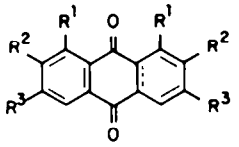
8 $X^1 = H, X^2 = X^3 = Cl$
9 $X^1 = H, X^2 = X^3 = Br$
10 $X^1 = X^3 = Cl, X^2 = H$
11 $X^1 = Cl, X^2 = H, X^3 = OCH_3$
12 $X^1 = H, X^2 = Cl, X^3 = OCH_3$
13 $X^1 = X^2 = X^3 = Cl$
14 $X^1 = Cl, X^2 = H, X^3 =$



4

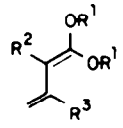


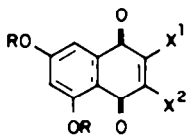
5 $X = Cl$
6 $X = Br$



7 $R^1 = R^3 = OC_2H_5, R^2 = H$
34 $R^1 = R^3 = OCH_3, R^2 = H$
38 $R^1 = OC_2H_5, R^2 = R^3 = CO_2CH_3$

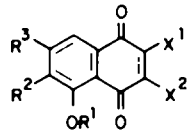
trimethylsilyloxybutadiene **25**. From 2,6-dichlorobenzoquinone, the important intermediate 2-chloro-6,8-dimethoxynaphthoquinone **15** could now be obtained on a fair scale in 39% yield. Flaviolin trimethyl ether **20** also became accessible in satisfactory yield (52%) from 2-chloro-5-methoxybenzoquinone **11** while the fundamental building block of many natural products 1,3,6,8-tetrahydroxyanthraquinone could be prepared as

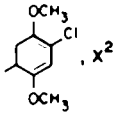




25 $R^1 = CH_3, R^2 = H, R^3 = OSi(CH_3)_3$
26 $R^1 = C_2H_5, R^2 = H, R^3 = CH_3$
27 $R^1 = CH_3, R^2 = R^3 = CO_2CH_3$
28 $R^1 = C_2H_5, R^2 = R^3 = CO_2CH_3$
29 $R^1 = R^3 = CH_3, R^2 = CO_2CH_3$
30 $R^1 = R^3 = CH_3, R^2 = COCH_3$

15 $X^1 = H, X^2 = Cl, R = CH_3$
16 $X^1 = H, X^2 = Cl, R = C_2H_5$
17 $X^1 = H, X^2 = Cl, R = C_2H_4OCH_3$
18 $X^1 = X^2 = H, R = C_2H_5$
19 $X^1 = Cl, X^2 = H, R = C_2H_5$
20 $X^1 = OCH_3, X^2 = H, R = CH_3$
21 $X^1 = X^2 = Cl, R = CH_3$
22 $X^1 = Cl, X^2 = OCH_3, R = CH_3$
23 $X^1 = X^2 = OCH_3, R = CH_3$



24 $X^1 =$  , $X^2 = H, R = C_2H_5$

35 $X^1 = R^2 = H, X^2 = Cl, R^1 = C_2H_5, R^3 = CH_3$
36 $X^1 = H, X^2 = Cl, R^1 = CH_3, R^2 = R^3 = CO_2CH_3$
37 $X^1 = H, X^2 = Cl, R^1 = C_2H_5, R^2 = R^3 = CO_2CH_3$
39 $X^1 = Cl, X^2 = H, R^1 = C_2H_5, R^2 = R^3 = CO_2CH_3$
40 $X^1 = H, X^2 = Cl, R^1 = R^3 = CH_3, R^2 = CO_2CH_3$
41 $X^1 = Cl, X^2 = H, R^1 = R^3 = CH_3, R^2 = CO_2CH_3$
42 $X^1 = H, X^2 = Cl, R^1 = R^3 = CH_3, R^2 = COCH_3$
43 $X^1 = X^2 = R^1 = R^2 = H, R^3 = CH_3$
44 $X^1 = X^2 = R^2 = H, R^1 = R^3 = CH_3$
45 $X^1 = X^2 = H, R^1 = R^3 = CH_3, R^2 = COCH_3$

31 $X^1 = H, X^2 = Br, R = CH_3$
32 $X^1 = Cl, X^2 = H, R = CH_3$
33 $X^1 = H, X^2 = OCH_3, R = CH_3$

its tetramethyl ether **34** either directly from 2,6-dichlorobenzoquinone (33%) or from the appropriate naphthoquinone **15** (89%).

1,1-Diethoxy-3-methylbutadiene **26** and 2,3-dicarbomethoxy-1,1-dialkoxybutadienes **27** and **28** gave the expected products while the first total synthesis of stypandrone as its methyl ether **45** was realized in an analogous manner. By condensing 2-acetyl-1,1-dimethoxy-3-methylbutadiene **30** with 2,6-dichlorobenzoquinone, a 25% yield of the corresponding naphthoquinone **42** was obtained. However, the removal of the remaining chlorine resulted in concomittant loss of the acetyl group. On the other hand, a reaction with chlorobenzoquinone gave two products resulting from attacks on both enedione systems. One of the products was obtained in 19% yield and was indistinguishable from a sample of the methyl ether of the natural product. An attempt to prepare the compound from benzoquinone gave very little desired substance (2%).

EXPERIMENTAL

M.ps were taken for samples in capillary tubes with a Thomas-Hoover apparatus (calibrated thermometer). The IR and UV spectra were determined with Beckman IR-12 and DK-1A spectrophotometers respectively. The NMR spectra were recorded with Varian A-60 and Bruker HX-90 spectrometers (tetramethylsilane as internal standard). Davison silica gel No. 923 was used for column chromatography, Baker-7G silica gel for preparative TLC and Woelm silica gel, activity III, for dry column chromatography.

Reaction of 2,6-dihalogenobenzoquinones with ketene acetals (Table 1).

Method A. The quinone and acetic acid were stirred at room temperature then cooled in a mixture of ethanol and liquid nitrogen or dry ice. Ketene acetal was added and the suspension allowed to warm slowly. Stirring was continued for a total of ~18 h then the crude product was evaporated under vacuum and chromatographed (dry column, benzene-ethyl acetate, 9:1).

Method B. The ketene acetal was added to a stirred paste of the quinone and acetic acid at room temperature. After the exothermic reaction had subsided, the mixture was refluxed for 1 h, evaporated under vacuum and chromatographed.

Method C. The ketene acetal was cooled in a mixture of ethanol and dry ice. Acetic acid was added at −70° and was followed by the quinone at various temperatures (−70, −22, 0, 20°). The reaction mixture was then allowed to warm slowly to room temperature, stirred for 18 h, evaporated and chromatographed.

Method D. To the ketene acetal cooled to −70° were added successively at the same temperature, acetic acid and the quinone. The mixture was allowed to come to room temperature (~45 min), then refluxed for 1 h, evaporated and chromatographed.

By the foregoing procedures the following products were obtained:

2-Chloro-6,8-dimethoxynaphthoquinone **15**, m.p. 208–209° (benzene) (lit.[3] dec. > 203°); δ(90 MHz, $CDCl_3$) 3.95 and 3.97 (2 × 3H, 2s, 6,8-OCH_3), 6.75 (1H, d, J = 2.5 Hz, 7-H), 7.10 (1H, s, 3-H) and 7.25 (1H, d, J = 2.5 Hz, 5-H); *m/e* 254/252 (M^+). This substance and a sample prepared earlier[3] were indistinguishable (IR and TLC in several solvent systems).

2-Chloro-6,8-diethoxynaphthoquinone **16**, m.p. 142.5–143.5° (petroleum ether, b.p. 90–120°); λ_{max} (ethanol) 219, 272, 415 nm (log ϵ 4.51, 4.13, 3.43); ν_{max} (KBr) 1665 cm^{-1}; δ(90 MHz, $CDCl_3$) 1.46 and 1.53 (6H, 2t, J = 7.0 Hz, $-OCH_2\underline{CH_3}$), 4.15 and 4.18 (4H, 2q, J = 7.0 Hz, $-O\underline{CH_2}CH_3$), 6.70 (1H, d, J = 2.5 Hz, 7-H), 7.10 (1H, s, 3-H) and 7.20 (1H, d, J = 2.5 Hz, 5-H); *m/e* 282/280 (M^+). Anal. Calc. for $C_{14}H_{13}O_4Cl$: C, 59.90; H, 4.67. Found: C, 59.81; H, 4.76%. Variable amounts of 4,6 - dichloro - 2 - ethoxy - 5 - hydroxybenzofuran **4** and ethyl 4,6 - dichlorohomogentisate **5** were also encountered but not evaluated.

2-Chloro-6,8-di(2-methoxyethoxy)naphthoquinone **17**, m.p. 134–135° (benzene-petroleum ether, b.p. 90–120°); λ_{max} (ethanol) 218, 272, 420 nm (log ϵ 4.68, 4.28, 3.65); ν_{max} (KBr) 1665 cm^{-1}; δ(60 MHz, $CDCl_3$) 3.47 and 3.52 (2 × 3H, 2s, $-OCH_3$), 3.67–4.42 (2 × 4H, 2m, $-OCH_2CH_2O-$), 6.84 (1H, d, J = 2.5 Hz, 7-H), 7.10 (1H, s, 3-H) and 7.24 (1H, d, J = 2.5 Hz, 5-H); *m/e* 342/340 (M^+) 282. Anal. Calc. for $C_{16}H_{17}O_6Cl$: C, 56.39; H, 5.03. Found: C, 56.64; H, 5.09%.

4,6-Dichloro-2-ethoxy-5-hydroxybenzofuran **4**, m.p. 107–108° (petroleum ether, b.p. 65–110°); ν_{max} (KBr) 3522, 3155, 3119 and 994 cm^{-1}; δ(60 MHz, $CDCl_3$) 1.47 (3H, t, J = 7.0 Hz, $-OCH_2\underline{CH_3}$), 4.27 (2H, q, J = 7.0 Hz, $-O\underline{CH_2}CH_3$), 5.55 and 5.66 (2 × 1H, 2s, 3-H and 5-OH) and 7.27 (1H, s, 7-H). The compound is labile and a correct analysis could not be obtained.

Ethyl 4,6-dichlorohomogentisate **5**, m.p. 147.5–148.0° (n-hexane); ν_{max} (KBr) 3360, 3230 and 1710 cm^{-1}; δ[60 MHz, $(CD_3)_2CO$] 1.20 (3H, t, J = 7.0 Hz, $-OCH_2CH_3$), 3.83 (2H, s, $-CH_2CO_2-$), 4.17

Table 1. Synthesis of 2-chloro-6,8-diethoxynaphthoquinone **16**

2,6-Dichloro-benzoquinone **8** (g)	Ketene diethyl acetal **2** (equiv.)	Acetic acid (equiv.)	Method	Yield of **16** (%)
0.180	5	0	A	0
0.180	5	2	A	62–76
0.885	5	2	A	40
1.00	5	2	A	28
0.500	2	2	A	8.5
0.500	5	5	A	27
0.500	5	2.5	A	44–52
0.500	10	5	A	45
0.885	5	1	B	20
0.885	5	2†	B	37
0.885	5	3	B	20
0.885	7	2	B	12
0.885	4	2	B	18
0.500	5	2.5	C(T_o = −70°)	52
0.500	5	2.5	C(T_o = −22°)	29
0.500	5	2.5	C(T_o = 0°)	31
0.500	5	2.5	C(T_o = 20°)	27
0.500	5	2.5	D	36

†With CF_3COOH the yield is 31%.

(2H, q, J = 7.0 Hz, $-O\underline{C}H_2CH_3$), 6.97 (1H, s, 3-H) and 8.35 (1H, broad s, 5-OH). Anal. Calc. for $C_{10}H_{10}O_4Cl_2$: C, 45.30; H, 3.80. Found: C, 45.52; H, 3.64%.

Ethyl 4,6-dibromohomogentisate **6**, m.p. 154–155° (benzene-petroleum ether, b.p. 90–120°); ν_{max} (KBr) 3430, 3360 and 1710 cm^{-1}; δ[90 MHz, $(CD_3)_2CO$] 1.17 (3H, t, J = 7.0 Hz, $-OCH_2\underline{C}H_3$), 3.80 (2H, s, $-CH_2CO_2-$), 4.10 (2H, q, J = 7.0 Hz, $-O\underline{C}H_2CH_3$) and 7.08 (1H, s, 3-H); *m/e* 356/354/352 (M^+). Anal. Calc. for $C_{10}H_{10}O_4Br_2$: C, 33.93; H, 2.85; Br, 45.15. Found: C, 34.07; H, 2.75; Br, 44.92%.

1,3,6,8-Tetraethoxyanthraquinone **7**, m.p. 154–156° (petroleum ether, b.p. 90–120°); λ_{max} (ethanol) 224, 282, 410 nm (log ε 4.63, 4.50, 3.78); ν_{max} (KBr) 1660 cm^{-1}; δ(60 MHz, $CDCl_3$) 1.45 and 1.51 (2 × 3H, 2t, J = 7.0 Hz, $-OCH_2CH_3$), 4.15 (4H, q, J = 7.0 Hz, $-OCH_2CH_3$), 6.70 (2H, d, J = 2.5 Hz, 2,7-H) and 7.25 (2H, d, J = 2.5 Hz, 4,5-H). Anal. Calc. for $C_{22}H_{24}O_6$: C, 68.73; H, 6.29. Found: C, 68.98; H, 6.11%.

Synthesis of other naphtoquinones using ketene acetals

5,7-*Diethoxynaphthoquinone* **18**

(a) This compound was prepared according to Method A from benzoquinone (500 mg, 4.62 mmols), ketene diethyl acetal[10] **2** (2.70 g, 23.3 mmols) and acetic acid (695 mg, 11.6 mmols). The naphthoquinone **18** was isolated by chromatography on silica gel (50g) (column, benzene-ethyl acetate 99:1) and purified by dry column chromatography (benzene) (160 mg, 14%), m.p. 128.5–130.0° (benzene-petroleum ether, b.p. 65–110°); λ_{max} (ethanol) 214, 257, 415 nm (log ε 4.57, 4.17, 3.60); ν_{max} (KBr) 1667 cm^{-1}; δ(90 MHz, $CDCl_3$) 1.43 and 1.51 (2 × 3H, 2t, J = 7.0 Hz, $-OCH_2CH_3$), 4.14 and 4.16 (2 × 2H, 2q, J = 7.0 Hz, $-OCH_2CH_3$), 6.70 (1H, d, J = 2.5 Hz, 6-H), 6.77 (2H, s, 2,3-H) and 7.18 (1H, d, J = 2.5 Hz, 8-H); *m/e* 246 (M^+). Anal. Calc. for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.56; H, 5.77%.

(b) When chlorobenzoquinone (500 mg, 3.50 mmols), ketene diethyl acetal **2** (2.30 g, 19.8 mmols) and acetic acid (525 mg, 8.75 mmols) interact according to method A, a crude product is obtained which is chromatographed on silica gel (column; 50 g). Benzene containing 2–5% ethyl acetate elutes a first zone consisting of 2-chloro-6,8-diethoxynaphthoquinone **16**, purified by preparative TLC (benzene-ethyl acetate 10:1) (24 mg, 2.5%) while use of the same solvent with 6–10% ethyl acetate allowed the separation of the unchlorinated quinone which was purified in the same way (60 mg, 7%).

2-*Chloro*-5,7-*diethoxynaphthoquinone* **19**. 2,5-Dichlorobenzoquinone **10** (500 mg, 2.82 mmols) is added at 0° to a mixture of ketene diethyl acetal **2** (1.64 g, 14.1 mmols) and acetic acid (425 mg, 7.10 mmols) according to method C. Preparative TLC. (benzene-ethyl acetate 10:1) of the partially purified product, gave the expected naphthoquinone **19** (71 mg, 8%), m.p. 145.5–146.5° (chloroform-petroleum ether b.p. 65–110°); λ_{max} (ethanol) 219, 271, 420 nm (log ε 4.60, 4.19, 3.59); ν_{max} (KBr) 1680 and 1655 cm^{-1}; δ (60 MHz, $CDCl_3$) 1.50 and 1.57 (2 × 3H, 2t, J = 7.0 Hz, $-OCH_2CH_3$), 4.21 (4H, q, J = 7.0 Hz, $-OCH_2CH_3$), 6.75 (1H, d, J = 2.5 Hz, 6-H), 7.05 (1H, s, 3-H) and 7.30 (1H, d, J = 2.5 Hz, 8-H). Anal. Calc. for $C_{14}H_{13}O_4Cl$: C, 59.90; H, 4.67; Cl, 12.63. Found: C, 59.64; H, 4.46; Cl, 13.01%.

2,5,7-*Trimethoxynaphthoquinone* (*Flaviolin trimethyl ether*) **20**. 2-Chloro-5-methoxybenzoquinone[11] **11** (250 mg, 1.45 mmol) reacts with ketene dimethyl acetal[12] **1** (640 mg, 7.25 mmols) and acetic acid (172 mg, 2.87 mmols) as in method B (the mixture is refluxed for 3 h). The crude product is chromatographed twice (dry column, benzene-ethyl acetate 1:1) and gave flaviolin trimethyl ether **20** (61 mg, 17%), m.p. 184–186° (benzene-petroleum ether, b.p. 90–120°) (lit.[13] 186–188°; lit.[14] 186–187°; lit.[15] 187°; lit.[16] 185–187°); δ(90 MHz, $CDCl_3$) 3.86, 3.93 and 3.96 (3 × 3H, 3s, 2,5,7-OCH_3), 6.01 (1H, s, 3-H), 6.73 (1H, d, J = 2.5 Hz, 6-H) and 7.25 (1H, d, J = 2.5 Hz, 8-H); *m/e* 248 (M^+). Anal. Calc. for $C_{13}H_{12}O_5$: C, 62.90; H, 4.87. Found: C, 63.04; H, 5.05%. (This substance and a sample of the authentic material are indistinguishable by the usual criteria: TLC in seven solvent systems; superposable IR spectra and mixed m.p.).

2,3-*Dichloro*-5,7-*dimethoxynaphthoquinone* **21**. Trichlorobenzoquinone[17] **13** (2.00 g, 9.45 mmols), ketene dimethyl acetal **1** (4.18 g, 47.5 mmols) and acetic acid (1.14 g, 19.0 mmols) were allowed to react according to method A. Addition of petroleum ether, b.p. 65–110°, to the reaction mixture precipitated the naphthoquinone **21** (550 mg, 22%), m.p. 200–201° (benzene); λ_{max} (ethanol) 220, 271, 292, 425 (log ε 4.58, 4.14, 4.11, 3.59); ν_{max} (KBr) 1670 cm^{-1}; δ(90 MHz, $CDCl_3$) 3.96 and 3.97 (2 × 3H, 2s, 5,7-OCH_3), 6.75 (1H, d, J = 2.5 Hz, 6-H) and 7.32 (1H, d, J = 2.5 Hz, 8-H); *m/e* 290/288/286 (M^+). Anal. Calc. for $C_{12}H_8O_4Cl_2$: C, 50.20; H, 2.81; Cl, 24.70. Found: C, 50.44; H, 2.65; Cl, 24.24.

2,3,5,7-*Tetramethoxynaphthoquinone* (*Spinochrome B tetramethyl ether*) **23**. A mixture of 2,3-dichloro-5,7-dimethoxynaphthoquinone **21** (250 mg, 0.871 mmol) and sodium methoxide (325 mg, 6.02 mmols) in anhydrous benzene was refluxed for 7 h, filtered and evaporated. The residue was chromatographed on silica gel (dry column, chloroform). A fast moving zone consisted of a product assumed to be 2-chloro-3,5,7-trimethoxynaphthoquinone **22** (152 mg, 62%), m.p. 157–158° (benzene-petroleum ether, b.p. 90–120°); ν_{max} (KBr) 1670 cm^{-1}; δ(90 MHz, $CDCl_3$) 3.95 and 3.97 (2 × 3H, 2s, 5,7-OCH_3), 4.30 (3H, s, 3-OCH_3), 6.70 (1H, d, J = 2.5 Hz, 6-H) and 7.31 (1H, d, J = 2.5 Hz, 8-H); *m/e* 284/282 (M^+) (an acceptable analysis could not be obtained).

The product from a second band was purified by preparative TLC (silica gel, benzene-ethyl acetate 5:1) and identified as spinochrome B tetramethyl ether **23** (26 mg, 11%), m.p. 126–127° (petroleum ether, b.p. 90–120°) (lit.[18] 132.0–132.5°; lit.[15] 131°; lit.[19] 130.0–130.5°); δ(90 MHz, $CDCl_3$) 3.92, 3.95, 4.01 and 4.08 (4 × 3H, 4s, 2,3,5,7-OCH_3), 6.67 (1H, d, J = 3.0 Hz, 6-H) and 7.25 (1H, d, J = 3.0 Hz, 8-H). The IR spectrum is identical to the one previously published.[18]

2-(4-*Chloro*-2,5-*dimethoxyphenyl*)-5,7-*diethoxynaphthoquinone* **24**. 2-Chloro-5-(4-chloro-2,5-dimethoxyphenyl) benzoquinone[20] **14** (500 mg, 1.58 mmol), acetic acid (237 mg, 3.95 mmols) and ketene diethyl acetal **2** (915 mg, 7.89 mmols) were mixed at −70° and the mixture allowed to warm slowly to room temp. (3 h), then stirred for 15 h. The residue obtained after evaporation of the volatile components under vacuum was twice chromatographed on silica gel (dry column, benzene) and gave the phenylnaphthoquinone **24** (210 mg, 34%), m.p. 191.0–192.5° (petroleum ether, b.p. 90–120°); ν_{max} (KBr) 1665 and 1655 cm^{-1}; δ(90 MHz, $CDCl_3$) 1.46 and 1.54 (2 × 3H, 2t, J = 7.0 Hz, 5,7-$OCH_2\underline{C}H_3$), 3.71 and 3.87 (2 × 3H, 2s, 2',5'-OCH_3), 4.19 (4H, q, 5,7-$OC\underline{H}_2CH_3$), 6.72 (1H, d, J = 2.5 Hz, 6-H), 6.83, 6.85 and 7.00 (3 × 1H, 3s, 3,3',6'-H), and 7.25 (1H, d, J = 2.5 Hz, 8-H). Anal. Calc. for $C_{22}H_{21}O_6Cl$: C, 63.89; H, 5.08. Found: C, 63.78; H, 4.99%.

Synthesis of naphthoquinones from 1,1-*dialkoxybutadienes*

2-*Chloro*-6,8-*dimethoxynaphthoquinone* **15**

A solution of 1,1-dimethoxy-3-trimethylsilyloxy-1,3-butadiene[21] **25** (5.80 g, 28.7 mmols) in anhydrous benzene (10 ml) was added dropwise to a suspension of 2,6-dichlorobenzoquinone **8** (5.00 g, 28.2 mmols) in the same solvent at room temp. The reaction mixture was stirred for 15 min, heated to reflux for 1 h and evaporated to dryness. The residue was heated at 140–150° for 2 h, refluxed in a mixture of methanol (25 ml) and 5% aqueous hydrochloric acid (10 ml) for 10 min, cooled and filtered. The crude product is stirred for 24 h in a mixture of chloroform (25 ml), methyl iodide (5 ml) and freshly prepared silver oxide (5g) (two more portions of methyl iodide—1.5 ml each—are added at regular intervals). The filtered reaction mixture was evaporated to dryness and the residue chromatographed on silica gel (column-chloroform). The naphthoquinone **15** was then purified by dry column chromatography (chloroform) (2.74 g, 39%) and was identical to the substance obtained earlier.

2-*Bromo*-6,8-*dimethoxynaphthoquinone* **31**

A similar reaction using 2,6-dibromobenzoquinone[22] **9** (2.44 g, 9.10 mmols) and 1,1-dimethoxy-3-trimethylsilyloxybutadiene **25** (1.85 g, 9.20 mmols) gave the naphthoquinone **31** (690 mg, 25%), m.p. 192–193° (benzene); λ_{max} (ethanol) 218, 271, 290, 415 nm (log ε 4.56, 4.09, 4.06, 3.60); ν_{max} (KBr) 1668 cm^{-1}; δ(90 MHz, $CDCl_3$) 3.94 and 3.97 (2 × 3H, 2s, 6,8-OCH_3), 6.72 (1H, d, J = 2.5 Hz, 7-H), 7.20 (1H, d, J = 2.5 Hz, 5-H), and 7.40 (1H, s, 3-H); *m/e* 298/296 (M^+).

Anal. Calc. for $C_{12}H_9O_4Br$: C, 48.51; H, 3.05; Br, 26.90. Found: C, 48.81; H, 2.84; Br, 26.81%.

2-*Chloro*-5,7-*dimethoxynaphthoquinone* **32**

A similar reaction with 2,5-dichlorobenzoquinone **10** (5.00 g, 28.2 mmols) and 1,1 - dimethoxy - 3 - trimethylsilyloxybutadiene **25** (5.80 g, 28.7 mmols) gave the expected naphthoquinone **32** (353 mg, 5%), m.p. 187.5–188.5° (benzene); λ_{max} (ethanol) 215, 262, 290, 420 nm (log ϵ 4.34, 3.86, 3.72, 3.13); ν_{max} (KBr) 1680 and 1655 cm^{-1}; δ(90 MHz, $CDCl_3$) 3.96 and 3.97 (2 × 3H, 2s, 5,7-OCH_3), 6.75 (1H, d, J = 2.5 Hz, 6-H), 7.16 (1H, s, 3-H) and 7.30 (1H, d, J = 2.5 Hz, 8-H); *m/e* 254/252 (M^+). Anal. Calc. for $C_{12}H_9O_4Cl$: C, 57.04; H, 3.59; Cl, 14.03. Found: C, 57.17; H, 3.54; Cl, 14.17%.

2,5,7-*Trimethoxynaphthoquinone* **20**

An analogous reaction between 2-chloro-5-methoxybenzoquinone **11** (1.00 g, 5.80 mmols) and 1,1 - dimethoxy - 3 - trimethylsilyloxybutadiene **25** (1.20 g, 5.95 mmols) gave the naphthoquinone **20** (purified by TLC-chloroform), (250 mg, 17%), m.p. 184–186°. This compound was identical to a substance obtained earlier.

2,6,8-*Trimethoxynaphthoquinone* **33**

A similar reaction involving 2 - chloro - 6 - methoxybenzoquinone[23] **12** (1.00 g, 5.80 mmols) and the same diene **25** (1.20 g, 5.95 mmols) gave the expected naphthoquinone **33** (750 mg, 52%), m.p. 197–198° (benzene) (lit.[11] 197–199°; lit.[24] 196–197°; lit.[3] 194–195°). This substance and a sample of the compound obtained earlier in this laboratory were identical (mixed m.p. and superposable IR spectra); its hydrolysis product was also identical to an authentic sample of 2 - hydroxy - 6,8 - dimethoxynaphthoquinone.

1,3,6,8-*Tetramethoxyanthraquinone* **34**

(a) A reaction between 2,6-dichlorobenzoquinone **8** (500 mg, 2.82 mmols) in benzene (3 ml) and an excess of 1,1 - dimethoxy - 3 - trimethylsilyloxybutadiene **25** (1.71 g, 8.47 mmols) in the same solvent (2 ml) was carried out in the usual way. The crude product after hydrolysis, methylation [dimethyl sulfate (2.5 ml added in several portions), anhydrous potassium carbonate (1.5 g) and boiling acetone (20 ml); 12 h], and filtration on silica gel (chloroform) was chromatographed on the same adsorbant (benzene containing 1 to 30% ethyl acetate) and gave 1,3,6,8-tetramethoxyanthraquinone **34** which was purified by dry column chromatography (silica gel, chloroform) (305 mg, 33%), m.p. 217–218° (methanol) (lit.[25] 221°; lit.[26] 225–226°; lit.[27] 220–221°; lit.[28] 224–225°; lit.[3] 217–218°). This substance and a sample prepared earlier[3] were indistinguishable (IR and TLC in several solvent systems).

(b) Alternately 2 - chloro - 6,8 - dimethoxynaphthoquinone **15** (500 mg, 1.98 mmol) in benzene (10 ml) could be treated with the same diene (500 mg, 2.48 mmols) in benzene (5 ml) at room temperature. The residue, after evaporation of the solvent, was heated at 150° for 12 h, hydrolyzed in the usual way, methylated as in section (a), and gave the anthraquinone **34** (575 mg, 89%).

2-*Chloro*-8-*ethoxy*-6-*methylnaphthoquinone* **35**

2,6-Dichlorobenzoquinone **8** (560 mg, 3.16 mmols), acetic acid (285 mg, 4.75 mmols) and 1,1 - diethoxy - 3 - methyl - 1,3 - butadiene[29] **26** (1.50 g, 9.65 mmols) were mixed at room temp. (water-bath), stirred for 30 min, heated at 90° for 2 h and finally refluxed for 1 h. The residue obtained after evaporation of the volatile components was chromatographed (dry column-petroleum ether, b.p. 65–110°—ethyl acetate 5:1) and gave the naphthoquinone **35** which was purified by preparative TLC (benzene-ethyl acetate 10:1) (210 mg, 27%), m.p. 126.0–127.5° (benzene-petroleum ether, b.p. 90–120°); λ_{max} (ethanol) 214, 262–273, 415 nm (log ϵ 4.56, 4.08, 3.64); ν_{max} (KBr) 1665 cm^{-1}; δ(90 MHz, $CDCl_3$) 1.52 (3H, t, J = 7.0 Hz, $-OCH_2CH_3$), 2.42 (3H, s, 6-CH_3), 4.17 (2H, q, J = 7.0 Hz, $-OCH_2CH_3$), 7.04 (2H, broad s, 3, 7-H) and 7.43 (1H, d, J = 2.0 Hz, 5-H). Anal. Calc. for $C_{13}H_{11}O_3Cl$: C, 62.28; H, 4.42; Cl, 14.14. Found: C, 61.98; H, 4.48; Cl, 13.93%.

6,7 - *Dicarbomethoxy* - 2 - *chloro* - 8 - *methoxynaphthoquinone* **36**

A mixture of 2,6-dichlorobenzoquinone **8** (500 mg, 2.80 mmols) and 2,3-dicarbomethoxy-1,1-dimethoxybutadiene[30] **27** (650 mg, 2.80 mmols) was prepared at room temp. then stirred at 80° for 3 h and at 110° for 2 h. The crude product twice chromatographed on silica gel (dry column, benzene-ethyl acetate 10:1, then benzene), gave the corresponding naphthoquinone **36** (395 mg, 41%), m.p. 147.0–147.5° (benzene-petroleum ether, b.p. 65–110°); λ_{max} (ethanol) 222, 255, 365 nm (log ϵ 4.46, 4.31, 3.78); ν_{max} (KBr) 1730 and 1680 cm^{-1}; δ(90 MHz, $CDCl_3$–C_6D_6 2:1) 3.69 (3H, s, 8-OCH_3), 3.83 and 3.84 (2 × 3H, 2s, 6,7-CO_2CH_3), 6.88 (1H, s, 3-H) and 8.35 (1H, s, 5-H); *m/e* 340/338 (M^+). Anal. Calc. for $C_{15}H_{11}O_7Cl$: C, 53.19; H, 3.27; Cl, 10.47. Found: C, 53.52; H, 3.31; Cl, 10.14%.

2,3 - *Dicarbomethoxy* - 1,1 - *diethoxy* - 1,3 - *butadiene* **28**

This compound was preapred, as for analogous compounds,[30] from ketene diethyl acetal **2** (29.2 g, 0.252 mols) and dimethyl acetylenedicarboxylate (35.8 g, 0.252 mol) in acetonitrile (50 ml). Fractionation of the crude product gave the diene **28** (30.5 g, 47%), b.p. 115–117°/0.3 mm; ν_{max} (film) 1720, 1600 and 1075 cm^{-1}; δ(60 MHz, CCl_4) 1.20 and 1.37 (2 × 3H, 2t, J = 7.0 Hz, $-OCH_2CH_3$), 3.57 and 3.67 (2 × 3H, 2s, CO_2CH_3), 4.00 and 4.20 (2 × 2H, 2q, J = 7.0 Hz, $-OCH_2CH_3$), 2.52 and 6.22 (2 × 1H, 2d, J = 2.0 Hz, 4-H_2). Anal. Calc. for $C_{12}H_{18}O_6$: C, 55.80; H, 7.02. Found: C, 55.56; H, 6.88%.

6,7 - *Dicarbomethoxy* - 2 - *chloro* - 8 - *ethoxynaphthoquinone* **37**

(a) An analogous reaction between 2,6-dichlorobenzoquinone **8** (500 mg, 2.80 mmols) and 2,3 - dicarbomethoxy - 1,1 - diethoxy - 1,3 - butadiene **28** (2.18 g, 8.45 mmols) gave two products after double chromatography on silica gel (dry column, benzene-ethyl acetate 5:1). A first zone consisted of the naphthoquinone **37** (455 mg, 46%), m.p. 147–149° (benzene-petroleum ether, b.p. 90–120°); λ_{max} (ethanol) 226, 252, 365 nm (log ϵ 4.49, 4.36, 3.81); ν_{max} (KBr) 1725, 1690 and 1660 cm^{-1}; δ(90 MHz, $CDCl_3$) 1.45 (3H, t, J = 7.0 Hz, $-OCH_2CH_3$), 3.95 (6H, s, CO_2CH_3), 4.06 (2H, q, J = 7.0 Hz, $-OCH_2CH_3$), 7.24 (1H, s, 3-H) and 8.36 (1H, s, 4-H). Anal. Calc. for $C_{16}H_{15}O_7Cl$: C, 54.48; H, 3.72; Cl, 10.05. Found: C, 54.57; H, 3.59; Cl, 10.08%.

A slower-moving band yielded 2,3,6,7 - tetracarbomethoxy - 1,8 - diethoxyanthraquinone **38** (110 mg, 7.5%), m.p. 174–175° (benzene-petroleum ether, b.p. 65–100°); λ_{max} (ethanol) 234, 355 nm (log ϵ 4.66, 3.91); ν_{max} (KBr) 1730 and 1670 cm^{-1}; δ(60 MHz, $CDCl_3$) 1.41 (6H, t, J = 7.0 Hz, $-OCH_2CH_3$), 3.97 (12H, s, CO_2CH_3), 4.17 (4H, q, J = 7.0 Hz, $-OCH_2CH_3$) and 8.67 (2H, s, 4,5-H); *m/e* 497 (M-OCH_3). Anal. Calc. for $C_{26}H_{24}O_{12}$: C, 59.08; H, 4.58. Found: C, 59.26; H, 4.73%.

(b) When the same reaction was conducted with one equivalent of the diene **28** (730 mg, 2.89 mmols) only the naphthoquinone **37** was obtained (550 mg, 56%) and required only one chromatographic separation (dry column, benzene-ethyl acetate 10:1).

6,7 - *Dicarbomethoxy* - 2 - *chloro* - 5 - *ethoxynaphthoquinone* **39**

A mixture of 2,5-dichlorobenzoquinone **10** (500 mg, 2.80 mmols) and 2,3 - dicarbomethoxy - 1,1 - diethoxybutadiene **28** (730 mg, 2.80 mmols) was heated at 110° for 4 h. Chromatography of the crude product on silica gel (dry column, benzene-ethyl acetate 10:1) gave two compounds which did not separate. Slow crystallisation of this mixture from benzene and petroleum ether, b.p. 65–110° gave large red and white crystals that could readily be isolated. The red crystals consisted of the naphthoquinone **39** (212 mg, 21%), m.p. 113–114° (benzene-petroleum ether, b.p. 65–110°); λ_{max} (ethanol) 220, 252, 370 nm (log ϵ 4.52, 4.36, 3.65); ν_{max} (KBr) 1740, 1725, 1680 and 1660 cm^{-1}; δ(90 MHz, $CDCl_3$) 1.40 (3H, t, J = 7.0 Hz, $-OCH_2CH_3$), 3.96 (6H, s, 6,7-CO_2CH_3), 4.03 (2H, q, J = 7.0 Hz, $-OCH_2CH_3$), 7.16 (1H, s, 3-H), and 8.48 (1H, s, 8-H). Anal. Calc. for $C_{16}H_{15}O_7Cl$: C, 54.48; H, 3.72; Cl, 10.05. Found: C, 54.69; H, 3.89; Cl, 10.43%.

The colourless compound was identified as the adduct, 6,7 - dicarbomethoxy - 2,4a - dichloro - 5,5 - diethoxy - 4a, 5,8,8a - tetrahydronaphthoquinone (400 mg, 32%), m.p. 143–144° (benzene-petroleum ether, b.p. 65–110°); ν_{max} (KBr) 1725, 1685 and 1655 cm^{-1}; δ(90 MHz, $CDCl_3$) 1.01 and 1.05 (2 × 3H, 2t, J = 7.0 Hz, $-OCH_2CH_3$), 2.80 (1H, dd, J = 8.0, 20.0 Hz, 8-H), 3.53 (1H, d, J = 20.0 Hz, 8-H), 3.69 (1H, d, J = 8.0 Hz, 8a-H), 3.41 and 3.44 (2 × 2H, 2q, J = 7.0 Hz, $-OCH_2CH_3$), 3.76 and 3.80 (2 × 3H, 2s, CO_2CH_3) and 7.18 (1H, s, 3-H). Anal. Calc. for $C_{16}H_{20}O_8Cl_2$: C, 49.67; H, 4.63. Found: C, 49.58; H, 4.48%.

7 - Carbomethoxy - 2 - chloro - 8 - methoxy - 6 - methylnaphthoquinone **40**

A mixture of 2,6-dichlorobenzoquinone **8** (2.00 g, 11.3 mmols) and 2 - carbomethoxy - 1,1 - dimethoxy - 3 - methyl - 1,3 - butadiene[23] **29** (2.12 g, 11.3 mmols) was kept at 130° for 3 h. The crude product was chromatographed twice on silica gel (dry column, benzene-ethyl acetate (10:1) then benzene for the second) and gave the naphthoquinone **40** (365 mg, 11%), m.p. 137.5–138.0° (petroleum ether, b.p. 90–120°); λ_{max} (ethanol) 218, 243(sh), 276, 352 nm (log ϵ 4.40, 4.27, 4.00, 3.53); ν_{max} (KBr) 1720 and 1670 cm^{-1}; δ(90 MHz, $CDCl_3$) 2.41 (3H, s, 6-CH_3), 3.89 and 3.98 (2 × 3H, 2s, 7-CO_2CH_3 and 8-OCH_3), 7.13 (1H, s, 3-H) and 7.84 (1H, s, 5-H). Anal. Calc. for $C_{14}H_{11}O_5Cl$: C, 57.06; H, 3.76; Cl, 12.03. Found: C, 57.17; H, 3.62; Cl, 12.21.

6 - Carbomethoxy - 2 - chloro - 5 - methoxy - 7 - methylnaphthoquinone **41**

In an analogous reaction, a mixture of 2,5 - dichlorobenzoquinone (1.00 g, 5.65 mmols) and 2 - carbomethoxy - 1,1 - dimethoxy - 3 - methylbutadiene **29** (1.06 g, 5.65 mmols) was heated at 110° for 1.5 h. The crude product was chromatographed on silica gel (dry column; benzene-ethyl acetate 10:1) and gave the desired quinone **41** (310 mg, 19%), m.p. 133–134° (petroleum ether, b.p. 90–120°); λ_{max} (ethanol) 207, 250, 275, 350 nm (log ϵ 4.41, 4.14, 3.96, 3.51); ν_{max} (KBr) 1725, 1675 and 1655 cm^{-1}; δ(90 MHz, $CDCl_3$) 2.41 (3H, s, 7-CH_3), 3.91 and 3.96 (2 × 3H, 2s, 5-OCH_3 and 6-CO_2CH_3), 7.18 (1H, s, 3-H) and 7.76 (1H, s, 8-H). Anal. Calc. for $C_{14}H_{11}O_5Cl$: C, 57.06; H, 3.76; Cl, 12.03. Found: C, 57.19; H, 3.65; Cl, 11.62%.

2 - Acetyl - 1,1 - dimethoxy - 3 - methyl - 1,3 - butadiene **30**

A mixture of pent - 3 - yn - 2 - one (2.00 g, 28.0 mmols) and ketene dimethyl acetal **1** (2.45 g, 28.0 mmols) were heated at 145–150° for 18 h in a sealed tube. Fractionation of the crude product gave the diene **30** (1.23 g, 28%), b.p. 65–70°/0.5 mm, which deteriorates rapidly; ν_{max} (film) 1695, 1640, 1585 and 1085 cm^{-1}; δ(90 MHz, $CDCl_3$) 1.87 (3H, m, 3-CH_3), 2.25 (3H, s, 2-$COCH_3$), 3.78 and 3.82 (2 × 3H, 2s, 1,1-OCH_3), 4.75 and 5.07 (2 × 1H, 2m, 4-H_2).

7-Acetyl - 2 - chloro - 8 - methoxy - 6 - methylnaphthoquinone **42**

2,6-Dichlorobenzoquinone **8** (840 mg, 4.75 mmols) was added to 2 - acetyl - 1,1 - dimethoxy - 3 - methylbutadiene **30** (760 mg, 4.75 mmols) and the mixture was stirred for 15 h. The crude product was twice chromatographed on silica gel (dry column; benzene-ethyl acetate 10:1) and gave 3-chlorostypandrone methyl ether **42** (330 mg, 25%), m.p. 135–136° (petroleum ether, b.p. 90–120°-benzene); λ_{max} (ethanol) 219, 242(sh), 272(sh), 307(sh), 352, 420 nm (log ϵ 4.22, 4.10, 3.89, 3.44, 3.44, 3.27); ν_{max} (KBr) 1690 and 1670 cm^{-1}; δ(90 MHz, $CDCl_3$) 2.34 (3H, s, 6-CH_3), 2.52 (3H, s, 7-$COCH_3$), 3.84 (3H, s, 8-OCH_3), 7.18 (1H, s, 3-H) and 7.76 (1H, s, 5-H); *m/e* 280/278 (M^+). Anal. Calc. for $C_{14}H_{11}O_4Cl$: C, 60.33; H, 3.98; Cl, 12.72. Found: C, 60.55; H, 3.98; Cl, 12.42%.

Reduction of **42**

A mixture of 7 - acetyl - 2 - chloro - 8 - methoxy - 6 - methylnaphthoquinone **42** (55 mg, 0.198 mmol), stannous chloride dihydrate (250 mg, 1.11 mmol), concentrated hydrochloric acid (0.6 ml) and acetic acid (0.6 ml) was refluxed for 1 h, cooled, diluted with water (2 ml) and treated with an aqueous solution (0.6 ml) of chromium trioxide (125 mg). Separation of the crude products, obtained by extraction with ethyl acetate, by preparative TLC (benzene-ethyl acetate 10:1) gave two products: 5 - hydroxy - 7 - methylnaphthoquinone (rameniaceone) **43** (9 mg, 24%), m.p. 123.5–124.5° (petroleum ether, b.p. 30–80°) (lit.[31] 125.5–126.5°; lit.[32] 125–126°); ν_{max} (KBr) 1670 and 1645 cm^{-1}; δ (90 MHz, $CDCl_3$) 2.42 (3H, s, 7-CH_3), 6.90 (2H, s, 2,3-H), 7.07 (1H, d, J = 2.0 Hz, 6-H) and 7.43 (1H, d, J = 2.0 Hz, 8-H); and 5 - methoxy - 7 - methylnaphthoquinone **44** (17 mg, 43%), m.p. 164.5–165.5° (petroleum ether, b.p. 90–120°) (lit.[31] 166.5–167.5°); ν_{max} (KBr) 1665 and 1655 cm^{-1}; δ(90 MHz, $CDCl_3$) 2.48 (3H, s, 7-CH_3), 3.99 (3H, s, 5-OCH_3), 6.83 (2H, s, 2,3-H), 7.10 (1H, broad s, 6-H) and 7.55 (1H, broad s, 8-H).

6 - Acetyl - 5 - methoxy - 7 - methylnaphthoquinone (Stypandrone methyl ether) **45**

Chlorobenzoquinone (254 mg, 1.78 mmol) and 2 - acetyl - 1,1 - dimethoxy - 3 - methylbutadiene **30** (285 mg, 1.78 mmol) were mixed at room temperature and stirred for 18 h. The crude product was chromatographed (dry column, benzene) and the quinonic material separated by preparative TLC (benzene) giving two products: stypandrone methyl ether **45** (83 mg, 19%), m.p. 100–1° (benzene-petroleum ether, b.p. 90–120°) (lit.[33] 100–1°); λ_{max} (ethanol) 215, 235, 274, 345 nm (log ϵ 4.26, 4.20, 3.77, 3.49); δ(90 MHz, $CDCl_3$) 2.36 (3H, s, 7-CH_3), 2.54 (3H, s, 6-$COCH_3$), 3.84 (3H, s, 5-OCH_3), 6.89 (2H, s, 2,3-H) and 7.75 (1H, s, 8-H) (this substance and the authentic material were indistinguishable by TLC in seven solvent systems, their IR spectra were identical and the mixture m.p. showed no depression) and 7 - acetyl - 2 - chloro - 8 - methoxy - 6 - methylnaphthoquinone **42** (45 mg, 9%).

Acknowledgements—The authors thank Dr. R. G. Cooke for a sample of stypandrone methyl ether and Dr. R. G. Coombe for those of 2,5,7 - trimethoxy - 1,4 - naphthoquinone and 2 - hydroxy - 6,8 - dimethoxy - 1,4 - naphthoquinone. Financial support from the Ministère de l'Éducation du Québec and from the National Research Council of Canada are acknowledged.

REFERENCES

[1]Part VIII. *J. Org. Chem.* **41**, 3018 (1976).
[2]S. M. McElvain and E. L. Engelhardt, *J. Am. Chem. Soc.* **66**, 1077 (1944).
[3]J. Banville, J.-L. Grandmaison, G. Lang and P. Brassard, *Can. J. Chem.* **52**, 80 (1974).
[4]J. Banville and P. Brassard, *J. Chem. Soc. Perkin I* 613 (1976).
[5]A. Castonguay and P. Brassard, *Synth. Comm.* **5**, 377 (1975).
[6]W. Mayer and R. Weiss, *Angew. Chem.* **68**, 680 (1956).
[7]J. Y. Savoie and P. Brassard, *Can. J. Chem.* **44**, 2867 (1966).
[8]S. M. McElvain and D. Kundiger, *J. Am. Chem. Soc.* **64**, 254 (1942).
[9]B. M. Mikhailov and L. S. Povarov, *Zhur. Obshch. Khim.* **29**, 2079 (1959); *Chem. Abstr.* **54**, 108512 (1960).
[10]S. M. McElvain and D. Kundiger, *Org. Synth.* **23**, 45 (1943).
[11]A. S. P. Lennart and B. Lindberg, *Acta. Chem. Scand.* **4**, 60 (1950).
[12]S. M. McElvain, H. I. Anthes and S. H. Shapiro, *J. Am. Chem. Soc.* **64**, 2525 (1942) (in this method benzene is advantageously replaced by xylene).
[13]J. E. Davies, F. E. King and J. C. Roberts, *J. Chem. Soc.* 2782 (1955).
[14]A. J. Birch and F. W. Donovan, *Aust. J. Chem.* **8**, 529 (1955).
[15]J. Smith and R. H. Thomson, *J. Chem. Soc.* 1008 (1961).
[16]R. G. Coombe, *Aust. J. Chem.* **25**, 881 (1972).
[17]R. H. Thomson, *J. Chem. Soc.* 1196 (1953).
[18]M. Okajima, *Sci. Pap. Inst. Phys. Chem. Res. (Japan)* **53**, 356 (1959).
[19]J. Gough and M. D. Sutherland, *Tetrahedron Letters* 269 (1964).
[20]T. Posternak, W. Alcalay, R. Luzzati and A. Tardent, *Helv. Chim. Acta* **31**, 525 (1948).
[21]J. Banville and P. Brassard, *J. Chem. Soc. Perkin I* 1852 (1976).
[22]H. van Erp, *Rec. Trav. Chim.* **30**, 284 (1911).
[23]I.S. Ioffe and A. F. Sukhima, *Zhur. Obshch. Khim.* **23**, 295 (1953); (*Chem. Abstr.* **48**, 2640d (1954)).
[24]R. G. Coombe, *Aust. J. Chem.* **27**, 1327 (1974).
[25]M. D. Sutherland and J. Wells, *Chem. and Ind.* 291 (1959).
[26]E. Bullock, D. Kirkaldy, J. C. Roberts and J. G. Underwood, *J. Chem. Soc.* 829 (1963).
[27]T. F. Low, R. J. Park, M. D. Sutherland and I. Vessey, *Aust. J. Chem.* **18**, 182 (1965).
[28]G. M. Holmwood and J. C. Roberts, *J. Chem. Soc.* (C), 3899 (1971).
[29]S. M. McElvain and L. R. Morris, *J. Am. Chem. Soc.* **74**, 2657 (1952).
[30]K. C. Brannock, R. D. Burpitt and J. G. Thweatt, *J. Org. Chem.* **28**, 1697 (1963).
[31]R. G. Cooke and H. Dowd, *Aust. J. Chem.* **6**, 53 (1953).
[32]G. Bendz and G. Lindberg, *Acta. Chem. Scand.* **24**, 1082 (1970).
[33]R. G. Cooke and L. G. Sparrow, *Aust. J. Chem.* **18**, 218 (1965).