Tetrahedron Vol. 43, No. 1, pp 225 to 234, 1987
Printed in Great Britain.

0040-4020/87 $5.00+.00

CONFIGURATION OF THE CYCLOBUTANE PHOTODIMERS OF 2-ETHOXY- AND 2-METHOXY-1,4-NAPHTHOQUINONE

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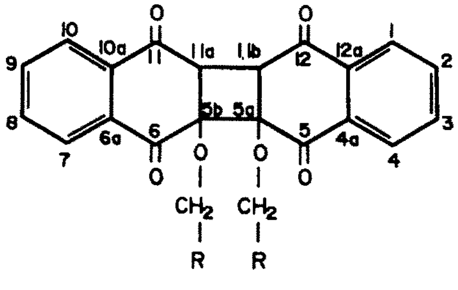
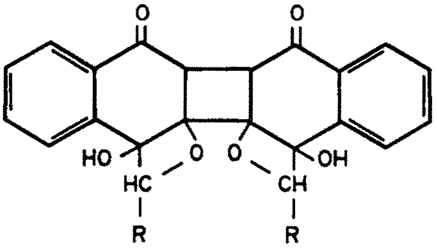
(*Received in UK* 12 *November* 1986)

Abstract - The structure and configuration of the C_4-dimers of 2-ethoxy- and 2-methoxy-1,4-naphthoquinone and related compounds are elucidated from an extensive ^1H and ^{13}C n.m.r. study. The importance of the sign of the proton-proton and ^{13}C-^1H coupling constants in determining the structures of these type of compounds is discussed. The assignment of signals was accomplished by selective population inversion (SPI) experiments. The use of reductive cleavage reactions to support structure deductions is also demonstrated. This approach to structural analysis should facilitate the characterisation of other cyclobutane compounds.

The photolysis of 2-methoxy- and 2-ethoxy-1,4-naphthoquinones in acetic anhydride solution has been reported to cause dimerisation[1] (1, 2) and subsequent cyclization of the alkoxy group to spiro-oxetanols (3, 4) in high yield. No attempt was made however to determine the steric arrangement around the cyclobutane ring. The structures of 1 and 2 were assigned[1] only by analogy to the photodimerisation of 2-methyl-1,4-naphthoquinone[2], whose dimeric products include all four possible configurations. We now wish to report on the elucidation of the structure and stereochemistry of 1 and 2 as well as an isomeric compound 12,[3] obtained from the ethanolysis of the C_4-dimers (5 or 6) of 2-chloro-1,4-naphthoquinone.[4,5]

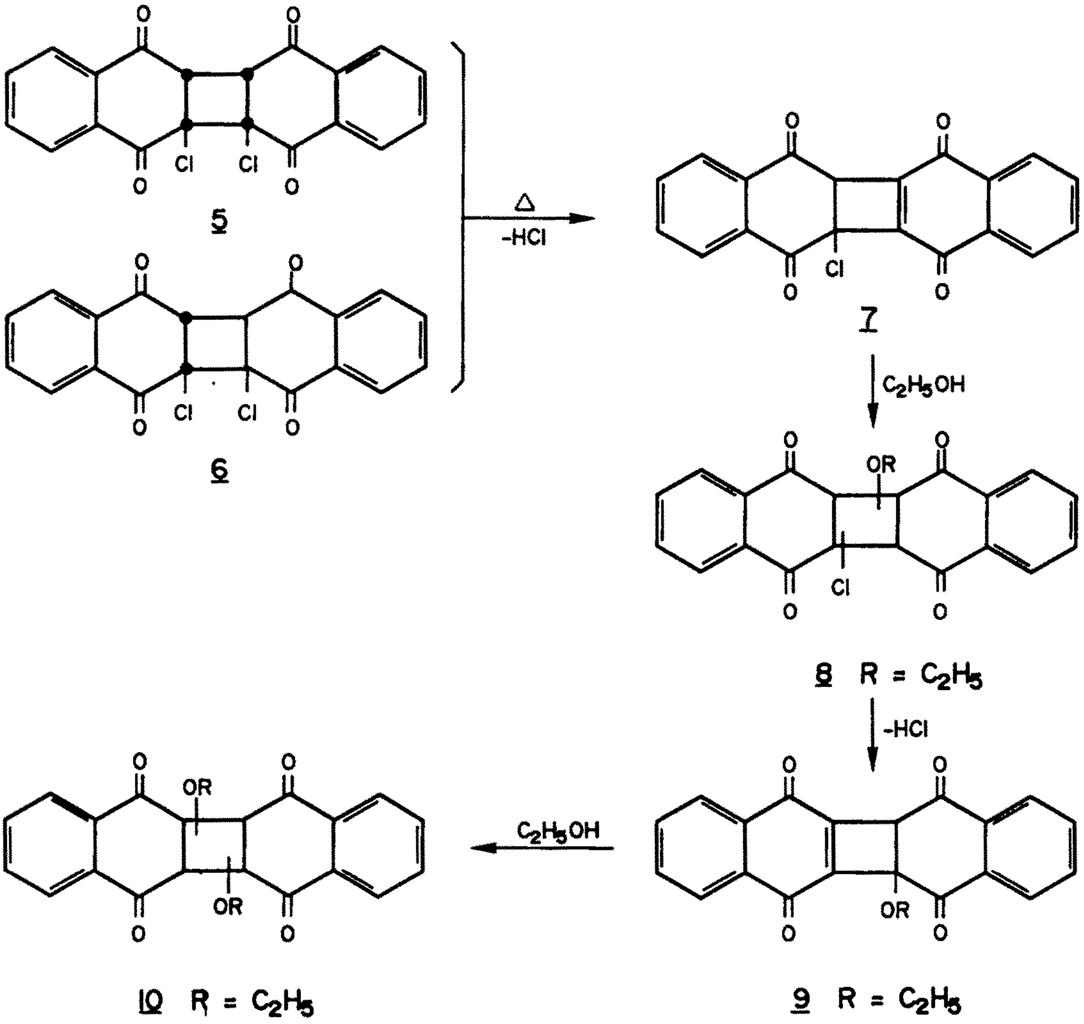


1 R = H
2 R = CH_3



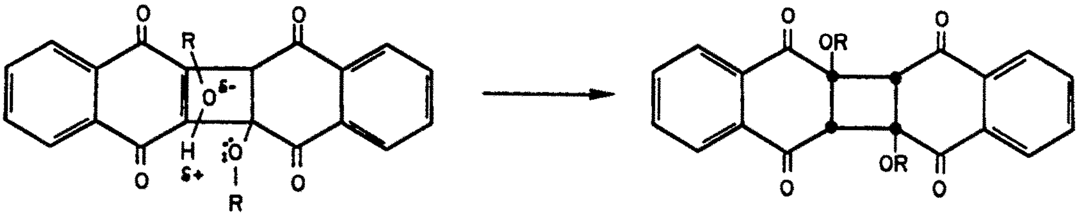
3 R = H
4 R = CH_3

It has recently been demonstrated[3] that treatment of 5 or 6 with ethanol under reflux conditions leads to the formation of the unsaturated compound 7, which acts as an intermediate in the formation of 10 from 5 or 6. The following reaction sequence was proposed:[3]



An alternative nucleophilic displacement of the halogen atom in 7 to produce 9 is improbable, since an S_N2-displacement would require concomitant inversion at the saturated cyclobutane carbon atom, whereas S_N1-displacement should involve the formation of a localised or delocalised carbonium ion which is destabilised by the adjacent carbonyl groups.

Due to hydrogen bonding between the oxygen atom of the ethoxy group and the acidic hydrogen atom of the approaching ethanol molecule, and also in the light of the low acidic character of ethanol, it can be assumed that the approaching ethanol molecule is probably polarised as shown in the transition state 11. It can be concluded that a *syn*-configurated head-to-tail compound 12 is probably produced via *cis* addition of ethanol to 9.



11 R = C_2H_5 12 R = C_2H_5

To gain more information on the structures of 1, 2 and 12 we conducted an extensive ^1H and ^{13}C n.m.r. study. The symmetry elements present in the dimers under discussion, as evidenced by the ^1H and ^{13}C n.m.r. spectra, render certain nuclei equivalent. We will, therefore, only refer to the one of the two equivalent nuclei with the lowest systematic number.

The ^1H n.m.r. spectra of 1, 2 and 12 ($CDCl_3$) exhibited signals from an ABCD spin system, attributable to the aromatic protons, and a singlet arising from the cyclobutane ring methine protons. The methyl protons of 2 were recorded as a triplet while the methylene protons however appeared not as a normal quartet but as the AB part of an ABX_3 spin system. This phenomenon can be attributed to the diastereotopic nature of the methylene protons by virtue of the chirality at C_5 or to restricted rotation in the ethoxy group. No attempt was made to distinguish between these two possibilities. Spectral analysis of the ABCD spin systems with the computer programme LAME[6] yielded the chemical shifts and coupling constants of the aromatic protons given in Table 1. Only the signals arising from one aromatic proton need be assigned in order to assign the remaining aromatic proton resonances unambiguously. This was accomplished with ^{13}C-{^1H}SPI experiments[5,7,8] by application of a selective π-pulse (τ = 0.051 s; γH_2 = 9.8 Hz) to the low-field ^{13}C side band, resulting from the directly bonded (C,H) coupling constant of the aromatic proton resonating at lowest field. The assignment of the aromatic ^1H resonances then follows from the assigned ^{13}C signals given in Table 2. Assignment of the aromatic proton resonances of 1 was accomplished by comparison with the corresponding values of 2.

Table 1 ^1H n.m.r. data of the dimers 1, 2 and 12 as well as the oxetanols 3, 4 and 13

	1	2	12	3	4	13
Proton	Chemical	shifts (δ);	p.p.m.	downfield	from internal	TMS
1-H	8.149	8.152	8.193	8.171	8.152	8.011
2-H	7.815	7.806	7.771	7.542	7.516	7.400
3-H	7.794	7.790	7.621	7.730	7.697	7.549
4-H	8.225	8.213	7.709	7.639	7.516	7.260
11a(5b)-H	3.947	3.952	3.791	3.181	3.121	3.323
OCH_n		3.283	3.550	4.794	4.896	4.498
		3.396	3.995	5.281		
CH_3	3.106	0.822	1.197		1.734	1.506
OH				5.294	5.309	5.155

	1	2	12	3	4	13
	Coupling constant (J) values in Hertz					
J(1-H,2-H)	7.90	7.96	8.01	7.95	7.97	8.04
J(1-H,3-H)	1.46	1.33	1.14	1.42	1.28	1.67
J(1-H,4-H)	0.36	0.59	0.61	0.52	0.51	
J(2-H,3-H)	7.38	7.32	7.42	7.29	7.14	7.52
J(2-H,4-H)	1.40	1.35	1.34	1.15	1.17	1.40
J(3-H,4-H)	7.92	7.99	7.86	7.96	7.92	7.98
RMS[a]	0.119	0.125	0.046	0.068	0.125	
J(11a or 5b-H,11b-H)[b]		+4.0	0	+10.19	+10.27	0
$^2J(CH_2)$		8.53	9.41	6.50		
$^3J(CH_nCH_3)$		7.03	7.01		6.30	6.40
Solvent	$CDCl_3$	$CDCl_3$	$CDCl_3$	$CDCl_3$	$CDCl_3$	$CDCl_3$ + $(CD_3)_2SO$
	500 MHz	100 MHz	100 MHz	100 MHz	100 MHz	500 MHz

[a] The weighted root mean squares deviation of the transition frequencies of the aromatic protons as given by LAME.[6]

[b] To be determined from the natural abundance ^{13}C satellite proton spectra. The signs were obtained from ^{13}C-{^1H}SPI experiments.

Protons above the plane of a benzene ring experience a shielding effect which causes the aromatic proton resonances of *syn*-configurated cyclobutane dimers to appear at a higher field than those of *anti* dimers.[5,9,10] The resonance positions of the C-1 and C-4 protons of the *syn* dimers are to higher field than those observed for the corresponding protons in *anti* dimers. The substituent on C-5a has only a small influence on the chemical shifts of the aromatic protons as is evidenced by comparison with the reported[5] chemical shift values of the C-1 and C-4 protons of the *anti* and *syn* C_4-dimers of 1,4-naphthoquinone. In the latter compounds the chemical shifts for the C-1 and C-4 protons are identical (*syn* δ 7.825; *anti* δ 8.204) whereas with substitution on C-5a a slight difference in the chemical shift values of C-1 and C-4 is observed. The chemical shift values of the C-1 and C-4 protons of 1 (δ 8.149 and δ 8.225) and 2 (δ 8.152 and δ 8.213) correspond closely with those observed for the corresponding protons of the *anti* dimers of 2-chloro-[5] and 2-methyl-1,4-naphthoquinone[2] proving that 1 and 2 also have the *anti*-configuration.

The chemical shifts of the aromatic protons of 12 do not correspond to any of the values that have been observed before. The chemical shift of C-1 is recorded at δ 8.193 whereas the C-4 proton appears at higher field at δ 7.709. This is a very strong indication that 12 must have the *syn* head-to-tail configuration. Steric repulsion between the ethoxy groups in the C-5a and C-11a positions causes a twist in the cyclobutane ring with the result that C-4 is moved to a position directly above the plane of the opposite benzene ring. The proton at C-1 is forced out of the sphere of influence of the opposite aromatic ring. This observation was confirmed by examination of molecular models.

An unambiguous distinction can be made between head-to-head and head-to-tail isomers and also between *syn* and *anti* head-to-tail isomers if the magnitude and sign of the proton-proton coupling constants between the cyclobutane ring methine protons are known.[5] The magnitude of these couplings has been determined from the natural-abundance ^{13}C satellite proton spectra while the signs of the methine proton-proton coupling constants were obtained from ^{13}C-{^{1}H}SPI experiments. The proton-proton coupling constant of the methine protons of 2 [J(11a-H,11b-H) = +4] indicates that 2 must possess a head-to-head structure. The magnitude of this coupling constant corresponds well to the value obtained[5] for the *anti*-configurated head-to-head dimer 6 of 2-chloro-1,4-naphthoquinone. The positive sign of the coupling constant is due to the *cis* vicinal coupling between the methine protons.

Further evidence for the head-to-head configuration of 2 was found from the sign of the ^{13}C-proton coupling constant over more than one bond [$^{>1}J$(CH)] determined from the ^{13}C-{^{1}H}SPI experiments.[5] The negative sign of $^{>1}J$(CH) can only be attributed to a geminal ^{13}C-proton coupling confirming the correctness of the allocated structure. The ^{13}C chemical shifts and (^{13}C,H)-coupling constants of the dimers 2 and 12 are given in Table 2.

No (^{1}H,^{1}H) or long-range (^{13}C,H) coupling constants could be detected between the methine protons nor between the methine protons and methine carbon atoms of the cyclobutane ring of 12 (see Tables 1 and 2). This situation is only possible in head-to-tail configurated dimers where the proton-proton coupling over four bonds is small and the dihedral angle between the methine proton and the methine carbon atom is in the order of 90°, resulting in a small or zero vicinal (^{13}C,H) coupling constant. From these considerations, as well as the observed aromatic proton chemical shifts, it must be concluded that 12 possesses a head-to-tail *syn*-configurated structure. Alternatively the vicinal (^{13}C,H) coupling between the corresponding nuclei of the *anti*-configurated head-to-tail dimer of 2-chloro-1,4-naphthoquinone was previously easily detected.[5]

Table 2 The ^{13}C chemical shifts and ^{13}C-H coupling constants of the dimers 2 and 12[a]

	2			12		
Carbon[b]	δ	^{1}J(CH)	$^{>1}J$(CH)	δ	^{1}J(CH)	$^{>1}J$(CH)
1	127.13 Dd	164.9	7.0	127.07 Dd	165.9	7.4
2	134.40 Dd	163.3	7.9	135.12 Dd	164.4	8.4
3	134.17 Dd	163.1	8.0	134.07 Dd	165.4	8.2
4	127.08 Dd	165.1	7.0	127.58 Dd	166.1	7.5
4a	136.42 Sm	-	-	133.96 St	-	7.0
5	190.29 St	-	4.0	191.42 Std	-	4.2;3.4
5a	86.00 St	-	9.0	79.07 St	-	7.2
10a(6a)	135.78 St	-	6.0	135.45 Std	-	7.1;2.0
11(6)	194.13 Std	-	6.1;3.8	190.14 St	-	4.7
11a(5b)	53.05 Dd	144.4	-4.3	59.15 D	140.9	0[c]
OCH_n	61.75 DDq	140.5;144.5	4.0	62.47 Tq	144.2	4.4
CH_3	14.63 Qt	127.4	3.0	15.13 Qt	126.5	2.7
Solvent	$CDCl_3$			$CDCl_3$		
Frequency	125.71			125.71		

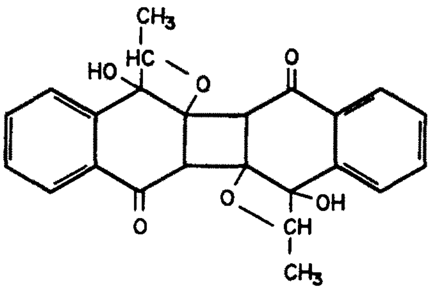
[a] Chemical shifts are relative to internal TMS and coupling constants are given in Hz. Symbols in upper case refer to the pattern resulting from directly bonded (C,H) coupling and those in lower case to patterns from (C,H) couplings over more than one bond.
S = singlet, D or d = doublet, T or t = triplet, Q or q = quartet and m = multiplet.

[b] Referring to the equivalent nucleus with the lowest number (see text).

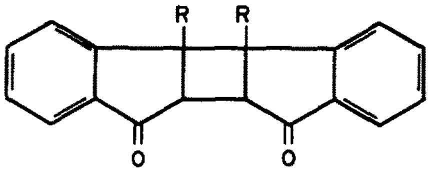
[c] The coupling over three bonds (proton with hydrogen bearing carbon atom) is so small that it could not be detected.

The ^{13}C n.m.r. data of 2 and 12 as collected in Table 2 have been obtained from proton noise decoupled and nuclear Overhauser enhanced (n.O.e.) single frequency ^{13}C n.m.r. spectra. In assigning the ^{13}C resonances extensive use has been made of off-resonance proton decoupled and selective proton decoupled ^{13}C n.m.r. spectra as well as ^{13}C-{^{1}H}SPI experiments. When an aromatic proton was selectively decoupled the ^{13}C signals of the carbon atoms three bonds away were affected most. When the low field proton (1-H) of 12, for example, was selectively irradiated the carbon resonances at δ_C 134.07 (C-3), 133.96 (C-4a) and 190.14 (C-12) were affected. By selectively inverting the populations of a transition of the cylcobutane ring proton the resonances of the carbon atom two bonds removed [δ_C 190.14 (C-12) and δ_C 79.07 (C-5a)] and those three bonds removed [δ_C 191.42 (C-5) and δ_C 135.45 (C-12a/C-6a)] were affected. Not only the assignment of the ^{13}C resonances but also the assignment of the aromatic proton resonances could be deducted from these experiments and are given in Tables 1 and 2.

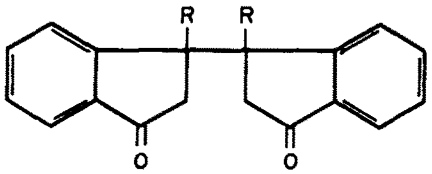
Chemical proof for the correctness of the allocated structures of 1, 2 and 12 was found from a study of the products obtained from the reductive cyclobutane ring cleavage of the corresponding spiro-oxetanols 3, 4 and 13. Compounds 3 and 4 were previously obtained[1] by sunlight irradiation of 1 or 2 in acetic anhydride respectively. In a similar way 13 was produced by irradiation of 12 in acetic anhydride.



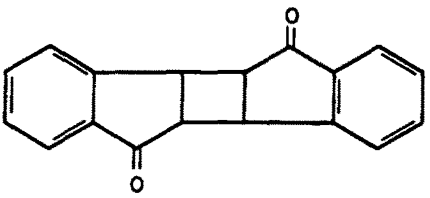
13



14 R = H
15 R = CH₃



16 R = H
17 R = CH₃

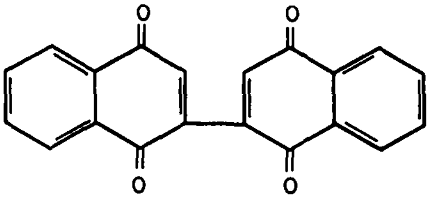


18

It is well known that treatment of 1,2-dicarbonyl substituted cyclobutane derivatives with zinc and zinc chloride in ethanol leads to cyclobutane ring cleavage.[11] The reductive ring cleavage of the diketones of the cyclobutane dimers of indene (14) and 3-methyl-indene (15) with zinc and zinc chloride in ethanol producing 16 and 17 respectively serve as typical examples.[11,12] On the other hand no cleavage is obtained in the case of 1,3-dicarbonyl substituted cyclobutane derivatives (18).[11]

Treatment of 3 or 4 (derived from 1 or 2 respectively) with zinc and zinc chloride in ethanol in both cases produced a yellow crystalline compound which was completely identical to 2,2'-bi[1,4-naphthoquinonyl] (19).[13] This result undoubtedly indicates that 3 and 4 are derived from cyclobutane dimers with a head-to-head structure. The formation of 19 from 3 or 4 is probably due to an initial cyclobutane ring cleavage whereby 20 is obtained. This is followed by cleavage of the oxetane ring, subsequent loss of two molecules aldehyde and enolyzation producing the tetraol 21 which is readily converted to 19 by dehydrogenation. Attempts to isolate 20 and 21 were fruitless.

On the other hand treatment of 13 (derived from 12) with zinc and zinc chloride in ethanol produced a product completely identical to an authentic sample of the tetraol 22.[14] We concluded that 13 as well as 12 exhibits head-to-tail cylcobutane structures which are not suitable for reductive cyclobutane ring cleavage.[11]



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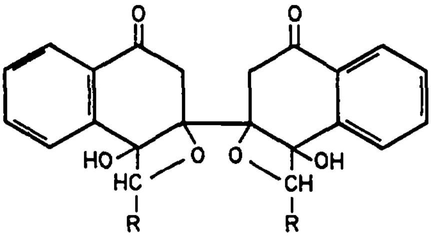
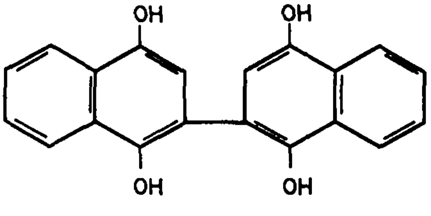
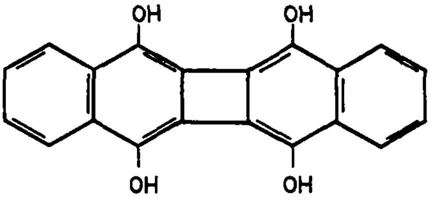


20 R = H, CH_3



21



22

With the ^1H and ^{13}C n.m.r. data now available for all four the possible C_4-dimers of 2-substituted-1,4-naphthoquinones it should be possible to deduce the configuration of an unknown C_4-dimer from only its ^1H n.m.r. spectrum and the value of the proton-proton coupling constant between the cyclobutane ring methine protons. The ^1H and ^{13}C data of the spiro-oxetanols 3, 4 and 13 are collected in Tables 1 and 3. The lowest field aromatic proton resonance can be assigned to 1-H. The assignment of the remaining aromatic proton resonances followed from spectral analysis and the assignment of the ^{13}C signals from off-resonance proton decoupled ^{13}C n.m.r. spectra. Further proof that 3 and 4 have the same *anti* head-to-head configuration and that 13 exhibits a *syn* head-to-tail configuration can be deduced from these data.

Table 3 The ^{13}C chemical shifts and ^{13}C-H coupling constants of the oxetanols 3, 4 and 13[a]

	3			4			13		
Carbon	δ	^{1}J(CH)	$>^{1}J$(CH)	δ	^{1}J(CH)	$>^{1}J$(CH)	δ	^{1}J(CH)	$>^{1}J$(CH)
1	126.57 Dd	163.8	7.3	127.72 Dd	164.5	7.5	124.87 Dd	162.6	7.4
2	126.64 Dd	162.0	7.6	125.91 Dm	160.0	-	127.54 Dd	163.2	7.7
3	134.52 Dd	161.2	8.3	135.04 Dm	160.0	-	133.40 Dd	162.3	8.5
4	128.28 Dd	162.2	7.9	128.83 Dd	162.3	7.5	127.60 Dd	159.5	6.7
4a	143.78 Sm	-	7.0	143.41 Sm	-	-	145.17 Sm	-	-
5	89.68 Sm	-	-	86.88 Sm	-	-	89.04 Sq	-	6.6
5a	72.75 Sm	-	-	74.17 Sm	-	-	69.12 Sm	-	-
10a(6a)	127.43 St	-	6.8	127.18 St	-	7.1	130.59 St	-	7.0
11(6)	190.36 Sd	-	3.9	190.18 Sd	-	3.9	191.43 Sdd	-	5.5;4.0
11a(5b)	44.81 Dd	146.0	6.1	45.33 Dd	146.2	6.1	58.70 D	136.5	-
OCH_n	84.99 T	154.1	-	91.43 Dq	155.0	4.9	88.67 Dm	153.4	-
CH_3	-	-	-	16.23 Q	127.5	-	17.19 Q	127.1	-
Solvent	$CDCl_3$ + $(CD_3)_2SO$			$CDCl_3$			$CDCl_3$ + $(CD_3)_2SO$		
Frequency	125.71			125.71			125.71		

[a] Units and abbreviations as in Table 2.

EXPERIMENTAL

Infrared spectra (KBr disc) were recorded on a Nicolet 5DX FT-spectrophotometer. Mass spectra were obtained at 70 eV on a VG 70-70 E mass spectrometer. Melting points are uncorrected. Elemental analyses were performed on a Hewlett-Packard analyser. The ^{1}H and ^{13}C n.m.r. spectra were recorded on a Varian XL-100-15 FT or a Bruker WM 500 spectrometer as indicated using saturated solutions in deuteriochloroform.

Photolysis of 2-methoxy-1,4-naphthoquinone

A solution of 0.2 g of the quinone in 20 mℓ of dichloromethane was photolyzed at 15°C for 72 hours using a Hanovia medium pressure mercury immersion lamp emitting predominantly UV light at 254, 265, 297, 313 and 366 nm. During this time the straw coloured product 1 (0.12 g, m.p. > 210° dec) crystallized from the reaction mixture which was completely identical to the dimer obtained[1] by irradiating the quinone in acetic anhydride at 365 nm.

Photolysis of 2-ethoxy-1,4-naphthoquinone

A solution of 0.2 g of the quinone in dichloromethane (20 mℓ) was photolyzed as described above for a period of 48 hours. The photoproduct 2 (0.9 g, m.p. > 230° dec) was separated from the unreacted monomer on a silica gel column with dichloromethane as eluate and recrystallized from ethanol. No oxetanol formation could be detected and the dimer 2 was completely identical to the dimer obtained[1] from photolysis in acetic anhydride.

Ethanolysis of 5 (or 6)[3]

A solution of 5 or 6 (0.2 g) in ethanol (20 mℓ) was refluxed and mechanically stirred. A yellowish solution was obtained within five minutes. The excess ethanol (10 mℓ) was removed under reduced pressure and 7 (0.15 g) was obtained. Prolonged treatment of 5, 6 or 7 as described above for 1 h produced a colourless crystalline product 12 (0.12 g, m.p. 126-128° dec) which was recrystallized from ethanol. ν_{max} 1680(s), 1585(s), 1265(s), 1240(s), 1050(s), 925(s) and

720(s) cm^{-1}; m/z 404(M$^+$), 202(M$^+$/2); Calc. for $C_{24}H_{20}O_6$: C, 71.28; H, 4.98%. Found: C, 71.30; H, 4.98%.

Spiro-oxetanol from 1 and 2

A solution of 1 (0.4 g) or 2 (0.4 g) in acetic anhydride (25 mℓ) was sealed in Pyrex test tubes and exposed to direct sunlight for a period of 10 days. The acetic anhydride was removed under reduced pressure and the colourless photoproduct 3 (0.32 g, m.p. 206-207°) or 4 (0.28 g, m.p. 230°C) was recrystallized from acetonitrile. Both oxetanols were completely identical to those obtained[1] by photolysis of 1 or 2 using the 365 nm line of a mercury source.

Spiro-oxetanol from 12

A solution of 12 (0.4 g) in acetic anhydride (15 mℓ) was exposed to direct sunlight as described above. The product 13 (0.35 g, m.p. 180°C) was obtained as described before. ν_{max} 3480(OH), 1690(C=O), 1590(s), 1270(s), 1160(s), 1040(s), 950(s) and 760(s) cm^{-1}; m/z 404(M$^+$), 202(M$^+$/2), 158(M$^+$/2 - CH_3CHO); Calc. for $C_{24}H_{20}O_6$: C, 71.28; H, 4.98%. Found: C, 71.29; H, 5.00%.

Reductive cyclobutane ring cleavage of 3 and 4

A solution of 3 (0.2 g) or 4 (0.2 g) in ethanol (20 mℓ) containing zinc chloride (0.2 g) and zinc powder (0.2 g) was refluxed for 3 hours. The warm reaction mixture was filtered and the filtrate was cooled to give yellow crystals (0.15 g and 0.085 g respectively). The m.p. (270°C), infrared and mass spectrum of the product was completely identical with an authentic sample of 19.[13]

Reductive cyclobutane ring cleavage of 13

A solution of 13 (0.2 g) in ethanol (20 mℓ) was treated with zinc and zinc chloride as described before. A colourless product (0.09 g) was obtained. The m.p. (260-265°C), infrared and mass spectrum was completely identical with an authentic sample of 22.[14]

REFERENCES

1. J.V. Ellis and J.E. Jones, *J. Org. Chem.*, 40, 485 (1975).
2. H. Werbin and E.T. Strom, *J. Am. Chem. Soc.*, 90, 7296 (1968).
3. J. Dekker, F.J.C. Martins, A.M. Viljoen and P.L. Wessels, *S. Afr. J. Chem.*, 32, 111 (1979).
4. F.J.C. Martins, J. Dekker and A.M. Viljoen, *S. Afr. J. Chem.*, 31, 29 (1977).
5. J. Dekker, F.J.C. Martins, A.M. Viljoen and P.L. Wessels, *S. Afr. J. Chem.*, 34, 76 (1981).
6. C.W. Haigh, *Annu. Rep. NMR Spectrosc.*, 4, 311 (1971).
7. K.G.R. Pachler and P.L. Wessels, *J. Magn. Reson.*, 12, 337 (1973).
8. T.G. Dekker, K.G.R. Pachler and P.L. Wessels, *Org. Magn. Reson.*, 8, 530 (1976).
9. C.E. Johnson and F.A. Bovey, *J. Chem. Phys.*, 29, 1027 (1958).

10. T.G. Dekker and J. Dekker, *J. S. Afr. Chem. Inst.*, 28, 122 (1975).

11. J. Dekker, F.J.C. Martins and J.A. Kruger, *Tetrahedron Lett.*, 2489 (1975).

12. J. Dekker, F.J.C. Martins and T.G. Dekker, *S. Afr. J. Chem.*, 30, 21 (1977).

13. D. Schulte-Frohlinde and V. Werner, *Chem. Ber.*, 94, 2726 (1961).

14. J.M. Bruce, *J. Chem. Soc.*, 2, 2782 (1962).