Reactions of tetrahalogeno-*o*-benzoquinones part VI*: Reactions of tetrachloro-*o*-benzoquinone with methyl naphthols—Formation of naphthoquinone methides

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Abstract. The oxidation of a few methyl naphthols with tetrachloro-*o*-benzoquinone (1) has been described. Reaction of 1-methyl-2-naphthol (4) with the quinone (1) was found to give the spirodimer, 1,1',2,2'-tetrahydro-3*H*-benzo (f) chromen-3-spiro-1'-naphthalene-2'-one (6) and a yellow solid which has been assigned the structure of 5,6,7,8-tetrachloro-1,4-benzodioxan-2-spiro-1'-naphthalen-2'-one (7) on the basis of chemical and spectral data. Among the other naphthols studied, 4-methyl-2-*t*-butyl-1-naphthol afforded 5,6,7,8-tetrachloro-1,4-benzodioxan-2-spiro-1'-naphthalen-3'-*t*-butyl-4'-one (22) while 2-methyl-1-naphthol and 4-methyl-1-naphthol gave 2-methyl-4,4-(tetrachloro-*o*-phenylenedioxy) naphthalen-1(4*H*)-one(15) and 4-methyl-2,2-(tetrachloro-*o*-phenylenedioxy) naphthelen-1(2*H*)-one (19) respectively. The present study has shown that oxidation of suitably substituted naphthols with the quinone (1) gives rise to naphthoquinone methides.

Keywords. Quinone oxidation; quinone methides; methyl naphthol reaction; dienone; benzodioxane; NMR and mass spectra.

1. Introduction

Quinone methides (Turner 1964; Schleigh 1971), implicated as intermediates in many chemical and biochemical processes, constitute a group of reactive organic compounds which can theoretically be derived from quinones by replacement of one of the carbonyl oxygen by a methylene or substituted methylene group. A number of quinone methides occur in nature as fungal metabolites and wood pigments (Turner 1964). Though unsubstituted benzo- and naphthoquinone methides have not been isolated in the pure state, many substituted para benzoquinone methides have been obtained as crystalline solids. Recent studies (Cook and Norcross 1956; Sheppard 1968; Murray 1968) on the oxidation of phenols having alkyl substituents with α-hydrogen atom(s) at ortho or para position to the hydroxyl group indicate that quinone methides are involved in many instances (Cook and Norcross 1956, 1959; Muller *et al* 1961; Bauer and Coppinger 1963; Stebbins and Sicilio 1970; Becker 1969; Findlay and Turner 1971; Bolon 1970).

Earlier studies (Kasturi *et al* 1969; unpublished) carried out in our laboratories on naphthols have shown that tetrachloro-*o*-benzoquinone (1) is an efficient phenol

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oxidising agent. We have observed that reaction of naphthols with the quinone initially leads to an oxydiphenol of the type 2 which undergoes intramolecular oxidative coupling to give spirodienone 3. As the use of the quinone 1 as a phenol oxidising agent has not received much attention, we thought it worthwhile to examine whether reaction of this quinone with ortho and para methyl substituted naphthols could give rise to quinone methides. The results of our studies on the oxidation of 1-methyl-2-naphthol, 2-methyl-1-naphthol, 4-methyl-1-naphthol and 2-*t*-butyl-4-methyl-1-naphthol using 1 are discussed in this paper.


SCHEME 1
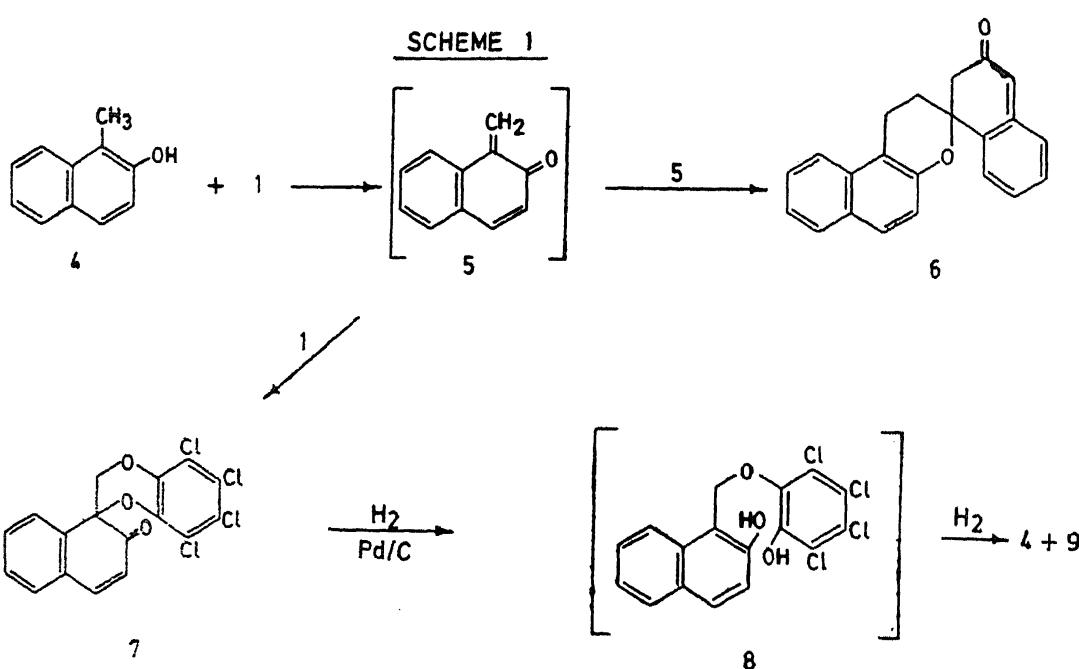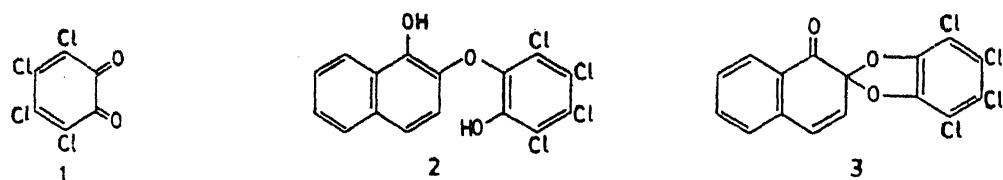
Oxidation of 1-methyl-2-naphthol (4) with one mole of the quinone 1 in refluxing benzene afforded after column chromatography two yellow solids. The spectral properties of the major product suggested that it was the spirodimer 6 which was confirmed by comparison with an authentic sample (Smith and Horner 1968). It has been well established by Dean and coworkers (Chauhan *et al* 1973) that the spirodimer results from dimerisation of 1,2-naphthoquinone-1-methide (5).

Elemental analysis and mass spectrum [M^+400 (^{35}Cl)] of the minor product showed the molecular formula to be $C_{17}H_8Cl_4O_3$. IR spectrum showed a strong absorption at 1690 cm^{-1} showing the presence of a conjugated carbonyl group. The NMR spectrum of the compound exhibited two doublets (J = 12 Hz) at 3·8 (1H) and 4·6 δ (1H), another doublet at 6·2 δ (J = 10Hz, 1H) and a complex multiplet between 7·4 and 7·75 δ(5H). The 1,4-benzodioxan structure 7 was assigned to this compound based on this data. The two doublets with equal coupling constants can be assigned to the methylene hydrogens. The mass spectral fragmentation further supports the structure. The base peak at m/e 156 can be assigned to an ion corresponding to

1,2-naphthoquinone methide resulting from a facile retro Diels-Alder type fragmentation of the molecular ion.

Catalytic hydrogenation of the compound provided further evidence for the assigned structure. Two moles of hydrogen were rapidly absorbed to give a mixture of 1-methyl-2-naphthol (4) and tetrachlorocatechol (9). The reductive ring opening of the spiro system (Pummerer and Cherbuliez 1914) gives rise to a benzylic ether 8 which rapidly undergoes benzylic cleavage to give the observed products (scheme 1).

SCHEME 2
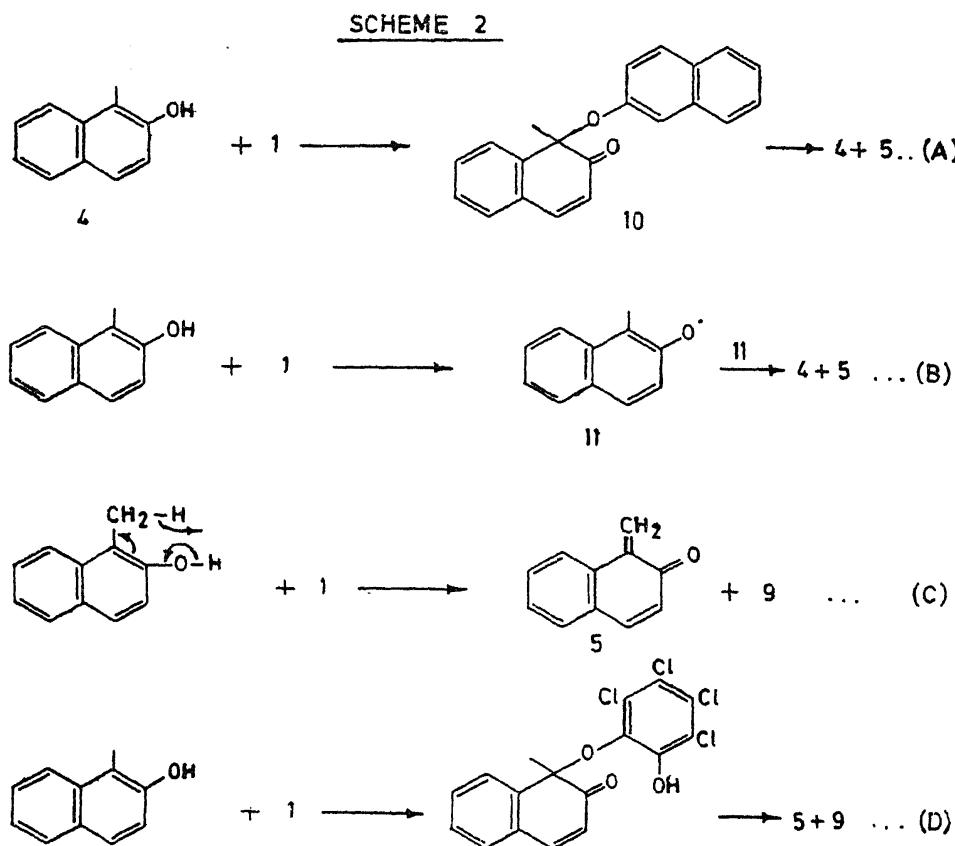
The benzodioxan 7 could be considered to be a Diels-Alder adduct of the initially formed naphthoquinone methide 5 and the quinone 1 (Horspool 1969), the former acting as the dienophile. The isolation of the spirodimer 6 as the main product of the reaction indicated the formation of the quinone methide 5 in the reaction. Based on these mechanistic considerations, the reaction of the naphthol 4 with 2 moles of the quinone was examined, when as expected, benzodioxan 7 was formed as the major product of the reaction.

Several mechanisms (Cook and Norcross 1959; Bauer and Coppinger 1963; Stebbins and Sicilio 1970; Becker 1969; Findlay and Turner 1971) have been postulated for the formation of quinone methide during phenol oxidations and accordingly, four different pathways can be visualised for the formation of the naphthoquinone methide 5 in the reaction described above (scheme 2). In the light of the earlier observations by Pummerer and Cherbuliez (1914) on the oxidation of the naphthol 4 with alkaline potassium ferricyanide it was thought possible to provide experimental evidence in favour of one of these pathways viz., path A in scheme 2, involving the formation of the quinol ether 10. It had been observed that ferricyanide oxidation of the naphthol 4 gave the quinol ether 10 which was found to be stable at room

SCHEME 3
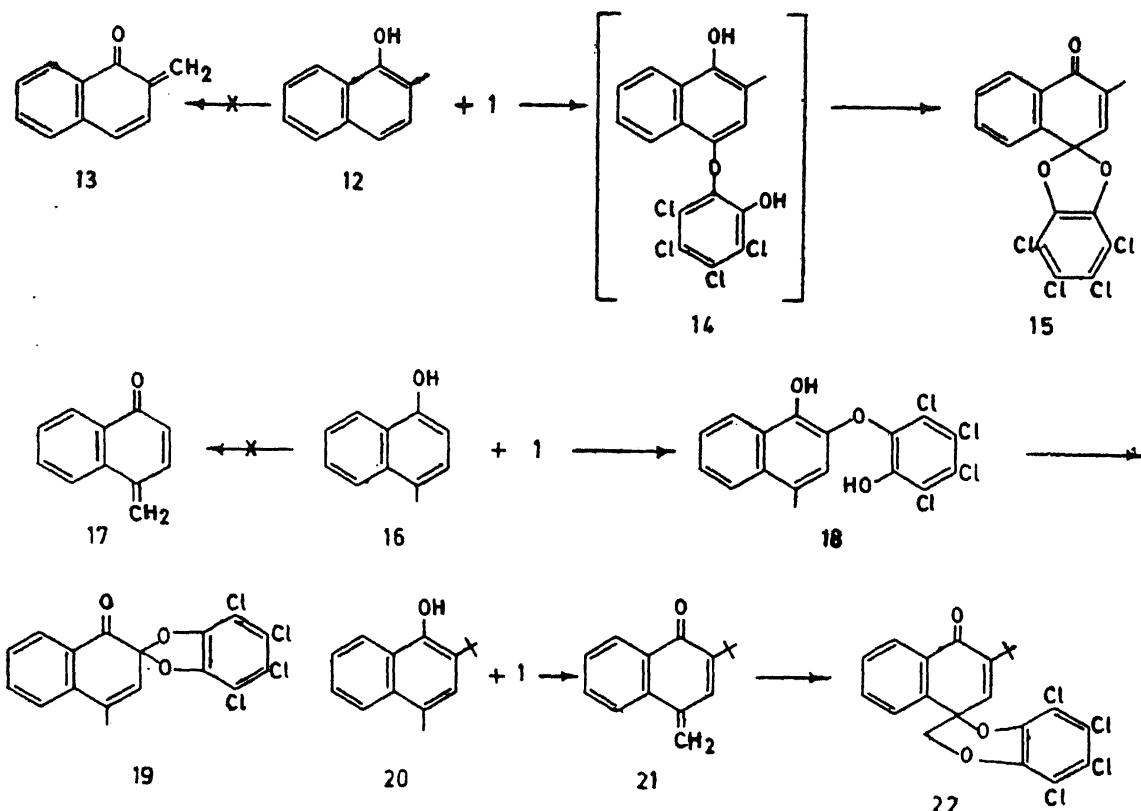
temperature (Pummerer and Cherbuliez 1914). However, it underwent dissociation in refluxing benzene or xylene giving the parent naphthol 4 and the dimer 6, the latter resulting presumably through the intermediacy of the naphthoquinone methide 5 (Smith and Horner 1938). Hence, if the quinol ether 10 were an intermediate in the reaction of the naphthol 4 with the quinone 1, it should be possible to isolate this compound by carrying out the reaction and subsequent purification at room temperature.

When the reaction was carried out at room temperature, it was found to be fast and was complete in 30 minutes (as seen by the disappearance of the naphthol in TLC). Preparative TLC (silica gel) of the reaction mixture afforded the benzodioxan 7 in small amounts (~3%) and an yellow semi-solid. A TLC comparison of this product in different solvent systems showed that it had a R_f value identical with those of the spirodimer 6 and the quinol ether 10. The NMR spectrum of the product, however, showed two singlets at 1·83 and 2·8δ, the latter one appearing along with a multiplet occurring between 2·0—3·2δ, three doublets at 6·08 (J=9Hz), 6·18 (J=10Hz) and 6·42δ (J=10Hz) of nearly equal intensity and a complex multiplet between 7·2—8·2δ. A comparison of the spectrum with those of the spirodimer 6 and the quinol ether 10 showed that the abovementioned semi-solid is a mixture of these two compounds. Thus, the two singlets and two of the doublets (those appearing at 6·08 and 6·42δ) are due to the quinol ether 10 while the multiplet between 2·0—3·2δ and the doublet at 6·18δ arise from the spirodimer 6. The integrated intensities of the various signals suggested that the two compounds are formed in nearly equal accounts. The NMR spectrum of a 1 : 1 mixture of 6 and 10 was found to be identical with that of the reaction product, confirming this. Because of

their identical R_f values, the separation of the product into the two components by preparative TLC was not possible.

This observation clearly shows that more than one reaction pathway is involved in the formation of the naphthoquinone methide. It is unlikely that under the mild conditions employed the quinol ether 10 could have dissociated to give the spiro-dimer 6.

The possible formation of naphthoquinone methides from methyl-l-naphthols was then examined. Reaction of 2-methyl-l-naphthol (12) with the quinone 1 afforded a white solid. The elemental analysis and mass spectrum [(M$^+$ 400 (^{35}Cl)] of the compound supported a molecular formula $C_{17}H_8Cl_4O_3$. The IR spectrum showed two absorptions at 1680 and 1658 cm^{-1} suggesting a *p*-dienone structure (Dimroth *et al* 1967; Hewitt 1971). The mass spectrum of the compound exhibited a fragment ion at m/e 385 (^{35}Cl) resulting from loss of 15 mass units from the molecular ion indicating the presence of a methyl group. Based on the above spectral data[*], the *p*-dienone structure 15 was assigned to this compound.

Reaction of 4-methyl-l-napthol with the quinone 1, expected to form the 1,4-naphthoquinone-4-methide 17, afforded an yellow solid spectral data of which were in agreement with the *o*-dienone structure 19. In the NMR spectrum, the methyl protons appeared as a doublet (J=1Hz) at 2·26δ, and the olefinic proton as a broad singlet at 6·12δ.

The intermediate formation of oxydiphenols 14 and 18 can be invoked to explain the formation of the dienones, 15 and 19 respectively (Kasturi *et al* 1969; unpublished).

The above observations indicated that in the case of 1-naphthol having an un-substituted ortho or para position the formation of oxydiphenols is preferred to that of the corresponding quinone methides. Hence, it was thought that by blocking the 2-position of 4-methyl-l-naphthol with a phenyl or *t*-butyl group coupling at this position could be prevented and thus force the formation of the 1, 4-naphthoquinone-4-methide. Bolon (1970a, b) had made a similar approach in the oxidation of 2,6-dimethylphenol.

Reaction of 4-methyl-2-*t*-butyl-l-naphthol (20) with 2 moles of quinone 1, in reflux-ing benzene led to a complex reaction mixture, (TLC). Preparative layer chromato-graphy of this afforded only one compound in pure state. The spectral data suggested the 1,4-benzodioxan structure 22 for this compound. The NMR spectrum showed signals due to the *t*-butyl protons at 2·33δ and the olefinic proton at 6·7δ. The methylene protons appeared as a singlet at 4·25δ. Mass spectrum of the compound had a fragment ion at m/e 212 arising from a facile retro Diels-Alder type fragmenta-tion. The formation of the benzodioxan strongly suggests that the 1,4-naphthoquin-one-4-methide (21) is formed during the oxidation of the naphthol 20.

2. Experimental

All melting points reported herein are uncorrected. The UV spectra were recorded in 95% ethanol on a Unicam SP 700A spectrometer and the IR spectra on Perkin-

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[*]Due to its very low solubility in all common organic solvents the NMR spectrum of the com-pound could not be recorded.

Elmer Model 700 or Carl-Zeiss UR 10 Spectrometer. The NMR spectra were recorded on a Varian HA-100D or T-60 Spectrometer. Chemical shifts are quoted in δ values relative to tetramethylsilane (TMS) as internal standard. Mass spectra were recorded on an Atlas CH-4 spectrometer with a built-in direct inlet system.

2.1. *Reaction of* 1-*methyl-2-naphthol* (4) *with tetrachloro-o-benzoquinone* (1)

(a) To a solution of the naphthol 4 (0·63 g) in dry benzene (50 ml) the quinone 1 (1g) was added and then heated under reflux for 6 hr. The reaction mixture was concentrated and the residue chromatographed over neutral alumina (50g). Elution with benzene-hexane (1 : 1) mixture gave an yellow solid, which on preparative TLC [silica gel, benzene-hexane (1 : 1)] gave 5,6,7,8-tetrachloro-1, 4-benzodioxan-2-spiro-1'-naphthalen-2'-one (7) (0.08 g), m.p. 211-212° (*in vacuo*) (benzene-hexane); M^+400 (^{35}Cl); IR (nujol): ν_{max} 1690 (conjugated C=O), 1620, 1600 and 1580 cm^{-1} (C=C); UV (EtOH) λ_{max} 220 (ϵ, 75, 400), 236 (40, 160) and 306 nm (10, 400); NMR (CDCl$_3$): 3·83 and 4·6 (AB pair, J=12 Hz, 2H, $-CH_2-O-$), 6·2 (d, J=10 Hz, 1H, C$-3'$H) and 7·4$-$7·75 (m, 5H, C$-4'$ H and ar$-$H); (Found: C, 51·18; H, 2·34; Cl, 34·94, C$_{17}$H$_8$Cl$_4$O$_3$ requires C, 50·79; H, 2·01 and Cl, 35·27%).

Further elution with benzene gave a highly viscous yellow liquid which on crystallisation from benzene-hexane afforded 1,1',2,2'-tetrahydro-3*H*-benzo (f) chromen-3-spiro-1'-naphthalen-2'-one (6) (0·4 g), m.p. 141-142° (m.p. 139-141°) (Smith and Horner 1938), identical with an authentic sample.

Further elution with more polar solvents gave a complex mixture of compounds which could not be purified.

(b) A solution of the naphthol 4 (0·63 g) in dry benzene (50 ml) was refluxed with the quinone 1 (2 g) for 6 hr. The concentrated reaction mixture was chromatographed over neutral alumina (75 g). Elution with benzene-hexane (1 : 1) mixture afforded the 1, 4-benzodioxan 7 (0·7 g) identical with the sample obtained in the above reaction. Further elution with benzene gave a viscous liquid preparative TLC (silica gel, benzene) of which afforded the 1, 4-benzodioxan 7 (0·05 g) and the spirodimer 6 (0·04 g).

(c) To a solution of the naphthol 4 (0·16 g) in dry benzene (10 ml) the quinone 1 (0·25 g) was added and the resulting solution allowed to stand at room temperature. A TLC examination after 30 min showed complete disappearance of the naphthol 4. The solution was concentrated to half its volume *in vacuo* at room temperature. Preparative TLC (silica gel, benzene) of the residue afforded the 1,4-benzodioxan 7 (0·015 g) and a mixture (0·07 g) of 1-methyl-1-(1-methyl-2-naphthyloxy)-naphthalen-2(1*H*)-one (10) and the spirodimer 6 as a semi-solid.

2.2. *Catalytic hydrogenation of the* 1,4-*benzodioxan* 7

A solution of the 1,4-benzodioxan 7 (0·4 g) in dry ethyl acetate (50 ml) was hydrogenated in presence of 10% palladium on carbon (0·1 g). Two moles of hydrogen ($\sim$50 ml) were rapidly absorbed. The catalyst was filtered off and the residue obtained on concentration of the filtrate subjected to preparative TLC [silica gel, benzene-chloroform (1 : 1)] to give 1-methyl-2-naphthol (4) (0·12 g) and tetrachloro-catechol (9) (0·2 g), identical with authentic samples.

2.3. *Reaction of 2-methyl-1-naphthol* (12) *with the quinone* 1

A mixture of the naphthol 12 (0·47 g) and the quinone 1 (1·5 g) in dry benzene (30 ml) was refluxed for 6 hr. The concentrated reaction mixture was chromatographed over neutral alumina (50 g). Elution with benzene-hexane (1 : 1) mixture gave 2-methyl-4,4-(tetrachloro-*o*-phenylenedioxy) naphthalen-1 (4*H*)-one (15) (0·49 g) as a white solid, m.p. 205° (*in vacuo*) (benzene); M^+ 400 (^{35}Cl); IR (nujol): ν_{max} 1680, 1658 (dienone doublet) and 1600 cm^{-1} (C=C); UV (Et OH); λ_{max} 219 (ϵ, 30, 700), 295 (3300) and 302 nm (3070) (Found: C, 50·98; H, 2·44; Cl, 35.66. $C_{17}H_8O_3Cl_4$ requires C, 50·79; H, 2·01 and Cl, 35·27%).

Further elution with benzene and other more polar solvents gave an intractable mixture of compounds.

2.4. *Reaction of 4-methyl-1-naphthol* (16) *with the quinone* 1

The quinone 1 (2 g) was added to a solution of the naphthol 16 (0.63g) in dry benzene (50 ml) and the resulting solution heated under reflux for 6 hr. Concentration of the reaction mixture followed by column chromatography over neutral alumina (75 g) afforded 4-methyl-2,2-(tetrachloro-*o*-phenylenedioxy)-naphthalen-1(2*H*)-one (19) (0·58 g) m.p. 177° (*in vacuo*) (benzene-hexane); IR (nujol): ν_{max} 1690 (conjugated C=O) and 1595 cm^{-1} (C=C); UV (EtOH): λ_{max} 220 (ϵ, 46, 600), 243 (49, 350), 304 (6430) and 370 nm (1670); NMR (CDCl$_3$) 2·26 (d, j=1 Hz, 3H, —CH=C—(CH$_3$)$_3$), 6, 12 (br.s, 1H, C—3H), 7·2—7·8 (m, 3H, ar—*H*) and 7·9—8·15 (m, 1H, C—8H). (Found: C, 50·82; H, 2·33; Cl, 35·30. $C_{17}H_8Cl_4O_3$ requires C, 50·79, H, 2·01 and Cl, 35·27%).

2.5. *Reaction of 2-t-butyl-4-methyl-1-naphthol* (20) *with the quinone* 1

A solution of the naphthol 20 (0.45 g) and the quinone 1 (1 g) in dry benzene (30 ml) was refluxed for 6 hr. The reaction mixture after concentration, was chromatographed over silica gel (50g). Elution with benzene-hexane (1 : 1) mixture afforded an yellow solid. Preparative TLC [silica gel, benzene-hexane (1 : 3)] of this solid gave 5,6,7, 8-tetrachloro-1,4-benzodioxan-2-spiro-1'-naphthalene-3'-*t*-butyl-4'-one(22) (0·22 g), m.p. 175-176° (*in vacuo*)(benzene-hexane); M^+ 456 (^{35}Cl); IR(nujol): ν_{max} 1662 and 1638 (dienone doublet) and 1605 cm^{-1} (C=C); UV (EtOH): λ_{max} 218 (ϵ, 71, 340), 238 (25, 840), 296 (5300) and 302 nm (4800); NMR (CDCl$_3$): 2·33 [s, 9H, —C(CH$_3$)$_3$], 4·2 (s, 2H, —CH$_2$—O), 6.7 (s, 1H, C—2'H), 7·4—7·3 (m, 3H, ar—H) and 8·0—8·36 (m, 1H, C—8'H) (Found: C, 55·38, H, 3·92; Cl, 31 16. $C_{21}H_{16}Cl_4O_3$ requires C, 55·05, H, 3.52 and Cl, 30.96%).

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