Quinones. Part 9.[1] Side-chain Alkylthiolation of Methyl-1,4-naphthoquinones

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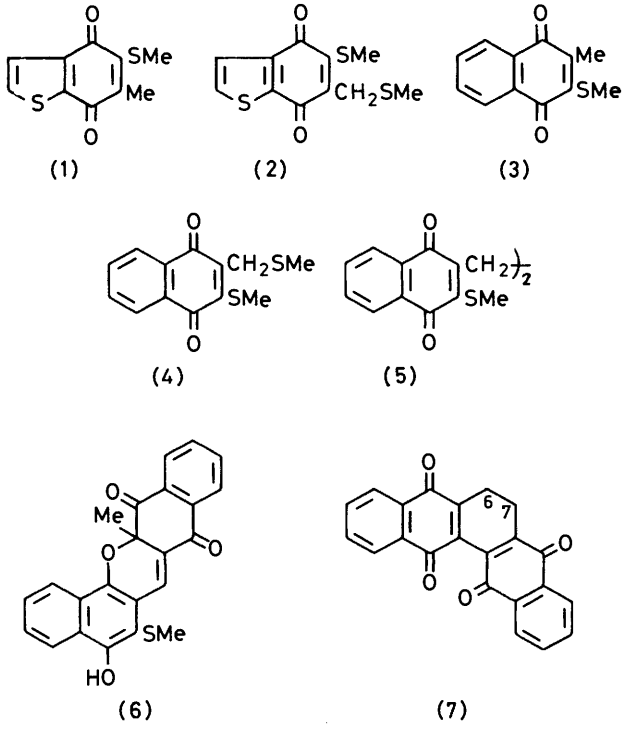
2-Methyl-1,4-naphthoquinones react with an excess of sodium methanethiolate to give methylthiomethyl derivatives. Corresponding products were obtained, but in lower yield, using α-toluene- and toluene-*p*-thiolates. With 3-chloro-2-methyl-1,4-naphthoquinone and methanethiolate, replacement of chlorine occurs before reaction with the side chain, while the minor products formed provide evidence that the side-chain alkylthiolation proceeds by addition of thiolate to the tautomeric quinone methide form of the methylquinone.

In connection with previous work on the structure of caldariellaquinone we synthesised[2] 6-methyl-5-methylthiobenzo[*b*]thiophen-4,7-quinone (1) by the reaction of 5-bromo-6-methylbenzo[*b*]thiophen-4,7-quinone with a small excess (14%) of sodium methanethiolate. A minor product of this reaction was found later to be 5-methylthio-(6-methylthiomethyl)benzo[*b*]thiophen-4,7-quinone (2). The structure of (2), $C_{11}H_{10}O_2S_3$, was evident from the n.m.r. spectrum which comprised two *S*-methyl singlets at δ 2.63 and 2.18, a methylene singlet at δ 3.90, and two doublets at δ 7.64 and 7.54 arising from the thiophen-ring protons. As the formation of (2) involves both nuclear and side-chain methylthiolation, which is new, the reaction was studied further using more readily available quinones.



(1) (2) (3) (4) (5) (6) (7)

RESULTS

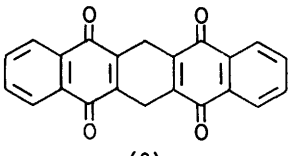
3-Chloro-2-methyl-1,4-naphthoquinone reacted with sodium methanethiolate (1.66 mol equiv.) at room temperature to give mainly 2-methyl-3-methylthio-1,4-naphthoquinone (3). The minor products did not include the di-methylthiolated product (4) but this was detected (t.l.c.) when 2 mol of sodium methanethiolate were used. Using a large excess of methanethiolate (10 mol equiv.) (4) was formed in 21% yield, better yields (51%) being obtained when 2-methyl-3-methylthio-1,4-naphthoquinone (3) was used as starting material. The structure of (4) was deduced from analytical and spectroscopic data (see Experimental section) and was confirmed by synthesis from 3-chloro-2-chloromethyl-1,4-naphthoquinone and the same reagent.

The minor products formed in the above reactions included the dimeric compounds (5) and (6). The n.m.r. spectrum of the biquinone (5), $C_{24}H_{18}O_4S_2$, displayed singlets at δ 3.21 ($-CH_2CH_2-$) and 2.40 (2 SMe) whereas the *O*-methyl analogue[3] resonates at δ 2.88 and 4.00. The red xanthene (6), $C_{23}H_{16}O_4S$, showed $\lambda_{max.}$ 478 nm, $\nu_{max.}$ 3 360, 1 702 (C-13 >C=O), and 1 654 cm^{-1}, and δ 8.41 (H-7), 7.30 (HO), 2.32 (SMe), and 1.58 (C-13a Me), and was generally very similar to the xanthene (6; Me in place of SMe)[4] [*cf.* $\lambda_{max.}$ 486 nm, $\nu_{max.}$ 3 370, 1 709, and 1 650 cm^{-1}, and for the acetate δ 7.95 (H-7), and 1.57 (C-13a Me)].

When a solution of 3-chloro-2-methyl-1,4-naphthoquinone and a large excess of sodium methanethiolate was left in a stoppered flask for two days, relatively little reaction ensued, giving low yields (<10%) of (3) and (4). However another minor product was isolated which we regard as the dihydropentaphenediquinone (7). It showed characteristic 1,4-naphthoquinone u.v. and i.r. spectra ($\lambda_{max.}$ 251 and 333 nm, $\nu_{max.}$ 1 675 and 1 660 cm^{-1}), and a typical 1,4-naphthoquinone n.m.r. spectrum at low field in addition to a singlet (4H) at δ 2.88 ($CDCl_3$) or 3.03 (CF_3CO_2D) [*cf.* (5; Et in place of SMe), δ ($CDCl_3$) 2.80 (4 H, s) and (CF_3CO_2D) 3.05]. In the mass spectrum the molecular ion is very weak with the base peak at *m/e* 338 ($M^+ - 2$), corresponding to pentaphenediquinone, followed by successive losses of four molecules of carbon monoxide from $M^+ - 2$. Easy aromatisation of the central ring of (7) is not surprising although it would be opposed by increased steric interaction between the C-13 and C-14 oxygens. Initially we considered that this biquinone might be the isomer (8), as its dehydroderivative, pentacene-5,14 : 7,12-diquinone, can be obtained[5] from 3-chloro-2-methyl-1,4-naphthoquinone on treatment with *N*-methylcyclohexylamine but the observed methylene resonance is at too high field.

When 2,3-dimethyl-1,4-naphthoquinone was left for a few hours with a large excess of sodium methanethiolate (20 mol) the di-methylthiolated product (10; R^1 = Me, R^2 = H) was obtained in good yield. Using a smaller excess of reagent (10 mol) and restricted access of air led to the formation of a mixture of the mono- (9; R = Me) and di-methylthiolated (10; R^1 = Me, R^2 = H) compounds.

The structures of these quinones were confirmed synthetically by nucleophilic substitution of 2,3-dichloromethyl- and 3-chloromethyl-2-methyl-1,4-naphthoquinones with sodium methanethiolate. Similarly, 2,3,6-trimethyl-1,4-naphthoquinone gave a good yield of the corresponding di-methyl-



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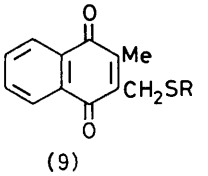

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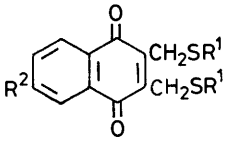

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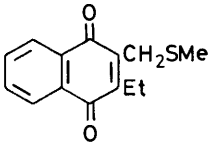

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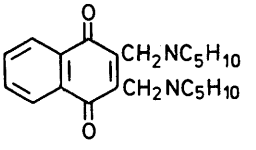
thiolated quinone (10; $R^1 = R^2 = Me$) whereas 3-ethyl-2-methyl-1,4-naphthoquinone reacted exclusively on the methyl side chain to give the methylthiomethyl derivative (11).

Reactions with two other thiolates were examined briefly.



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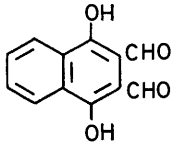

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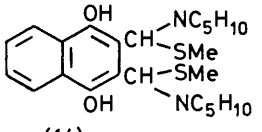

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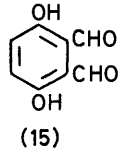

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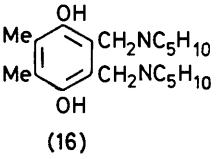

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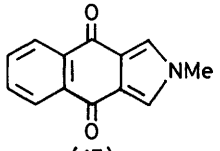

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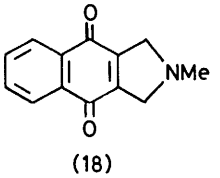

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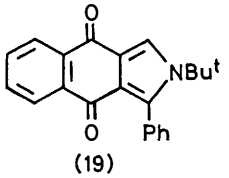

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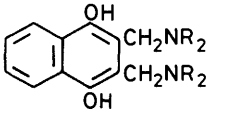
With sodium α-toluenethiolate, 2,3-dimethyl-1,4-naphthoquinone gave a mixture of (9; $R = PhCH_2$) (mainly) and (10; $R^1 = PhCH_2$, $R^2 = H$); even after heating at 55—60 °C with a 20-fold molar excess of reagent and then leaving overnight, some unchanged starting quinone remained. The reaction of 2,3-dimethyl-1,4-naphthoquinone with a large excess of sodium toluene-*p*-thiolate was similar although yields of (9; $R = p\text{-}MeC_6H_4$) and (10; $R^1 = p\text{-}MeC_6H_4$, $R^2 = H$) were somewhat lower and more by-products were observed. The two *p*-tolylthiomethyl derivatives were also prepared from the appropriate chloromethylquinone by nucleophilic substitution by toluene-*p*-thiolate. In the mass spectrum of the bis-(*p*-tolylthiomethyl)quinone the base peak appears at *m/e* 273 ($M^+ - C_7H_9S_2$), probably corresponding to a tetracene derivative for which several structures can be written.

It was desirable to relate the products from side-chain alkylthiolation to those obtained by side-chain amination.[6] To this end 2,3-bis(methylthiomethyl)-1,4-naphthoquinone (10; $R^1 = Me$, $R^2 = H$) was treated with piperidine (2 mol) in order to obtain the bis(aminomethyl)quinone (12) or its more stable quinol.[6] Five coloured products were formed, the major one being the pale yellow diformylquinol (13) [ν_{CO} 1 640 cm^{-1}, δ 13.55 (HO) and 10.55 (CHO)]. Several routes to (13) are possible, one of which proceeds by hydrolysis of the tetrasubstituted quinol (14). The analogue (15) was previously obtained [6] by oxidation of (16) with a limited amount of chromic acid.

The reaction of 2,3-bis(methylthiomethyl)-1,4-naphthoquinone with dimethylamine was even more complex, but methylamine gave one major product identified as the isoindolequinone (17) [ν_{CO} 1 657 cm^{-1}, δ 7.36 (2 H, s, H-1 and -3)]. The reaction presumably proceeds by oxidation of the quinone (18) formed by nucleophilic displacement of both methylthio-groups in (10; $R^1 = Me$, $R^2 = H$). A similar intermediate compound is probably involved in the formation of the isoindolequinone (19) on treatment of 3-benzyl-2-methyl-1,4-naphthoquinone with t-butylamine.[7]

DISCUSSION

This new side-chain alkyl(aryl)thiolation reaction bears an obvious resemblance to the side-chain amination of alkylated quinones,[6,8] a reaction that is effected by leaving the quinone in contact with an excess of a secondary aliphatic amine, with or without solvent, the product being the quinol, *e.g.* (20) from 2,3-dimethyl-1,4-naph-



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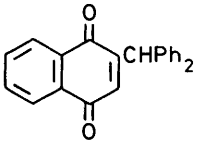

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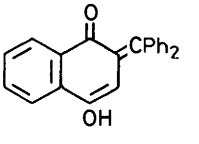

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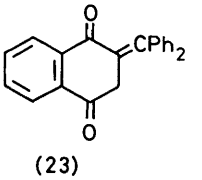

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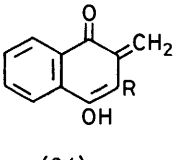

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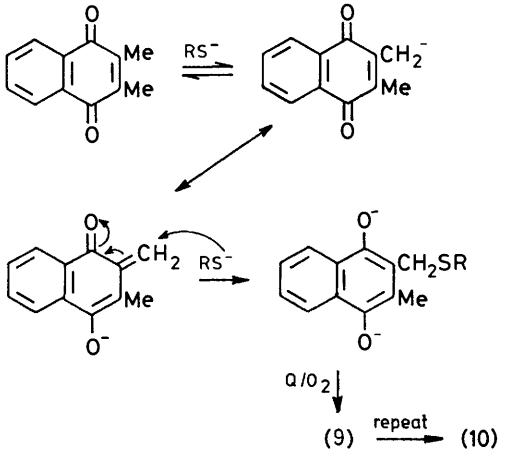
thoquinone, which is usually isolated by removal of solvent and the excess of amine. This difference in end-product is not of great significance as some of our reaction solutions showed relatively little colour prior to work-up, more colour developing, *i.e.* oxidation of quinols to quinones, during the isolation procedures.

We regard the alkylthiolation as a three-step process (Scheme 1), the thiolate acting first as a base to remove a proton from an α-carbon atom, and secondly as a nucleophile by conjugate addition to the quinone methide so formed to give the quinol dianion which is finally oxidised, mainly by air, although the starting quinone is no doubt involved to some extent. That oxygen is required for the oxidation step(s) was readily demonstrated by allowing the reaction to proceed in a stoppered flask. Yields of thiolated products were invariably low, and when 2,3-dimethyl-1,4-naphthoquinone was treated with 10 mol of sodium toluene-*p*-thiolate in that way scarcely any side-chain reaction occurred. However, when the stopper was removed, allowing free access

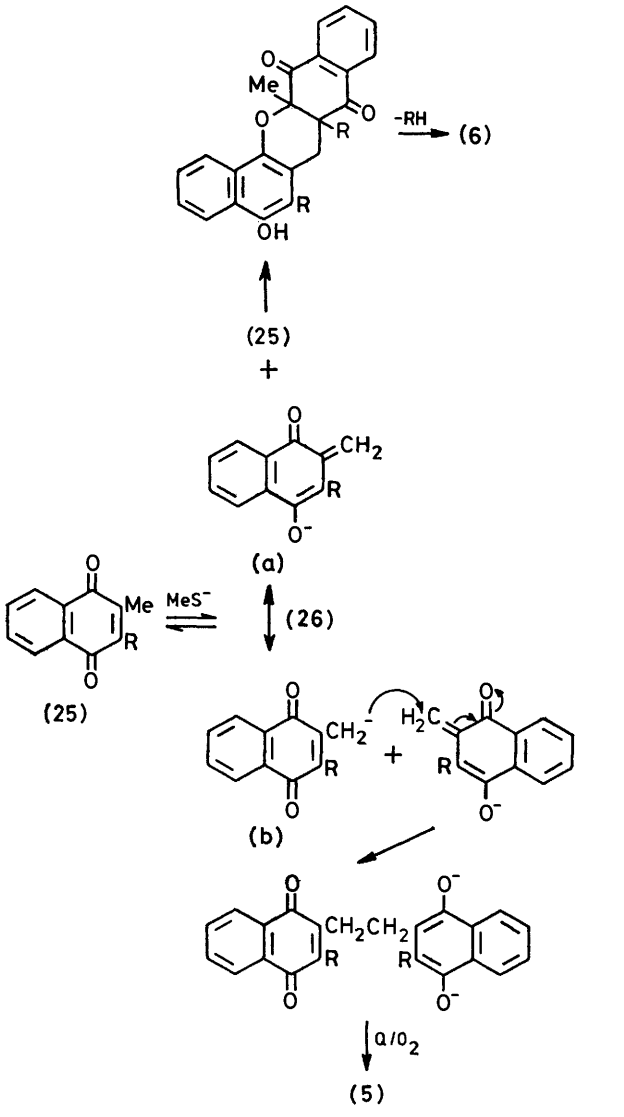


SCHEME 1

of air, the reaction continued in the normal way. The conversion Q–Me ⟶ Q–CH_2SR requires two mol of thiolate but in practice a substantial excess is required in order to obtain a good yield since quinone methide anions can react in other ways [8,9] (*e.g.* with themselves or with the protonated species), and some thiolate is inevitably consumed by oxidation (by air and starting quinone) to disulphide. This may be offset to some extent by a competing reaction, $Q–CH_2^- + RSSR \longrightarrow RQ–CH_2SR + RS^-$, but for *p*-tolylthiolation, at least, this is not important as very little of (9; R = *p*-MeC_6H_4) and (10; R^1 = *p*-MeC_6H_4, R^1 = H) were formed when 2,3-dimethyl-1,4-naphthoquinone was treated with sodium methanethiolate (1 mol) and di-*p*-tolyl sulphide (10 mol). Thus the thiolate anions are involved in three reactions, proton abstraction, nucleophilic addition, and oxidation, all of which relate to the electron density on sulphur. It is therefore not surprising that the side-chain reaction proceeds most efficiently with methanethiolate and least with toluene-*p*-thiolate (*cf.* pK_a values, MeSH 10.3, $PhCH_2SH$ 9.43, *p*-MeC_6H_4SH 7.08).[10] In the reactions of α-toluene- and toluene-*p*-thiolate with 2,3-dimethyl-1,4-naphthoquinone, yields of dialkyl-(aryl)thiomethylquinones (10) were less than 15% and much starting quinone remained at the end of the reaction period. If the reaction with toluene-*p*-thiolate was prolonged the *p*-tolylthiomethylquinones (9; R = *p*-MeC_6H_4) and (10; R^1 = *p*-MeC_6H_4, R^2 = H) gradually disappeared with concomitant consumption of all the starting quinone and the appearance of two more polar products which have not been examined. The course of the side-chain reaction is also influenced by the redox potential of the alkylated quinone which affects the extent of thiolate oxidation, and by the nature of the alkyl side chains. In one example, methylthiolation of 3-ethyl-2-methyl-1,4-naphthoquinone gave the isomer (11) only, which is consistent with the greater acidity of the methyl compared to the methylene group, formation of the primary anion ($Q–CH_2^-$) being preferred. Similar observations have been made in other reactions involving quinone α-carbanions where ethyl groups are usually inert.[3,11]

The participation of quinone methide tautomers in the reactions of alkylated quinones has frequently been invoked although they have never been directly detected in these reactions. Recently, Russian workers [12] have been able to isolate the diphenylmethylquinone (21) in both its quinone methide (22) and diketo (23) tautomeric forms. However, this is a very favourable case, and the isolation of a quinone methide (24) derived from a simple methylquinone is unlikely. (4-Benzyl-1,2-naphthoquinone has also been isolated in a tautomeric form which in that case is a *p*-quinone methide.[13]) Indirect evidence for the participation of (24) or its anion, in our experiments comes from the minor products isolated from the reaction between 3-chloro-2-methyl-1,4-naphthoquinone and sodium methanethiolate, namely (5) and (6). (Minor products were observed in most of the alkylthiolation reactions but were not investigated.) The xanthene (6) arises (Scheme 2) by cycloaddition [9b,14,15] of the quinone methide (26a; R = MeS) to the precursor quinone (25; R = Cl or MeS) followed by elimination of hydrochloric acid or methanethiol. The product described in the Experimental section is the xanthene (6) but on one occasion we also isolated a trace of the red chloroxanthene (6; Cl in place of MeS) ($C_{22}H_{13}ClO_4$ by accurate mass measurement). The dimer (5) is most probably formed by Michael addition of the carbanion (26b; R = MeS) to the quinone methide, followed by oxidation for which there is ample precedent.[3,16] It is not known whether this conjugate addition involves the quinone methide or its anion (as written), as (5) was isolated when the reaction with 3-chloro-2-methyl-1,4-naphthoquinone was conducted with less than 2 mol of sodium methanethiolate, but it seems likely that the anion takes part in the preparative side-chain alkylthiolations (Scheme 1) where a large excess of thiolate was employed. The formation of the dimeric compounds (5) and (6) could be detected when only 1 mol of thiolate was used with 3-chloro-2-methyl-1,4-naphthoquinone showing that some attack had occurred on the methyl group, but subsequent addition of RS^- to the quinone methide did not occur in the absence of an excess of reagent, the product being mainly 2-methyl-3-methylthio-1,4-naphthoquinone resulting from normal nucleophilic displacement. The other very minor pro-

duct (7) obtained from one of these reactions probably is not formed directly from a quinone methide, and we speculate that it derives from the biquinone (5) by further reaction with thiolate (Scheme 3) to give the pentacyclic



SCHEME 2

phenediquinone (27). Reduction of the 6,7-double bond, which would relieve the steric interaction of the C-13 and C-14 carbonyl groups, could occur by a redox reaction with thiolate followed by rearrangement of the monoquinol (or its dianion).

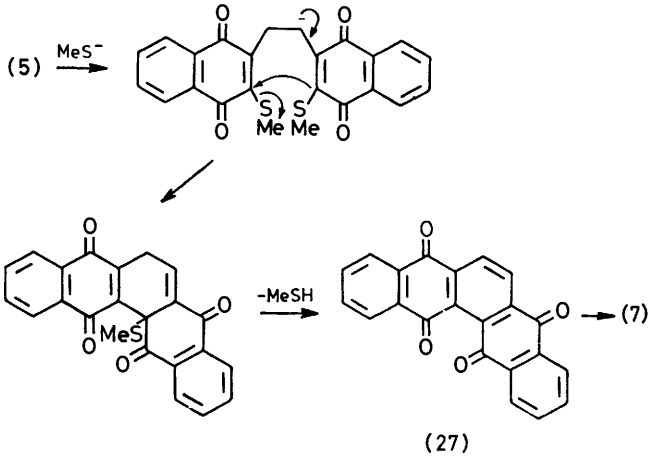
EXPERIMENTAL

Spectra were measured in ethanol (u.v.), KBr (i.r.), or deuteriochloroform (n.m.r.) unless stated otherwise.

Sodium Methanethiolate.—This was prepared by passing an excess of methanethiol gas through methanolic sodium methoxide, and evaporating the solution to dryness *in vacuo*. The deliquescent white solid was stored in a desiccator.

5-Methylthio-6-(methylthiomethyl)benzo[b]*thiophen-4,7-quinone* (2).—The reaction of 5-bromo-6-methylbenzo[*b*]thiophen-4,7-quinone and sodium methanethiolate to give 6-methyl-5-methylthiobenzo[*b*]thiophen-4,7-quinone is described in ref. 2. Elution of the minor orange band which separated on preparative t.l.c. afforded the *methylthio-(methylthiomethyl)quinone* as orange-red needles, m.p. 158—159° (from ethanol) (3%) (Found: M^+, 269.984 0. $C_{11}H_{10}O_2S_3$ requires M, 269.984 2); $\lambda_{max.}$ 239, 275, 330, and 467 nm (log ε 4.19, 3.88, 3.80, and 3.29); $\nu_{max.}$ 1 660 and 1 638 cm^{-1}; δ 7.64 and 7.54 (each 1 H, d, J 5 Hz, H-2 and -3), 3.90 (2 H, s, Q–CH_2–S), 2.63 (3 H, s, Q–SMe), and 2.18 (3 H, s, CH_2–S*Me*); *m/e* 270 (M^+, 50%), 255 (50), 240 (47), 224 (45), 223 (50), 222 (100), 209 (8), 190 (18), 139 (7), 111 (10), and 110 (13).

Reaction of 3-Chloro-2-methyl-1,4-naphthoquinone with Sodium Methanethiolate.—(i) Sodium methanethiolate (0.56 g, 1.66 mol) in methanol (5 ml) was added to 3-chloro-2-methylnaphthoquinone (1 g) in benzene (20 ml) and methanol (10 ml). The mixture was stirred for 1 h and then evaporated. The residue was separated on silica gel, eluting with benzene containing increasing amounts of



SCHEME 3

chloroform, to give 2-methyl-3-methylthio-1,4-naphthoquinone (3) as yellow needles, m.p. 91—92° (lit.,[17] 91—92°) (from ethanol) (0.55 g); δ 2.66 (3 H, s, SMe) and 2.31 (3 H, s, Q–Me). Further elution with light petroleum (b.p. 60—80°)–ether gave a fraction which was separated by preparative t.l.c. on silica gel in ethyl acetate–benzene (1 : 19), followed by ethyl acetate–light petroleum (1 : 4), into *8,13-dihydro-5-hydroxy-13a-methyl-6-methylthio-8,13-dioxodibenzo*[b,h]*xanthen* (6) as red prisms, m.p. 190—191° (decomp.) (from chloroform–light petroleum) (36 mg) (Found: M^+, 338.076 5. $C_{23}H_{16}O_4S$ requires M, 338.076 9); $\lambda_{max.}$ 248, 265sh, 312sh, 319, 350sh, and 478 nm (log ε 4.37, 4.23, 4.10, 4.12, 3.74, and 3.82); $\nu_{max.}$ 3 360, 1 702, 1 654, and 1 590 cm^{-1}; δ 8.41 (1 H, s, H-7), 8.56—8.16, 7.92—7.78 and 7.80—7.66 (total 8 H, m, ArH), 7.30 (1 H, s, exchanges with CD_3OD, OH), 2.32 (3 H, s, SMe), and 1.58 (3 H, s, C-13a-Me); *m/e* 388 (M^+, 40%), 373 (10), 342 (40), 341 (100), 312 (8), 105 (16), and 77 (14); and *1,2-bis-(3-methylthio-1,4-naphthoquinon-2-yl)ethane* (5) as yellow needles, m.p. 203° (from chloroform–light petroleum) (10 mg) (Found: M^+, 434.065 1. $C_{24}H_{18}O_4S_2$ requires M, 434.064 7); δ 8.12—7.96 and 7.75—7.60 (each 4 H, m, ArH), 3.21 (4 H, s, Q–CH_2), and 2.40 (6 H, s, SMe); *m/e* 434 (M^+, 100%), 387 (17), 372 (26), 371 (13), 218 (16), 217 (32), 189 (5), 184 (7), 115 (9), 105 (10), 85 (13), 83 (23), and 76 (13).

(ii) A mixture of 3-chloro-2-methyl-1,4-naphthoquinone (0.2 g), sodium methanethiolate (0.7 g, 10 mol) in benzene (5 ml), and methanol (10 ml) was stirred under a drying tube for 4 h and poured into a mixture of ether (50 ml) and 10% w/v potassium dihydrogen phosphate–water (50 ml). The organic phase was dried ($MgSO_4$) and evaporated, and the residue separated by preparative t.l.c. on silica in benzene. The upper orange band was removed to give 3-*methylthio*-2-(*methylthiomethyl*)-1,4-*naphthoquinone* as orange needles, m.p. 128—129° (from ethanol) (48 mg) (Found: C, 59.3; H, 4.8; S, 24.5%; M^+, 264.027 7. $C_{13}H_{12}O_2S_2$ requires C, 59.1; H, 4.6; S, 24.3%; M, 264.027 8); $\lambda_{max.}$ 250sh, 261, 323, and 434 nm (log ε 4.16, 4.21, 3.56, and 3.36); $\nu_{max.}$ 1 660, 1 650, and 1 590 cm^{-1}; δ 8.15—8.0 and 7.76—7.64 (each 2 H, ArH), 3.93 (2 H, s, CH_2SMe), 2.67 (3 H, s, Q–SMe), and 2.18 (3 H, s, CH_2SMe); *m/e* 264 (100%), 249 (63), 236 (5), 245 (8), 234 (100), 218 (50), 217 (56), 216 (100), 203 (11), 189 (10), 184 (13), 128 (8), 115 (14), 113 (14), 105 (10), 104 (19), and 76 (40).

(iii) To a solution of 3-chloro-2-methyl-1,4-naphthoquinone (0.5 g) in benzene (8 ml) was added sodium methanethiolate (1.75 g, 10 mol) in methanol (18 ml). The flask, almost full, was left stoppered for 50 h. Benzene (80 ml) and 10% w/v potassium dihydrogen phosphate–water (100 ml) were added and the organic phase was washed with water, dried ($MgSO_4$), and evaporated. The residue (264 mg) was separated by preparative t.l.c. on silica gel in benzene into 2-methyl-3-methylthio-1,4-naphthoquinone (3) (33 mg), 3-methylthio-2-(methylthiomethyl)-1,4-naphthoquinone (4) (55 mg), and 6,7-*dihydropentaphene*-5,14 : 8,13-*diquinone* (7) as yellow prisms, subl. 250—260° (8 mg) (Found: $M^+ - 2$, 338.057 9. $C_{22}H_{12}O_4$ requires $M - 2$, 338.057 9); $\lambda_{max.}$ ($CHCl_3$) 251, 270sh, 295sh, and 333 nm (log ε 4.38, 4.24, 4.11, and 3.76); $\nu_{max.}$ 1 675, 1 660, and 1 594 cm^{-1}; δ 8.20—8.08 and 7.82—7.70 (each 4 H, m, ArH), and 2.88 (4 H, s, H-6 and -7); *m/e* 342 (2%), 340 (M^+, 3.5), 339 (14), 338 (100), 310 (35), 282 (28), 254 (16), 226 (9), and 224 (8).

Reaction of 2-*Methyl*-3-*methylthio*-1,4-*naphthoquinone with Sodium Methanethiolate*.—2-Methyl-3-methylthio-1,4-naphthoquinone (120 mg) in benzene (3 ml) was stirred with sodium methanethiolate (390 mg, 10 mol) for 4 h in a flask protected by a drying tube. The mixture was poured into ether–aqueous potassium dihydrogen phosphate and the ethereal layer was washed with water, dried ($MgSO_4$), and evaporated. The residue was crystallised from ethanol to give 3-methylthio-2-(methylthiomethyl)-1,4-naphthoquinone (4), m.p. 128—129° (74 mg), identical with that obtained above.

This compound was also obtained by stirring 2-chloro-3-chloromethyl-1,4-naphthoquinone [18] (34 mg) in benzene (2 ml) with sodium methanethiolate (19.4 mg) in methanol (1 ml) for 24 h. The mixture was filtered and evaporated, and the residue purified by preparative t.l.c. on silica gel in chloroform. The main orange band afforded 3-methylthio-2-(methylthiomethyl)-1,4-naphthoquinone (4) as yellow needles, m.p. 128—129° (from ethanol) (15 mg), identical with that obtained above.

Reaction of Alkylated 1,4-*Naphthoquinones with Sodium Methanethiolate*.—(i) 2,3-Dimethyl-1,4-naphthoquinone (0.508 g) in benzene (10 ml) was stirred with sodium methanethiolate (3.82 g, 20 mol) in methanol for 12 h in a flask protected by a drying tube. The mixture was added to benzene (50 ml) and aqueous potassium dihydrogen phosphate, and the organic phase was washed with water, dried, and evaporated to give a crystalline residue (0.67 g). Crystallisation from ethanol gave 2,3-*bis*(*methylthiomethyl*)-1,4-*naphthoquinone* (10; R^1 = Me, R^2 = H) as orange-red needles, m.p. 85–86° (0.43 g) (Found: C, 60.3; H, 5.3; S, 22.8%; M^+, 278.043 2. $C_{14}H_{14}O_2S_2$ requires C, 60.4; H, 5.05; S, 23.0%; M, 278.043 4); $\lambda_{max.}$ 252.5, 267, 273sh, and 335 nm (log ε 4.19, 4.15, 4.14, and 3.50); δ 8.12—8.06 and 7.80—7.67 (each 2 H, A_2B_2, ArH), 3.78 (4 H, s, Q–CH_2–S), and 2.19 (6 H, s, SMe); *m/e* 278 (M^+, 8%), 231 (16), 230 (28), 216 (10), 215 (100), 184 (5), 128 (5), and 76 (6).

(ii) The above experiment was repeated in a stoppered flask for 2 days using half the amount of sodium methanethiolate (10 mol). The residue after work-up was separated by preparative t.l.c. on silica gel in benzene followed by ethyl acetate–light petroleum (1 : 9). The main band was passed down a column of silica gel in ether–petrol (1 : 9) to give 2-*methyl*-3-*methylthiomethyl*-1,4-*naphthoquinone* (9; R = Me) as yellow needles, m.p. 61.5—62° (from light petroleum–ethanol) (48 mg) (Found: C, 67.2; H, 5.3; S, 13.8%; M^+, 232.055 5. $C_{13}H_{12}O_2S$ requires C, 67.2; H, 5.2; S, 13.8%; M, 232.055 8); $\lambda_{max.}$ 252, 265—272, and 329.5 nm (log ε 4.16, 4.15, and 3.51); $\nu_{max.}$ (KBr) 1 660, 1 614, and 1 594 cm^{-1}; δ 8.15—8.02 and 7.76—7.63 (each 2 H, m, ArH), 3.72 (2 H, s, Q–CH_2–S), 2.24 (3 H, s, SMe), 2.15 (3 H, s, Q–*Me*); *m/e* 232 (M, 75%), 217 (28), 187 (7), 186 (100), 185 (25), 158 (16), 157 (18), 129 (11), 128 (28), 127 (11), 105 (9), 77 (11), and 76 (20); and 2,3-bis(methylthiomethyl)-1,4-naphthoquinone, m.p. 85—86° (97 mg), identical to that obtained in (i). Another fraction (159 mg) containing more (9; R = Me) and (10; R^1 = Me, R^2 = H) was not purified further.

2-Methyl-3-(methylthiomethyl)-1,4-naphthoquinone was also prepared from 3-chloromethyl-2-methyl-1,4-naphthoquinone [18] (0.64 g) in benzene (13 ml) by stirring with sodium methanethiolate (0.2 g) in methanol (3 ml) for 24 h. After filtration and evaporation, the residue was purified by preparative t.l.c. on silica gel in benzene, the main yellow band (0.41 g) yielding the desired quinone, m.p. 61.5—62°, identical to that obtained above. 2,3-Bis(methylthiomethyl)-1,4-naphthoquinone (10; R^1 = Me, R^2 = H) was obtained similarly from 2,3-bis(chloromethyl)-1,4-naphthoquinone.[18] The crude product crystallised from ethanol as orange-red needles, m.p. 85—86°, identical with those obtained in (i).

(iii) 2,3,6-Trimethyl-1,4-naphthoquinone (0.264 g) in benzene (7 ml) was treated with sodium methanethiolate (1.84 g, 20 mol) in the usual way. Work-up and preparative t.l.c., gave 6-*methyl*-2,3-*bis*(*methylthiomethyl*)-1,4-*naphthoquinone* (10; R^1 = R^2 = Me) (280 mg) as orange needles, m.p. 93—93.5° (from chloroform–light petroleum) (Found: C, 61.8; H, 5.7; S, 22.0%; M^+, 292.059 2. $C_{15}H_{16}O_2S_2$ requires C, 61.6; H, 5.5; S, 21.9%; M, 292.059 1); δ 7.97 (1 H, d, J 8 Hz, H-8), 7.88br (1 H, s, H-5), 7.49 (1 H, dd, J 8 and 2 Hz, H-7), 3.76 (4 H, s, Q–CH_2–S), 2.43 (3 H, s, 6-Me), and 2.18 (6 H, s, SMe); *m/e* 292 (M^+, 7%), 246 (10), 245 (53), 244 (71), 231 (10), 230 (37), 229 (100), 199 (7), 198 (21), 171 (10), 119 (15), 118 (7), 115 (11), and 89 (10).

(iv) As in (iii), 3-ethyl-2-methyl-1,4-naphthoquinone (0.19 g) [19] in benzene (4 ml) was stirred with sodium methanethiolate (0.69 g) in methanol (8.5 ml) for 4 h. Work-up gave 2-*ethyl*-3-(*methylthiomethyl*)-1,4-*naphthoquinone* (11) (0.19 g) as orange-yellow needles, m.p. 63.5—64° (from light petroleum) (Found: C, 68.3; H, 5.9; S, 13.0%; M^+, 246.071 7. $C_{14}H_{14}O_2S$ requires C, 68.3; H, 5.7; S, 13.0%; M, 246.071 3); δ 8.14—8.02 and 7.75—7.62 (each

2 H, A_2B_2 m, ArH), 3.71 (2 H, s, Q–CH_2–S), 2.70 (2 H, q, *J* 8 Hz, Q–CH_2Me), 2.20 (3 H, s, SMe), and 1.18 (3 H, t, *J* 8 Hz, CH_2Me); *m/e* 246 (M^+, 9%), 200 (21), 199 (17), 198 (100), 197 (13), 128 (8), and 76 (12). The identical quinone was obtained by leaving a mixture of 3-chloromethyl-2-ethyl-1,4-naphthoquinone [18] (78 mg) and sodium methanethiolate (24.5 mg) in benzene–methanol overnight. The product, needles, had m.p. 63.5—64°.

Reaction of 2,3-Dimethyl-1,4-naphthoquinone with Thiolates.—(*a*) Sodium α-toluenethiolate was prepared by adding α-toluenethiol (9.87 g) to sodium methoxide (from 1.744 g sodium, 15 mol) in methanol (60 ml). This solution was added quickly to 2,3-dimethyl-1,4-naphthoquinone (0.94 g) in benzene (20 ml). The mixture was stirred under a drying tube for 8 h, and then poured into ether–aqueous potassium dihydrogen phosphate. Evaporation of the dried ethereal layer left a yellow oil (4 g) which was chromatographed on dry silica eluting with ether–light petroleum (1 to 10%) to give dibenzyl disulphide; unchanged dimethylnaphthoquinone; *3-benzylthiomethyl-2-methyl-1,4-naphthoquinone* (9; R = $PhCH_2$) as yellow needles, m.p. 89.5—91° (from chloroform–light petroleum) (0.5 g) (Found: C, 74.1; H, 5.3; S, 10.2%; M^+, 308.086 9. $C_{19}H_{16}O_2S$ requires C, 74.1; H, 5.2; S, 10.4%; *M*, 308.087 0); $\lambda_{max.}$ 247sh, 251, 264, 269sh, and 331 nm (log ε 4.18, 4.20, 4.12, 4.12, and 3.47); δ 8.15—7.99 and 7.74—7.62 (each 2 H, m, ArH), 7.37—7.18 (5 H, m, Ph), 3.83 (2 H, s, $-CH_2-S-$), 3.67 (2 H, s, $-CH_2-S-$), and 2.16 (3 H, s, Q–Me); *m/e* 308 (M^+, 5%), 217 (56), 187 (11), 186 (100), 128 (11), 123 (22), 92 (5), 91 (79), 77 (10), and 76 (8); and *2,3-bis(benzylmethylthio)-1,4-naphthoquinone* (10; R^1 = $PhCH_2$, R^2 = H) as yellow needles, m.p. 88—89° (from ethanol) (0.28 g) (Found: C, 72.3; H, 5.3; S, 14.9%; M^+, 430.106 0. $C_{26}H_{22}O_2S_2$ requires C, 72.5; H, 5.2; S, 14.9%; *M*, 430.106 0); $\lambda_{max.}$ 247sh, 253, 264, and 336 nm (log ε 4.28, 4.29, 4.19, and 3.58); δ 8.11—7.99 and 7.74—7.62 (each 2 H, m, ArH), 7.36—7.13 (10 H, br s, Ph), 3.76 (4 H, s, $-CH_2-S-$), and 3.58 (4 H, s, $-CH_2-S-$); *m/e* 430 (M^+, 1.5%), 339 (28), 217 (9), 216 (13), 215 (75), 184 (19), 128 (13), 121 (12), 92 (25), 91 (100), 77 (7), and 76 (8). A further fraction (0.183 g) contained (9; R = $PhCH_2$) and (10; R^1 = $PhCH_2$, R^2 = H).

(*b*) Toluene-*p*-thiol (8.45 g) was added to sodium methoxide (from 1.456 g sodium, 20 mol) in methanol (45 ml). This solution was added quickly to 2,3-dimethyl-1,4-naphthoquinone (0.6 g) in benzene (45 ml). After stirring for 4 h, the mixture was poured into benzene–aqueous potassium dihydrogen phosphate. The dried benzene layer was evaporated, and the crude product was separated by preparative t.l.c. on silica in benzene to give di-*p*-tolyl disulphide (174 mg); *2-methyl-3-p-tolylthiomethyl-1,4-naphthoquinone* (9; R = *p*-MeC_6H_4) as orange needles, m.p. 93—94° (from methanol) (207 mg) (Found: C, 73.8; H, 5.4; S, 10.4%; M^+, 308.086 9. $C_{19}H_{16}O_2S$ requires C, 74.0; H, 5.2; S, 10.4%; *M*, 308.087 0); $\lambda_{max.}$ 251, 262, and 333 nm (log ε 4.27, 4.20, and 3.45); δ 8.13—8.0 and 7.75—7.63 (each 2 H, m, ArH), 7.34 and 7.06 (each 2 H, d, *J* 8 Hz, MeC_6H_4), 4.04 (2 H, s, Q–CH_2–S), 2.31 (3 H, s, ArMe), and 1.88 (3 H, s, Q–Me); *m/e* 308 (M^+, 40%), 293 (8), 157 (8), 128 (13), 124 (100), 123 (9), and 91 (19); and *2,3-bis-(p-tolylthiomethyl)-1,4-naphthoquinone* (10; R^1 = *p*-MeC_6H_4, R^2 = H) as orange-red needles, m.p. 112—113° (from methanol) (174 mg) (Found: C, 72.6; H, 5.5; S, 15.2%; M^+, 430.106 0. $C_{26}H_{22}O_2S_2$ requires C, 72.5; H, 5.2; S, 14.9%; *M*, 430.106 0); $\lambda_{max.}$ 253.5, 268sh, and 335 nm (log ε 4.40, 4.29, and 3.62); δ 8.12—8.0 and 7.77—7.63 (each 2 H, m, ArH), 7.22 and 7.04 (each 4 H, d, *J* 8 Hz, MeC_6H_4), 3.52 (4 H, s, Q–CH_2–S), and 2.31 (6 H, s, ArMe); *m/e* 430 (M^+, 4%), 309 (18), 308 (84), 307 (84), 274 (32), 273.091 4 (100) ($C_{19}H_{13}O_2$ requires 273.091 5), 246 (21), 215 (33), 184 (23), 159 (9), 128 (17), 127 (7), 125 (8), 124 (79), 123 (89), 92 (11), 91 (79), 79 (28), 78 (8), 77 (26), and 76 (13). Starting quinone (211 mg) and two unidentified colourless bands were also obtained.

2-Methyl-3-*p*-tolylthiomethyl-1,4-naphthoquinone was also prepared from 3-chloromethyl-2-methyl-1,4-naphthoquinone (58 mg) and toluene-*p*-thiol (40 mg) by heating under reflux in benzene (5 ml) for 3 h, followed by addition of more thiol (20 mg) and further heating for 2 h. The mixture was then evaporated to dryness and the residue crystallised from methanol to give the desired quinone as orange needles, m.p. 93—94° (21 mg), identical with that obtained above.

Similarly, 2,3-bis(chloromethyl)-1,4-naphthoquinone (195 mg) in benzene (15 ml) was stirred overnight with toluene-*p*-thiol (205 mg). More thiol (109 mg) was then added, and the mixture was heated under reflux for 6 h and then worked up. The main orange band on preparative t.l.c. afforded 2,3-bis-(*p*-tolylthiomethyl)-1,4-naphthoquinone which crystallised from methanol as orange-red needles, m.p. 112—113° (200 mg), identical with those described above.

Reactions of 2,3-Bis(methylthiomethyl)-1,4-naphthoquinone.—(i) *With piperidine.* 2,3-Bis(methylthiomethyl)-1,4-naphthoquinone (196 mg) in benzene (4 ml) was stirred with dry piperidine (0.15 ml) for 36 h. The mixture was separated by preparative t.l.c. on silica gel in chloroform. The band of second highest R_F value yielded *2,3-diformyl-1,4-naphthoquinol* (13) which separated from aqueous ethanol as pale yellow crystals, m.p. >165° (decomp.; gas evolved at 183°) (30 mg) (Found: C, 66.5; H, 3.7%; M^+, 216.041 8. $C_{12}H_8O_4$ requires C, 66.65; H, 3.7%; *M*, 216.042 2); $\lambda_{max.}$ 249, 278sh, 401, 419, and 450sh nm (log ε 4.28, 3.95, 3.75, 3.75, and 3.37); $\nu_{max.}$ 1 640, 1 610, 1 580, and 1 500 cm^{-1}; δ 13.53 (2 H, s, OH), 10.55 (2 H, s, CHO), and 8.50—8.38 and 7.83—7.72 (each 2 H, dd, *J* 6 and 3 Hz, ArH); *m/e* 216 (M^+, 100%), 188 (35), 187 (13), 131 (9), 105 (10), and 77 (10).

(ii) *With methylamine.* 2,3-Bis(methylthiomethyl)-1,4-naphthoquinone (195 mg) in benzene (4 ml) was stirred overnight with methylamine (33% w/w in EtOH; 1 ml). *2-Methylbenzo[f]isoindole-4,9-quinone* (17) (73 mg) was deposited after 2 days. It sublimed at >325° to give fine needles, m.p. 340—350° (Found: C, 74.0; H, 4.0; N, 6.7%; M^+, 211.063 6. $C_{13}H_9NO_2$ requires C, 73.9; H, 4.3; N, 6.6%; *M*, 211.063 3); $\lambda_{max.}$ (MeOH) 245, 263, 272sh, 330sh, and 354 nm (log ε 4.40, 4.21, 4.13, 3.68, and 3.69); $\nu_{max.}$ 1 657, 1 595, and 1 585 cm^{-1}; δ 8.30—8.18 and 7.74—7.62 (each 2 H, m, ArH), 7.36 (2 H, s, H-1 and -3), and 3.82 (3 H. s, NMe); *m/e* 211 (M^+, 100%), 183 (10), 182 (5), 170 (17), 154 (5), 142 (8), and 114 (10) {*cf.* isoindole-4,7-quinone,[20] $\nu_{max.}$ 1 647 and 1 582 cm^{-1}; δ ([$^2H_6$]Me_2CO) 7.50}.

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