8. *Side-chain Amination: A New Reaction of Nuclear-alkylated Quinones.*

By D. W. Cameron, P. M. Scott, and Lord Todd.

Fully alkylated quinones readily undergo a novel amination, involving reaction in a tautomeric form at carbon atoms adjacent to the nucleus. Duroquinone, for example, yields 2,3-dimethyl-5,6-bispiperidinomethylquinol (whose structure is confirmed by synthesis) together with the corresponding tris- and tetrakis-derivatives. The process appears to be general and is compared with well-known reactions involving amination of the quinone nucleus.

Primary and secondary amines have long been known to react with quinones, yielding amino-quinones in which the amine residue is attached directly to the quinonoid ring system. Such reactions generally proceed by one or other of two mechanistic pathways. The first [1] consists of nucleophilic 1,4-addition of the amine to give an amino-quinol which on oxidation yields the corresponding amino-quinone; the latter may then undergo a second amination in the same way. Alternatively, amination of a substituted quinone may occur by simple displacement of groups (*e.g.*, halogen, alkoxyl) already present.[2] In the first pathway the equivalent of 1 mole of oxygen is consumed for each entering amino-group,[3] whereas no oxidation is involved in the second.[4] In both, no more than two amino-groups can be introduced into one quinone residue and the position of entry of the second amino-group is controlled by the position of the first; thus 1,4-benzoquinone gives exclusively 2,5-diaminated benzoquinones and 1,4-naphthaquinone gives monoamino-derivatives.

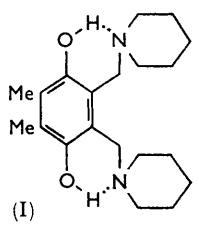
A study of the reaction between alkylated quinones and amines has now disclosed a third general type of amination, hitherto unobserved, which is related to the above-mentioned type involving oxidation but differs from it in a number of important respects. This work was undertaken as a result of studies on the erythroaphins [4] which behave in this respect like simple fully alkylated quinones. When duroquinone is kept in contact with an excess of piperidine the colourless basic 2,3-dimethyl-5,6-bispiperidinomethylquinol (I) is produced in 55% yield. Like duroquinol itself, the compound (I) is insoluble in aqueous alkali; its infrared spectrum contained no carbonyl absorption in the solid state but had a very strong, broad band extending from *ca.* 3300 to 2300 cm.$^{-1}$ centred at

[1] See, *e.g.*, Fieser and Fieser, " Advanced Organic Chemistry," Reinhold, New York, 1961, p. 853.
[2] See, *e.g.*, Buckley, Henbest, and Slade, *J.*, 1957, 4891.
[3] James and Weissberger, *J. Amer. Chem. Soc.*, 1938, **60**, 98.
[4] Cameron, Cromartie, Hamied, Scott, and Todd, *J.*, 1964, 62.

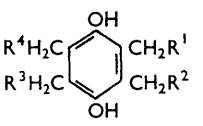
approximately 2800 cm.$^{-1}$ and attributable to a strongly bonded hydroxyl (the spectrum obtained in carbon tetrachloride solution was in this respect similar). It has been shown [5] that OH • • • N bonding as indicated in (I) is considerable, though the compounds examined were simpler and the effect was not so marked as in (I). This spectroscopic evidence precluded the isomeric structure (II; $R^1 = R^4 =$ piperidino, $R^2 = R^3 = H$) which would show non-bonded hydroxyl, and final proof of structure (I) was obtained by its synthesis from *o*-xyloquinol by the action of formaldehyde and piperidine by the standard procedure.[6] A similar aminomethylation of *p*-xyloquinol yielded the isomer (II; $R^1 = R^3 =$ piperidino, $R^2 = R^4 = H$) although previous workers,[7] using admittedly milder conditions, have failed to effect this reaction. Compounds analogous to (I) were also obtained from duroquinone with morpholine and cyclohexylamine; the orientation of these products was assumed on the basis of their infrared characteristics and by analogy with the piperidine product. No similar derivative was obtained on treatment with ammonia, which merely converted the duroquinone into diduroquinone.[8] The action of aromatic amines was not investigated since it has already been reported [9] that duroquinone is converted into duroquinol when heated with aniline to 220° and that no other product can be isolated.

The formation of compound (I) presumably proceeds by addition of piperidine to a tautomeric form (III) of duroquinone, followed by oxidation of the resulting aminated quinol (II; $R^1 =$ piperidino, $R^2 = R^3 = R^4 = H$) and further addition of piperidine to the resulting quinone. This is, in principle, similar to the reaction of sodiomalonic ester with duroquinone to yield the coumarin (IV), which Smith and his colleagues [10] consider to proceed by an initial nucleophilic addition of malonate ion to the tautomer (III). The tautomer (III) is evidently of transient existence; it does not appear to have been detected by any physical means although it is of some interest that photolysis of *o*-nitrotoluene has been reported to yield a compound (V) the spectrum of which could be measured.[11]

Of three possible diaminated duroquinols, only (I) appears to be produced in the reaction with piperidine, so that the first piperidino-group which enters the molecule must exercise significant control over the direction of further amination. This was perhaps to be



(I)



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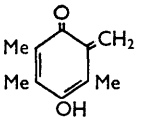

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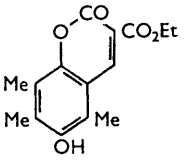

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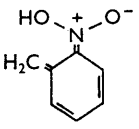

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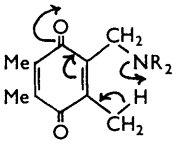
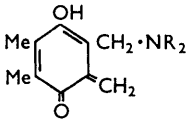


(VI)



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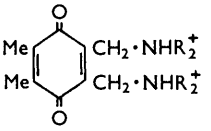


(VIII)

expected since it is clear from considerations to be discussed later that the piperidino-groups in (I) are by no means insulated from the chromophoric system. Of the possible reactive forms of the intermediate aminated quinone (VI), structure (VII) may be favoured by a process such as that depicted in (VI), although we have no evidence for this other

[5] Freedman, *J. Amer. Chem. Soc.*, 1961, **83**, 2900.
[6] Caldwell and Thompson, *J. Amer. Chem. Soc.*, 1939, **61**, 765.
[7] Caldwell and Thompson, *J. Amer. Chem. Soc.*, 1939, **61**, 2354.
[8] Smith, Tess, and Ullyot, *J. Amer. Chem. Soc.*, 1944, **66**, 1320.
[9] Rügheimer and Hankel, *Ber.*, 1896, **29**, 2171.
[10] Smith and Denyes, *J. Amer. Chem. Soc.*, 1936, **58**, 304.
[11] Wettermark, *Nature*, 1962, **194**, 677.

than the exclusive formation of (I) in the overall reaction. Preliminary attempts to isolate the intermediate monopiperidino-quinol appeared unpromising and were not pursued, but both 2-methyl-3,5,6-trispiperidinomethylquinol (II; $R^1 = R^2 = R^3 =$ piperidino, $R^4 = H$) and 2,3,5,6-tetrakispiperidinomethylquinol (II; $R^1 = R^2 = R^3 = R^4 =$ piperidino) have been obtained, the former as a by-product in preparing the bis-piperidino-compound and the latter, in low yield, by prolonged treatment of duroquinone or of the tris-compound with piperidine. In all the amination reaction mixtures, a deep red colour of variable intensity developed but no attempt was made to isolate the substance(s) responsible for it.

Comparison of the aminations described above with the common nuclear amination of quinones by nucleophilic addition reveals two obvious differences. In the first place, whereas nuclear amination never introduces more than two amine residues, the side-chain amination can readily do so. In the former, the electron-donating effect of the nuclear nitrogens presumably prevents further attack. In the latter the effect of the nitrogen on the chromophore is much less, although it clearly exists, since side-chain amination becomes progressively more difficult as the number of amino-groups increases and since there is a strong directive effect, already mentioned, in the amination of quinone (VI) to give the bis-derivative (I). Interaction is also evident in the quinols from a consideration of the ultraviolet spectra; the absorption maxima for duroquinol and the bis-, tris-, and tetrakis-piperidinomethyl derivatives are at 289, 304, 309, and 313 mμ, respectively, indicating a bathochromic shift of *ca.* 5 mμ for each piperidino-group introduced.

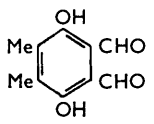
The second difference between nuclear and side-chain amination is that in the latter the products isolated are normally quinols rather than quinones. The quinol form is, of course, stabilised by the strong hydrogen-bonding mentioned in discussing the infrared absorption of compound (I), but the corresponding quinones appear to be unstable and we have been unable to prepare any of them in the benzoquinone series in a free state. Thus, oxidation of the bispiperidinomethyl quinol (I) with oxides of nitrogen [12] gave the dinitrate of the dication (as VIII) in high yield as a stable crystalline water-soluble compound, the structure of which was confirmed spectroscopically; attempts to liberate the free quinone from it yielded no tractable product other than a small amount of the quinol (I). Aminated quinones such as (VI) must, however, have at any rate a transient existence as intermediates in the amination reactions. The reaction of duroquinone with piperidine is accompanied by an uptake of oxygen corresponding to 1·25 mol. in 6 hours and 1·53 mol. after 23 hours; thereafter, only a very slow uptake occurs. This uptake is intermediate between that required for the production of the bis- (1 mol.) and the tris-piperidinomethyl derivative (2 mol.) on the basis of the mechanism proposed and agrees with the observation that a mixture of these two substances is the major product of the reaction.

Oxidation of the quinol (I) with a limited amount of chromic acid yielded, not the corresponding quinone, but a yellow, crystalline, acidic compound $C_{10}H_{10}O_4$, evidently the dialdehyde (IX) or, less probably, its tautomer (X). Like salicylaldehyde, this product, can be extracted from ether with sodium hydrogen carbonate and its infrared spectrum shows bands corresponding both to bonded hydroxyl (3000 cm.$^{-1}$) and bonded carbonyl (1636 cm.$^{-1}$); the simplicity of its nuclear magnetic resonance (n.m.r.) spectrum excludes possible unsymmetrical cyclic structures.

In order to test the generality of the amination described above we have examined a number of other substituted quinones and have obtained broadly similar results. Thus, 2,3-dimethyl-1,4-naphthaquinone, on treatment with piperidine, gave 2,3-bispiperidinomethyl-1,4-naphthaquinol, while ψ-cumoquinone (trimethyl-1,4-benzoquinone) and its 2-bromo-derivative both yielded 2-piperidino-3,5,6-trispiperidinomethylquinol (XI; $R^1 = R^2 = R^3 = R^4 =$ piperidino). In the last two instances amination must also occur by the two commoner routes, *viz.*, nuclear amination by addition and by displacement of a

[12] Cf. Brook, *J.*, 1952, 5040.

halogen atom. It has been reported [13] that treatment with an appropriate quantity of methylamine converts 2-methyl-1,4-naphthaquinone into its 3-methylamino-derivative; with aromatic bases a similar reaction ensues.[14] We found that treatment with an excess of piperidine yielded 2-piperidino-3-piperidinomethyl-1,4-naphthaquinone (as XII) as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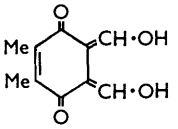
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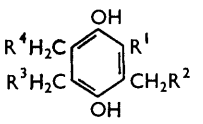
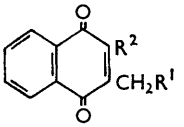

(XI)


(XII)

unstable red crystals which decomposed slowly in solution on exposure to light. The production of a quinone rather than a quinol in this instance is noteworthy; it probably reflects the lower oxidation–reduction potential of the nuclear-piperidinonaphthaquinones than of benzoquinones. 2-Hydroxy-1,4-naphthaquinone (lawsone) yields, with formaldehyde and amines, the corresponding 3-aminomethyl derivatives which like (XII) are rather unstable,[15] but attempts to prepare them by treatment of 2-hydroxy-3-methyl-1,4-naphthaquinone (phthiocol) failed, presumably because of the resistance of the phthiocol anion to nucleophilic attack.

In addition to the reactions mentioned above, some other substituted quinones have been observed to yield basic materials on similar treatment, but because of their instability the products were not obtained pure. 1,2,3,4-Tetrahydroanthraquinone gave, with piperidine, a basic solid but attempts to purify it by recrystallisation failed because of elimination reactions leading to anthraquinone, the only product isolated; this " dehydrogenation " of tetrahydroanthraquinone with cyclohexylamine or aniline has been reported by other workers.[16] Similarly, certain heavily substituted naphthaquinones obtained by degradation of the protoaphins [17] were converted almost quantitatively by piperidine into basic products which were too unstable to be purified; their formation was accompanied by an uptake of 1—1·25 mol. of oxygen, corresponding to the introduction of one piperidino-group per molecule of quinone.

The structural assignments made earlier were fully consistent with proton magnetic resonance spectra (40 Mc./sec.). These were relatively simple, owing to the absence of spin–spin interaction (except for those within the piperidino-groups). For the piperidino-substituted compounds so far described, singlets were consistently observed within the ranges 0·10—0·43, 6·22—6·71, and 7·85—7·99 τ, corresponding to protons of OH, Ar·CH_2·N, and Ar·CH_3 groups, respectively. In the unsymmetrical compounds (II; $R^1 = R^2 = R^3$ = piperidino, R^4 = H) and (XI; $R^1 = R^2 = R^3 = R^4$ = piperidino) the second of these spectral regions contained three singlets instead of one, reflecting the small environmental differences between the three nuclear methylene groups. The corresponding peak in the spectrum of cation (VIII) was shifted to 5·60 τ, providing the only exception to these general assignments. The protons of piperidino-groups themselves were generally observed as composite bands of relative intensities 2 : 3 within the ranges 7·52—7·61 and 8·45—8·55 τ, respectively. However, shifts to lower field appeared in the spectra both of cation (VIII) (6·61, 8·21 τ) and of compounds such as (XII; $R^1 = R^2$ = piperidino) in which piperidine was directly attached to a quinone nucleus (6·54, 8·32 τ). The intensities of all peaks in the various spectra were consistent with the structural assignments.

Experimental

Unless otherwise stated, infrared spectra were measured for Nujol and/or hexachlorobutadiene mulls. Nuclear magnetic resonance spectra were obtained at 40 Mc./sec. Points

[13] Asano and Hase, *J. Pharm. Soc. Japan*, 1941, **61**, 55.
[14] Golovanova, *Zhur. obschei Khim.*, 1948, **18**, 835.
[15] Vaughan, Habil, McElhinney, Takahashi, and Waters, *J. Org. Chem.*, 1961, **26**, 2392.
[16] Skita and Müller, *Ber.*, 1931, **64**, 1152.
[17] Cameron, Cromartie, Kingston, and Todd, *J.*, 1964, 51.

of reference are quoted as chemical shifts on the τ scale and have been measured against tetramethylsilane as internal reference. Oxygen uptakes were measured in a microhydrogenator filled with carbon dioxide-free air.

2,3-*Dimethyl*-5,6-*bispiperidinomethylquinol*.—(*a*) *From duroquinone*. A solution of duroquinone (1·0 g.) in redistilled piperidine was left at room temperature for 35 hr., then evaporated, and the residue was recrystallised from ethanol, to yield the *bispiperidino methyl-quinol* (I) as long, colourless needles, m. p. 161—162° (1·1 g.), identical with a specimen synthesised as described below (mixed m. p.; spectra). It was soluble in dilute hydrochloric acid from which it was reprecipitated with sodium hydroxide. The amination consumed 1·25 mol. of oxygen in 6 hr. and 1·53 in 23 hr., and then a little more very slowly [Found: C, 72·3; H, 9·7; N, 8·1; *C*-Me, 8·4%; *M*, (cryoscopic), 323. $C_{20}H_{32}N_2O_2$ requires C, 72·3; H, 9·7; N, 8·4; *C*-Me, 9·0%; *M*, 332]; $\lambda_{max.}$ (*a*) in ether, 304 mμ (log ε 3·70), (*b*) in 3N-HCl, 297 mμ (log ε 3·65); $\nu_{max.}$ 2800br cm.$^{-1}$; n.m.r. (*a*) in CCl_4, 0·18 (OH), 6·51 (Ar·CH_2·N), 7·59 (piperidino-CH_2·N), 7·99 (Ar·Me), 8·48 (piperidino-CH_2), (*b*) in $CHCl_3$, 6·39, 7·52, 7·85, 8·48.

2,5-Bisdimethylaminomethyl quinol [6] had n.m.r. peaks (in $CHCl_3$) at 0·27 (OH), 3·53 (Ar·H), 6·45 (Ar·CH_2·N), 7·71 (N-Me).

(*b*) *From o-xyloquinol*. *o*-Xyloquinol [18] (1·1 g.), ethanol (20 ml.), piperidine (2 ml.), and 40% aqueous formaldehyde (1·5 ml.) were warmed at 80° under nitrogen for 3 hr., then cooled and concentrated to small bulk. The solid (1·28 g.) which separated was recrystallised from ethyl acetate, giving prisms m. p. 159°, soluble in dilute acid. This appeared to consist of mixed crystals of the desired product with the corresponding monoamino-quinol (Found: C, 72·1; H, 9·6; N, 7·5%). This product (289 mg.) was warmed at 80° a further 2·5 hr. under nitrogen with piperidine (0·2 ml.) and aqueous formaldehyde (0·15 ml.) in ethanol (10 ml.). Concentration and cooling gave 2,3-dimethyl-5,6-bispiperidinomethyl quinol (62 mg.), m. p. 159—160° identical with compound (I) above.

2,5-*Dimethyl*-3,6-*bispiperidinomethylquinol*.—2,5-Dimethylquinol (70 mg.), piperidine (0·16 ml.), and 40% aqueous formaldehyde (0·12 ml.) in ethanol (5 ml.) were refluxed under nitrogen for 40 min. Similar further quantities of reagents and solvent were then added and the mixture was refluxed a further hour. Concentration and cooling afforded the *product* (91 mg.), colourless plates, m. p. 198—200° (decomp.) (from ethyl acetate), soluble in dilute acid (Found: C, 72·5; H, 9·4; N, 8·2. $C_{20}H_{32}N_2O_2$ requires C, 72·3; H, 9·7; N, 8·4%); $\lambda_{max.}$ (in dioxan), 263 and 307 mμ (log ε 3·35 and 3·65); $\nu_{max.}$ 2800br cm.$^{-1}$; n.m.r. (in CCl_4), 0·1 (OH), 6·45 (Ar·CH_2·N), 7·53 (piperidino·CH_2·N), 7·99 (Ar·Me), 8·44 (piperidino·CH_2).

Action of Other Amines on Duroquinone.—(*a*) Treatment of duroquinone (220 mg.) with morpholine (4 ml.), as for piperidine, yielded 2,3-*dimethyl*-5,6-*bismorpholinomethylquinol* (135 mg.), m. p. 208—209° (decomp.) (Found: C, 64·7; H, 8·6; N, 8·2. $C_{18}H_{28}N_2O_4$ requires C, 64·3; H, 8·4; N, 8·3%); $\lambda_{max.}$ (in dioxan), 303 mμ (log ε 3·71); $\nu_{max.}$ 2800 cm.$^{-1}$.

(*b*) Duroquinone (282 mg.), treated with cyclohexylamine (5 ml.), similarly yielded 2,3-*biscyclohexylaminomethyl*-5,6-*dimethylquinol* (191 mg.) which crystallised as colourless needles from the reaction mixture and had m. p. 191° (decomp.) (from benzene–cyclohexane) [Found: C, 73·3; H, 10·1; N, 7·9%; *M* (cryoscopic), 373. $C_{22}H_{36}N_2O_2$ requires C, 73·3; H, 10·1; N, 7·8%; *M*, 360·5]; $\lambda_{max.}$ (in dioxan), 258 and 303 mμ (log ε 3·53 and 3·61); $\nu_{max.}$ 3280 (NH) and 2700br cm.$^{-1}$.

(*c*) Duroquinone (104 mg.) in dioxan (2 ml.) saturated with ammonia was left overnight at room temperature, then evaporated; the residue, when recrystallised, yielded starting material (60 mg.), m. p. and mixed m. p. 110—111°.

(*d*) Duroquinone (50 mg.) in dioxan (5 ml.) was heated with concentrated aqueous ammonia (5 ml.) at 80° for 3 hr., two further quantities of ammonia solution (2 ml.) being added hourly. Evaporation and recrystallisation yielded diduroquinine [8] (16 mg.), m. p. and mixed m. p. 203—206° (from ethanol).

Methyltrispiperidinomethylquinol.—The mother-liquors from the first recrystallisation of the bispiperidinomethyl-quinol (I), prepared by method (*a*) above, were diluted with water to give a colourless solid (0·4 g.), which was recrystallised, first from ethanol and then from methanol, to yield *methyltrispiperidinomethylquinol*, soft, colourless needles, m. p. 163·5—164·5° (135 mg.) (Found: C, 72·3; H, 10·1; N, 10·3. $C_{25}H_{41}N_3O_2$ requires C, 72·3; H, 9·9; N, 10·1%); $\lambda_{max.}$ (in ether) 309 mμ (log ε 3·76); $\nu_{max.}$ 2800br cm.$^{-1}$; n.m.r. (in CCl_4) 6·35, 6·47;

[18] Baker and Brown, *J.*, 1948, 2303.

6·68 (Ar·CH_2·N), 7·56 (piperidino·CH_2·N), 7·99 (Ar·Me), and 8·50 (piperidino·CH_2). This was soluble in dilute acid and its m. p. was depressed in admixture with the bispiperidinomethylquinol (I).

Tetrakispiperidinomethylquinol.—(*a*) *From duroquinone.* A solution of duroquinone (1·0 g.) in piperidine (10 ml.) was left for 2 weeks at room temperature. *Tetrakispiperidinomethylquinol* (75 mg.) was then filtered off and recrystallised from ethanol–chloroform as colourless needles, soluble in dilute acid but insoluble in alkali, not melting but decomposing on rapid heating at *ca.* 240° [Found: C, 71·9; H, 9·7; N, 11·4%; *M* (cryoscopic), 496. $C_{30}H_{50}N_4O_2$ requires C, 72·2; H, 10·1; N, 11·2%; *M*, 499]; $\lambda_{max.}$ (in ether), 313 mμ (log ε 3·84); $\nu_{max.}$ 2940, 2900br, 1518, 1488, 1387, 1370, 1340, 1327, 1301, 1282, 1269, 1258, 1235, 1215, 1190, 1150, 1115, 1065, 1040, 1027, 995, 986, 962, 860, 835, 788, 781, and 755 cm.$^{-1}$; n.m.r. (in $CHCl_3$) 6·38 (Ar·CH_2·N), 7·45 (piperidino·CH_2·N), and 8·51 (piperidino·CH_2).

(*b*) *From methyltrispiperidinomethylquinol.* The trispiperidinomethyl-quinol (74 mg.), when kept in piperidine (2 ml.) for 36 hr., gave the tetra-substituted product (18 mg.) after recrystallisation, whose infrared spectrum was identical with that of the material prepared by method (*a*).

2,3-*Dimethyl*-5,6-*bispiperidinomethyl*-1,4-*benzoquinone Dinitrate.*—The bispiperidinomethylquinol (I) (79 mg.) was added to a solution of oxides of nitrogen [12] (0·25 ml.) in dry carbon tetrachloride (8 ml.), and the mixture was left for 8 min. Decantation, trituration of the residue with ethanol, and recrystallisation from methanol yielded the *dinitrate* (as VIII) (73 mg.), yellow plates, m. p. 189—190° (decomp.) (Found: C, 52·9; H, 6·7; N, 12·4. $C_{20}H_{32}N_4O_8$ requires C, 52·6; H, 7·1; N, 12·3%); $\lambda_{max.}$ (in H_2O), 260, 305, and 358 mμ (log ε 4·16, 2·67, and 2·73); $\nu_{max.}$ 2795, 2720, 2600 (NH^+), 1660 (C=O), and 1350 (NO_3^-) cm.$^{-1}$; n.m.r. (in D_2O; reference H_2O τ 5·28), 5·60 (quinone CH_2·N^+), 6·61 (piperidino·CH_2·N^+), 7·90 (quinone-Me), and 8·21 (piperidino·CH_2).

The dinitrate was dissolved in water, neutralised with aqueous sodium hydrogen carbonate, and extracted with ether. The extract was washed and dried. Evaporation gave a yellow gum, which yielded the bispiperidinomethyl-quinol (I) (10 mg.) on recrystallisation from ethanol–water. No other crystalline product could be isolated.

Oxidation of Quinol (I).—A solution of the bispiperidinomethyl-quinol (I) (3·0 g.) in warm acetic acid (12 ml.) was treated with a warm solution of chromium trioxide (1·5 g.) in 50% aqueous acetic acid (12 ml.), and then the mixture was poured into water (60 ml.), cooled, and filtered, to yield 3,6-*dihydroxy*-4,5-*dimethylphthalaldehyde* (IX), which crystallised from ethanol–water and sublimed at 100°/10^{-4} mm. (254 mg.). Recrystallisation from ethanol gave yellow plates, m. p. 166—167°, soluble in alkali [Found: C, 62·0; H, 5·1; N, 0·0%; *M* (cryoscopic), 197. $C_{10}H_{10}O_4$ requires C, 61·9; H, 5·2%; *M*, 194]; $\lambda_{max.}$ (in EtOH), 244, 276, and 400 mμ (log ε 4·23, 3·92, and 3·84); $\nu_{max.}$ 3000 (OH), 1636 (C=O), 1591, and 1577 (C=C) cm.$^{-1}$; n.m.r. (in CCl_4), −2·44 (OH), −0·68 (CH), 7·72 (Ar·Me). Treated in ethanolic solution with Brady's reagent it gave a red precipitate.

Salicylaldehyde, has n.m.r. peaks (in CCl_4) at −1·10 (OH) and 0·20 (CH).

Piperidinotrispiperidinomethylquinol.—(*a*) ψ-Cumoquinone (99 mg.) dissolved readily in piperidine (2 ml.), forming a deep purple solution. After one day, solvent was evaporated and the resulting gum crystallised from ethanol, yielding colourless needles of the *product* (45 mg.), m. p. 197—198° (decomp.), giving a deep purple colour with ferric chloride [Found: C, 72·0; H, 10·1; N, 11·6%; *M* (cryoscopic), 490. $C_{29}H_{48}N_4O_2$ requires C, 71·9; H, 10·0; N, 11·6%; *M*, 485]; $\lambda_{max.}$ (in dioxan), 310 mμ (log ε 3·78); $\nu_{max.}$ at 2800br cm.$^{-1}$, n.m.r. (in CCl_4), 0·43 (OH), 6·22, 6·34, 6·71 (Ar·CH_2·N), 7·55 (piperidino·CH_2·N), 8·45 (piperidino·CH_2).

(*b*) 2-Bromo-3,5,6-trimethyl-1,4-benzoquinone [19] (101 mg.) and piperidine (2 ml.) were left overnight, the deep purple solution filtered from piperidinium bromide (m. p. 238—240°), and the filtrate evaporated to yield colourless needles (29 mg.) m. p. and mixed m. p. 196—197° (from ethanol). Their ultraviolet and infrared spectra were identical with those of the product of method (*a*).

2,3-*Bispiperidinomethyl*-1,4-*naphthaquinol.*—A solution of 2,3-dimethyl-1,4-naphthaquinone (1·1 g.) in piperidine (15 ml.), left at room temperature in the dark for 5 hr., deposited 2,3-*bispiperidinomethyl*-1,4-*naphthaquinol* (1·3 g.) which formed colourless needles (from cyclohexane), m. p. (rapid heating) *ca.* 160° (decomp.). The compound was somewhat unstable and on gentle

[19] Smith and Miller, *J. Amer. Chem. Soc.*, 1942, **64**, 440; Smith and Wiley, *ibid.*, 1946, **68**, 887.

heating or on storage at room temperature slowly became pink (Found: C, 75·0, 74·8; H, 8·3, 9·0; N, 7·6. $C_{22}H_{30}N_2O_2$ requires C, 74·5; H, 8·5; N, 7·9%); $\lambda_{max.}$, (*a*) in ether, 252, 333, and 346 mμ (log ε 4·47, 3·76, and 3·79), (*b*) in 3N-HCl, 218, 245, and 338 mμ (log ε 4·55, 4·42, and 3·62); $\nu_{max.}$ 2950, 2860, 2800br, 1594, 1520, 1486, 1449, 1377, 1336, 1308, 1270, 1205, 1185, 1154, 1120, 1105, 1067, 1038, 1024, 1010, 982, 967, 955, 906, 880, 855, 830, 784, 775, 769, and 652 cm.$^{-1}$; n.m.r. (in CCl_4), 2·60—2·86 (Ar·H), 6·36 (Ar·CH_2·N), 7·53 (piperidino·CH_2·N), and 8·45 (piperidino·CH_2). When the above amination was carried out overnight instead of for 5 hr., no crystalline product was obtained.

2-*Piperidino*-3-*piperidinomethyl*-1,4-*naphthaquinone*.—2-Methyl-1,4-naphthaquinone (350 mg.) was dissolved in piperidine (3 ml.), giving a red solution which was left for 13 hr. in the dark. Piperidine was then removed under reduced pressure and the residue was, with some difficulty, recrystallised from methanol, giving 2-*piperidino*-3-*piperidinomethyl*-1,4-*naphthaquinone* (290 mg.) which was unstable to light in dilute solution. The reaction proceeded with uptake of 1·9 mol. of O_2 and was virtually complete after 5 hr. The pure compound, m. p. 72°, was obtained as red needles by recrystallisation from methanol in the dark (seeding was essential to induce crystallisation) (Found: C, 74·8; H, 8·1; N, 8·2. $C_{21}H_{26}N_2O_2$ requires C, 74·5; H, 7·7; N, 8·3%); $\lambda_{max.}$ (in EtOH), 247, 283, and 501 mμ (log ε 4·16, 4·08, and 3·51); $\nu_{max.}$ 1673, 1633 (C=O), 1600, and 1555 (C=C) cm.$^{-1}$; n.m.r. (in CCl_4) 1·76—2·56 (Ar·H), 6·54 (piperidino·CH_2·N), 6·59 (quinone-CH_2·N), 7·61 (piperidino·CH_2·N), 8·32, and 8·55 (piperidino·CH_2).

2-*Piperidino*-1,4-*naphthaquinone*.—Prepared as described by Crosby and Lutz,[20] this had m. p. 91—94° (lit., 94—96°) and $\lambda_{max.}$ (in EtOH), 240, 277, and 469 mμ (log ε 4·15, 4·28, and 3·63); $\nu_{max.}$ 1676 (C=O), 1625, and 1592 (C=C) cm.$^{-1}$; n.m.r. (in CCl_4), 1·95—2·72 (Ar·H), 4·11 (quinone-H), 6·55 (piperidino·CH_2·N), and 8·29 (piperidino·CH_2).

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[20] Crosby and Lutz, *J. Amer. Chem. Soc.*, 1956, **78**, 1233.