Dimerisation of 2-Alkyl-1,4-naphthoquinones in the Presence of t-Butylamine

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Treatment of certain 2-alkyl-1,4-naphthoquinones with ethanolic t-butylamine resulted in dimerisation to give 12H-dibenzo[b,h]fluorene derivatives (II). Mixtures of these naphthoquinones gave low yields of mixed dimers of the same type.

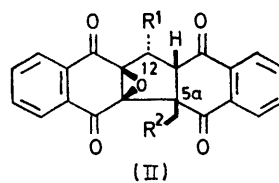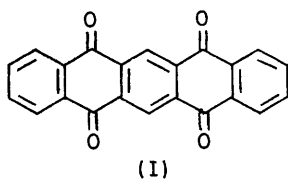DIMERISATION of naphthoquinones has received consider-able attention in recent years and a variety of products have been isolated, their nature depending on the reagents and the conditions.[1] Dimerisation of 2-alkyl-1,4-naph-thoquinones in the presence of N-methylcyclohexylamine

[1] (a) F. M. Dean and L. E. Houghton, J. Chem. Soc. (C), 1971, 1920 and references therein; (b) K. Chandrasenan and R. H. Thomson, Tetrahedron, 1971, **25**, 2529; (c) W. Storck and G. Manecke, Chem. Ber., 1971, **104**, 1207; (d) I. Baxter, D. W. Cameron, and R. B. Titman, J. Chem. Soc. (C), 1971, 1253; (e) I. Baxter, D. W. Cameron, J. K. M. Sanders, and R. B. Titman, J.C.S. Perkin I, 1972, 2046; (f) K. Hallmayer, Arch. Pharm., 1972, **305**, 776; (g) H. Brockmann and H. Laatsch, Tetrahedron Letters, 1973, 3695.

has been reported and the structures of the products have been shown to depend upon the nature of the alkyl group. Thus 2-methyl-1,4-naphthoquinone yields pentacene-5,14:7,12-diquinone (I),[1d] and 2-ethyl- and 2-benzyl-1,4-naphthoquinones give 12H-dibenzo[b,h]fluorene derivatives of type (II).[1e] 2-Isopropyl-1,4-naphthoquinone does not yield a dimer under similar conditions.[1e] We describe here an investigation into the scope of this reaction. In particular, we have studied the possibility of achieving crossed dimerisation of 2-alkyl-1,4-naphthoquinones. We have also investigated five durther examples of self-dimerisation involving 2-alkyl-1,4-naphthoquinones.

In the earlier work,[1e] N-methylcyclohexylamine was used as the dimerisation reagent but we have now found

quinones (IIIa and c) with ethanolic t-butylamine gave the crossed dimer (IIe) in addition to the self-dimers (I) and (IId). Likewise the quinones (IIIb and c) gave the mixed dimer (IIf).

The stereochemistry of the dimer (IIa) was assigned previously by the use of Eu(dpm)$_3$-induced shifts;[1e] similar shifts are observed with the dimers (IIc—f), indicating that they all possess the same stereochemistry. In addition, these compounds, like compound (IIa), also show the small coupling (J 1 Hz) between the 12- and 12a-protons.

In all three examples discussed above only a single mixed dimer could be detected in each reaction. Certain trends are apparent: namely in mixed dimerisations (i) when 2-methyl-1,4-naphthoquinone is used then the

(I)

(II)

a; R^1= R^2 Me   f; R^1= Ph, R^2= Me
b; R^1= H, R^2= Me   g; R^1= R^2= CH$_2$Ph
c; R^1= Me, R^2= H   h; R^1= R^2 p - MeO·C$_6$H$_4$
d; R^1= R^2 Ph   i; R^1= R^2 p - NO$_2$·C$_6$H$_4$
e; R^1= Ph, R^2 H

(III)
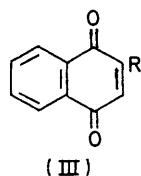
a; R = Me   e; R = p - MeO·C$_6$H$_4$·CH$_2$
b; R = Et   f; R = p - NO$_2$·C$_6$H$_4$·CH$_2$
c; R = CH$_2$Ph   g; R = CHPh$_2$
d; R = CH$_2$CH$_2$Ph

(IV)
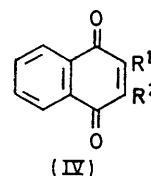
a; R^1= CH$_2$ == CMe , R^2= NHBu^t
b; R^1= Br, R^2 = NHBu^t
c; R^1= Et , R^2 = OEt
d; R^1= Et , R^2 = OH

that the more volatile t-butylamine is equally satisfactory in effecting dimerisation of the quinones (IIIb and c) and have used this amine almost exclusively in the work described below.

When an equimolar mixture of quinones (IIIa and b) was kept in ethanolic solution in the presence of either N-methylcyclohexylamine or t-butylamine, three products were obtained, namely the known dimers (I) and (IIa) and a new compound, identified on the basis of its spectral properties as an epoxide of type (II), derived from one molecule of each of the quinones (IIIa and b). In principle, these two quinones may react to give either of the two crossed dimers (IIb and c); these two alternatives were readily distinguished by n.m.r. spectroscopy. Thus the new epoxide showed two methyl signals at τ 8·35 and 8·12, the former being a doublet and the latter a singlet, supporting structure (IIc). Reaction of the

methyl group is always found at the angular 5a-position and (ii) when 2-benzyl-1,4-naphthoquinone is used the phenyl group is always at C-12.

The phenethyl-, p-methoxybenzyl-, and p-nitrobenzyl-1,4-naphthoquinones (IIId—f) all readily underwent self-dimerisation in good yield to give compounds of type (II), presumably (IIg—i). The n.m.r. spectra of these compounds were in agreement with these overall structures but in the case of the latter two products it was impossible to confirm their stereochemistry by Eu(dpm)$_3$-induced shifts because of their low solubility in suitable solvents. 2-Diphenylmethyl-1,4-naphthoquinone (IIIg) was recovered unchanged from ethanolic t-butylamine.

2-Isopropyl-1,4-naphthoquinone does not yield a dimer on treatment with either ethanolic N-methylcyclohexylamine[1e] or t-butylamine. Using neat t-butylamine we again failed to isolate a dimer, although

many products were detected by t.l.c. The only product isolated was the aminated quinone (IVa).

2-Bromo-3-methyl- and 2-methyl-1,4-naphthoquinones react similarly in the presence of amine, insofar as they both yield the pentacene (I).[1d] This similarity in behaviour does not extend to 2-bromo-3-ethyl- and 2-ethyl-1,4-naphthoquinones. Thus although 2-ethyl-1,4-naphthoquinone yields the dimer (IIa) on treatment with t-butylamine, we were unable to detect this dimer in the analogous reaction with 2-bromo-3-ethyl-1,4-naphthoquinone. The products isolated from this reaction were the amino-quinone (IVb), which could arise via the well documented amine-induced dealkylation of quinones,[2] and the ethoxy-quinone (IVc). The quinone (IVc) was rather unstable and on attempted crystallisation or sublimation gave the related known hydroxy-quinone (IVd),[3] from which the quinone (IVc) was readily recovered by treatment with diazoethane.

We are unable to make any definitive comments on the mechanism of formation of compounds of type (II), which may, in principle, involve radicals and/or anions. However the following points are relevant. U.v.,[4] e.s.r.,[5] and n.m.r.[6] spectroscopic evidence for the presence of radicals in solutions containing quinones and amines has been presented. In addition, when the dimerisation of the quinone (IIIe) was performed in deuteriomethanol and the reaction mixture quenched, after a short time, with acetic acid, we were unable to detect any deuterium incorporation into the starting material by n.m.r. spectroscopy. Failure to observe isotopic exchange suggests that if carbanions are formed under these conditions their formation is slow with respect to subsequent reaction steps. In this connection, although Clark, Hutchinson, and Wilson[5] were able to demonstrate base-catalysed isotopic exchange in methyl quinones using triethylamine, they failed to recover isotopically labelled quinone when the secondary amines piperidine or pyrrolidine were used because of the intervention of a fast, complex reaction.

The alkyl quinones used in this investigation were prepared either by known literature procedures or by the radical alkylation method recently introduced.[7]

EXPERIMENTAL

Unless otherwise stated i.r. spectra were measured for Nujol mulls and u.v. and visible spectra for solutions in ethanol. N.m.r. spectra were measured at 100 MHz for solutions in deuteriochloroform with tetramethylsilane as internal reference. All integrations gave results consistent with the structural assignments.

Preparation of 2-Alkyl-1,4-naphthoquinones.—The following quinones were prepared from 1,4-naphthoquinone and the appropriate carboxylic acid by the method of Jacobsen and Torsell;[7] yields were in the range 25—55%: (a) 2-

benzyl-1,4-naphthoquinone, m.p. 94° (lit.,[1e] 94—95°); (b) 2-*phenethyl*-1,4-*naphthoquinone* (IIId), m.p. 44—45° (from methanol) (Found: C, 82·1; H, 5·5. $C_{18}H_{14}O_2$ requires C, 82·4; H, 54·%), τ (CDCl₃) 7·1br (s, CH₂·CH₂), 3·28 (s, CH=C), 2·79 (s, ArH), and 2·4—1·8 (m, ArH); (c) 2-(p-*methoxybenzyl*)-1,4-*naphthoquinone* (IIIe), m.p. 80—81° (from methanol) (Found: C, 78·0; H, 4·9. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·1%), $\lambda_{max.}$ 246, 251, and 335 nm (log ε 4·27, 4·27, and 3·42), $\lambda_{infl.}$ 262 nm (log ε 4·12), τ 6·24 (s, OMe), 6·18 (d, J 1 Hz, CH₂Ar), 3·43 (t, J 1 Hz, CH=C), 3·16 and 2·86 (2d, J 8 Hz, ArH), and 2·4—1·8 (m, ArH); (d) 2-(p-*nitro-benzyl*)-1,4-*naphthoquinone* (IIIf), m.p. 186—188° (from benzene) (Found: C, 69·8; H, 4·0. $C_{17}H_{11}NO_4$ requires C, 69·6; H, 3·8%), $\lambda_{max.}$ 253, 264, and 332 nm (log ε 4·38, 4·34, and 3·54), $\lambda_{infl.}$ 247 nm (log ε 4·33); (e) 2-(diphenyl-methyl)-1,4-naphthoquinone (IIIg), m.p. 187° (lit.,[8] 189°) (from methanol).

Dimerisation of 2-Alkyl-1,4-naphthoquinones.—(a) *Quinones* (IIIa *and* b). A mixture of quinones (IIIa) (1·72 g) and (IIIb)[9] (1·84 g), N-methylcyclohexylamine (3 ml), and 95% ethanol (400 ml) was kept overnight in an open vessel. The mixture was filtered to give pentacene-5,14:7,12-diquinone (I) (0·14 g), m.p. >350°, identical spectroscopically with an authentic sample.[1d] After a further 24 h, the original filtrate had deposited a solid (0·80 g), which when recrystallised five times from benzene gave c-5b,11a-*epoxy*-5a,5b,-11a,c-12a-*tetrahydro*-r-5a,t-12-*dimethyl*-12H-*dibenzo*[b,h]-*fluorene*-5,6,11,13-*tetraone* (IIc) (0·23 g), m.p. 279—281° (Found: C, 74·6; H, 4·4%; M⁺, 372. $C_{23}H_{16}O_5$ requires C, 74·2; H, 4·3%; M, 372), $\lambda_{max.}$ (CHCl₃) 306 nm (log ε 3·66), τ 8·35 (d, J 7 Hz, CH·CH₃), 8·12 (s, Me), 7·26 (d, J 1 Hz, CH·CH·CO), 6·05 (m, J 7 and 1 Hz, CH₃·CH·CH), and 2·5—1·8 (m, ArH). Preparative layer chromatography on silica of the mother liquors from the recrystallisations and elution with benzene–chloroform (1 : 1) gave the epoxide (IIa) (0·54 g), m.p. and mixed m.p. 198—199° (from benzene).[1e]

A similar reaction with t-butylamine in place of N-methylcyclohexylamine gave the same products in similar yields.

(b) *Quinones* (IIIa *and* c). A mixture of the quinones (IIIa) (0·65 g) and (IIIc) (0·94 g), t-butylamine (1 ml), and 95% ethanol (150 ml) was kept for 3 days in an open vessel. The precipitate was collected, boiled with benzene, and filtered off. The insoluble material (0·02 g) was identified as the quinone (I). The filtrate was evaporated and purified by preparative layer chromatography on silica. Elution with benzene gave the known dimer[1e] (IId) (0·2 g), m.p. 250—260°, and c-5b,11a-*epoxy*-5a,5b,11a,c-12a-*tetrahydro*-r-5a-*methyl*-t-12-*phenyl*-12H-*dibenzo*[b,h]*fluorene*-5,6,11,13-*tetraone* (IIe) (30 mg), m.p. 244—246° (from benzene–light petroleum) (Found: C, 77·7; H, 4·5%; M⁺, 434. $C_{28}H_{18}O_5$ requires C, 77·4; H, 4·2%; M, 434), $\nu_{max.}$ 1710, 1690, and 1670 cm⁻¹, τ 8·35 (s, Me), 6·99 (d, J 1 Hz, CH·CH·CO), 4·82 (d, J 1 Hz, PhCH·CH), 2·76 (s, Ph), and 2·4—1·8 (m, ArH).

(c) *Quinones* (IIIb *and* c). A mixture of the quinones (IIIb) (0·71 g) and (IIIc) (0·94 g), t-butylamine (1 ml), and ethanol (150 ml) was kept for 3 days. The resulting precipitate gave, by preparative layer chromatography as above, the

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[3] S. C. Hooker, *J. Amer. Chem. Soc.*, 1936, **58**, 1174.

[4] T. Yamaoka and S. Nagakura, *Bull. Chem. Soc. Japan*, 1971, **44**, 1780, 2971.

[5] V. M. Clark, D. W. Hutchinson, and R. G. Wilson, *Chem. Comm.*, 1968, 52.

[6] I. Baxter and J. K. M. Sanders, *J.C.S. Chem. Comm.*, 1974, 255.

[7] N. Jacobsen and K. Torssell, *Annalen*, 1972, **763**, 135; *Acta. Chem. Scand.*, 1973, **27**, 3211.

[8] L. F. Fieser and M. A. Peters, *J. Amer. Chem. Soc.*, 1931, **53**, 4080.

[9] L. F. Fieser, W. P. Campbell, E. M. Fry, and M. D. Gates, *J. Amer. Chem. Soc.*, 1939, **61**, 3216.

dimer (IId) [1e] (0·30 g), m.p. 250—260°, and c-5b,11a-*epoxy*-r-5a-*ethyl*-5a,5b,11a,c-12a-*tetrahydro*-t-12-*phenyl*-12H-*di*-benzo[b,h]*fluorene*-5,6,11,13-*tetraone* (IIf) (22 mg), m.p. 186—188° (from benzene–light petroleum) (Found: C, 77·3; H, 4·5%; M^+, 448. $C_{29}H_{20}O_5$ requires C, 77·7; H, 4·5%; M, 448), $\nu_{max.}$ 1705, 1690, and 1675 cm^{-1}, τ 9·42 (t, J 7 Hz, $CH_2 \cdot CH_3$), 8·35 and 6·82 (2 × sextet, J 7 Hz, $CH_2 \cdot CH_3$), 6·71 (d, J 1 Hz, CH·CH·CO), 4·73 (d, J 1 Hz, PhCH·CH), 2·76 (s, Ph), and 2·4—1·8 (m, ArH).

(*d*) *Quinone* (IIId). A mixture of the quinone (0·92 g), t-butylamine (0·5 ml), and ethanol (60 ml) was kept in an open vessel in the dark for 2 days, and filtered to give, probably, t-12-*benzyl*-c-5b,11a-*epoxy*-5a,5b,11a,c-12a-*tetrahydro*-r-5a-*phenethyl*-12H-*dibenzo*[b,h]*fluorene*-5,6,11,13-*tetraone* (IIg) (0·5 g), m.p. 123—125° (from benzene–light petroleum) (Found: C, 80·4; H, 5·1. $C_{36}H_{26}O_5$ requires C, 80·3; H, 4·9%), τ 2·9—1·8 (ArH) and a complex series of overlapping multiplets derived from the aliphatic protons at τ 8·4—5·4 [confident assignment of the signals of this region was impossible with the exception of a broadened singlet at τ 6·88 (12a-H)].

(*e*) *Quinone* (IIIe). A mixture of the quinone (1·0 g) and t-butylamine (1 ml) in ethanol (100 ml) was kept for 2 days. The precipitate was collected and recrystallised from glacial acetic acid to give presumably c-5b,11a-*epoxy*-5a,5b,11a,c-12a-*tetrahydro*-r-5a-(p-*methoxybenzyl*)-t-12-(p-*methoxy*-*phenyl*)-12H-*dibenzo*[b,h]*fluorene*-5,6,11,13-*tetraone* (IIh) (0·75 g), m.p. 250—252° (Found: C, 75·6; H, 4·8. $C_{36}H_{26}O_7$ requires C, 75·8; H, 4·6%); $\nu_{max.}$ 1710sh, 1700, and 1680 cm^{-1}, τ (CF$_3$·CO$_2$H) 6·98 and 5·27 (2d, J 14 Hz, CH_2Ar), 6·43 (d, J 1 Hz, CH·CO), 6·19 and 5·96 (2s, OMe), 4·62 (d, J 1 Hz, PhCH·CH), 3·64 and 3·35 (2d, J 8 Hz, ArH), 2·85 and 26·0 (2d, J 8 Hz, ArH), and 2·2—1·6 (m, ArH).

(*f*) *Quinone* (IIIf). This reaction was carried out as described for quinone (IIId) and gave presumably c-5b,11a-*epoxy*-5a,5b,11a,c-12a-*tetrahydro*-r-5a-(p-*nitrobenzyl*)-t-12-(p-*nitrophenyl*)-12H-*dibenzo*[b,h]*fluorene*-5,6,11,13-*tetraone* (IIi) (0·75 g), m.p. >320° (from dimethylformamide) (Found: C, 68·0; H, 3·4; N, 4·7. $C_{34}H_{20}N_2O_9$ requires C, 68·0; H, 3·4; N, 4·7%), $\nu_{max.}$ 1710, 1700, and 1680 cm^{-1}, insoluble in the usual n.m.r. solvents. The spectrum of a solution in concentrated sulphuric acid showed δ [p.p.m. downfield from the high-field doublet (J 14 Hz) of an AB quartet] 1·55 (d, J 14 Hz, CHAr), 0·4br (s, CH·CO), 2·34br (s, PhCH·CH), 3·38 and 4·54 (2d, J 8 Hz, ArH), and 4·7—5·4 (m, ArH).

Reaction between 2-*Isopropyl*-1,4-*naphthoquinone and* t-*Butylamine.*—A mixture of the quinone [10] (0·7 g) and the amine (50 ml) was kept for 7 days and evaporated to dryness. The residue was partitioned between dilute hydrochloric

acid and ether. The organic phase was collected, dried (MgSO$_4$), and evaporated. Preparative layer chromatography of the residue on silica gave 2-*isopropenyl*-3-t-*butylamino*-1,4-*naphthoquinone* (IVa) (20 mg), m.p. 110—111° (from light petroleum) (Found: C, 75·9; H, 7·2; N, 5·0%; M^+, 269. $C_{17}H_{19}NO_2$ requires C, 75·8; H, 7·1; N, 5·2%; M, 269), $\nu_{max.}$ 3360, 1681, 1643, 1618, and 1597 cm^{-1}, τ (CDCl$_3$) 8·59 (s, Bu^t), 7·99br (s, CH$_2$=CMe), 5·40br (s, NH), 4·96br and 4·50br (2s, CH_2=C), and 2·35—1·85 (m, ArH).

Reaction between 2-*Bromo*-3-*ethyl*-1,4-*naphthoquinone and* t-*Butylamine.*—A mixture of the quinone (0·74 g), the amine (1 ml), and ethanol (50 ml) was kept in the dark for 3 days and evaporated to dryness. The residue was dissolved in the minimum volume of hot methanol and the solution cooled to give unchanged starting material (0·31 g). The mother liquors were evaporated to dryness and the residue purified by preparative layer chromatography on silica (benzene), to give (i) unchanged starting quinone (0·16 g), (ii) 2-ethoxy-3-ethyl-1,4-naphthoquinone (20 mg) as a gum, $\nu_{max.}$ 1670br cm^{-1}, τ (CDCl$_3$) 8·87 and 8·58 (2t, J 7 Hz, 2 × CH_3·CH$_2$), 7·35 (q, J 7 Hz, CH$_2$·CH_3), 5·56 (q, J 7 Hz, O·CH_2·CH$_3$), and 2·5—1·8 (m, ArH), identical with the material obtained by treatment of 2-ethyl-3-hydroxy-1,4-naphthoquinone [3] with ethereal diazoethane, and (iii) 2-*bromo*-3-t-*butylamino*-1,4-*naphthoquinone* (20 mg), m.p. 119—120° (from methanol) (Found: C, 54·7; H, 4·7; N, 4·4. $C_{14}H_{14}BrNO_2$ requires C, 54·5; H, 4·6; N, 4·5%), τ (CDCl$_3$) 8·47 (s, Bu^t), 4·9br (NH), and 2·45—1·85 (m, ArH).

2-*Ethyl*-3-*hydroxy*-1,4-*naphthoquinone* (IVd).—To a solution of 2-ethyl-1,4-naphthoquinone (1 g) in ethanol (10 ml) was added a solution of anhydrous sodium carbonate (0·2 g) in water (5 ml) and 30% hydrogen peroxide (1 ml). After 15 min the solution was diluted with water (100 ml) and the precipitate (0·7 g) collected, dried, and dissolved in concentrated sulphuric acid (5 ml). After 10 min the solution was poured onto ice to give the quinone (0·5 g), m.p. 137—138° (from ethanol) (lit.,[3] 137—138°).

2-*Bromo*-3-t-*butylamino*-1,4-*naphthoquinone* (IVb).—To a suspension of 2,3-dibromo-1,4-naphthoquinone (1·58 g) in ethanol (100 ml) was added t-butylamine (1·1 g). The mixture was stirred at room temperature for 24 h, and evaporated to dryness. Recrystallisation of the residue gave the title quinone (1·0 g), m.p. 119—120° (from methanol), identical with the material obtained above.

[10] L. F. Fieser and F. C. Chang, *J. Amer. Chem. Soc.*, 1942, **64**, 2043.