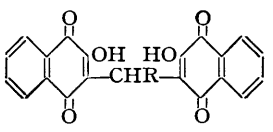
240. *Quinones. Part I. Chloroalkylation.*

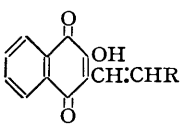
By R. H. Thomson.

1 : 4-Naphthaquinones (but not benzoquinones) may be chloroalkylated by saturating their solutions in cold acetic acid containing an aldehyde with dry hydrogen chloride. 1 : 4-Naphthaquinone gave the 2 : 3-bischloromethyl compound (V), 2-methyl-1 : 4-naphthaquinone gave the 3-derivatives (IV; R = Me; R′ = H, Me, and Ph), 2-ethyl-1 : 4-naphthaquinone gave the analogues (IV; R = Et; R′ = H and Me) and 2-chloro-1 : 4-naphthaquinone gave its 3-chloromethyl derivative (IV; R = Cl; R′ = H). The scope of the reaction appears to be limited. Yields are 50—60%. Catalytic reduction of the chloromethylquinones (except V), followed by oxidation, afforded diquinones (*e.g.*, VI).

A variety of compounds may be obtained by the reaction of aldehydes with naphthaquinones. For instance, Hooker and Carnell (*J.*, 1894, **65**, 76) prepared diquinones of type (I) by heating various aldehydes with 2-hydroxy-1 : 4-naphthaquinone in alcohol, and Hooker (*J.*, 1896, **69**, 1362; *J. Amer. Chem. Soc.*, 1936, **58**, 1163) obtained alkenylhydroxyquinones of type (II) by using a large excess of the aldehyde in hot acetic–hydrochloric acid. By the latter method Brockmann and Müller (*Annalen*, 1939, **540**, 51) obtained both alkyl- and alkenyl-naphthazarins, but 1 : 4-naphthaquinone and certain alkyl derivatives condense with equimolecular amounts of aldehydes under these conditions to give anthocyanidins of type (III) (Raudnitz and Puluj, *Ber.*, 1931, **64**, 2212; Fieser and Fieser, *J. Amer. Chem. Soc.*, 1941, **63**, 1574).



(I)



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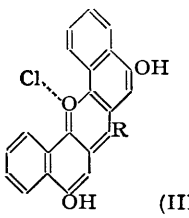
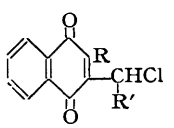


(III)

It is now found that chloroalkylquinones of type (IV) can be obtained in 50—60% yield by the interaction of aldehydes and naphthaquinones in cold glacial acetic acid in the presence of hydrochloric acid. 2-Methyl-1 : 4-naphthaquinone reacted with formaldehyde, acetaldehyde, and benzaldehyde, to give the chloroalkylquinones (IV; R = Me; R′ = H, Me, and Ph respectively) but chloroalkylation did not occur with propaldehyde, 2-formylthiophen, or 2-naphthaldehyde. In all cases the solution became red (owing to anthocyanidin formation) and when the reaction failed it was usually possible to isolate some 3-chloro-2-methyl-1 : 4-naphthaquinone from the tarry product. (The anthocyanidin and the chloromethylquinone were isolated from a blank reaction when no aldehyde was present.) 2-Ethyl-1 : 4-naphthaquinone gave chloromethyl and chloroethyl derivatives; reaction with benzaldehyde yielded a small amount of an unidentified chlorine-free compound, m. p. 280°. Although chloromethylation of 2-chloro-1 : 4-naphthaquinone proceeded smoothly, attempted reactions with acetaldehyde and benzaldehyde afforded only 2 : 3-dichloro-1 : 4-naphthaquinone in low yield. 2-Hydroxy-1 : 4-naphthaquinone did not react with aldehydes in the cold; when heated it condensed with formaldehyde to give (I; R = H) (previously obtained by Fieser *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 3214, under very similar conditions) but did not condense with benzaldehyde or acetaldehyde (cf. Hooker, *loc. cit.*). 1 : 4-Naphthaquinone readily formed the bischloromethyl derivative (V) and reaction with acetaldehyde gave, in minute quantity, a chlorine-free compound which appears to be (VII); with benzaldehyde (III; R = Ph) was obtained even in the cold. Attempts to chloroalkylate benzoquinones were unsuccessful; with benzoquinone and its 2 : 5-dichloro- and 2 : 6-dimethyl derivatives, the products were mixtures of chloroquinols, and an attempt to chloromethylate chalkone produced the hydrochloride only.

Chloroalkylation is thus a limited reaction although fortunately chloromethylation, which is likely to be the most useful, is the most successful. The reaction is very similar to Hooker's (*loc. cit.*) alkenylation process which proceeds *via* an "aldol." At low temperatures a replacement reaction would give rise to a chloroalkyl group but may be succeeded, according to the conditions, by an elimination reaction to form an alkenyl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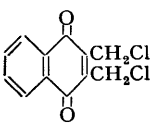
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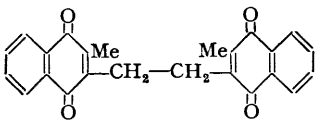
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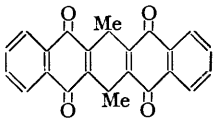
(VII)

group. This complication is absent in chloromethylation. The first step in the reaction is presumably co-ordination of carbonyl-oxygen with a proton, and hence quinone and aldehyde compete, and both chloroalkylation and hydrochloric acid addition can proceed simultaneously, the latter predominating with the more reactive benzoquinones.

Catalytic reduction of the chloroethyl and chlorobenzyl compounds proceeded smoothly in glacial acetic acid, but 2-chloro-3-chloromethyl- and 3-chloromethyl-2-methyl-1 : 4-naphthaquinone formed very insoluble precipitates (quinhydrones?) during reduction, and the ultimate yields of 2-chloro-3-methyl- and 2 : 3-dimethyl-1 : 4-naphthaquinone respectively were very poor. By working in dimethylformamide solution precipitation was avoided and diquinones (*e.g.*, VI) were obtained on subsequent oxidation. These diquinones were also formed by reaction of the chloromethylquinones with silver powder. Attempts to convert (V) into a *cyclo*butene derivative by various methods were of no avail. The products formed were apparently more complex as they did not sublime in a high vacuum.

Experimental

3-*Chloromethyl*-2-*methyl*-1 : 4-*naphthaquinone*.—A solution of 2-methyl-1 : 4-naphthaquinone (1 g.) in glacial acetic acid (10 c.c.) containing aqueous formaldehyde (3 c.c.; 36%) was cooled in ice-water, and dry hydrogen chloride passed in for 30 minutes. The solution became red and, after being kept overnight, blue, and was then poured on ice. The dull pink precipitate was washed with water until orange-brown and crystallised from alcohol (charcoal) in light yellow needles, m. p. 107—108° (58%). The yield was not appreciably affected by raising the temperature to 60°, increasing the time of reaction and the amount of formaldehyde, or using paraformaldehyde.

1 : 2-*Bis*-(2-*methyl*-1 : 4-*naphthaquinon*-3-*yl*)*ethane*.—(*a*) A suspension of silver powder (1 g.) in dry benzene (10 c.c.) containing 3-chloromethyl-2-methyl-1 : 4-naphthaquinone (0·3 g.) was refluxed for 5 hours, then filtered, and the residue extracted twice with boiling benzene. The combined filtrates were concentrated and allowed to cool. Light yellow needles, m. p. 269—270° (28%), separated. (*b*) The chloromethylquinone (0·4 g.) in dimethylformamide (15 c.c.) was hydrogenated in the presence of 2% palladised strontium carbonate (1 g.) until 1·5 mols. of hydrogen were taken up. After removal of the catalyst a solution of chromium trioxide (0·2 g.) in water (2 c.c.) was added and the mixture heated on the water-bath for 20 minutes. The suspension obtained was diluted with water and filtered. The *product* crystallised from glacial acetic acid in yellow leaflets, m. p. 269—270° (77%) (Found: C, 77·6; H, 5·1. $C_{24}H_{18}O_4$ requires C, 77·8; H, 4·9%). When the hydrogenation was carried out in glacial acetic acid (30 c.c.) containing anhydrous sodium acetate (0·4 g.) and with a palladised barium sulphate catalyst, a purple precipitate appeared and the hydrogen uptake was slow and incomplete. Working up as before yielded 2 : 3-dimethyl-1 : 4-naphthaquinone, m. p. and mixed m. p. 126° (70 mg.).

3-1′-*Chloroethyl*-2-*methyl*-1 : 4-*naphthaquinone*.—Dry hydrogen chloride was passed into a solution of 2-methyl-1 : 4-naphthaquinone (1 g.) in glacial acetic acid (10 c.c.) containing acetaldehyde (1 c.c.) for 10 minutes, with cooling in ice-water. Next morning the red solution was poured on ice, and the precipitate washed with a little cold alcohol and crystallised from the same solvent (charcoal) in yellow needles, m. p. 145—146° (55%) (Found: C, 66·7; H, 4·7. $C_{13}H_{11}O_2Cl$ requires C, 66·5; H, 4·7%). This reaction failed when concentrated hydrochloric acid was used. The *chloroethylquinone* (0·5 g.) in glacial acetic acid (20 c.c.) containing anhydrous sodium acetate (0·5 g.) was hydrogenated in the presence of 5% palladised barium

sulphate (0·1 g.). After absorption of 2 mols. of hydrogen the suspension was filtered and oxidised for 15 minutes on the water-bath with a solution of chromium trioxide (0·25 g.) in water (2 c.c.). 3-Ethyl-2-methyl-1 : 4-naphthaquinone was isolated by dilution with water. It crystallised from methanol in light yellow needles, m. p. and mixed m. p. 72—73° (82%).

3-α-*Chlorobenzyl*-2-*methyl*-1 : 4-*naphthaquinone*.—A cooled mixture of 2-methyl-1 : 4-naphthaquinone (1 g.), benzaldehyde (0·7 c.c.), and glacial acetic acid (10 c.c.) was treated with dry hydrogen chloride for 30 minutes, set aside overnight, and poured into water. The *product* crystallised from alcohol in light yellow needles, m. p. 103° (44%) (Found: C, 73·0; H, 4·5. $C_{18}H_{13}O_2Cl$ requires C, 72·8; H, 4·4%). Catalytic hydrogenation and subsequent oxidation afforded 3-benzyl-2-methyl-1 : 4-naphthaquinone, m. p. and mixed m. p. 108° (95%).

3-*Chloromethyl*-2-*ethyl*-1 : 4-*naphthaquinone*.—A cold mixture of 2-ethyl-1 : 4-naphthaquinone (1 g.), aqueous formaldehyde (3 c.c.; 36%), and acetic acid (8 c.c.) was saturated with dry hydrogen chloride for 15 minutes, and worked up next day. Crystallisation from methanol (charcoal) gave yellow needles, m. p. 86—87° (53%) (Found: C, 66·6; H, 4·5. $C_{13}H_{11}O_2Cl$ requires C, 66·5; H, 4·7%).

1 : 2-*Bis*-(2-*ethyl*-1 : 4-*naphthaquinon*-3-*yl*)*ethane*.—This was obtained from 3-chloromethyl-2-ethyl-1 : 4-naphthaquinone by (*a*) refluxing in dry benzene with silver powder, or (*b*) hydrogenation over palladised barium sulphate in glacial acetic acid–anhydrous sodium acetate, followed by chromic acid oxidation. The *diquinone* crystallised from glacial acetic acid in light yellow needles, m. p. 267° (62%) (Found: C, 78·45; H, 5·55. $C_{26}H_{22}O_4$ requires C, 78·35; H, 5·55%).

3-1′-*Chloroethyl*-2-*ethyl*-1 : 4-*naphthaquinone*.—A cooled mixture of 2-ethyl-1 : 4-naphthaquinone (1 g.), acetaldehyde (1 c.c.), and glacial acetic acid (10 c.c.) was treated with dry hydrogen chloride for 15 minutes and the *product* was isolated after 3 hours. It crystallised from methanol in yellow needles, m. p. 103° (63%) (Found: C, 67·4; H, 5·4. $C_{14}H_{13}O_2Cl$ requires C, 67·55; H, 5·4%).

2 : 3-*Diethyl*-1 : 4-*naphthaquinone*.—This was obtained from the above chloroethylquinone by catalytic hydrogenation and subsequent oxidation. The *product* was purified by vacuum-sublimation (thrice), yielding yellow needles, m. p. 72—73° (90%) (Found: C, 78·25; H, 6·5. $C_{14}H_{14}O$ requires C, 78·45; H, 6·6%).

2-*Chloro*-3-*chloromethyl*-1 : 4-*naphthaquinone*.—A mixture of 2-chloro-1 : 4-naphthaquinone (1 g.), aqueous formaldehyde (3 c.c.; 36%), and glacial acetic acid (15 c.c.) was cooled in ice-water and saturated with dry hydrogen chloride for 20 minutes. After several hours the crystals were collected and recrystallised from alcohol in lemon-yellow blades, m. p. 119° (50%) (Found: C, 54·5; H, 2·5. $C_{11}H_6O_2Cl_2$ requires C, 54·8; H, 2·5%). A little more was obtained by dilution of the reaction mixture after filtration.

1 : 2-*Bis*-(2-*chloro*-1 : 4-*naphthaquinon*-3-*yl*)*ethane*.—Prepared from 2-chloro-3-chloromethyl-1 : 4-naphthaquinone by (*a*) reaction with silver powder in boiling benzene or (*b*) hydrogenation in dimethylformamide over palladised strontium carbonate and subsequent oxidation, the *diquinone* crystallised from dimethylformamide in pale yellow leaflets, m. p. 302° (Found: C, 64·5; H, 3·1. $C_{22}H_{12}O_4Cl_2$ requires C, 64·25; H, 2·95%). When the hydrogenation was carried out in glacial acetic acid a trace of 2-chloro-3-methyl-1 : 4-naphthaquinone was isolated.

2 : 3-*Bischloromethyl*-1 : 4-*naphthaquinone*.—A cooled mixture of 1 : 4-naphthaquinone (1 g.), aqueous formaldehyde (6 c.c.; 36%), and glacial acetic acid (15 c.c.) was saturated with dry hydrogen chloride for 30 minutes. Next morning the crystals were washed with alcohol and recrystallised from the same solvent, forming stout yellow-brown needles, m. p. 142—143° (58%) (Found: C, 56·5; H, 3·0; Cl, 27·7. $C_{12}H_8O_2Cl_2$ requires C, 56·5; H, 3·15; Cl, 27·8%). By the same procedure, using acetaldehyde (1 c.c.) in place of formalin, a product was obtained which after extraction with boiling alcohol (20 c.c.) and crystallisation from glacial acetic acid (charcoal) formed yellow needles, m. p. 304° (decomp., darkening from 270°) (12 mg.) (Found: C, 77·85; H, 4·4. $C_{24}H_{16}O_4$ requires C, 78·25; H, 4·4%). The *substance* gave a negative Craven test (*J.*, 1931, 1605) and no colour on warming with Claisen's alkali.

Addition of Hydrochloric Acid to 2 : 5-*Dichlorobenzoquinone*.—A suspension of 2 : 5-dichlorobenzoquinone (1 g.) in glacial acetic acid (10 c.c.) and aqueous formaldehyde (6 c.c.; 36%) was cooled in ice-water and saturated with dry hydrogen chloride for 15 minutes. The quinone dissolved, forming an orange-red solution, the colour subsequently faded, and colourless crystals separated. These were collected (0·52 g.; m. p. 170—200°), and crystallised first from benzene and then from glacial acetic acid, forming needles, m. p. 230—232° (0·24 g.). Oxidation with chromic acid yielded chloranil, m. p. 290° (in sealed tube). Concentration of the benzene

mother-liquor gave a product, m. p. 130—140° (70 mg.), which on oxidation yielded trichlorobenzoquinone, m. p. 170°. When the addition reaction was repeated in the absence of formaldehyde the initial crop of crystals had m. p. 135° (0·75 g.) (trichloroquinol has m. p. 136°). Reactions with other benzoquinones were similar.

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