# A New Route to 4-Hydroxytetralones and 1-Naphthols

By **Nigel J. P. Broom** and **Peter G. Sammes,*** Department of Organic Chemistry, The University of Leeds, Leeds LS2 9JT

The lithium salts, derived from position 3 of phthalides by treatment with hindered bases, participate in Michael addition reactions with a variety of conjugated olefins. For singly-activated olefins the conjugate anion reacts intramolecularly with the lactone group to produce 4-hydroxytetralones in moderate to good yield. Dehydration of these hydroxytetralones, by brief treatment with acid, produces the corresponding α-naphthol. Substituted phthalides react similarly making the method a general one for the production of substituted α-naphthols.

THE formation of carbanions from phthalides has been noted in a variety of reactions reported in the literature, and an example is the base-catalysed condensation of aldehydes with phthalide (1) in which reaction at position 3 of the phthalide nucleus occurs.[1] Eugster and his colleagues showed that the sodium salt of phthalide (1)

(1)   (2)

(3)

(4)
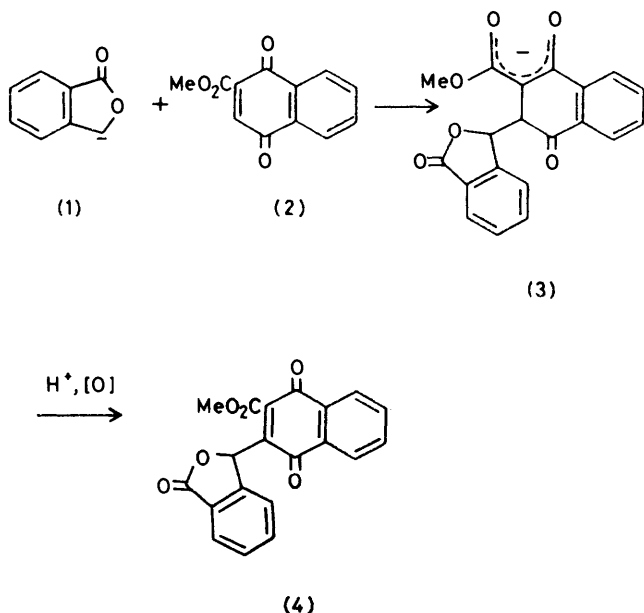
reacted with the substituted naphthoquinone (2) by Michael addition to produce the adduct (3), which, after protonation and oxidation, gave the quinone (4).[2] That the anion (3) does not undergo intramolecular reaction between the carbanion and the lactone function of the phthalide residue was considered to be a consequence of the stabilised nature of the carbanion adduct, akin to that of a β-dicarbonyl anion. It was therefore considered that, if a less activated Michael acceptor were used, subsequent intramolecular cyclisation between the lactone function and the conjugate anion might occur.

In order to test this hypothesis the lithium anion of phthalide was produced by reaction with freshly-prepared lithium di-isopropylamide in tetrahydrofuran at —40 °C. An orange colour was noted and ascribed to formation of the carbanion (5). Addition of acrylonitrile, as a solution in tetrahydrofuran, resulted in

rapid loss of the colour as the temperature of the reaction mixture was raised from —40 °C to room temperature. Quenching of the reaction mixture with dilute acid and ether extraction afforded a solid, identified as a 1 : 1 mixture of epimers of 2-cyano-4-hydroxytetralone (6) which were not readily separated. ¹H N.m.r. evidence showed that the cyano-group adopted a pseudo-equatorial orientation,[3] the proton at C-2 appearing as a double doublet at δ 3.82 (J 5, 15 Hz) and 4.36 (J 6.5, 12 Hz) in the two epimers. The former can be assigned to the *trans*-isomer (6a), in which the hydroxy group at position 4 shields the proton at C-2; the latter is the *cis*-isomer (6b). In this product no enolisation of the β-keto-nitrile system was apparent from the n.m.r. spectrum. Further proof of the structure of the adduct was obtained by addition of a small drop of trifluoro-acetic acid to the n.m.r. sample solution in deuterio-chloroform, which caused a rapid change in the n.m.r. pattern, to that of the known aromatic dehydration product, 2-cyano-1-naphthol (7).[4] A possible course of the reactions leading to the tetralones (6) is given in the Scheme 1. Using the above reaction conditions, the

(5)

(6)
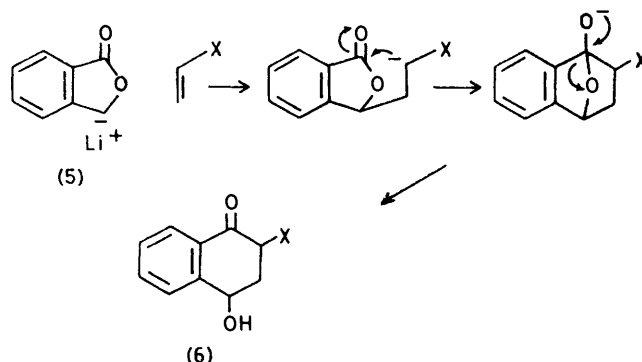
SCHEME 1

anion (5) was reacted with a series of other Michael acceptors and these results are outlined in Table 1.

When the reaction was conducted with methyl 3-methylcrotonate the derived tetralones (8) were isolated as an unstable yellow oil. The ¹H n.m.r. spectrum of the material showed a *ca.* 2 : 1 ratio between the main products, with signals belonging to the C-4 and C-2 protons occurring as singlets at δ 4.64 and 4.00 in the
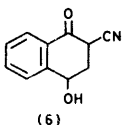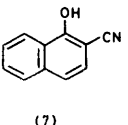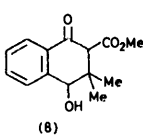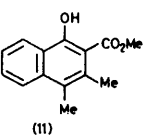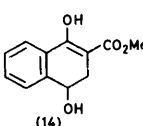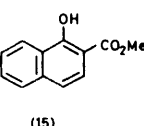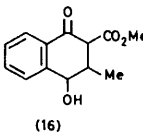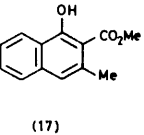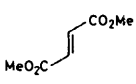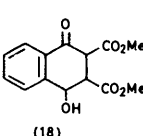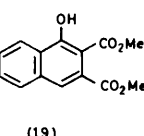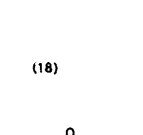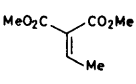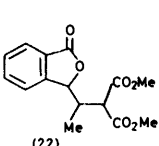
major isomer and at 4.62 and 3.52 in the minor one. Some enolisation of the β-keto-ester system was also apparent by the appearance of a small amount of an acidic proton at lower fields. Acetylation of the mixture, using pyridine–acetic anhydride as the reagent,

TABLE 1

Tetralones and napthols from phthalide [a]

Michael acceptor	Product [b]	Yield [c] %	Naphthol	Yield [d] %
(CN structure)	(6)	39	(7)	74
(CO₂Me, Me, Me structure)	(8)	37	(11)	65 (35) [e]
(CO₂Me structure)	(14)	37	(15)	72
(CO₂Me, Me structure)	(16)	48	(17)	68
(CO₂Me, MeO₂C structure)	(18)	44	(19)	82
(CO₂Me, CO₂Me structure)	(18)	44	(19)	78
(MeO₂C, CO₂Me, Me structure)	(22)	45		
(Me, Me, Me ketone structure)	(23)	20		

[a] General reaction conditions as described in the Experimental section. No attempts to optimise yields were made. [b] As mixtures of epimers. [c] Isolated yields based on starting phthalide. [d] Yields from isolated tetralones. [e] Overall yield from phthalide, without isolation of the intermediate tetralone.

afforded, as the major product, the monoacetate (9); small quantities of the diacetate (10) were also isolated from this reaction.

On treatment of the hydroxy-ketone (8) with either boron trifluoride–ether in dichloromethane or a catalytic amount of toluene-p-sulphonic acid in benzene at reflux,

dehydration, accompanied by concomitant methyl migration, occurred to give the naphthol (11). Treatment of either the alcohol (8) or the monoacetates (10) with boron trifluoride–ether in the presence of ethane-1,2-dithiol afforded not only the corresponding naphthol (11) but quantities of the 4-thio-substituted tetralone (13), presumably formed by trapping of the intermediate carbocation (12) (Scheme 2).

The behaviour of a variety of other Michael acceptors was also studied (Table 1). The adduct from methyl acrylate was found to exist mainly in the enolic form (14); acid-catalysed dehydration afforded the known naphthol (15). Corresponding dehydration of the adducts (16) from methyl crotonate gave loss of water without methyl migration. The naphthol (17) obtained from the sequence of reactions has the expected n.m.r. spectrum and showed a m.p. of 84—86 °C compared to the 109—110 °C reported for the isomeric 2-methoxy-carbonyl-4-methyl-1-naphthol.[5]

The ¹H n.m.r. spectrum of the methoxycarbonyl derivative (18), obtained from the reaction with dimethyl fumarate, showed that ca. half the product was in the enolic form and the presence of two exchangeable singlets at δ 12.40 and 12.44 indicated that there were two enolic epimers. Furthermore, irradiation at the frequency of the (broad) C-4 proton signal at δ 5.0 caused the C-3 proton doublets of epimers (19a) and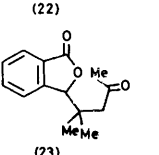 (19b), at δ 4.06 (J 3 Hz) and 3.94 (J 6 Hz) to collapse to singlets. The adduct (18) obtained from reaction of the phthalide anion with dimethyl maleate was very similar, and again about half the material was in the enolic form, although only one of the enol isomers was observed, that with the C-3 proton at δ 4.06 (d, J 3 Hz) and the enolic proton at δ 12.46. Dehydration of the adducts from either dimethyl fumarate or dimethyl maleate gave a naphthol, m.p. 102—103 °C, assigned the structure (19). It showed $\nu_{max.}$ 3 400—3 000, 1 720, and 1 685 cm⁻¹; δ 3.88 (3 H, s), 3.42 (3 H, s), 7.36 (1 H, s, H-4), 7.42—7.70 (3 H, m), 8.22—8.38 (1 H, m, H-8), and 11.68 (1 H, s, exchangeable with D₂O). An accurate mass measurement and microanalytical data confirmed the molecular formula $C_{14}H_{12}O_5$; the known isomeric 4-methoxycarbonyl derivative, of m.p. 144 °C,[6] can be discounted. A compound assigned the structure of the naphthol (19) had previously been reported by us to have been prepared in low yield by the oxidation of 2,3-bis(methoxycarbonyl)-1,4-dihydronaphthol (20) with manganese dioxide.[7] A direct comparison between this material, m.p. 145—160 °C (decomp.), and the naphthol (19), m.p. 102—103°, showed that they were different. Preparation of a fresh sample of the oxidation product, using the literature method, followed by extensive purification, gave material of m.p. 240—246 °C (decomp.). Although its i.r. spectrum and ¹H n.m.r. spectrum at 60 MHz were very similar to those of the naphthol (19), examination of the ¹H n.m.r. spectra at 100 MHz showed differences in the aromatic region, the proton at position 4 being absent. Careful mass-spectral examination showed a parent ion corresponding to a molecular formula of

(8)   (12)   (11)

H^+
$-H_2O$

$HSCH_2CH_2SH$

(13)

SCHEME 2

$C_{28}H_{22}O_{10}$, and thus the oxidation product must be the dimer of structure (21). Attempts to prepare the dimer (21), by direct oxidation of the naphthol (19) with manganese dioxide, failed.

Reaction of the phthalide anion with highly activated acceptors, such as dimethyl ethylidenemalonate, proceeded without subsequent cyclisation, to give the substituted phthalide (22). Under the standard reaction conditions mesityl oxide behaved similarly to produce, as the major product, the phthalide adduct (23).

A brief study was also undertaken of the use of substituted phthalides in this naphthol preparation. For this purpose 6-methoxyphthalide (24) [8] and 4-methoxyphthalide (25) were prepared. Towards the preparation of the latter compound Buehler et al. con-

(21)
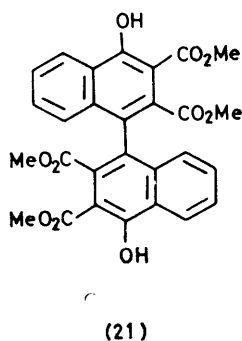
densed 3-hydroxybenzoic acid with formaldehyde to give two principal compounds, m.p. 175 and 254 °C, the higher-melting component being 4-hydroxyphthalide,[9] which could be methylated to the required phthalide (25). The structure of the unknown compound, m.p. 177—179 °C (from water) was not previously determined. A spectroscopic examination of this material established a molecular formula of $C_{10}H_8O_4$ and the presence of a

cyclic five-membered aromatic lactone; $v_{max.}$ 1 740 cm^{-1}; $\delta_{[(CD_3)_2CO]}$ 5.20 (2 H, s), 5.34 (4 H, s), 7.18 (1 H, d, J 8 Hz), and 7.46 (1 H, d, J 8 Hz). Of the two possible

TABLE 2 [a]

Phthalide	Michael acceptor	Product [b]	Yield [c]	Naphthol	Yield [d]
(24)		(29)	41	(30)	52
(25)		(31)	48	(32)	53
(25)		(33)	58	(34)	43
(25)		(35)	34	(36)	67
(25)		(37)	30	(28)	52

[a] See Table 1 for footnotes b—d.

structures for this material, either (26) or (27), the chemical shifts are best in agreement with the structure (26). The results of the reactions of the 4- and 6-

methoxyphthalide with some Michael acceptors are detailed in Table 2. Of particular note is the reaction of the phthalide (25) with crotonolactone. In principle the observed naphthol product (28) could itself be used as a substituted phthalide for sequential reaction with
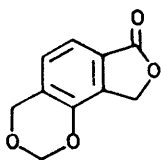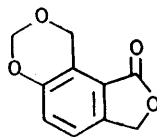
(26)   (27)

further crotonolactone units. Such a sequence of reactions would constitute a general method for aromatic homologation.

Subsequent to our initial report on this work [10] several other groups have utilised activated phthalides (29) for related purposes. These include the use of 3-cyanophthalides,[11] 3-arylthiophthalides,[11] and 3-aryl-sulphonylphthalides.[12] Attempts to utilise methyl 2-methylbenzoate in place of phthalide gave, instead, the products of self-condensation. Staunton and colleagues have shown, however, that such self-condensations, occurring during formation of the corresponding carbanion, can be minimised by the presence of substituents, such as a methoxy-group, adjacent to the ester group.[13]

Recently the phthalide ion (5) has been shown capable of reacting with benzynes to form anthraquinones.[14]

EXPERIMENTAL

M.p.s were determined on a hot-stage apparatus and are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 157G spectrometer on solutions in chloroform, unless otherwise stated, and u.v. spectra were recorded for ethanolic solutions with a Pye-Unicam SP800 instrument. ^{1}H N.m.r. spectra were determined on a JEOL MH100 instrument using deuteriochloroform as solvent and tetramethyl-silane as internal reference. Mass spectra were recorded by P.C.M.U., Harwell. All solvents were dried and distilled before use. Thin-layer chromatography (t.l.c.) was carried out on Merck Kieselgel GF$_{254}$; preparative t.l.c. was carried out on 1-mm thick plates of silica. Light petroleum refers to the fraction of boiling range 60—80 °C. Base-catalysed reactions were routinely carried out under a blanket of dry nitrogen or argon.

General Procedure for Phthalide Reactions.—To a stirred solution of di-isopropylamine (0.31 ml, 2.25 mmol) in tetrahydrofuran (12 ml) at −40 °C was slowly added a solution of n-butyl-lithium (2.5M, 1.07 ml, 2.25 mmol) in hexane. After 15 min a solution of phthalide (288 mg, 2.15 mmol) in tetrahydrofuran (6 ml) was added at −40 °C to produce an orange solution. After a further 15 min at −40 °C the reactant (2.15 mmol) (see Table 1) was added as a solution in tetrahydrofuran (1 ml), and the stirred mixture left for a further 30 min before allowing it to warm to room temperature. The mixture was poured into 2N hydrochloric acid (40 ml), extracted with ether (4 × 40 ml),

and the combined extracts dried (Na$_2$SO$_4$) and evaporated. Where necessary the reaction mixture was purified by preparative t.l.c. (CHCl$_3$) to give the hydroxytetralones (see Table 2).

The isolated tetralones, generally as mixtures of isomers, showed the following properties:

2-Cyano-4-hydroxytetralone (6) was isolated as a white amorphous solid, m.p. 116—118 °C; ν$_{max.}$ 3 460, 2 240, and 1 680 cm^{-1}; δ (*ca.* 1:1 mixture of epimers) 2.56—2.94 (2 H, 3-CH$_2$), 2.75—3.40 (1 H, br s, OH), 3.82 (0.5 H, dd, *J* 5, 11 Hz, exchanged with D$_2$O, 2-CH), 4.36 (0.5 H, dd, *J* 6.5, 12 Hz, exchanged with D$_2$O, 2-CH), 4.92—5.16 (1 H, 4-CH), 7.25—8.07 (4 H, aromatic H) (Found: *M*$^+$, 187, 0.633. C$_{11}$H$_9$NO$_2$ requires *M*, 187.063 3).

4-Hydroxy-2-methoxycarbonyl-3,3-dimethyltetralone (8) was isolated as a viscous oil; ν$_{max.}$ 3 470, 3 310, 1 765, and 1 690 cm^{-1}; δ (mixture of isomers) 1.07, 1.10, 1.16, 1.18 (6 H, s, Me), 3.15—3.64 (1 H, br s, OH), 3.74 and 3.76 (3 H, s, CO$_2$Me), 3.52 and 4.00 (1 H, s, 2-CH), 4.62 and 4.64 (1 H, s, 4-CH), and 7.25—7.99 (4 H, aromatic H) (Found: *M*$^+$, 248.104 0. C$_{14}$H$_{16}$O$_4$ requires *M*, 248.104 9).

4-Hydroxy-2-methoxycarbonyltetralone (14) was isolated as a viscous yellow oil; ν$_{max.}$ 3 600—3 170, 1 735, 1 685, 1 645, 1 615, 1 600, and 1 570 cm^{-1}; δ 2.56—3.11 (1 H, br s, exchanged with D$_2$O, OH), 2.73 (2 H, d, *J* 6 Hz, 3-CH$_2$), 4.72 (1 H, t, *J* 6 Hz, 4-CH), 7.06—7.72 (4 H, aromatic H), and 12.22 (1 H, exchanged with D$_2$O, enol).

4-Hydroxy-2-methoxycarbonyl-3-methyltetralone (16) was isolated as a viscous yellow oil; ν$_{max.}$ 3 540—3 200, 1 740, 1 680, 1 650, 1 635, and 1 600 cm^{-1}; δ (mixture of epimers) 0.71—1.20 (3 H, 3-Me), 2.38—2.81 and 2.98—3.18 (1 H, 3-CH), 2.91—3.47 (1 H, exchanged with D$_2$O, OH), 3.28 (0.5 H, 2-CH), 3.76 and 3.81 (3 H, s, CO$_2$Me), 4.40 and 4.68 (1 H, 4-CH), 7.11—7.94 (4 H, aromatic H), and 12.18 (0.5 H, s, exchanged with D$_2$O, enol) (Found: *M*$^+$, 234.089 9. C$_{13}$H$_{14}$O$_4$ requires *M*, 234.089 2).

4-Hydroxy-2,3-bismethoxycarbonyltetralone (18). Material from dimethyl fumarate was isolated as a viscous oil; ν$_{max.}$ 3 560—3 120, 1 740, 1 680, 1 650, 1 610, 1 600, and 1 570 cm^{-1}; δ (as a mixture of isomers) 3.39—3.82 (1 H, br s, exchanged with D$_2$O, OH), 3.52, 3.56, 3.68, 3.77, and 3.82 (6 H, s, CH$_2$Me), 3.80—4.26 (1.5 H, 2-CH and 3-CH), 5.04 (1 H, 4-CH), 7.18—7.94 (4 H, aromatic H), and 12.40 and 12.44 (0.5 H, exchanged with D$_2$O, enol) (Found: *M*$^+$, 278.079 1. C$_{14}$H$_{14}$O$_6$ requires *M*, 278.079 0).

Material obtained from dimethyl maleate was essentially the same as the latter product but contained only one enolic epimer; δ (mixture of keto and enol isomers) 2.85—3.24 (1 H, br s, exchanged with D$_2$O, OH), 3.58, 3.60, 3.78, 3.82, and 3.84 (6 H, s, CO$_2$Me), 3.75—4.22 (1.5 H, 2-CH and 3-CH), 5.04 (1 H, 4-CH), 7.11—8.00 (4 H, aromatic H), and 12.46 (0.5 H, exchanged with D$_2$O, enol) (Found: *M*$^+$, 278.078 4. C$_{14}$H$_{14}$O$_6$ requires *M*, 278.079 0).

2-Cyano-1-naphthol (7).—The tetralone (6) (170 mg, 0.91 mmol) was dissolved in trifluoroacetic acid (2 ml). After 20 min the reaction mixture solidified, chloroform was added, and the mixture filtered. The solid was dissolved in 0.5N sodium hydroxide, neutralised with hydrochloric acid, and extracted into dichloromethane. The organic phase was dried (Na$_2$SO$_4$) and evaporated to give the naphthol (113 mg, 74%), m.p. (methanol–benzene) 176—177 °C (lit.,[4] 178 °C).

Methyl 1-Hydroxy-3,4-dimethyl-2-naphthoate (11).—The tetralone (8) (152 mg) in dichloromethane (3 ml) was treated with boron trifluoride–ether (30 ml) at room temper-

ature for 15 min. The solution was poured into water (10 ml) and extracted with dichloromethane (3 × 7 ml). Work-up afforded the naphthoate (32 mg, 65%), m.p. (ethanol) 84—85 °C; $\lambda_{max.}$ 359 (ε 2 980), 309 (2 050), 296 (2 660), 285 (3 020), 263 (23 720), 255 (23 360), and 220 nm (27 310); $\nu_{max.}$ 3 500—3 000, 1 650, and 1 585 cm^{-1}; δ 2.50 (3 H, s), 2.58 (3 H, s), 3.96 (3 H, s), 7.32—7.68 (2 H, m), 7.96 (1 H, dd, J 3, 10 Hz), 8.42 (1 H, dd, J 2, 10 Hz), and 11.88, (1 H, s, exchanged with D$_2$O) (Found: M^+, 230.094 0. C$_{14}$H$_{14}$O$_3$ requires M, 230.094 2). When the preparation was repeated without isolation of the intermediate tetralone, the overall yield of naphthoate was 35%.

Methyl 1-Hydroxy-2-naphthoate (15).—The tetralone (14) (87 mg) in dichloromethane (3 ml) was treated with boron trifluoride–ether (2 drops) and the reaction mixture worked up as described above, after 15 min. The naphthoate had m.p. (ethanol) 76—77 °C (lit.,[6] 76—78 °C); δ 3.96 (3 H, s), 7.18—7.76 (4 H, m), 8.28—8.44 (1 H, m), and 11.82 (1 H, s, exchanged with D$_2$O).

Methyl 1-Hydroxy-3-methyl-2-naphthoate (17).—The tetralone (16) (180 mg) in dichloromethane (10 ml) was treated with boron trifluoride–ether (3 drops) at room temperature for 15 min before work-up in the normal manner. The naphthoate had m.p. (ethanol) 84—86 °C; $\lambda_{max.}$ 366sh (ε 3 200), 352 (3 800), 290 (3 570), 280 (4 350), 259 (33 690), 250 (30 520), and 217 nm (22 590); $\nu_{max.}$ (Nujol) 1 650 cm^{-1}; δ 2.53 (3 H, s), 3.90 (3 H, s), 6.96 (1 H, s), 7.22—7.52 (3 H, m), 8.20—8.32 (1 H, m), and 12.52 (1 H, s, exchanged with D$_2$O) (Found: C, 72.2; H, 5.5; C$_{13}$H$_{12}$O$_3$ requires C, 72.2; H, 5.6%).

Dimethyl 1-Hydroxynaphthalene-2,3-dicarboxylate (19).— The tetralone (18) (80 mg) was treated with boron trifluoride–ether (2 drops) in dichloromethane (3 ml) at room temperature for 15 min. Extraction, in the normal manner, gave the *ester* (62 mg, 82%), m.p. (ethanol) 102—108 °C; $\lambda_{max.}$ 355 (ε 5 630), 343 (5 630), 302 (2 750), 290 (4 120), 280 (4 550), 252sh (32 500), 249 (33 370), and 232 nm (28 600); $\nu_{max.}$ (Nujol) 3 400—3 000, 1 700, and 1 685 cm^{-1}; δ 3.88 (3 H, s), 3.92 (3 H, s), 7.36 (1 H, s, 4-CH), 7.42—7.70 (3 H, m), 8.22—8.38 (1 H, m, 8-CH), and 11.68 (1 H, s, exchanged with D$_2$O, enol) (Found: C, 64.2; H, 4.7%; M^+, 260.067 2. C$_{14}$H$_{12}$O$_5$ requires C, 64.6; H, 4.65%; M, 260.068 4). The tetralone from dimethyl maleate gave the identical naphthol to that from dimethyl fumarate.

Acetylation of the Tetralone (8).—The tetralone mixture (380 mg) was acetylated with acetic anhydride (3 ml) in pyridine (3 ml) for 16 h, then poured into water (10 ml) and extracted with dichloromethane. The extract was washed with water, dried (Na$_2$SO$_4$), and evaporated to dryness. The residue was separated by preparative t.l.c. [ether–light petroleum (7 : 3)] to afford, as the less-polar product, the monoacetates (9) (250 mg, 56%) as an oil; $\nu_{max.}$ 1 740 and 1 690 cm^{-1}, δ (mixture of isomers) 1.15 (6 H), 2.10 and 2.24 (3 H, MeCO), 3.76 and 3.80 (3 H, MeO), 3.60 and 4.00 (1 H, 2-CH), 5.96, 6.12 (1 H, 4-CH), 7.25—7.65 (3 H, m), and 8.00—8.14 (1 H) (Found: M^+, 290.115 6. C$_{16}$H$_{18}$O$_5$ requires M, 290.115 4). The diacetate (10) (76 mg, 15%) was isolated as a pale yellow oil; $\nu_{max.}$ 1 770, 1 725, and 1 600 cm^{-1}; δ 1.22 (3 H, s), 1.26 (3 H, s), 2.06 (3 H, s), 2.32 (3 H, s), 3.85 (3 H, s), 5.75 (1 H, s), and 7.25—7.44 (4 H, aromatic H) (Found: M^+, 332.125 7. C$_{18}$H$_{20}$O$_6$ requires M, 332.126 0).

When the monoacetate (9) (67 mg) was treated with ethane-1,2-dithiol (0.02 ml) and boron trifluoride–ether

(0.02 ml) in dichloromethane (3 ml) at room temperature for 15 min, work-up by pouring the mixture into saturated sodium hydrogencarbonate solution (15 ml) and extraction into dichloromethane gave the naphthoate (11) (13 mg, 25%) and the sulphide (12) (21 mg, 28%) as an oil. The latter, as a mixture of isomers, showed $\nu_{max.}$ 1 740 and 1 680 cm^{-1}; δ 1.24 (3 H, s), 1.34 (3 H, s), 1.67 (1 H, m, exchanged with D$_2$O), 2.60—2.85 (4 H, m), 3.82 (3 H, s), 3.96 (1 H, s), 4.18 (1 H, s), 7.25—7.52 (3 H, m), and 8.02—8.22 (1 H, m) (Found: M^+, 324.085 3. C$_{16}$H$_{20}$O$_3$S$_2$ requires M, 324.085 2).

Oxidation of Dimethyl 1-Hydroxy-1,4-dihydronaphthalene-2,3-dicarboxylate (2).—The dihydronaphthol[7] (252 mg) in benzene (10 ml) was stirred with manganese dioxide (1 g) for 12 h. The mixture was filtered and the filtrate, evaporated to small bulk, was subjected to preparative t.l.c. to give 2,3-bismethoxycarbonylnaphthalene (100 mg, 42%), m.p. 48—49 °C (lit.,[15] 49—50 °C), and 1,1'-*dihydroxy-2,2',-3.3'-tetrakismethoxycarbonyl-4,4'-binaphthyl* (21) (70 mg, 13%), m.p. (benzene) 240—246 °C (decomp.): $\nu_{max.}$ (Nujol) 1 730 and 1 665 cm^{-1}; δ (100 MHz) 3.45 (6 H, s), 3.96 (6 H, s), 7.20—7.72 (6 H, m), 8.50—8.65 (2 H, m), 13.00 (2 H, s, exchanged with D$_2$O) (Found: C, 65.1; H, 4.6%; M^+, 518.121 5. C$_{28}$H$_{22}$O$_{10}$ requires C, 64.9; H, 4.3%; M, 518.121 3).

Attempted oxidation of the naphthol (19) with manganese dioxide in benzene did not give the dimer (21).

3-(2,2-Dimethoxycarbonyl-1-methylethyl)phthalide (22).— Reaction between the lithium salt of phthalide (266 mg, 2 mmol), prepared using lithium di-isopropylamide (1 equiv.) as base in tetrahydrofuran (10 ml), and dimethyl ethylidene-malonate (316 mg, 2 mmol) in tetrahydrofuran (2 ml) at −40 °C for 2 h, followed by warming to room temperature over 1 h, afforded, after work-up and preparative t.l.c., the *title phthalide* (246 mg, 45%), as a mixture of isomers; $\nu_{max.}$ 1 755 and 1 730 cm^{-1}; δ 0.62 and 1.26 (3 H, Me), 2.82—3.16 (1 H, 1'-CH), 3.64, 3.68, 3.76, and 3.82 (7 H, 2 × CO$_2$Me and 2'-CH), 5.54 and 5.70 (1 H, 3-CH), and 7.37—7.95 (4 H, aromatic H) (Found: M^+, 292.094 4. C$_{15}$H$_{16}$O$_6$ requires M, 292.094 7).

3-(1,1-Dimethyl-3-oxobutyl)phthalide (23).—Reaction between the lithium salt of phthalide (268 mg, 2 mmol), prepared using lithium di-isopropylamide (1 equiv.) in tetrahydrofuran (20 ml), and mesityl oxide (196 mg, 2 mmol) at −40 °C for 1 h, and then warming to room temperature during 1 h afforded, after work-up, the *title phthalide* (95 mg, 20%) as a viscous yellow oil; $\nu_{max.}$ 1 725 and 1 685 cm^{-1}; δ 1.03 (3 H, s), 1.10 (3 H, s), 2.16 (3 H, s, CO$_2$Me), 2.48 and 2.90 (2 H, AB q, 2'-Me), 5.97 (1 H, s, 3-CH), 7.36—7.64 (3 H, m), and 7.98—8.15 (1 H, m) (Found: M^+, 232.110 2. C$_{14}$H$_{16}$O$_3$ requires M, 232.109 9).

4-Hydroxy-2-methoxycarbonyl-7-methoxy-3,3-dimethyl-tetralone (29).—6-Methoxyphthalide (24)[8] (164 mg, 1 mmol) in tetrahydrofuran (1 ml) was added to a solution of lithium di-isopropylamide (1 equiv.) in tetrahydrofuran (10 ml) at −40 °C. After 15 min methyl 3-methylcrotonate (114 mg, 1 mmol) in tetrahydrofuran (1 ml) was added and the solution left at −40 °C for 30 min, and then allowed to warm to room temperature during 1 h. Work-up in the normal manner followed by preparative t.l.c. [chloroform–methanol (97 : 3)] afforded the *title tetralone* (115 mg, 41%) as an oil; $\nu_{max.}$ 3 600, 3 225, 1 750, and 1 690 cm^{-1}; δ (an isomeric mixture) 1.08, 1.12, and 1.15 (6 H), 2.60—2.90 (1 H, s, exchanged with D$_2$O), 3.45 and 3.96 (1 H, 2-CH), 3.75 (3 H), 3.80 (3 H), 4.46 and 4.52 (1 H, 4-CH), and 7.00—

7.45 (3 H) (Found: M^+, 278.117 7. $C_{15}H_{18}O_5$ requires M, 278.115 4).

Methyl 1-*Hydroxy*-7-*methoxy*-3,4-*dimethyl*-2-*naphthoate* (30).—The tetralone (29) (80 mg) in dichloromethane (5 ml) was treated with boron trifluoride–ether (2 drops) at room temperature for 15 min. Work-up afforded the *naphthol* (30) (38 mg, 51%), m.p. (ether–light petroleum) 103—104 °C; $\lambda_{max.}$ 373 (ε 2 360), 296sh (5 910), 274 (18 900), and 238 nm (23 940); $\nu_{max.}$ 1 650 cm^{-1}; δ 2.44 (3 H, s), 2.48 (3 H, s), 3.90 (3 H, s), 3.96 (3 H, s), 7.14 (1 H, dd, J 3, 9 Hz), 7.60 (1 H, d, J 3 Hz), 7.72 (1 H, d, J 9 Hz), and 11.64 (1 H, s, exchanged with D_2O) (Found: C, 69.5; H, 6.2%; M^+, 260.104 7. $C_{15}H_{16}O_4$ requires C, 69.5; H, 5.8%; M, 260.105 5).

4-*Methoxyphthalide* (25).[9]—Hydrogen chloride gas was bubbled through a stirred solution of *m*-hydroxybenzoic acid (25 g), 40% formaldehyde solution (500 ml), concentrated hydrochloric acid (500 ml), and concentrated sulphuric acid (25 ml) at 30—40 °C for 2 h. The mixture was then cooled and the precipitate filtered to give 4-hydroxyphthalide (5.5 g), m.p. (water) 253—254 °C (lit.,[9] 254 °C). The filtrate was diluted with water and, after 20 h the precipitate collected to give the *phthalide* (26) (4.0 g), m.p. (H_2O) 177—179 °C; $\lambda_{max.}$ 304 (ε 1 780), 228sh (3 740), and 220 nm (5 520); $\nu_{max.}$ (Nujol) 1 740 cm^{-1}; $\delta[(CD_3)_2CO]$ 5.20 (2 H, s), 5.34 (4 H, s), 7.18 (1 H, d, J 8 Hz), and 7.46 (1 H, d, J 8 Hz) (Found: M^+, 192.042 2. $C_{10}H_8O_4$ requires M, 192.042 3).

4-Methoxyphthalide (25) was prepared according to the method of Buehler *et al.*[9] from 4-hydroxyphthalide; it had m.p. 125—126 °C (lit.,[9] 127 °C); $\lambda_{max.}$ 293 (ε 1 565), 233sh (3 615), and 220 nm (4 435); $\nu_{max.}$ 1 735 cm^{-1}; δ 3.90 (3 H, s), 5.22 (2 H, s), 6.98—7.14 (1 H, m), 7.34—7.52 (2 H, m).

Reactions of 4-*Methoxyphthalide* (*see Table* 2).—Condensations were carried out on a 2-mmol scale using the general method described above. Dehydrations of the hydroxytetralones were achieved using boron trifluoride–ether in dichloromethane.

(a) *Methyl* 3-*methylcrotonate*. The tetralone (31) was isolated as a viscous yellow oil; $\nu_{max.}$ 3 620—3 250, 1 740, 1 685, and 1 585 cm^{-1}; δ 1.08 (3 H, s), 1.24 (3 H, s), 2.90—3.18 (1 H, br s, exchanged with D_2O), 3.76 (3 H, s), 3.86 (3 H, s), 4.10 (1 H, s, 2-CH), 4.78 (1 H, s, 4-CH), 7.06 (1 H, d, J 7.5 Hz), 7.28 (1 H, t, J 7.5 Hz), 7.50 (1 H, d, J 7.5 Hz) (Found: M^+, 278.116 1. $C_{15}H_{18}O_5$ requires M, 278.115 4). Dehydration afforded *methyl* 1-*hydroxy*-5-*methoxy*-3,4-*dimethyl*-2-*naphthoate* (32), m.p. (ethanol) 93—94 °C; $\lambda_{max.}$ 371 (ε 2 310), 347sh (1 880), 313 (2 780), 301 (2 710), 299 (2 600), 21 (21 670), and 222 nm (3 322); $\nu_{max.}$ (Nujol) 1 650 and 1 585 cm^{-1}; δ 2.40 (3 H, s), 2.60 (3 H, s), 3.77 (3 H, s), 3.86 (3 H, s), 6.78 (1 H, d, J 7.5 Hz), 7.17 (1 H, t, J 7.5 Hz), 7.88 (1 H, d, J 7.5 Hz), and 11.40 (1 H, exchanged with D_2O) (Found: M^+, 260.105 5. $C_{15}H_{16}O_4$ requires M, 260.104 9).

(b) *Methyl crotonate*. The tetralone (33) was isolated as a viscous oil; $\nu_{max.}$ 3 620—3 160, 1 730, 1 680, 1 645, and 1 580 cm^{-1} (Found: M^+, 264.096 9. $C_{14}H_{16}O_5$ requires M, 264.099 7). Dehydration gave *methyl* 1-*hydroxy*-5-*methoxy*-3-*methyl*-2-*naphthoate* (34), m.p. (ether–light petroleum) 154—155 °C; $\lambda_{max.}$ 370sh (ε 3 540), 362 (3 840), 307 (3 075), 294 (2 950), 282 (3 010), 252 (33 820), and 218 nm (13 230);

$\nu_{max.}$ 1 645 and 1 580 cm^{-1}; δ 2.62 (3 H, s), 3.94 (6 H, s), 6.81 (1 H, d, J 7.5 Hz), 7.24 (1 H, t, J 7.5 Hz), 7.40 (1 H, s), 7.82 (1 H, d, J 7.5 Hz), and 11.40 (1 H, s, exchanged with D_2O) (Found: C, 68.3; H, 5.7; $C_{14}H_{14}O_4$ requires C, 68.3; H, 5.7%).

(c) *Dimethyl maleate*. The tetralone (35) was isolated as a viscous oil; $\nu_{max.}$ 3 600—3 200, 1 735, 1 690, 1 655, 1 630, and 1 580 cm^{-1} (Found: M^+, 308.091 0. $C_{15}H_{16}O_7$ requires M, 308.089 6). Dehydration of the tetralone afforded *dimethyl* 1-*hydroxy*-5-*methoxynaphthalene*-2,3-*dicarboxylate* (36), m.p. (ether–light petroleum) 106—107 °C; $\lambda_{max.}$ 366 (ε 4 930), 354 (5 110), 310 (3 010), 299 (2 610), 249 (38 060), and 224 nm (34 440); $\nu_{max.}$ (Nujol) 1 725 and 1 665 cm^{-1}; δ 3.88 (3 H, s), 3.92 (6 H, s), 6.90 (1 H, d, J 7.5 Hz), 7.38 (1 H, t, J 7.5 Hz), 7.78 (1 H, s), 7.86 (1 H, d, J 7.5 Hz), and 11.58 (1 H, s, exchanged with D_2O) (Found: C, 62.0; H, 4.9; $C_{15}H_{14}O_6$ requires C, 62.0; H, 4.9%).

(d) *Crotonolactone*. The tetralone (37) was isolated as an amorphous solid, m.p. 164—166 °C; $\nu_{max.}$ (Nujol) 3 450—3 120, 1 760, 1 655, and 1 585 cm^{-1}; $\delta[(CD_3)_2CO]$ 2.98—3.30 (2 H, m), 3.68—3.80 (1 H, m), 3.90 (3 H, s), 4.36—4.66 (2 H, m), 5.40 (1 H, m), and 7.20—7.48 (3 H, m) (Found: M^+, 248.068 3. $C_{13}H_{12}O_5$ requires M, 248.068 5). Dehydration, using neat trifluoroacetic acid, afforded 1-*hydroxy*-3-*hydroxymethyl*-5-*methoxy*-2-*naphthoic acid* 2,3-*lactone* (28), m.p. (chloroform–light petroleum) 205—206 °C; $\nu_{max.}$ 3 400 and 1 728 cm^{-1}; δ 4.08 (3 H, s), 5.50 (2 H, s), 7.09 (1 H, d, J 8 Hz), 7.56 (1 H, t, J 8 Hz), 7.86 (1 H, s), 8.03 (1 H, d, J 8 Hz), and 8.60 (1 H, s, exchanged with D_2O) (Found: M^+, 230.058 3. $C_{13}H_{10}O_4$ requires M, 230.057 9).

REFERENCES

[1] P. Dieckman, *Ber.*, 1914, **47**, 1439; R. L. Horton and K. C. Murdock, *J. Org. Chem.*, 1960, **25**, 938; H. Zimmer and R. D. Barry, *J. Org. Chem.*, 1964, **29**, 3070.
[2] W. von Trueb and C. H. Eugster, *Helv. Chim. Acta*, 1972, **55**, 969; A. von Braun and C. H. Eugster, *Helv. Chim. Acta*, 1972, **55**, 974.
[3] *cf.* A. S. Kende, J. Belletine, T. J. Bentley, E. Hume, and J. Airey, *J. Amer. Chem. Soc.*, 1975, **97**, 4425.
[4] J. A. McRae and L. Merion, *Canad. J. Res.*, 1937, **15B**, 480.
[5] R. S. Desai, K. S. Ratha, and R. C. Shah, *Proc. Ind. Acad. Sci.*, 1946, **23A**, 187.
[3] ' Dictionary of Organic Compounds,' eds. I. Heilbron and H. M. Bunbury, Eyre and Spottiswoode Ltd., London, 1965.
[7] B. J. Arnold, S. M. Mellows, P. G. Sammes, and T. W. Wallace, *J.C.S. Perkin I*, 1974, 401.
[8] S. N. Chakravarti and W. H. Perkin, *J. Chem. Soc.*, 1929, 196.
[9] C. A. Buehler, J. A. Powers, and J. G. Michels, *J. Amer. Chem. Soc.*, 1944, **66**, 417.
[10] N. J. P. Broom and P. G. Sammes, *J.C.S. Chem. Comm.*, 1978, 162.
[11] G. A. Kraus and H. Sugimoto, *Tetrahedron Letters*, 1978, 2263.
[12] F. M. Hauser and R. P. Rhee, *J. Org. Chem.*, 1978, **43**, 178.
[13] F. J. Leeper and J. Staunton, *J.C.S. Chem. Comm.*, 1978, 406.
[14] P. G. Sammes and D. J. Dodsworth, *J.C.S. Chem. Comm.*, 1979, 33.
[15] S. M. Mellows, Ph.D. Thesis, University of London, 1970.