Lead(IV) Ester and Electrochemical Oxidations of Phenolic Compounds: a Comparative Study

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Oxidation of 3-acetyl-1-propyl-5,6,7,8-tetrahydro-2-naphthol (**6**) with lead(IV) acetate or lead(IV) benzoate is shown to produce almost entirely the *o*-quinol esters, (**8**) and (**20**), respectively. By contrast, electrochemical oxidation of (**6**) in acetic acid at a platinum anode leads largely to the corresponding *p*-quinol acetate (**7**) in addition to (**8**), and also to other products [(**10**) and (**11**)]. Structure (**8**) was assigned unambiguously from a two-dimensional homonuclear shift-correlated ^{13}C spectrum obtained by using a symmetrised INADEQUATE program, and an *X*-ray crystal structure determination was carried out on the benzoate (**20**). Treatment of the *o*-quinol acetate (**8**) with acetic anhydride containing sulphuric acid leads to the diacetate (**9a**), whereas dissolution of the *p*-quinol acetate (**7**) in dichloromethane containing ethanolic sulphuric acid produces the phenol (**12**). Saponification of either (**12**) or (**9a**) gives the 2′,6′-dihydroxyacetophenone (**9b**), a useful precursor to proxicromil (**2**).

Derivatives of 5-hydroxy-4-oxo-4*H*-1-benzopyran-2-carboxylic acid, *e.g.* sodium chromoglycate (**1**) (INTAL †) and proxicromil (**2**), are well known anti-allergic compounds used for the prophylactic treatment of asthma.[1] The 2-carboxychromone moieties in molecules like (**1**) and (**2**) are conveniently synthesized from the corresponding 2′-hydroxyacetophenones by Claisen condensations with diethyl oxalate and acid-catalysed cyclisations [*viz.* (**3**) ⟶ (**4**) ⟶ (**5**)]. A popular and attractive route to 2′,6′-dihydroxyacetophenones (**3**) involves oxidation of a 2′-hydroxyacetophenone using lead(IV) acetate (LTA),[2] followed by Thiele rearrangement of the resulting quinol acetate[3] and saponification, *i.e.* (**6**) ⟶ (**7**)/(**8**) ⟶ (**9a**) ⟶ (**9b**). The oxidations of phenols by LTA and related oxidants,[4] however, are not without practical difficulties (*e.g.* lead residues), and their regiospecificities (*i.e. o- versus p*-acetoxylations) are not always predictable.[2] In connection with investigations of a synthesis of the 2′,6′-dihydroxyacetophenone precursor (**9b**) of proxicromil (**2**) we have examined the specificities of acetoxylations of the phenol (**6**), using both LTA and an electrochemical procedure.[5]

Treatment of the 2′-hydroxyacetophenone (**6**), easily available from 5,6,7,8-tetrahydro-2-naphthol (Scheme 1),[6] with LTA in dichloromethane at room temperature resulted in smooth acetoxylation to one major quinol acetate which was isolated as a viscous oil in 90% yield; a minor (< 5%) isomeric quinol acetate was also separated by chromatography. By contrast, when a solution of (**6**) in glacial acetic acid containing tetrabutylammonium acetate was electrolysed at a platinum anode (1.0 V *versus* saturated calomel electrode), chromatography resulted in the separation of four principal products (combined yield *ca.* 87%), the least of which showed spectroscopic data identical with those of the major quinol acetate derived from the LTA oxidation of (**6**). The constitutions of the two additional minor products resulting from anodic acetoxylation of (**6**) were shown to be (**10**) and (**11**), but the major product had spectral data identical with those of the minor quinol acetate produced in the LTA oxidation.

A clue to the constitutions of the isomeric quinol acetates produced in the anodic and LTA oxidations was obtained from inspection of their u.v. absorption data. Thus, whereas the major product from the LTA oxidation of (**6**) showed an extended conjugation absorption maximum at 339 nm (ε 7 300) the major, isomeric quinol acetate from the corresponding anodic acetoxylation exhibited a weaker absorption (ε 3 600) at much shorter wavelength ($\lambda_{max.}$ 278 nm). These data alone led us to the tentative assignments of structures (**8**) and (**7**) for the principal products of the LTA and anodic oxidations, respectively. The assignments were supported by chemical investigation, together with data from detailed n.m.r. studies.

Thus, treatment of the *p*-quinol acetate (**7**) with sulphuric acid in dichloromethane led to the product (**12**) of simple dienone–phenol rearrangement, whereas similar treatment of the *o*-quinol acetate (**8**) instead produced the benzylic acetate (**15**), presumably *via* the triene intermediate (**14**). Dissolution of (**8**) in acetic anhydride containing a few drops of concentrated sulphuric acid gave rise to the diacetoxyacetophenone (**9a**), which could be correlated with (**12**). Thus, depending on

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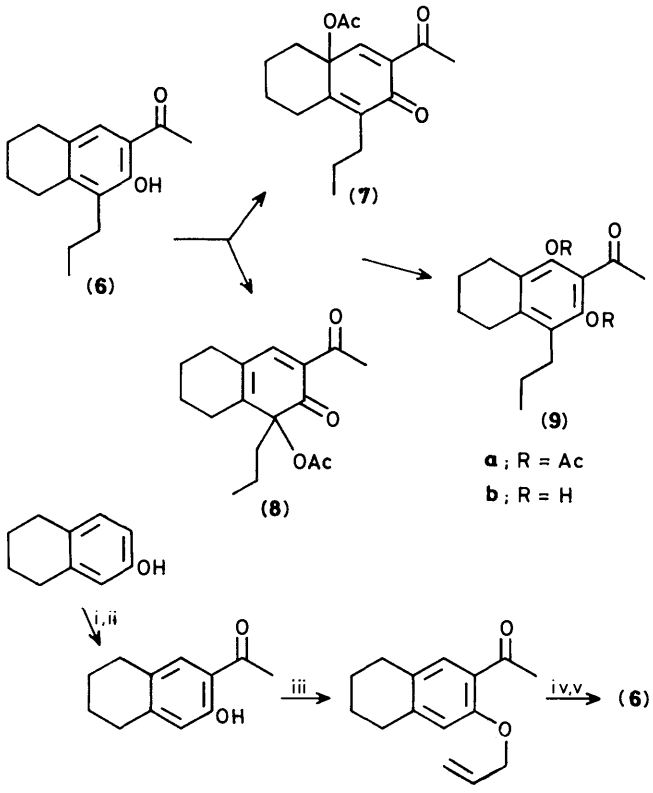
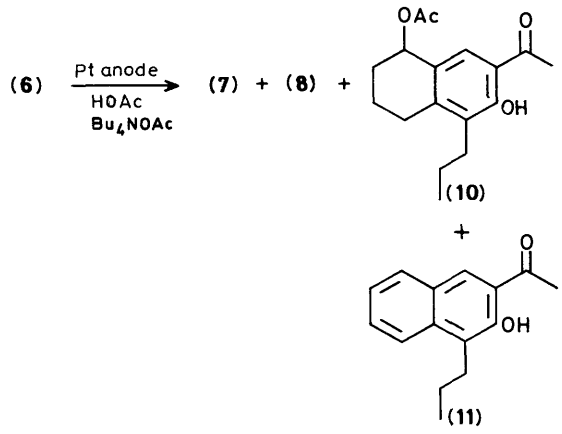
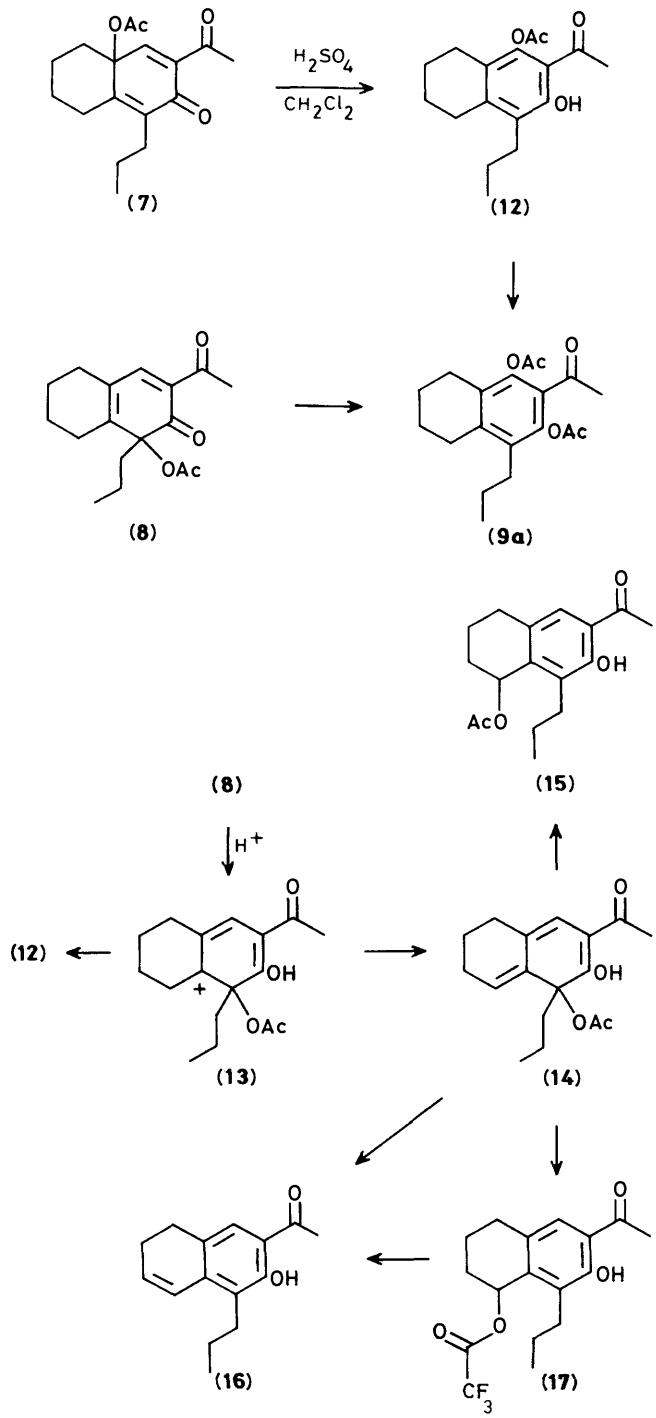


Scheme 1. *Reagents:* i, Ac_2O, H_2SO_4; ii, $AlCl_3$, NaCl, 170 °C; iii, $CH_2{=}CHCH_2Br$, K_2CO_3, Me_2NCHO; iv, heat; v, Pd–C, H_2



conditions, either of the *p*- and *o*-quinol acetates (**7**) and (**8**) can be used to access the bisacetate (**9a**), and hence the target 2′,4′-dihydroxyacetophenone (**9b**).

The constitutions of the products, summarised in Scheme 2, resulting from the reaction between the *o*-quinol acetate (**8**) and trifluoroacetic acid (TFA) proved especially illuminating, and provided the final necessary correlations to suppport the assignment of the two structures (**7**) and (**8**). The acetate (**12**) produced on treatment of (**8**) with TFA is presumably derived from the cation (**13**) by three 1,2-acetate shifts in an extended dienone–phenol rearrangement (see foregoing discussion), whereas the dihydronaphthalene (**16**) could be formed from (**14**) by a 1,4-elimination of acetic acid. The formation of (**17**) from (**14**) is most likely the result of an acid-promoted S_N1' or S_N2' reaction; this transformation is similar to the change (**14**) ⟶



Scheme 2.

(**15**) for which an S_Ni' mechanism is also available. On boiling the trifluoroacetate (**17**) in xylene for 6 h, the dihydronaphthalene (**16**) was secured in good yield. In addition, hydrolysis of (**17**), followed by treatment of the resulting carbinol with acetyl chloride, afforded the acetate (**15**). These experiments thus fully correlated the substitution patterns in (**15**), (**16**), and (**17**).

Although the n.m.r. data for the isomeric quinol acetates (**7**) and (**8**) showed many features in common, significant differences were observed in the chemical shifts associated with the acetoxy portions in the two isomers, *viz.* δ_H 2.08 (**7**) and 2.14

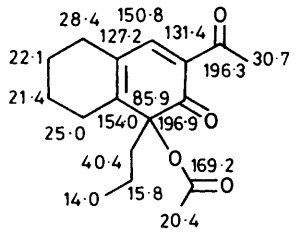
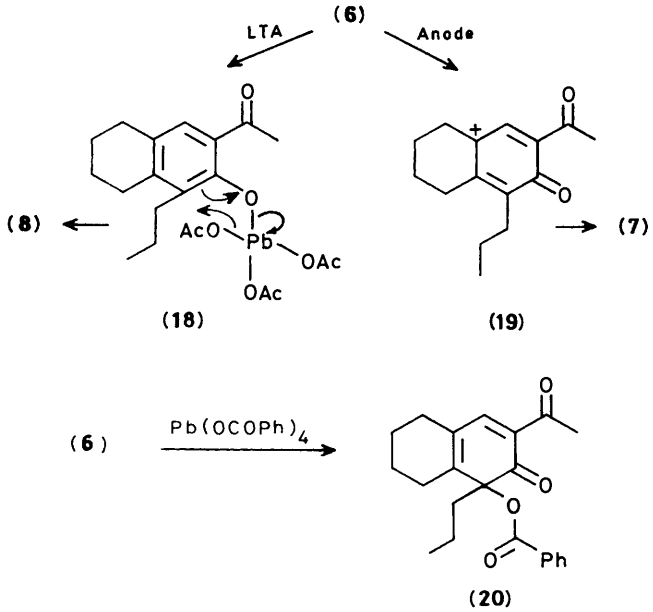


Figure 1. ^{13}C Shifts for structure (**8**)



(**8**) ($OCOCH_3$); δ_C 75.6 (**7**) and 85.9 (**8**) (*C*OAc), and also in the chemical shifts of their olefinic hydrogen atoms, δ_H 7.27 (**7**) and 7.56 (**8**). A two-dimensional (2D) heteronuclear (^{13}C–^1H) correlation spectrum of the *o*-quinol acetate (**8**), which was optimised for one-bond couplings, proved that the methylene carbon (δ 40.4) was directly bonded to the two hydrogen atoms with resonances at δ 1.89 and 1.71. Furthermore the observed non-equivalence of these two hydrogen atoms in the ^1H n.m.r. spectrum supported their proximity to the chiral centre. From the n.m.r. point of view, however, the most obvious difference between the isomeric acetates (**7**) and (**8**) was that whereas in (**7**) the *C*–OAc centre and the =C*H* are separated by only two bonds, in (**8**) the same atoms are separated by four bonds. For this reason we recorded two 2D heteronuclear correlation spectra, for (**8**), with input parameters which corresponded to J_{CH} values of 8 and 10 Hz. Although not all the expected correlations were present in either spectrum, there was a correlation of *C*–OAc and CH_2Et which favoured (**8**) over the alternative structure (**7**).

Finally, definitive evidence in favour of the assignment of structure (**8**) was obtained from a 2D homonuclear shift-correlated ^{13}C n.m.r. spectrum produced using a symmetrised INADEQUATE program. After an acquisition time of 60 h on a saturated solution of the sample in $CDCl_3$, we obtained a set of one-bond correlations which defined the connectivity shown in Figure 1. In particular, the quaternary carbon centre (δ 85.9) was shown to be directly bonded to the carbonyl carbon (δ 196.9), the olefinic carbon (δ 154.0), and the methylene carbon of the propyl side-chain (δ 40.4). All the expected correlations were present, and none was left unaccounted for.

The regioselectivities observed in the acetoxylations of (**6**) by LTA and by the electrochemical procedure are to some measure consistent with literature precedent. Thus, the *o*-quinol acetate (**8**) is probably produced from the LTA oxidation of (**6**) by a two-electron oxidation involving an intramolecular displacement *via* the aryloxy-lead derivative (**18**). Likewise, the predominant formation of the *p*-quinol acetate, (**7**) from electrochemical oxidation of (**6**) can be ascribed to a field effect at the anode which favours the localisation of the positive charge in the cyclohexadienyl cation intermediate (**19**) at the carbon centre *para* to the carbonyl group.

As a corollary to our studies we also examined the reaction between the phenol (**6**) and lead tetrabenzoate.[7] This oxidation led to a single, highly crystalline quinol ester, m.p. 88.5—89.5 °C, the n.m.r. chemical shift data of which [*i.e.* δ_C 86.3 (*C*OCOPh)] correlated with the *o*-quinol acetate structure (**8**). This assignment (**20**) to the benzoate was confirmed by an *X*-ray crystallographic analysis.

Experimental

Light petroleum (the fraction of b.p. 40—60 °C) was distilled before use. Solutions of products in organic solvents were dried over magnesium sulphate. Fluka Kieselgel G was used for column chromatography, and Fluka HF_{254} silica gel for t.l.c. M.p.s were determined with a Reichert Kofler micro hot stage. U.v. spectra were obtained for ethanolic solutions using either a Unicam SP800 or a Philips PU8720 spectrophotometer. I.r. spectra were recorded for chloroform solutions with a Perkin-Elmer 710B or a Pye Unicam SP3-100 instrument. Solutions in deuteriochloroform, with tetramethylsilane as internal standard, were used for the determination of n.m.r. spectra; routine ^1H spectra were recorded with a Perkin-Elmer R32 or a Bruker WP80SY instrument; other ^1H and ^{13}C n.m.r. spectra were obtained with a Bruker WM250 or an AM400 spectrometer. Shifts are expressed in p.p.m. downfield from Me_4Si. Accurate mass measurements in mass spectra were determined with a VG Micromass 7070E instrument.

Electrochemistry: General Procedure.—The electrolyses were performed in a standard **H**-cell equipped with ground glass joints and divided by a fine glass sinter. The platinum anode comprised a 4 × 7 mm piece of foil fused to a platinum wire. The stainless steel cathode measured *ca.* 8 × 30 mm. The cell potentials were maintained by a Hi-Tek DT2101 potentiostat, and were measured against a silver–silver perchlorate reference electrode; they are reported relative to a standard calomel electrode. The electrolysis solutions were stirred magnetically, and all experiments were conducted at room temperature.

3-*Acetyl*-1-*propyl*-5,6,7,8-*tetrahydro*-2-*naphthol* (**6**).—The naphthol was prepared from 5,6,7,8-tetrahydro-2-naphthol, according to Scheme 1.[6]

1-*Acetoxy*-3-*acetyl*-1-*propyl*-5,6,7,8-*tetrahydronaphthalen*-2(1H)-*one* (**8**).—A solution of 3-acetyl-1-propyl-5,6,7,8-tetrahydro-2-naphthol (2 g, 8.6 mmol) in dry dichloromethane (40 ml) was added to a slurry of LTA (5.8 g, 13.1 mmol) in dry dichloromethane (40 ml). The mixture was stirred at 25 °C for 1.5 h, and then the solids were removed by filtration. The filtrate was extracted with saturated aqueous sodium hydrogen carbonate (2 × 10 ml) and water (10 ml), and then dried. Evaporation under reduced pressure left a bright yellow oil (2.2 g, 90%) which solidified to produce the naphthalenone, m.p. 48—52 °C; $\lambda_{max.}$(EtOH) 235 (ε 5 950), 339 (6 200), 392infl nm (1 480); $\nu_{max.}$ 2 920, 2 870, 1 730, 1 677, 1 637, 1 543, and 1 360 cm^{-1}. The n.m.r. spectroscopic properties of the naphthalenone were investigated in detail, and the following procedures were

employed in obtaining the relevant data: (*a*) 400 MHz ^1H spectrum and 2D homonuclear shift-correlated spectrum for ^1H couplings using the COSY microprogram; (*b*) 100.6 MHz ^{13}C spectrum and the DEPT sequence to determine C/H multiplicities, homonuclear shift correlated spectra for ^{13}C one-bond couplings using INADEQ (1D) and INADSYM (2D) icroprograms; (*c*) 2D heteronuclear ($^{13}C/^1H$) shift-correlated spectra using the XHCORR microprogram; three spectra were obtained with different delays which were determined by the input J_{CH} values [140 Hz (for one-bond couplings), and 10 and 8 Hz (for two- and three-bond couplings)]. δ_H* 0.86 (t, *J* 7.3 Hz, 3 × 11-H), 1.14—1.25 (m, 10a-H), 1.23—1.33 (m, 10b-H), 1.65—1.73 (m, 2 × 6-H plus 2 × 7-H), 1.69—1.77 (part obscured ddd, J^2 11.9 Hz, 9a-H), 1.83—1.90 (ddd, J^2 11.9 Hz, 9b-H), 2.05—2.10 (m, 8a-H), 2.14 (3 × 13-H), 2.18—2.22 (m, 8b-H), 2.30—2.38 (m, 2 × 5-H), 2.49 (3 × 15-H), and 7.56 (4-H); δ_C see Figure 1 (Found: C, 70.3; H, 7.95%; *m/z*, 290.1504. $C_{17}H_{22}O_4$ requires C, 70.3; H, 7.6%; *M*, 290.1516).

Anodic Oxidation of 3-*Acetyl*-1-*propyl*-5,6,7,8-*tetrahydro*-2-*naphthol* (**6**).—The platinum anode and the stainless steel cathode were placed in the electrolysis cell containing a solution of tetrabutylammonium acetate (1.20 g, 4 mmol) in glacial acetic acid (40 ml) and the naphthol (**6**) (101 mg, 0.4 mmol) was then dissolved in the anolyte. Electrolysis was carried out at an anode potential of 1.00 V for 8 h, and the glacial acetic acid was then removed under reduced pressure. The residue was dissolved in water (20 ml) and the solution was then extracted with light petroleum (3 × 20 ml). The combined extracts were dried, filtered, and evaporated to leave a viscous yellow oil (110 mg). Chromatography on silica gel (10 g) [light petroleum–ether (10:1 v/v) as eluant] afforded the following.

(i) 5-*Acetoxy*-3-*acetyl*-1-*propyl*-5,6,7,8-*tetrahydro*-2-*naphthol* (**10**) (eluted first) (5.7 mg, 5%) as a bright yellow solid, m.p. 58—60 °C; $\lambda_{max.}$(EtOH) 222 (ε 1 650), 253 (2 810), and 303 nm (445); $\nu_{max.}$ 2 950, 1 730, 1 640, 1 375, and 1 245 cm^{-1}; δ_H 1.00 (t, *J* 7 Hz, CH_2CH_3), 2.09 ($OCOCH_3$), 2.63 ($COCH_3$), 1.20—3.00 (m, 5 × CH_2), 6.04 (br t, CHOAc), 7.68 (=CH), and 12.66 (OH); δ_C 14.5 (CH_2CH_3), 17.9, 21.6, 21.8, 26.5, 26.7, 27.3, 28.5, 70.3 (*C*–OAc), 117.6, 125.4, 129.7, 130.4, 145.3, 160.0, 170.8 ($OCOCH_3$), and 204.4 ($COCH_3$); *m/z* 290 (10.5%), 230 (95), and 201 (64) (Found: *m/z*, 290.1509. $C_{17}H_{22}O_4$ requires *M*, 290.1518).

(ii) 3-*Acetyl*-1-*propyl*-2-*naphthol* (**11**) (eluted second) (4.8 mg, 5%) as a yellow solid, m.p. 62—63.5 °C; $\lambda_{max.}$(EtOH) 222 (ε 29 400), 250infl (41 100), 255 (42 200), 262infl (35 400), 287infl (5 820), 295 (8 300), 306 (8 100), and 400br nm (2 140); $\nu_{max.}$ 3 050br, 2 925, 2 870, 1 637, 1 570, 1 310, 1 146, 1 100, 948, and 887 cm^{-1}; δ_H 1.05 (t, *J* 7 Hz, CH_2CH_3), 1.69 (*ca.* quint, CH_2CH_3), 2.83 ($COCH_3$), 3.10 (*ca.* dd, $ArCH_2$), 7.28—7.46 (m, ArH), 7.55—7.75 (m, ArH), 7.85—8.05 (m, 2 × ArH), 8.33 (4-H), and 11.97 (OH); *m/z* 228 (41%), 199 (100), and 181 (34) (Found: C, 79.0; H, 7.2%; *m/z*, 228.1158. $C_{15}H_{16}O_2$ requires C, 78.9; H, 7.1%; *M*, 228.1150). The compound was identical with the product formed from dehydrogenation of (**6**) by 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (procedure as for the dehydrogenation of tetralin).[8]

(iii) An unresolved 5:2 mixture of the quinol acetates (**7**) and (**8**) (*ca.* 40%) (eluted third). The isomers were separated by h.p.l.c. on a Waters Associates liquid chromatograph using a silica Rad Pak in a RCM 100 column (8 × 100 mm; 10 μm particle size), eluted with light petroleum–ether (u.v. detection). This gave (a) 4a-*acetoxy*-3-*acetyl*-1-*propyl*-5,6,7,8-*tetrahydro*-*naphthalen*-2(4aH)-*one* (**7**), as pale yellow oil; $\lambda_{max.}$(EtOH) 246infl (ε 5 690), 278infl (3 630), and 320infl nm (880); $\nu_{max.}$ 2 910, 2 860, 1 740, 1 690, 1 650, and 1 360 cm^{-1}; δ_H 0.93 (t, *J* 7 Hz, CH_2CH_3), 1.26 (2 H, *ca.* td), 1.40 (2 H, *ca.* sextet, CH_2CH_3), 1.7 (2 H, br m), 1.90 (1 H, *ca.* tt), 2.08 ($OCOCH_3$), 2.0—2.15 (1 H, m), 2.33—2.5 (3 H, m), 2.55 ($COCH_3$), 2.75—2.82 (1 H, m), and 7.27 (=CH); δ_C 14.1 (CH_2CH_3), 20.5 (CH_2), 21.1 ($O{\cdot}COCH_3$), 22.7 (CH_2), 26.9 (CH_2), 27.6 (CH_2), 27.9 (CH_2), 30.9 ($COCH_3$), 39.7 (CH_2Et), 75.6 (C-4a), 134.6 (C-1 or -3), 137.6 (C-1 or -3), 151.2 (C-4), 153.8 (C-8a), 168.9 (OCO), 183.2 ($COCH_3$), and 198.9 (C-2); *m/z* 290 (2%), 248 (26), 232 (33), 206 (85), and 178 (100) (Found: *m/z*, 290.1521. $C_{17}H_{22}O_4$ requires *M*, 290.1518); and (b) 1-*acetoxy*-3-*acetyl*-1-*propyl*-5,6,7,8-*tetrahydronaphthalen*-2(1H)-*one* (**8**), which showed chromatographic and spectroscopic data identical with those of the compound produced on treatment of (**6**) with LTA.

Table 1. Progressive additions of acid to the *p*-quinol acetate (**7**)

t/min	Acid solution	No. drops added
0	10 ml EtOH, 1 drop conc. H_2SO_4	1
20	10 ml EtOH, 1 drop conc. H_2SO_4	1
51	10 ml EtOH, 5 drops conc. H_2SO_4	1
60	10 ml EtOH, 10 drops conc. H_2SO_4	1
70	10 ml EtOH, 20 drops conc. H_2SO_4	1
80	EtOH–H_2SO_4 10:1 v/v	1
90	conc. H_2SO_4	1
100	conc. H_2SO_4	1

Rearrangement of the p-*Quinol acetate* (**7**) *by Acid into the Acetoxynaphthol* (**12**).—The *p*-quinol acetate (**7**) (2.0 mg, 0.007 mmol) was dissolved in dichloromethane (2 ml) that had previously been saturated with water. The acid-catalysed rearrangement was monitored by t.l.c. analysis as progressively larger amounts of sulphuric acid were added to the stirred solution, as indicated in Table 1. After 110 min the mixture was extracted with saturated brine (2 × 2 ml) and water (2 ml). The organic phase was dried and filtered, and the solvent removed under reduced pressure to give the pale yellow crystalline acetoxynaphthol (**12**) (1.2 mg, 60%). The ^1H n.m.r. spectrum was identical with that obtained for material prepared from the *o*-quinol acetate (**8**) (see later).

Rearrangement of the o-*Quinol Acetate* (**8**) *by Acid into the Acetoxynaphthol* (**15**).—Concentrated sulphuric acid (2 drops) and ethanol (1 drop) were added to a stirred solution of the *o*-quinol acetate (**8**) (40 mg, 0.14 mmol) in dichloromethane (40 ml). The mixture was stirred for 15—20 min, and then one further drop of concentrated sulphuric acid was added. After a total of 65 min the solution had attained a deep orange colour, and at this point it was extracted with saturated brine (2 × 30 ml) and with water (30 ml). The separated organic phase was dried and filtered, and the solvent was then removed under reduced pressure. The residue was purified by preparative t.l.c. [light petroleum–ether (5:1 v/v)] to give the crystalline acetoxynaphthol (**15**) (10.9 mg, 27%), m.p. 107—109 °C, which showed spectroscopic data identical with those of an authentic sample (see later).

Rearrangement of the o-*Quinol Acetate* (**8**) *by Sulphuric Acid and Acetic Anhydride* (*Thiele Conditions*) *into* 2-*Acetyl*-1,3-*diacetoxy*-4-*propyl*-5,6,7,8-*tetrahydronaphthalene* (**9a**).—A solution of the acetoxynaphthalen-2(1*H*)-one (**8**) (1.39 g, 4.79 mmol) in acetic anhydride (3.8 ml) was added to a solution of concentrated sulphuric acid (0.1 ml) in acetic anhydride (0.4 ml). The mixture was stirred at 25 °C for 0.75 h and then poured

* Hydrogen atoms are numbered according to the carbon atoms to which they are attached. The *carbon* atoms of the side-chains are numbered as follows: $-CH_2CH_2CH_3$ C-9, C-10, and C-11, respectively; $-OCOCH_3$ C-12 and C-13; $-COCH_3$ C-14 and C-15.

onto ice–water and stirred for a further 1 h. The precipitate was filtered off and recrystallised from ethanol to give the *resorcinol diacetate* (0.38 g, 25%) as colourless crystals, m.p. 102.5—103.5 °C; $\nu_{max.}$(CHCl$_3$) 1 755, 1 688, and 1 600 cm^{-1}; δ_H 0.97 (t, *J* 7.3 Hz, CH_2CH_3), 1.45 (2 H, *ca.* sext, CH_2CH_3), 1.75 (4 H, m), 2.26 (6 H, 2 × OCO*Me*), 2.40 (3 H, COMe), 2.42 (2 H, m), 2.53 (2 H, t, *J* 6 Hz), and 2.72 (2 H, t, *J* 6 Hz); δ_C 14.6 (q), 20.6 (q), 20.7 (q), 21.7 (t), 22.2 (t), 22.5 (t), 23.7 (t), 26.8 (t), 28.7 (t), 30.8 (q), 125.9, 128.5, 131.6, 140.0, 143.2, 143.7, 168.4, 169.2, and 199.0 (Found: C, 68.7; H, 7.5%; *m/z*, 332.1602. $C_{19}H_{24}O_5$ requires C, 68.7; H, 7.3%; *M*, 332.1621).

Saponification of the Diacetate (**9a**) *to* 2-*Acetyl*-4-*propyl*-5,6,7,8-*tetrahydronaphthalene*-1,3-*diol* (**9b**).—The resorcinol diacetate (**9a**) (0.2 g) was added to a degassed solution of aqueous sodium hydroxide (1 ml; 2M) in methanol (5 ml). The resulting mixture was stirred at 25 °C for 20 min and then poured into 0.3M hydrochloric acid (10 ml). The mixture was extracted with dichloromethane (3 × 10 ml), and the extracts were then evaporated to leave a yellow gum. Chromatography on silica [3:1 dichloromethane–light petroleum (b.p. 40—60 °C) and light petroleum–ether (10:1) as eluants], followed by crystallisation gave the resorcinol (0.09 g, 60%) as colourless crystals, m.p. 59—62 °C; $\lambda_{max.}$(EtOH) 279 (ε 11 000) and 363 nm (2 100); $\nu_{max.}$(CHCl$_3$) 3 590 and 1 623 cm^{-1}; δ_H 0.99 (t, *J* 7 Hz, CH_2CH_3), 1.3—1.7 (2 H, m), 1.7—1.95 (4 H, m), 2.4—2.9 (6 H, m), 2.75 (COMe), 8.89 (s, OH), and 10.1 (s, chelated OH); δ_C 14.5 (q), 22.2 (t), 22.4 (t), 22.4 (t), 22.6 (t), 22.7 (t), 27.1 (t), 27.6 (t), 33.6 (q), 108.1, 114.5, 118.5, 144.9, 156.2, 156.6, and 205.3 (Found: C, 72.4; H, 8.3%; *m/z*, 248.1408. $C_{15}H_{20}O_3$ requires C, 72.55; H, 8.1%; *M*, 248.1411).

Trifluoroacetic Acid-catalysed Rearrangement of the o-*Quinol Acetate* (**8**) *to Compounds* (**12**), (**16**), *and* (**17**).—A solution of 1-acetoxy-3-acetyl-1-propyl-5,6,7,8-tetrahydronaphthalen-2-(1*H*)-one (**8**) (0.50 g, 1.72 mmol) in dichloromethane (10 ml) was added to freshly distilled trifluoroacetic acid (7.04 g, 61.7 mmol). The resulting solution was stirred under nitrogen for 4 h, and then benzene (20 ml) was added. The solvents were removed under reduced pressure, and the residue was then taken up in benzene (30 ml); this solution was evaporated under reduced pressure to give a brown oil (0.55 g). Chromatography over silica gel (10 g) [light petroleum–ether (20:1 ⟶ 10:1 v/v) as eluant] afforded the following.

(i) 4-*Acetoxy*-3-*acetyl*-1-*propyl*-5,6,7,8-*tetrahydro*-2-*naphthol* (**12**) (eluted last) (80 mg, 16%) as a pale yellow solid, m.p. 94—96 °C; $\lambda_{max.}$(EtOH) 224 (ε 6 800), 272 (4 900), and 351 (12 570); $\nu_{max.}$ 1 750, 1 620, 1 365, and 1 110 cm^{-1}; δ_H 1.00 (t, *J* 7.2 Hz, CH_2CH_3), 1.3—1.85 (m, 3 × CH_2), 2.38 ($OCOCH_3$), 2.60 ($COCH_3$), 2.4—2.85 (3 × CH_2), and 12.98 (OH); δ_C 14.6 (CH_2CH_3), 21.2 ($OCOCH_3$), 21.8 (CH_2), 22.1 (CH_2), 22.5 (CH_2), 23.5 (CH_2), 27.5 (2 × CH_2), 31.8 ($COCH_3$), 115.0 (C-3), 120.45 (C-1 or -4a), 127.8 (C-4a or -1), 145.3 (C-4 or 8a), 146.9 (C-8a or -4), 159.3 (C-2), 168.9 ($OCOCH_3$), and 203.0 ($COCH_3$); *m/z* 290 (14%), 248 (66), and 219 (100) (Found: C, 71.1; H, 7.8%; *m/z*, 290.1494. $C_{17}H_{22}O_4$ requires C, 70.3; H, 7.6%; *M*, 290.1518).

(ii) 3-*Acetyl*-1-*propyl*-5,6-*dihydro*-2-*naphthol* (**16**) (eluted second) (22 mg, 6%) as a light yellow solid, m.p. 66.5—67.5 °C; $\lambda_{max.}$(EtOH) 226 (ε 12 080), 288infl, 300 (12 000), 307 (12 225), and 365 nm (2 990); $\nu_{max.}$ 1 625, 1 370, and 1 315 cm^{-1}; δ_H 0.99 (t, *J* 7 Hz, CH_2CH_3), 1.50 (m, CH_2CH_3), 2.30 (m, CH_2), 2.62 ($COCH_3$), 2.6—2.8 (m, 2 × CH_2), 6.35 (*ca.* dt, J_{cis} 10.6 Hz, 7-H), 6.80 (*ca.* dt, J_{cis} 10.6 Hz, 8-H), and 7.37 (4-H); *m/z* 230 (81%), 215 (34), 202 (19), and 201 (100) (Found: C, 78.1; H, 8.1%; *m/z*, 230.1302; $C_{15}H_{18}O_2$ requires C, 78.2; H, 7.9%; *M*, 230.1306).

(iii) 3-*Acetyl*-1-*propyl*-8-*trifluoroacetoxy*-5,6,7,8-*tetrahydro*-2-*naphthol* (**17**) (eluted first) (262 mg, 42%) as an off-white solid, m.p. 76.5—78.5 °C; $\nu_{max.}$ 1 770, 1 640, 1 575, 1 310, and 1 150 cm^{-1}; δ_H 0.98 (t, *J* 7 Hz, CH_2CH_3), 1.2—1.7 (3 H, m), 1.8—1.95 (3 H, m), 2.25—2.95 (4 H, m), 2.64 ($COCH_3$), 6.38 (*ca.* t, 8-H), 7.49 (4-H), and 12.37 (OH) (Found: C, 59.65; H, 5.5%; *m/z*, 344.1204. $C_{17}H_{19}F_3O_4$ requires C, 59.3; H, 5.6%; *M*, 344.1235).

6-*Acetyl*-8-*propyl*-1,2,3,4-*tetrahydronaphthalene*-1,7-*diol*.—Aqueous sodium hydroxide [300 mg, 7.5 mmol in water (1 ml)] was added to a solution of the trifluoroacetoxy compound (**17**) (99.8 mg, 3 mmol) in methanol (5 ml). The resulting deep yellow solution was diluted with methanol (5 ml), and then stirred for 20 min. The methanol was removed under reduced pressure, and then water (5 ml) was added to the residue and the pH of the mixture adjusted to 7 with 2M hydrochloric acid. The aqueous solution was saturated with solid sodium chloride, and then extracted with ether (3 × 10 ml). The dried extracts were filtered and evaporated to give the *naphthol* (73 mg, 98%) as a white solid, m.p. 131—132 °C; $\lambda_{max.}$(EtOH) 224 (ε 35 150), 267 (18 610), and 356 (5 960); $\nu_{max.}$ 3 400br, 3 150—2 750, 2 950, 1 640, 1 370, and 1 310 cm^{-1}; δ_H 1.03 (t, *J* 7 Hz, CH_2CH_3), 1.40—2.30 (7 H, m), 1.60 (exchanged with D_2O, OH), 2.63 ($COCH_3$), 2.65—2.93 (3 H, m), 5.04 (1 H, *ca.* t, 1-H), 7.44 (5-H), and 12.40 (1 H, s, intensity only partly reduced on D_2O shake, chelated OH); *m/z* 248 (36%), 230 (41), 215 (23), and 201 (53) (Found: C, 72.3; H, 8.3%; *m/z*, 248.1402. $C_{15}H_{20}O_3$ requires. C, 72.55; H, 8.1%; *M*, 248.1412).

8-*Acetoxy*-3-*acetyl*-1-*propyl*-5,6,7,8-*tetrahydro*-2-*naphthol* (**15**).—A solution of the foregoing alcohol (53.2 mg, 0.2 mmol) in acetyl chloride (5 ml) was kept at 25 °C with occasional swirling, for 20 min. The excess of acetyl chloride was removed under reduced pressure and the residue was chromatographed on silica gel [light petroleum–ether (10:1 v/v) as eluant] to give the *acetoxynaphthol* (21 mg, 35%), which crystallised from ether–light petroleum as a white lustrous solid, m.p. 108—109 °C; $\lambda_{max.}$(EtOH) 224 (ε 17 120), 265 (9 460), and 355 nm (2 790); $\nu_{max.}$ 3 250—2 750br, 2 900, 1 725, 1 635, 1 365, 1 305, and 945 cm^{-1}; δ_H 0.98 (t, *J* 7 Hz, CH_2CH_3), 1.35—1.95 (5 H, m), 2.06 ($OCOCH_3$), 2.1—2.9 (5 H, m), 2.62 ($COCH_3$), 6.13 (*ca.* t, 8-H), 7.43 (4-H), and 12.35 (OH); *m/z* 290 (4%), 231 (21), 230 (100), 215 (23), and 201 (41) (Found: C, 70.1; H, 7.7%; *m/z*, 290.1474. $C_{17}H_{22}O_4$ requires C, 70.3; H, 7.6%; *M*, 290.1518).

Conversion of the Trifluoroacetoxynaphthol (**17**) *into the Dihydronaphthol* (**16**).—A solution of the ester (**17**) (20 mg, 0.06 mmol) in xylene (2 ml) was boiled under reflux for 6 h, and the xylene was removed under reduced pressure. The residue was purified by preparative t.l.c. [light petroleum–ether (10:1 v/v)] to give the dihydronaphthol (10 mg, 74%) as a pale yellow solid, m.p. 66.5—67.5 °C, which showed spectroscopic data identical with those of previously obtained material.

3-*Acetyl*-1-*benzoyloxy*-1-*propyl*-5,6,7,8-*tetrahydronaphthalen*-2(1H)-*one* (**20**).—The tetrahydronaphthol (**6**) (0.20 g, 0.86 mmol) and lead tetrabenzoate (0.6 g, 0.86 mmol) were suspended in dry dichloromethane (3 ml), and the resulting mixture was stirred for 2 h. The mixture was filtered and the solids were washed with dichloromethane. The combined organic solutions were evaporated under reduced pressure, and the residue was triturated with light petroleum. Evaporation of the filtered solution afforded a bright yellow solid (0.42 g), which was purified by chromatography over silica gel [light petroleum–ether (5:2 v/v)] to give the *benzoate* (0.25 g, 82%) as a yellow solid, m.p. 88.5—89.5 °C (from pentane); $\lambda_{max.}$(EtOH) 234 (ε 25 350) and 341 nm (8 100); $\nu_{max.}$ 3 040, 2 925, 2 865, 1 710, 1 675, 1 635, 1 600, 1 540, 1 357, 1 317, and 1 230 cm^{-1}; δ_H 0.92 (t, *J* 7 Hz, CH_2CH_3), 1.10—2.50 (complex m, 6 × CH_2), 2.52 ($COCH_3$), 7.42—7.62 (m, 4-H + 3 × ArH), and 8.04—

Table 2. Fractional atomic co-ordinates for the benzoate (**20**)

Atom	*x/a*	*y/b*	*z/c*
C(1)	0.0512(1)	0.2717(2)	0.2919(1)
C(2)	−0.0494(1)	0.3261(3)	0.2826(1)
C(3)	−0.0908(1)	0.3557(3)	0.3647(1)
C(4)	−0.0452(2)	0.3079(3)	0.4406(1)
C(5)	0.0423(2)	0.2302(3)	0.4508(1)
C(6)	0.0789(2)	0.1785(4)	0.5422(1)
C(7)	0.1781(3)	0.1286(5)	0.5492(2)
C(8)	0.1982(3)	0.0336(4)	0.4718(2)
C(9)	0.1782(2)	0.1215(3)	0.3861(2)
C(10)	0.0877(1)	0.2052(2)	0.3799(1)
C(11)	0.1101(2)	0.4099(3)	0.2679(1)
C(12)	0.1116(2)	0.5452(3)	0.3305(2)
C(13)	0.1738(2)	0.6734(3)	0.3067(2)
C(14)	0.0100(1)	0.0346(3)	0.2202(1)
C(15)	0.0252(1)	−0.0691(2)	0.1465(1)
C(16)	0.0907(2)	−0.0386(3)	0.0892(1)
C(17)	0.1010(2)	−0.1380(3)	0.0201(2)
C(18)	0.0471(2)	−0.2651(4)	0.0079(2)
C(19)	−0.0170(3)	−0.2971(3)	0.0643(2)
C(20)	−0.0286(2)	−0.1990(3)	0.1343(2)
C(21)	−0.1823(2)	0.4345(4)	0.3667(2)
C(22)	−0.2230(3)	0.5271(7)	0.2911(3)
O(1)	0.0625(1)	0.1628(2)	0.2214(1)
O(2)	−0.0898(1)	0.3465(2)	0.2096(1)
O(14)	−0.0424(1)	0.0107(2)	0.2746(1)
O(21)	−0.2191(2)	0.4289(4)	0.4337(2)
H(4)	−0.073(2)	0.322(3)	0.493(2)
H(6a)	0.075(2)	0.268(3)	0.585(2)
H(6b)	0.038(2)	0.095(4)	0.560(2)
H(7a)	0.192(2)	0.064(4)	0.599(2)
H(7b)	0.227(3)	0.231(5)	0.545(3)
H(8a)	0.259(2)	−0.005(4)	0.476(2)
H(8b)	0.150(2)	−0.069(4)	0.472(2)
H(9a)	0.177(2)	0.053(3)	0.335(2)
H(9b)	0.229(2)	0.199(4)	0.382(2)
H(11a)	0.084(1)	0.442(2)	0.207(1)
H(11b)	0.174(2)	0.373(3)	0.267(1)
H(12a)	0.052(2)	0.583(3)	0.336(2)
H(12b)	0.129(2)	0.510(3)	0.390(2)
H(13a)	0.153(2)	0.702(4)	0.243(2)
H(13b)	0.241(2)	0.631(4)	0.304(2)
H(13c)	0.172(2)	0.758(5)	0.344(2)
H(16)	0.127(2)	0.061(3)	0.098(1)
H(17)	0.150(2)	−0.113(4)	−0.021(2)
H(18)	0.054(2)	−0.336(4)	−0.043(2)
H(19)	−0.061(2)	−0.377(4)	0.057(2)
H(20)	−0.071(2)	−0.219(3)	0.171(2)
H(22a)	−0.245(3)	0.457(5)	0.255(3)
H(22b)	−0.183(3)	0.573(6)	0.254(3)
H(22c)	−0.271(3)	0.588(5)	0.307(2)

8.10 (2 H, m, *o*-ArH); δ_C 14.25 (q), 15.93 (t), 21.45 (t), 22.16 (t), 25.14 (t), 28.44 (t), 30.88 (q), 40.58 (t), 86.30, 127.53, 128.50 (2 × ArC), 129.91 (2 × ArC), 131.75, 133.43, 150.82, 153.96, 164.96, 196.71, and 196.92 (Found: C, 75.0; H, 7, 1%. $C_{22}H_{24}O_4$ requires C, 75.0; H, 6.9%).

Crystallographic Analysis of the Benzoate (**20**).—*Crystal data.* $C_{22}H_{24}O_4$; M = 352.43. Monoclinic, a = 14.608(1), b = 8.693(1), c = 15.280(1) Å, β = 96.26(1)°, U = 1 928.84 Å^3, Z = 4, D_c = 1.21 g cm^{-3}, $F(000)$ = 752, space group $P2_1/n$, Cu-K_α radiation, λ = 1.541 78 Å, μ(Cu-K_α) = 6.75 cm^{-1}.

A crystal of approximate dimensions 0.45 × 0.35 × 0.1 mm was mounted on an Enraf-Nonius CAD4 diffractometer and 25 reflections were used to determine accurate lattice parameters.

Table 3. Bond lengths (Å) for the benzoate (**20**), with standard deviations in parentheses

C(1)–C(2)	1.536(3)	C(9)–C(10)	1.502(3)
C(1)–C(10)	1.507(3)	C(11)–C(12)	1.514(3)
C(1)–C(11)	1.544(3)	C(12)–C(13)	1.506(4)
C(1)–O(1)	1.456(2)	C(14)–C(15)	1.479(3)
C(2)–C(3)	1.475(3)	C(14)–O(1)	1.352(2)
C(2)–O(2)	1.217(2)	C(14)–O(14)	1.207(2)
C(3)–C(4)	1.339(3)	C(15)–C(16)	1.390(3)
C(3)–C(21)	1.505(3)	C(15)–C(20)	1.376(3)
C(4)–C(5)	1.439(3)	C(16)–C(17)	1.385(3)
C(5)–C(6)	1.509(3)	C(17)–C(18)	1.357(4)
C(5)–C(10)	1.348(3)	C(18)–C(19)	1.369(5)
C(6)–C(7)	1.505(4)	C(19)–C(20)	1.392(4)
C(7)–C(8)	1.498(5)	C(21)–C(22)	1.478(5)
C(8)–C(9)	1.515(4)	C(21)–O(21)	1.207(3)

Table 4. Bond angles (°) for the benzoate (**20**), standard deviations in parentheses

C(2)–C(1)–C(10)	116.3(2)	C(1)–C(10)–C(5)	119.9(2)
C(2)–C(1)–C(11)	106.9(2)	C(1)–C(10)–C(9)	117.8(2)
C(2)–C(1)–O(1)	108.4(2)	C(5)–C(10)–C(9)	122.2(2)
C(10)–C(1)–C(11)	111.0(2)	C(1)–C(11)–C(12)	115.2(2)
C(10)–C(1)–O(1)	110.6(2)	C(11)–C(12)–C(13)	113.0(2)
C(11)–C(1)–O(1)	102.7(1)	C(15)–C(14)–O(1)	112.4(2)
C(1)–C(2)–C(3)	116.9(2)	C(15)–C(14)–O(14)	125.4(2)
C(1)–C(2)–O(2)	119.6(2)	O(1)–C(14)–O(14)	122.3(2)
C(3)–C(2)–O(2)	123.5(2)	C(14)–C(15)–C(16)	122.3(2)
C(2)–C(3)–C(4)	118.1(2)	C(14)–C(15)–C(20)	118.2(2)
C(2)–C(3)–C(21)	123.0(2)	C(16)–C(15)–C(20)	119.6(2)
C(4)–C(3)–C(21)	118.9(2)	C(15)–C(16)–C(17)	120.0(2)
C(3)–C(4)–C(5)	126.3(2)	C(16)–C(17)–C(18)	120.2(3)
C(4)–C(5)–C(6)	117.4(2)	C(17)–C(18)–C(19)	120.3(3)
C(4)–C(5)–C(10)	119.9(2)	C(18)–C(19)–C(20)	120.3(3)
C(6)–C(5)–C(10)	122.7(2)	C(15)–C(20)–C(19)	119.4(3)
C(5)–C(6)–C(7)	113.2(2)	C(3)–C(21)–C(22)	120.9(3)
C(6)–C(7)–C(8)	111.8(3)	C(3)–C(21)–O(21)	118.5(3)
C(7)–C(8)–C(9)	111.6(3)	C(22)–C(21)–O(21)	120.5(3)
C(8)–C(9)–C(10)	112.6(2)	C(1)–O(1)–C(14)	115.9(1)

Intensity data were collected using an ω/2θ scan for 1 ⩽ θ ⩽ 76. A total of 4 024 independent reflections was measured of which 2 312 had $I \geqslant 3\sigma(I)$ and were considered observed and used in the subsequent refinement. The data were corrected for Lorentz and polarisation factors but no absorption corrections were made. Crystallographic calculations were performed using the CRYSTALS system of programs.[9] The structure was solved by direct methods using the MULTAN program.[10] Least-squares refinement including anisotropic thermal parameters for non-hydrogen atoms and isotropic refinement of hydrogen atoms located in a difference Fourier synthesis terminated at R 0.0417 (R_w 0.0515). A final difference map showed no features in excess of 0.15 e Å^{-3}.

The crystal structure is shown in Figure 2. Final atomic co-ordinates and bond lengths and angles are shown in Tables 2—4. The cyclohexane ring adopts the expected half-chair conformation with C(7) and C(8) 0.31 and 0.39 Å respectively above and below the plane containing the other four atoms. The cyclohexadienone ring is in an envelope conformation with C(1) 0.22 Å above the plane containing the remaining five atoms. The bond angle at C(4) within this ring is enlarged to 126.3°. This is the first report of structural parameters for the cyclohexa-2,4-dienone ring; the only previously published reference contains no co-ordinate data.[11] The acetyl C(21) is twisted 13° out of conjugation with the cyclohexadienone. The remaining

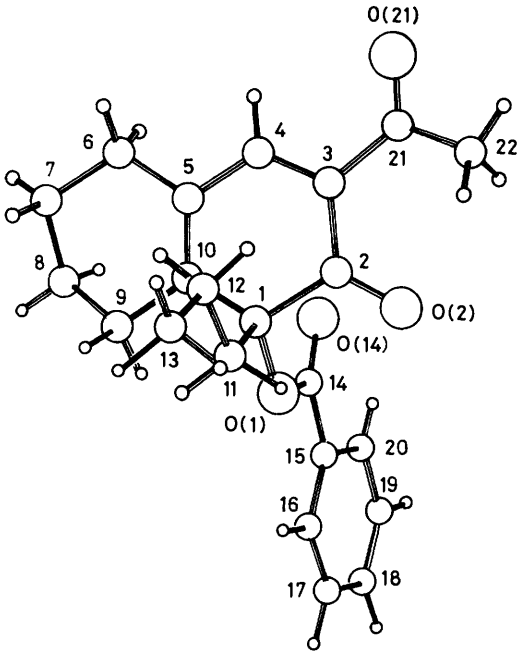


Figure 2. Crystal structure of the benzoate (**20**)

geometric data are unexceptional. Thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.*

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* See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1988, Issue 1, section 5.6.3.

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