

The Reactivity of Polyhydric Phenols Towards Air and *m*-Chloroperbenzoic Acid. The Nature of the Monomeric Products

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The products of a series of polysubstituted phenols, previously shown to exhibit increasing reactivity towards oxygen, were characterised when air and *m*-chloroperbenzoic acid were used separately as oxidants.

The latter reagent gave compounds derived from oxidation of the unsaturated side-chains and, for the more reactive phenols, products derived by oxidation at the aromatic nucleus. In the case of air, only the more reactive phenols gave products, and these were mainly derived by oxidation at the aromatic nucleus. In particular 2,4-di-isopentenylphloroglucinol gave 3,4-dihydroxy-2,4-di-isopentenylcyclohexa-1,5-dione which was isomerised in sodium carbonate to 3,4-dihydroxy-2-isopentenyl-4-isohexenylcyclopent-2-enone. 2,4,6-Tri-isopentenylphloroglucinol gave 3,4-dihydroxy-2,4,6-tri-isopentenylcyclohex-2-en-1,5-dione which, on prolonged exposure to air, afforded 3,5-dihydroxy-2,5-di-isopentenylcyclopent-2-ene-1,4-dione.

IN an earlier paper¹ of this series we drew attention to the differences in reactivity of a series of substituted polyhydric phenols towards oxygen, in relation to the specific question of the aerial-oxidation of the hop constituents, the deoxyhumulones (1). By competitive experiments it was shown that the higher the number of substituents on the benzenoid system, the greater the reactivity, and that certain substituents were more effective than others. Thus alkyl or alkenyl, and hydroxy groups conferred greater reactivity than acyl groups. The products of these oxidations were known to be complex, and only in the case of the deoxyhumulones (1) were they characterised, albeit incompletely. In the preceding paper, those products and their interrelationships have been discussed in more detail, and we now describe the characterisation of some of the aerial-oxidation products of the other polyhydric phenols. In the investigations of aerial-oxidations of hop constituents it has often proved valuable to use chemical reagents, *e.g.* lead tetra-acetate,² organic

peracids,³ and persulphate salts⁴ to obtain oxidation products which are also formed amongst those derived from air; notable examples include cohulupone,^{5,6} tricyclodehydroisohumulone,² and humulinone.⁷⁻⁹ We therefore also examined the products obtained when *m*-chloroperbenzoic acid was used as an oxidant for this series of phenols. Peracid reagents are particularly associated with attack at double bonds¹⁰ whereas reagents such as lead tetra-acetate are more likely to initiate reaction on the aromatic nucleus where the resulting free radicals are highly stabilised.

Each of the series of phenols (2)–(7) (of which aceto-deoxyhumulone (6) is the subject of the preceding paper) was allowed to react separately with air and the peracid. Whilst the latter reacted with all the compounds, air, as expected,¹ gave no reaction with the first three, but reacted readily with (5), (6), and (7).

The simplest of the phenols (2) reacted smoothly with *m*-chloroperbenzoic acid to give the hydroxychroman (8) in high yield, whose structure followed unambiguously from its spectral data. In particular the cyclisation of the side-chain [presumably as its epoxide (cf.

¹ E. Collins, G. D. John and P. V. R. Shannon, *J.C.S. Perkin I*, 1975, 96.

² J. A. Elvidge, D. R. J. Laws, J. D. McGuinness, and P. V. R. Shannon, *Chem. and Ind.*, 1974, 573.

³ B. E. Connett and J. A. Elvidge, *J. Chem. Soc. (C)*, 1968, 1193.

⁴ E. Byrne, D. M. Cahill, and P. V. R. Shannon, *J. Chem. Soc. (C)*, 1970, 938.

⁵ L. O. Spetsig, M. Steninger, and S. Brohult, European Brewery Convention, Proceedings of 6th Congress, Copenhagen, 1957, 22, 1957.

⁶ P. M. Brown, J. S. Burton, and R. Stevens, *J. Chem. Soc.*, 1964, 4774.

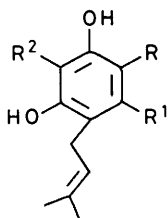
⁷ A. H. Cook and G. Harris, *J. Chem. Soc.*, 1950, 1873.

⁸ F. Alderweireldt and M. Verzele, *Bull. Soc. chim. belges*, 1957, 66, 391.

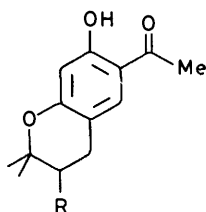
⁹ A. H. Cook, G. A. Howard, and C. A. Slater, *J. Inst. Brewing*, 1955, 61, 321.

¹⁰ H. O. House, 'Modern Synthetic Reactions', W. A. Benjamin, New York, 1965, 105.

ref. 11)] to give the hydroxychroman ring system was confirmed by the α carbonyl proton signal at τ 6.17,



- (1) R = COCH₂CHMe₂, R¹ = OH, R² = CH₂CH:CMe₂
 (2) R = Ac, R¹ = R² = H
 (3) R = Ac, R¹ = H, R² = CH₂CH:CMe₂
 (4) R = Ac, R¹ = OH, R² = H
 (5) R = H, R¹ = OH, R² = CH₂CH:CMe₂
 (6) R = Ac, R¹ = OH, R² = CH₂CH:CMe₂
 (7) R = R² = CH₂CH:CMe₂, R¹ = OH



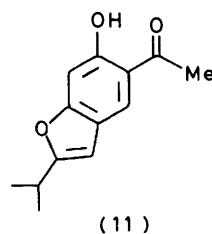
- (8) R = OH
 (9) R = OToS
 (10) R = H

(dd, J_{AX} 8.4 J_{BX} 9.1 Hz) and associated CH₂ multiplet centred on τ 7.14 (J_{AB} 16.6 Hz). The magnitudes of the coupling constants are in accord with a time-averaged conformation with an equatorial OH group. Tosylation of (8) in pyridine gave the tosylate (9) which was reduced with lithium aluminium hydride to the crystalline chroman (10) identical to an authentic sample.¹² Treatment of (8) with *p*-toluenesulphonic acid in refluxing benzene gave the benzofuran (11) rather than the chromen (12). Similar ring contractions have been anticipated previously.¹³ Peracid oxidation of aldehydes structurally related to (2) can give both hydroxychroman or 2-(1-methyl-1-hydroxy)ethylidihydrofuran ring systems.¹⁴

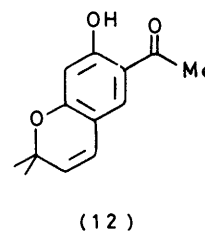
The di-isopentenyl analogue of (2), (3)¹⁵ gave a more complex mixture with the peracid. Column chromatography afforded a mixture of two components, barely separated by t.l.c. The field desorption (FD) mass-spectrum¹⁶ on the mixture gave a single molecular ion of 304 a.m.u. (100%) showing the addition of 1 oxygen atom to (3) and the u.v. spectrum (λ_{max} 289 nm) was

typical of a dihydroxydialkylacetophenone with a substituted *para*-OH group ($\lambda_{(alkali)max}$ 288 nm).

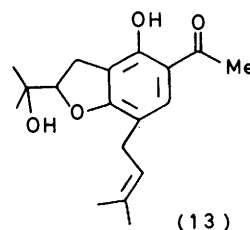
In the ¹H n.m.r. spectrum of this mixture, four high-field singlets could be seen at τ 8.81, 8.75, 8.70, and 8.66 suggesting both the 2-(1-hydroxy-1-methylethyl)dihydrofuran and the 2,2-dimethyl-3-hydroxydihydrofuran grouping respectively. The associated carbonyl methine proton signals could be seen at τ 5.26 (t, J 9 Hz) and 6.15 (t, J 6 Hz), and two distinct low-field chelated OH signals appeared at τ -2.54 and -2.86. The allylic methylene signal was observed at τ 6.8, hence the structures (13) and (14) are proposed for these two components. The products of oxidative cyclisation of



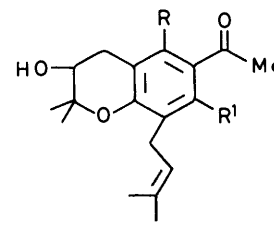
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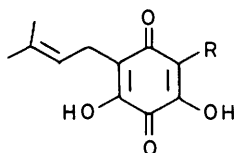
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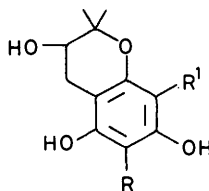
(13)



- (14) R = OH, R¹ = H
 (15) R = H, R¹ = OH



- (16) R = Ac
 (31) R = CH₂CH:CMe₂



- (17) R = H, R¹ = Ac
 (18) R = Ac, R¹ = H
 (19) R = CH₂CH:CMe₂, R¹ = Ac
 (32a) R = CH₂CH:CMe₂, R¹ = H
 (32b) R = H, R¹ = CH₂CH:CMe₂
 (33) R = CH₂CH₂CMe₂, R¹ = Ac

the alternative side-chain [*e.g.* (15)] would be expected to show the remaining =CH·CH₂- signal at τ 6.6 as in the starting phenol (3), but the observed (C-3) allylic

¹¹ L. Crombie, D. E. Games, N. J. Haskins, and G. F. Reed, *J.C.S. Perkin I*, 1972, 2241.

¹² B. S. Bajwa, P. Lal, and T. R. Seshadri, *Indian J. Chem.*, 1971, 9, 19.

¹³ B. W. Bencze, J. Eisenbeiss, and H. Schmid, *Helv. Chim. Acta.*, 1956, 39, 928.

¹⁴ W. Steck, *Canad. J. Chem.*, 1971, 49, 2298.

¹⁵ A. C. Jain, P. Lal, and T. R. Seshadri, *Tetrahedron*, 1970, 26, 2631.

¹⁶ H. D. Beckey and H. R. Schulten, *Angew. Chem. Internat. Edn.*, 1975, 14, 403.

methylene signals in (13) and (14) appear at τ 6.8 as for C-3 in (3).

The phenol (4), also unreactive to air, gave three isolable products with equimolar amounts of the peracid.

The least-polar red, semisolid compound, M^+ 250 (100%) (FD), showed a u.v. spectrum almost identical with that of humuloquinone¹⁷. The ^1H n.m.r. spectrum, apart from the expected isopentenyl and acetyl signals, showed the anticipated very low field OH signal τ -8.65 due to the 6-membered chelated OH group and this product must, therefore, be the dehydroacetohumulone (16).

The remaining two compounds were obtained as a sharp melting (179–181 °C) solid mixture, giving a single spot on t.l.c. FD and (EI) mass spectra indicated a common molecular ion of 252 a.m.u. The u.v. spectrum, whilst typical of the basic monosubstituted acylphloroglucinol in neutral solution, showed a bathochromic shift of the main band in alkali from 292 to 325 nm suggesting a free *para*-OH group. The ^1H n.m.r. spectrum, in keeping with the presence of a mixture, showed two major O-CMe signals at τ 8.58 and 8.68 with two minor signals at τ 8.71 and 8.62, but indicated only the hydroxychroman ring system (τ 6.22, t, J = 7 Hz). In the low-field region two singlets were seen, the major one, at τ -3.68, was consistent with the *ortho*-cyclised hydroxypyran structure (17). Presumably smaller amounts of the *para*-cyclised isomer (18) were also present in the mixture.

Of the remaining three phenols (5), (6), and (7), all of which are sufficiently reactive to undergo oxidation in air,¹ the aerial-oxidation products of the acetodeoxyhumulone (6) have already been discussed (see preceding paper). Oxidation of (6) with 1 mole equivalent of *m*-chloroperbenzoic acid gave the oily hydroxychroman (19) identical in all respects with the sample obtained by aerial oxidation (see preceding paper). The other major product obtained was the tricyclic chroman (20). The latter, which showed the expected u.v. spectrum and a single (molecular) ion m/e 336 in the FD mass spectrum, gave evidence of the two oxidised ring systems, the hydroxypyran and 2(1-methyl-1-hydroxyethyl)dihydrofuran, with triplets in the ^1H n.m.r. spectrum at τ 6.21 (J = 6 Hz) and 5.29 (J = 9 Hz) respectively. A low-field singlet (1 H) at τ -3.75, and the fact that (20) was formed easily from (19) with the peracid, established the orientation of the two rings as shown and the compound was identical to that formed from (6) in air (see preceding paper). The peracid reaction on (6) also gave smaller amounts of a mixture of isomeric tricyclic compounds which were not completely characterised but whose spectroscopic properties indicated different combinations of the dihydropyran and dihydrofuran ring system.

The dialkenylphloroglucinol (5) when kept for several months at ambient temperatures, slowly oxidised to two observable new products of higher polarity. The most

polar, from its FD and EI mass spectra, showed M^+ 278.152 3 ($\text{C}_{16}\text{H}_{22}\text{O}_4$), *i.e.* the addition of one oxygen atom to (5), and showed a base peak at m/e 69, suggesting the cleavage of a dimethylallyl group at an sp^3 ring carbon. In the ^1H n.m.r. spectrum the normal signals from the side-chain vinylic methyls and hydrogens were evident as were the corresponding methylene signals (τ 6.95, d, J = 7 Hz and τ 7.4, m) (from C-6 and C-4 respectively). The only other signals apart from the quaternary OH proton (τ 7.85 s,) were two lines centred in τ 6.5 and a minor broad singlet at τ 4.02. These signals were in keeping with the nuclear methylene (AB system) and vinyl hydrogen groups in the tautomeric pair (21) and (22) respectively. The former signal was very close to that at τ 6.47 (m) for the incompletely characterised tetrahydro-analogue reported earlier.¹⁸ The cyclohexane (21)/(22) was readily isomerised under alkaline conditions to the cyclopentenone (23) whose u.v. spectrum [λ_{max} 270 nm, λ_{max} (acid) 253 nm] was almost identical to that of its tetrahydro-analogue (24) m.p. 156 °C.¹⁸ Hydrogenation of (23) gave (24), m.p. 155–156 °C, whose ^1H n.m.r. spectrum was identical to that reported.¹⁸

The formation of (23) [rather than the isomer (25)] from (21) contrasts with the ring contraction of humulone (26) to the isohumulones (27) and supports the suggestion of Shaw¹⁹ that the anomalous acid and base-catalysed ring-contraction of the model humulone (28) to (29) must be preceded by deacylation of (28) to (30). Similar conclusions may be drawn from results with the tetrahydro-derivative of (22)¹⁸ and it seems clear that the absence of the exocyclic carbonyl in humulones (26) confers the alternative regiospecificity on the ring contraction. The second product of aerial-oxidation of (5) was a red oil which was obtained as a red gum after chromatography. FD mass spectrometry (M^+ 276) showed that addition of one oxygen to, and removal of two hydrogens from, (5) had occurred, and the ^1H n.m.r. spectrum showed only the signals of the now identical dimethylallyl side-chains. The u.v. spectrum and elemental analysis confirmed the quinone structure (31).

The effect of peracid on (5) was to produce both compounds (21) and (31), the former in much diminished yield, but in addition, attack at the double-bonds gave much larger amounts (*ca.* 20%) of a crystalline solid whose mass spectra (EI and FD) confirmed the gain of 1 oxygen atom (M^+ 278 a.m.u.) and whose u.v. spectrum closely resembled that of the starting phenol. The hydroxychroman structures (32a or b) were indicated by the ^1H n.m.r. resonances at τ 6.24 (t, J = 6 Hz, 1 H) 7.4 (m, 2 H) and 8.76, and 8.72 (2 s, 6 H) which replaced those of one of the dimethylallyl side-chains of (5). Small-scale hydrogenation and Friedel-Crafts acetylation of (32) gave a single product, M^+ (FD) 322 a.m.u. whose u.v. spectrum [λ_{max} (EtOH) 293 nm, λ_{max} (alkaline EtOH) 240sh and 336 nm] EI, mass spectrum, and t.l.c.

¹⁸ W. J. G. Donnelly and P. V. R. Shannon, *J. Chem. Soc. (C)*, 1970, 524.

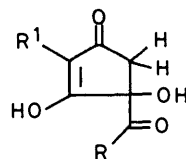
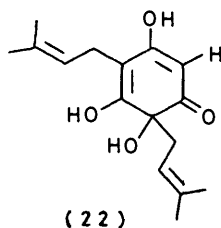
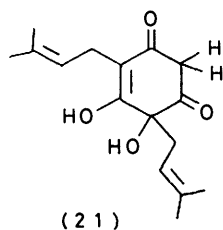
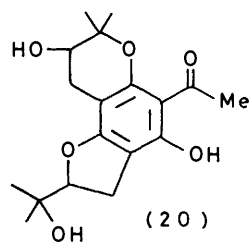
¹⁹ S. J. Shaw, *Chem. Comm.*, 1968, 183.

¹⁷ G. Harris, G. A. Howard, and J. R. A. Pollock, *J. Chem. Soc.*, 1952, 1906.

characteristics were identical with the hydroxychroman (33) (see preceding paper). Hence the orientation (32a) follows for the unsaturated hydroxychroman.

The final phenol (7) in the series had been shown earlier¹ by kinetic studies to be the most reactive to oxygen, and this was borne out in the present work. After 3 weeks in the air at 0 °C the oily phenol (7) had partly oxidised to two main products. Column chromatography gave the first as an oil, M^+ 346.2125 ($C_{21}H_{30}O_4$). Fragment ions in the EI mass spectrum at $M - 69$, $M - 55 - 69$ and m/e 69 and 55, corresponding to cleavage of dimethylallyl side-chains both α and β to a ring, implied their attachment to sp^3 and sp^2 hybridised

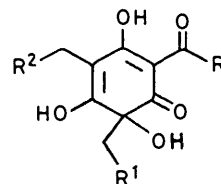
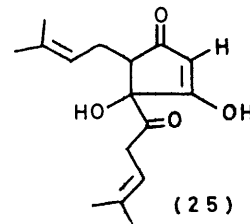
simple showing two distinct dimethylallyl side-chains, and the resonances of the methylene doublets (τ 7.47 and 6.92, each $J = 7$ Hz) established the structure (36). As expected the i.r. showed a strong OH stretching band at



(23) $R = R^1 = CH_2 \cdot CH : CMe_2$

(24) $R = R^1 = CH_2CH_2CMe_2$

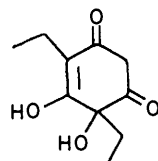
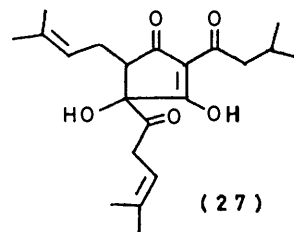
(29) $R = R^1 = Et$



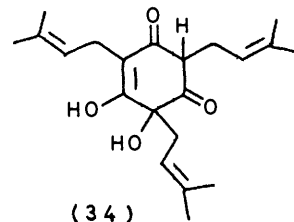
(26) $R = CH_2CHMe_2$

$R^1 = R^2 = CH : CMe_2$

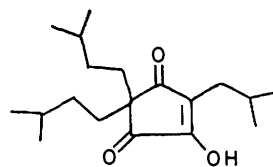
(28) $R = Me, R^1 = R^2 = Me$



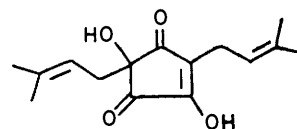
(30)



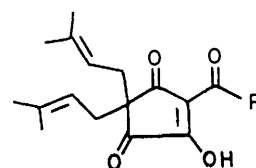
(34)



(35)



(36)



(37)

carbons respectively. The u.v. spectrum was very similar to that of compound (22). From the 1H n.m.r. spectrum it was evident that the three dimethylallyl side-chains of (7) remained unaffected. The $C=CMe_2$ signals (τ 8.30 and 8.36) and the corresponding olefinic signal (τ 4.95) were accompanied by two multiplet signals in the ratio 2 : 1 at τ 7.4 (4 H) and 6.98 (2 H), characteristic of singly and double allylic CH_2 groups respectively. A four-line signal centred on τ 6.57 (1 H) ($J_{AX} + J_{BX}$ 12 Hz) could be assigned to the ring-methine proton of a cyclohexadienone (*cf.* ref. 20) and the above facts lead only to the diastereomeric structures (34). The non-conjugated carbonyl group was confirmed by a band at 1720 cm^{-1} in the i.r. spectrum.

The second compound, obtained pure only after p.l.c., was shown by FD and EI mass spectrometry to have M^+ 264.1353 ($C_{15}H_{20}O_4$). The molecular formula implied a gain of two oxygen atoms and a loss of an isohexenoyl side-chain from a ring-contracted form as in (25). The u.v. spectrum [λ_{max} (acid EtOH) 275 nm, λ_{max} (alkaline EtOH) 240 and 325 nm] was also in accord with a 5-membered ring and was very similar to that of the diketone (35).²¹ The 1H n.m.r. spectrum was unusually

ν_{max} 3620 cm^{-1} and the adsorption in the $C=O$ region (ν_{max} 1745 and 1690 cm^{-1}) was very similar to that (1740 and 1680 cm^{-1}) for (35).²¹

It seemed possible that the diketone (36) might be formed directly from (34) in air.

²⁰ 'High Resolution N.M.R. Spectra Catalogue', Spectrum 512, Varian Associates, Palo Alto, California, 1962.

²¹ J. S. Burton and R. Stevens, *J. Chem. Soc.*, 1963, 4382.

In fact (34), at room temperature (as in oil) for two days gave, after p.l.c., a 55% yield of the diketone (36), identical characterisation (t.l.c. and u.v., n.m.r., and i.r. spectra) with the sample isolated from oxidation of the phenol (7). This evidently ready conversion is relevant to the problem of the formation of hulupones (37) in air.²² (cf. ref. 23).

Oxidation of (7) with peracid gave a very complex mixture from which only small amounts of (34) could be isolated.

The range of structures established for the oxidation products of these phenols (a) from air and (b) from peracid tends to indicate a different function for each of the oxidants. Both reagents can oxidise the unsaturated side-chains, but whilst peracid is predictably unselective, oxygen shows a more discriminative reactivity. Both reagents will attack the aromatic nucleus, but only in the more highly substituted phenols.

The validity of the use of *m*-chloroperbenzoic acid to simulate the effect of oxygen on this group of multi-functional compounds must, therefore, be considered carefully.

EXPERIMENTAL

General conditions are as described in the preceding paper. Light petroleum refers to that of b.p. 40–60 °C unless stated otherwise. FD refers to field desorption mass-spectra. I.r. spectra were measured in chloroform solutions. Where spectral data (u.v., n.m.r., or mass) have been deposited as Supplementary publication (SUP No. 22144, 13 pp.) for a compound the name is asterisked.*

Aerial Oxidation of 2,4-Dihydroxy-5-isopentenylacetophenone (2).—The above ketone (15 mg), m.p. 144 °C (lit.,¹⁵ 144–145 °C) was dissolved in deuteriochloroform (0.5 ml) in an n.m.r. tube and left to oxidise slowly at 20 °C for 20 weeks. The solvent level was maintained at 0.5 ml and progress of autoxidation was followed by n.m.r. spectroscopy. No sign of oxidative breakdown was observed.

Peracid Oxidation.—The ketone (2) (100 mg), *m*-chloroperbenzoic acid (100 mg) and *p*-toluenesulphonic acid (4 mg) were dissolved in chloroform (12 ml) and the mixture stirred at 19 °C for 2½ h. The mixture was then washed with dilute aqueous sodium carbonate (2 × 50 ml) and water (2 × 50 ml) and then dried (MgSO₄·H₂O). Evaporation of the solvent under reduced pressure gave a white solid (88 mg). Recrystallisation from light petroleum (b.p. 30–40 °C) and chloroform gave 6-acetyl-3,7-dihydroxy-2,2-dimethylchroman (8)* as colourless crystals (65 mg), m.p. 135.5–136.5 °C, (Found: C, 65.8, H, 6.6. C₁₃H₁₆O₄ requires C, 66.1; H, 6.8%).

Tosylation.—The hydroxychroman (8) (100 mg) and *p*-toluenesulphonyl chloride (84 mg) were dissolved in dry pyridine (4 ml) and the mixture stirred at 20 °C for 6 days. Chloroform (25 ml) was added and the mixture washed with dilute hydrochloric acid (0.5M; 8 × 20 ml) and water (6 × 25 ml). The chloroform layer was dried (MgSO₄·H₂O) and evaporation of the solvent under reduced pressure gave

a brown oil (97 mg). Chromatography on silicic acid (25 × 2.5 cm) and elution with ether–light petroleum (2 : 3) afforded a white solid (30 mg). Recrystallisation from light petroleum (b.p. 30–40 °C) and chloroform gave colourless crystals of the tosylate (9)* (16 mg), m.p. 114.5–116 °C (Found: M⁺, 390.114 2. C₂₀H₂₂O₆S requires M, 390.113 7).

Reduction of the Tosylate (9).—The above tosylate (20 mg) in freshly dried ether (100 ml) was treated with an excess of lithium aluminium hydride, added slowly at such a rate that the reaction mixture boiled gently. When reduction was complete (t.l.c.), the excess of reagent was destroyed with moist ether. The reaction mixture was then poured onto an excess of ice-cold dilute sulphuric acid. The ether layer was washed with water (2 × 25 ml), dried (MgSO₄·H₂O), and evaporation of the solvent under reduced pressure gave a solid (14 mg). P.l.c. gave a white solid (8 mg), which after recrystallisation from light petroleum and chloroform afforded the chroman (10) (3 mg), m.p. 114–115 °C, identical in all respects (t.l.c., u.v., and n.m.r.) with an authentic sample,¹² m.p. 115–116 °C, mixed m.p. 113.5–115.5 °C.

Dehydration of (8) to the Benzofuran (11).—The hydroxychroman (8) (50 mg) was gently heated under reflux in benzene (10 ml) with *p*-toluenesulphonic acid (50 mg) under a slow stream of oxygen-free nitrogen. The dehydration was followed by t.l.c. After 2 h, the mixture was concentrated (140 mg), ether (25 ml) was added to it, and the mixture extracted with aqueous sodium carbonate (1% w/v; 4 × 25 ml). The ether layer was washed with water (4 × 25 ml) and dried (MgSO₄·H₂O). Evaporation of the solvent under reduced pressure yielded a brown oil (24 mg), which gave a single spot on t.l.c. P.l.c. afforded a crystalline solid (10 mg). Recrystallisation (× 2) from light petroleum (b.p. 30–40 °C) at low temperature yielded 5-acetyl-6-hydroxy-2-isopropylbenzo[b]furan (11)* as yellow crystals (2 mg), m.p. 57–58.5 °C (Found: C, 71.0; H, 6.4. C₁₃H₁₄O₃ requires C, 71.5; H, 6.5%).

Aerial Oxidation of 2,4-Dihydroxy-3,5-di-isopentenylacetophenone (3).—The ketone (3) (15 mg), m.p. 108 °C (Lit.¹⁵ 109–110 °C) in deuteriochloroform (0.5 ml) was kept in an n.m.r. tube at 20 °C for 19 weeks, progress of autoxidation being followed by n.m.r. No sign of oxidative breakdown was observed.

Peracid Oxidation.—The ketone (3) (200 mg), *m*-chloroperbenzoic acid (250 mg), and *p*-toluenesulphonic acid (25 mg) were stirred in chloroform (25 ml) for 1 h at 19 °C. Work-up as for compound (2) yielded an orange gum (240 mg), which was chromatographed in silicic acid (27 × 2.5 cm).

Elution with ethyl acetate–light petroleum (2 : 3) gave a mixture of two spots (barely separated) as an oil (40 mg), identified as (13)* and (14)*, R_F = 0.60, 0.58 (CHCl₃). Elution with ethyl acetate–light petroleum (7 : 3), gave an oil (140 mg), which after repeated p.l.c. gave a single spot in several t.l.c. systems, R_F = 0.28 in chloroform, λ_{max}. 285 and 315sh nm, λ_{max}. (alkaline EtOH) 287 and 345 nm. Analysis by FD mass spectrometry and n.m.r. spectroscopy showed this oil (20 mg) to be a complex mixture.

Aerial Oxidation of 2,4,6-Trihydroxy-3-isopentenylacetophenone (4).—The above ketone (15 mg), m.p. 171–172 °C (lit.,²⁴ 172°) in deuteriochloroform (0.5 ml) was kept in an n.m.r. tube at 20 °C for 20 weeks. Progress of autoxidation

* For details of the Supplementary publications scheme, see Notice to Authors No. 7, *J.C.S. Perkin I*, 1976, Index issue.

²² J. P. Regan, European Brewery Convention, Proceedings of 12th Congress, Interlaken, 1969, 471.

²³ W. Reininger, *Chem. Ber.*, 1973, **106**, 1309.

²⁴ W. Riedl, J. Nickl, K. H. Risse, and R. Mitteldorf, *Chem. Ber.*, 1956, **89**, 1849.

was monitored by n.m.r.; no sign of change was observed over this period.

Peracid Oxidation.—The ketone (4) (250 mg), *m*-chloroperbenzoic acid (250 mg), and *p*-toluenesulphonic acid (10 mg) were stirred in chloroform (30 ml), at 20 °C for 2 h. Work-up as for the oxidation of compound (2) gave a red oil (240 mg). Chromatography of this oil on silicic acid (27 × 2.5 cm) and elution with ethyl acetate–light petroleum (1 : 4) gave an oil (45 mg) which after p.l.c. gave the *quinone* (16) (12 mg) as a red gum which could not be recrystallised (Found: C, 62.2; H, 5.5. C₁₃H₁₄O₅ requires C, 62.4; H, 5.6%).

Elution with ethyl acetate–light petroleum (2 : 3), gave an oil (55 mg), which after careful recrystallisation from chloroform and light petroleum (b.p. 30–40 °C) afforded a yellow crystalline mixture (18 mg) of the two isomeric hydroxychromans (17) and (18).^{*} These isomers were inseparable by chromatography or recrystallisation, and gave a *single* spot on t.l.c. The sample had m.p. 179–181 °C (Found: C, 61.9; H, 6.1. C₁₃H₁₆O₅ requires C, 61.9; H, 6.4%).

Peracid Oxidations of Deoxyacetohumulone (6).—(i) With 1 mole/1 mole. Deoxyacetohumulone (6) (200 mg), m.p. 78–79 °C (lit.,²⁵ 78–79 °C), *m*-chloroperbenzoic acid (150 mg), and *p*-toluenesulphonic acid (8 mg) were stirred in chloroform (24 ml) at 20 °C for 1.5 h. Work-up as for the oxidation of (2) gave a brown oil (208 mg). P.l.c. (plates 3 × 20 × 20 cm) afforded unchanged deoxyacetohumulone (71 mg) and a band containing the major components of the reaction (85 mg). Column chromatography on silicic acid (15 × 2.5 cm) and elution with ethyl acetate–light petroleum (1 : 4) afforded the hydroxychroman (19) as an oil (19 mg), identified unambiguously by comparison (u.v., t.l.c., and n.m.r.) with the sample obtained by aerial oxidation of (6) (see preceding paper).

Elution with ethyl acetate–light petroleum (2 : 3) afforded a solid (12 mg). Recrystallisation from boiling chloroform, acetone, and light petroleum (b.p. 30–40 °C) afforded crystals of the *hydroxychroman* (20)^{*} m.p. 197.0–199.5 °C (softening at 196.0 °C) (Found: M⁺, 336.157 1. C₁₈H₂₄O₆ requires M, 336.157 3).

(ii) With 2 mole/1 mole. Deoxyacetohumulone (6) (200 mg), *m*-chloroperbenzoic acid (230 mg), and *p*-toluenesulphonic acid (25 mg) in chloroform (25 ml), were stirred at 20 °C for 0.5 h. Work-up as before gave a yellow solid (208 mg), which was chromatographed on silicic acid (25 × 3.0 cm).

Elution with ethyl acetate–light petroleum (1 : 4) gave the hydroxychroman (19) (8 mg) as an oil, which was identical in all respects to that obtained above.

Elution with ethyl acetate–light petroleum (2 : 3) afforded the tricyclic compound (20) as a solid (35 mg), m.p. 196–199.5 °C, mixed m.p. 196–198 °C identical to that obtained above.

Conversion of Compound (19) *into* (20).—The hydroxychroman (19) (28 mg), *m*-chloroperbenzoic acid (20 mg) and *p*-toluenesulphonic acid (2 mg) were stirred in chloroform (10 ml) at 19 °C for 0.5 h; work-up as for compound (2) gave a yellow solid (21 mg). P.l.c. yielded a pale cream solid (8 mg) which was recrystallised from chloroform and light petroleum (b.p. 30–40 °C) to give the colourless solid (20), m.p. 195–198 °C. Its u.v. and ¹H n.m.r. spectra were identical to those for the specimen (m.p. 197.0–199.5°) described above.

Oxidations of Di-isopentenylphloroglucinol (5).—(a) *Aerial*

oxidation. The phenol (5) (2.5 g; oil) was set aside to oxidise in the air at 20 °C for 3 months. The oil was then chromatographed on silicic acid (36 × 3.5 cm).

Elution with ether–light petroleum (1 : 4) gave a red oil (51 mg) which was purified by p.l.c. to yield the *p-quinone* (31) as a red gum (17 mg). It was identical (t.l.c., u.v., i.r., and n.m.r.) to the sample obtained from the peracid oxidation of (5) (see below). Elution with ether–light petroleum (2 : 3) gave the starting phenol (5) as an oil (1.12 g).

Elution with ether–light petroleum (7 : 3) gave the *cyclohexadione* (21)^{*} as an oil (145 mg), which gave a single spot on t.l.c., R_F 0.36 (Found: M⁺, 278.152 3. C₁₆H₂₂O₄ requires M, 278.151 8).

Isomerisation of compound (21) *to* (23). The dione (21) (140 mg) in methanol (3 ml) was added to boiling aqueous sodium carbonate (0.1M; 20 ml) under nitrogen. After 20 min the mixture was poured onto ice, acidified (4N-HCl), and extracted into ether. The ether layer was washed with water (3 × 20 ml) and dried (MgSO₄·H₂O). Evaporation of the solvent under reduced pressure yielded an oil (129 mg). Chromatography on silicic acid (26 × 2.0 cm) and elution with redistilled ethyl acetate–light petroleum (2 : 3) gave the cyclopentenone (23)^{*} as an oil (35 mg). The oil was unstable and high-resolution mass spectrometry was not immediately available. After 4 weeks FD mass spectrometry gave *m/e* 278 (48%) (M⁺), 294 (100%) (M⁺ + O), 310 (62%) (M + O₂).

Hydrogenation of compound (23) *to* (24). The cyclopentenone (23) (35 mg) in ethanol (4 ml) was hydrogenated over 10% palladium on charcoal (25 mg) at 19 °C and atmospheric pressure. After uptake of 2 mole equiv. of hydrogen, the catalyst was filtered off and the solvent evaporated under reduced pressure to leave a gum (22 mg). Crystallisation at 0 °C gave a solid which after recrystallisation (× 2) from chloroform and light petroleum (b.p. 30–40 °C) gave (23) as a colourless solid (5 mg), m.p. 155–156 °C (lit.,¹⁸ 157.7–158 °C). The u.v. and ¹H n.m.r. spectra of (24) were identical to those reported¹⁸ for (23).

(b) *Peracid oxidation of* (5). Di-isopentenylphloroglucinol (5) (1.175 g), *m*-chloroperbenzoic acid (520 mg), and *p*-toluenesulphonic acid (100 mg) were stirred in chloroform at 19 °C for 0.5 h. Work-up was as described above, and an oil was obtained (1.24 g), which was chromatographed on silicic acid (30 × 2.5 cm).

Elution with ether–light petroleum (1 : 4) yielded the *quinone* (31)^{*} as a red gum (168 mg) (Found: C, 69.6; H, 7.1. C₁₆H₂₀O₄ requires C, 69.5; 7.3%). Elution with ether–light petroleum (7 : 3) gave the dione (21) as an oil (12 mg). Its t.l.c. and u.v., i.r., and n.m.r. spectra were identical to those of the characterised sample obtained from the air oxidation of (5).

Elution with ether–light petroleum (4 : 1) gave crude (32a) (121 mg) which, after p.l.c. gave an oil (51 mg). Crystallisation from chloroform and light petroleum (b.p. 30–40 °C) gave a brown solid (22 mg), recrystallisation (× 2) of which gave the *hydroxychroman* (32a)^{*} as brown crystals (10 mg), m.p. 52–53.5 °C (Found: M⁺, 278.151 5. C₁₆H₂₂O₄ requires M, 278.151 8).

Hydrogenation. The hydroxychroman (32a) (10 mg) in ethanol (3 ml) was hydrogenated over 5% palladium on charcoal (10 mg) at 20 °C and atmospheric pressure. After uptake of 1 mole equiv. of hydrogen (≈ 0.6 ml), the catalyst

²⁵ E. Collins and P. V. R. Shannon, *J.C.S. Perkin I*, 1973, 419.

was filtered off and the solvent evaporated under reduced pressure to leave an oil (9 mg), which gave a single spot on t.l.c., λ_{\max} 278 and 290 nm, λ_{\max} (alkaline EtOH) 270sh, 282sh, 292sh, and 333 nm.

Acylation of the hydrogenation product. The above hydrogenated product (9 mg) and aluminium chloride (15 mg) were stirred in nitrobenzene (2.5 ml) and acetyl chloride (0.2 ml) was added slowly. The mixture was stirred at 20 °C for 3 days. T.l.c. analysis showed the formation of one spot of lower polarity than the starting compound.

Ether (25 ml) was added and the mixture extracted with sodium hydroxide solution (1M; 30 ml). The alkaline phase was washed with ether (3 × 20 ml), acidified (4N-HCl) and extracted into ether (3 × 20 ml), and dried (MgSO₄·H₂O). The solvent was removed under reduced pressure to leave an oil (7 mg). This was subjected to p.l.c. and afforded an oil (ca. 1 mg), λ_{\max} 293 nm, λ_{\max} (alkaline EtOH) 240sh and 336 nm. This compound was identified unambiguously as the saturated and acylated hydroxychroman (33) and shown to be identical to a fully characterised sample of the hydroxychroman (33) (see preceding paper) (t.l.c., u.v., and EI mass spectrum).

Oxidations of Tri-isopentenylphloroglucinol (7).—(a) *Aerial oxidation at 0 °C.* The trisubstituted phenol (7)¹ (1.01 g) was kept at 0 °C and left to autoxidise slowly over 3 weeks. The oil was then chromatographed on silicic acid (column 35 × 2.5 cm). Elution with ether–light petroleum (3 : 7) yielded the *dione* (34)* as an oil (60 mg) (Found: M^+ , 346.212 5. C₂₁H₃₀O₄ requires M , 346.214 3).

Elution with ether–light petroleum (7 : 3) gave a yellow oil (110 mg) which was purified by p.l.c. to give the *cyclopentenone* (36)* as a yellow gum (55 mg) (Found: M^+ , 264.135 3. C₁₅H₂₀O₄ requires M , 264.136 2).

The remaining complex mixture of minor oxidation products were washed off the column using methanol to leave a thick brown gum (675 mg).

Aerial oxidation of compound (34) to (36).—The dione (34) (35 mg) from the aerial oxidation of (7) was kept as an oil to oxidise at 20 °C for 2 days. T.l.c. analysis showed the formation of one red spot. P.l.c. afforded the compound (36) as a yellow oil (15 mg), whose t.l.c. and other properties (u.v., i.r., and n.m.r.) were identical to those of the sample obtained from the air oxidation of the phenol (7).

(b) *Peracid oxidation.* The phenol (7) (0.505 g), *m*-chloroperbenzoic acid (270 mg), and *p*-toluenesulphonic acid in chloroform (20 ml) were stirred at 19 °C for 0.5 h. The mixture was worked up as for the oxidation of compound (2) to give an orange oil (460 mg). Chromatography on a silicic acid column (17 × 2.0 cm) and elution with ether–light petroleum (1 : 4) afforded an oil (25 mg), which gave a single spot on t.l.c. It was shown to be identical to the dione (34) by comparison (t.l.c., u.v., n.m.r.) with the sample obtained from aerial oxidation of (7).

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