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THE OXIDATION OF SOME PYROGALLOL AND PURPUROGALLIN DERIVATIVES

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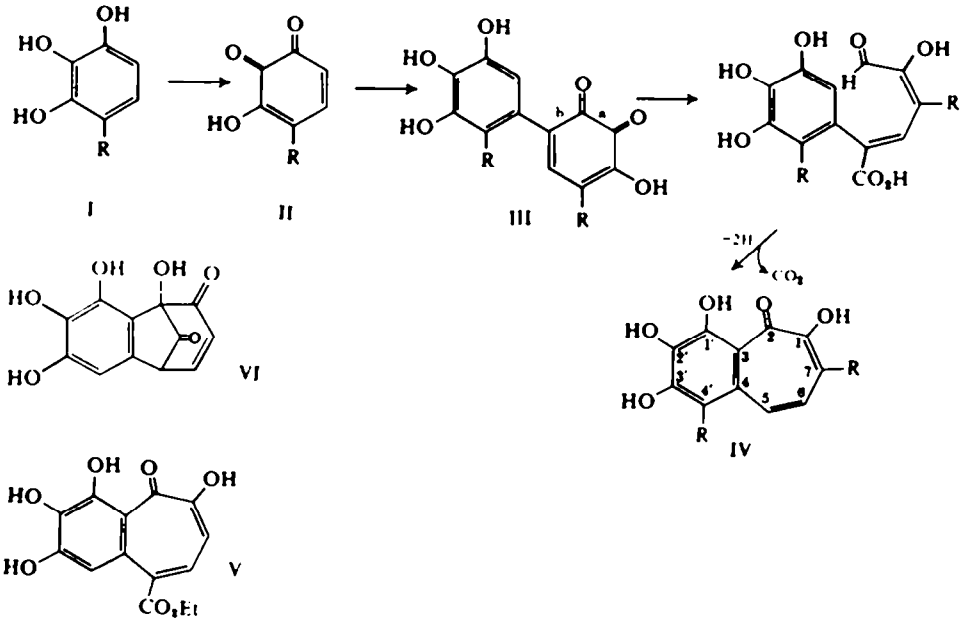
Abstract—The oxidation products of a number of 4- and 5-monosubstituted and 4,6-disubstituted pyrogallols are discussed. 4-Alkylpyrogallols yield the corresponding 4',7-dialkylpurpurogallins and the structures of the products resulting from the further oxidation of these compounds with alkaline hydrogen peroxide are elucidated. Oxidation of 5-mono and 4,6-dialkylpyrogallol derivatives yield characteristic white and yellow dimers respectively. Evidence is presented in favour of a tricyclododecane formulation for the former and a dibenzodioxin structure for the latter type of dimer. The transformation of the dibenzodioxin dimers to benzocyclopentadioxepin isomers on treatment with base is described.

IN AN earlier paper[1] a mechanism for the conversion of pyrogallol (I; R = H) into purpurogallin (IV; R = H) which was based on the intermediate formation of the hydroxyquinone II (R = H) and its dimerization to the tetrahydroxydipheno-*o*-quinone (III; R = H) was suggested. The mechanism predicts that 4-substituted pyrogallols would be oxidized to 4',7-disubstituted purpurogallins IV provided that the substituent group did not radically modify the nucleophilic (position 6) and electrophilic (position 5) reactivities of the hydroxyquinone II which are necessary for its subsequent dimerization. On the other hand 5-substituted pyrogallols would not be expected to give purpurogallins except in those cases, such as gallic acid, where the 5-substituent may be eliminated during the reaction.[2] The present communication describes experiments undertaken some 15 years ago to test these conclusions; the oxidation of a number of 4- and 5-substituted and 4,6-disubstituted pyrogallols have been examined and where substituted purpurogallins have been obtained the further oxidation of these products with alkaline hydrogen peroxide has been studied, in part to establish the constitution of the substituted purpurogallins and in part to prepare new substituted tropolones. The results, which support on the whole the proposed mechanism, are reported† but publication was delayed until further evidence concerning certain abnormal products and reactions was supplied by later work‡. Some of the earlier results have, not unexpectedly, been anticipated by others and particularly noteworthy contributions to this field of investigation have been

† In Ph.D. theses (A. C. and P. B. T.)[3]
‡ N. M .W. and E. H.

[1] A. Critchlow, R. D. Haworth and P. L. Pauson, *J. Chem. Soc.* 1318 (1951).
[2] W. Crow, and R. D. Haworth, *J. Chem. Soc.* 1325 (1951).
[3] A. Critchlow and P. B. Tinker, Ph.D. Theses, Sheffield University, 1953 and 1954.

made.[4–6,7–14] A recent communication[15] now makes it necessary to describe our results in this field.



The isolation[4,7] of the ethyl purpurogallin-5-carboxylate (V) by the oxidation of pyrogallol in ethanol solution is particularly important in connection with the mechanism of formation of purpurogallin. Full experimental details for the preparation of V are not available and in our hands low yields (10%) were experienced, but PMR measurements confirm the structure of the ester. The isolation of V does not however necessarily establish the dimeric structure (VI) as an intermediate in the reaction as concluded by Salfeld[6] and Horner;[7,8] thus V could be derived by rupture of bond (a) of III (as opposed to bond (b) as previously suggested[1]) followed by cyclization.

The oxidation of 4-substituted pyrogallols

Horner *et al.*[11] have oxidized 4-halogen substituted pyrogallol derivatives I (R = Cl or Br) to the corresponding 4',7-dihalogenopurpurogallins (IV; R = Cl or Br). Similar results were obtained in our work and the predicted orientation of the halogen substituents has also been supported by the PMR spectra of these compounds

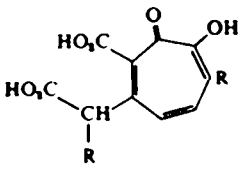
[4] J. C. Salfeld, *Angew. Chem.* **69**, 723 (1957).
[5] J. C. Salfeld, *Chem. Ber.* **93**, 737 (1960).
[6] J. C. Salfeld and E. Baume, *Chem. Ber.* **93**, 745 (1960).
[7] L. Horner and W. Durckheimer, *Z. Naturforsch.* **14B**, 741 (1959).
[8] L. Horner, K. H. Weber and W. Durckheimer, *Chem. Ber.* **94**, 2883 (1961).
[9] L. Horner and S. Gowecke, *Chem. Ber.* **94**, 1267 (1961).
[10] L. Horner, S. Gowecke and W. Durckheimer, *Chem. Ber.* **94**, 1276 (1961).
[11] L. Horner and W. Durckheimer, *Chem. Ber.* **95**, 1206 (1962).
[12] L. Horner and W. Durckheimer, *Chem. Ber.* **95**, 1219 (1962).
[13] L. Horner, W. Durckheimer, K. H. Weber and K. Dolling, *Chem. Ber.* **97**, 312 (1964).
[14] M. Mupakami, K. Suzuki and E. Mishima, *J. Chem. Soc. Japan* **75**, 620 (1954).
[15] H. J. Teuber, P. Heinrich and M. Dietrich, *Liebigs Ann.* **696**, 64 (1966).

all of which showed a pair of ortho coupled protons in the tropolone ring (e.g. 1,1',2',3'-tetra-O-methyl-4',7-dibromopurpurogallin, showed an AB quartet τ 2·35 and 3·01, J_{AB} 13 c/s). When the dibromo-derivative IV (R = Br) was oxidized with alkaline hydrogen peroxide a surprising result† was obtained; the only isolable products were the bromine free dibasic acid VII (R = H) and the anhydride VIII both of which have previously been derived by an analogous oxidation of purpurogallin itself.[16] It was shown that 4',7-dibromopurpurogallin on treatment with alkali (20% caustic soda at 90° for 5 min) gave an infusible polymeric material and up to 30% yields of purpurogallin (Horner[11] reports 57%) which would of course be converted to VII (R = H) and VIII by peroxide. The mechanism whereby the bromine is removed is obscure; it appears as bromide ion and similar experiments with simpler bromophenols gave an analogous liberation of bromide ion, the percentage eliminated being shown as follows in the bracket: 4-bromopyrogallol (81%), tribromopyrogallol (95%), tribromoresorcinol (74%), 5,6-dibromoresorcinol (13%), 4-bromocatechol (15%), *o*- and *p*-bromophenol (0%). The elimination of bromine from the purpurogallin derivative shows several analogies to the base catalysed conversion of 7-bromo-2,2'-diphenylcycloheptanone to 2,2'-diphenylcycloheptanone observed by Corey[17] and of iodine from certain ketosteroids observed by Djerassi[18] and in both of these examples the halogen atom has a positive character. The model experiments also show that an increase in the number of phenolic OH groups increases the tendency for bromine elimination and it is also probable that the reducing properties of the pyrogallol nucleus plays an important role in the conversion of IV (R = Br) to IV (R = H).

4-Methylpyrogallol[19] (I; R = Me) was converted by the action of potassium iodate into 4',7-dimethylpurpurogallin (IV; R = Me) which gave a 2',3'-dimethyl ether with diazomethane in an analogous fashion to purpurogallin itself. As expected from its structure dimethylpurpurogallin (IV; R = Me) failed to react with bromine but oxidation with alkaline hydrogen peroxide was abnormal and the expected tropolone carboxylic acid (VII; R = Me) was not obtained. The deep purple coloured product, isolated in poor yield, lacked tropolone and carboxylic acid properties and reacted as a phenolic quinone towards ferric chloride and 2,4-dinitrophenylhydrazine. Methylation yielded a dimethyl ether which showed a band at 1698 cm^{-1} in the IR and formed a crystalline mono-2,4-dinitrophenylhydrazone. The PMR spectra of the phenolic quinone, its methyl ether and methyl ether 2,4-dinitrophenylhydrazone (in CF_3CO_2H) showed two ortho coupled aromatic protons (τ 1·6 and 2·6, J 10 c/s) and two Me groups attached to aromatic or quinonoid systems (τ 7·32 and 7·80) and were consistent with the structure IX proposed for the phenolic quinone. The mode of formation of IX from dimethylpurpurogallin presumably involves a base catalysed contraction of the tropolone ring[20] and parallels the oxidative transformation of colchicine to colchinol.[21]

† This result was briefly reported by P. L. Paulson, *Chem. Rev.* **55**, 1 (1955).

[16] R. D. Haworth and J. D. Hobson, *J. Chem. Soc.* 561 (1951).
[17] E. Corey and J. Lyle, *J. Amer. Chem. Soc.* **75**, 4973 (1953).
[18] G. Rosenkranz, O. Mancera, J. Gatica and C. Djerassi, *J. Am. Chem. Soc.* **72**, 4078 (1950).
[19] A. Critchlow, R. D. Haworth and P. L. Pauson, *J. Chem. Soc.* 1318 (1951).
[20] P. L. Pauson, *Chem. Rev.* **55**, 1 (1955).
[21] J. W. Cook and J. D. Loudon, *Quart. Rev.* **5**, 99 (1951).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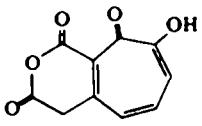
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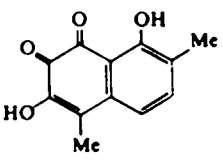
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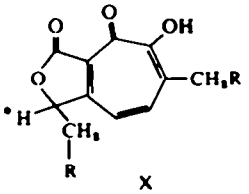
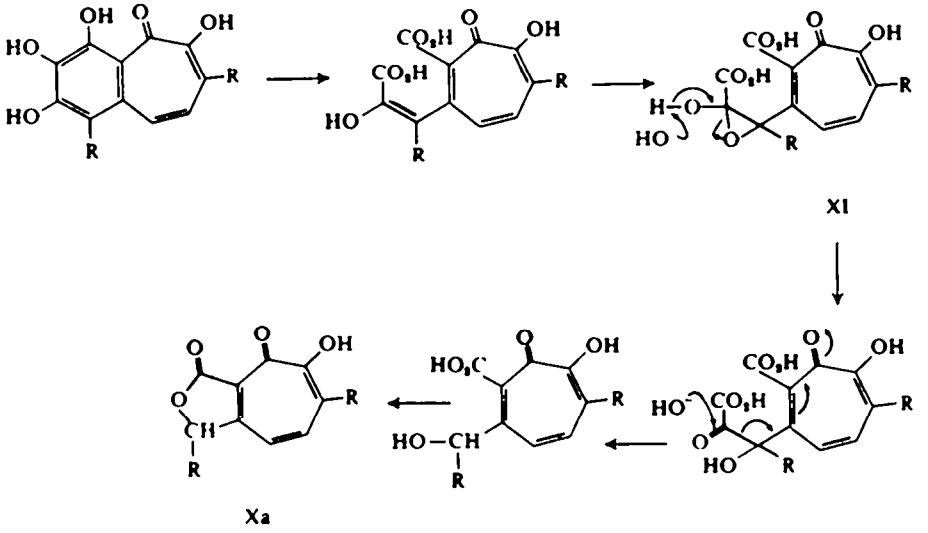

X

4-Ethylpyrogallol, prepared from gallacetophenone,[21,22] was oxidized by periodate in good yield to 4',7-diethylpurpurogallin (IV; R = Et) which with diazomethane gave a 2',3'-O-methyl ether. When the diethylpurpurogallin was oxidized with peroxide a pale yellow compound, which exhibited typical tropolone colour reactions[20] with ferric chloride and copper acetate, was obtained. The UV spectrum showed a degree of fine structure which resembled those of the more complex alkyltropolones and in the IR spectrum bands at 1621 and 1558 cm^{-1} which were attributed to the tropolone nucleus. An additional band at 1770 cm^{-1} was ascribed to an unsaturated γ-lactone but conclusive chemical evidence for the proposed structure X (R = Me) was not obtained. The PMR spectrum of X (R = Me) was consistent with the proposed formulation as the lactone of 7-ethyl-4-(α-hydroxypropyl)-tropolone-3-carboxylic acid and showed a strongly hydrogen bonded OH group, two ortho coupled aromatic protons (τ 2·3 and 2·9, J 10·5 c/s) and two Me groups adjacent to methylene (τ 8·7 and 8·96). One of these methylene groups—attached to the tropolone ring—was clearly evident as the characteristic 1:3:3:1 quartet (τ 7·1) but the other appeared as a very broad multiplet (τ 8·0) which presumably results from its position adjacent to the Me and the methine group. This analysis was supported by the appearance of the absorption of the methine hydrogen (X, *) which was present as a distinct quartet (1:1:1:1) typical of an ABX system (τ 4·60, J_{AX} = 4 c/s, J_{BX} = 7 c/s). The low field position of this quartet is in harmony with the location of the methine group next to the tropolone ring and the lactone oxygen (cf. phthalide methylene group at τ 4·65). The indication of two active hydrogens (Zerewitinoff) in X (R = Me) results probably from the participation in this test of the methine hydrogen in addition to the OH of the tropolone ring.

4-n-Propyl-[21,22] and 4-n-butylpyrogallols[21,22] were also oxidized by potassium iodate to the di-n-propyl- and di-n-butylpurpurogallins IV (R = n-Pr or n-Bu) respectively. Further peroxide oxidation of these compounds gave characteristic yellow crystalline derivatives whose reactions and spectroscopic (UV, IR and PMR) properties were consistent with their formulation (X: R = Et or n-Pr) as analogues of the Et compound discussed above. The formation of structure Xa for this series of products may be envisaged as a variation of the peroxide oxidation of purpurogallin itself[15] and is rationalised below. Decomposition of the intermediate XI in the manner indicated leads to Xa, and alternatively fission of the epoxide ring of XI, accompanied by decarboxylation, leads to VII.

4-Methoxypyrogallol (I; R = OMe), prepared by the action of alkaline hydrogen peroxide on 2,3-dihydroxy-4-methoxybenzaldehyde,[24] and 4-aminopyrogallol (I; R = NH_2) obtained by reduction of 4-nitropyrogallol,[25] gave deep red solutions with

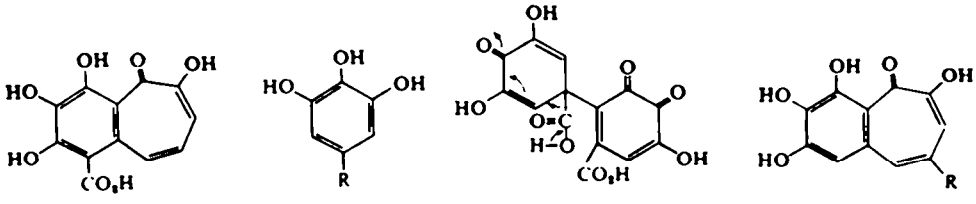
[22] S. S. Israelstam and H. Stephen, *J. S. African Chem. Inst.* **26**, 41 (1943).
[20] M. C. Hart and E. H. Woodruff, *J. Am. Chem. Soc.* **58**, 1937 (1936).
[24] E. Späth and E. Dobrovolny, *Ber. Dtsch. Chem. Ges.* **71**, 1831 (1938).
[25] A. Einhorn, J. Cobliner and H. Pfeiffer, *Ber. Dtsch. Chem. Ges.* **37**, 100 (1904).



XI

Xa

potassium iodate which did not yield purpurogallins. These failures were not unexpected as both the OMe and amino groups would diminish the necessary electrophilic character of position 5 of the intermediate II and in addition it is probable that these groups would facilitate oxidation to the corresponding 2,3-dihydroxy-*p*-benzoquinone. Again we have been unable to convert pyrogallol-4-carboxylic acid (I; R = CO_2H), prepared by a variation of the method of Baker and Smith,[36] or 4-nitropyrogallol[36] (I; R = NO_2) into purpurogallins presumably because the carboxyl and nitro groups reduce the necessary nucleophilic character of position 6 in the intermediate II. These groups, on the other hand, do not interfere with the electrophilic nature of position 5 and when a mixture of pyrogallol and pyrogallol-4-carboxylic acid was oxidized with iodate a small yield of a carboxylic acid, possibly purpurogallin-4'-carboxylic acid (XII) which gave purpurogallin on sublimation, was obtained.



XII XIII XIV XV

The oxidation of 5-substituted pyrogallols

Although as indicated above mechanistic considerations preclude the transformation of 5-mono and 4,6-disubstituted pyrogallols to purpurogallin derivatives the nature of the oxidation products of these types of pyrogallol have also been investigated. Gallic acid (XIII, R = CO_2H) provides a special case and its oxidation to purpurogallin-4-carboxylic acid (XV, R = CO_2H) is dependent on the ready elimination of the carboxyl group from the intermediate quinone dimer XIV. Both 5-methyl-[37] and

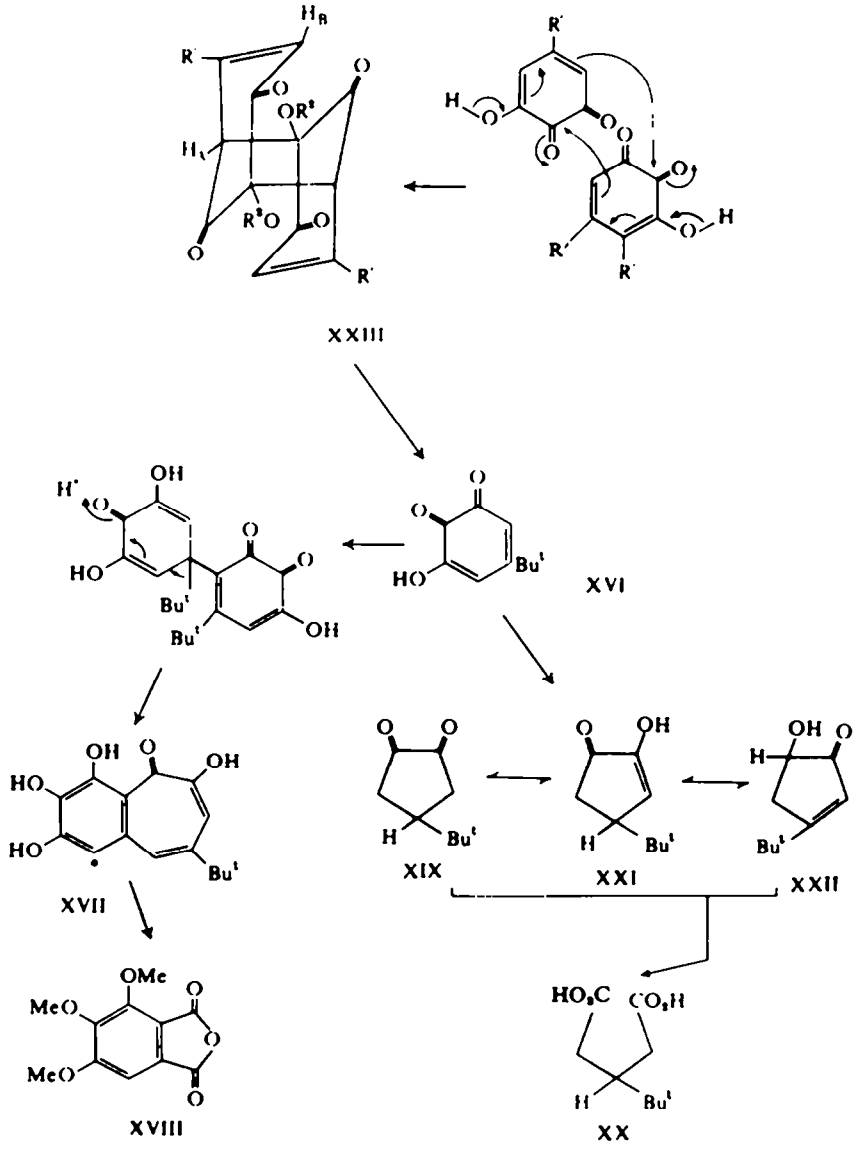
[36] W. Baker and H. A. Smith, *J. Chem. Soc.* 2542 (1931).

[37] Y. Ashina and M. Yusue, *Ber. Dtsch. Chem. Ges.* **69**, 2327 (1936).

5-t-butylpyrogallols[28] (XIII; R = Me and R = t-Bu) when treated with potassium iodate gave characteristic white crystalline products. 5-t-Butylpyrogallol (XIII, R = t-Bu) was prepared from pyrogallol, t-butanol and zinc chloride according to Stockelbach,[28] who however formulated the compound as the expected 4-t-butyl isomer I (R = t-Bu). However the PMR spectrum of the compound and its tri-O-acetate showed a sharp two proton singlet in the aromatic region and its 1,2-di-O-acetate (ν_{max} 3200, 1760, 1710 cm^{-1}) showed a two proton AB system (J_{AB} 3 c/s) in the aromatic region These results and those of the acid and base catalysed degradation of its oxidation product, discussed below, are most reasonably rationalised in terms of the 5-t-butyl structure for the parent pyrogallol. Electrophilic substitution of pyrogallol (e.g. acylation and alkylation) normally proceeds exclusively with the formation of 4-mono- and 4,6-di-substituted products. Thus t-butylation of pyrogallol with excess of alkylating agent gives a good yield of the 4,6-di-t-butyl compound. However under the conditions for the formation of the mono-t-butyl pyrogallol when the phenol and t-butanol are approximately equimolar it is suggested that the 4-isomer is first formed (kinetic control) and subsequently rearranges to the presumed thermodynamically more favourable 5-t-butyl derivative. Rearrangement does not occur with the 4,6-di-t-butyl product since a 4,5-orientation of alkyl groups would in this case be predictably less stable. The oxidation products of 5-methyl- and 5-t-butylpyrogallol resembled in many respects a presumed dimeric form of 3-hydroxy-*o*-benzoquinone (II; R = H) obtained by Perkin and Steven[29] and for which Teuber[15] recently proposed a novel tricyclododecane structure. Thus the compounds were high melting, difficulty soluble and showed strong bands at 1750, 1690 and 1620 cm^{-1} in the IR and in the UV λ_{max} were observed at 278 and 235 mμ. The mol. wt. (360) of the compound derived from 5-t-butylpyrogallol was determined by mass spectrometry and showed it to be a dimer, and a dimeric structure has similarly been assumed for the compound obtained by oxidation of 5-methylpyrogallol. Acetylation proceeded readily in acetic anhydride and sulphuric acid to give di-acetylderivatives and zinc dust reduction gave the parent pyrogallol derivatives. Perkin and Steven[29] observed that the dimeric form of the hydroxy-*o*-quinone (II; R = H) was readily converted to purpurogallin by warming in water, but under the same conditions the methyl and t-butyl analogues were comparatively stable, although warming the compounds with acetone, alcohol or chloroform gave light-red solutions due presumably to a partial dissociation into the parent hydroxy-*o*-quinone. Warming the t-butyl compound with acids or bases however gave products whose formation can only be rationalised in terms of an initial dissociation to the monomeric hydroxy-*o*-quinone (XVI) followed by further reaction. Refluxing in acid gave, in poor yield, a compound showing the typical spectroscopic properties of a purpurogallin derivative and which gave a dimethyl ether with diazomethane and a tetramethyl ether with dimethyl sulphate. The compound analysed as a mono-t-butylpurpurogallin and has been formulated as 6-t-butylpurpurogallin (XVII); support for this structure was obtained by the isolation of trimethoxyphthalic anhydride (XVIII)[30] after oxidation of the tetramethyl ether and by the PMR spectra of the compound and its methyl ethers which showed a singlet aromatic proton (XVII, •) and two meta coupled protons in the tropolone

[28] F. E. Stocklebach, *U.S. Pat.*, 2, 137, 815; *Chem. Abstr.* 33, 1764 (1939).
[29] A. G. Perkin and A. B. Steven, *J. Chem. Soc.* 802 (1906).
[30] J. A. Barltrop and J. S. Nicholson, *J. Chem. Soc.* 120 (1948).

ring. On treatment with base the oxidation product of 5-t-butylpyrogallol gave initially a deep red solution rapidly fading to yellow on warming and which on acidification gave a weakly acidic substance with a strong caramel odour. The substance formed a dioxime and bis-2,4-dinitrophenylhydrazone which have been formulated as derivatives of 4-t-butylcyclopenta-1,2-dione (XIX) and oxidation gave, in small amount, a dicarboxylic acid (isolated as its *p*-toluimide) formulated therefore as XX. TLC resolved the original alkaline degradation product into two major components. The first of these on the basis of analytical and spectroscopic data was assigned the monoenolic structure XXI which was supported by its methylation (diazomethane or dimethyl sulphate) to a monomethyl ether which gave a 2,4-dinitrophenylhydrazone. The



PMR spectrum of the second component, which could not be obtained pure as judged by TLC, was interpreted in terms of the tautomeric structure XXII and further chemical evidence which will support this assignment is being sought. Analysis of the original mixture of products resulting from the alkaline degradation (XXI and XXII) based on the t-butyl absorptions in the PMR spectrum (XXI, τ 9·08 and XXII, τ 8·80) indicated a 2:1 ratio of XXI to XXII. The derivation of XXI and XXII presumably results from an initial dissociation of the 5-t-butylpyrogallol oxidation product to the monomeric quinone followed by a benzilic acid change and loss of carbon dioxide to give the parent 1,2-cyclopentadione (XIX) in an analogous manner to the change observed by Campbell in the aerial oxidation of 4,6-di-t-butylpyrogallol.[31]

The structures XXIII (R′ = Me or t-Bu; R^2 = H) proposed for the oxidation products of 5-methyl- and 5-t-butylpyrogallol have been deduced from the spectroscopic data and from the property of ready dissociation into the monomeric quinonoid form observed for t-butyl compound. The PMR of the oxidation products (Table 1) were notable for their simplicity which combined with the UV and IR characteristics have been interpreted in terms of the dimeric structures XXIII (R′ = Me or t-Bu, R^2 = H). Similar formulations have recently been proposed[15,33] for the oxidation products of several hydroxy-*o*-quinones. In particular the structure XXIII (R^1 = R^2 = H) was suggested for the white dimer of 3-hydroxy-*o*-benzoquinone previously isolated.[29] This independent structural assignment confirms the chemical relationship of this substance to the 5-methyl- and 5-t-butylpyrogallol oxidation products which has been referred to above.

TABLE 1. PMR SPECTRA IN $CF_3 \cdot CO_2H$: τ VALUES (RELATIVE INTENSITIES FOLLOWED BY MULTIPLICITY IN PARENTHESES)

Compound	R^1	COMe	H_A	H_B
XXIII (R^1 = Me, R^2 = COMe)	7·58 (3, d)	7·62 (3, s)	5·95 (1, d)	3·45 (1, m)
XXIII (R^1 = *t*-Bu, R^2 = H)	8·64 (9, s)	—	5·67 (1, d)	3·25 (1, d)
XXIII (R^1 = *t*-Bu, R^2 = COMe)	8·62 (9, s)	7·65 (3, s)	5·62 (1, d)	3·28 (1, d)

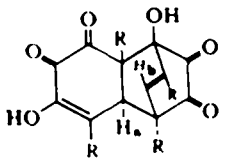
m = multiplet, d = doublet, s = singlet.

5-Bromopyrogallol, prepared by reduction of tribromopyrogallol with zinc in acetic acid,[33] was converted by potassium iodate into a product which is tentatively regarded as the bromo analogue of XXIII (R′ = Me or t-Bu, R^2 = H) but sufficient material was not available for a more detailed analysis. The oxidation of 5-methylpyrogallol to XXIII (R^1 = Me, R^2 = H) proceeds rapidly such that in a mixed oxidation of pyrogallol and 5-methylpyrogallol only purpurogallin (IV; R = H) and the dimer XXIII (R^1 = Me, R^2 = H) were obtained, there being no trace of the mixed oxidation product XV (R = Me). 5-Nitropyrogallol[34] was readily oxidized to a deep red aqueous solution by iodate but no crystalline product could be isolated in this case.

[31] T. W. Campbell, *J. Am. Chem. Soc.* **73**, 4190 (1951).
[33] H. J. Teuber and G. Steinmetz, *Chem. Ber.* **98**, 666 (1965).
[29] J. F. Moore and R. M. Thomas, *J. Am. Chem. Soc.* **39**, 987 (1917).
[34] H. Barth, *Monatschefte* **1**, 882 (1880).

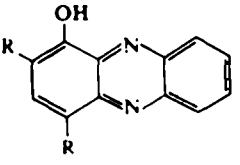
The oxidation of 4,6-disubstituted pyrogallols

The oxidation of 4,6-disubstituted pyrogallol derivatives has been investigated during the course of this work by several workers notably Flaig[35,36] and Salfeld[6,7] and the latter proposed structures XXIV (R = Et or t-Bu) for the characteristic products formed on oxidation of 4,6-diethyl- (XXV; R = Et) and 4,6-di-t-butyl-pyrogallol (XXV; R = t-Bu). These proposals were based on spectroscopic and analytical data, the ready reduction of the t-butyl dimer to the parent pyrogallol formation of the phenazine XXVI (R = Et or t-Bu) with *o*-phenylenediamine, formation of mono- and di-acetyl derivatives and the general chemical similarity in chemical and physical properties to several *o*-benzoquinone dimers[37–40] such as XXVII

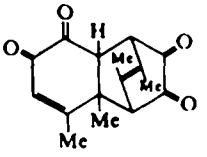


XXIV

XXV



XXVI



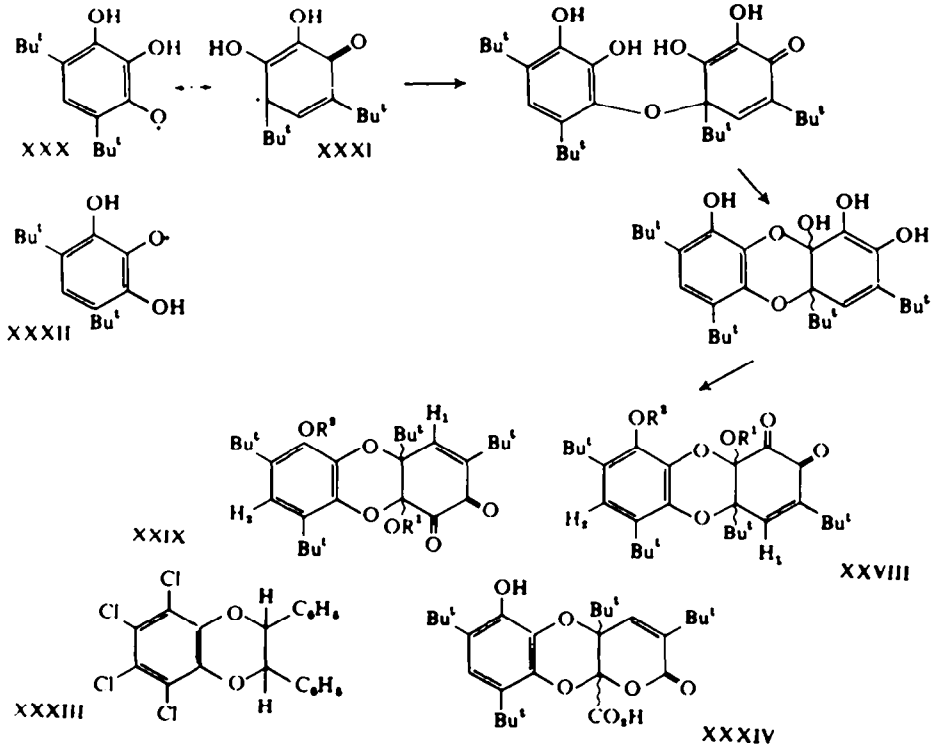
XXVII

whose structures have been investigated by other workers. In the present work similar dimeric products have been prepared by oxidation with *p*-benzoquinone or potassium iodate of 4,6-diethyl- and 4,6-di-t-butylpyrogallol. The properties and chemical reactions of the t-butyl dimer agree closely with those reported by Salfeld for this compound but a discrepancy in colour (yellow as opposed to white) and m.p. (132–133° as opposed to 142–151°) was observed for the diethyl analogue. In addition the latter was reduced back to 4,6-diethyl pyrogallol a reaction not reported by Salfeld. However it is clear from the published[40] spectroscopic data of quinone dimers such as XXVII that they differ significantly from the yellow dimeric products obtained from the 4,6-dialkylpyrogallols. Thus dimers of the type XXVII show four distinct carbonyl bands in the IR (1770, 1740, 1721 and 1690 cm^{-1}) whereas the dimeric form of 4,6-di-t-butylpyrogallol for example shows only two at 1759 and 1689 cm^{-1}. Similar significant differences were apparent in the UV and visible spectra and the PMR spectra did not show absorption which could be associated with H_a or H_b in structure XXIV. These observations indicated that further investigation of these compounds was required.

The PMR spectra of the 4,6-di-t-butyl-3-hydroxy-*o*-benzoquinone dimer and its derivatives (Table 2) all showed two uncoupled protons (τ 2·94 to 3·23) which could only be assigned to protons attached to an aromatic nucleus or in the β-position of an $\alpha\beta$-unsaturated carbonyl system. The dimer contained two OH groups and the spectrum of the diacetate indicated that one was phenolic (Me of acetate, τ 7·60) and the other aliphatic (Me of acetate, τ 7·82). On this basis the spectrum of the

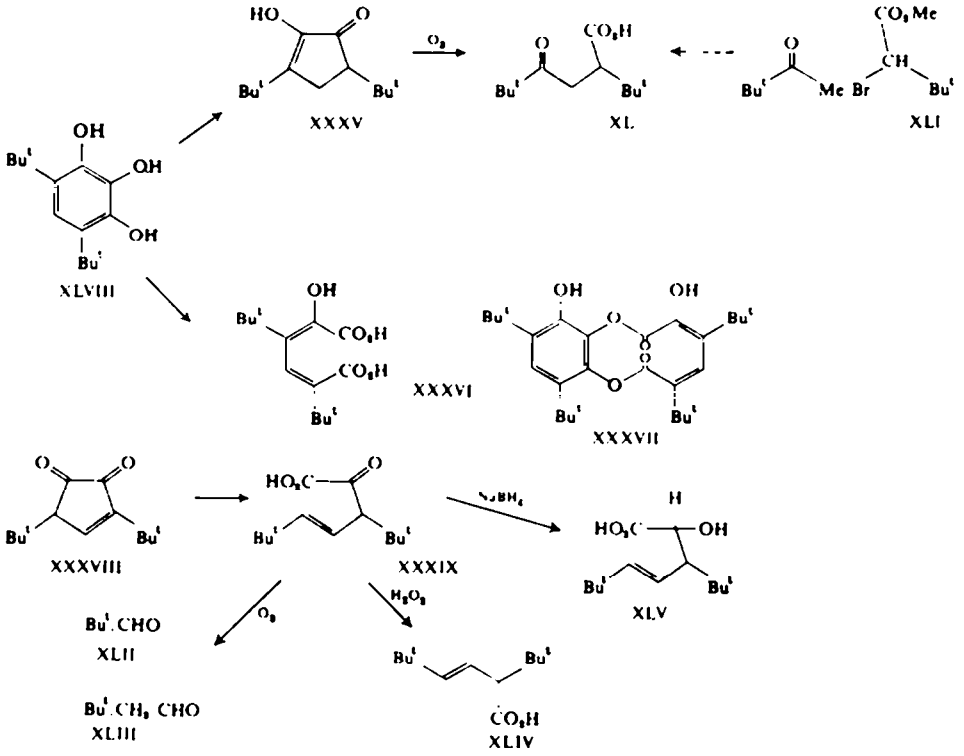
[35] W. Flaig, T. Ploetz and A. Biergaus, *Liebigs Ann.* **597**, 196 (1955).
[36] W. Flaig, *Biochemistry of Wood*, IV*th International Congress of Biochemistry* p. 227. Pergamon Press, London (1958).
[37] A. A. Patchett and B. Witkop, *J. Org. Chem.* **22** 1477 (1957).
[38] J. Harley-Mason and A. H. Laird, *J. Chem. Soc.* 1718 (1958).
[39] L. Horner and K. Sturm, *Liebigs Ann.* **597**, 1 (1955).
[40] E. Adler, R. Magnusson, B. Berggren and A. Thomelius, *Acta Chem. Scand.* **14**, 515 (1960).

monoacetate was interpreted as being due to a phenolic acetate (Me of acetate, τ 7·60). Interpretation of the IR spectra of the two acetates did not allow this distinction to be clearly made. Taken in conjunction with the other chemical and physical data referred to above which indicated a structure containing two carbonyl functions one of which had $\alpha\beta$ unsaturation (IR ν_{max} 1689 and 1618 cm^{-1}) and ether linkages (ν_{max} 975 cm^{-1}) the new evidence has been interpreted in terms of the dibenzodioxin formulae XXVIII or XXIX ($R^1 = R^2 = H$) for the t-butyl dimer. An analogous structure XXVIII or XXIX ($R^1 = R^2 = H$ and Et for t-Bu) presumably represents the structure of the product from 4,6-diethylpyrogallol but a similar detailed analysis of this compound has not been carried out. The compound did however show in the IR ν_{max} >CO 1764, 1689 cm^{-1} and its PMR spectrum was quite analogous to the di-t-butyl dimer (Table 2) showing two OH groups (τ 4·71, 5·39), two singlet hydrogens (τ 3·25, 3·46) and four Et groups distinguished most easily by analysis of the Me signals which indicated that three were in similar chemical environments (τ 9·02) and one was distinct (τ 8·81).



Structures XXVIII or XXIX ($R^1 = R^2 = H$) could arise by a number of routes. Thus if the reaction proceeds by a free radical mechanism then structure XXVIII ($R^1 = R^2 = H$) would be formed by a pairing of the phenoxy radical XXX and its mesomeric form XXXI with the subsequent changes as depicted. Structure XXIX ($R^1 = R^2 = H$) would be formed analogously by an initial pairing of the radicals XXXI and XXXII). Alternatively if the reactions proceed via quinone intermediates either of the proposed structures for the dimeric products could arise by Diels–Alder

addition of the quinone carbonyl groups to the double bond of a further quinone molecule. This type of addition of *o*-quinones to olefinic double bonds has been observed;[41] thus condensation of tetrachlor-*o*-benzoquinone and stilbene gives the benzdioxan XXXIII. It has not been possible to define the geometry of the ring fusion nor to distinguish between the two alternative structures XXVIII or XXIX ($R^1 = R^2 = H$). Molecular models indicate a degree of steric repulsion between two of the t-butyl groups in XXVIII ($R^1 = R^2 = H$) such as to favour XXIX ($R^1 = R^2 = H$) and this latter formulation is used in the subsequent discussions; additional evidence is clearly desirable. Lengthy peroxide treatment of the di-t-butylpyrogallol dimer gave a colourless lactonic acid formulated as the pyranobenzodioxin (XXXIV) on the basis of the IR (ν_{max} 1762, 1709 and 993 cm^{-1}) and PMR spectra (four t-butyl groups τ 8·65 (2), 8·80, 9·00; the β-proton of an $\alpha\beta$-unsubstituted lactone τ 3·74, and one aromatic proton τ 3·17). Alkaline degradation of the lactonic acid gave equimolar quantities of the cyclopentanedione (XXXV) and the dicarboxylic acid (XXXVI) which Campbell[31] has shown previously to be degradation products of the parent 4,6-di-t-butylpyrogallol.



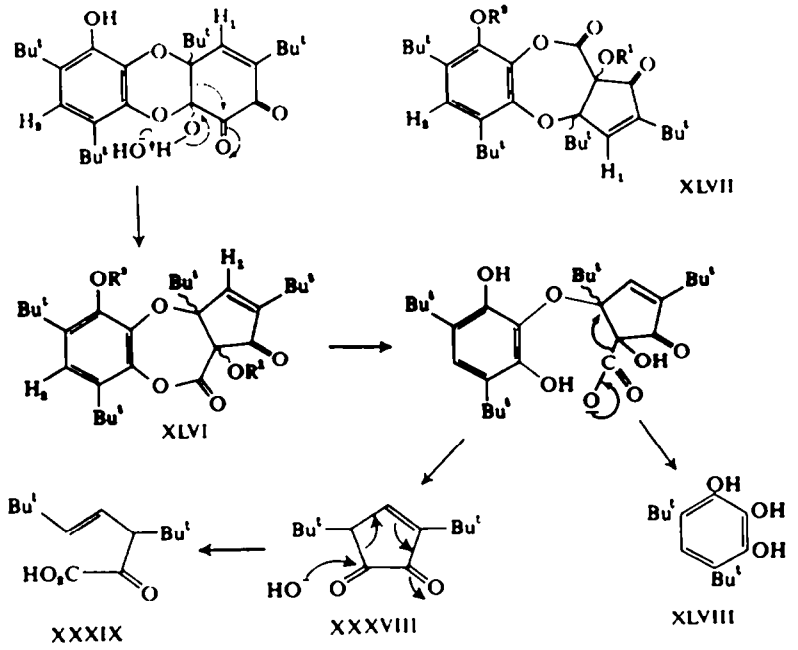
The yellow 4,6-di-t-butyl-3-hydroxy-*o*-benzoquinone dimer (XXVIII or XXIX; $R^1 = R^2 = H$) underwent a remarkable change on melting or on treatment with a catalytic amount of base to a white isomeric compound which Salfeld and Baume[7] formulated as XXXVII since it gave 4,6-di-t-butylpyrogallol (XLVIII) and 3,5-di-t-butylcyclopent-3-en-1,2-dione (XXXVIII) on further alkaline degradation. Teuber

[41] L. Horner and L. Merz, *Liebigs Ann.* **570**, 89 (1950).

et al.[15] recently described a product identical to the white dimer resulting from oxidation of 4,6-di-t-butylpyrogallol with Fremy's salt, and an exchange of samples with Professor Teuber has confirmed this identity. In the present work additional products which have been isolated from prolonged alkaline degradation of the white dimer are 3,5-di-t-butylcyclopent-2-en-2-ol-1-one (XXXV), in small amount the dicarboxylic acid XXXVI (both are breakdown products of 4,6-di-t-butylpyrogallol[31]) and the keto acid XXXIX which is derived from XXXVIII by base cleavage. Further proof of the structure of 3,5-di-t-butylcyclopent-2-en-2-ol-1-one (XXXV) was obtained by ozonolysis which gave the keto acid XL whose structure was corroborated by synthesis. Thus treatment of the α-bromoester XLI and t-butyl methyl ketone with sodamide readily afforded the methyl ester of XL.

Proof of the structure of the other keto acid XXXIX was obtained from its IR spectrum (ν_{max} 1733 (>CO), 1709 (—CO_2H) and 1650 (>C=C<) cm^{-1}) and PMR spectrum which showed two t-butyl groups (τ 8·98, 9·03) in addition to a three proton ABX pattern from the allylic system (AB, τ 4·70 and 4·77; X, τ 6·13; J_{AB} 15 c/s, J_{AX} 0 c/s, J_{BX} 9 c/s). Proof also followed from its ozonolysis to give 1,1,1-trimethylacetaldehyde (XLII) and 2,2,2-trimethylpropionaldehyde (XLIII) both of which were isolated and identified as their 2,4-dinitrophenylhydrazones. Peroxide oxidation of XXXIX gave 5,5-dimethyl-2-t-butyl-hex-2-enoic acid (XLIV), and sodium borohydride reduction 6,6-dimethyl-3-t-butyl-2-hydroxyhept-3-enoic acid (XLV).

The mono- and di-acetates of the yellow dimer XXVIII or XXIX (R′ = H, R^2 = CO·Me and XXVIII or XXIX; R^1 = R^2 = CO·Me) both underwent analogous transformations with alkali to give the monoacetate of the white dimeric form; the former when treated with a catalytic amount and the latter with one equivalent of base. Following the assignment of the phenolic acetate structure to the monoacetate



of the yellow form the rearrangement has been formulated therefore as an α-ketol rearrangement[42] initiated by abstraction of a proton from the hemi-acetal group of XXVIII or XXIX ($R^1 = R^2 = H$) and giving rise to the benzocyclopentadioxepin structure for the white dimer XLVI or XLVII ($R^1 = R^2 = H$).

The PMR and IR spectra of the white form and its derivatives (Table 2) prepared by methods analogous to those described[7] were in agreement with the assigned structure XLVI or XLVII ($R^1 = R^2 = H$). The transformation of the yellow to the white form and the mechanism of the alkaline degradation of the white form to 4,6-di-t-butyl pyrogallol and the cyclopentene-1,2-dione are illustrated in the annexed scheme. The parallel rearrangement was observed with the Et analogue of XXVIII or XXIX ($R^1 = R^2 = H$) but the product was readily decomposed with alkali and on recrystallization, giving products presumed to arise by degradation of the parent pyrogallol.

TABLE 2. SOME DERIVATIVES OF 4,6-DI-BUTYLPYROGALLOL. PMR SPECTRA IN $CDCl_3$ (τ VALUES) AND IR CARBONYL ABSORPTIONS

Compound	H_1, H_2	OH*	OMe	COMe	t-Bu	ν_{max} CO (cm^{-1})
XXIX; $R^1 = R^2 = H$	3·15, 3·23	4·5, 5·35	·	—	8·60, 8·85(3)	1759, 1689
XXIX; $R^1 = R^2 = COMe$	3·01, 3·01	—	·	7·60, 7·82	8·65, 8·75 / 8·85, 8·90	1785, 1762, 1687
XXIX; $R^1 = H$, $R^2 = COMe$	3·13, 2·94	5·40	· ·	7·60	8·65, 8·81 / 8·84, 8·93	1768, 1745, 1689
XLV; $R^1 = R^2 = H$	2·95, 2·95	4·5, 5·65	· ·	—	8·62(2), 8·66 / 9·07	1754, 1728
XLV; $R^1 = R^2 = COMe$	3·09, 2·80	· ·	·	7·63, 7·90	8·60, 8·70(2) / 9·06	1785, 1762, 1725
XLV; $R^1 = H$, $R^2 = COMe$	2·95, 2·82	5·69	·	7·69	8·64, 8·69 / 8·72 9·07	1785, 1762, 1739
XLV; $R^1 = H$ $R^2 = Me$	2·92 2·92	5·75	6·22	· ·	8·62(2) 8·68 / 9·10	1749, 1720
XLV; $R^1 = COMe$, $R^2 = Me$	3·07, 2·92	· ·	6·25	—, 7·90	8·65(3), 9·08	1760, 1750, 1725
	Aromatic-H					
XLVII; R = H	3·2	4·8	· · ·	—	8·70(2)	
XLVII; R = COMe	3·05	4·3	—	7·63	8·60, 8·66	
	Vinylic-H					
XXXVIII	3·25	—	· —	· ·	8·74, 8·97	
XXXV	—	4·19	·	—	8·75, 9·03	
XXXIX	4·70, 4·77	· ·	·	· ·	8·98, 9·03	
XLIII	4·40, 4·39	· ·	·	· ·	8·82, 8·90	

Figures in parentheses refer to numbers of t-butyl groups.
* Hydroxyl group assignments were established by deuteration studies.

EXPERIMENTAL

All m.ps are uncorrected. Except where otherwise stated "potassium iodate solution" refers to a soln of KIO_3 (6 g) in water (100 ml).

4-Substituted pyrogallol derivatives. 4-Methyl-,[10] 4-ethyl-,[37,38] 4-n-propyl-,[37,31] 4-n-butyl-,[39,38] 4-methoxy-,[34] 4-nitro-[38] and 4-amino-[38] pyrogallols were prepared by published methods.

[42] S. Selman and J. F. Eastham, *Quart. Rev.* **14**, 221 (1960).

4-Carboxypyrogallol. A paste of finely powdered pyrogallol (100 g), $KHCO_3$ (200 g) and water (50 ml) was heated at 90° under a stream of N_2 and over 2 hr the bath temp raised to 135° and maintained at this temp until water was no longer evolved or the mixture began to char. After cooling the product was dissolved in water (1000 ml), acidified (15N HCl) and the 2,3,4-trihydroxybenzoic acid (90 g) collected, m.p. 210° (d), (lit[36] m.p. 206–208°).

5-Substituted pyrogallol derivatives. 5-Nitro-[36] and 5-methylpyrogallol[37] were produced by published methods. 5-t-Butylpyrogallol was prepared according to the method of Stockelbach.[38] Revision of the structure of the product formed in this reaction from 4 to 5-t-butylpyrogallol is discussed above.

5-Bromopyrogallol. To a soln of tribromopyrogallol (2 g) in AcOH acid (3·5 ml) and water (0·4 ml) was added Zn dust and the mixture heated under reflux for ½ hr, poured into water (100 ml) and filtered. The soln was extracted with ether (3 × 100 ml) and evaporation of the ether gave a gum which on sublimation (130°, 0·1 mm) and crystallization from Chf containing a few drops of acetone gave *5-bromopyrogallol* (0·1 g) as off white needles, m.p. 148° (d). (Found: C, 35·8; H, 2·6; Br, 38·5. $C_6H_5O_3Br$ requires: C, 35·2; H, 2·4; Br, 39·0%.)

The oxidation of 4-substituted pyrogallols

4',7-Dimethylpurpurogallin (IV; R = Me). 4-Methylpyrogallol (20 g) was dissolved in water (250 ml), the soln cooled to 10° and filtered. KIO_4aq (220 ml) was added with rapid stirring (2 hr) and after ½ hr the product was collected and crystallized from dioxan as orange-red needles (7 g), m.p. 199°, (Critchlow, Haworth and Pauson give, m.p. 185°). (Found: C, 63·0; H, 4·5. Calc. for $C_{18}H_{12}O_6$: C, 62·9; H, 4·9%.)

4',7-Diethylpurpurogallin (IV; R = Et) prepared from 4-ethylpyrogallol as above crystallized from EtOH as orange needles, m.p. 152–153°. (Found: C, 65·6; H, 6·0. $C_{16}H_{16}O_6$ requires: C, 65·2; H, 5·8%.)

4',7-Di-n-propylpurpurogallin (IV; R = n-Pr) prepared from 4-n-propylpyrogallol as above crystallized from EtOH as orange needles, m.p. 125°. (Found: C, 66·8; H, 6·5. $C_{17}H_{20}O_6$ requires: C, 67·1; H, 6·6%.)

4',7-Di-n-butylpurpurogallin (IV; R = n-Bu) prepared from 4-n-butylpyrogallol as above crystallized from EtOH as orange plates, m.p. 138°. (Found: C, 68·7; H, 7·1. $C_{18}H_{24}O_6$ requires: C, 68·7; H, 7·2%.)

2'3'-Di-O-methyl-4',7-dimethylpurpurogallin. Excess ethereal diazomethane was added to a suspension of 4',7-dimethylpurpurogallin (0·3 g) in ether (30 ml) and after 2 hr removal of the solvent and crystallization from ether gave the *di-O-methyl ether* as orange needles (0·12 g), m.p. 125°. (Found: C, 65·4; H, 5·7. $C_{14}H_{16}O_6$ requires: C, 65·2; H, 5·8%.)

2'3'-Di-O-methyl-4',7-diethylpurpurogallin prepared as above from 4',7-diethylpurpurogallin crystallized from MeOH as red needles, m.p. 82–83°. (Found: C, 67·2; H, 6·8. $C_{17}H_{20}O_6$ requires: C, 67·1; H, 6·6%.)

Oxidation of 4',7-dibromopurpurogallin. A soln of NaOH (44 g) in water (200 ml) was heated to 95° and 4',7-dibromopurpurogallin (10 g) followed by H_2O_2 (100 vols, 15 ml) added. Once the rapid effervescence had ceased the soln was cooled, acidified with 40% H_2SO_4 and extracted continuously with ether (24 hr). The ether solution deposited a brown solid which sublimed (200°, 0·05 mm) and crystallized from cyclohexane gave 3-methyltropolone (0·5 g), m.p. and mixed m.p. 73–74°. The residual ether soln after drying (Na_2SO_4) and evaporation gave a residue which crystallized from AcOH to give tropolone-3,4-dicarboxylic anhydride (0·5 g), m.p. and mixed m.p. 150°.

Oxidation of 4',7-dimethylpurpurogallin. Water (140 ml) was heated to 95° and NaOH (30 g) added; then with rapid stirring 4',7-dimethylpurpurogallin (4 g) and H_2O_2 (100 vols, 11 ml). After the effervescence had ceased the soln was cooled, acidified (10N H_2SO_4, 80 ml) the *3,8-dihydroxy-4,7-dimethyl-1,2-naphthoquinone* which separated, was collected and crystallized as irregular prisms (0·3 g), m.p. 228° (d). The PMR spectrum ($CF_3{\cdot}CO_2H$) showed two 3 proton singlets (τ 7·80, 7·32) and a 2 proton AB system (τ 1·6, 2·6; J_{AB} 10 c/s).

The product was dissolved in MeOH (5 ml) and treated with excess ethereal diazomethane. After 3 hr removal of the ether and crystallization of the residue from MeOH gave deep red needles of *3,8-dimethoxy-4,7-dimethyl-1,2-naphthoquinone*, m.p. 149°. (Found: C, 68·0; H, 5·6; OMe, 24·6. $C_{14}H_{14}O_4$ requires: C, 68·3; H, 5·7; OMe, 25·0%), ν_{max} (nujol) at 1698 cm^{-1}. The PMR spectrum ($CF_3{\cdot}CO_2H$) showed four 3 proton singlets (τ 7·45, 7·25, 5·75, 5·35), and a 2 proton AB system

(τ 1·45, 2·45; J_{AB} 9 c/s). The quinone reacted with 2,4-dinitrophenylhydrazine in EtOH to give the *mono-2,4-dinitrophenylhydrazone* crystallizing as purple needles, m.p. 270–275° (d). (Found: C, 56·3; H, 4·2; N, 13·6. $C_{20}H_{16}O_7N_4$ requires: C, 56·4; H, 4·2; N, 13·2%.) The PMR spectrum showed four 3 proton singlets (τ 7·45, 7·25, 5·75, 5·35), a 2 proton AB system (τ 1·6, 2·75; J_{AB} 10 c/s) and a 3 proton ABX system, AB (τ 1·4, 2·0; J_{AB} 10 c/s, J_{AX} 3 c/s, J_{BX} 0 c/s), X (τ 0·75).

Oxidation of 4',7-*diethylpurpurogallin*. KOH (57 g) was added to boiling water (160 ml), 4',7-diethylpurpurogallin (5 g) was then added with rapid stirring followed by H_2O_2 (100 vols, 25 ml) in 5 ml portions. After 5 min the soln was cooled, $NaHSO_3$ (0·5 g) added and the soln made acid with 15N H_2SO_4. Extraction with ether gave a brown gum which crystallized from EtOH to give the lactone of *7-ethyl-4-(α-hydroxy-n-propyl)tropolone-3-carboxylic acid*, (X; R = Me), (0·2 g) as pale yellow needles, m.p. 156–157°. (Found: C, 66·3; 66·4; H, 5·9, 6·0. $C_{13}H_{14}O_4$ requires: C, 66·6; H, 5·9%), Zerewitinoff estimation gave values of 1·9 and 1·8 per mole and the equiv wt by titration was 233; ν_{max} (nujol) at 1770, 1621, 1558 cm^{-1}; λ(max) (EtOH) 255, 266, 295 (inflexion), 309, 319, 357, 372 and 392 mμ with log ε 4·3, 4·22, 3·22, 3·61, 3·70, 3·65, 3·73 and 3·86 respectively. The PMR spectrum is discussed on p. 2832.

Oxidation of 4',7-*di-n-propylpurpurogallin*. Oxidation of 4',7-di-n-propylpurpurogallin, as above, gave *the lactone of 7-n-propyl-4-(α-hydroxy-n-butyl)tropolone-3-carboxylic acid* (X; R = Et) crystallizing from EtOH as yellow needles, m.p. 140–141°. (Found: C, 68·3; H, 7·1. $C_{14}H_{16}O_4$ requires: C, 68·7; H, 6·9%), ν_{max} (nujol) at 1772 and 1620 cm^{-1}, equiv wt by titration 262.

Oxidation of 4',7-*di-n-butylpurpurogallin*. Oxidation of 4',7di-n-butylpurpurogallin, as above, gave *the lactone of 7-n-butyl-4-(α-hydroxy-n-pentyl)tropolone-3-carboxylic acid*, (X; R = n-Pr), crystallizing from EtOH as yellow needles, m.p. 152°. (Found: C, 70·3; H, 7·6. $C_{17}H_{22}O_4$ requires: C, 70·3; H, 7·6%), ν_{max} (nujol) at 1771 and 1620 cm^{-1}, equiv wt by titration 288.

The oxidation of 5-substituted pyrogallols

Oxidation of 5-methylpyrogallol. KIO_3aq (16 ml) was added to an ice cold soln of 5-methylpyrogallol (2 g in 50 ml). The ppt was collected, triturated with acetone to give *2,7-dihydroxy-5,10-dimethyl tricyclo*[5,3,1,$1^{3,6}$]*dodeca-4,9-diene-3,8,11,12-tetraone* (XXIII; R^1 = Me, R^2 = H), (1·2 g), m.p. 210° (d). (Found: C, 60·4; H, 4·6. $C_{14}H_{12}O_6$ requires: C, 60·8; H, 4·4%), ν_{max} (nujol) at 1752 and 1689 cm^{-1}. The acetate was formed by boiling in Ac_2O (3 ml) containing one drop of 36N H_2SO_4 for 10 min and crystallized from Ac_2O as plates, m.p. 295° (d). (Found: C, 59·6; H, 4·5. $C_{18}H_{16}O_8$ requires: C, 60·0; H, 4·4%), ν_{max} (nujol) at 1764 and 1685 cm^{-1}. The PMR spectrum ($CF_3{\cdot}CO_2H$) showed a 6 proton singlet (τ 7·6), a 6 proton doublet (τ 7·54, J 2 c/s), a two proton doublet (τ 5·82, J 4 c/s) and a two proton multiplet (τ 3·45).

Oxidation of pyrogallol and 5-methylpyrogallol. A soln of pyrogallol (1 g) and 5-methylpyrogallol (2 g) in water (50 ml) was treated dropwise with KIO_3aq. After addition of 16 ml the yellow solid which separated was collected, triturated with acetone, to give a product m.p. 210° undepressed on admixture with the oxidation product of 5-methylpyrogallol. Further addition of KIO_3aq precipitated a red solid which after sublimation and crystallization from EtOH gave needles, m.p. and mixed m.p. with purpurogallin, 272°.

Oxidation of 5-t-butylpyrogallol. KIO_3aq (148 ml) was added over a period of 1 hr to a solution of 5-t-butylpyrogallol (20 g) in water (1 l.) and the *2,7-dihydroxy-5,10-di-t-butyl tricyclo*[5.3.1.$1^{3,6}$] *dodeca-4,9-diene-3,8,11,12-tetraone* (XXIII; R^1 = t-Bu, R^2 = H) which separated was collected and crystallized from Chf as plates (18 g), m.p. 205–210°. (Found: C, 66·7; H, 6·9 $C_{16}H_{18}O_8$ requires: C, 66·7; H, 6·7%), ν_{max} (nujol) at 1760 and 1689 cm^{-1}. The PMR spectrum ($CF_3{\cdot}CO_2H$) showed an 18 proton singlet (τ 8·65), and a 4 proton AB system (τ 5·65, 3·25, J_{AB} 2·5 c/s). Acetylation (Ac_2O and H_2SO_4) gave an *acetyl derivative*, crystallizing from AcOH as needles, m.p. 305° (d). (Found: C, 64·4; H, 6·2. $C_{18}H_{14}O_4$ requires: C, 64·8; H, 6·3%), ν_{max} (nujol) at 1764 and 1693 cm^{-1}. The PMR spectrum ($CF_3{\cdot}CO_2H$) showed an 18 proton singlet (τ 8·62), a 6 proton singlet (τ 7·66) and a 4 proton AB system (τ 3·26, 5·62, J_{AB} = 2 c/s).

The oxidation product (1 g) was refluxed for 3 hr with Zn (5 g) and 2N HCl (50 ml). Extraction of the soln with ether (4 × 50 ml), evaporation of the ether and crystallization of the residue from Chf gave 5-t-butylpyrogallol (0·05 g), m.p. and mixed m.p. 137°.

4-t-Butylcyclopent-2-en-2-ol-1-one (XIX). The oxidation product of 5-t-butylpyrogallol above (1 g) was dissolved in 1N NaOH (50 ml) and the soln kept at 60° for ½ hr before acidification with 1N H_2SO_4. Extraction with ether and removal of the ether gave a gum which on sublimation

(100°/8 mm) gave an semi-solid material. Treatment with 2,4-dinitrophenylhydrazine gave *4-t-butylcyclopent-1,2-dione-bis-2,4-dinitrophenylhydrazine* which crystallized from pyridine as needles, m.p. 277–279°. (Found: C, 49·1; H, 4·5; N, 22·4. $C_{31}H_{33}O_8N_8$ requires: C, 49·0; H, 4·28; N, 21·8%.) Treatment with hydroxylamine gave the *di-oxime* which crystallized from EtOH as needles, m.p. 222–223°. (Found: C, 58·6; H, 8·7. $C_9H_{16}O_3N_2$ requires: C, 58·7; H, 8·7%.)

Preparative TLC (silica gel using Chf containing 2% MeOH as developing solvent) resolved the semi-solid material into two components R_f 0·5 and R_f 0·28. The faster running material crystallized from light petroleum (b.p. 60–80°) as plates of *4-t-butylcyclopent-2-en-2-ol-1-one* (XXI; 0·1 g), m.p. 125–127°. (Found: C, 69·8; H, 8·7. $C_9H_{14}O_2$ requires: C, 70·1; H, 9·1%), ν_{max} (nujol) at 1720 and 1650 cm^{-1}. The PMR spectrum ($CDCl_3$) showed a one proton doublet (τ 3·38, J 3 c/s), a one proton singlet (τ 5·4) removed by D_2O shake, a one proton multiplet (τ 7·4), a 2 proton quartet of an A_2B system (τ 7·68, J_{AB} 5 c/s) and a 9 proton singlet (τ 9·07).

The slower running material probably *3-t-butylcyclopent-2-en-5-hydroxy-1-one* (XXII) crystallized from light petroleum (b.p. 60–80°) as needles m.p. 115–119°. (Found: C, 69·8; H, 8·6. $C_9H_{14}O_2$ requires: C, 70·1; H, 9·1%.) The PMR spectrum ($CDCl_3$) showed a one proton triplet (τ 4·5, J 2 c/s), a one proton quartet (τ 5·65), a 2 proton multiplet (τ 6·9) and a 9 proton singlet (τ 8·80).

4-t-Butylcyclopent-2-en-2-methoxy-1-one. (a) After shaking a soln of 4-t-butylcyclopent-2-en-2-ol-1-one (0·1 g) 2N NaOH (4 ml) and Me_2SO_4 (0·16 g) for 1 hr the oily ppt was collected and crystallized from light petroleum (b.p. 60–80°); the *methyl ether* (0·05 g) separated as needles, m.p. 67°. (Found: C, 71·5; H, 9·6. $C_{10}H_{16}O_2$ requires: C, 71·4; H, 9·5%.) (b) 4-t-Butylcyclopent-2-en-2-ol-1-one (0·5 g) was treated at 0° for 4 days with excess ethereal diazomethane (40 ml) when removal of the solvent gave a gum which was treated with 2,4-dinitrophenylhydrazine. The resultant mixture was triturated with EtOH–dioxan and the insoluble portion crystallized from pyridine to give the bis-dinitrophenylhydrazone of 4-t-butylcyclopent-1,2-dione, m.p. and mixed m.p. 276–278°. The soluble portion crystallized from EtOH as needles (0·05 g) of the *2,4-dinitrophenylhydrazone of 4-t-butylcyclopent-2-en-2-methoxy-1-one*, m.p. 191°. (Found: N, 16·0. $C_{16}H_{20}N_4O_5$ requires: N, 16·1%.)

3-t-Butylglutaric acid (XX). The oxidation product of XXIII (R^1 = t-Bu, R^2 = H; 1 g) was dissolved in 1N NaOH (50 ml) and kept at 60° for ½ hr before acidification with 1N H_2SO_4. Extraction with ether and removal of the solvent gave a gum which on sublimation (100°/8 mm) yielded semi-solid material (0·6 g). The latter was dissolved in acetone (20 ml) containing solid $KHCO_3$ and treated with 5% $KMnO_4$ until a permanent pink colour remained for 10 min. The soln was diluted (200 ml), treated with SO_2 and continuously extracted with ether for 20 hr. Removal of the ether gave an oil which was distilled (90°/0·2 mm) then heated at 180° for 2 hr with *p*-toluidine (0·4 g). On cooling the product, after trituration with 2N HCl was collected and crystallized from benzene to give the *3-t-butylglutaric acid* p-*toluimide* (0·3 g) as needles, m.p. 166°. (Found: C, 74·1; H, 7·7; N, 5·8. $C_{16}H_{21}NO_3$ requires: C, 74·1; H, 8·1; N, 5·4%.)

6-t-Butylpurpurogallin (XVII). The oxidation product of XXIII (R^1 = t-Bu, R^2 = H; 5 g) was refluxed in EtOH (100 ml) containing 1N HCl (100 ml) for 4 days under a stream of N, when the solvents were removed and the residue dissolved in EtOH (20 ml). The product which separated was sublimed (150–160°, 0·5 mm) and crystallized from EtOH to give *6-t-butylpurpurogallin* as orange plates, (0·5 g), m.p. 278° (d). (Found: C, 64·9; H, 6·0. $C_{14}H_{16}O_5$ requires: C, 65·2; H, 5·6%.) The PMR spectrum (in acetone) showed a singlet proton (τ 2·95) and a two proton AB quartet (τ 2·5, 2·6, J_{AB} 3 c/s).

2',3'-Di-O-methyl-6-t-butylpurpurogallin. Treatment of 6-t-butylpurpurogallin (0·5 g) with excess ethereal diazomethane for 3 hr gave on removal of the solvent the *dimethyl ether* (0·2 g) crystallizing as orange needles from MeOH, m.p. 147–148°. (Found: C, 67·4; H, 6·4. $C_{17}H_{20}O_5$ requires: C, 67·1; H, 6·6%.) The PMR spectrum ($CDCl_3$) showed a 9 proton singlet (τ 8·60), two 3 proton singlets (τ 5·95, 6·02) a one proton singlet (τ 3·25) and a 2 proton AB quartet (τ 2·6, 2·7, J_{AB}. 3 c/s).

1,1',2',3'-Tetra-O-methyl-6-t-butylpurpurogallin. The dimethyl ether above (0·35 g) was suspended in Me_2SO_4 (1 ml), 65% KOHaq (5 ml) added and the soln heated to initiate the reaction. When this subsided the soln was cooled, diluted and the product collected by ether extraction. Removal of the ether and crystallization of the residue from light petroleum (b.p. 40–60°) gave the *tetramethyl ether* as prisms, m.p. 103°. (Found: C, 69·1; H, 7·34. $C_{19}H_{24}O_5$ requires: C, 68·7; H, 7·3%.)

Oxidation of 1,1',2',3'-tetra-O-methyl-6-t-butylpyrpurogallin. The tetramethyl ether above was dissolved in acetone (5 ml) and 2% $KMnO_4$ (47 ml) added over 36 hr. The suspension was then

clarified by passage of SO_2, acidified and extracted with ether for 10 hr. Removal of the ether gave a brown gum which sublimed and crystallized from ether gave trimethoxyphthalic anhydride, m.p. and mixed m.p. 143–144°.

The oxidation of 4,6-*di-t-butylpyrogallol*

Oxidation of 4,6-*di-t-butylpyrogallol*. A soln of KIO_3 (13·5 g) in water (200 ml) was added with stirring to a soln of 4,6-di-t-butylpyrogallol (36 g) in acetone (200 ml) and water (200 ml). After 30 min when the intense purple colour had changed to brown the soln was extracted with ether (3 × 500 ml), the ether extract dried (Na_2SO_4) and evaporated. Recrystallization of the residue from light petroleum (b.p. 60–80°) gave 4a,10a-*dihydro*-6,10a-*dihydroxy*-3,4a,7,9-*tetra-t-butyldibenzo-p-dioxin*-1,2-*dione* (XXIX, $R^1 = R^2 = H$), (35 g), m.p. 160–161°, (Flaig, Ploetz and Biergaus[34] give m.p. 153–161°). (Found: C, 71·0; H, 8·7. Calc. for $C_{28}H_{40}O_6$: C, 71·4; H, 8·5%), ν_{max} (nujol) at 3500, 1759, 1618 and 975 cm^{-1}. The mono- and di-acetates of the dimer were obtained substantially as described by Salfeld. The mol. wt. determined ebullioscopically gave a value of 223–230 in Chf. The mol. wt determined cryoscopically in benzene gave a value of 515 ($C_{28}H_{40}O_6$ requires: 472). On boiling the benzene soln the colour changed from yellow to dark brown when cryoscopic measurements gave a value of 948, $(C_{28}H_{40}O_6)_2$ requires 944, after 5 days at 20° the soln was yellow and a value of 500 was obtained.

Action of barium hydroxide on XLVI ($R^1 = R^2 = H$). A soln of XLVI ($R^1 = R^2 = H$; 5 g) in MeOH (250 ml) was treated with sat $Ba(OH)_2$aq (125 ml) and refluxed whilst a stream of N was passed. After 90 min the soln was cooled acidified (2N HCl) and extracted with ether (2 × 500 ml). After drying (Na_2SO_4) and removal of the ether the residue was chromatographed in light petroleum (b.p. 40–60°) on alumina (300 g, Brockmann grade V, acid washed). Elution with the same solvent gave 3,5-*di-t-butylcyclopent*-3-*en*-1,2-*dione* (XXXVIII, 1·78 g) crystallizing from light petroleum (b.p. 60–80°) as orange needles, m.p. 65° (Salfeld and Baume[7] give m.p. 66°). (Found: C, 74·8; H, 9·4. Calc. for $C_{13}H_{20}O_2$: C, 74·9; H, 9·7%), the PMR spectrum ($CDCl_3$) showed two 9 proton singlets (τ 8·74, 8·97) and two 1 proton doublets (τ 3·25, 7·38; J_{AX} 3 c/s). Elution with light petroleum (b.p. 40–60°): ether (1:1) gave 4,6-di-t-butylpyrogallol m.p. and mixed m.p. of the triacetate 169–170°.

Action of 1N NaOH *on* XLVI ($R^1 = R^2 = H$). Finely ground XLVI ($R^1 = R^2 = H$; 6 g) was heated at 100° with 1N NaOH (300 ml) for 5 hr when the pH was adjusted to 9 (2N AcOH) and the soln extracted with ether (3 × 500 ml). Removal of the ether gave XXXV m.p. and mixed m.p. 105–106°. (Found: C, 74·2; H, 10·7. Calc. for $C_{18}H_{32}O_2$: C, 74·3; H, 10·5%), ν_{max} (nujol) at 3300, 1685 and 1640 cm^{-1}. The PMR spectrum showed two 9 proton singlets (τ 8·75, 9·03), 3 protons in an ABC pattern (τ 7·76) and a 1 proton singlet (broad) (τ 4·19). The aqueous soln remaining after ether extraction on standing gave a white solid which was collected, recrystallized from water, decomposed with 1N H_2SO_4 and the organic material extracted into ether. Removal of the solvent, distillation (b.p. 113–116° (9 m.m.) and crystallization from light petroleum (b.p. 40–60°) gave 6,6-*dimethyl*-3-*t-butyl*-2-*oxo-hept*-4-*enoic acid* (XXXIX) as small needles (1·95 g), m.p. 48–50°. (Found: C, 68·7; H, 9·7. $C_{13}H_{22}O_3$ requires: C, 69·0; H, 9·8%), ν_{max} (nujol) at 1733, 1709 and 1650 cm^{-1}. The PMR spectrum of the keto acid ($CDCl_3$) showed two 9 proton singlets (τ 8·98, 9·03) and a 3 proton ABX pattern, AB (τ 4·70, 4·77) X (τ 6·13), (J_{AB} 15 c/s, J_{AX} 0 c/s, J_{BX} 9 c/s). The *semicarbazone* of the keto acid XXXIX had m.p. 186–187°. (Found: C, 58·9; H, 8·7; N, 14·7. $C_{14}H_{25}N_3O_3$ requires: C, 59·3; H, 8·9; N, 14·8%.) The 2,4-*dinitrophenylhydrazone* of the keto acid had m.p. 236–237° d. (Found: C, 56·8; H, 6·5; N, 13·9. $C_{19}H_{26}N_4O_6$ requires: C, 56·1; H, 6·5; N, 13·8%.)

The residual aqueous soln, on removal of the keto acid sodium salt above, was acidified (1N HCl) and extracted with ether (3 × 500 ml) and the extract dried (Na_2SO_4). Removal of the ether gave a gum which triturated with benzene gave the acid XXXVI, m.p. 158–159° (Flaig and Schulz[49] gives m.p. 160°). The benzene soln on evaporation gave a further quantity of the keto acid (1·02 g).

Action of 1N NaOH *on* 4,6-*di-t-butylpyrogallol*. 4,6-Di-t-butylpyrogallol (0·5 g) was heated at 100° with 1N NaOH (50 ml) for 90 min and steam distilled until 3,5-di-t-butylcyclopent-2-en-2-ol-1-one (0·22 g), m.p. and mixed m.p. 105–106°, ceased to pass over. Acidification (HCl) of the residual soln gave XXXVI (0·25 g), m.p. and mixed m.p. 158–159°.

Action of 1N NaOH *on* 3,5-*di-t-butylcyclopent*-3-*en*-1,2-*dione*. The cyclopentendione XXXVIII (0·4 g) was heated with 1N NaOH for 5 hr at 100°. Acidification of the soln gave XXXIX (0·34 g), after extraction with ether, m.p. and mixed m.p. 48–50°.

[49] W. Flaig and H. Schulze, *Liebigs Ann.* **575**, 231 (1952).

Ozonolysis of the keto-acid XXXIX. Ozone was passed through a soln of the Na salt of XXXIX (1·0 g) in AcOH (100 ml) until no further uptake was observed. The ozonide was decomposed with Zn dust and steam and the products steam distilled. Addition of 2,4-dinitrophenylhydrazine to the steam distillate gave a ppt which was separated by chromatography on alumina (200 g acid washed) using light petroleum (b.p. 40–60°). The first fractions gave 1,1,1-trimethylacetaldehyde 2,4-dinitrophenylhydrazone (0·28 g), m.p. 209–211°, (lit m.p. 210°). (Found: C, 50·1; H, 5·7; N, 20·5. Calc. for $C_{11}H_{14}N_4O_4$: C, 49·6; H, 5·3; N, 21·0%.) Elution with light petroleum (b.p. 40–60°): benzene (1:1) gave 2,2,2-trimethylpropionaldehyde 2,4-dinitrophenylhydrazone (0·14 g), m.p. 139–140°, (lit. m.p. 140°). (Found: C, 51·4; H, 6·2; N, 19·7. Calc. for $C_{12}H_{16}N_4O_4$: C, 51·4; H, 5·8; N, 20·0%.)

Hydrogen peroxide oxidation of the keto acid XXXIX. A soln of the Na salt of XXXIX (0·5 g) in water (10 ml) was cooled in ice, H_2O_2 (0·3 ml, 100 vol) added and the soln stood at room temp for 20 hr. Acidification gave a ppt which on crystallization from EtOH–water gave *5,5-dimethyl-2-t-butyl-hex-2-enoic acid* (XLIV; 0·22 g), m.p. 71–72°. (Found: C, 72·4; H, 10·7. $C_{12}H_{22}O_2$ requires: C, 72·7; H, 11·2%), ν_{max} (nujol) at 1705 and 1660 cm^{-1}. The PMR spectrum ($CDCl_3$) gave two 9 proton singlets (τ 8·82, 8·90) and a 3 proton ABX pattern (AB, τ 4·39, 4·40; X, τ 7·21; J_{AB} 3 c/s, J_{AX} 0 c/s, J_{BX} 4 c/s).

Sodium borohydride reduction of the keto-acid XXXIX. A soln of XXXIX (1·0 g) and $NaBH_4$ (1·0 g) in alcohol (17 ml) and water (10 ml) containing 2N NaOH (7 ml) was refluxed for 1 hr before acidification (2N HCl) and extraction with ether (4 × 50 ml). Removal of ether drying the extract (Na_2SO_4) gave a residue which after crystallization from light petroleum (b.p. 60–80°) gave *6,6-dimethyl-3-t-butyl-2-hydroxyhept-3-enoic acid* (XLV; 0·54 g), m.p. 101–102°. (Found: C, 68·8; H, 10·2. $C_{13}H_{24}O_3$ requires: C, 68·4; H, 10·5%), ν_{max} at 3370, 1715 cm^{-1}. Acetylation gave *6,6-dimethyl-3-t-butyl-2-acetoxyhept-3-enoic acid*, m.p. 97–98°. (Found: C, 66·8; H, 9·7. $C_{15}H_{26}O_3$ requires: C, 66·6; H, 9·7%), ν_{max} at 1754, 1698 cm^{-1}.

Hydrogen peroxide oxidation of XXIX ($R^1 = R^2 = H$). The dimer XXIX ($R^1 = R^2 = H$; 5·0 g) was treated with a solution of H_2O_2 in ether (0·63M, 25 ml) at room temp and the mixture allowed to stand for 10 months. Excess H_2O_2 was then destroyed with $FeSO_4$aq and the ether soln was shaken with $NaHCO_3$aq. After removal of the ether the residue was boiled with benzene, dissolved in moist ether and shaken with 2N HCl. Evaporation of the ether and crystallization from benzene gave *4a,10a-dihydro-6-hydroxy-2-oxo-3,4a,7,9-tetra-t-butyl-2H-pyrano-2,3-benzodioxin-10a-carboxylic acid* (XXIV; 1·78 g), m.p. 202–203° d. (Found: C, 68·8; H, 8·2. $C_{28}H_{40}O_7$ requires: C, 68·8; H, 8·3%), ν_{max} 3529, 3407, 1762, 1709, 1646, 1608, 993 cm^{-1}. The PMR spectrum ($CDCl_3$) showed two 9 proton singlets (τ 8·80, 9·0), one 18 proton singlet (τ 8·65), two 1 proton singlets (τ 3·17, 3·74).

Action of 2N NaOH *on the lactonic acid* XXXIV. The acid XXXIV (0·05 g) was heated at 100° with 2N NaOH (2 ml) for 2 hr and the mixture then steam distilled. The steam distillate was extracted with ether; removal of the ether gave *3,5-di-t-butylcyclopent-2-en-2-ol-1-one* (0·015 g), m.p. and mixed m.p. 105–106°. The residue from steam distillation yielded after acidification (2N HCl) and ether extraction the acid XXXVI (0·027 g), m.p. and mixed m.p. 158–159°.

Ozonolysis of 3,5-di-t-butylcyclopent-2-en-2-ol-1-one (XXXV). Ozone was passed through a soln of XXXV (1·0 g) in AcOH (100 ml) until no further uptake occurred. Steam distillation of the soln followed by ether extraction of the residue (4 × 100 ml) gave, after removal of the ether *5,5'-dimethyl-2-t-butyl-4-oxohexanoic acid* (XL; 0·55 g), b.p. 150–155°/15 mm, which crystallized from light petroleum (b.p. 60–80°), m.p. 82–83°. (Found: C, 67·2; H, 10·5. $C_{12}H_{22}O_3$ requires: C, 67·3; H, 10·4%), ν_{max} 1715 and 1705 cm^{-1}. The PMR spectrum ($CDCl_3$) showed two 9 proton singlets (τ 8·89, 9·00), and a 3 proton A_2B pattern (A_2, τ 7·28, B, τ 7·45; J_{AB} 4 c/s).

Synthesis of 5,5'-dimethyl-2-t-butyl-4-oxo-hexanoic acid (XL)

Methyl-3,3'-dimethyl-2-bromobutanoate. t-Butylacetic acid (17 g) was refluxed with $SOCl_2$ (40 ml) for 2 hr when the excess $SOCl_2$ was removed by evaporation. Bromine (25 g) was added dropwise during 2 hr at room temp and the mixture then refluxed for 3 hr, cooled and poured into MeOH (120 ml), stood overnight and poured into ice water (300 ml). The oil which separated was extracted into ether (4 × 500 ml), the ether extracts washed with Na_2CO_3aq, dried (Na_2SO_4), evaporated and distilled to give methyl *3,3'-dimethyl-2-bromobutanoate* (27·6 g), b.p. 181–182°. (Found: C, 40·6; H, 6·5; Br, 35·6. $C_7H_{13}BrO_2$ requires: C, 40·2; 6·3; Br, 38·2%), ν_{max} 1755 cm^{-1}.

5,5'-Dimethyl-2-t-butyl-4-oxohexanoic acid. Methyl 3,3'-dimethyl-2-bromobutanoate (26 g) was added to the Na salt of pinacolone prepared by dissolving Na (3 g) in liquid ammonia, displacing

the ammonia with dry ether, adding pinacolone (13 g) and stirring for 1 hr and the mixture refluxed for 3 hr. The ether soln was then washed with water, dried (Na_2SO_4) and evaporated to yield crude *methyl-5,5'-dimethyl-2-t-butyl-4-oxohexanoate* (2·0 g), b.p. 115–117°/12 mm. The latter was refluxed with 2N NaOH (25 ml) for 6 hr, the soln acidified (2N HCl) and extracted with ether (3 × 25 ml); the ether extracts were dried (Na_2SO_4) and distilled to give *5,5'-dimethyl-2-t-butyl-4-oxo-hexanoic acid* (0·3 g). b.p. 150°/15 mm, m.p. and mixed m.p. 82–83°. The product was identical (IR) with the product of ozonolysis of 3,5-di-t-butylcyclopent-2-en-2-ol-1-one.

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