Spirans. Part 15.[1] The Effect of Ring Size upon the Regioselective Oxidative Coupling of Heterocyclic Phenols

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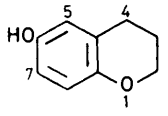
The oxidation of 2,3-dihydro-2,2,4,6,7-pentamethylbenzofuran-5-ol (7b) by alkaline potassium hexacyanoferrate(III) gives a complex mixture from which three products have been isolated and identified; all result from oxidation at the 6-methyl group only. Although unidentified products may have resulted from oxidation at the 4-methyl group, the evidence supports the view that the size of the heterocyclic ring determines the regioselectivity. The products are 2,2',3,3'-tetrahydro-2,2,2',2',4,4',7,7'-octamethyl-6,6-ethylenebisbenzofuran-5,5'-diol (8), which gives the spiran (11), 2,2',3,3',7',8'-hexahydro-2,2,2',2',4,4',7',9-octamethyl-6*H*-pyrano[2,3-*f*]benzofuran-6-spiro-6'(5'H)-benzofuran-5'-one, upon further oxidation, and the related trimer (12), the structure of which is partly disclosed by hydrolysis (by silica) of the acetal grouping. The size of the heterocyclic ring has little effect upon the ease of sigmatropic rearrangement in the spiran (11), but influences the ease with which this dissociates to give a quinone methide and thence the trimer (12).

With mild base 4-chloromethyl-2,3-dihydro-2,2,6,7-tetramethylbenzofuran-5-ol (7e) gave a trimer isomeric with compound (12).

SCANDINAVIAN workers[2] have amply demonstrated that in the benzopyran derivative (1) the two positions *ortho* to the hydroxy-group are not equivalent. Electrophilic substitution (bromination, protodetritiation) strongly favours the 5-position whereas in most phenols



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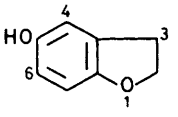
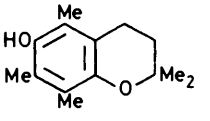


(2)

there is little selectivity and in the benzofuran derivative (2) substitution occurs mainly at the other *ortho* position, *i.e.*, position 6. Another markedly regioselective reaction is the hexacyanoferrate(III) oxidation of the tocopherol analogue (3) in which only the 5-methyl group appears to be attacked.[3,4] In effect, dehydrogenation gives the quinone methide (4) which rapidly dimerizes by (2 + 4) cycloaddition to produce the spirodimer (5) along with a little of the trimer (6), formed by the addition of another quinone methide molecule to the spiran.[3,5] Whether the dihydropyran ring is again the deciding factor is not known, since the only comparable dihydrofuran that has been examined is compound (7a), which is oxidized at the 6-methyl group, but has no 4-methyl group that could compete with it.[6] We have now examined the oxidation of the benzofuran analogue (7b) and find that, indeed, the changed ring size does permit oxidation at the alternative position, although with a selectivity that at best is only moderate. Some of the other consequences of reducing the ring size are also discussed.

The oxidation of the dihydrobenzofuranol (7b) by alkaline hexacyanoferrate(III) differed from that of the comparable chromanol (3) in being slow and not very efficient, much of the phenol being recovered. The products formed a complex mixture that has not yet been fully resolved, although it is clear that a major constituent is the bisphenol (8). Neither of the other



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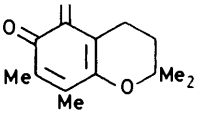

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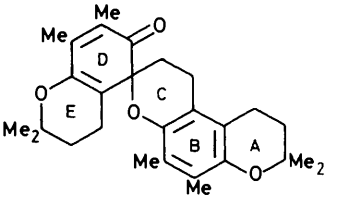

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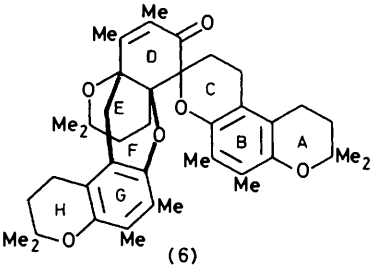

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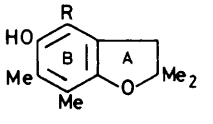
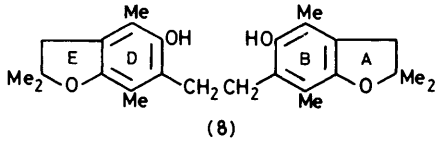


(7) a; R = H d; R = CH_2OH
b; R = Me e; R = CH_2Cl
c; R = CHO

possible bisphenols (9; $n = 2$) or (10) was detected. When oxidized separately the bisphenol (8) readily supplied the spirodimer (11), yet this was not itself detected in the reaction mixture. It must have been present, however, because the derived trimer (12) was easily

isolated and could reasonably have been formed only by way of the addition to the spirodimer of another quinone methide unit. Another trimer-like substance was obtained, but nothing is known about its structure; it is likely to be a mixture of very similar substances since, in



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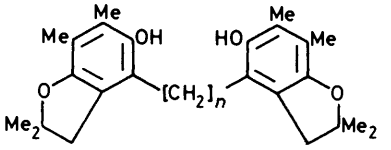

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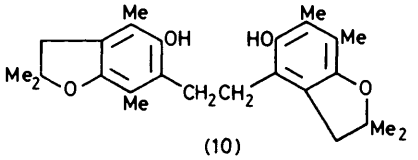

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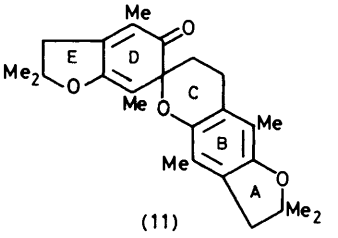
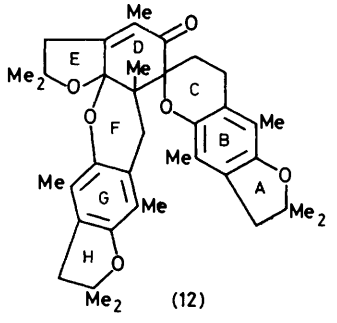
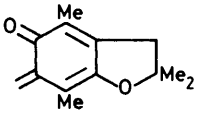


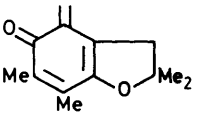
(11)



(12)



(13a)



(13b)

all, there are 64 ways of combining quinone methide units (13a) and/or (13b) to form trimers similar to (12).

While certain of the oxidation products are of well known types that are easily recognized by standard techniques, it is not a simple matter to identify individual regioisomers. The n.m.r. spectrum of the bisphenol (8) (Table 1) contains the requisite number of

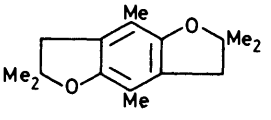
TABLE 1

^{1}H N.m.r. spectra[a] of simple derivatives of 2,3-dihydrobenzofuran at 220 MHz in $CDCl_3$ (δ scale)

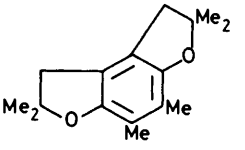
	Ring A		Ring B		Other	
Compd.	Me	CH_2	Me	OH[b]	CH_2	CHO
(7c)	1.46	3.21	2.12 2.15	11.06		9.84
(7d)	1.42	2.88	2.08 2.13	6.9	4.72	
(8)	1.45	2.93	2.12 2.21	5.61	2.72	
(9; $n = 1$)	1.44	2.98	2.08	4.74	3.73	
(14a)	1.43	2.87	2.03			
(14b)	1.44	2.85	2.06			

[a] All resonances appeared as singlets; relative intensities were appropriate to the assignments. [b] Resonances sometimes broad, always removed by D_2O.

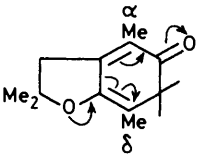
sharp bands, but there is no easy way of distinguishing this isomer from the symmetrical alternative (9; $n = 2$) or even from the bisphenol (10) of mixed origin. The problem arises from the very close similarity of the two moieties involved, as illustrated by the ^{1}H n.m.r. spectra of the isomeric bisfurans (14a) and (14b) (Table 1), but fortunately it can be resolved by reference to the spirans and trimers which are more amenable to study. The spiran contains a cyclohexadienone ring which must be substituted as in structures (15a) or in (15b). In the ^{1}H



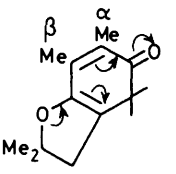
(14a)



(14b)



(15a)



(15b)

(16)

n.m.r. spectrum the methyl resonances of the latter system should be well separated with the β-methyl band at low fields (in the aryl methyl region) because of electron-withdrawal by the carbonyl group. The same effect operates in the other system (15a), but here it is countered by electron release from the heterocyclic oxygen atom so now the δ-methyl band should remain close to the α-methyl band. Thus, these bands provide a means of orientation for rings D, provided that they can

be securely identified. The spiran possesses two aromatic methyl groups that resonate at δ 2.02 and 2.06 and two vinylic methyl groups that resonate as a single band at δ 1.81 (Table 2), a distribution which obviously requires system (15a) for ring D. Moreover, these assignments can be confirmed in a manner described below. We show next that the methyl distributions in rings B and D of compound (11) are the same by allowing the sigmatropic rearrangement [7] indicated in structures (16) to interchange them. No new methyl bands appear and the compound suffers no constitutional change, hence the two systems AB and DE in the spiran have the same orientation. The symmetrical structure (8) for the bisphenol follows automatically.

TABLE 2

^{1}H N.m.r. spectra [a] for the spiran (11), the trimer (12), and the hemiacetal (19)

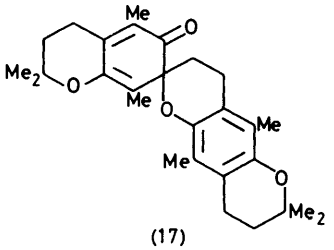
Assignments for Me groups of spiran (11)	Methyl resonances [b] (11)	(12)	(19)	Methylene resonances [c] (11)	(12)	(19)
		1.14 [d]	1.14 [d]	1.3	1.6	
		1.28	1.28	1.9	2.1	2.1
Ring E *gem*	1.37	1.36	1.31	2.6	2.6	2.6
		1.38	1.34	2.70	2.7	2.7
		1.38	1.40	2.91	2.8	1.8
	1.42	1.43	1.48		3.1	3.1
Ring A *gem*	1.44	1.50	1.50			
	1.44	1.50	1.77			
Ring D vinylic	1.80	1.77	1.94			
	1.80	1.94	2.00			
Ring B aromatic	2.02	2.00	2.05			
	2.06	2.04	2.07			

[a] At 220 MHz in $CDCl_3$, δ scale. [b] The relative intensities of the bands are in agreement, but specific assignments can be made only for the spiran (11). [c] In general these bands were complex, ill-resolved multiplets. [d] Angular methyl group.

The sigmatropic rearrangement (16) is already familiar from earlier studies [7] upon the spiran (5) in the tocopherol series and from our own study [1] of the isomer (17). At 18 °C the ^{1}H n.m.r. spectrum of spiran (11) (in $CDCl_3$) is blurred in part, but if the temperature is lowered all the bands are sharp by −5 °C. If the temperature is raised the blurring increases until coalescence of aromatic and vinylic methyl signals is attained at 45 °C. These figures are very like those for the parallel spiran [1] (17), with pyran instead of furan rings, which rearranges more easily than does its better known regioisomer (5).

When heated in chlorobenzene the spiran (11) is converted into one of the trimers obtained by oxidizing the phenol (7), and in this respect the reactivity of the spiran is intermediate between the spiran [1] (17), which is very sensitive to heat, and the isomer [7] (5), which is not. Evidently, the size of the fused heterocyclic ring is as important as its disposition. Since only the quinone methide (13a) can have been produced by the dissociation, recombination to form trimer must lead to a structure such as compound (12). Here, ring F might have the alternative orientation as in compound (18), which thus avoids the acetal grouping, and the stereochemistry of the cycloaddition that forms ring F is unknown except that it can be assumed to be a (4 + 2) addition suprafacial in both components. Indeed, no such trimer has a known stereochemistry [3,8-10] so we have made stereochemical assignments the goal of a separate study. The main features of the trimer (12) are not in doubt, however, since it behaves as an unsaturated ketone with four aromatic methyl groups, one vinylic methyl group, and seven *gem* or angular methyl groups that can be counted in the ^{1}H n.m.r. spectrum (Table 2). Had ring D been orientated in the alternative fashion [compound (15b)], this count would have shown two vinylic methyl groups and six *gem* or angular methyl groups as, for example, it does for trimer (6). This result confirms the orientations arrived at above.

It has also been possible to adduce evidence that the trimer is the acetal (12) and does not have the regioisomeric arrangement shown in compound (18) (there is precedent for both kinds of arrangement [9,10]). The ^{13}C n.m.r. spectrum (Table 3), besides confirming other findings, displays a peak at δ_C 102.64 p.p.m. which is not found in the spectra of the spirans or of the parent phenols (Table 4), but which corresponds well with the acetal peak in several comparable compounds (aflatoxin B_1,[11] δ_C 113.6; sterigmatocystin,[11] 113.1; and averrufin,[12] 100.9 p.p.m.). Long residence of the trimer on a silica column induces the addition of the elements of water. The i.r. and the ^{1}H n.m.r. spectrum (Table 2) of the yellow product show that two hydroxy-groups are present, the other main features remaining much the same. The mass spectrum is virtually unchanged and does not display a molecular ion peak 18 a.m.u. above the molecular ion peak of the original trimer, which shows that dehydration is very easy. All this is compatible with a partial hydrolysis of the acetal group contained in compound (12); and of the two rings we chose to open the furanoid ring E in order to relieve marked strain in ring D. Hence, we propose structure (19) for the new compound. Of course, the other ring could open as well to give an enedione of type (20), and recyclization could give a hemiacetal epimeric with (19) at the starred atom. While the presence of much of the enedione itself should perhaps be excluded because the ^{13}C n.m.r. spectrum (Table 3) shows only one ketonic carbon resonance, the equilibrium it allows between two hemiacetals appears likely. The compound behaves chromatographically as



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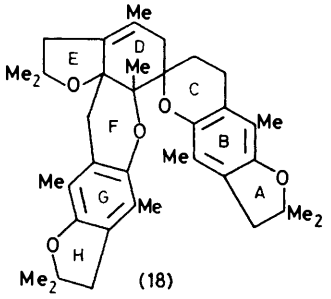

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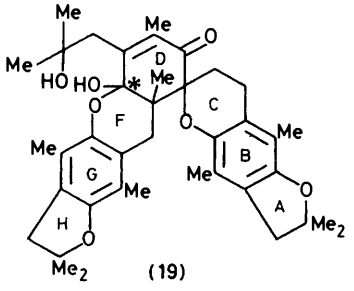

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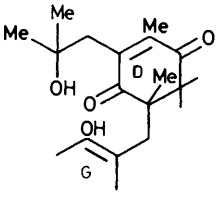

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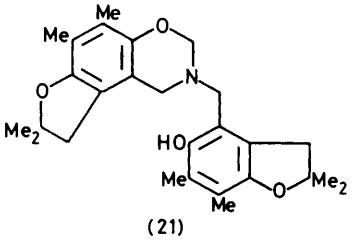

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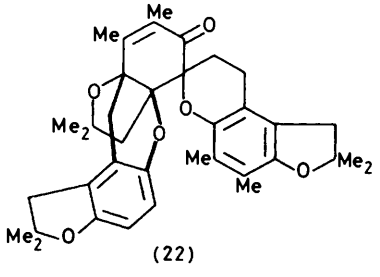


(22)

a single substance, and it crystallizes well and has a sharp melting point, yet in the ^{1}H n.m.r. spectrum some of the bands of the original trimer appear to have become double, and there are also ' too many ' peaks in the ^{13}C n.m.r. spectrum (Table 3). The latter spectrum does tend to confirm the presence of two hemiacetals (in solution) because it includes two singlets close together, near δ_C 102 and 103 p.p.m., both of which have to be assigned to acetal carbon.

Because none of the identified oxidation products included one with a nucleus derived from the quinone methide (13b), we thought it advisable to examine such a compound made in a controlled manner. The phenol (7a) was treated with hexamine in acetic acid and gave the bright yellow aldehyde (7c), along with the tertiary amine (21), and borohydride reduction supplied the

TABLE 3

^{13}C N.m.r. spectra [a] of the trimer (12) and the hemiacetal (19)

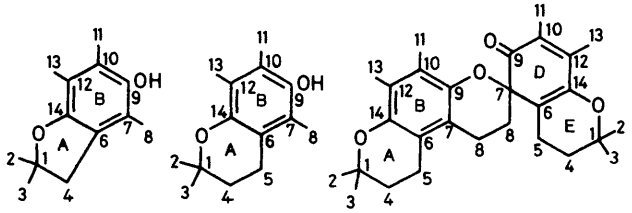
Mult.[b]	Trimer (12)	Hemiacetal (19)	Mult.[b]	Trimer (12)	Hemiacetal (19)
s	195.84	195.85			81.76
s	152.64	152.70	s	81.62	81.68
		150.73	s	79.27	79.27
s	150.53	150.55	t	42.71	43.09
s	150.44	150.43	t	42.61	42.62
s	144.56	144.59	t	42.14	42.13
		142.50			41.96
s	126.88	126.85			41.68
		123.25			41.48
s	123.08	123.14	t	30.34	30.23
s	122.84	122.85	qq	29.45	29.48
		122.65			29.34
		120.27	qqq	28.49	28.53
s	120.09	120.10			27.53
		119.69	t	23.48	23.48
s	119.27	119.27	q	22.23	22.27
s	118.77	118.79	t	20.83	20.86
s	115.07	116.63	q	12.65	12.68
s	115.35	115.27	q	12.11	12.10
s	112.84	112.88	q	11.86	11.86
		112.72	q	11.15	11.19
s	102.64	103.10	q	10.93	10.97
		102.69			
		85.10			
s	84.64	84.70			

[a] Determined for solutions in $CDCl_3$ at 25.5 MHz; chemical shifts are given as shifts (p.p.m.) from TMS on the δ scale. [b] Refers to trimer (12) only.

alcohol (7d). We noted in passing that the mass spectrum of the aldehyde contains particularly strong $(M + 1)^+$ and $(M + 2)^+$ peaks, while that of the alcohol contains a very strong $(M - 1)^+$ peak; such behaviour is reminiscent of that of quinones and their related quinols.[13] Hydrogen chloride converted the alcohol (7d) into the halide (7e) which was a sensitive compound and was, therefore, not purified, but treated at once with aqueous sodium hydrogencarbonate to produce the evanescent quinone methide (13b) and so a trimer, possibly compound (22). The intermediate spiran was not observed. The structure assigned to the new trimer is tentative in some respects. It is clearly of the same general type as the other, in that the compound behaves as an unsaturated ketone, and its mass spectrum is dominated by the fragment ions $M^+/2$ and $M^+/3$, the molecular ion itself being relatively weak. Yet some properties are so unusual that at first the compound was thought to be of a substantially different kind. Analytically, the compound was found to be a hemihydrate, the i.r. spectrum showing a very broad hydroxylic band, obviously the result of strong hydrogen bonding. The ^{1}H n.m.r. spectrum seemed surprisingly simple when obtained in the usual way (in $CDCl_3$ at ambient temperatures), but was found to have the proper complexity

TABLE 4

^{13}C N.m.r.[a] of the dihydrobenzofuranol (7b), the chromanol (3), and the spiran (5)



(7b)* (3)* (5)*

Mult.	(5)	(3)	(7b)	Assignment [b]	Mult.	(5)	(3)	(7b)	Assignment [b]
s	202.09			D9	t	32.89	33.05	42.80	A5
s	145.60			D14	t	32.42			B8
s	145.46	145.52	145.12	B9	t	28.14			E5
s	144.63	144.42	150.90	B14	q	27.43			E2
					q	26.28 [c]			E3
s	142.83			D12	q	26.28 [c]	26.66 [d]	28.43 [d]	A2, 3
s	126.93			D6	t	20.01	21.05		A4
s	123.17	122.42	122.90	B6	t	17.8' [d]			D8, E4
s	121.98	120.96	121.34	B7	q	13.88			D13
s	115.35	118.44	117.35	B12	q		12.17	12.80	B8
s	115.07	116.96	115.59	B10					
s	114.70			D10	q	11.84			D11
s	80.35			D7	q	11.73	11.76	12.16	B11
s	73.67			E1	q	11.19	11.24	12.01	B13
s	72.21	72.37	84.98	A1					

[a] Determined for solutions in $CDCl_3$ at 25.2 MHz; chemical shifts are given as shifts (p.p.m.) from TMS on the δ_C scale. [b] To facilitate comparisons within this Table carbon atoms are numbered in association with particular rings as shown (the numbering herein is not that used in the rest of the paper, which is IUPAC numbering). Most of the assignments are tentative in that several could be interchanged with equivalent ones and still give a satisfactory fit. [c] The band at this point is extremely strong and is believed to consist of three signals that have not been resolved. [d] A strong band, believed to consist of two nearly identical signals.

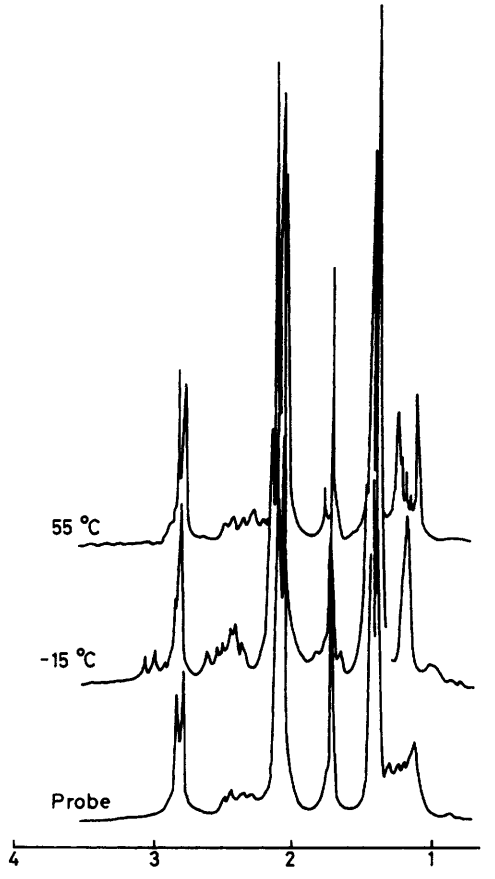


FIGURE 1 ^{1}H N.m.r. spectra (δ scale) for the trimer (22) determined at 220 MHz in $CDCl_3$ at the temperatures indicated

when examined in other conditions. The simplicity is partly a result of accidental coincidence of resonances and partly a result of broadenings that arise from conformational changes on the n.m.r. time scale. At lower temperatures the spectrum (Figure 1) is much sharper and displays a series of multiplets similar to those in other spirans.[10] In this sharper spectrum the relative intensities for methyl bands show that there are five near δ 2.1; if pyridine is added to the sample the band can be seen to split into four discrete peaks (Figure 2), but we have not found a way of confirming five. These five correspond to four aromatic methyl groups and one vinylic methyl group. A single methyl band near δ 1.7 corresponds to the other vinylic methyl group. Near δ 1.4 four geminal methyl groups provide three distinct peaks however the spectrum is obtained, whereas the remaining two geminal methyl groups exhibit different behaviour. At −15 °C one of them appears to lie under the band at δ 1.4, while the other occurs near δ 1.2 (Figure 1). At ordinary temperatures both methyl signals broaden considerably and form two humps near δ 1.1 and 1.3. At + 55 °C these peaks become sharp and occur near δ 1.1 and 1.22. A detailed explanation has to await the stereochemical studies mentioned above, but conclusions of importance for the present discussion can readily be extracted by the use of trifluoroacetic acid-induced line broadening.[14] Since all the aromatic systems in structure (22) are 6-hydroxychroman derivatives, all closely associated protons should suffer reversible line broadening when the sample is treated with trifluoroacetic acid, to leave the vinylic methyl signals sharp against a diffuse background (aside from the geminal

methyl bands). Figure 2 shows the result, which confirms the assignments and, in particular, confirms that in this trimer ring D has the orientation found in compound (15b) and not found in structure (15a).

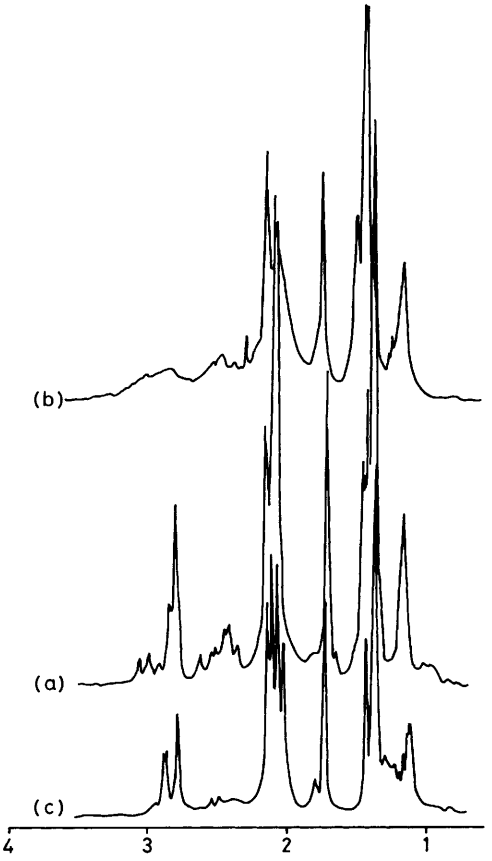


FIGURE 2 ^{1}H N.m.r. spectra (δ scale) for the trimer (22) determined at 220 MHz in $CDCl_3$: (a) at −15 °C; (b) at −15 °C after the addition of trifluoroacetic acid (*ca.* 6 drops); (c) at 32 °C after the addition of pyridine (*ca.* 7 drops)

Trimer (22) differed from all the oxidation products, so we are left with no direct evidence that the oxidation can attack the 4-methyl group of the phenol (7b) although, of course, such attack could be partly responsible for the unidentified substances. The main result, however, does confirm the idea that, in 6-hydroxy-1-benzopyran derivatives like compound (3), the specific oxidation is directed by the dihydropyran ring and that the effect is an activation of the 5-methyl group rather than a deactivation of the 7-methyl group.

EXPERIMENTAL

The Oxidation of 2,3-*Dihydro*-2,2,4,6,7-*pentamethylbenzofuran*-5-*ol* (7b).—The benzofuranol (3 g) in benzene (100 ml) was shaken with potassium hexacyanoferrate(III) (7.1 g) in 0.2M sodium hydroxide (100 ml) for 0.5 h. The benzene layer was then washed with water (2 × 50 ml), dried (Na_2SO_4), and concentrated under reduced pressure to leave a dark brown oil (2.8 g). After the oil had been dissolved in cyclohexane (70 ml) and left overnight it deposited solid A (66 mg). The cyclohexane was removed under reduced pressure and the residue was dissolved in light petroleum (70 ml) and kept at 5 °C for 8 h, during which time the solution (solution S) deposited more solid; this was heated in light petroleum (40 ml) and the insoluble part (110 mg) was combined with solid A, and the soluble part (0.6 g) formed solid B.

Solution S was then concentrated, but no more solid was obtained. Complete removal of the solvent left a brown oil that was subjected to chromatography on silica with elution by diethyl ether–light petroleum (7 : 3 v/v). After the first material appeared in the eluate the first cut was made at 130 ml. Removal of the solvent left a semisolid that was separated by boiling methanol into an insoluble part, C1, and a solution. Concentration of the solution to half its bulk induced the separation, when cold, of solid C2, and dilution of the filtrate with water provided a third solid, C3. In later work C3 could be better obtained by using neutral alumina instead of silica for chromatography.

The second cut was made after a further 40 ml. The contents of this fraction proved to be an oil that supplied a further quantity of solid C1 when treated with a little methanol. A third cut was made after another 140 ml. The contents again formed a semisolid; separation by means of hot light petroleum gave additional quantities of solid A (insoluble) and solid B (soluble).

Several further cuts were made, but no fraction supplied any single, identifiable products.

Solid A (combined yields 206 mg) separated from ethanol or diethyl ether to give 2,2′,3,3′-*tetrahydro*-2,2,2′,2′,4,4′-7,7′-*octamethyl*-6,6′-*ethylenebisbenzofuran*-5,5′-*diol* (8) as prisms, m.p. 208—210 °C; $\nu_{max.}$ (KBr) 3 300br cm^{-1} (strong, OH); $\delta(CDCl_3)$ 1.47 (12 H, s, *gem*-Me), 2.12 (6 H, s, Ar-Me), 2.20 (6 H, s, Ar-Me), 2.94 (4 H, s, CH_2CH_2), and 5.60br (2 H, s, removed by D_2O, OH) (Found: C, 75.9; H, 8.4. $C_{26}H_{34}H_4$ requires C, 76.1; H, 8.3%). The mass spectrum shows that the molecular ion *m/e* 410 breaks down into fragment ions *m/e* 218 ($C_{12}H_{15}O{\cdot}CH{=}CH_2^+$) and 205 ($C_{12}H_{15}O{\cdot}CH_2^+$), other strong peaks being formed from these by loss of Me groups.

Solid B (combined yields 1.0 g) was identified as the starting benzofuranol by m.p., mixed m.p., and spectroscopic methods.

Solid C1 (250 mg) crystallized from ethanol or from acetone to give the trimer (12), 2,2′,3,3′,6a,7,7′,8′,10,11-*decahydro*-2,2,2′,2′,4,4′,6a,8,9′,10,10,12-dodecamethyl-5H-*xantheno*[2,3-b:10a, 5-b′]*bisfuran*-6-*spiro*-6′-*pyrano*[2,3-f]-*benzofuran*-5-*one* as faintly yellow hexagonal prisms, m.p. 239—241 °C; $\nu_{max.}$ (KBr) 1 674 cm^{-1} (conj. ketone) (Found: C, 76.5; H, 7.9%; M^+, 612.346 05. $C_{39}H_{48}O_6$ requires C, 76.4; H, 7.9%; M^+, 612.345 07). Other spectroscopic details are discussed in the text.

Solid C2 (60 mg) separated from methanol to give 2,2′,-3,3′,5a,7′,8,8′,9a,10-*decahydro*-5a-*hydroxy*-6-(2-*hydroxy*-2-*methylpropyl*)-2,2,2′,2′,4,4′,7,9′,9a,11-*decamethyl*-8H-*furo*-[2,3-b]*xanthen*-9-*spiro*-6′-*pyrano*[2,3-f]*benzofuran*-8-*one* (19) as bright yellow, thick hexagonal prisms, m.p. 160—163 °C; $\nu_{max.}$ (KBr) 3 564 (OH) and 1 667 cm^{-1} (conj. ketone) (Found: C, 74.5; 74.6; H, 8.0, 8.1. $C_{39}H_{50}O_7$ requires C, 74.3; H, 8.0%). The mass spectrum contained no peak appropriate to a molecule $C_{39}H_{50}O_7$, but indicated a molecular ion at *m/e* 612 ($C_{39}H_{48}O_6$ requires M^+, 612) that collapsed *via* a dimer (*m/e* 408) to a monomer (*m/e* 204). The n.m.r. spectrum is detailed in the text. This compound is probably not a primary oxidation product because it can be

formed by passing the trimer (12) through a silica column, though not through a column of neutral alumina. Trimer (12) was purified by recrystallization until no trace of the bright yellow compound (19) could be detected visually, by t.l.c., or by i.r. and n.m.r. spectroscopy, and a sample (300 mg) in diethyl ether was passed down a column of silica (3 × 15 cm). which resembled that used for the separation of oxidation products. Elution with diethyl ether–light petroleum (3 : 20 v/v) took several days and the contents of the total eluate were yellow and were heated with methanol to recover the trimer (slightly soluble; 160 mg) and to isolate compound (19) as bright yellow hexagonal prisms (60 mg), m.p. and mixed m.p. 160—162 °C, further identified spectroscopically.

Solid C3 (100 mg) was too soluble in the usual solvents for effective recrystallization, but was purified by rechromatography on neutral alumina to give a substance that resembled the trimer (12) and which crystallized from aqueous ethanol to form irregular pale yellow *plates*, m.p. 139—141 °C; $\nu_{max.}$ (KBr) 1 670 cm^{-1} (conj. ketone) (Found: C, 76.4; 76.3; H, 7.9, 7.9. $C_{39}H_{48}O_6$ requires C, 76.4; H, 8.0%). The mass spectrum gave *m/e* 612 for the molecular ion ($C_{39}H_{48}O_6$ corresponds to *m/e* 612) with major fragmentations to give ions at *m/e* 408 and 204. T.l.c. in various systems disclosed only a single component. The structure has not been fully established.

2,2′,3,3′,7′,8′-Hexahydro-2,2,2′,2′,4,4′,7′,9-octamethyl-6H-pyrano[2,3-f]benzofuran-6-spiro-6′-benzofuran-5′-one [Spiran (11)].—The ethylenebisbenzofurandiol (8) (115 mg) in benzene (10 ml) was oxidized with potassium hexacyanoferrate(III) (1 g) in 0.2M sodium hydroxide (10 ml), the mixture being vigorously stirred for 45 min. The organic layer was washed with water and dried in the routine manner and the solvent was removed under reduced pressure (without the use of heat) to leave a yellow solid. This crystallized from methanol to give the spiran (11) as bright yellow, felted *needles* (105 mg), m.p. 144—145 °C; $\nu_{max.}$ (KBr) 1 633 and 1 657 cm^{-1} (conj. ketone) (Found: C, 76.5; H, 8.0. $C_{26}H_{32}O_4$ requires C, 76.4; H, 7.9%). The mass spectrum showed the expected molecular ion at *m/e* 408 with the only major fragment ion at *m/e* 204. The n.m.r. spectrum is discussed above.

This spiran (44 mg) was heated in boiling chlorobenzene (7 ml) for 3 h. The colour slowly faded and removal of the solvent under reduced pressure left a faintly yellow solid which, when crystallized from ethanol, supplied the trimer (12) as very pale yellow, thin prisms (41 mg), m.p. and mixed m.p. 240—241 °C, further identified spectroscopically.

2,3-Dihydro-4-hydroxymethyl-2,2,6,7-tetramethylbenzofuran-5-ol (7d).—2,3-Dihydro-2,2,6,7-tetramethylbenzofuran-5-ol (1 g) and hexamethylenetetra-amine (2.7 g) were heated together in refluxing aqueous acetic acid (1 : 1, 50 ml) for 1.5 h. During this time a faintly yellow solid separated from the hot solution and when collected (hot) and crystallized from acetone it gave *2,3-dihydro-4-(3,4,5,6-tetrahydro-6,6,8,9-tetramethyl-2H-furo[3,2-f][1,3]benzoxazin-5-ylmethyl)-2,2,6,7-tetramethylbenzofuran-5-ol* (21) as large prisms (205 mg), m.p. 199—200 °C, δ (at 60 MHz) 1.43 (12 H, s, *gem*-Me), 2.13 (s, 12 H, Ar-Me), 2.26 (4 H, s, furan-CH_2), 3.86 (2 H, s, Ar-CH_2N), 3.96 (2 H, s, Ar-CH_2N), and 4.81 (2 H, s, OCH_2N) (Found: C, 73.7; H, 7.9; N, 3.4. $C_{26}H_{33}O_4N$ requires C, 73.8; H, 7.9; N, 3.3%). The mass spectrum displayed the molecular ion at *m/e* 437 with major fragment ions at *m/e* 233 ($C_{14}H_{19}NO_2$) and 204 ($C_{13}H_{16}O_2$); from the latter loss of Me gave another important fragment ion at *m/e* 189.

When the hot mother liquor was allowed to cool it deposited a solid which, when recrystallized from aqueous acetic acid, supplied *2,3-dihydro-5-hydroxy-2,2,6,7-tetramethylbenzofuran-4-carbaldehyde* (7c) as thick yellow prisms (410 mg), m.p. 108 °C; $\nu_{max.}$ (KBr) *ca.* 1 640br cm^{-1} (H-bonded CHO); δ 1.46 (6 H, s, *gem*-Me), 2.12 (3 H, s, Ar-Me), 2.15 (3 H, s, Ar-Me), 3.21 (2 H, s, ring-CH_2), 9.84 (1 H, s, CHO), and 11.06 (1 H, s, removed by D_2O, OH) (Found: C, 70.5; H, 7.3. $C_{13}H_{16}O_3$ requires C, 70.9; H, 7.3%). In the mass spectrometer several samples under various conditions failed to show a peak at *m/e* 220 ($C_{13}H_{16}O_3$ requires M^+, 220), but a strong peak at *m/e* 221 was always present along with a corresponding peak at *m/2e* 110.5; it seems that the compound picks up one hydrogen atom as do quinones.

Sodium borohydride (0.2 g) in water (20 ml) was added to the aldehyde (0.5 g) in tetrahydrofuran (THF) (freshly distilled; 15 ml) at 0 °C. The stirred solution lost its colour after 5 min and acetic acid was added to destroy the excess of reductant. The solution was diluted with water (50 ml) and the desired product extracted into diethyl ether, recovered in the usual way, and crystallized from ethyl acetate–light petroleum to give the *hydroxymethylbenzofuranol* (7d) as long prisms (0.4 g), m.p. 147—148 °C; $\nu_{max.}$ (KBr) 3 510sh and 3 330br cm^{-1} (OH); δ 1.42 (6 H, s, *gem*-Me), 2.08 (3 H, s, Ar-Me), 2.13 (3 H, s, Me), 2.88 (2 H, s, ring-CH_2), 4.72 (2 H, s, CH_2OH), and 6.9br (s, removed by D_2O, OH) (Found: C, 70.1; H, 8.2. $C_{13}H_{18}O_3$ requires C, 70.2; H, 8.2%). The mass spectrum of this compound was again somewhat unusual. The molecular ion at *m/e* 222 was observed, but was weak, a peak at *m/e* 220 being much more prominent; the compound appears to lose one or two hydrogen atoms easily, again as quinols do. Peaks corresponding to (M^+ — Me), (M^+ — H_2O), and (M^+ — CH_2OH) were observed as usual.

Trimer (22).—The foregoing hydroxymethylbenzofuran (7d) (0.40 g) was dissolved in diethyl ether (sodium-dry; 60 ml), which contained a molecular-sieve dehydrating agent, and treated with a slow stream of hydrogen chloride (dried by H_2SO_4) for 1 h at −5 °C. The mixture was kept for 2 h at 0 °C and the solution was decanted off and concentrated under reduced pressure without the application of heat. The residual solid (0.42 g) was used for the next step without purification.

The solid was dissolved in diethyl ether (150 ml) and shaken for 15 min with aqueous sodium hydrogencarbonate (7%; 100 ml); the initial yellow colour quickly faded. The ethereal layer was washed with water (2 × 70 ml), dried (Na_2SO_4), and concentrated under reduced pressure to leave a pale yellow solid that crystallized from ethanol to give the trimer (22), *1,1′,2,2′,4′,5′,7,8-octahydro-2,2,2′,2′,8′,-9,9′,10,13,13-decamethyl-6a,10a-ethano-oxy-8′H,11H-furo[3,-2-a]xanthen-7-spiro-6′-pyrano[3,2-e]benzofuran* as the hemihydrate as thick prisms (0.20 g), m.p. 222—223 °C [Found (samples dried routinely at room temperature) C, 75.3; 75.4; H, 8.2, 8.3; (samples dried under reduced pressure at 110 °C for several hours) C, 75.7, 75.5; H, 8.2, 8.2. $C_{39}H_{48}O_6$ requires C, 76.5; H, 7.9. $C_{39}H_{48}O_6 \cdot 0.5H_2O$ requires C, 75.4; H, 8.0%]. Spectroscopic and other findings are discussed in the text. The mother liquors yielded a substance that was purified on a column of silica to give a very small quantity of *2,2′,3,3′-tetrahydro-2,2,2′,2′,-6,6′,7,7′-octamethyl-4,4′-methylenebisbenzofuran-5,5′-diol* (9;

n = 1), m.p. 206 °C [Found (mass spectrally): M, 386. $C_{25}H_{32}O_4$ requires M, 386], further identified by the ^1H n.m.r. spectrum (Table 1).

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