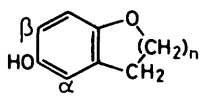
Spirans. Part 14.[1] Regioisomeric Quinone Methides and Spirodimers Related to Tocopherol

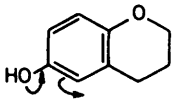
By **Francis M. Dean,* David A. Matkin,** and **Mohamed O. A. Orabi,** The Robert Robinson Laboratories, University of Liverpool, Liverpool L69 3BX

Evidence is provided that the quinone methide (5), 3,4-dihydro-2,2,5,8-tetramethyl-7-methylene-2*H*-benzo[*b*]-pyran-6(7*H*)-one, is more, not less, readily formed than its regioisomer, the corresponding 5-methylenebenzo-pyran-6-one (4), and consequently that 'bond fixation' and allied geometrical constraints (Mills–Nixon effects) cannot be responsible for the regioselective oxidative dimerisation of tocopherol. The quinone methide (5) obtained transitorily by treating 7-chloromethyl-3,4-dihydro-2,2,5,8-tetramethyl-2*H*-benzo[*b*]pyran-6-ol (11) with hydrogen carbonate ion rapidly forms the corresponding spirodimer (7), 3,3',4,4',8,9-hexahydro-2',2',5,5',-7,7,8',10-octamethylbenzo[1,2-*b*:4,5-*b*']dipyran-2-spiro-7'(6'*H*)-[1]benzopyran-6'-one and trimer (12), which is the main product. The spirodimer (7) reverts to quinone methide (5) near 80 °C and is, therefore, rapidly transformed into the trimer at this temperature, whereas the regioisomeric spirodimer (6), previously recognised as the product from the oxidations, is stable. The difference in reactivity between the known quinone methide (4) and the new one (5) is thought to be associated with the benzylic methylene groups of the terminal pyran rings.

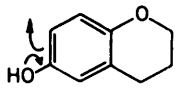
In simple phenols, the two *ortho*-positions are more or less equivalent as regards their propensity to undergo electrophilic attack. One of the chief anomalies is found in 6-hydroxychroman (1; $n = 2$), which is selectively attacked by electrophiles at the α-position whereas its ring homologues (1; $n = 1, 3$) or the equivalent but non-heterocyclic 4-methoxy-3-methylphenol



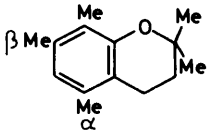
(1)



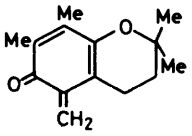
(2a)



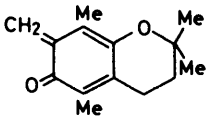
(2b)



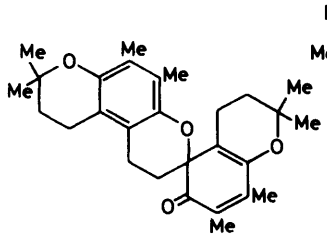
(3)



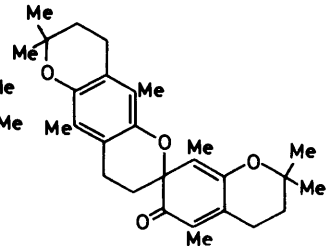
(4)



(5)



(6)

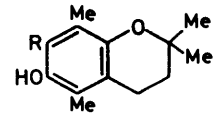


(7)

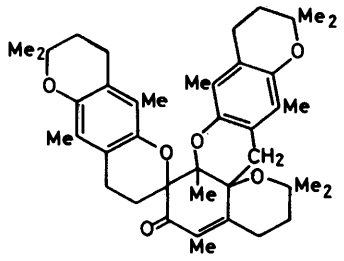
are attacked mainly at the β-position.[2,3] Some authors have sought to explain these and similar variations (Mills–Nixon effects[4]) by assuming that the size of the heterocyclic ring determines the nature of the bond common to the two rings (*i.e.* its length, angle, and order), consequently affecting the other benzenoid positions unequally. In particular, it has often been argued that the double-bond distribution (2a) would be thermodynamically preferred to that in (2b) and consequently that release of electrons from the hydroxy-group (arrows) would occur by preference towards the α-position (bond fixation theory). The same kind of arguments have been used to explain the fact that oxidations of tocopherols and their analogue (3) occurs specifically at the α-methyl group, never at the β-methyl group. Thus the analogue (3) could in theory be oxidised (dehydrogenated) giving either or both of the quinone methides (4) and (5), but the former has always been considered to be thermodynamically the more stable and this was thought to explain why (3) is oxidised at the α-methyl group to give the spirodimer (6) and not at the β-methyl group to give the isomer (7). But neither our own [5] nor the earlier calculations [6] of activation energies for quinonoid Wheland transition states showed sufficient sensitivity to the lengths and angles at the common bond nor has any independent experimental evidence been adduced for the presumed thermodynamical stabilities of the two quinone methides. We now offer direct evidence that the quinone methide (5) is probably more, not less stable than (4), and consequently that the regiospecificity in oxidation of the 5-methyl group in the 6-hydroxychroman nucleus is not determined by quinone methide formation, whether as envisaged by other authors [7] or by us,[5] even though quinone methides are undoubtedly produced by the oxidation.[8]

Because the spirodimer (7) is not available by the oxidation method we prepared it in another way beginning with 2,5-dimethylbenzene-1,4-diol. This compound reacts in acid media with 3-methylbut-2-en-1-ol to give a mixture of the monopyran (8) and a dipyran, but we found difficulty in obtaining the aldehyde (9) from the former, only the method with dichloromethyl methyl ether [9] being satisfactory. Borohydride reduction was normal, and the alcohol (10) so obtained readily supplied the halide (11) when treated with hydrogen chloride. With weak base (hydrogen carbonate ion) the halide instantly turns yellow because it forms the quinone

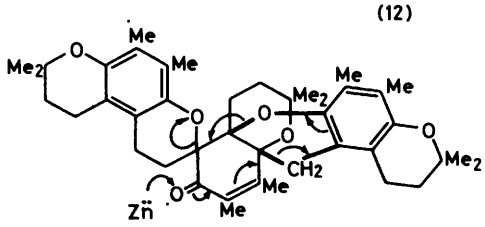
methide (5), but the expected spirodimer (7) was not the major product because another addition converted most of the material into the trimer (12). Structure (12) is assigned mainly on account of precedents [10-12] consistent with i.r. absorption at 1 675 cm^{-1} (conjugated ketone) and a lack of methyl resonances above δ 1.2 in the ^1H n.m.r. spectrum which suggests that all the angular methyl groups are adjacent to oxygen atoms. Such trimers are too stable to heat to provide quinone methides by cycloreversion under practicable conditions,[12] so we took up an observation made by Skinner and Parkhurst [11] who noted that the isomeric trimer (13), from quinone methide (4), is sensitive to zinc in acetic anhydride. They suggested that a concerted



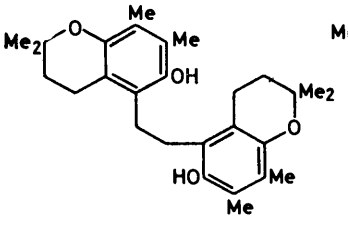
(8) R = H
(9) R = CHO
(10) R = CH_2OH
(11) R = CH_2Cl



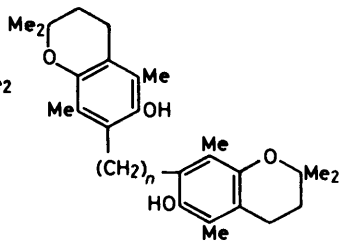
(12)



(13)



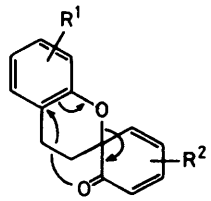
(14)



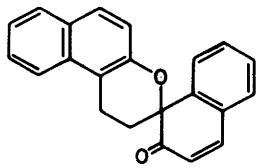
(15)

process as indicated by arrows in (13) could account for the reduction, in part, to the ethylenebischromanol (14). We found that although a similar reduction of trimer (12) by zinc in acetic anhydride or acetic acid gives chiefly other products, the desired ethylenebischromanol (15; $n = 2$) is obtainable in moderate yield and can be oxidised by hexacyanoferrate(III) to the requisite spiran (7).

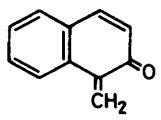
The spiran (7) is a yellow compound sensitive to light, which bleaches it in a few hours. It is also unusually sensitive to heat. At ordinary temperature its ^1H n.m.r. spectrum consists of bands greatly broadened by the sigmatropic rearrangement [13] indicated in diagram (16)—



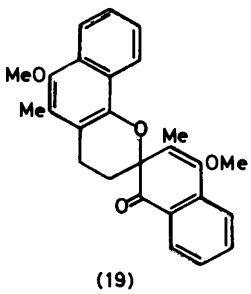
(16)



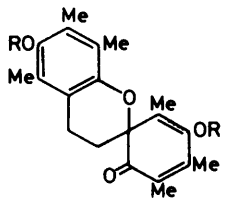
(17)



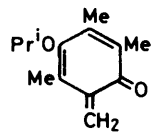
(18)



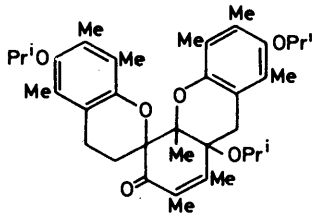
(19)



(20) R = Me
(21) R = Pr^i



(22)



(23)

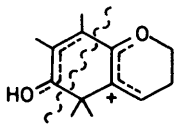
while the spirodimer (17) becomes a useful source [14] of quinone methide (18) only at temperatures above 160 °C.

It is evident, therefore, that the thermal sensitivity of the spirodimer (7) is unusual and partly controlled by the annelation with the dihydropyran rings. To make this point clearer we studied the spirans (19), (20), and (21) available from prior studies.[15] None of these compounds exhibited signs of sigmatropic rearrangement at temperatures up to 120 °C and the first two resisted any

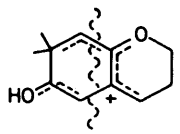
change *via* a quinone methide monomer to a trimer. The spiran (21) did show a slow change but this was irreversible. The new material could not be fully purified since it seemed to consist of a mixture of two very closely related substances, probably stereoisomers; however, we do not doubt that it is essentially the trimer (23) derived from the quinone methide (22). Thus the mass spectrum gave 618 as the molecular weight, the i.r. spectrum indicated an unsaturated ketone ($\nu_{max.}$ 1 682 cm^{-1}), and the ^1H n.m.r. spectrum showed a new band at δ 1.5 consonant with a (new) angular methyl group. We had expected the first two spirans to be thermally stable compared with the annelated spirans because steric hindrance from the *ortho*-substituents prevents their methoxy-groups from lying in the plane of the rings and therefore from engaging their lone pairs in p-π stabilisations.[16] We had expected the isopropyl ether to behave similarly, but models now showed that while there are indeed important steric interactions they cannot be wholly relieved by rotation, *i.e.* there is no conformation in which the isopropyl methyl groups do not collide in some way with the *ortho*-substituents. Hence despite its size the isopropyl group could well be less of a bar to electronic interaction than the methyl of the methoxy group.

From these results we conclude that cycloreversion of spirodimers into quinone methide monomers is expedited by alkoxy-groups, the more so if these form part of a dihydropyran ring annelated in a particular way. Until the necessary calculations can be completed we offer qualitative reasons derived from our analysis of the regiospecificity of electrophilic attack of 6-hydroxychroman (1; $n = 2$) and its ring homologues.[5] There the key feature was that the benzylic methylene group of the heterocyclic ring had to be included in the analysis because its hyperconjugative interactions with the benzenoid orbitals are significant. Only within the geometry of the dihydropyran ring can the orbitals of this methylene group be correctly aligned with the benzene orbitals without at the same time reducing the important interactions with the heterocyclic oxygen atom. The main energy changes are felt in the inner orbitals, not in the frontier orbital. Pictorially we show the π-system for electrophilic substitution at the α-position in diagram (24), where the benzylic methylene group is treated as an sp^2 carbon. When a node splits the system as symmetrically as possible it produces two moieties each with an oxygen atom and three carbon atoms. The positive charge is placed so as to emphasise the simultaneous interactions with ring oxygen and benzylic carbon atoms. There is no corresponding diagram for β-substitutions; in diagram (25) the same placing for the positive charge is impossible without fragmentation of the π-system or cross conjugation or gross loss of symmetry in the orbital concerned.

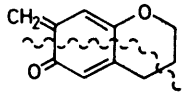
Applied to the quinone methides, similar criteria are easily met for isomer (5), which permits analysis into two transoid segments each with one oxygen and four carbon atoms as in (26). The dipolar form (27) points comparison and contrast with the preceding case. For isomer (4) no equivalent can be found; perhaps (28) is the nearest, but it leaves out the important benzylic methylene group. Finally, diagram (29) illustrates the operation of these criteria in both components during cycloreversion as the starred bonds break; thus the quinone methide (5) should be readily formed from spiran (7). By the same criteria, however, the quinone



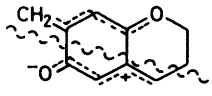
(24)



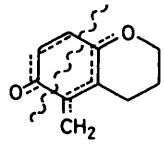
(25)



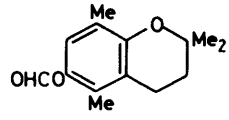
(26)



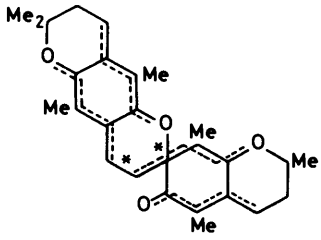
(27)



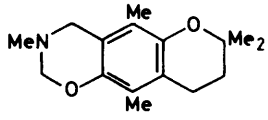
(28)



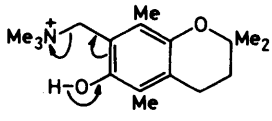
(30)



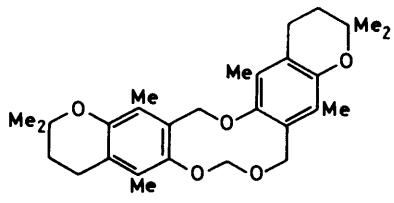
(29)



(31)



(32)



(33)

methide should be particularly efficient in cycloadditions, which explains why we obtained mainly the trimer (12) when we had hoped to prepare the spirodimer (7) in the same way as its isomer (6).

We conclude with a note on synthetical matters. The Vilsmeier–Haack method failed to convert the chromanol (8) into the aldehyde (9), only the formate (30) being formed. As pointed out above, the chromanol is not activated towards the requisite β-substitution and other authors [17] have remarked that the less reactive phenols may give formates instead of aldehydes. The vigorous conditions of the Duff process (hexamethylenetetramine in boiling acetic acid) gave some of the aldehyde, but it was accompanied by the 1,3-oxazine derivative (31).

The i.r. spectrum is devoid of bands attributable to carbonyl, hydroxy-, or imino-groups, while the ^{1}H n.m.r. spectrum evidences the presence of an *N*-methyl group and two isolated methylene groups. The mass spectrum is dominated by a fragmentation in which C_2H_5N is lost, no doubt because of a cycloreversion generating the quinone methide (5) and $MeN{:}CH_2$. The ease of quinone methide formation might also be invoked to account for the presence of the cyclic amine since the intermediate salt (32) should readily afford the quinone methide (5) and there seem to be parallels already in the literature.[18] Attempts to obtain the halide (11) by direct chloromethylation may also have failed for similar reasons, the product being a mixture that failed to yield any single substance. A similar product often contaminated the trimer (12) when this was made by treating the crude halide (11) with hydrogen carbonate ion, and it could then be obtained pure and identified as the 1,5,7-trioxacyclodecane derivative (33). Again no carbonyl or hydroxy-groups were detected by i.r. spectroscopy, and this time the ^{1}H n.m.r. spectrum showed three isolated methylene bands at low fields. The mass spectrum showed two very marked fragmentations; first the molecular ion lost a fragment of 30 m.u. (CH_2O) and then the ion produced (436 m.u.) collapsed into (2 mol. equiv. of) the quinone methide (5) (218 m.u.).

EXPERIMENTAL

I.r. spectra were determined upon mulls in paraffin. ^{1}H N.m.r. spectra were determined upon solutions in deuteriotrichloromethane, usually at 100 MHz. Light petroleum refers to the fraction b.p. 60—80 °C. Molecular weights were determined mass spectroscopically.

2,2,5,8-*Tetramethylchroman*-6-*ol* (8).—2,5-Dimethylbenzene-1,4-diol (8 g) was heated under reflux in formic acid (98%; 75 ml) and tetrahydrofuran (20 ml) and 3-methylbut-2-en-1-ol (2.5 g) in tetrahydrofuran (20 ml) was added drop by drop during *ca.* 3.5 h. After a further 3 h under reflux the products were isolated in the usual way and obtained as an oil that was boiled in methanol (75 ml) containing concentrated hydrochloric acid (1 ml) for 20 min. Volatilisation of solvents and reagent under reduced pressure and neutralisation of the residue by means of sodium hydrogen carbonate supplied a sticky pink material which was left in contact with light petroleum. The residual starting diol crystallised (4.2 g) and was removed. The solution supplied a purplish solid that was dissolved in ethyl acetate (100 ml) and shaken with palladium-on-charcoal (10%; 0.5 g) under hydrogen for several hours; recovered from this treatment it formed a pale yellow gum that was fractionated on a column of silica (100 g) by means of ether–light petroleum (1 : 20) giving the first product. This was purified from light petroleum to furnish 2,3,4,7,8,9-hexahydro-2,2,5,7,7,10-hexamethylbenzo[1,2-*b*:4,5-*b*']-dipyran as prisms (450 mg), m.p. 192—194 °C (lit.,[18] 193—196 °C). The second product was eluted by means of ether–light petroleum (1 : 5) and crystallised from light petroleum to give the chroman-6-ol as needles (3.1 g), m.p. 78—78.5 °C (lit.,[19] 77—78 °C, 86—87.5 °C).

Reactions of 2,2,5,8-*Tetramethylchroman*-6-*ol* (8).—(i) *With dimethylformamide.* The chromanol (0.5 g) was added to a mixture of phosphoryl chloride (2.5 ml) and dimethylformamide (20 ml) that had been freshly made and allowed to cool to room temperature. Little happened at ordinary temperature so the reaction mixture was heated on a steam-bath for 45 min whereupon it turned deep red. It was cooled, poured onto ice, and the products isolated from it in the usual way giving a light yellow oil which, when purified on a column of silica (50 g) from ether–light petroleum (1 : 5 v/v), supplied 2,2,5,8-*tetramethylchroman*-6-*yl formate* (30) as an oil (0.5 g) crystallising from a small volume of light petroleum chilled in ice as large rhombs, m.p. 35—38 °C, $\nu_{max.}$ (Nujol) 1 718 cm^{-1} (ester C:O), δ 1.30 (s, 6 H, *gem*-Me_2), 2.00 (s, 3 H, $ArCH_3$), 2.12 (s, 3 H, $ArCH_3$), 1.78 (t, 2 H, *J* 7 Hz, 3-CH_2), 2.60 (t, 2 H. *J* 7 Hz, 4-CH_2), 6.64 (s, 1 H, ArH), and 8.23 (s, 1 H, HC:O) (Found: C, 71.9; H, 7.9. $C_{14}H_{18}O_3$ requires C, 71.8; H, 7.7%). The major fragmentation of the molecular ion, *m/e* 234, gave a fragment ion at *m/e* 206 ($M^{\cdot+}$ − CO).

Later fractions from the chromatography gave a solid (20 mg) crystallising from light petroleum as needles, m.p. 43—46 °C, with hydroxylic absorption at 3 520 and 3 440 cm^{-1} but no carbonyl absorption. The molecular weight (*m/e* 206) indicates isomerism with the starting chromanol and the substance may be a dihydrobenzofuran derivative but it was not examined further.

(ii) *With hexamethylenetetramine* (Duff reaction). The chromanol (0.74 g) was heated with hexamethylenetetramine (2.0 g) in boiling aqueous acetic acid (1 : 1 v/v) (40 ml) for 2.5 h and the mixture was then diluted with water (250 ml) and the products collected into ether (3 × 80 ml), washed with water, and freed from acid by means of sodium hydrogen carbonate. Obtained from the ether in the usual way, the products formed a yellow oil that was mixed with light petroleum and kept at 0 °C. The solid so made was crystallised from light petroleum to give 6-*hydroxy*-2,2,5,8-*tetramethylchroman*-7-*carbaldehyde* (9) as yellow rhombs (0.27 g), m.p. 88—89 °C, $\nu_{max.}$ (Nujol) 1 636 (conj. C:O with hydrogen bonding), δ 1.31 (s, 6 H, *gem*-Me_2), 1.82 (t, 2 H, *J* 7 Hz, 3-CH_2), 2.11 (s, 3 H, ArMe), 2.40 (s, 3 H, ArMe), 2.69 (t, 2 H, *J* 7 Hz, 4-CH_2), 10.28 (s, 1 H, CH:O), and 11.78 (s, removed by D_2O, 1 H, bonded OH) (Found: C, 71.7; H, 7.8%; *M*, 234. $C_{14}H_{18}O_3$ requires C, 71.8; H, 7.7%; *M*, 234).

All light petroleum mother-liquors from the aldehyde were combined and the contents subjected to thick-layer chromatography on silica. Ether–light petroleum developed a band R_F 0.4 that was extracted with ether–acetone. The extract provided a solid that crystallised from light petroleum to give 2,3,4,7,8,9-*hexahydro*-3,5,7,7,10-*pentamethylpyrano*[2,3-g]-1,3-*benzoxazine* (31) as cream coloured rhombs (70 mg), m.p. 107 °C, $\lambda_{max.}$ 226, 294 (infl., and 298 nm (log ε 3.90, 3.65, and 3.68), δ 1.28 (s, 6 H, *gem*-Me_2), 1.76 (t, 2 H, *J* 7 Hz, pyran 3-CH_2), 1.95 (s, 3 H, ArMe), 2.04 (s, 3 H, ArMe), 2.55 (s, 3 H, NMe), 2.60 (t, 2 H, *J* 7 Hz, pyran 4-CH_2), 3.99 (s, 2 H, $ArCH_2N$), and 4.63 (s, 2 H, $O{\cdot}CH_2{\cdot}N$) (Found: C, 73.6; H, 9.1; N, 5.5. $C_{16}H_{23}NO_2$ requires C, 73.5; H, 8.9; N, 5.4%). The mass spectrum indicates that the molecular ion at *m/e* 261 loses $MeNCH_2$ to give a quinone methide, *m/e* 218, as the major fragment ion by a retro-Diels–Alder reaction.

(iii) *With dichloromethyl methyl ether.* Dichloromethyl methyl ether (4.0 g) was added during 5 min to a stirred solution of the chromanol (4.1 g) and titanium(IV) chloride (2.2 ml) in dichloromethane (200 ml); then the flask was capped with a drying tube and the deep violet solution kept for 35 min. 2M-Hydrochloric acid was added to the reaction mixture of 0 °C and the products were isolated by means of

ether (600 ml), washed with dilute hydrochloric acid and then water, recovered by evaporation of solvent, and freed from coloured tar by means of charcoal in light petroleum (60 ml). Concentration of the filtrate supplied the carbaldehyde (9) as yellow rhombs (4.3 g), m.p. 88—89 °C, identical with a sample from (ii) above. This method was used for preparative purposes.

7-Chloromethyl-2,2,5,8-tetramethylchroman-6-ol (11).—Sodium borohydride (1.0 g) in water (10 ml) was slowly added to a stirred solution of the chromancarbaldehyde (9) (4.0 g) in tetrahydrofuran (100 ml) at 0 °C. As soon as the mixture was bleached (*ca.* 3—4 min) the reaction was quenched with acetic acid and the mixture diluted with water (400 ml). The product was isolated by means of ether (2 × 150 ml) as a solid, which when purified from ether–light petroleum, furnished 7-hydroxymethyl-2,2,5,8-tetramethylchroman-6-ol (10) as needles (4.0 g), m.p. 124—126 °C (lit.,[20] 124—125 °C) (Found: C, 70.9; H, 8.6. Calc. for $C_{14}H_{20}O_3$; C, 71.2; H, 8.5%).

Hydrogen chloride (dried by passage through sulphuric acid) was rapidly bubbled into 7-hydroxymethyl-2,2,5,8-tetramethylchroman-6-ol (1.5 g) in ether (dried over sodium; 100 ml) at 0 °C and containing water-adsorbent molecular sieve (10 g) and protected by a drying tube. When hydrogen chloride was no longer absorbed, the flow was stopped and the solution kept at 0 °C for 1 h. Evaporation of the volatile materials under reduced pressure left a solid that was dissolved in the minimum amount of fresh ether and induced to crystallise by the addition of a little cold, light petroleum giving the *chloromethylchromanol* as needles (1.22 g), m.p. 85—87 °C (decomp.), $\nu_{max.}$ 3 300 (OH), δ 1.29 (s, 6 H, *gem*-Me_2), 1.78 (t, 2 H, *J* 7 Hz, 3-CH_2), 2.10 (s, 3 H, ArMe), 2.21 (s, 3 H, ArMe) 2.61 (t, 2 H, *J* 7 Hz, 4-CH_2), and 4.74 (s, 2 H, $ArCH_2Cl$) (Found: C, 66.3; H, 7.9. $C_{14}H_{19}ClO_2$ requires C, 66.0; H, 7.5%). No OH resonance could be found in the ^1H n.m.r. spectrum. The mass spectrum gave *m/e* 254 and 256 for the molecular ions (Cl isotopes) and showed a major collapse by loss of HCl to give a quinone methide fragment ion at *m/e* 178.

The Trimer (12).—The chloromethylchromanol (11) (1.5 g) in ether (500 ml) was shaken in a separating funnel with saturated aqueous sodium hydrogen carbonate (4 × 200 ml). At first the ether layer was intensely yellow but eventually the colour faded to a pale lime colour and, after being dried (Na_2SO_4), it was concentrated under reduced pressure to leave a gummy yellow residue. This was dissolved in a little ether and gradually treated with light petroleum until a light yellow powder separated. Crystallisation of the powder from acetone–light petroleum gave the trimeric spiran, *3′,4,4′,7,8,9,10′,11′,12′,15′-decahydro-2′,2′,5,5′,7,7,-7a′,9′,10,12′,12′,14′-dodecamethylbenzo*[1,2-b:4,5-b′]*dipyran-2(3H)-spiro-7′(2′H)-xantheno*[6,7-b:9a,1-b′]*dipyran-6′-one*, as cream needles (0.9 g), m.p. 221—223 °C (decomp.), $\nu_{max.}$ 1 675 (conj. C:O), δ (100 MHz) 1.18, 1.24, 1.41, 1.74, and 2.14 (all 3 H), 1.27 and 1.29 (each 6 H), and 2.00 (9 H) (all singlets), and *ca.* 2.6 (m) and 1.7 (m) (Found: C, 77.0; H, 8.3. $C_{42}H_{54}O_6$ required C, 77.0; H, 8.3%). The mass spectrum gave for the molecular ion a peak at *m/e* 654 with a major loss of 218 m.u. ($C_{14}H_{18}O_2$) corresponding to loss of one benzopyran quinone-methide segment.

On some occasions the chloromethylchromanol was prepared as above but, instead of being purified, was subjected at once to the treatment with sodium hydrogen carbonate. The trimer was obtained as before, but its mother liquors contained products that had to be separated by thick layer chromatography on silica with development by ether–light petroleum (1 : 2 v/v) and extraction by acetone. One product invariably present had R_F 0.3 and crystallised from light petroleum to give *2,2,2′,2′,5,5′,8,8′-octamethyl-7,7′-methylenebischroman-6-ol* (15; *n* = 1) as needles, m.p. 173.5—175 °C, $\nu_{max.}$ 3 440 cm^{-1} (OH), δ 1.28 (s, 12 H, *gem*-Me_2), 1.76 (t, 4 H, *J* 7 Hz, 3-CH_2), 2.02 (s, 6 H, ArMe), 2.21 (s, 6 H, ArMe), 2.58 (t, 4 H, *J* 7 Hz, 4-CH_2), 3.97 (s, 2 H, bridge CH_2), and 5.13 (bs, 2 H removed by D_2O, OH) (Found: C, 76.25; H, 8.7%; *M*, 424. $C_{27}H_{36}O_4$ requires C, 76.4; H, 8.55%; *M*, 424). On one occasion only the reaction appeared to take a substantially different course; instead of the trimer (12), we isolated the simpler spiran (7) (see below), and instead of the methylenebischromanol we isolated *2,3,4,9,12,13,14,17-octahydro-2,2,5,10,12,12,15,18-octamethyldi*[1]*benzopyrano*[6,7-d:6′,7′-h][1,3,7]*trioxacyclodecane* (33) which had m.p. 188—190 °C (decomp.) and δ 1.29 (s, 12 H, gem-Me_2), 1.79 (two almost coincident triplets, 4 H, *J* 7 Hz, 3- and 13-CH_2), 1.93, 2.00, 2.07 and 2.12 (all s, 3 H, ArMe), 2.63 (two almost coincident triplets, 4 H, *J* 7 Hz, 4- and 14-CH_2), 3.91 (bs, 2 H, $ArCH_2$-O), 4.01 (s, 2 H, $ArCH_2O$), and 4.69 (s, 2 H, O·CH_2·O) but neither carbonyl nor hydroxy-absorption in the i.r. region (Found: $M^{\cdot+}$, 466.2895. $^{12}C_{29}{}^1H_{38}{}^{16}O_5$ requires *M*, 466.2711). The initial fragmentation in the mass spectrometer involved the loss of 30 m.u. (CH_2O) followed by scission of the remainder into (two equal) ions, *m/e* 218.

Reduction of Trimeric Spiran (12).—(i) *With zinc in acetic acid.* The spiran (1.5 g) in acetic acid (60 ml) and tetrahydrofuran (30 ml) was heated (steam-bath) with zinc dust (40 g) and occasional stirring for 75 min. The mixture was filtered hot, and the residues washed with hot tetrahydrofuran (3 × 20 ml); filtrate and washings were combined, poured into water (600 ml), and extracted with ethyl acetate (2 × 200 ml). The extract was washed with water (2 × 250 ml), saturated aqueous sodium hydrogen carbonate (2 × 200 ml), and finally water (500 ml) and dried (Na_2SO_4). Removal of the ethyl acetate under reduced pressure left a gummy foam which collapsed to a powder (325 mg) when kept in contact with light petroleum (50 ml) for *ca.* 1 h. Crystallised from acetone–light petroleum, the powder supplied *2,2,2′,2′,5,5′,8,8′-octamethyl-7,7′-ethylenebischroman-6-ol* (15; *n* = 2) as tiny crystals (325 mg) of the solvate with acetone but which, after drying *in vacuo* at 120 °C had m.p. 242 °C (decomp.), $\nu_{max.}$ 3 350 (OH) and 1 628 (aromatic) cm^{-1}, δ 1.32 (s, 12 H; gem-Me_2), 1.82 [t, 4 H, 7 Hz, 3(3′)-CH_2], 2.17 (s, 6 H, ArMe), 2.26 (s, 6 H, ArMe), 2.69 [t, 4 H, *J* 7 Hz, 4(4′)-CH_2], and 2.81 (s, 4 H, CH_2CH_2 bridge). In the mass spectrum the molecular ion appeared at *m/e* 438 ($C_{28}H_{38}O_4$ requires *M*, 438) and the major fission was bisection into equal fragments $C_{14}H_{19}O_2$ with *m/e* 219. The *acetone solvate* gave an identical mass spectrum (Found: C, 75.1; H, 8.5. $C_{28}H_{38}O_4$·C_3H_6O requires C, 75.0; H, 8.9%).

The mother liquors were concentrated to about a third of their bulk and next day the precipitate was collected and purified from light petroleum to give *substance A* as needles (0.88 g), m.p. 263—264 °C (decomp.).

(ii) *With zinc in acetic anhydride.* The trimer (0.2 g) was reduced by zinc dust (1 g) and sodium acetate (0.4 g) in boiling acetic anhydride (8 ml) during 2 h; the hot mixture was then filtered and the residues washed with hot tetrahydrofuran. The filtrate and washings were combined and concentrated under reduced pressure leaving a solid that was extracted with tetrahydrofuran (2 × 10 ml). The extract

was poured into water (200 ml) and re-extracted with ether (2 × 100 ml). The ether solution was washed with saturated aqueous sodium hydrogen carbonate and then water and finally dried (Na_2SO_4). Removal of the ether left a solid that dissolved in a boiling mixture (20 ml) of ether and light petroleum (b.p. 40—60 °C) (1 : 5 v/v). The solution deposited a powder that furnished the ethylenebischromanol (15; $n = 2$) as its *diacetate*, which separated from acetone–light petroleum as needles (40 mg), m.p. 258—259 °C (subl.), $\nu_{max.}$ 1 745 cm^{-1} (aryl acetate) (Found: C, 73.1; H, 8.2. $C_{32}H_{42}O_6$ requires C, 73.5; H, 8.1%). The mass spectrum showed the expected molecular ion at *m/e* 522 and successive losses of keten giving fragment ions at *m/e* 480 and 438.

The products left after removal of the diacetate were separated by chromatography on thick silica plates from ether–light petroleum (2 : 1 v/v). One had R_F 0.6 and was recovered by elution with acetone–ether and crystallised from a small amount of light petroleum to give substance A as tiny crystals (12 mg), m.p. 263—264 °C. The other had R_F 0.35 and when isolated in the same way and crystallised from light petroleum afforded substance B as small needles (45 mg), m.p. 211—215 °C.

The Spiran (7).—During this preparation light was excluded as far as possible by wrapping all apparatus in aluminium foil. The ethylenebischromanol (15; $n = 2$) (100 mg) in benzene (35 ml) was added to potassium hexacyanoferrate(III) (1.0 g) and sodium hydroxide (1.0 g) in deaerated water (50 ml) and stirred vigorously under nitrogen for 1 h. The organic layer was washed with brine (2 × 100 ml), dried (Na_2SO_4), and concentrated under reduced pressure without application of heat leaving a yellow gum. This dissolved in hexane (*ca.* 5 ml) and then at 0 °C deposited the spiran, 3,3′,4,4′,8,9-*hexahydro*-2′,2′,5,5′,7,7,8′,-10-*octamethylbenzo*[1,2-b:4,5-b′]*dipyran*-2-*spiro*-7′(6′H)-[1]-*benzopyran*-6′-*one*, as a yellow crystalline powder (60 mg) $\lambda_{max.}$ (EtOH) 236, 294infl, 298 and 354br nm, $\nu_{max.}$ 1 660 and 1 644 cm^{-1} (conj. C:O), δ (chlorobenzene at 28 °C), 1.07 (s, 3 H) and 1.17 (s, 9 H, gem-Me_2), 1.72, 1.89, 2.07, and 2.10 (each s, 3 H, vinylic and aromatic Me), *ca.* 2.4 (mm, 6 H, benzylic CH_2), and *ca.* 1.5 (mm, 6 H, other CH_2) (Found: *M*, 436.261 59. $^{12}C_{28}{}^{1}H_{36}{}^{16}O_4$ requires *M*, 436.261 34). The mass spectrum showed a peak at *m/e* 438 as well as that at 436 and so behaved as do quinonoid compounds. No true m.p. could be observed; at 100 °C the powder loses its colour and eventually melts at 221 °C, *i.e.* at the m.p. of trimer (12).

Reduced by ascorbic acid (80 mg) in water (2 ml) at room temperature the spiran (12 mg) in ethanol (15 ml) was completely bleached in 1 min. Water (3 drops) was added and the mixture left until no more solid separated. The solid (9 mg), m.p. 241—243 °C, was identified spectroscopically with the ethylenebischromanol (15; $n = 2$).

Conversion of the Spiran (6) *into Trimer of Quinone Methide* (4).—When the spiran (6) (163 mg) was heated in chlorobenzene (7 ml) at 120 °C little change occurred during 2 h as revealed by t.l.c. The solution was, therefore, kept at *ca.* 140 °C for 6 h and the solvent removed under reduced pressure. Light petroleum (b.p. 80—100 °C) was added and removed first at 110 °C under ordinary pressure and then *in vacuo*. The residue consisted of the trimer (13) (158 mg), m.p. 124—126 °C, raised to 130—131 °C by trituration with a little methanol (lit.,[11] m.p. 128—130 °C), identified by its n.m.r. spectrum which at 220 Hz showed methyl singlets at δ 1.22, 1.28, 1.30, 1.47, 1.67, 1.96, 2.08, 2.12, 2.18, and 2.22 (all 3 H), and 1.25 (6 H).

[0/1496 *Received*, 30*th September*, 1980]

REFERENCES

[1] Part 13, F. M. Dean, G. A. Herbin, D. A. Matkin, A. W. Price, and M. L. Robinson, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1986.

[2] K.-G. Svensson, H. Selander, M. Karlsson, and J. L. G. Nilsson, *Tetrahedron*, 1973, **29**, 1115; H. Selander and J. L. G. Nilsson, *Acta Chem. Scand.*, 1971, **25**, 1182; 1972, **26**, 2433.

[3] J. L. G. Nilsson, H. Selander, H. Sievertsson, I. Skånberg, and K.-G. Svensson, *Acta Chem. Scand.*, 1971, **25**, 94.

[4] G. W. Wheland, ' Resonance in Organic Chemistry ', Wiley, New York, 1955, pp. 496—498.

[5] J. M. Behan, F. M. Dean, and R. A. W. Johnstone, *Tetrahedron*, 1976, **32**, 167.

[6] H. C. Longuet-Higgins and C. A. Coulson, *Trans. Faraday Soc.*, 1946, **42**, 756.

[7] J. L. G. Nilsson, H. Selander, H. Sievertsson, and I. Skånberg, *Tetrahedron*, 1970, **26**, 879; R. T. Borchardt and L. A. Cohen, *J. Am. Chem. Soc.*, 1973, **95**, 8308; W. Dürkheimer and L. A. Cohen, *ibid.*, 1964, 4388.

[8] J. L. G. Nilsson, J. O. Brånstad, and H. Sievertsson, *Acta Pharm. Suecica*, 1968, **5**, 509; D. A. Bolon, *J. Org. Chem.*, 1970, **35**, 715, 3666.

[9] H. Gross, A. Rieche, and G. Mathhey, *Chem. Ber.*, 1963, **96**, 308.

[10] A. Merijan, B. A. Shoulders, and P. D. Gardner, *J. Org. Chem.*, 1963, **28**, 2148.

[11] W. A. Skinner and R. M. Parkhurst, *J. Org. Chem.*, 1964, **29**, 3601; W. A. Skinner and P. Alaupovic, *ibid.*, 1963, **28**, 2854.

[12] M. S. Chauhan, F. M. Dean, S. McDonald, and M. L. Robinson, *J. Chem. Soc., Perkin Trans. 1*, 1973, 359.

[13] H. A. Lloyd, E. A. Sokolski, B. S. Strauch, and H. M. Fales, *Chem. Commun.*, 1969, 299; M. S. Chauhan, F. M. Dean, and M. L. Robinson, *ibid.*, 1971, 1141; C. J. Dixie and I. O. Sutherland, *ibid.*, 1972, 646.

[14] M. S. Chauhan, F. M. Dean, and M. L. Robinson, *J. Chem. Soc., Perkin Trans. 1*, 1973, 120.

[15] F. M. Dean and D. A. Matkin, *J. Chem. Soc., Perkin Trans. 1*, 1977, 2289.

[16] G. Baddeley, N. H. P. Smith, and M. A. Vickars, *J. Chem. Soc.*, 1956, 2455; W. G. B. Huysmans, W. J. Mijs, and J. G. Westra, *Tetrahedron*, 1969, **25**, 2249.

[17] T. M. Cresp, R. G. F. Giles, M. V. Sargent, C. Brown, and D. O'N. Smith, *J. Chem. Soc., Perkin Trans. 1*, 1974, 2435; T. M. Cresp, M. V. Sargent, J. A. Elix, and D. P. H. Murphy, *J. Chem. Soc., Perkin Trans. 1*, 1973, 340.

[18] D. D. Reynolds and B. C. Cossar, *J. Heterocycl. Chem.*, 1971, **8**, 611; D. J. Fields, J. B. Miller, and D. D. Reynolds, *J. Org. Chem.*, 1962, **27**, 2749.

[19] J. L. G. Nilsson, H. Sievertsson, and H. Selander, *Acta Chem. Scand.*, 1968, **22**, 3160; V. L. Frampton, W. A. Skinner, P. Cambour, and P. S. Baily, *J. Am. Chem. Soc.*, 1960, **82**, 4632.

[20] T. Nakamura and S. Kijima, *Chem. Pharm. Bull.*, 1972, **20**, 1681.