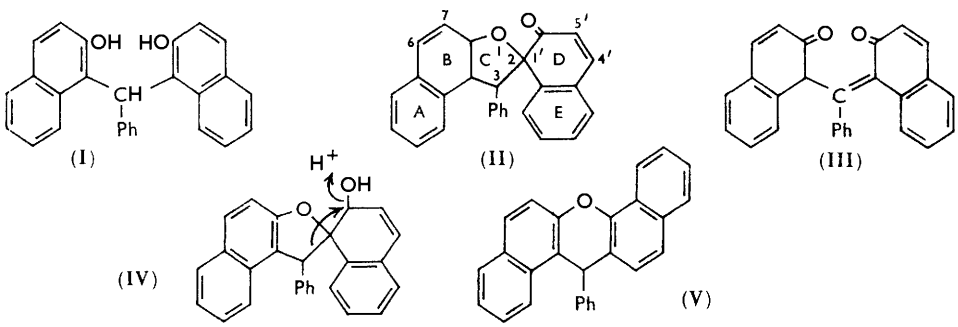
61. *Spirans. Part V.* Diastereoisomeric Grisenones obtained by Oxidative Cyclisation.*

By F. M. Dean and H. D. Locksley.

Both (racemic) diastereoisomers of 4,5:2′,3′-dibenzo-3-phenylgrisa-2′,4′-dien-6′-one have been made by oxidative cyclisation of " benzaldi-β-naphthol " (1,1′-benzylidenedi-2-naphthol) and have been assigned configurations by three methods.

The discussion includes brief comments on the stereochemistry of the catechins and on the synthesis of unsymmetrical xanthens.

That hypobromite oxidation [1] of di-(2-hydroxy-1-naphthyl)methane gives the spiran (II; H for Ph) was first appreciated by Pummerer and Cherbuliez.[2] Although other views have been expressed,[1,3] the spiran structure is currently accepted; [4] and many allied reactions have been described,[5] notably by Smiles and his collaborators.[6] Related oxidative cyclisations are now believed to be important steps in the biosynthesis of certain plant products,[7] and several laboratory syntheses along these lines have been successful.[5,8] Nevertheless, little is known about the mechanism of the cyclisation itself, so we are examining the behaviour of the dinaphthylmethane (I). This compound was chosen because it can be oxidised, by a very wide variety of reagents, to the spiran (II) where diastereoisomeric forms are possible. The production of one racemic diastereoisomer rather than the other can be expected to throw some light on the manner of cyclisation, and in fact different types of oxidising agent have different results: hypobromite, for example, gives one diastereoisomer of (II), and plumbic acetate in pyridine the other. However, this paper is concerned only with proofs of structure and configuration.



The substance obtained by oxidising the diphenol (I) with hypobromite was formulated [3,9,10] as the diketone (III), a view never revised in spite of the parallel work on the spiran (II; H for Ph). That the product is not a diketone and should properly be regarded as the spiran (II) follows most clearly from the ultraviolet spectrum (Fig. 1). Nearly

* Part IV, *J.*, 1962, 4745.

[1] Abel, *Ber.*, 1892, **25**, 3483.
[2] Pummerer and Cherbuliez, *Ber.*, 1914, **47**, 2957.
[3] Dischendorfer, *Ber.*, 1926, **59**, 774.
[4] Chatterjea, *J. Indian Chem. Soc.*, 1958, **35**, 37; 1950, **27**, 375; Sestanj, *Arhiv Kem.*, 1951, **23**, 81.
[5] Day, Nabney, and Scott, *J.*, 1961, 4067.
[6] Smiles and his co-workers, *J.*, 1930, 959; 1937, 1016, 1931; 1938, 2022.
[7] Åkermark, Erdtman, and Wachtmeister, *Acta Chem. Scand.*, 1959, **13**, 1855; Erdtman and Wachmeister, in " Festschrifte Artur Stoll," Birkhauser, Basle, 1957, p. 144; Barton and Cohen, *loc. cit.*, p. 117.
[8] Hassall and Lewis, *J.*, 1961, 2321; Davidson and Scott, *J.*, 1961, 4075.
[9] Kohn and Ostersetzer, *Monatsh.*, 1918, **39**, 299.
[10] Kohn and Schwartz, *Monatsh.*, 1925, **46**, 273.

the same as that of the simpler analogue, this spectrum indicates isolated β-naphthol and benzylideneacetone chromophores as in structure (II), and shows no sign of the very extended stilbene-derived chromophore in (III). In confirmation, the compound absorbs at 1675 cm.$^{-1}$ (as do authentic cyclohexenones), whereas the monoxime and mono-2,4-dinitrophenylhydrazone have no strong absorption in the carbonyl stretching region. The presence in structure (II) of an α-ketol ether grouping accounts for the reduction of the compound to the original dinaphthol (I) by zinc.[10] The spiran discussed so far may now more conveniently be called spiran A.

Oxidation of the benzylidenedinaphthol (I) by plumbic acetate in pyridine generates very little spiran A, the main product being an isomeric ketone, spiran B, having $\nu_{max.}$ 1675 cm.$^{-1}$. Spiran B must also be represented by structure (II), for it gives a monoxime almost transparent in the carbonyl region, its ultraviolet absorption spectrum (Fig. 1) hardly differs from that of spiran A, and reductive acetylation regenerates the dinaphthol (I) as the acetate. Thus spirans A and B are the two diastereoisomeric racemates corresponding to structure (II). Confirmation of this comes from the behaviour of the derived allylic alcohols (IV) obtained by borohydride reduction: the two alcohols give the same xanthen (V) on treatment with sulphuric acid, presumably because of the Wagner shift indicated by the arrows in (IV). Unlike the original di-β-naphthol (I), xanthen (V) is derived from one β- and one α-naphthol residue, and its constitution therefore provides evidence that in the allylic alcohols (and consequently in spirans A and B) an oxygen atom does indeed link a β-position in one naphthalene nucleus with an α-position in the other.

Each representing a racemate, the structures to be allocated to spirans A and B are (VI) and (VII). These compounds, and the more complex ones to be considered shortly, are, for systematic purposes, later assigned unambiguous stereochemical designations by the (*R*,*S*) symbolism of Cahn, Ingold, and Prelog.[11] To expedite discussion, however, spiran (VII) is temporarily called a *cis*-3-phenylgrisan to indicate that the phenyl substituent is on the same side of ring C as ring E. Structure (VI) then represents the *trans*-3-phenylgrisan. We offer three lines of evidence identifying spiran A as the *trans*- and spiran B as the *cis*-isomer.

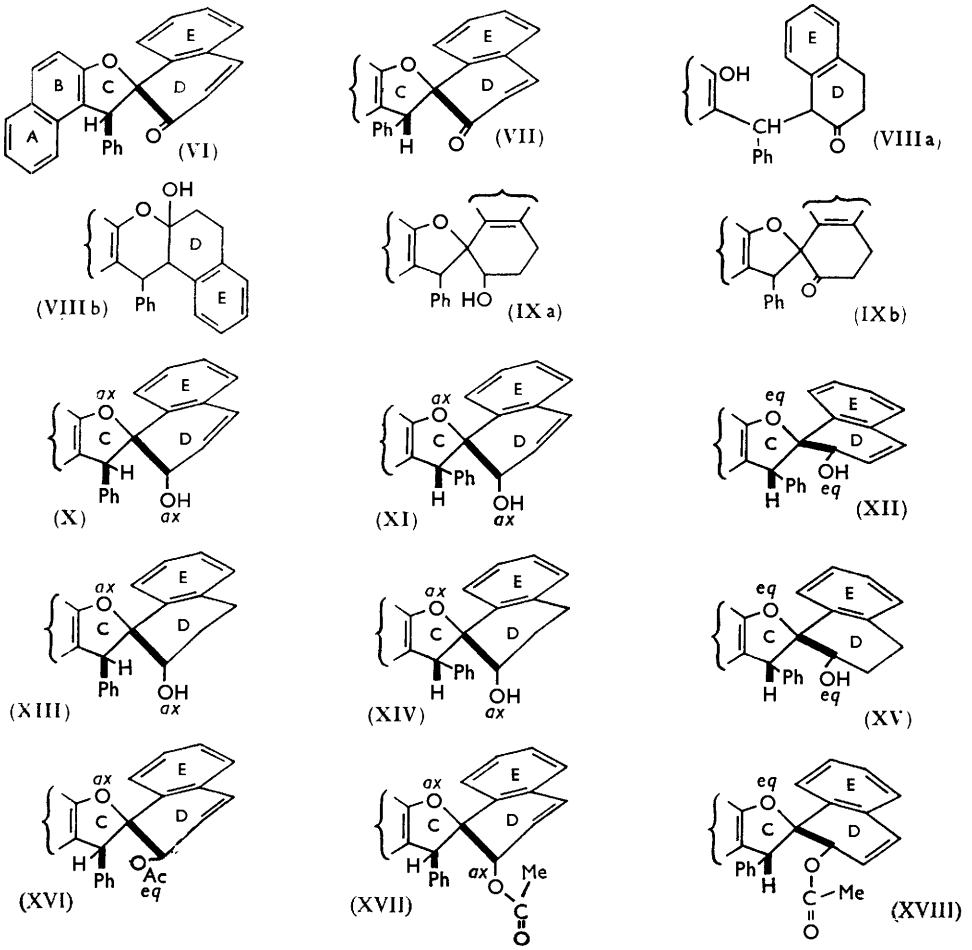
Largely because of their low solubilities, spirans A and B themselves could not be examined conveniently, so we examined instead the more soluble allylic alcohols notwithstanding the extra problems posed by their additional asymmetric centres. Geometrical isomerism about ring D bears no simple relation to that about ring C and therefore has to be described in independent terms. Substituents on the same side of ring D as the coumaran-oxygen atom can be called *syn*-substituents, those on the other side *anti*-substituents. The method is that adopted for the perhydrophenanthrenes [12] where a somewhat similar problem arises.

Hydrogenation of spiran A led to a saturated alcohol A that resisted oxidation by chromic oxide in pyridine to a ketone, and gave an acetate with $\nu_{max.}$ 1763 cm.$^{-1}$, a rather high value for such a derivative. These facts suggested that hydrogenation might have severed the ether link in the α-ketol group, and that the phenolic ketone (VIIIa) so formed had undergone the expected cyclisation to the hemiketal (VIIIb). But this view was discarded because the methyl ether of the alcohol could not be prepared by means of methanolic hydrogen chloride and, when prepared otherwise, was stable to acids. In spite of its other properties, the saturated alcohol is of type (IXa) because the acetate is produced by hydrogenation of the acetate of allylic alcohol A which must be of type (IV). From spiran B, on the other hand, hydrogenation produced a ketone of type (IXb) and the related saturated alcohol was accessible only with difficulty by the catalytic method. That this saturated alcohol is also of type (IXa) was confirmed by demonstrating that the acetate is obtainable by hydrogenation of the acetate of allylic alcohol B. It also follows

[11] Cahn, Ingold, and Prelog, *Experientia*, 1956, **12**, 81.
[12] Linstead and Walpole, *J.*, 1939, 842.

that each allylic alcohol has the same configuration as the related saturated alcohol. Finally, all these alcohols can be allocated the *anti*-configuration because, in either of the spirans (VI) and (VII), ring A and the 3-phenyl substituent tend to screen their side of the molecule from attack.

In writing the structures (VI) and (VII) for the spirans, one is guided by general conformational theory, which predicts that the coumaran-oxygen atom would be a pseudoaxial substituent with respect to ring D, leaving the more commodious pseudo-equatorial position for the benzylidene group. The same considerations apply to the alcohols, and with the configurational arguments given above, indicate for allylic alcohol A the structure (X), and for allylic alcohol B the structure (XI). Now this conclusion about allylic alcohol B is not entirely valid, because scale models show that in this, the *cis*-isomer, the 3-phenyl substituent approaches close enough to one end of ring E to experience marked repulsion. Thus structure (XI) contains an element of compression



which can, however, be eliminated by conformational inversion to what would normally be the less favourable arrangement, *i.e.*, to structure (XII) where the benzylidene group occupies the pseudoaxial position. Evidence offered below suggests that conformational inversion does occur but is not quite complete. Similarly, diagram (XIII) satisfactorily describes the saturated alcohol A, but diagram (XIV) for saturated alcohol B requires supplementation by diagram (XV).

Of the allylic alcohols, B is converted into xanthen (V) very much faster than A when the reagent is sulphuric acid (Figs. 2 and 3). Hence B is the alcohol containing either the element of compression, as in (XI), or the benzylidene group disposed in a manner particularly favourable for migration, as in (XII) where it is pseudoaxial. Thus spiran A is the *trans*- and spiran B the *cis*-3-phenylgrisenone.

The foregoing argument would fail if the rates of transformation were determined by the configuration of the hydroxyl groups at position 6′, although this is improbable since acids detach hydroxyl groups without difficulty from allylic alcohols. Indeed, by using aqueous hydrochloric acid in acetic acid the hydroxyl group may be removed from allylic alcohol A without the Wagner change's being involved. This reagent converts allylic alcohol B into the xanthen as before, but alcohol A into an acetate isomeric with that obtained by using acetic anhydride and pyridine. Both acetates afford xanthen (V) with sulphuric acid, and the new one is regarded as the *syn*-epimer (XVI).

The allylic alcohols were acetylated in basic media to avoid epimerisation and give the *anti*-acetates which were examined for their H^1-resonance spectra.* A peak due to the

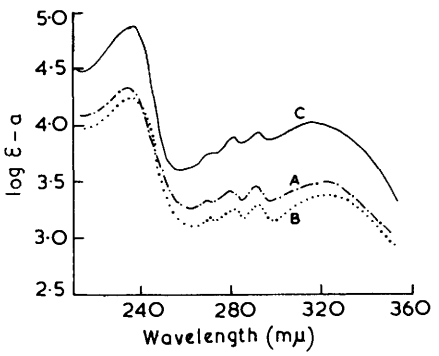


FIG. 1. Ultraviolet spectra of grisadienones: (A) spiran A (VI) ($a = 0{\cdot}5$); (B) spiran B (VII) ($a = 0{\cdot}5$); (C) 4,5:2′,3′-dibenzogrisan-2′,4′-dien-6′-one (II; H for Ph) ($a = 0$). (All in ethanol at concentrations between 10^{-3}M and 10^{-4}M.)

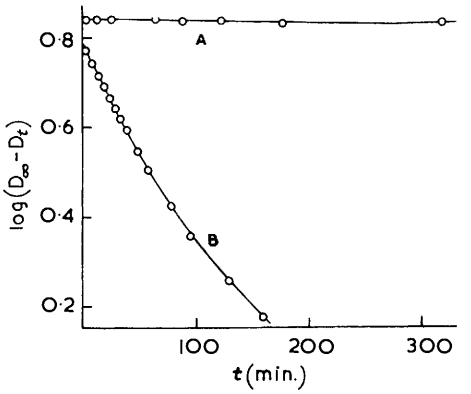


FIG. 2. Rates of conversion of allylic alcohols A and B into xanthen (V). D = Optical density at 305 mμ (see Fig. 3) of 1 cm. thickness of a $1{\cdot}12 \times 10^{-4}$M-solution of the alcohol in acetic acid containing sulphuric acid (30 ml./l.) at 30° ± 0·5°. For A, $k = 1{\cdot}54 \times 10^{-3}$ min.$^{-1}$. For *B*, $k = 99{\cdot}8 \times 10^{-3}$ min.$^{-1}$.

methyl protons of the acetyl group in allylic acetate B appeared at the expected point (τ 8·31) and had the appropriate intensity. In contrast, allylic acetate A gave a peak of the expected intensity but at a position (τ 8·56) indicative of shielding by olefinic or aromatic systems.[13] Diagram (XVII) depicts allylic acetate A with the methyl group shielded by the *trans*-3-phenyl substituent, a situation not possible in the *cis*-3-phenyl epimer (XVIII). Scale models confirm that, whatever the configurations at the 6′-positions, acetates in the *trans*-3-phenyl series will suffer this shielding while those in the *cis*-series will not. Again it follows that spiran A is the *trans*- and spiran B the *cis*-isomer.

The hydroxyl stretching frequencies of the allylic and of the corresponding saturated alcohols were kindly determined for us by Dr. G. Eglinton and his associates. As well as confirming the configurations allotted so far, these results (Fig. 4) disclose more exactly than the others the part played by conformational inversion. As none of the alcohols

* In deuterochloroform with tetramethylsilane as internal reference.

[13] Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, Oxford, 1959.

exhibited absorption due to unbonded hydroxyl no straightforward estimate of hydrogen-bonding shifts could be made, and for this and other reasons it was thought advisable to interpret the results by reference to data from model compounds reproducing the major stereochemical and structural features involved. Suitable models were tetra-*O*-methyl-epicatechin [XIX; (+)-form shown] and tetra-*O*-methylcatechin [XX; (−)-form shown]. Unfortunately there has been dispute about the conformation of the latter.[14–16] It is agreed that the epicatechin derivative is the *cis*-isomer having a pseudoequatorial aryl substituent at position 2 and a pseudoaxial hydroxyl group at position 3, the heterocyclic ring having the half-chair shape as in (XXI). Here the hydroxyl group is placed so that it can form a hydrogen bond with the ring oxygen atom or with the π-electrons of the

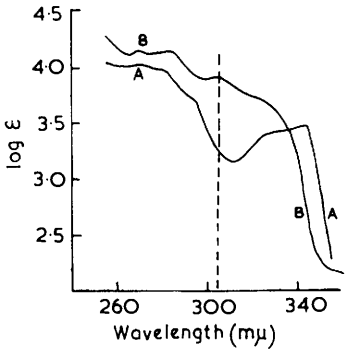


FIG. 3. Ultraviolet spectra of allylic alcohols A and B (curve A) and of xanthen (V) (curve B).

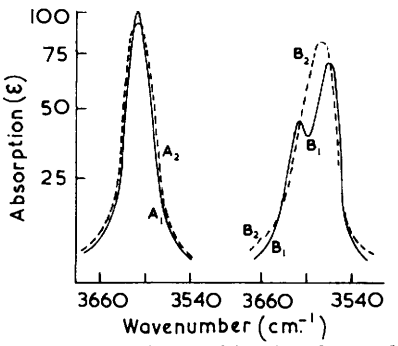


FIG. 4. Hydroxyl stretching bands of allylic and of saturated alcohols A and B: (A_1) allylic alcohol A: $\nu_{max.}$ 3608 (ε 100; Δ^a 20) (Δ^a refers to $\nu_{\frac{1}{2}}$); (A_2) saturated alcohol A: $\nu_{max.}$ 3605 (ε 95; Δ^a 21); (B_1) allylic alcohol B: $\nu_{max.}$ 3609, 3581(ε 45, 70) (Δ^a 45 overall); and (B_2) saturated alcohol B: $\nu_{max.}$ 3591 (ε 85; Δ^a 37). (All for 0·822M-solutions in carbon tetrachloride. Four-fold dilution produced no change in peak positions or shapes.)

aryl substituent. Free axial * secondary alcohols absorb[17] near 3630 cm.$^{-1}$. The epicatechin absorbs at 3587 cm.$^{-1}$, revealing a shift much too large to be due to π-electron bonding.[18] Hence bonding to *p*-electrons in phenoxide oxygen takes precedence over that to π-electrons and results in a shift of 43 cm.$^{-1}$.

On general grounds, tetra-*O*-methylcatechin (XX) would be expected to adopt conformation (XXII) where both substituents are disposed pseudoequatorially, a view supported by nuclear magnetic resonance studies.[16] This conformation precludes bonding to ring oxygen while permitting that to the aryl substituent. As free equatorial secondary alcohols[17] absorb near 3623 but the catechin derivative absorbs at 3594 cm.$^{-1}$, a shift of about 29 cm.$^{-1}$ has to be accounted for. Before the importance of bonding to π-electrons was fully appreciated, this shift was ascribed[15] to " weakened " bonding to oxygen, the molecule having adopted an unfavourable conformation to make this possible. Now, however, this shift merely confirms the existence of bonding to the aryl group in (XXII).

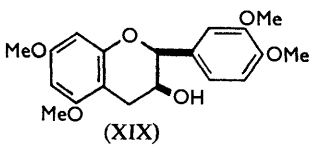
* In what follows it is assumed that the difference between a true and a pseudo-conformation will be immaterial.

[14] Roberts, *Chem. and Ind.*, 1955, **631**, 1551; Whalley, " The Stereochemistry of the Chromans and Related Compounds," Symposium on Vegetable Tannins, Cambridge, April 1956, Society of Leather Trades' Chemists, Croydon, 1956, p. 151.
[15] Birch, Clark-Lewis, and Robertson, *J.*, 1957, 3586.
[16] Clark-Lewis and Jackman, *Proc. Chem. Soc.*, 1961, 165.
[17] Cole, Jeffries, and Müller, *J.*, 1959, 1222; Cole and Jeffries, *J.*, 1956, 4391.
[18] Schleyer, Wintner, Trifan, and Backsai, *Tetrahedron Letters*, 1959, No. 14, 1.

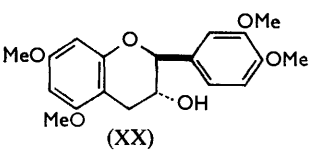
In spite of the stereochemical restrictions and other complexities in the catechin derivatives, the observed shifts are little different from those noted in simpler systems.[17-19]

Being pseudoaxial alcohols able to undergo bonding only to π-electrons, allylic alcohol A (X) and its saturated counterpart (XIII) should absorb near 3601 cm.$^{-1}$ (*i.e.*, 3630 — 29 cm.$^{-1}$). The observed frequencies agree (Fig. 4), the narrowness of the single bands showing that, in both cases, only one conformation is significant. In contrast, allylic alcohol B has dual absorption (Fig. 4). The stronger band tallies with structure (XII) which corresponds to absorption near 3580 cm.$^{-1}$ since the frequency (3623 cm.$^{-1}$) appropriate to a pseudoequatorial alcohol would here be lowered by about 43 cm.$^{-1}$ on account of bonding to oxygen. The weaker band, we think, might originate from the uninverted conformer (XI) in which bonding is again restricted to π-electrons. Although the absorption by saturated alcohol B takes the form of a single peak, this is very wide (Fig. 4) and seems to be composed of two overlapping bands; its position and shape are consistent with an alcohol composed of approximately equal amounts of two conformers (XIV) and (XV), and indicate that conformational inversion is less important for the saturated than for the allylic alcohol B. Scale models confirm the point, for they show the clearance between the 3-phenyl substituent and ring E to be greater in the saturated than in the unsaturated alcohol.

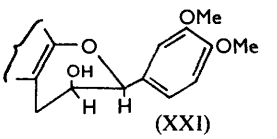
Compression between the 3-phenyl substituent and ring E in the *cis*-series has other consequences. Scale models show that a major increase in compression results whenever the sp^2-carbon at position 6′ in (VII) changes to the sp^3-state: changes at positions 4′ and 5′ matter much less. This explains why spiran A readily affords saturated alcohol A (IXa) when hydrogenated, whereas spiran B tends to give only the ketone (IXb). Though we made no measurements, it was obvious that borohydride reduction of spiran A is much faster than that of spiran B. Spiran A yields a 2,4-dinitrophenylhydrazone with some difficulty: spiran B does not react at all.



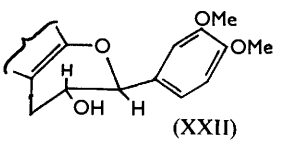
(XIX)



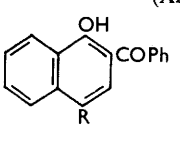
(XX)



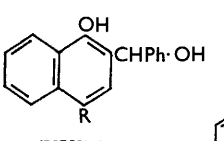
(XXI)



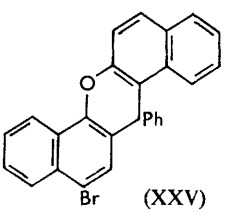
(XXII)



(XXIII)



(XXIV)



(XXV)

The xanthen (V) closely resembled the symmetrical analogue, obtained by dehydration of the dinaphthol (I), in spectroscopic properties and in forming a highly coloured xanthylium salt when oxidised. Further identification was effected synthetically. However, the methods available for the synthesis of unsymmetrical xanthens seem so limited in scope and efficiency [20] that conversion of the symmetrical (and therefore relatively easily obtainable) dinaphthol (I) into the unsymmetrical xanthen (V) may offer hope of a new method of value, and one of us (H. D. L.) is pursuing the matter. The required definitive synthesis was achieved from α-naphthyl benzoate, which was isomerised to the *o*-hydroxyketone (XXIII; R = H) by boron fluoride at 200° (better than earlier methods [21,22]).

[19] Flett, *Spectrochim. Acta*, 1957, **10**, 21; Baker and Shulgin, *J. Amer. Chem. Soc.*, 1958, **80**, 5388; Büchi, Crombie, Godin, Kaltenbronn, Siddalingaiah, and Whiting, *J.*, 1961, 2843.

[20] Campbell, in " Chemistry of Carbon Compounds," ed. Rodd, Elsevier Publ. Co., Amsterdam, 1959, Vol. IVB, p. 966; Wawzonek, in " Heterocyclic Compounds," ed. Elderfield, Wiley and Sons, Inc., New York, 1951, Vol. II, p. 419.

[21] Anderson and Thomas, *J. Amer. Chem. Soc.*, 1943, **65**, 234.

[22] *E.g.*, Edminson and Hilditch, *J.*, 1910, **97**, 226.

Borohydride reduction of the derived bromo-ketone (XXIII; R = Br) supplied an alcohol (XXIV; R = Br) which was unstable and was therefore used without purification. In acidic media, condensation of this alcohol with β-naphthol furnished the bromoxanthen (XXV), catalytic reduction then giving the xanthen (V). The presence of bromine was necessary because the alcohol (XXIV; R = H) undergoes self-condensation in acid in preference to reacting with β-naphthol. This second route to unsymmetrical xanthens is also being studied further.

Experimental

(2*RS*,3*RS*)-3-*Phenyl*-4,5:2′,3′-*dibenzogrisa*-2′,4′-*dien*-6′-*one* (*Spiran* A) (VI).—The part solution, part suspension prepared by mixing " benzaldi-β-naphthol " (I) (3·8 g.) and 10% aqueous potassium hydroxide (15 ml.) was treated during about 10 min. with bromine (2 g.) in 10% potassium hydroxide (15 ml.). The treatment was repeated after 1 hr. and again 1 hr. after that. Next day the yellow precipitate was collected, washed with water, dried in air, and purified on a column of alumina from which light petroleum (b. p. 60—80°) eluted unidentified, colourless material and then benzene eluted a yellow solid. Crystallised from ethanol, this gave the 3-phenylgrisenone as pale yellow needles (2·3 g.), m. p. 214—216° (Kohn and Schwartz [10] give m. p. 216°) (Found: C, 86·5; H, 5·0. Calc. for $C_{27}H_{18}O_2$: C, 86·6; H, 4·9%). The oxime had m. p. 205° (decomp.) (lit.,[10] 209°). The 2,4-*dinitrophenylhydrazone* crystallised from ethanol in red plates, m. p. 170° (decomp.) (Found: N, 9·8. $C_{33}H_{22}N_4O_5$ requires N, 10·0%).

This grisenone (0·5 g.) was reduced with acetic anhydride (10 ml.), zinc dust (2 g.), and pyridine (4 drops) at 100° for 1·5 hr. The cooled product was stirred with water and the acetic acid neutralised with sodium hydrogen carbonate. The product was isolated with chloroform (3 × 30 ml.), recovered by evaporation, and crystallised from ethanol, giving " benzaldi-β-naphthol " (I) as the diacetate, m. p. and mixed m. p. 201—203°.

(2*RS*,3*SR*)-3-*Phenyl*-4,5:2′,3′-*dibenzogrisa*-2′,4′-*dien*-6′-*one* (*Spiran* B) (VII).—Powdered plumbic acetate (5 g.) was sifted into an agitated solution of " benzaldi-β-naphthol " (5 g.) in pyridine (30 ml.). The acetate dissolved rapidly, the mixture became dark red, and a solid slowly separated. After 30 hr., the mixture was poured into water and the solid collected and passed in benzene down a column of acid-washed alumina. Evaporation of the eluate supplied a solid (4·4 g.) from which ethanol washed impurities, leaving the *dibenzogrisadienone* as cream needles, m. p. 259—262° (from ethyl acetate) [Found: C, 86·6; H, 5·0%; *M* (Rast), 376. $C_{27}H_{18}O_2$ requires C, 86·6; H, 4·9%; *M*, 374]. This compound is much less soluble than the geometrical isomer (spiran A) in the usual solvents. The infrared spectra of these two isomers are very similar, the clearest difference being at 854 cm.$^{-1}$ where spiran A has a peak of medium intensity and spiran B is transparent. (These and other figures are quoted for mulls in paraffin.)

A 2,4-dinitrophenylhydrazone could not be obtained. The *oxime* crystallised from benzene in rosettes, m. p. 216—217° (212° if crystallised from acetic acid) (Found, on specimen burnt with tungsten trioxide: C 83·4; H, 5·1; N, 3·5. $C_{27}H_{19}NO_2$ requires C, 83·3; H, 4·9; N, 3·6%).

By the method used for spiran A, spiran B gave an acetate that was purified on alumina and eluted by benzene–light petroleum (b. p. 60—80°). Recrystallisation from ethanol gave " benzaldi-β-naphthol " (I) as the diacetate (0·33 g.), m. p. and mixed m. p. 201—203°.

(2*RS*,3*RS*,6′*RS*)-3-*Phenyl*-4,5:2′,3′-*dibenzogrisa*-2′4′-*dien*-6′-*ol* (X).—After addition of potassium borohydride (0·30 g.) to spiran A (1·7 g.) in methanol (150 ml.) containing water (10 ml.), the colour of the solution faded during 20 min. Neutralised with hydrochloric acid and evaporated *in vacuo*, the solution furnished a solid that, purified from ethanol, gave the 3-*phenylgrisadienol* as needles (0·86 g.), m. p. 215—217°, having no carbonyl absorption (Found: C, 86·3; H, 5·5. $C_{27}H_{20}O_2$ requires C, 86·1; H, 5·4%). The *acetate*, obtained by the use of acetic anhydride and pyridine, separated from ethanol in needles, m. p. 182—184°, $\nu_{max.}$ 1748 cm.$^{-1}$ (Found: C, 83·4; H, 5·5. $C_{29}H_{22}O_3$ requires C, 83·2; H, 5·3%).

(2*RS*,3*SR*,6′*RS*)-3-*Phenyl*-4,5:2′,3′-*dibenzogrisa*-2′,4′-*dien*-6′-*ol* (XI) *and* (XII).—Solutions of spiran B (2·8 g.) in tetrahydrofuran (100 ml.) and potassium borohydride (0·6 g.) in water (8 ml.) were mixed and kept for 35 min. When isolated as was the foregoing isomer, this *phenylgrisadienol* crystallised from ethanol in rods (1·9 g.), m. p. 199—201°, having no carbonyl absorption (Found: C, 85·8; H, 5·6%). The mother-liquors contained starting material (0·3 g.). Interaction with acetic anhydride and pyridine gave the *acetate* which separated from ethanol in plates, m. p. 201—203°, $\nu_{max.}$ 1751 cm.$^{-1}$ (Found: C, 82·8; H, 5·5%).

(2*RS*,3*RS*,6′*RS*)-3-*Phenyl*-4,5:2′,3′-*dibenzogris*-2′-*en*-6′-*ol* (XIII).—Spiran A (1·03 g.) and 10% palladium–charcoal (1 g.) were shaken together in ethanol (250 ml.) under hydrogen (uptake *ca.* 2 mol., 133 ml.). Removal of the catalyst and solvent left the *gris*-2′-*en*-6′-*ol* as a gum which crystallised when kept and then separated from benzene–light petroleum (b. p. 60—80°) in needles (0·62 g.), m. p. 192—194°, insoluble in alkali and having neither carbonyl absorption nor a ferric reaction (Found: C, 85·6, 85·6; H, 5·9, 5·8. $C_{27}H_{22}O_2$ requires C, 85·7; H, 5·9%). Its *acetate* formed rods, m. p. 203—205° (from ethanol) (Found: C, 82·3; H, 5·8%). When made by shaking the appropriate 6′-acetoxygrisa-2′,4′-diene (0·24 g.) with 10% palladium–charcoal (0·20 g.) in tetrahydrofuran (250 ml.) until reaction ceased, this acetate was obtained as needles (0·21 g.), m. p. 203—205°, but the needles and rods suffered no depression in m. p. when mixed and were spectroscopically indistinguishable.

(2*RS*,3*RS*,6′*RS*)-6′-*Methoxy*-3-*phenyl*-4,5:2′,3′-*dibenzogris*-2′-*ene*.—The foregoing alcohol withstood for one week the action of methanol saturated with hydrogen chloride, but when kept with methyl iodide (5 ml.), silver oxide (0·20 g.), and dimethylformamide (60 ml.) for 2 days, it (0·20 g.) underwent considerable methylation. Insoluble matter was removed, further quantities of methyl iodide (5 ml.) and silver oxide (0·20 g.) were added, and the mixture was kept for another 2 days. Insoluble matter was again removed, and the filtrate poured into water containing enough potassium cyanide to keep all silver compounds in solution. Isolated by means of chloroform, the product was a solid which crystallised from methanol giving the 6′-*methoxygrisene* as needles (0·20 g.), m. p. 190—192° (Found: C, 85·3; H, 6·2; OMe, 8·3. $C_{27}H_{21}O{\cdot}OMe$ requires C, 85·7; H, 6·2; OMe, 7·9%). This ether was unaffected by boiling aqueous-methanolic hydrochloric acid.

(2*RS*,3*SR*)-3-*Phenyl*-4,5:2′,3′-*dibenzogris*-2′-*en*-6′-*one* (IXb).—When spiran B (2·0 g.) in tetrahydrofuran (200 ml.) was shaken under hydrogen with 10% palladium–charcoal, the reaction slackened after the absorption of about 1·5 mol. (192 ml.). The reaction was then interrupted and the gum left after removal of the catalyst and the solvent was kept in contact with ethyl acetate to induce crystallisation. Recrystallised from the same solvent, the product supplied the 3-*phenylgris*-2′-*en*-6′-*one* as rods (1·0 g.), m. p. 227—230°, $\nu_{max.}$ 1718 cm.$^{-1}$ (Found: C, 86·2; H, 5·5. $C_{27}H_{20}O_2$ requires C, 86·1; H, 5·4%). The *oxime* formed slightly straw-coloured needles, m. p. 260° (decomp.) (Found: C, 83·2; H, 5·7; N, 3·5. $C_{27}H_{21}NO_2$ requires C, 82·8; H, 5·4; N, 3·6%).

(2*RS*,3*SR*,6′*RS*)-3-*Phenyl*-4,5:2′,3′-*dibenzogris*-2′-*en*-6′-*ol* (XIV) *and* (XV).—(i) The above grisen-6′-one (2·1 g.) in tetrahydrofuran (50 ml.) containing water (6 ml.) was reduced at 55° by addition of potassium borohydride (0·5 g.) in ~1 hr. Next day the residual borohydride was decomposed by dilute hydrochloric acid, and the resulting mixture was evaporated to dryness *in vacuo* at $\gtrsim$45°. The required material was extracted with chloroform and, after evaporation, formed a gum crystallising in contact with methanol. Recrystallisation from methanol gave the 3-*phenylgrisen*-6′-*ol* as needles (1·8 g.), m. p. 208—210° (Found: C, 85·4; H, 6·0. $C_{27}H_{22}O_2$ requires C, 85·2; H, 6·0%). (ii) Spiran B was hydrogenated as before but the reaction was allowed to continue until no more hydrogen was absorbed. Isolated in the usual fashion and crystallised from methanol or ethyl acetate, the product was obtained as a mixture of two kinds of crystal. The infrared spectrum pointed to the presence of the grisen-6′-one (IXb) and of the derived alcohol (IXa), but the mixture could not be resolved by fractional crystallisation or by chromatography. A small quantity of needles was separated by hand-picking and identified with material prepared as in (i).

(2*RS*,3*SR*,6′*RS*)-6′-*Acetoxy*-3-*phenyl*-4,5:2′,3′-*dibenzogris*-2′-*ene*.—(i) The appropriate 3-phenylgrisen-6′-ol (0·27 g.) was treated with acetic anhydride (3 ml.) and pyridine (0·3 ml.) at 60° for 1 hr. Isolated in the usual way, the *acetate* separated from ethanol in needles (0·10 g.), m. p. 226—228° (Found: C, 83·1; H, 6·1. $C_{29}H_{24}O_3$ requires C, 82·8; H, 5·8%). (ii) When the appropriate 6′-acetoxy-3-phenylgrisadiene (0·79 g.) was hydrogenated as was the diastereoisomer above, the resulting 6′-acetoxy-3-phenylgrisene separated from ethanol in needles (0·55 g.), m. p. 226—228°, not depressed on admixture with a sample made as in (i). The esters prepared by methods (i) and (ii) could not be differentiated spectroscopically.

2-*Benzoyl*-4-*bromo*-1-*naphthol* (XXIII; R = Br).—Boron trifluoride was bubbled into molten 1-naphthyl benzoate (68 g.) at 100° until no more dissolved, whereafter the temperature was raised to 190—200° and kept there for 40 min., still with the gas passing in. The dark red mass so formed was cooled and mixed with acetic acid (100 ml.). Dark yellow crystals (*ca.* 60 g.) appeared and, after some time, were collected, washed with a little acetic acid, and

found to consist of a boron complex. The boron was removed by dissolution of the crystals in a boiling mixture of ethanol (120 ml.), water (50 ml.), and sodium acetate (25 g.). This solution deposited 2-benzoyl-1-naphthol in yellow needles (38 g.), m. p. 66° (lit.,[21] 65°; many different m. p. values have been recorded [22]) (Found: C, 82·0; H, 5·1. Calc. for $C_{17}H_{12}O_2$: C, 82·2; H, 4·9%). This ketone (10 g.) in acetic acid (120 ml.) was slowly treated with bromine in acetic acid until no further precipitate appeared: crystallised from acetic acid, the product gave 2-benzoyl-4-bromo-1-naphthol in bright yellow rods (10·2 g.), m. p. 146—148°, giving a dark green ferric reaction in ethanol. Dischendorfer [23] records m. p. 146·5°.

7-Bromo-9-phenyl-1,2:5,6-dibenzoxanthen (XXV).—Potassium borohydride (1·0 g.) was shaken with the bromo-ketone (XXIII; R = Br) (2 g.) in tetrahydrofuran (15 ml.) containing water (0·5 ml.): slight warming was needed to complete discharge of the initial yellow hue. The insoluble inorganic salts were removed and washed with a little tetrahydrofuran which was then added to the filtrate. The filtrate was dried ($MgSO_4$) and evaporated, at 40°, under reduced pressure. The gum left seemed very unstable and was therefore used without delay. It was dissolved in acetic acid (10 ml.) and mixed with a solution of β-naphthol (8 g.) in acetic acid (10 ml.) and concentrated hydrochloric acid (1 ml.). After 2 hr. at 100°, the solution had deposited crystals which were purified from ethanol–acetone, giving the *bromoxanthen* in rhombs (0·85 g.), m. p. 189—191° (Found: C, 74·0; H, 4·1; Br, 18·2. $C_{27}H_{17}BrO$ requires C, 74·2; H, 3·9; Br, 18·3%).

9-Phenyl-1,2:5,6-dibenzoxanthen (V).—The foregoing bromoxanthen was stable to reduction by hydrazine and palladium–carbon. A mixture of the bromoxanthen (0·45 g.), Raney nickel (1 g.), potassium hydroxide (3 g.), water (0·2 ml.), tetrahydrofuran (5 ml.), and ethanol (25 ml.) was shaken under hydrogen (uptake complete in *ca.* 24 hr.). The filtrate from the catalyst was acidified with concentrated hydrochloric acid, and the potassium chloride that separated was removed. Evaporation left a gum which solidified and recrystallised from acetic acid–light petroleum (b. p. 60—80°), giving the *dibenzoxanthen* as needles (0·22 g.), m. p. 217—219° (Found: C, 90·6; H, 5·6. $C_{27}H_{18}O$ requires C, 90·5; H, 5·1%).

Oxidation of the xanthen (0·62 g.) in hot acetic acid (60 ml.) by chloranil [24] (0·31 g.), in hot acetic acid (15 ml.) at once furnished a deep red solution which was boiled under reflux for 3 min., cooled to 70°, and treated with 70% perchloric acid (2 ml.) in acetic acid (3 ml.). Upon further cooling, the solution deposited a solid which, purified from acetic acid containing perchloric acid, gave *9-phenyl-1,2:5,6-dibenzoxanthylium perchlorate* in orange-red needles, m. p. 282° (decomp.) (Found: C, 70·1, 70·3; H, 4·0, 4·0. $C_{27}H_{17}ClO_5$ requires C, 71·0; H, 3·8%). (Explosions made it difficult to obtain accurate analyses.)

Action of Acids on (2RS,3RS,6'RS)-3-Phenyl-4,5:2',3'-dibenzogrisa-2',4'-dien-6'-ol.—(i) *Hydrochloric acid.* The alcohol (1·2 g.) was stable in acetic acid (30 ml.) on the steam-bath, but when water (0·3 ml.) and concentrated hydrochloric acid (0·1 ml.) were added a slow change occurred. After 3 hr. the yellow solution was concentrated *in vacuo*. A gum remained and was kept with a little ethanol until it crystallised. Purified from ethanol, the product gave what is believed to be *(2RS,3RS,6'SR)-6'-acetoxy-3-phenyl-4,5:2',3'-dibenzogrisa-2',4'-diene* (XVI) as needles (0·9 g.), m. p. 176—178° [171—180° in admixture with the (6'*RS*)epimer], $\lambda_{max.}$ 1746 cm.$^{-1}$ (Found: C, 83·3; H, 5·45. $C_{29}H_{22}O_3$ requires C, 83·2; H, 5·3%). (ii) *Sulphuric acid.* The alcohol (0·84 g.) was heated on the steam-bath with sulphuric acid (0·1 ml.) in acetic acid (20 ml.). After 1·5 hr. the solution was cooled and the crystalline precipitate (0·68 g.) collected and identified by mixed m. p. and spectroscopy as nearly pure 9-phenyl-1,2:5,6-dibenzoxanthen. The mother-liquor furnished a little more of this xanthen, contaminated by traces of a pink substance. When the alcohol was replaced by its acetate or by the epimeric acetate produced in (i), the dibenzoxanthen was formed in corresponding yield.

Action of Acids on (2RS,3SR,6'RS)-3-Phenyl-4,5:2',3'-dibenzogrisa-2',4'-diene-6'-ol.—In conditions as in (i) or (ii) above, this alcohol (0·10 g.) gave 9-phenyl-1,2:5,6-dibenzoxanthen as needles (0·07 g.), m. p. 215—217°, identified by mixed m. p. and spectroscopy. The derived acetate behaved in the same way.

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[23] Dischendorfer, *Monatsh.*, 1944, **75**, 25.
[24] Roberts and Robinson, *J.*, 1934, 1650.