

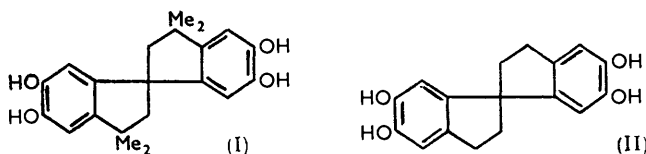
253. Some Bis-1 : 1'-spiroIndanes.

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Bis-3 : 4-dimethoxyphenethyl ketone (III) reacts with phosphorus oxychloride in benzene to give 5 : 6 : 5' : 6'-tetramethoxybis-1 : 1'-spiroindane (V), *via* the indene (IV). The structure of the spiran (V) was established by oxidation to the known *spiro*-anhydride (VI) of the acid (VII), and to the diketone (VIII) which possesses two reactive methylene groups.

The oxidation of the derived tetrahydroxybis-1 : 1'-spiroindane (II) throws light on the known remarkable behaviour on oxidation of the related *C*-tetramethyl derivative (I).

CERTAIN phenols, in which electrophilic substitution occurs *para* to a hydroxyl group, condense with acetone under acidic conditions to give derivatives of 3 : 3 : 3' : 3'-tetramethylbis-1 : 1'-spiroindane, a reaction which probably involves the intermediate formation of phorone. Thus catechol and acetone give 5 : 6 : 5' : 6'-tetrahydroxy-3 : 3 : 3' : 3'-tetramethylbis-1 : 1'-spiroindane (I),^{1,2} *o*-cresol and acetone give 6 : 6'-dihydroxy-3 : 3 : 5 : 3' : 3' : 5'-hexamethylbis-1 : 1'-spiroindane,^{3,4} and pyrogallol and acetone give 5 : 6 : 7 : 5' : 6' : 7'-hexahydroxy-3 : 3 : 3' : 3'-tetramethylbis-1 : 1'-spiroindane.⁵



The bis*spiro*cyclopentene system in (I) is remarkably stable. It survives vigorous treatment with nitric acid and ethanol which causes oxidation to the related bis-*o*-quinone in 80% yield;^{6,1} this is a most unusual way to prepare an *o*-quinone. Again aerial oxidation of the spiran (I) in alkaline solution causes symmetrical rupture of both catechol nuclei without degradation, to give in 75% yield 2 : 3 : 2' : 3'-tetra(carboxymethylene)-4 : 4 : 4' : 4'-tetramethylbis-1 : 1'-*spiro*cyclopentane.² Neither of these properties is shown by 5 : 6-dihydroxyindane; this yields an unstable red *o*-quinone only by oxidation with silver oxide in ether.² It is probable, therefore, that the abnormal properties of the spiran (I) are connected with the fact that both the carbon atoms attached to each catechol

¹ Baker, *J.*, 1934, 1678.

² Baker and McGowan, *J.*, 1938, 347.

³ Fisher, Furlong, and Grant, *J. Amer. Chem. Soc.*, 1936, **58**, 820.

⁴ Baker and Besly, *J.*, 1939, 1421.

⁵ Baker and Besly, *J.*, 1939, 195.

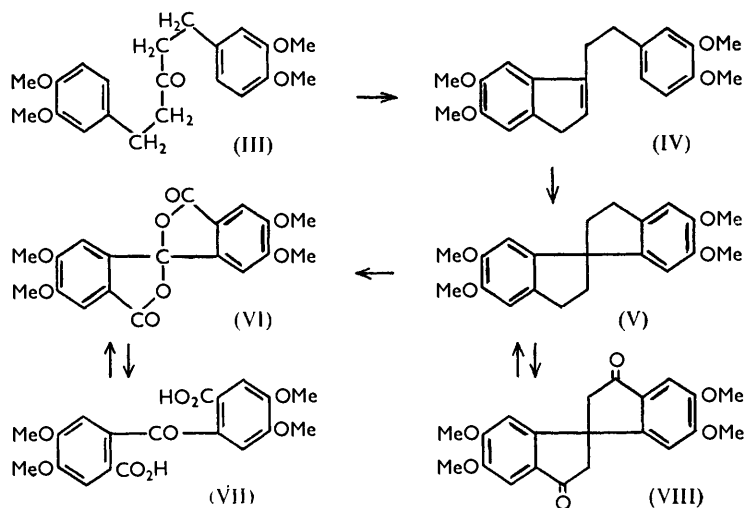
⁶ Fabinyi and Székely, *Ber.*, 1905, **38**, 2307.

nucleus are quaternary, thus not only preventing attack at these positions and at the carbon atoms themselves, but also oxidation *via* intermediate methylenequinones.

To obtain further information, the synthesis of 5:6:5':6'-tetrahydroxybis-1:1'-*spiroindane* (II) was undertaken and its properties were investigated. In brief the unsubstituted methylene groups at positions 3 and 3' do not permit the abnormally easy oxidation to the bis-*o*-quinone, and no clear-cut reaction but much degradation occurs as the result of alkaline oxidation.

The synthesis was achieved as follows. Di-3:4-dimethoxyphenethyl ketone (III), prepared by catalytic reduction of diveratrylideneacetone, undergoes cyclodehydration to 5:6:5':6'-tetramethoxybis-1:1'-*spiroindane* (V) in 91% yield when boiled with phosphorus oxychloride in benzene. Cyclodehydration of the ketone (III) with polyphosphoric acid for 2½ hours also gave the spiran (V) and a little of the isomeric 3-(3:4-dimethoxyphenethyl)-5:6-dimethoxyindene (IV); but after reaction for only 1 hour the yield of the spiran was very small and that of the indene much higher. The indene, therefore, is an intermediate in the production of the spiran (V), and was converted into it by phosphorus oxychloride in boiling benzene or by stannic chloride in chloroform.

Cyclodehydration of the ketone (III) to a saturated compound, C₁₇H₁₂(OMe)₄, might theoretically proceed in twenty-three different ways to give structurally isomeric tetramethoxy-derivatives of seven parent hydrocarbons, and there are in addition twenty racemic geometrical isomerides. A unique solution to the problem is afforded by the following facts which establish the structure as racemic 5:6:5':6'-tetramethoxybis-1:1'-*spiroindane* (V).

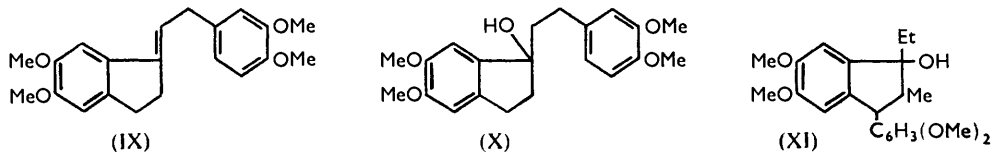


(a) When oxidised with potassium permanganate the product gave the known *spiro*-anhydride ⁷ (VI) of 4:5:4':5'-tetramethoxybenzophenone-2:2'-dicarboxylic acid (VII). This proves that there is *one* single-carbon bridge between the two dimethoxyphenyl nuclei and establishes the two new positions of attachment of carbon atoms to these nuclei. The free dicarboxylic acid (VII), not previously known, was obtained by alcoholic alkaline hydrolysis of the *spiro*-anhydride followed by acidification. (b) Oxidation of the product (V) by chromium trioxide gave a diketone (VIII), which on Clemmensen reduction reverted to the starting material (V). The ultraviolet absorption of the diketone shows that the carbonyl groups are each adjacent to an aryl nucleus, so that in the cyclodehydration product there must be methylene groups similarly attached. (c) The diketone (VIII) gives a dibenzylidene derivative when condensed with benzaldehyde in presence of ethanolic sodium

⁷ Oliverio and Boumis, *Gazzetta*, 1951, **81**, 581.

ethoxide. This establishes the presence of a methylene group adjacent to each carbonyl group in the diketone, and therefore of a $-\text{CH}_2\cdot\text{CH}_2-$ group attached to each dimethoxyphenyl nucleus in (V), thus leading to (V) as the only structure for the saturated, cyclised product $\text{C}_{17}\text{H}_{12}(\text{OMe})_4$.

The intermediate, unsaturated compound is almost certainly the indene (IV) rather than the isomeric methyleneindane (IX), and it must result from the dehydration of the



initially formed tertiary alcohol (X). There are several reasons for preferring the indene structure (IV), and an extremely close analogy for its formation is provided by dehydration of the tertiary indanol (XI) to the indene and not the (known) ethylideneindane.⁸

The ultraviolet absorption spectra of a few of the substances mentioned in this paper are recorded in the Table.

The spectra of 5 : 6 : 5' : 6'-tetramethoxybis-1 : 1'-spiroindane (V) and of its 3 : 3 : 3' : 3'-tetramethyl derivative [tetramethyl ether of (I)]¹ are almost identical. The spectrum of the diketone (VIII) is very similar to that of 2 : 2'-diacetyl-4 : 5 : 4' : 5'-tetramethoxydibenzyl⁹ which contains the same chromophoric groups; if the carbonyl groups in the oxidation product of (V) were in positions 2 and 2' the spectrum would resemble that of the parent bis-1 : 1'-spiroindane (V) and this is not the case.

Ultraviolet absorption maxima in ethanol.

Substance	λ (m μ)	$\log_{10} \epsilon$	λ (m μ)	$\log_{10} \epsilon$	Substance	λ (m μ)	$\log_{10} \epsilon$	λ (m μ)	$\log_{10} \epsilon$
(V)	232	4.16	287, 291	3.99, 3.98	(VIII)	236	4.51	268.5, 311.5	4.26, 4.16
Me_4 ether of (I)	232	4.22	286, 291	4.01, 3.99	(IV)	218	4.45	273, 296	4.00, 3.73

EXPERIMENTAL

Di-3 : 4-dimethoxyphenethyl Ketone (III).—Diveratrylideneacetone, prepared from veratraldehyde and acetone,¹⁰ was obtained in different experiments either as bright yellow needles, m. p. 84°, or plates, m. p. 122—123°. Previous workers^{11,12} have recorded m. p. 84°, except Haworth and Lamberton¹³ who obtained both forms which they probably rightly regarded as dimorphic modifications; it is, however, just possible that the two might be geometrical isomerides. Catalytic reduction of the diveratrylideneacetone (64 g.) in ethyl acetate (400 ml.) in presence of Raney nickel at 4 atm. and room temperature until a colourless solution was obtained, filtration, and concentration gave the ketone (III) as colourless needles (62 g.; 95%), m. p. 85° (oxime, m. p. 138.5°; lit.,¹⁰ m. p. 138—139°; semicarbazone, m. p. 189°).

Cyclodehydration of Di-3 : 4-dimethoxyphenethyl Ketone (III).—(a) *With phosphorus oxychloride.* 5 : 6 : 5' : 6'-Tetramethoxybis-1 : 1'-spiroindane (V). The ketone (11.4 g.) was boiled for 4 hr. with phosphorus oxychloride (45 ml.) in anhydrous benzene (114 ml.), and the solution which had become deep blue was then cooled and added to ice-water (400 g.). The combined benzene layer and an extract were shaken 3 times with 5% aqueous sodium hydroxide, then with water, dried, and distilled, and the residue which solidified was crystallised from methanol (30 ml.) at 0°, giving 5 : 6 : 5' : 6'-tetramethoxybis-1 : 1'-spiroindane (V) as radiating crystal aggregates (9.64 g.), m. p. 80—81° [Found: C, 73.9; H, 6.9; OMe, 35.4. $\text{C}_{17}\text{H}_{12}(\text{OMe})_4$ requires C, 74.1; H, 7.1; OMe, 36.5%]. No hydrogen was absorbed by this compound on attempted catalytic reduction.

⁸ Müller, Mészáros, Körmendy, and Kucsman, *J. Org. Chem.*, 1952, **17**, 787.

⁹ Battersby and Binks, *J.*, 1955, 2897.

¹⁰ Sugawara and Yoshikawa, *J.*, 1933, 1584.

¹¹ Stobbe and Haertel, *Annalen*, 1909, **370**, 104.

¹² Dickinson, Heilbron, and Irving, *J.*, 1927, 1892.

¹³ Haworth and Lamberton, *J.*, 1946, 1003.

(b) *With polyphosphoric acid.* 3-(3 : 4-Dimethoxyphenethyl)-5 : 6-dimethoxyindene (IV). (i) The finely powdered ketone (III) (8 g.) was added to polyphosphoric acid (84% of P_4O_{10} ; 80 g.) at 60°, and the mixture stirred at this temperature for 1 hr. The dark product was then stirred into 5% hydrochloric acid (150 ml.) at 0°, and after being kept at room temperature for some hours, the product was collected, washed several times with 5% aqueous sodium hydroxide and then with water, dried *in vacuo*, and extracted with ether (3 × 50 ml.). The ether-insoluble material crystallised from methanol as needles (1.8 g., 24%), m. p. 135° [Found: C, 74.2; H, 7.0; OMe, 36.6. $C_{17}H_{12}(OMe)_4$ requires C, 74.1; H, 7.1; OMe, 36.5%]. This 3-(3 : 4-dimethoxyphenethyl)-5 : 6-dimethoxyindene (IV), when reduced in ethanol at room temperature and pressure in presence of Adams platinum oxide catalyst, absorbed 1.04 mol. of hydrogen. The ether-soluble material was recovered and crystallised several times from methanol, giving needles (0.32 g., 5%), m. p. 81°, undepressed on admixture with 5 : 6 : 5' : 6'-tetramethoxybis-1 : 1'-spiroindane (V) prepared as described above.

(ii) A similar reaction carried out over a period of 2½ hr. gave the indene (IV) (0.12 g., 1.5%), and the bis-1 : 1'-spiroindane (V) (3.5 g., 46%).

Cyclisation of 3-(3 : 4-Dimethoxyphenethyl)-5 : 6-dimethoxyindene (IV).—(a) *With phosphorus oxychloride.* Cyclisation under the conditions described for the similar cyclodehydration of the ketone (III) gave the bis-1 : 1'-spiroindane (V) in 60% yield.

(b) *With stannic chloride.* The indene (2.2 g.) was dissolved in dry (K_2CO_3) chloroform (100 ml.), and stannic chloride (2 ml.) was added slowly. The green solution which gradually became bluish-purple was kept at 20° for 50 hr., then poured into 10% aqueous hydrochloric acid and ice, and shaken, and the chloroform layer and extract were separated, washed several times with dilute acid and then alkali, dried, and distilled. The residue was crystallised from a small volume of methanol at 0°, giving the spiran (V) (1.3 g., 60%), m. p. and mixed m. p. 81° (Found: C, 73.9; H, 7.1%).

5 : 6 : 5' : 6'-Tetrahydroxybis-1 : 1'-spiroindane (II).—5 : 6 : 5' : 6'-Tetramethoxybis-1 : 1'-spiroindane (V) (3 g.) was refluxed with glacial acetic acid (25 ml.) and aqueous hydrobromic acid (*d* 1.5; 25 ml.) for 5 hr., and the resulting deep-blue solution added to ice-water (500 g.) and repeatedly extracted with ether (total 300 ml.). The washed, dried extract yielded a residue which was taken up in chloroform (400 ml.), boiled with charcoal, concentrated (to 300 ml.), and kept at 0°; the resulting solid crystallised at 0° from a small volume of methanol containing a little acetic acid. The microcrystalline product had m. p. 290° and was difficult to purify. Treatment with boiling acetic anhydride and anhydrous sodium acetate for 4 hr. and addition of water gave the *tetra-acetyl derivative* which separated from methanol as plates, m. p. 200° [Found: C, 66.5; H, 5.5; Ac, 39.2. $C_{17}H_{12}O_4Ac_4$ requires C, 66.4; H, 5.4; Ac, 38.1%].

4 : 5 : 4' : 5'-Tetramethoxybenzophenone-2 : 2'-dicarboxylic Acid (VII) and its spiro-Anhydride (VI).—Finely powdered 5 : 6 : 5' : 6'-tetramethoxybis-1 : 1'-spiroindane (V) (3.6 g.) was added to a stirred solution of potassium permanganate (10 g.) in water (600 ml.) on a boiling-water bath, and after 1 hr. powdered potassium permanganate was added in portions (1 g. each) until no further reaction occurred (total, 17 g. during 2 hr.). The solution was then cleared by sulphur dioxide, concentrated (to *ca.* 200 ml.), and cooled and the solid collected, washed, and dried. This product (0.77 g.) was then crystallised from 50% acetic acid giving the *spiro-anhydride* (VI) of 4 : 5 : 4' : 5'-tetramethoxybenzophenone-2 : 2'-dicarboxylic acid as needles, m. p. 295° [Found: C, 61.3; H, 4.5; OMe, 33.0. Calc. for $C_{15}H_4O_4(OMe)_4$: C, 61.3; H, 4.3; OMe, 33.3%], undepressed on admixture with an authentic specimen, m. p. 296°, prepared as described below. This anhydride does not dissolve in 10% aqueous sodium hydroxide.

When the anhydride (VI) (0.086 g.) was warmed with 10% ethanolic potassium hydroxide (5 ml.) the clear solution subsequently deposited needles of the crude potassium salt (0.096 g.) of the related acid. This salt when dissolved in water (2 ml.) and acidified with 10% hydrochloric acid in the cold gave a precipitate which was collected, washed with cold water, and dried *in vacuo*, giving 4 : 5 : 4' : 5'-tetramethoxybenzophenone-2 : 2'-dicarboxylic acid (VII), which melts at 295° after conversion into the anhydride (VI) [Found: C, 58.4; H, 5.0; OMe, 33.4%; equiv., 194. $C_{13}H_4O(OMe)_4(CO_2H)_2$ requires C, 58.5; H, 4.6; OMe, 31.8%; equiv., 195]. It dissolves readily in 10% aqueous sodium hydroxide or sodium carbonate.

spiro-Anhydride of 4 : 5 : 4' : 5'-Tetramethoxybenzophenone-2 : 2'-dicarboxylic Acid (VI).—Difficulty was encountered in repeating the oxidation of 2 : 2'-dimethyl-4 : 5 : 4' : 5'-tetramethoxydiphenylmethane by the procedure described by Oliverio and Boumis.⁷ The finely powdered substance (2.5 g.) was added to a stirred solution of potassium permanganate (6 g.)

in water (250 ml.) on a boiling-water bath. After 2 hr. powdered potassium permanganate (4 g.) was added, and 2 hr. later the hot solution was filtered to remove manganese dioxide and starting material (1.5 g. recovered), then acidified with hydrochloric acid and boiled until no further precipitate was formed. This anhydride (VI) was collected, washed, dried (yield, 0.6 g., 50% after allowance for recovered material), and crystallised from 1 : 1 chloroform-methanol (16 ml.), giving needles, having m. p. 296° which could not be raised by repeated crystallisation. Oliverio and Boumis⁷ record m. p. 305°; it is possible that this m. p. was corrected.

5 : 6 : 5' : 6'-Tetramethoxybis-1 : 1'-spiroindane-3 : 3'-dione (VIII).—5 : 6 : 5' : 6'-Tetramethoxybis-1 : 1'-spiroindane (V) (0.9 g.) was added to a solution of chromium trioxide (1.6 g.) in acetic acid (6 ml.) and water (6 ml.); after being stirred for 2 hr. and being kept for 24 hr., the mixture was poured into 10% sulphuric acid (100 ml.). The precipitated, washed solid was crystallised twice from a mixture of acetic acid (4 ml.) and methanol (1 ml.), giving the dione (VIII) as prisms (0.48 g., 50%), m. p. 265° [Found: C, 68.3; H, 5.6; OMe, 34.8. C₁₇H₈O₂(OMe)₄ requires C, 68.5; H, 5.4; OMe, 33.7%]. The dibenzylidene derivative was prepared in 50% yield from the dione (VIII), sodium ethoxide, and benzaldehyde in boiling ethanol (5 hr.); after addition of hydrochloric acid and evaporation, the residue was crystallised twice from methanol, giving yellow needles, m. p. 216° [Found: C, 77.1; H, 5.2; OMe, 21.8. C₃₁H₁₆O₂(OMe)₄ requires C, 77.2; H, 5.2; OMe, 22.8%].

Reduction of 5 : 6 : 5' : 6'-Tetramethoxybis-1 : 1'-spiroindane-3 : 3'-dione (VIII).—A mixture of the dione (VIII) (0.8 g.), amalgamated zinc (3.5 g.), concentrated hydrochloric acid (10 ml.), water (5 ml.), and acetic acid (5 ml.) was boiled for 1½ hr., then cooled, and the product crystallised from acetic acid (2 ml.) at 0°. The product, after being freed from oily material on a porous plate, separated at 0° from methanol (2 ml.) and a little light petroleum (b. p. 60–80°) in crystals (0.44 g., 60%), m. p. 80–81°, undepressed on admixture with a specimen of 5 : 6 : 5' : 6'-tetramethoxybis-1 : 1'-spiroindane (V).

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