# **770.** *Flavothebaone. Part VII.*[1] *The Synthesis of 1,2,7,10-Tetramethoxybenzo*[a]*fluorene (Compound D).*

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The structure of 1,2,7,10-tetramethoxybenzo[*a*]fluorene (compound D), a key degradation product of flavothebaone has been confirmed by synthesis.

In Part II of this series,[2] the structures of flavothebaone trimethyl ether pseudomethine (I) and the nitrogen-free degradation products, compounds B (II; R = Ac), C (II; R = Me), and D (II; R = H) were elucidated. The structure (II; R = H) for the last of these, with which the nuclear magnetic resonance spectrum has been found compatible, has been confirmed by synthesis, by cyclodehydration of the arylidene-2-tetralone (III) prepared

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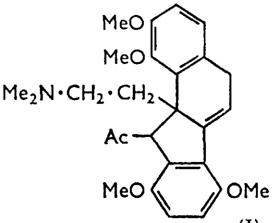
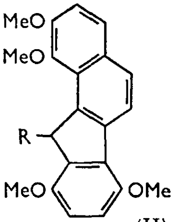
[1] Part VI, Bentley and Ringe, *J. Org. Chem.*, 1957, **22**, 599.
[2] Bentley, Dominguez, and Ringe, *J. Org. Chem.*, 1957, **22**, 409.

by acid-catalysed condensation of 2,5-dimethoxybenzaldehyde and 7,8-dimethoxy-2-tetralone.

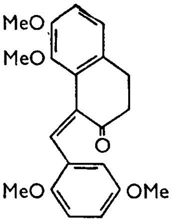
This condensation proceeded in poor yield to give a yellow αβ-unsaturated ketone, the nuclear magnetic resonance spectrum of which contains a symmetrical multiplet centred at τ 7·2, almost identical in shape and position with the $A_2B_2$ multiplet of 7,8-dimethoxy-2-tetralone. This compound must, therefore, have the structure (III) arising from condensation in the α-position since the product of condensation at the β-position would not contain such an $A_2B_2$ system. The infrared ($\nu_{\max.}$ 1689 cm.$^{-1}$) and ultraviolet spectra ($\lambda_{\max.}$ 225 mμ, ε 23,600) are also compatible with the structure (III). This ketone, when heated with polyphosphoric acid, afforded compound D.



(I)

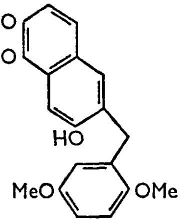


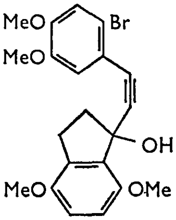
(II)



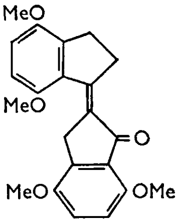
(III)

(IV)





(V)



(VI)

The base-catalysed condensation of 2,5-dimethoxybenzaldehyde and 7,8-dimethoxy-2-tetralone, however, afforded only phenolic material showing no infrared carbonyl absorption. This material readily gave a methyl ether and coupled in alkaline solution with diazotised amines, to give an orange azo-compound, and these reactions indicate that the material is a β-naphthol having a free α-position; it must then have the structure (IV), with which the nuclear magnetic resonance spectrum is compatible. It is of interest that the product (III) of acid-catalysed condensation is not converted into the isomer (IV) on prolonged boiling with ethanolic potassium hydroxide (it is recovered unchanged), and the phenol (IV) is recovered unchanged on treatment with polyphosphoric acid under conditions suitable for the conversion of the tetralone (III) into compound D; more vigorous conditions simply caused extensive decomposition of the phenol. Further, base-catalysed condensation of β-tetralone with methyl oxalate involves reaction at position 3.[3]

An alternative attempt to synthesise the benzofluorene by reaction of the Grignard reagent derived from 2-bromo-4,5-dimethoxyphenylacetylene and methylmagnesium iodide with 4,7-dimethoxyindan-1-one, followed by reduction and cyclodehydration of the expected product (V), failed; condensation under a variety of conditions afforded only the product (VI) of self-condensation of the indanone.

## EXPERIMENTAL

1-(2,5-*Dimethoxybenzylidene*)-7,8-*dimethoxy*-2-*tetralone* (III).—Concentrated hydrochloric acid (3·5 ml.) was slowly added to a boiling solution of 2,5-dimethoxybenzaldehyde (1·7 g.) and

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[3] Soffer, Stewart, and Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 1556.

7,8-dimethoxy-2-tetralone[4] (2·1 g.) in ethanol (100 ml.), and the mixture was then boiled for 1 hr. The mixture was cooled, poured into water, and neutralised with sodium hydrogen carbonate, after which the product was isolated by ether-extraction. Evaporation of the ether solution afforded a pale brown gum, which solidified to a yellow powder on trituration with ether. The solid crystallised from aqueous ethanol, 1-(2,5-*dimethoxybenzylidene*)-7,8-*dimethoxy*-2-*tetralone* (0·26 g.) being obtained as yellow needles, m. p. 167—168° (Found: C, 71·1; H, 6·3. $C_{21}H_{22}O_5$ requires C, 71·2: H, 6·3%). A further 0·8 g. was recovered from the ether used for the trituration by evaporation and chromatographic purification on silica gel; elution of the column with 1 : 1 light petroleum (b. p. 40—60°)–benzene (1 : 1) and with benzene afforded unchanged aldehyde and tetralone, respectively, and elution with 1 : 1 ether–benzene (1 : 1) gave the condensation product.

1,2,7,10-*Tetramethoxybenzo*[a]*fluorene* (II; R = H).—A mixture of 1-(2,5-dimethoxybenzylidene)-7,8-dimethoxy-2-tetralone (0·17 g.), phosphorus pentoxide (2·04 g.), and phosphoric acid (1·36 g.) was heated on a water-bath for 20 min., after which ice was added and the blue gelatinous precipitate was extracted with benzene. The benzene solution was washed with water, dried ($Na_2SO_4$), and chromatographed on silica gel. Elution with benzene gave a cream-coloured powder that was chromatographed in 3 : 2 light petroleum (b. p. 40—60°)–benzene on silica gel (5 g.). Elution with 120 ml. of 2 : 3 light petroleum–benzene gave a solid (0·04 g.) which, on recrystallisation from ethanol, afforded 1,2,7,10-tetramethoxybenzo[*a*]fluorene (compound D) (0·034 g.), m. p. 152—153° alone or mixed with material prepared by the degradation of flavothebaone (lit.,[2] 152°).

3-(2,5-*Dimethoxybenzyl*)-7,8-*dimethoxy*-2-*naphthol* (IV).—A solution of potassium hydroxide (2·35 g.) in water (5 ml.) and methanol (10 ml.) was added dropwise to a boiling solution of 2,5-dimethoxybenzaldehyde (3·14 g.) and 7,8-dimethoxy-2-tetralone (3·88 g.) in methanol (60 ml.), and the mixture was then heated for 1½ hr., cooled, and poured into water. The precipitate was isolated by ether-extraction, a brown oil being obtained. This was chromatographed in 2 : 3 light petroleum (b. p. 40—60°) and benzene over silica gel (80 g.). Elution with 9 : 1 benzene–light petroleum (b. p. 40—60°) (600 ml.) gave a mixture of the aldehyde and tetralone, but elution with benzene (2·7 l.) afforded 3-(2,5-*dimethoxybenzyl*)-7,8-*dimethoxy*-2-*naphthol* (IV) (4·8 g.), which was obtained as pale pink needles, m. p. 111—112°, on recrystallisation from aqueous methanol (Found: C, 70·9; H, 6·35; OMe, 34·6. $C_{21}H_{22}O_5$ requires C, 71·2; H, 6·3; 4OMe, 35·0%). The *methyl ether* was obtained by use of methyl sulphate and alkali, as pale orange needles, m. p. 106—107° (from aqueous ethanol) (Found: C, 71·5; H, 6·7. $C_{22}H_{24}O_5$ requires C, 71·7; H, 6·6%).

2-(4,7-*Dimethoxyindan*-1-*ylidene*)-4,7-*dimethoxyindan*-1-*one* (VI).—Dry benzene (30 ml.) was added to a solution of ethylmagnesium bromide (from magnesium, 0·2 g., and ethyl bromide, 0·9 g.) in ether, and the ether removed by distillation. The mixture was cooled and 2-bromo-4,5-dimethoxyphenylacetylene (2·0 g.) was added followed, after 2 hours' heating under reflux, by 4,7-dimethoxyindan-1-one[5] (1·6 g.) in dry benzene (20 ml.). This mixture was heated under reflux for 2½ hr. and left overnight. Ammonium chloride solution was then added and the organic layer separated; the aqueous layer was extracted with ether, and the combined benzene and ether solution dried and evaporated, leaving a brown solid (1·6 g.) from which 2-(4,7-*dimethoxy*-1-*indanylidene*)*indan*-1-*one* (0·3 g.), m. p. 204—205° (Found: C, 71·9; H, 6·0. $C_{22}H_{22}O_5$ requires C, 72·0; H, 6·1%), was recovered by recrystallisation from methanol; unchanged 2-bromo-4,5-dimethoxyphenylacetylene (1·1 g.) was obtained from the mother-liquors.

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[4] Soffer, Stewart, Cavagnol, Gellerson, and Bowler, *J. Amer. Chem. Soc.*, 1950, **72**, 3704.

[5] Arnold and Zaugy, *J. Amer. Chem. Soc.*, 1941, **63**, 1317.