c 1.11) λ_{max} 2350; 2650; 3150 Å. ϵ_{max} 21,800; 14,900; 6010.

Anal. Calcd. for $C_{25}H_{28}O_5$: C, 73.5; H, 6.9. Found: C, 73.5; H, 6.9.

Flavothebaone trimethyl ether hexahydrodesazamethine (II, R = Et). Flavothebaone trimethyl ether desazamethine (10 g.) in glacial acetic acid (150 ml.) was hydrogenated over platinum oxide (0.2 g.) at 50–70°C. when 3 moles of hydrogen were absorbed in 6 hr. The catalyst was then removed, the filtrate concentrated in vacuo and water added. The product was collected and washed with water; yield quantitative. Recrystallization from 50% ethanol gave the pure *flavothebaone trimethyl ether hexahydrodesazamethine* as white plates, m.p. 167–168°C.; $[\alpha]_D^{22}$ +210° ($CHCl_3$, c 1.40) λ_{max} 2200; 3000 Å. ϵ_{max} 26,400; 4070.

Anal. Calcd. for $C_{26}H_{30}O_5$: C, 73.9; H, 7.1. Found: C, 73.6; H, 7.0.

Flavothebaone trimethyl ether tetrahydrodesazamethine (III, R = $CH{=}CH_2$). Dihydroflavothebaone trimethyl ether dihydromethine (4.4 g.) was heated with 30% hydrogen peroxide (4 ml.) for 30 min. on the steam bath and the solution then evaporated to dryness *in vacuo*. The *N*-oxide was decomposed at 110–120°C./0.1 mm. The residual hard brown glass was treated with hot 2*N* hydrochloric acid and the white product collected, washed with water and recrystallized from aqueous alcohol; yield, 2 g. (50%), m.p. 149–152°C. Recrystallization from 50% ethanol afforded pure *flavothebaone trimethyl ether tetrahydrodesazamethine* as white plates, m.p. 151–152°C.; $[\alpha]_D^{22}$ +260° ($CHCl_3$, c 1.63). λ_{max} 2250; 3000 Å. ϵ_{max} 21,300; 5840.

Anal. Calcd. for $C_{26}H_{28}O_5$: C, 74.3; H, 6.7. Found: C, 74.0; H, 6.5.

Reduction. The tetrahydrodesazamethine (1 g.) was hydrogenated in glacial acetic acid (20 ml.) with platinum oxide (0.05 g.). One mole of hydrogen was taken up to give the hexahydrodesazamethine m.p. 165–167°C. undepressed on mixing with the product from the reduction of the desazamethine.

Flavothebaone Trimethyl Ether Dihydrodesazamethine (IV, R = $CH{=}CH_2$). Flavothebaone trimethyl ether dihydromethine (6 g.) was heated with 30% hydrogen peroxide (6 ml.) for 30 min. on the steam bath and the solution then evaporated to dryness at 100°C./20 mm. The *N*-oxide was decomposed at 120–150°C./0.1 mm. The residue was treated with warm 2*N* hydrochloric acid and the white product collected and washed with water; yield, 3.9 g., m.p. 200–208°C. Recrystallization from ethanol afforded 2.9 g. (54%) of the *flavothebaone trimethyl ether dihydrodesazamethine* as white prisms, m.p. 209–212°C. which was improved to 211–212°C. on further recrystallizations from ethanol. $[\alpha]_D^{20}$ +189° ($CHCl_3$, c 1.37) λ_{max} 2200; 2850 Å. ϵ_{max} 37,600; 16,250.

Anal. Calcd. for $C_{26}H_{26}O_5$: C, 74.6; H, 6.2. Found: C, 74.5; H, 6.2.

Reduction. Dihydrodesazamethine (1 g.) was hydrogenated in glacial acetic acid (25 ml.) with platinum oxide (0.05 g.) when 2 moles of hydrogen were absorbed in 1.5 hr. to give the hexahydrodesazamethine, m.p. 167–168°C. and showing no depression in m.p. on mixing with the product from reduction of desazamethine.

Hofmann Degradation of Dihydroflavothebaone Trimethyl Ether Dihydromethine. Dihydroflavothebaone trimethyl ether dihydromethine methiodide (5.9 g.) was converted into the methohydroxide by stirring with silver oxide and water. The dry methohydroxide was decomposed at 220–230°. The following fractions were obtained from the residue.

1. *Basic material* (0.8 g.), shown to be undegraded base.
2. *Polymerized material* (1.3 g.)
3. *Neutral material* (1.8 g.). From this fraction, by chromatography on alumina was recovered 1.2 g. of *Compound G* (V) obtained as colorless prisms m.p. 223° on recrystallization from methanol or on sublimation. $[\alpha]_D^{22}$ +376.5 ($CHCl_3$, c 2.25) λ_{max} 2950 Å; ϵ_{max} 4467.

Anal. Calcd. for $C_{25}H_{28}O_5$: C, 73.9; H, 6.40. (3) OMe, 22.9. Found: C, 74.2; H, 6.4; OMe, 21.4.

A small amount (0.05 g.) of Compound D (see part II) was also obtained.

Hofmann degradation of dihydroflavothebaone trimethyl ether methine. The methine methiodide (6.6 g.) was converted into the methohydroxide by stirring with silver oxide and water. The methohydroxide was heated at 210° for 30 min. The residue, when worked up in the usual way afforded 2.1 g. of undegraded methine base and 1.05 g. of neutral material, which gave, on chromatographic separation on alumina, 0.56 g. of *Compound H* (VI), white prisms on sublimation and recrystallization from methanol. $[\alpha]_D^{20}$ +484.6° ($CHCl_3$, c 1.31) λ_{max} 2250; 2825 Å. ϵ_{max} 23,410; 11,963.

Anal. Calcd. for $C_{25}H_{24}O_4$: C, 74.2; H, 5.9; (3) OMe, 23.0. Found: C, 74.4; H, 5.8; OMe, 22.0.

Hydrogenation of compound H. Compound H (0.08 g.) was hydrogenated in glacial acetic acid, and from the product Compound G was isolated (5 mg.) m.p. 218–220° $[\alpha]_D^{20}$ +377° ± 20° (Compound G m.p. 223°, $[\alpha]_D$ +376.5°).

ABERDEEN, SCOTLAND

[COMMUNICATION FROM THE CHEMISTRY DEPARTMENT, THE UNIVERSITY, ABERDEEN]

Flavothebaone. Part V.[1] Anomalous Beckmann Transformations

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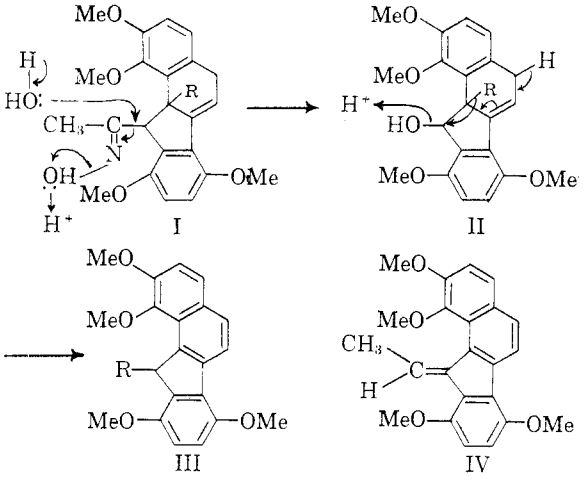
Flavothebaone trimethyl ether ψ-methine oxime on Beckmann transformation affords a *neo*methine with loss of acetonitrile. This on dehydration suffers migration of the side-chain giving a chrysofluorene derivative. Analogous compounds may be prepared from nitrogen-free derivatives of the ψ-methine. A nitrile is likewise formed by Beckmann transformation of flavothebaone trimethyl ether hexahydrodesazamethine; the further degradation of this nitrile has been studied.

In a search for a suitable method of further degradation of flavothebaone trimethyl ether ψ-methine (I, R = $CH_2CH_2NMe_2$)[2] and its derivatives[1] the Beckmann transformation of the oximes was investigated. The ψ-methine oxime is in this way readily transformed into a *neo*methine which is unaffected by acids and alkalis. The composition of the new base is $C_{25}H_{31}NO_5$ and the ultraviolet spectrum is very similar to that of the ψ-methine. The infrared spectrum shows that it is hydroxylic

(1) K. W. Bentley, J. Dominguez, and J. P. Ringe, *J. Org. Chem.*, **22**, 422 (1957).

(2) K. W. Bentley, J. Dominguez, and J. P. Ringe, *J. Org. Chem.*, **22**, 409 (1957).

and nonketonic. We propose, therefore, the structure (II, R = $CH_2CH_2NMe_2$) for this base. Dehydration of the *neo*methine with formic acid affords the anhydro*neo*methine, which has been assigned the structure of 11-β-dimethylaminoethyl-1,2,7,10-tetramethoxychrysofluorene (III, R = $CH_2CH_2NMe_2$).

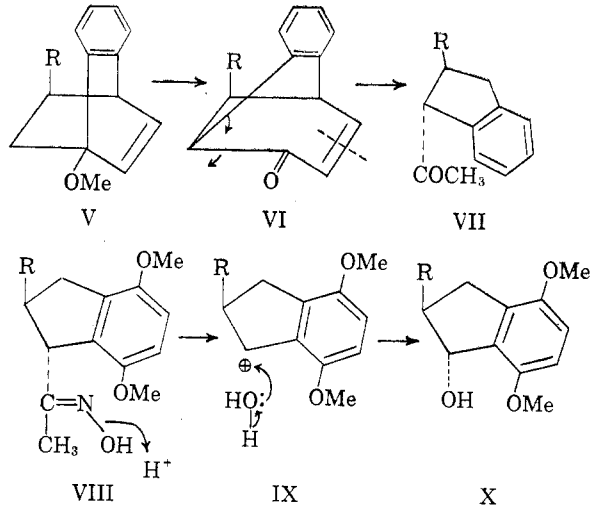


Degradation of the *neo*methine N-oxide was also accompanied by dehydration and rearrangement, the product being the chrysofluorene (III, R = $CH{=}CH_2$) which on reduction afforded the ethyl compound (III, R = Et).

Degradation of the desaza-ψ-methine oxime (I, R = $CH{=}CH_2$) affords a small amount of the desaza*neo*methine (II, R = $CH{=}CH_2$) but mainly the chrysofluorene (III, R = $CH{=}CH_2$). This is presumably due to the greater ease with which the vinyl group migrates in comparison with the β-dimethylaminoethyl group. The dihydrodesaza-ψ-methine oxime (I, R = Et) likewise gives (II, R = Et) and a very small amount of (III, R = Et), which may also be obtained from (II, R = Et) by dehydration with formic acid.

The migration of the side chain is apparently stereospecific as the vinyl-compound (III, R = $CH{=}CH_2$) and the ethyl compound (III, R = Et) obtained by these processes are optically active. They may be racemized by heating with alkalies, and these facts support the location of the vinyl and ethyl groups at position 11. The fact that the compound (IV) is not obtained by this process may be attributed to the fact that the surrounding methoxyl groups prevent a planar arrangement of such a molecule, whatever the position of the methyl group.

The conversion of flavothebaone trimethyl ether methine, which has the steric arrangement (VI), into the ψ-methine would be expected to give the *trans* arrangement of side chain and $COCH_3$ groups (VII) though a *cis* arrangement could subsequently arise in alkaline solution. (No evidence has been obtained of the production of two forms of the ψ-methine.) If the ψ-methine has the *trans* arrangement the Beckmann transformation could occur as shown in VIII → X; elimination of the $CH_3C(=NOH)$— group from the oxime (VIII) would give the carbonium ion (IX), stabilized by resonance in the aromatic nucleus; the hydroxyl group could then add on either side of the five-membered ring, but an addition *trans* to the side chain would be sterically more favorable, (IX), and would then give an arrangement suitable for a 1,2-shift of the side chain on dehydration.



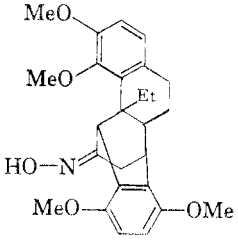
Alternatively, if the Beckmann transformation proceeds by a bimolecular process, the side chain would be expected to migrate as the acetonitrile is eliminated, and the intervention of the *neo*methine would not be expected. However, if the side chain and CH_3CO groups are *cis* in the ψ-methine, a bimolecular process would give the neomethine with a *trans* arrangement of side chain and hydroxyl group suitable for a subsequent 1,2-shift. We have no further evidence on the disposition of groups in the ψ-methine, but from work on flavothebaone trimethyl ether hexahydrodesazamethine oxime described below, we favor the *trans* arrangement of side chain and CH_3CO group and the production of a carbonium ion in the Beckmann process.

The Beckmann transformation of flavothebaone trimethyl ether hexahydrodesazamethine oxime (XI)[1] likewise proceeds readily to give a nitrile of composition $C_{26}H_{31}NO_5$ (Compound K), isomeric with the oxime. The ultraviolet spectrum of the product is similar to that of the parent oxime, and the infrared spectrum shows that it is hydroxylic and nonketonic. Hydrolysis of the nitrile affords the corresponding acid (Compound L) $C_{26}H_{32}O_7$. Fission of the oxime (XI) could occur in two ways, giving the nitriles XII or XIII, and this process is closely analogous to the Beckmann transformations of camphor oxime[3,4] (XIV) and dihydrocodeinone

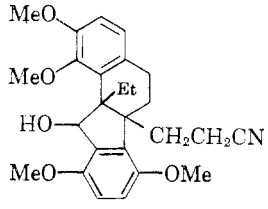
(3) M. A. Behal, *Bull. soc. chim. France*, **13** (3), 836 (1895).

(4) F. Tiemann, *Ber.*, **30**, 321 (1897).

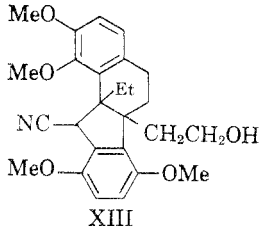
oxime[5] (XVI) to XV and XVII, respectively, and by analogy the structure (XII) seems more likely than XIII for Compound K. Only one oxime can be obtained from the hexahydrodesazamethine and on steric grounds this is most probably constituted with the N—OH bond *trans* to the ring junction carbon atom; rearrangement of this would give XII. This formulation for Compound K is supported by the following further degradations.



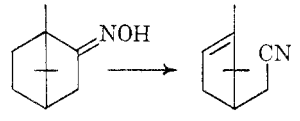
XI



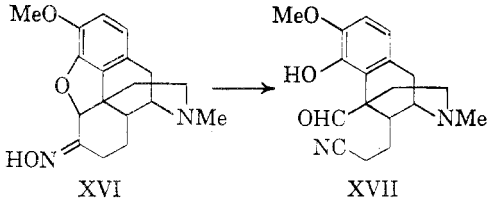
XII



XIII



XIV XV

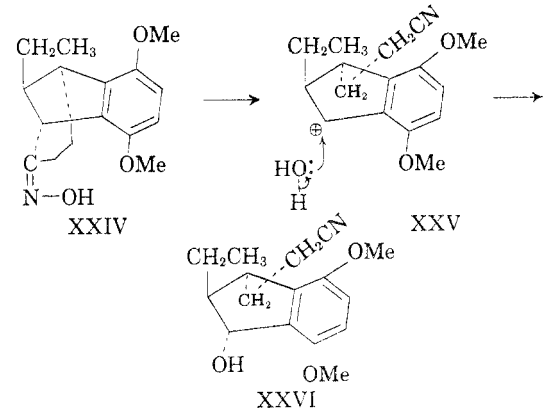


XVI XVII

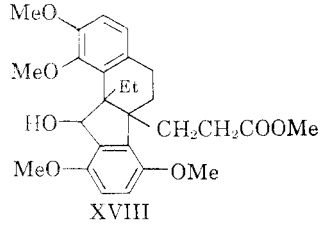
Hydrolysis of the nitrile, followed by esterification affords Compound L methyl ester (XVIII), which on treatment with phenylmagnesium bromide yields the carbinol (XIX), Compound M. Dehydration of Compound M with acetic anhydride and formic acid affords two substances, neither of which was the simple anhydro compound (XX). The first of these, Compound N, $C_{38}H_{38}O_4$, has lost two molecules of water and must therefore have the structure XXI, and must arise by migration of the ethyl side chain, as in the conversion of the *neo*methine derivatives into derivatives of chrysofluorene. The other possible structure (XXII), based on the constitution (XIII) for the nitrile, would require the five-membered ring and the CPh_2 group to be planar, and this would be impossible on steric grounds, owing to hindrance between the phenyl and methoxyl groups.

The second product of dehydration, Compound O, has the composition $C_{38}H_{40}O_5$ and arises by the loss of one molecule of water. The optical rotation, $[\alpha]_D$ −83° compared with that of Compound M (−14.6°) is not consistent with the formulation (XX) as no asymmetric center is involved or directly influenced by the dehydration of (XIX) to (XX), and the ultraviolet spectrum [which is quite different from that of the highly conjugated Compound N (XXI)] clearly shows that the substance is not styrenoid. The most acceptable structure for Compound O is clearly the cyclic ether structure (XXIII).

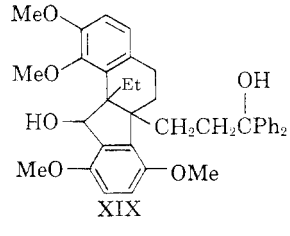
To explain the facile 1,2-shift of the ethyl group with dehydration in going from Compound M (XIX) to Compound N (XXI) it is necessary to



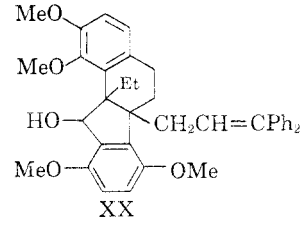
XXIV XXV XXVI



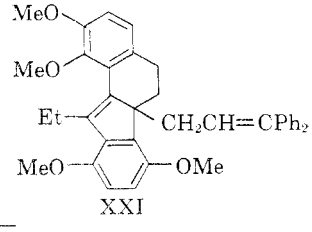
XVIII



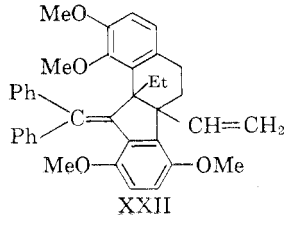
XIX



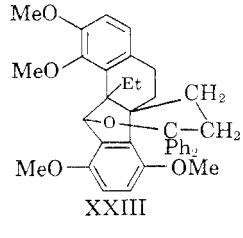
XX



XXI



XXII



XXIII

(5) C. Schöpf, *Ann.*, **452**, 211 (1927).

postulate a *trans* arrangement of the ethyl and hydroxyl groups. From our previous discussion of the rearrangement of thebainequinol to flavothebaone (Part III of this investigation) the steric arrangement of the oxime (XI) is seen to be as shown in XXIV and a concerted opening of the six-membered ring and addition of hydroxyl would give a *cis* arrangement of Et and OH. However, opening of the ring to give the carbonium ion (XXV), which would be stabilized by the adjacent aromatic nucleus (*cf.* the rearrangement of the ψ-methine oxime), would be followed by addition of the hydroxyl group in the least-hindered position, *i.e.*, *trans* to the adjacent ethyl group, giving a constitution for Compounds K, L, and M suitable for the subsequent dehydration and 1,2-shift.

EXPERIMENTAL

Beckmann rearrangement of flavothebaone trimethyl ether ψ-methine oxime. Flavothebaone trimethyl ether ψ-methine oxime (20 g.) was slowly added to purified thionyl chloride (25 ml.) at 0° over 40 min. The mixture was allowed to stand in the ice bath for 1 hr. and the excess of thionyl chloride then removed *in vacuo* at 20°. The very viscous residue was treated with ice and dilute hydrochloric acid when a considerable amount of crystalline material was obtained. This was collected, washed with ice water, dissolved in hot water and aqueous sodium carbonate added to the solution. The precipitated base was collected and recrystallized from 35% ethanol when *flavothebaone trimethyl ether* neo*methine* was obtained as colorless needles, m.p. 147°; $[\alpha]_D^{15}$ +103° (EtOH, c 1.5).

Anal. Calcd. for $C_{25}H_{31}NO_5$: C, 70.5; H, 7.4; N, 3.3. Found: C, 70.5; H, 7.6; N, 2.9.

The *picrate*, prepared in and recrystallized from ethanol, was obtained as yellow irregular plates m.p. 171–172°.

Anal. Calcd. for $C_{31}H_{34}N_4O_{12}$: C, 57.1; H, 5.0. Found: C, 57.4; H, 5.0.

Rearrangement of flavothebaone trimethyl ether neomethine in formic acid. A solution of flavothebaone trimethyl ether *neo*methine (1 g.) in 100% formic acid (20 ml.) was refluxed for 3 hr., the color changing from dark blue to red and finally to dark green. Water was added, the solution basified with ammonia and extracted with benzene. The benzene solution was washed with water, dried, concentrated to about 20 ml. and light petroleum (b.p. 50–60°) added to product a faint turbidity and the solution was then chromatographed on alumina. A blue fluorescent band (ultraviolet light) was eluted with benzene giving a brown oil, which was dissolved in ethanol and converted into the picrate: yield 0.20 g. Recrystallization from ethanol afforded *flavothebaone trimethyl ether anhydroneomethine* (III, R = $CH_2CH_2NMe_2$) *picrate* as yellow plates, m.p. 223° (dec.).

Anal. Calcd. for $C_{31}H_{32}N_4O_{11}$.EtOH: C, 58.0; H, 5.6; N, 8.2. Found: C, 58.3; H, 5.5; N, 7.9.

The *free base* was obtained by adding ammonia to the picrate and extracting the resulting mixture with ether. It could not be obtained crystalline, but the ultraviolet spectrum indicated a chrysofluorene structure λ_{max} 2250, 2700, 3250 Å, ϵ_{max} 41,800, 55,000, 11,100.

On adding an alcoholic solution of *s*-trinitrobenzene to a solution of the base in alcohol, a deep red solution was formed, indicating complex formation although no crystalline derivative was obtained.

The degradation of flavothebaone trimethyl ether neomethine N-oxide. Flavothebaone trimethyl ether *neo*methine (5 g.) and 30% hydrogen peroxide (5 ml.) were heated together on the steam bath for 30 min., the excess of hydrogen peroxide was removed at 100°/20 mm. and the N-oxide then decomposed at 150°/0.1 mm. A dark tar was formed which was extracted with ether and 2*N* hydrochloric acid. A considerable amount of material was insoluble and was treated separately.

The ether extract was washed with 2*N* hydrochloric acid, then water, dried over sodium sulfate and evaporated. The residue (1 g.) was dissolved in benzene and passed down an alumina column and a blue fluorescent band (ultraviolet light) was then eluted with benzene, but the eluate gave only a small amount of a brown oil.

The acid extract was basified with ammonia and extracted with chloroform to give 1.3 g. of a dark brown base that could not be purified.

The ether and acid insoluble portion was extracted with benzene and the solution passed down an alumina column. The first blue fluorescent band (in ultraviolet light) was eluted with benzene and afforded 0.5 g. of a light yellow oil, which, on crystallization from methanol, gave 0.3 g. of 1,2,7,10-*tetramethoxy*-11-*vinylchrysofluorene* (Compound I) as white prisms, m.p. 100–102° improved to 103° on further recrystallization; $[\alpha]_D^{19}$ −134° ($CHCl_3$, c 0.4); λ_{max} 2300, 2750, 3350 Å; ϵ_{max} 51,400, 62,300, 14,500.

Anal. Calcd. for $C_{23}H_{22}O_4$: C, 76.2; H, 6.1. Found: C, 76.2, 76.5; H, 5.8, 6.0.

The *s-trinitrobenzene* complex was obtained as dark red needles m.p. 153–154° from ethanol.

Anal. Calcd. for $C_{23}H_{22}O_4.{}^1/_2C_6H_3N_3O_6$: C, 66.6; H, 5.1; N, 4.5. Found: C, 66.3; H, 5.3; N, 4.4.

The 2,4,6-*trinitrotoluene complex* prepared in and recrystallized from ethanol, was obtained as bright red needles, m.p. 127–128°.

Anal. Calcd. for $C_{23}H_{22}O_4.C_7H_5N_3O_6$: C, 61.1; H, 4.6; N, 7.1. Found: C, 60.8; H, 4.9; N, 6.9.

The *picrate*, prepared in and recrystallized from ethanol, was obtained as very deep red needles, m.p. 131°.

Anal. Calcd. for $C_{23}H_{22}O_4.{}^1/_2C_6H_3N_3O_7$: C, 65.5; N, 5.0; N, 4.4. Found: C, 65.4; H, 4.8; N, 4.2.

Reduction of 1,2,7,10-tetramethoxy-11-vinylchrysofluorene. 1,2,7,10-Tetramethoxy-11-vinylchrysofluorene (0.5 g.) in glacial acetic acid (20 ml.) was hydrogenated over platinum oxide (0.05 g.) when one molar proportion of hydrogen was absorbed. The catalyst was removed and the filtrate concentrated *in vacuo* and water added. The product was collected and washed with water. The yield was quantitative. Recrystallization from methanol afforded 1,2,7,10-*tetramethoxy*-11-*ethylchrysofluorene* (Compound J) as white needles m.p. 153–154°; $[\alpha]_D^{16}$ −93° ($CHCl_3$, c 0.32); λ_{max} 2250, 2750, 3350 Å; ϵ_{max} 51,300, 79,000, 13,800.

Anal. Calcd. for $C_{23}H_{24}O_4$: C, 75.8; H, 6.6. Found: C, 75.4; H, 6.6.

The *s-trinitrobenzene complex* was obtained as red needles, m.p. 178–179° from ethanol.

Anal. Calcd. for $C_{23}H_{24}O_4.{}^1/_2C_6H_3N_3O_6$: C, 66.3; H, 5.5; N, 4.5. Found: C, 66.1; H, 5.6; N, 4.4.

Flavothebaone trimethyl ether desaza-ψ-methine oxime. A solution of flavothebaone trimethyl ether desaza-ψ-methine (2.5 g.) and hydroxylamine hydrochloride (2.5 g.) in ethanol (25 ml.) and pyridine (12 ml.) was refluxed 4 hr. Water was added, the product collected from the cold solution and recrystallized from methanol to give *flavothebaone trimethyl ether desaza-ψ-methine oxime* as white needles, m.p. 208°; $[\alpha]_D^{20}$ +241° ($CHCl_3$, c 0.69).

Anal. Calcd. for $C_{25}H_{27}NO_5$: C, 71.2; H, 6.5. Found: C, 70.9; H, 6.6.

Beckmann rearrangement of flavothebaone trimethyl ether desaza-ψ-methine oxime. Thionyl chloride (2 ml.) was added to flavothebaone trimethyl ether desaza-ψ-methine oxime (2.5 g.) in chloroform (25 ml.), slowly with constant shaking at −10° (ice-salt bath). A deep green solution was formed which was allowed to stand for 30 min. in an ice bath. The chloroform was evaporated *in vacuo* below 40° and methanol containing a few drops of ammonia was added to the residue to remove the last traces of thionyl chloride. The methanol was evaporated and the residue dissolved in a 1:1 mixture

of benzene and light petroleum (b.p. 50–60°) and passed down an alumina column. A blue fluorescent band (ultraviolet light) was eluted with benzene, the eluate evaporated and the residue crystallized from methanol to give 0.95 g. of product, m.p. 110–130°. Two recrystallizations from methanol afforded 0.45 g. of *flavothebaone trimethyl ether desaza*neo*methine* as pale yellow prisms, m.p. 167–168° which was depressed to 158–160° on mixing with the desaza-ψ-methine (m.p. 167–168°); $[\alpha]_D^{20}$ +11.9° ($CHCl_3$, c 1.43); λ_{max} 2200, 2550, 3050; ϵ_{max} 28,800, 11,800, 5420.

Anal. Calcd. for $C_{23}H_{24}O_5$: C, 72.6; H, 6.4. Found: C, 72.3; H, 6.4.

The alcoholic liquors on treatment with *s*-trinitrobenzene, afforded 0.6 g. of the *s*-trinitrobenzene complex of 1,2,7,10-tetramethoxy-11-vinylchrysofluorene as deep red prisms, m.p. 150–152°.

Rearrangement of the desaza*neo*methine to the fully aromatic Compound I was extremely easy and great care had to be taken to avoid this in the Beckmann rearrangement. Boiling a methanolic solution 1 min. in the presence of the merest trace of thionyl chloride was sufficient to cause complete rearrangement.

The preparation of 1,2,7,10-tetramethoxy-11-vinylchrysofluorene from the Beckmann rearrangement was carried out most simply as follows:

Thionyl chloride (2 ml.) was added to the desaza-ψ-methine oxime (2.5 g.) in chloroform (25 ml.) with constant shaking below −5°. After standing for 30 min., the chloroform was removed *in vacuo*, ice water added to the residue and the brown solid collected, washed with water, and dried in the oven at 100°. It was dissolved in a 1:1 mixture of benzene and light petroleum (b.p. 50–60°) and the blue fluorescent band (ultraviolet light) eluted with benzene. Evaporation of the solvent afforded a light yellow substance which on recrystallization from methanol gave 1.2 g. of 1,2,7,10-tetramethoxy-11-vinylchrysofluorene as very pale yellow prisms, m.p. 103° alone or mixed with a specimen prepared from degradation of flavothebaone trimethyl ether *neo*methine N-oxide.

*Reduction of flavothebaone trimethyl ether desaza*neo*methine.* Flavothebaone trimethyl ether desaza*neo*methine (0.35 g.) in ethyl acetate (15 ml.) was hydrogenated over platinum oxide (0.05 g.) when one molar equivalent was absorbed in 10 min. The catalyst was removed, the filtrate evaporated, and the residue recrystallized from methanol when *flavothebaone trimethyl ether dihydrodesaza*neo*methine* was recovered as light brown prisms m.p. 160–161°; $[\alpha]_D^{22}$ +133° ($CHCl_3$, c 1.52); λ_{max} 2600, 3050 Å; ϵ_{max} 11,200, 5240.

Anal. Calcd. for $C_{23}H_{26}O_5$: C, 72.2; H, 6.9. Found: C, 72.4, 72.2; H, 6.9, 7.1.

Flavothebaone trimethyl ether dihydrodesaza-ψ-methine oxime. This substance, prepared in exactly the same way as the desaza-ψ-methine oxime, was obtained as pale brown prisms m.p. 177° on recrystallization from 50% ethanol; $[\alpha]_D^{21}$ +305° ($CHCl_3$, c 0.68).

Anal. Calcd. for $C_{25}H_{29}NO_5$: C, 70.9; H, 6.9; N, 3.3. Found: C, 70.9; H, 6.7; N, 3.3.

Beckmann rearrangement of flavothebaone trimethyl ether dihydrodesaza-ψ-methine oxime. Thionyl chloride (3 ml.) was added slowly to a solution of flavothebaone trimethyl ether dihydrodesaza-ψ-methine oxime (3.7 g.) in chloroform (35 ml.) below −5°. The deep green solution was allowed to stand for 30 min. and the chloroform was then removed *in vacuo* at 40°. The residue was triturated with methanol to give a brown crystalline material which, after recrystallization from methanol, afforded 1.5 g. of flavothebaone trimethyl ether dihydrodesaza*neo*methine as brown prisms, m.p. 160–161° alone or mixed with a specimen prepared by reduction of the desaza*neo*methine. A further 0.6 g. was recovered from the alcoholic mother liquors.

Unlike the Beckmann rearrangement of the desaza-ψ-methine oxime, none of the fully aromatic Compound J was obtained. In an experiment where the chloroform solution (after addition of thionyl chloride) was refluxed for 10 min., the main product was still the dihydrodesaza*neo*methine although the liquors, after purification by chromatography, afforded a small amount of the chrysofluorene.

Rearrangement of flavothebaone trimethyl ether dihydrodesazaneomethine in formic acid. A solution of flavothebaone trimethyl ether dihydrodesazaneomethine (0.2 g.) in 100% formic acid (10 ml.) was boiled under reflux for 17 hr., during which the color changed from deep blue to dark brown. Water was then added and the product extracted with ether and the ether extract washed with 2*N* sodium carbonate, and water, and dried. Evaporation of the ether afforded only amorphous material which was dissolved in a 1:1 mixture of benzene and light petroleum (b.p. 50–60°) and the resulting solution passed down a column of alumina. A blue fluorescent band (ultraviolet light) was eluted with benzene, and after evaporation of the eluate, recrystallization of the residue from methanol gave 0.1 g. of 1,2,7,10-tetramethoxy-11-ethylchrysofluorene (Compound J) as white needles, m.p. 154° alone or mixed with a specimen obtained from the reduction of Compound I. A *s*-trinitrobenzene complex was formed, m.p. 174–176° undepressed on mixing with the complex of Compound J.

Action of alcoholic potassium hydroxide on 1,2,7,10-tetramethoxy-11-vinylchrysofluorene. 1,2,7,10-Tetramethoxy-11-vinylchrysofluorene (0.2 g.) in a 10% alcoholic potassium hydroxide solution (20 ml.) was refluxed for 6 hr., the solution was cooled, water was added and the mixture extracted with benzene. The benzene extract was washed with water, dried over sodium sulphate, and concentrated to about 10 ml. Light petroleum (b.p. 50–60°) was added to the extract to produce a faint turbidity and the resulting solution chromatographed on alumina. A blue fluorescent band (ultraviolet light) was eluted with a 1:1 mixture of benzene and light petroleum, which afforded, after evaporation of the eluate and recrystallization of the residue from methanol, 0.1 g. of *rac-1,2,7,10-tetramethoxy-11-vinylchrysofluorene* as yellow crystals m.p. 152–160°, $[\alpha]_D$ 0.0. The ultraviolet spectrum was very similar to that of the starting material; λ_{max} 2250, 2750, 3300 Å; ϵ_{max} 44,300, 58,300, 11,700.

Racemization of 1,2,7,10-tetramethoxy-11-ethylchrysofluorene. 1,2,7,10-Tetramethoxy-11-ethylchrysofluorene (0.2 g.) in a 10% alcoholic potassium hydroxide solution (20 ml.) was refluxed for 24 hr. Water was then added and the product collected and recrystallized from methanol when *rac-1,2,7,10-tetramethoxy-11-ethylchrysofluorene* was obtained as cream needles, m.p. 128–130°, $[\alpha]_D$ 0.0.

The *s*-trinitrobenzene complex prepared in ethanol, was obtained as red prisms m.p. 156–158°.

The Beckmann rearrangement of flavothebaone trimethyl ether hexahydrodesazamethine oxime. Flavothebaone trimethyl ether hexahydrodesazamethine oxime (9 g.) in chloroform (90 ml.) was cooled to −10° in an ice-salt bath and thionyl chloride (4.5 ml.) was added slowly, the temperature being maintained between −5° and −10°. A deep green solution was formed which was kept in the ice-salt bath for 30 min. The mixture was then evaporated to dryness under reduced pressure and methanol (50 ml.) was added to the residue. A homogeneous solution was first formed from which a greenish-white crystalline material separated and this was collected to give 6 g. of crude Compound K m.p. 184–188°. Recrystallization from methanol gave 4.85 g. (54%), m.p. 191–193° and further recrystallizations from methanol afforded pure Compound K, as white needles m.p. 194–195°; $[\alpha]_D^{24}$ −17.5° ($CHCl_3$, c 1.00); λ_{max} 2200, 2900 Å; ϵ_{max} 21,000, 7320.

Anal. Calcd. for $C_{26}H_{31}NO_5$: C, 71.4; H, 7.2; N, 3.2. Found: C, 71.9, 71.7; H, 7.2, 6.9; N, 2.9.

Compound K exhibits an intense blue color in concentrated sulfuric acid.

The hydrolysis of Compound K. Compound K (12 g.) was added to a solution of potassium hydroxide (60 g.) in ethanol (300 ml.) and water (25 ml.) and the mixture boiled under reflux for 17 hr. Compound K dissolved as the hydrolysis

proceeded and ammonia was evolved. After cooling, water (700 ml.) was added, the mixture acidified with concentrated hydrochloric acid, and the product extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and evaporated, and the residue was dissolved in hot aqueous alcohol and filtered hot [Norit]. The product was collected from the cooled filtrate and washed with a little 50% ethanol when 11 g. of light brown crystalline material, m.p. 165–167°, was obtained. Recrystallization from 50% ethanol afforded Compound L as white prisms, m.p. 166–167°; $[\alpha]_D^{21}$ −18.2° ($CHCl_3$, c 0.99).

Anal. Calcd. for $C_{26}H_{32}O_7$: C, 68.4; H, 7.1. Found: C, 68.6; H, 7.2.

The *methyl ester*, prepared by esterification of the acid with diazomethane in ether, was recrystallized from methanol when it was obtained as white rods, m.p. 161–162°.

Anal. Calcd. for $C_{27}H_{34}O_7$: C, 68.9; H, 7.3. Found: C, 68.9; H, 7.2.

Reaction of methyl ester of Compound L with phenylmagnesium bromide. Compound L methyl ester (11 g., 0.023 mol.) in benzene (120 ml.) was added over a period of 15 min. to a stirred mixture of phenylmagnesium bromide [prepared from magnesium (9 g.) and bromobenzene (42 ml.) in the usual way] and ether (100 ml.). The mixture was refluxed for 3 hr. with stirring, and then poured onto crushed ice (400 g.) and concentrated hydrochloric acid (65 ml.). The aqueous layer was extracted with benzene (2 × 100 ml.) and the combined benzene-ether solution washed with 2*N* hydrochloric acid, water, 5% sodium hydroxide, and finally water. Most of the solvent was then removed and the residue steam distilled for 6 hr. to remove biphenyl. The residual liquid was extracted with ether when 13 g. of product was obtained. Recrystallization of this from ethanol gave Compound M as white prisms, m.p. 174–175°; $[\alpha]_D^{20}$ −14.6° ($CHCl_3$, c 0.82).

Anal. Calcd. for $C_{38}H_{42}O_6$: C, 76.8; H, 7.1. Found: C, 76.8; H, 6.8.

Dehydration of Compound M with acetic anhydride and formic acid. A solution of Compound M (1 g.) in acetic anhydride (8 ml.) and 100% formic acid (5 ml.) was refluxed for 2 hr., during which the initial deep blue color quickly turned to red. Water was added to the mixture and the precipitated light brown, amorphous material recrystallized from ethanol when Compound N was obtained as white needles, m.p. 164°; $[\alpha]_D^{20}$ +92° ($CHCl_3$, c 0.31); λ_{max} 2275, 2550, 2675, 2900, 3000, 3100, 3200 Å; ϵ_{max} 52,480, 25,700, 18,200, 19,050, 18,000, 19,000, 18,000.

Anal. Calcd. for $C_{38}H_{38}O_4$: C, 81.7; H, 6.9. Found: C, 81.6; H, 6.7.

The alcoholic liquors (from recrystallization of Compound N) were evaporated and the residue dissolved in a 1:1 mixture of benzene and light petroleum (b.p. 50–60°) and the solution passed down an alumina column. A blue fluorescent band (ultraviolet light) was eluted, the eluate evaporated, and the residue recrystallized three times from ethanol when Compound O was obtained as white needles, m.p. 153–154° which was depressed to 125° on mixing with a sample of Compound N; $[\alpha]_D^{20}$ −83° ($CHCl_3$, c 0.85); λ_{max} 2150, 2775 Å; ϵ_{max} 22,910, 7586.

Anal. Calcd. for $C_{38}H_{40}O_5$: C, 79.1; H, 7.0. Found: C, 79.4, 79.5; H, 6.7, 7.3.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, THE UNIVERSITY, ABERDEEN]

Structure of Isothebaine

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4,6-Dimethoxy-5-ethoxyaporphine has been synthesized by a combination of the Bischler-Napieralski *iso*-quinoline and the Pschorr phenanthrene syntheses, and found to be identical with *iso*thebaine ethyl ether.

During the period of active growth of *Papaver orientale* the plant contains appreciable quantities of thebaine, but after the ripening and withering of the aerial plant very little, if any, of this alkaloid can be extracted. At the same time, however, the roots are found to contain a phenolic, optically active alkaloid, isothebaine, isomeric with thebaine.[1,2] It was originally postulated that thebaine is converted into isothebaine in the plant. Klee[3] examined the base thoroughly and found that Hofmann degradation of the methyl ether proceeded *via* a mixture of an optically inactive methine, and an optically active isomethine, to a trimethoxyvinylphenanthrene, which on oxidation, followed by decarboxylation, afforded a trimethoxyphenanthrene, isolated as the picrate. This was believed by Klee to be identical with the picrate of 3,4,5-trimethoxyphenanthrene obtained by Vongerichten and Dittmer[4] from morphenol (II) and subsequently synthesised by Pschorr and Koch.[5] On this basis Klee allotted structure I to isothebaine, the phenolic —OH being placed at C_4, without proof, to account for the apparent difficulty of methylation of the base (nascent diazomethane in *iso*amyl ether).

More recently Schlittler and Müller[6] have repeated these degradations and obtained the trimethoxyphenanthrene as a crystalline solid, which was found to be identical with the product of decarboxylation of synthetic 3,4,5-trimethoxyphenanthrene-9-carboxylic acid. Kiselev and Konovalova, who isolated[7] *iso*thebaine from *Papaver*

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