*baone monomethyl ether hydrochloride* separated and was collected and recrystallized from water, when it was obtained as yellow prisms, m.p. 310° (dec.), (lit.[2] 308°).

*Anal.* Calcd. for $C_{25}H_{25}O_5N\cdot HCl^1/_2H_2O$: C, 64.5; H, 5.8; Cl, 7.6. Found: C, 64.1, H, 6.0; Cl, 7.3.

*Flavothebaone monomethyl ether*, prepared from the hydrochloride, was obtained as stout yellow prisms, m.p. 272° (lit.[2] 272°) on recrystallization from 90% methanol (the base was very sparingly soluble in anhydrous methanol).

*Anal.* Calcd. for $C_{25}H_{25}O_5N\cdot 1^1/_2H_2O$: C, 67.1; H, 6.3. Found: C, 67.1; H, 6.0.

*Thebainequinol monomethyl ether B.* Methyl sulfate (25 ml.) was slowly added with stirring to a boiling solution of thebainequinol (5 g.) and potassium hydroxide (35 g.) in 50% 2-ethoxyethanol (150 ml.) over a period of 40 min. The mixture was cooled and diluted with water (150 ml.) and the solid product was collected. Thebainequinol monomethyl ether B was obtained as colorless needles, m.p. 258° on recrystallization from 2-ethoxyethanol. (Schöpf, von Gottberg, and Petri[2] give m.p. 238° for a thebainequinol monomethyl ether prepared from thebainequinol and methyl *p*-toluenesulfonate.)

*Anal.* Calcd. for $C_{26}H_{27}O_5N$: C, 72.0; H, 6.2. Found: C, 72.0; H, 6.3.

*Rearrangement of thebainequinol monomethyl ether B.* The rearrangement of thebainequinol monomethyl ether B in a mixture of acetic and hydrochloric acids afforded a flavothebaone monomethyl ether hydrochloride, m.p. 320°.

*Anal.* Calcd. for $C_{25}H_{25}O_5N.HCl.1^1/_2H_2O$: C, 62.1; H, 6.0. Found: C, 62.3; H, 5.8.

The free base was obtained as yellow prisms, m.p. 248–249°.

*Anal.* Calcd. for $C_{25}H_{25}O_5N.H_2O$: C, 68.6; H, 6.1. Found: C, 68.9; H, 5.8.

*Acknowledgments.* We wish to thank Sir Robert Robinson for his constant interest and advice and Dr. H. M. E. Cardwell for much helpful discussion.

ABERDEEN, SCOTLAND

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

# Flavothebaone. Part IV.[1] Degradation of *N*-Oxides and Exhaustive Methylation of Reduced Methines

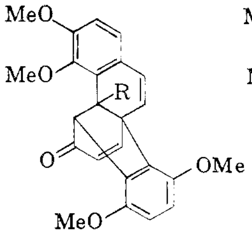
K. W. BENTLEY, J. DOMINGUEZ, AND J. P. RINGE

*Received September 25, 1956*

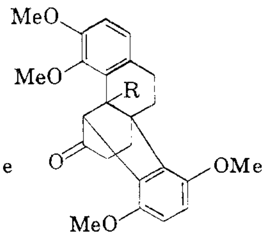
Flavothebaone trimethyl ether methine *N*-oxide has been degraded to a desaza-compound, alkaline rearrangement of which affords the desaza-ψ-methine also obtainable from the ψ-methine *N*-oxide. The trimethyl ether methine has been hydrogenated to a tetrahydro-compound also obtained from dihydroflavothebaone trimethyl ether methine. The *N*-oxides of these bases have been degraded to desaza-compounds which are not identical with the products of Hofmann degradation of the metho-hydroxides. The Hofmann products are believed to be of the thebenone type. The various desaza-methines have been related by hydrogenation.

It has previously been shown[2] that the degradation of *N*-oxides of methine bases in the morphine-thebaine group proceeds with the elimination of dimethylhydroxylamine and formation of vinyl compounds, in cases where there is no free hydroxyl group at position 4. Application of this reaction to flavothebaone trimethyl ether methine (I, R = $CH_2CH_2NMe_2$) affords the desaza-methine (I, R = CH = $CH_2$) which is shown by the ultraviolet spectrum to be a genuine derivative of the methine. Hydrogenation of the desazamethine (I, R = CH = $CH_2$) affords the hexahydrodesazamethine (II, R = Et). When the desazamethine is heated with alcoholic potassium hydroxide it undergoes the ψ-methine rearrangement[2] giving flavothebaone trimethyl ether desaza-ψ-methine (III, R = CH = $CH_2$) also obtainable by the thermal decomposition of the ψ-methine *N*-oxide. Hydrogenation of the desaza-ψ-methine affords the dihydroderivative (III, R = Et).

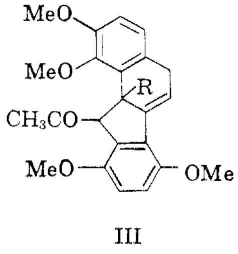
Catalytic hydrogenation of flavothebaone trimethyl ether methine affords dihydroflavothebaone trimethyl ether dihydromethine (II, R = $CH_2CH_2$-$NMe_2$) also obtainable by the catalytic reduction of dihydroflavothebaone trimethyl ether methine (IV, R = $CH_2CH_2NMe_2$) (Part III). Degradation of the *N*-oxide of dihydroflavothebaone trimethyl ether dihydromethine affords the desaza-compound (II, R = CH = $CH_2$) which yields (II, R = Et) on hydrogenation; (II, R = Et) is also obtained by the



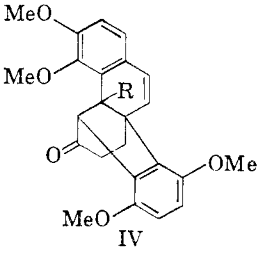
I



II



III



IV

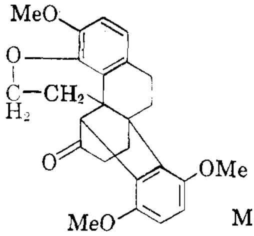
---

[1] Part III: K. W. Bentley, J. Dominguez, and J. P. Ringe, *J. Org. Chem.*, 22, 418 (1957).

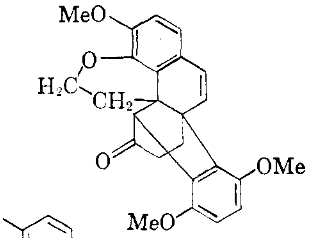
[2] K. W. Bentley, J. C. Ball, and J. P. Ringe, *J. Chem. Soc.*, 1963 (1956).

hydrogenation of the desaza-methine (IV, R = CH $=CH_2$) obtained from (IV, R = $CH_2CH_2NMe_2$) via the *N*-oxide.

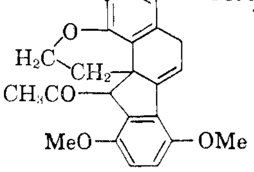
Dry distillation of the methohydroxide of (II, R = $CH_2CH_2NMe_2$) affords a nitrogen-free substance, Compound G, that is not identical with the desaza-compound (II, R = CH $=$ $CH_2$). Compound G has the composition $C_{25}H_{26}O_5$, and cannot be hydrogenated; its infrared spectrum contains no vinyl absorption band, and we believe that it is a thebenone-type of compound of structure (V). Similarly the dry distillation of the methohydroxide of (IV, R = $CH_2CH_2NMe_2$) affords a nitrogen-free substance, Compound H, different from the vinyl-compound (IV, R = CH=$CH_2$); this has the composition $C_{25}H_{24}O_5$, contains a styrenoid chromophore and is, we believe, the thebenone-type compound (VI). Hydrogenation of Compound H on a very small scale afforded a small amount of Compound G. The methoxyl determinations on Compounds G and H support these formulas. The optical rotations of Compound G (+376.5°) and Compound H (+484.6°) are much larger than those of any of the vinyl compounds obtained from the *N*-oxides, and are roughly of the same order as that of Compound F (+764°) (Part II), which is believed to be (VII).



V



VI



VII

From the products of these two Hofmann degradations a very small amount of Compound D (Part II) was obtained; this, we believe, arose via the ψ-methine from a small amount of unreduced flavothebaone trimethyl ether methine in the starting material, and has no structural significance.

## EXPERIMENTAL

*Dihydroflavothebaone trimethyl ether dihydromethine.* (II, R = $CH_2CH_2NMe_2$). Flavothebaone trimethyl ether methine (4.2 g.) in glacial acetic acid (40 ml.) was shaken under hydrogen with platinum oxide (0.2 g.) 450 ml. (2 mol. equiv.) of hydrogen were absorbed. *Dihydroflavothebaone trimethyl ether* dihydromethine (4.0 g.) was recovered from the solution and obtained as colorless prisms m.p. 155–156° from 50% ethanol. $[\alpha]^{20}_{D}$ +175° ($CHCl_3$ c 2.37) $\lambda_{max}$ 2950 Å; $\epsilon_{max}$ 4370.

*Anal.* Calcd. for $C_{28}H_{35}O_5N$: C, 72.2; H, 7.6; Found: C, 72.4; H, 7.4.

The *perchlorate*, prepared in and recrystallized from ethanol, was obtained as colorless plates, m.p. 255°.

*Anal.* Calcd. for $C_{28}H_{35}O_5N{\cdot}HClO_4{\cdot}{}^1/_2H_2O$: C, 58.4; H, 6.4. Found: C, 58.3; H, 6.4.

The *picrate*, prepared in ethanol and recrystallized from *iso*amyl alcohol, was obtained as yellow plates, m.p. 195°.

*Anal.* Calcd. for $C_{28}H_{35}O_5N{\cdot}C_6H_3O_7N_3$: C, 58.8; H, 5.5; N, 8.1. Found: C, 58.7; H, 5.6; N, 8.1.

The *methiodide*, prepared in benzene and recrystallized from water, was obtained as colorless needles, m.p. 244–245° (dec.).

*Anal.* Calcd. for $C_{28}H_{35}O_5N{\cdot}CH_3I$: C, 57.3; H, 6.3; I, 20.9. Found: C, 57.0; H, 6.1; I, 20.6.

This base was also obtained by the hydrogenation of dihydroflavothebaone trimethyl ether methine.

*Flavothebaone trimethyl ether desazamethine* (I, R = CH=$CH_2$). Flavothebaone trimethyl ether methine (20 g.) was heated with 30% hydrogen peroxide for 30 min. on the steam bath and the light yellow solution then evaporated to dryness at 100°C./20 mm. The *N*-oxide was decomposed by heating to 170°C./15–20 mm. in an oil bath. The brown residue was crushed in a mortar, washed with 2*N* hydrochloric acid and then water, and digested with alcohol (50 ml.) for 15 min. on the steam bath. After cooling, the product was collected and washed with alcohol: yield, 12 g. (67%), m.p. 226–232°C. Recrystallization from ethanol afforded *flavothebaone trimethyl ether desazamethine* as white needles, m.p. 233–234°C., $[\alpha]^{21}_{D}$ −71.5° ($CHCl_3$ c 1.37), $\lambda_{max}$ 2300; 2750; 3100 Å: $\epsilon_{max}$ 27,000; 11,500; 5620. It was light sensitive in the same way as the methine.

*Anal.* Calcd. for $C_{26}H_{24}O_5$: C, 75.0; H, 5.8. Found: C, 74.7; H, 5.9.

*Flavothebaone trimethyl ether desaza-ψ-methine* (III, R= CH=$CH_2$). Flavothebaone trimethyl ether ψ-methine (5 g.) was heated with 30% hydrogen peroxide (5 ml.) on the steam bath for 30 min. and the deep red solution then evaporated to dryness at 80°C./20 mm. The ψ-methine *N*-oxide was decomposed at 160–170°C./0.05 mm. to give a black tar, which was extracted with warm benzene and filtered from insoluble material. The benzene solution was washed with 2*N* hydrochloric acid, then water, dried (sodium sulfate), and concentrated to about 20 ml. Petroleum ether (b.p. 50–60°C.) was added to produce a faint turbidity and this solution passed down an alumina column. A blue fluorescent band (ultraviolet light) was eluted with benzene, and after evaporation, afforded 1 g. of a light yellow oil. Trituration with alcohol gave 0.7 g. of pale yellow crystalline material, m.p. 160–163°C. Further recrystallizations from methanol afforded the pure *flavothebaone trimethyl ether desaza-ψ-methine* as very pale yellow needles, m.p. 167–168°C., $[\alpha]^{24}_{D}$ +142° ($CHCl_3$, c 1.22) $\lambda_{max}$ 2300; 2650; 3150 Å; $\epsilon_{max}$ 20,900; 14,900; 5910.

*Anal.* Calcd. for $C_{25}H_{26}O_5$: C, 73.9; H, 6.4. Found: C, 73.6; H, 6.2.

*Alkaline rearrangement of flavothebaone trimethyl ether desazamethine to the desaza-ψ-methine.* Flavothebaone trimethyl ether desazamethine (5 g.) and a solution of potassium hydroxide (40 g.) in alcohol (200 ml.) and water (20 ml.) were boiled under reflux for 6 hr. The solution was then cooled, water (200 ml.) was added and the product collected. Recrystallization from methanol gave 2.8 g. (57%) of the desaza-ψ-methine as brown needles m.p. 165–168°C. Further recrystallization from methanol afforded the product as pale yellow needles m.p. 167–168°C. undepressed on mixing with the desaza-ψ-methine prepared by the degradation of ψ-methine *N*-oxide.

*Flavothebaone trimethyl ether dihydrodesaza-ψ-methine* (III, R=Et). The desaza-ψ-methine (1 g.) in glacial acetic acid (20 ml.) was hydrogenated over platinum oxide (0.05 g.) when 1 mole of hydrogen was absorbed. The catalyst was removed and water added to the filtrate to give a quantitative yield of product, m.p. 160–163°C. Recrystallization from ethanol afforded *flavothebaone trimethyl ether dihydrodesaza-ψ-methine* as white prisms m.p. 163°C.; $[\alpha]^{23}_{D}$ +268° ($CHCl_3$, c 1.11) $\lambda_{max}$ 2350; 2650; 3150 Å. $\epsilon_{max}$ 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) $\lambda_{max}$ 2200; 3000 Å. $\epsilon_{max}$ 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=CH₂). 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). $\lambda_{max}$ 2250; 3000 Å. $\epsilon_{max}$ 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) $\lambda_{max}$ 2200; 2850 Å. $\epsilon_{max}$ 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) $\lambda_{max}$ 2950 Å; $\epsilon_{max}$ 4467.

*Anal.* Calcd. for $C_{25}H_{26}O_5$: 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) $\lambda_{max}$ 2250; 2825 Å. $\epsilon_{max}$ 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

K. W. BENTLEY AND J. P. RINGE

*Received September 25, 1956*

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).