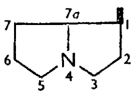
922. *The* Senecio *Alkaloids. Part XIII.** *The Absolute Configuration of Heliotridane* (1-*Methylpyrrolizidine*) *and the* "*Necine*" *Bases.*

By F. L. Warren and M. E. von Klemperer.

Heliothidane is converted by three successive Hofmann reactions into (+)-3-methylheptane, from which the absolute configuration of heliotridane, and hence the "necine" bases, is deduced.

The several "necine" bases, which are hydroxylated 1-methylpyrrolizidines, have been extensively studied and assigned relative configurations at their asymmetric centres.[1] Leonard[2] has recently deduced an absolute configuration on the basis of a correlation between the molecular-rotational shifts of *iso*retronecanol and (—)-lupinine, the structure of the latter being fully defined by Cookson[3] on the basis of the degradation by Karrer and his co-workers to (—)-4-methylnonane.[4]

We have now degraded heliotridane (I) to (+)-3-methylheptane which is assigned configuration (IV) (*D* on Klyne's symbolism,[5] *S* on that of Cahn, Ingold, and Prelog[6]), and have so established conclusively, but contrary to the deductions from molecular rotational shifts,[2] that the orientation of heliotridane at position 1 is *S* (Cahn, Ingold, and Prelog's symbolism[6]).



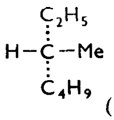
(I)

$C_3H_7\cdot CH(NMe_2)\cdot CHMe\cdot C_2H_5$

(II)

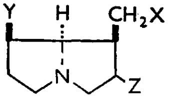
$C_2H_5\cdot CH{=}CH\cdot CHMe\cdot C_2H_5$

(III)

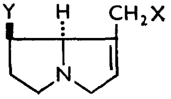


$$H-\overset{C_2H_5}{\underset{C_4H_9}{C}}-Me$$

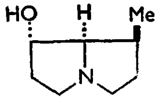
(IV)



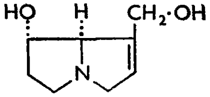
	X	Y	Z
(I) Heliotridane	H	H	H
(V) Platynecine	OH	OH	H
(VI) Retronecanol	H	OH	H
(VII) *iso*Retronecanol	OH	H	H
(VIII) Rosmarinecine	OH	OH	OH



	X	Y
(IX) Retronecine	OH	OH
(X) Deoxyretronecine	H	OH
(XI) Supinidine	OH	H



(XII) Oxyheliotridane



(XIII) Heliotridine

Heliotridane (I) has been obtained by several methods but the preparation from readily available material was best carried out by the following procedure. Retrorsine or isatidine was catalytically hydrogenolysed and then further hydrolysed to retronecanol[7, 8] which was dehydrated with sulphuric acid and reduced in the presence of platinum to heliotridane (I).[9] This was submitted to two successive Hofmann degradations with

---

* Part XII, *J.*, 1955, 65.

[1] Cf. Warren, *Progress Chem. Org. Natural Products*, 1955, **12**, 198; Adams and Gianturco, *Angew. Chem.*, 1957, **69**, 5.

[2] Leonard, *Chem. and Ind.*, 1957, 1455.

[3] Cookson, *ibid.*, 1953, 337.

[4] Karrer, Canal, Zohner, and Widner, *Helv. Chim. Acta*, 1928, **11**, 1062.

[5] Klyne, "Progress in Stereochemistry," Butterworths, London, 1954, p. 205.

[6] Cahn, Ingold, and Prelog, *Experientia*, 1956, **12**, 85.

[7] Barger, Seshadri, Watt, and Yabuta, *J.*, 1935, 11.

[8] Leisegang and Warren, *J.*, 1949, 486.

[9] Konawolowa and Orékhoff, *Bull. Soc. chim. France*, 1937, 1285; cf. Adams and Rogers, *J. Amer. Chem. Soc.*, 1941, **63**, 228.

reduction at each stage as described by Men'shikov[10] to give 4-dimethylamino-3-methylheptane (II). This amine (II) has now been converted into its methiodide which by a third Hofmann reaction yielded a hydrocarbon envisaged in accordance with the Hofmann rule[11] as 5-methylhept-3-ene (III). This methylheptene was reduced catalytically to partially racemised (+)-3-methylheptane (IV), $[\alpha]_D$ +4·1°, compared with the value $[\alpha]_D$ +4·6° given by Levene and Marker[12] for their synthetic product or +12·0° for their calculated maximum rotation.

The ready dehydration of platynecine to anhydroplatynecine[13] necessitates that the methyl group in heliotridane must be *trans* to the 7*a*-hydrogen atom,[14] so that Men'shikov's (−)-heliotridane is now (1*S*,7*aS*)-1-methylheliotridane (I).

The absolute configurations of the hydroxy-derivatives of this (1*S*,7*aS*)-1-methylpyrrolizidine pivot on the relative orientation of the hydroxyl groups of platynecine which is fully established by two different methods (Adams and Van Duuren[15] and by these laboratories[16]) and which now becomes (1*S*,7*R*,7*aR*)-1 : 7-bishydroxymethylpyrrolizidine (V). The structures of retronecanol[7] (VI), *iso*retronecanol[17] (VII), rosmarinecine[16,18] (VIII), retronecine[14] (IX), isatinicine (retronecine *N*-oxide),[8] deoxyretronecine[8] (X), and supinidine[19] (XI) follow logically from their structural relations with platynecine. The change in the orientation of the 7-hydroxyl group of retronecanol and retrorsine then gives oxyheliotridane[17] (XII) and heliotridine[17] (XIII) respectively.

EXPERIMENTAL

4-*Dimethylamino*-3-*methylheptane*.—Heliotridane, b. p. 166°/700 mm., d_4^{16} 0·940, $[\alpha]_D^{16}$ −111° (pure liquid) (Adams and Rogers[20] give b. p. 165—166°, d_4^{34} 0·911, $[\alpha]_D^{14}$ −91°), was submitted twice to the Hofmann degradation and reduction of the product at each stage as described by Men'shikov,[10] to give 4-dimethylamino-3-methylheptane, b. p. 180°/700 mm., $[\alpha]_D^{20}$ −0·59° (pure liquid), d_4^{20} 0·948 (Found: C, 76·4; H, 14·5. Calc. for $C_{10}H_{23}N$: C, 76·35; H, 14·7%). Men'shikov[10] gives b. p. 180—181°.

The tertiary base (8 g.) in acetone (20 ml.) was treated slowly with methyl iodide (5 ml., 1·5 mol.) in acetone (10 ml.). The product crystallised from acetone, to give the *methiodide*, m. p. 184°, $[\alpha]_D^{26}$ +5·9° (*c* 1 in ethanol) (Found: C, 44·0; H, 8·9. $C_{11}H_{26}NI$ requires C, 44·1; H, 8·7%).

3-*Methylheptane*.—The methiodide (16 g.) in water was stirred for 12 hr. with silver oxide, prepared from silver nitrate (9 g.). The solution was evaporated to dryness under reduced pressure at 40°, and then at 130°/20 mm. with a cold trap at −70°. The distillate was taken up in ether, and the solution washed, dried, and distilled, to give 5-methylhept-3-ene (1·35 g.), b. p. 110—120°, $[\alpha]_D^{20.5}$ −1·7° (*c* 18 in methanol).

5-Methylhept-3-ene (1·0 g.) in methanol in the presence of platinum oxide absorbed 200 ml. of hydrogen in 20 min. The product was poured into water, taken up in ether, washed and evaporated through a fractionating column. The product distilled at 110—115° to a colourless liquid, d_4^{19} 0·720, $[\alpha]_D^{20.5}$ +4·1° (Found: C, 84·6; H, 15·8. Calc. for C_8H_{18}: C, 84·1; H, 15·9%). Levene and Marker[12] give d_4^{22} 0·710, $[\alpha]_D^{22}$ +4·55°.

The authors gratefully acknowledge grants to assist this work from the South African Council for Scientific and Industrial Research and from African Explosives and Chemical Industries.

DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, UNIVERSITY OF NATAL,
PIETERMARITZBURG, SOUTH AFRICA.
[*Received, June* 16*th*, 1958.]

[10] Men'shikov, *Ber.*, 1935, **68**, 1555; *Bull. Acad. Sci. U.R.S.S. Ser. Chim.*, 1937, 1035 (*Brit. Abs.*, AII, 1938, 162).

[11] Hanhart and Ingold, *J.*, 1927, 997.

[12] Levene and Marker, *J. Biol. Chem.*, 1931, **91**, 763.

[13] Konowalowa and Orechoff, *Ber.*, 1935, **69**, 1908.

[14] Leonard and Felly, *J. Amer. Chem. Soc.*, 1950, **72**, 2537; cf. refs.

[15] Adams and Van Duuren, *J. Amer. Chem. Soc.*, 1954, **76**, 6379.

[16] Dry, Koekemoer, and Warren, *J.*, 1955, 59.

[17] Men'shikov and Kurzokov, *J. Gen. Chem. U.R.S.S.*, 1949, **19**, 1702.

[18] Richardson and Warren, *J.*, 1943, 452.

[19] Men'shikov and Gurevich, *J. Gen. Chem. U.R.S.S.*, 1949, **19**, 1382.

[20] Adams and Rogers, *J. Amer. Chem. Soc.*, 1941, **63**, 234.