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THE EMDE DEGRADATION OF RHOEADINE AND RHOEAGENINE METHIODIDES

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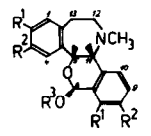
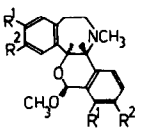
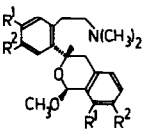
In connection with a systematic investigation of the alkaloids of Papaver rhoeas, we have studied[1] the chiroptical properties of some rhoeadine (B/D cis) (I) and isorhoeadine (B/D trans) (II) derivatives. By the Emde degradation of rhoeadinemethiodide (I.CH_3I), we obtained the substance (+)-III. Very recently, Rönsch[2] reported that the main products of the Emde degradation of the methiodides of 1-epi-alpinine (B/D cis) (IV) and O-methyl-alpinigenine (B/D trans) (V) (Ref.[3]) are (-)-VI and (+)-VI. Since the alkaloids rhoeadine (I) and 1-epi-alpinine (IV) have the same absolute configuration at all the centers of chirality[4,5], these two substances give rise to the products III and VI whose CD spectra should be similar to each other; the CD bands at c. 280 nm have, however, opposite signs (Table 1). This finding induced us to study the Emde degradation of rhoeadine (I) and rhoeagenine (VII) in more detail.



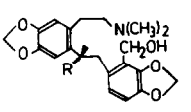
I $R^1+R^2=OCH_2O$, $R^3=CH_3$
IV $R^1=R^2=OCH_3$, $R^3=CH_3$
VII $R^1+R^2=OCH_2O$, $R^3=H$



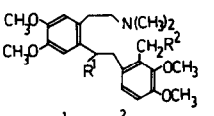
II $R^1+R^2=OCH_2O$
V $R^1=R^2=OCH_3$



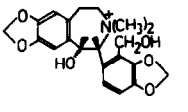
III $R^1+R^2=OCH_2O$
(-)-VI $R^1=R^2=OCH_3$



VIII R=H
XI R=OH



IX $R^1=OH$, $R^2=H$
X $R^1=H$, $R^2=OH$



XII

An aqueous suspension of rhoeadinemethiodide (I.CH_3I) was treated with sodium amalgam (3%), the mixture left standing for 24 h at room temperature, and subjected to column chromatography on alumina. The main reaction product was the already earlier described[1] substance III (m.p. 134-35°). The more polar fractions gave the optically inactive substance VIII (m.p. 136-37°, acetate m.p. 71-73°) whose PMR spectrum (Table 2) is consistent with the proposed structure. For the side product of the Emde degradation of 1-epi-alpinine (IV), Rönsch[2] proposed structure IX ($[\alpha]_D^{23}$ -4.6° in methanol). Since the PMR spectrum of the substance VIII resembles that of the Rönsch product (Table 2), the substance IX (Ref.[2]) has the correct structure X. The structure X is supported by the singlets at 2.87 ppm (Ar-CH_2-CH_2-Ar) and 4.72 ppm (Ar-CH_2-OH).

The aqueous suspension of rhoeageninemethiodide (VII.CH_3I) was mixed with sodium amalgam (3%) and left standing for 24 h at room temperature to afford a mixture of three substances. Column chromatography on alumina gave two substances in pure state. The main reaction product was a substance of m.p. 135-36°. On the basis of the PMR spectral data (Table 2), this substance has structure XI. The IR and PMR spectra show that the minor substance of m.p. 136-37° (optically inactive) is identical with the side product VIII obtained by the Emde degradation of rhoeadinemethiodide (I.CH_3I).

Reduction of rhoeageninemethiodide (VII.CH_3I) with sodium borohydride in water gave rhoeageninediolmethiodide (XII) in quantitative yield. The Emde degradation of this compound afforded the same products as those obtained from rhoeageninemethiodide (VII.CH_3I). Obviously, the Emde degradation of rhoeageninemethiodide (VII.CH_3I) is a two step process, i.e. reduction of the half-acetal group of VII.CH_3I is followed by the Emde degradation.

Since the results of this work are at variance with the results published in paper[2], further studies are required to gain deeper insight into the stereochemistry of the products of the Emde degradation of alkaloids with a trans-rheadane skeleton.

Table 1 Optical Rotatory Values and CD Data

Compound	$[\alpha]_D$	λ nm($\Delta\varepsilon$), EtOH	λ nm($\Delta\varepsilon$), HCl/EtOH
III (ref.[1])	+15°(MeOH)	296(−3.50), 279(+1.39), 241(+2.74), 227(−0.87)	297(−2.10), 279(+0.97), 243(+1.50), 230(−0.90)
VI[a] (ref.[2])	+14°(MeOH)	282(+1.01)[c]	
VI[b] (ref.[2])	−15°(MeOH)	282(−1.01)[c]	
XI	+112°(MeOH) +63°($CHCl_3$)	296(+2.29), 242(+5.90)	296(+4.02), 238(+5.66)
Diacetate of XI	+64°(MeOH)	298(+3.69), 278(−0.37), 239(+4.58)	298(+3.06), 272(−0.32), 241(+4.13)

[a] from V, [b] from IV, [c] in MeOH

Table 2 PMR Spectral Data[6]

	III (ref.[1])	VIII	Acetate of VIII	X (ref.[2])	XI	Diacetate of XI
H-1,4	6.70s (1H) 7.08s (1H)	6.58s (1H) 6.70s (1H)	6.63s (1H) 6.72s (1H)	6.61s 6.65s	6.58s (1H) 7.02s (1H)	6.57s (1H) 6.87s (1H)
H-5	5.30q (1H) J = 15.0	2.82s (4H)	2.77s (4H)	2.87s	4.92q (1H) J = 13.5	6.08q (1H) J = 14.0
H-11	2.4-3.1m (2H)				2.3-3.3m (2H)	2.3-3.3m (2H)
H-6	5.72s (1H)	4.70s (2H)	5.13s (2H)	4.72s	4.70s (2H)	5.08s (2H)
H-9,10	6.57d (1H) 6.80d (1H) J_{ortho}=8.0	6.65s (2H)	6.68s (2H)	6.82q J=8.5	6.67s (2H)	6.40d (1H) 6.63d (1H) J_{ortho}=8.0
H-12,13	2.4-3.1m (4H)	2.1-3.0m (4H)	2.2-3.0m (4H)		2.3-3.3m (4H)	2.3-3.3m (4H)
$N(CH_3)_2$	2.27s (6H)	2.27s (6H)	2.30s (6H)	2.31s	2.10s (6H)	2.23s (6H)
O-CH_2-O	5.93s (2H) 6.02q (2H) J_{gem}=1.2	5.88s (2H) 5.93s (2H)	5.90s (2H) 5.98s (2H)	– –	5.93s (2H) 5.97s (2H)	5.90s (2H) 5.92s (2H)
CH_3CO	–	–	2.07s (3H)	–	–	1.98s (3H) 2.07s (3H)
CH_3O	3.53s (3H)	–	–	3.85-3.90	–	–

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2. H. Rönsch, Tetrahedron Letters 1972, 4431.
3. The substance IV has already earlier been designated cis-alpinine and the substance V epialpinine; the prefix epi- is used only for alkaloids with a trans-rheadane skeleton and stable configuration at C-6 (M. Shamma, J.A. Weiss, S. Pfeifer, and H. Döhnert, Chem. Commun. 1968, 212).
4. M. Shamma, J.L. Moniot, W.K. Chan, and K. Nakanishi, Tetrahedron Letters 1971, 4207.
5. C.S. Huber, Acta Cryst. B28, 982 (1972).
6. PMR spectra were measured in $CDCl_3$ with TMS as internal standard at 60 MHz. The numbering system of all the compounds is the same as in formula I.