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SYNTHESIS OF HOMOPROAPORPHINE RELATED COMPOUNDS

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Catalytic hydrogenation of the enone **III** on platinum oxide gave a mixture of the alcohols VIa and VIb, but on palladium-charcoal afforded the ketone V, which was also obtained from VIb. Treatment of the alcohol VIa or VIb with hydrogen on platinum oxide yielded an epimeric mixture of VIa and VIb.

Previously we have reported a synthesis of (±)-kreysiginone (I) and its epimer (II),[1] and a stereochemical study in a catalytic reduction of both compounds.[2] In this communication we wish to describe on the structure of reduced products of the enone III,[3] derived from II, under several conditions.

Treatment of the dienone II, whose stereochemistry was determined,[3,4] with concentrated hydrochloric acid in glacial acetic acid at 20 - 25° for 24 h gave the enone (III), mp 197 - 198°

(lit.,[3] mp 197 - 198°), in 62 % yield in addition to the known homoaporphine (IV), mp 241 - 243° (lit.,[3] mp 241 - 242°). The structure of III was determined by ir [ν_{max} (KBr) 1690 cm^{-1}], mass [m/e 341 (M^+)] and nmr [δ ($CDCl_3$) 2.17 (2H, d, J 2.0 Hz, C_{13} - H_2), 3.61 (3H, s, OCH_3), 5.93 (1H, d, J 10.5 Hz, C_{10} - H), and 6.90 (1H, dd, J 10.5 and 2 Hz, C_9 - H) spectra.[3]

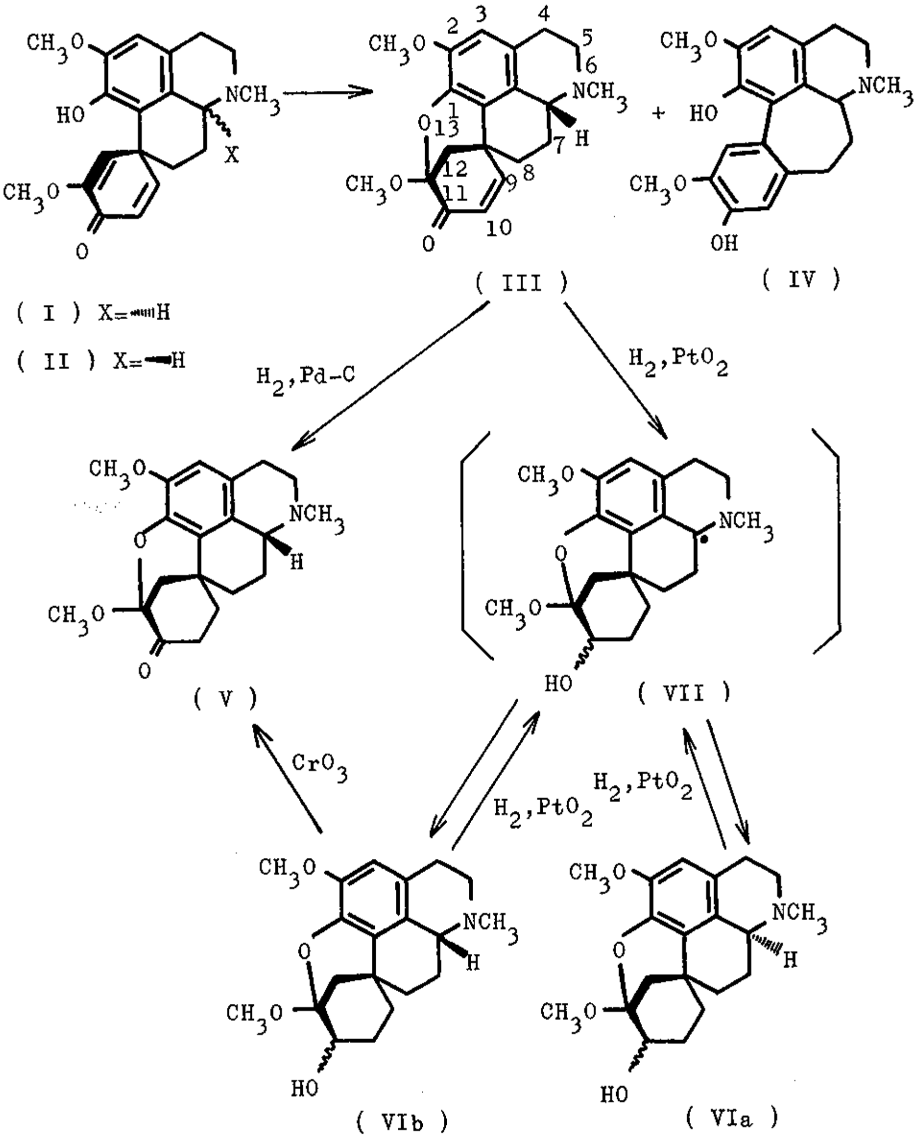
Catalytic reduction of this enone III on 20 % palladium-charcoal in ethanol at room temperature and atmospheric pressure afforded in 63 % yield the cyclohexanone derivative V, which was characterised as methiodide, mp 255 - 257° (decomp.). The free base (V) revealed the presence of cyclohexanone system at 1730 cm^{-1} in ir spectrum ($CHCl_3$), and nmr spectrum ($CDCl_3$) showed three methyl resonances at 2.39 (NCH_3, s), 3.56 (aliphatic OCH_3, s) and 3.79 (aromatic OCH_3, s) and an aromatic proton at 6.53 but no olefinic proton.

On the other hand, hydrogenation of III on platinum oxide in methanol at room temperature and atmospheric pressure gave a mixture of the cyclohexanols VIa and VIb in a ratio of 1 : 2, which were separated by silica gel column chromatography. The first eluate furnished VIa, one of the cyclohexanols as colourless prisms, mp 113 - 115°, and the other VIb was characterised as methiodide, mp 250 - 252° (decomp.). The ir spectrum (KBr) of both cyclohexanols showed hydroxyl group at 3560 cm^{-1} but lacked carbonyl absorption. The nmr ($CHCl_3$) spectrum of the former revealed signals at 2.42 (NCH_3, s), 3.40 (aliphatic OCH_3, s), 3.83 (aromatic OCH_3, s) and 6.57 (aromatic H, s), and that of the second one (VIb) showed closely similar resonances at 2.36 (NCH_3, s), 3.36 (OCH_3, s), 3.80 (OCH_3, s) and 6.52 (aromatic H, s). An oxidation of the second cyclohexanol VIb with chromic anhydride-pyridine complex[5] in methylene chloride at room temperature gave the cyclohexanone V [methiodide, mp 254 - 256° (decomp.)] which was identical with the sample V, prepared from the enone III by direct reduction, in ir spectral comparison. However, oxidation of the first cyclohexanol VIa under the same condition in case of VIb afforded a tarry oil, ν_{max} 1720 cm^{-1}, which was different from the cyclohexanone V.

On the ground of this fact, the second cyclohexanol could be assigned the structure VIb which had the relative configuration between the C_{6a}-hydrogen and the C_{8a}-C_9 bond to be cis, but the stereochemistry of a hydroxyl group could not be determined. The first cyclohexanol would be assigned trans isomer VIa. Both cyclohexanols VIa and VIb were treated with hydrogen over platinum oxide in methanol to give a same mixture of two cyclohexanols VIa and VIb in a ratio of 1 : 2. It has been well known that in a hydrogenation on the platinum, catalyst abstracts the C_1-hydrogen in 1-monosubstituted 1,2,3,4-tetrahydroisoquinoline ring to form the radical, which is then hydrogenated to afford a mixture of the starting material and C_1-epimer.[2,6] This supports that the first cyclohexanol is assigned structure VIa and that the cyclohexanone III was absorbed on the catalyst and then homolytic removal of the hydrogen at the C_{6a}-position gave an intermediate VII which was then reduced to the cyclohexanols VIa and VIb.

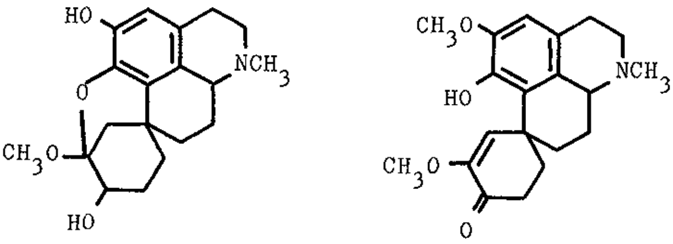
The above hydrogenation demonstrates the second epimerisation of the homoproaporphine system in the presence of platinum catalyst.[2]

Chart 1


(I) X=H
(II) X=H
(III)
(IV)
(V)
(VII)
(VIb)
(VIa)
H2,Pd-C
H2,PtO2
H2,PtO2
H2,PtO2
CrO3
CH3O
HO
NCH3
O
OH
1
2
3
4
5
6
7
8
9
10
11
12
13

Recently, Šantavý[7,8] isolated a new alkaloid, kesselringine (VIII) which has a similar structure to our product VI. From our work and the isolation of dihydrokreysiginone (IV),[9] the cyclohexanone V or the cyclohexanols VIa and VIb would be an intermediate for the biogenesis of kesselringine (VIII) from kreysiginone (I) and dihydrokreysiginone (IX).

Chart 2



(VIII) (IX)

The attempted elucidation of the configuration of the cyclohexanols VIa and VIb is currently in progress.

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