

CATALYTIC HYDROGENATION OF (\pm)-KREYSIGINONE

Tetsuji Kametani,* Fumio Satoh, and Keiichiro Fukumoto

Pharmaceutical Institute, Tohoku University, Aobayama, Sendai, Japan

Hideo Sugi and Kazuo Kigasawa

Grelan Pharmaceutical Co. Ltd., Sakurashinmachi, Setagayaku, Tokyo, Japan

Catalytic hydrogenation of the isomeric homoproaporphines (Va and Vb) and the deuterated dienones VIa and VIb in the presence of platinum afforded the same mixture of cyclohexanols (VIIa and VIIb). In contrast, palladium reduction of the hydrochloride of Va provided the cyclohexanone (VIIIa) while that of Vb gave a mixture of the cyclohexanone (VIIIb) and the cyclohexenone (IX).

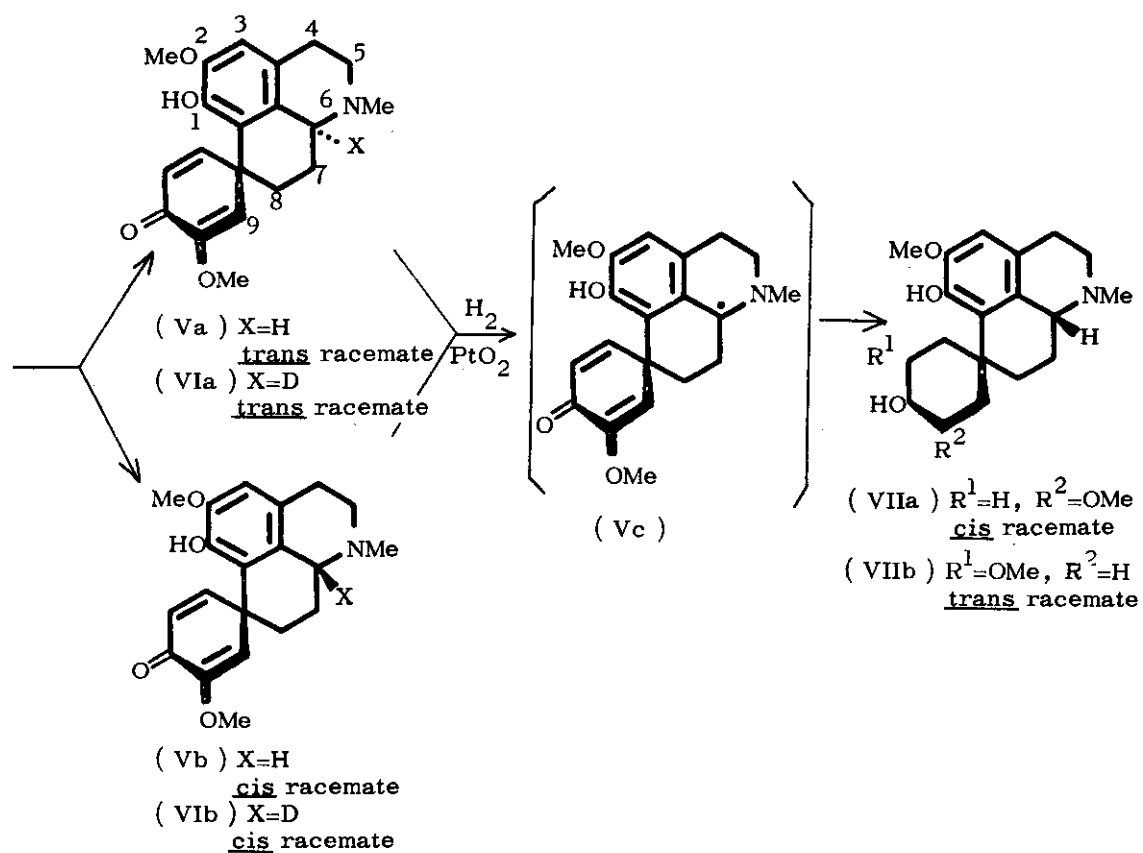
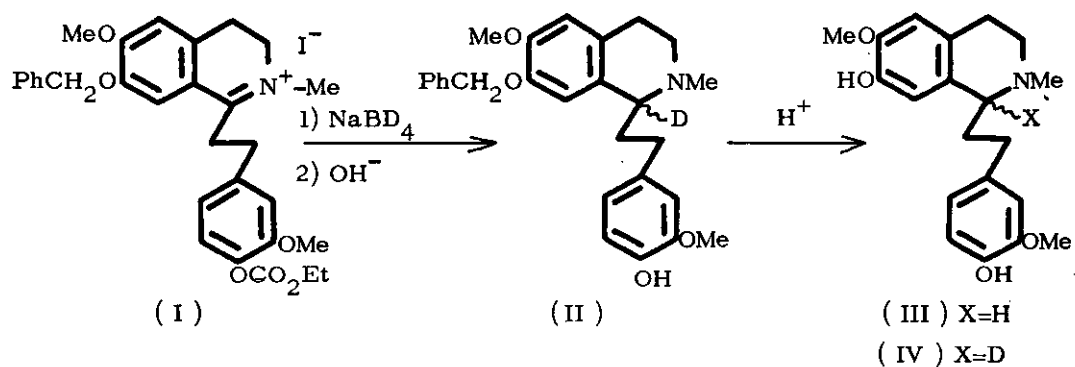
In a previous study involving the homoproaporphine alkaloid kreysiginone, we described the synthesis and separation of the two isomeric dienones (Va and Vb), obtained by phenolic oxidation of the diphenolic phenethylisoquinoline (III).¹ Since hydrogenation experiments have been shown to be useful in establishing the configuration of reduced morphinandienones,² we now report the results of hydrogenating the two dienones (Va and Vb) in the presence of platinum and palladium catalysts.

Catalytic hydrogenation of either of the isomeric dienones (Va and Vb) in methanol in the presence of platinum oxide afforded a mixture of the cyclo-

hexanols (VIIa and VIIb). Trituration of the mixture with benzene and crystallization of the resulting solid from methanol gave one of the cyclohexanols (VIIa or VIIb) as needles, mp $196 - 198^{\circ}$ (decomp.). The other cyclohexanol (VIIa or VIIb) was characterized as its hydrochloride, prisms from ethanol-ether, mp $257 - 259^{\circ}$ (decomp.). The nmr spectrum of the free base of the first cyclohexanol (in CDCl_3) showed signals at 2.42 (NMe, s), 3.42 (aliphatic OMe, s), 3.60 ($\text{C}_{6a}\text{-H}$, broad signal), 3.85 (aromatic OMe, s), and 6.48 ppm ($\text{C}_3\text{-H}$), and that of the second isomer revealed a closely similar resonances. The structures of both cyclohexanols (VIIa and VIIb) were supported by other physical data.

In view of this conversion of both dienones (Va and Vb) into a mixture of the same cyclohexanols (VIIa and VIIb) and based on a previous study regarding the configuration of homoproaporphines,³ the relative configuration between the $\text{C}_{6a}\text{-hydrogen}$ and the $\text{C}_{8a}\text{-C}_9$ bond of the cyclohexanone system of Va and Vb should be trans and cis, respectively. It would appear that the platinum catalyst abstracts the $\text{C}_{6a}\text{-hydrogen}$ from the dienones (Va and Vb) to give the common intermediate (Vc), which is then hydrogenated to afford the same products (VIIa and VIIb). A similar behavior was noted when optically active protoberberines and 1-benzylisoquinolines were catalytically hydrogenated with platinum catalyst to furnish the corresponding racemic products.⁴

In addition, the dienones (VIa and VIb) deuterated at the $\text{C}_{6a}\text{-position}$, synthesized by reduction of the dihydroisoquinoline methiodide (I) with sodium borodeuteride to the tetrahydroisoquinoline (II) followed by acid-catalyzed debenzylation and phenolic oxidation of the resulting diphenolic 1- d_1 -tetrahydroisoquinoline (IV), were hydrogenated over platinum oxide to give the same cyclohexanols (VIIa and VIIb) obtained from dienones (Va and Vb). This supports the hypothesis that all

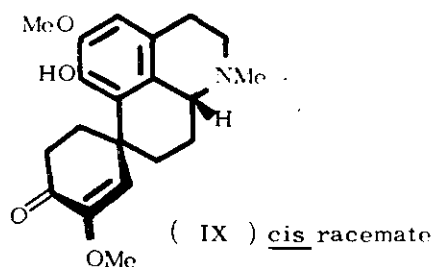
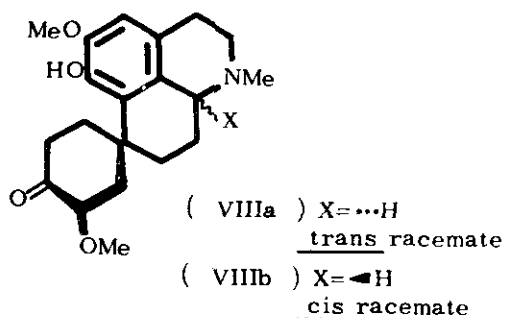


the dienones are absorbed on the catalyst followed by homolytic removal of the hydrogen at the C_{6a}-position to give the common intermediate (Vc) which is then reduced to the same products (VIIa and VIIb).

On the other hand, catalytic hydrogenation of the dienone (Va) hydrochloride in the presence of 10 % palladium-on-charcoal afforded the cyclohexanone (VIIIa): ν_{\max} 1720 cm⁻¹ (C=O); nmr spectrum (in CDCl₃) revealed three methyl resonances at 2.43 (NMe, s), 3.43 (aliphatic OMe, s), and 3.80 ppm (aromatic OMe, s).

In contrast, the same treatment of the dienone (Vb) gave a mixture of the cyclohexanone (VIIIb) and the cyclohexenone (IX). The latter compound was isolated as leaves, mp 198 - 200° (decomp.) (from methanol). Its ir [ν_{\max} (KBr) 1672 and 1620 cm⁻¹ (C=C)] spectrum was in good accord with a cyclohexenone system and its nmr (in CDCl₃) spectrum showed signals at 2.45 (NMe, s), 3.62 (olefinic OMe, s); 3.90 (aromatic OMe, s) and 5.90 ppm (C₉-H, s).

The above hydrogenations demonstrate the novel epimerization of the homo-proaporphines (Va and Vb) in the presence of platinum catalyst. The attempted elucidation of the configuration of the resulting cyclohexanols (VIIa and VIIb) is currently in progress.



ACKNOWLEDGEMENT We thank Miss R. Kato, Miss C. Yoshida, Mrs. A. Sato, Mrs. C. Koyanagi, and Miss A. Ujiie for spectral measurements and microanalyses.

REFERENCES

- 1 T. Kametani, K. Fukumoto, H. Yagi, and F. Satoh, Chem. Commun., 1967, 878; J. Org. Chem., 1968, 33, 690.
- 2 L. J. Haynes, G. E. M. Husbands, and K. L. Stuart, J. Chem. Soc. (C), 1968, 951.
- 3 T. Kametani, F. Satoh, H. Yagi, and K. Fukumoto, J. Chem. Soc. (C), 1970, 382.
- 4 T. Kametani and M. Ihara, J. Chem. Soc. (C), 1968, 191; T. Kametani, M. Ihara, and K. Shima, J. Chem. Soc. (C), 1968, 1619.

Received, 1st August, 1973