HETEROCYCLES, Vol. 2, No. 6, 1974

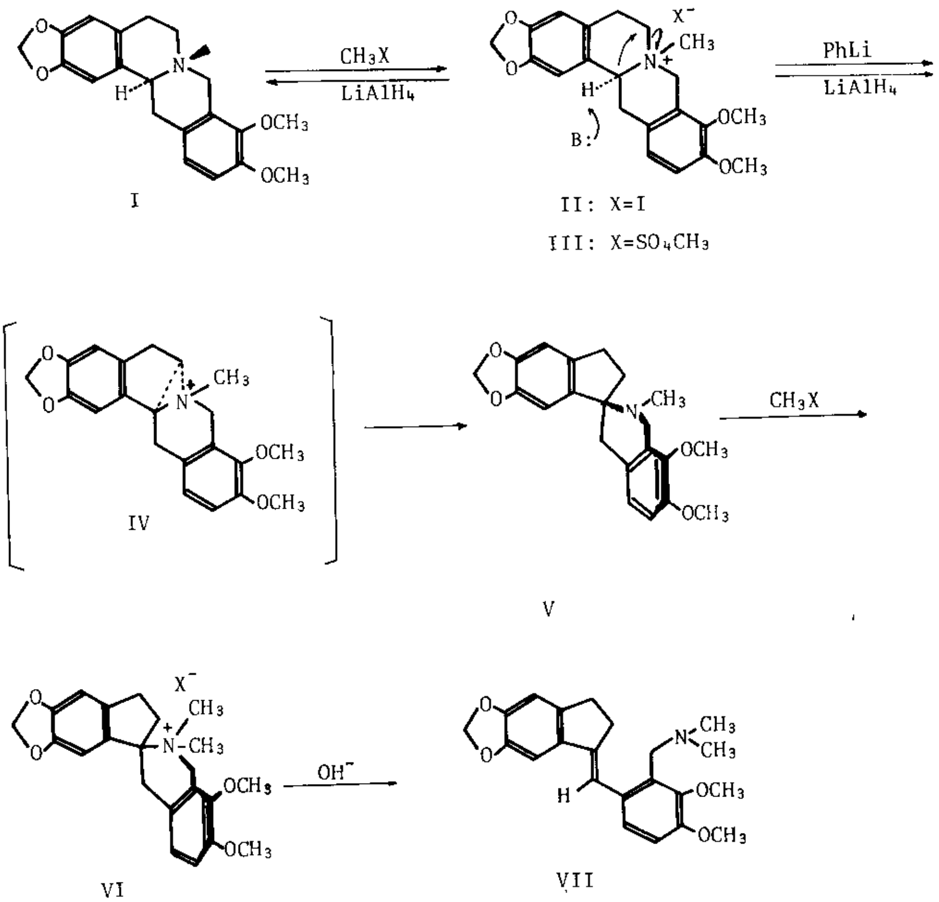
PHENYLLITHIUM-INDUCED REARRANGEMENT OF N-METHYLTETRAHYDROBERBERINIUM SALTS

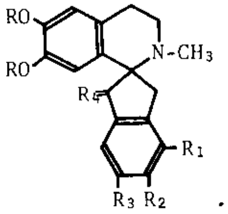
Yoshikazu Kondo* and Tsunematsu Takemoto
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai, Japan
and
Kazue Kondo
Chemical Research Institute of Non-Aqueous Solutions
Tohoku University, Katahira-cho, Sendai, Japan

In the presence of phenyllithium or lithium alanate, *dl*-*N*-methyltetrahydroberberinium salts underwent rearrangement to *N*-methyl-7,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-spiro-1´-5´,6´-methylenedioxyindane (V). The structure of V has been proven by chemical and spectral means.

Although several light- and base-induced rearrangements of the phenolic protoberberinium salts into the ochotensine type alkaloids (VIII-X) were reported[1-5], the non-phenolic protoberberinium salts were quite stable to these reagents.

When *dl*-*N*-methyltetrahydroberberinium salts were treated with phenyllithium under Stevens rearrangement conditions a tertiary base (V), mp 117-118°, was obtained by alumina column chromatography (12-25% yield). Compound V showed the composition $C_{21}H_{23}O_4N$, which was established by mass spectral (M^+ 353) and elemental analyses[6], and gave a picrate, mp 237-238° (decomp.), $C_{27}H_{26}O_{11}N_4$. V revealed absorption maxima in the uv spectrum at 230 nm (sh. ε 13170) and 287





VIII: $R_1=R_2=OH$, $R_3=H$, $R_4=CH_2$

IX: $R_1=H$, $R_2=R_3=OH$, $R_4=CH_2$

X: $R_1=R_2=OCH_3$, $R_3=H$, $R_4=H_2$

nm (ε 5830) showing the presence of the tetrahydroisoquinoline nucleus. The nmr spectrum ($CDCl_3$) showed signals at δ 2.26 (s, $>N-CH_3$), 2.85 (m, 4H, methylenes), 3.30 (m, 4H, methylenes), 3.83 (s, 2 × $-OCH_3$), 5.77 (s, $-O-CH_2-O-$), 6.41 (s, benzene H), 6.56 (s, benzene H) and 6.78 ppm (s, 2 × benzene H). V readily reacted with methyl iodide or dimethyl sulfate to yield a dimethyl quarternary salt, amorphous solid (VI, X=I or SO_4CH_3).

The quarternary salt (VI) on treatment with caustic alkaline solution afforded a single methine base (VII), mp 118-119°, $C_{22}H_{25}O_4N$. Compound VII showed an absorption maximum at 298 nm (ε 17200) which resembled that of a stilbene[7]. The nmr spectrum of VII showed two multiplets (each 2H) at ca 2.5 and 2.8 ppm, and a triplet (1H, J=1.5 Hz) at 6.68 ppm which indicated the presence of the benzylideneindane structure, and a pair of doublets (each 1H, J=1.4 Hz) at 3.63 and 3.70 ppm assignable to an aminomethyl group. The methine base (VII) on treatment with methyl iodide afforded a quarternary iodide, which was unreactive to caustic alkaline solution under various conditions.

In the light of these results the structure of compound V was assigned to be *N*-methyl-7,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-spiro-1′-5′,6′-methylenedioxyindane.

Compound V was also obtainable in maximally 62.4% yield, together with tetrahydroberberine (I)[8], on refluxing of *N*-methyltetrahydroberberinium iodide (II) or the methosulfate (III) with lithium alanate in tetrahydrofuran.

Since this rearrangement may conform to the S_Ni mechanism[9], the conformation of the product is inevitably shown as V.

REFERENCES

1 M. Shamma and C. D. Jones, *J. Amer. Chem. Soc.*, *1969*, **91**, *4009*; *ibid.*, *1970*, **92**, *4943*.

2 M. Shamma and J. F. Nugent, *Tetrahedron Letters, 1970, 2625.*

3 Idem, *Chem. Commun., 1971, 1642; Tetrahedron, 1973,* **29**, *1265.*

4 B. Nalliah, R. H. F. Manske, R. Rodrigo, and D. B. MacLean, *Tetrahedron Letters, 1973, 2795.*

5 T. Kametani, M. Takemura, and K. Fukumoto, *Heterocycles, 1974,* **2**, *433.*

6 All compounds gave satisfactory elemental analyses.

7 P. B. Russell, *J. Amer. Chem. Soc., 1956,* **78**, *3115.*

8 M. Tomita and T. Ibuka, *Yakugaku Zasshi, 1962,* **82**, *1652.*

9 E. M. Kaiser and D. W. Slocum, 'Organic Reactive Intermediates', ed. by S. P. McManus, Academic Press, New York, 1973, p. 381.

Received, 2nd September, 1974