

PHENYLITHIUM-INDUCED REARRANGEMENT OF N-METHYLTETRAHYDROBERBERINIUM SALTS

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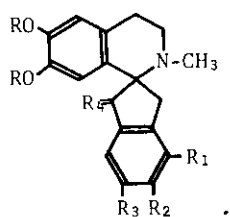
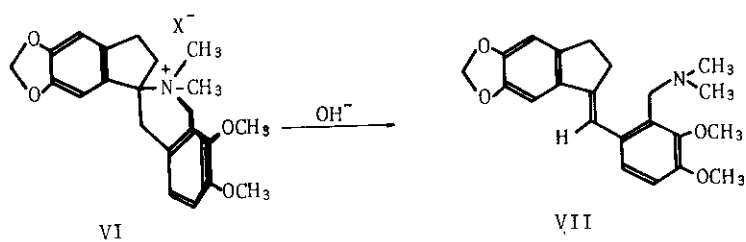
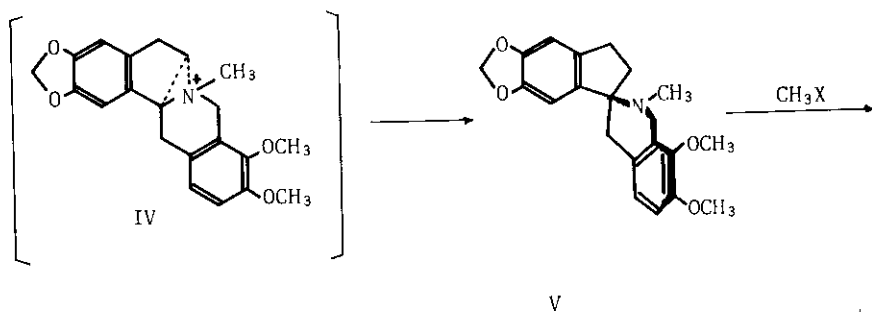
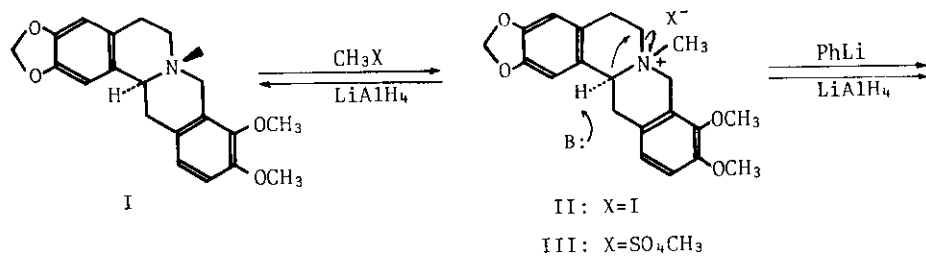
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In the presence of phenyllithium or lithium alanate, *dl*-*N*-methyltetrahydroberberinium salts underwent rearrangement to *N*-methyl-7,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-spiro-1'-5',6'-methylenedioxyindane (V). The structure of V has been 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<sup>1-5</sup>, 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<sup>6</sup>, 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.  $\epsilon$  13170) and 287



VIII: R<sub>1</sub>=R<sub>2</sub>=OH, R<sub>3</sub>=H, R<sub>4</sub>=CH<sub>2</sub>

IX: R<sub>1</sub>=H, R<sub>2</sub>=R<sub>3</sub>=OH, R<sub>4</sub>=CH<sub>2</sub>

X: R<sub>1</sub>=R<sub>2</sub>=OCH<sub>3</sub>, R<sub>3</sub>=H, R<sub>4</sub>=H<sub>2</sub>

nm ( $\epsilon$  5830) showing the presence of the tetrahydroisoquinoline nucleus. The nmr spectrum ( $\text{CDCl}_3$ ) showed signals at  $\delta$  2.26 (s,  $>\text{N}-\text{CH}_3$ ), 2.85 (m, 4H, methylenes), 3.30 (m, 4H, methylenes), 3.83 (s,  $2 \times -\text{OCH}_3$ ), 5.77 (s,  $-\text{O}-\text{CH}_2-\text{O}-$ ), 6.41 (s, benzene H), 6.56 (s, benzene H) and 6.78 ppm (s,  $2 \times$  benzene H). V readily reacted with methyl iodide or dimethyl sulfate to yield a dimethyl quarternary salt, amorphous solid (VI,  $\text{X}=\text{I}$  or  $\text{SO}_4\text{CH}_3$ ).

The quarternary salt (VI) on treatment with caustic alkaline solution afforded a single methine base (VII), mp 118-119°,  $\text{C}_{22}\text{H}_{25}\text{O}_4\text{N}$ . Compound VII showed an absorption maximum at 298 nm ( $\epsilon$  17200) which resembled that of a stilbene<sup>7</sup>. 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 benzyli-deneindane 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)<sup>8</sup>, on refluxing of *N*-methyltetrahydroberberinium iodide (II) or the methosulfate (III) with lithium alanate in tetrahydrofuran.

Since this rearrangement may conform to the  $\text{S}_{\text{Ni}}$  mechanism<sup>9</sup>, the conformation of the product is inevitably shown as V.

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