The authors wish to thank Dr. Setsuzo Tejima of the University of Hokkaido for his valuable discussion; Takeda Chemical Industries Co., Ltd. and Dai-ichi Seiyaku Co., Ltd. for their supplies of the starting materials; and members of the Central Analysis Room of this Faculty and those of Seikagaku-Kogyo Co., Ltd. for carrying out the elemental analyses.

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Received November 22, 1966

Chem. Pharm. Bull. 15(4) 545~547 (1967)

UDC 547.892.2.07

Tricyclic Amines from Azabicyclic Compounds through Carbenes

We have reported[1] our studies on the reactions of carbonium ions generated at 9-position of azabicyclo[3.3.1]nonane and 8-position of azabicyclo[3.2.1]octane. We now report on the extension of these studies to include reactions with carbenes at the same positions because these reactions would contribute to the conformations of these azabicyclic compounds.[2]

Sodium salt obtained from 3-methyl-3-azabicyclo[3.3.1]nonan-9-one[3] tosylhydrazone (I) of m.p. 186° (decomp.) was decomposed at 170° in Diglyme[4] to give a tricyclic amine (Ⅱ), $C_9H_{15}N$, b.p$_{77}$ 109~110°, in 67% yield (*Anal.* Calcd. for $C_9H_{15}N$: C, 78.77; H, 11.02; N, 10.21. Found: C, 78.90; H, 10.96; N, 10.09). Ⅱ was characterized as a crystalline methiodide (Ⅲ), $C_{10}H_{18}NI \cdot 1/2H_2O$, m.p. 230°, and a picrate, $C_{15}H_{18}O_7N_4$, m.p. 180~195°. Ⅱ showed no absorption in the ultraviolet region and the NMR (nuclear magnetic resonance) spectrum showed no absorption corresponding to any olefinic proton; but infrared absorption of Ⅱ at 3030 cm^{-1} suggested the presence of a cyclopropane ring in Ⅱ. Hofmann degradation of Ⅲ afforded an unsaturated amine (Ⅳ), which formed crystalline hydrochloride of m.p. 181~183° (decomp.) (*Anal.* Calcd. for $C_{10}H_{18}NCl$: C, 63.98; H, 9.67; N, 7.46. Found: C, 63.64; H, 9.61; N, 7.37). The presence of an exocyclic methylene in Ⅳ was shown by infrared absorptions at 3080, 1651, and 867 cm^{-1}, and NMR absorptions at 4.96 and 4.83 p.p.m. The notable end absorption of Ⅳ in ultraviolet region indicated a conjugation of the cyclopropane ring and the exocyclic methylene. Furthermore, NMR spectrum of the methiodide (V) of Ⅳ indicated the presence of a dimethylaminomethylene group like $(CH_3)_2N\text{-}CH_AH_B\text{-}\overset{|}{C}H_X\text{-}$: H_A 3.53 p.p.m. (quartet), H_B 3.10 p.p.m. (quartet), $J_{AB}=13.5$, $J_{AX}=5.5$, $J_{BX}=8.5$ (c.p.s.). Hofmann degradation of V gave *m*-xylene which was identified by means of infrared, ultraviolet, and NMR spectrometry, and gas-liquid chromatography.

Different from Ⅱ, the unsaturated amine (Ⅳ) easily took up hydrogen chloride or acetic acid to give Ⅵ (hydrochloride, m.p. 179°, and methiodide, m.p. 166° (decomp.)) or Ⅶ (picrate, m.p. 155~164°). Osmium tetroxide oxidation of Ⅳ afforded a diol (Ⅷ) of

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m.p. 76.5～78° which was further treated with periodic acid to give an aminoketone (IX) (hydrochloride, m.p. 196～197.5° (decomp.); picrate, m.p. 183～186°). Treatment of IX with hydrochloric acid gave a chloramino-ketone (X) (hydrochloride m.p. 196° (decomp.); picrate, m.p. 172～173.5°). The infrared absorption of IX at 1715 cm^{-1} and its notable end absorption in ultraviolet region indicated the conjugation of the cyclopropane ring with the five-membered ring ketone5); and the infrared absorption of X at 1710 cm^{-1} and absence of ultraviolet absorption also showed a conversion of IX to the saturated six-membered ring ketone (X). Based on these data, II was designated as 3-methyl-3-azatricyclo[6.1.0.0^{5,9}]nonane.

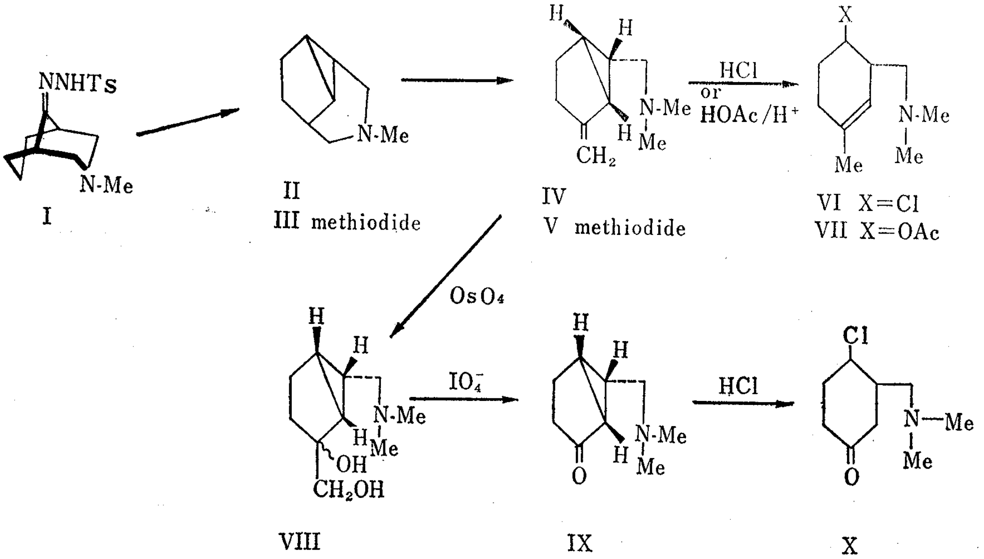

Chart 1.

On the other hand, sodium salt obtained from 3-methyl-3-azabicyclo-[3.2.1]octan-8-one3) tosylhydrazone (XI) of m.p. 147° (decomp.) was treated under the same condition as before to give a tricyclic amine (XII), $C_8H_{13}N$, b.p.$_{75}$ 83～86° (*Anal.* Calcd. for $C_8H_{13}N$: C, 77.99; H, 10.64; N, 11.37. Found: C, 77.69; H, 10.62; N, 11.28). XII was unstable to air and acids, and characterized as methiodide (XIII), $C_9H_{16}NI$, m.p. 215° (decomp.), or picrate, $C_{14}H_{16}O_7N_4$, m.p. 153° (decomp.). Infrared absorption of XII at 3030 cm^{-1} also indicated the presence of a cyclopropane ring. Mass spectrometry of XII suggested the structure of 2-methyl-2-azatricyclo[5.1.0.0^{4,8}]octane; the most intense fragmentation peak at m/e 94 was indicative of N-methylpyridinium ion (XIV) which may be generated from M-1$^+$(XV) by removal of ethylene. Disappearance of the peak at m/e 58 corresponding to $(CH_3)_2N^+=CH_2$,6) which was marked in the spectrum of II, also ruled out the other possible formula (XVI) having two methylene groups at the nitrogen atom. As for the chemical proof, Hofmann degradation of XIII reverted it to XII by liberation of methanol when the reaction was carried out in water, but gave a methoxy-amine (XVII) when reacted in methanol and its NMR spectrum exhibited one proton signal at 2.4～2.9 p.p.m., showing the presence of one hydrogen at the carbon bearing the dimethyl-amino group. Contrasted with II, which was stable to hydrogenation, XII easily took up one mole of hydrogen to afford 3-methyl-3-azabicyclo[3.2.1]octane (XVIII) and 3-methyl-3-azabicyclo[3.3.0]octane (XIX), which were

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identified with the synthetic samples as methiodides of m.p. 270° (decomp.) and m.p. 203~204.5°, respectively. The former was synthesized by the Wolff-Kishner reduction of 3-methyl-3-azabicyclo[3.2.1]octan-8-one and the latter by the method of Rice and Grogan.[7] Based on these facts, the structure of XII was designated as 2-methyl-2-azatricyclo[$5.1.0.0^{4,8}$]octane.

In these reactions, reaction by-products were also investigated in both azabicyclononane and -octane compounds, but any products corresponding to an isomer of the tricyclic amine (II or XII) could not be isolated. Consequently, it was concluded that the insertion reaction of these carbenes, which are supposed as intermediates in these reactions, proceeds uniquely into the opposite side of N-methyl group in the case of azabicyclononane system and into the same side in the case of azabicyclo-öctane.

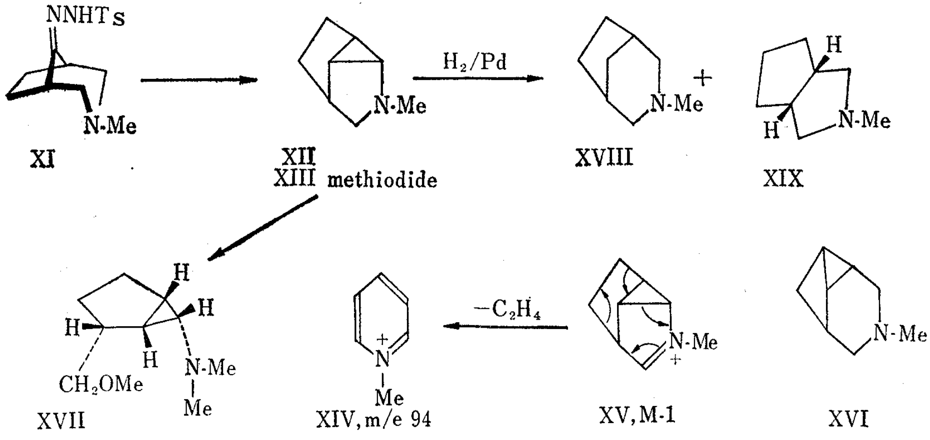

Chart 2.

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Received December 14, 1966

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Chem. Pharm. Bull.
15(4) 547~548 (1967)

UDC 581.19 : 582.823 : 547.918

The Sapogenin Constituent of the Seeds of *Camellia sasanqua* Thunb.

In relation to the study on theasapogenols[1~4] obtained from the seeds saponin of *Thea sinensis* L. (Japanese name: cha), hitherto engaged in this laboratory, we have

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