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INTRAMOLECULAR CYCLIZATION OF A DIENO-NITRILE:
SYNTHESIS OF A NEW MONOTERPENE ALKALOID

Yasuo BUTSUGAN, Shigeo YOSHIDA, Masao MUTO, and Tadaaki BITO
Department of Synthetic Chemistry, Nagoya Institute of Technology,
Gokiso-cho, Showa-ku, Nagoya, Japan

Teruo MATSUURA and Ruka NAKASHIMA
Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Kyoto, Japan

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We wish to report an intramolecular cyclization between nitrile and conjugated diene moieties leading to a monoterpene alkaloid with a pyridine nucleus. Rose bengal-sesitized photooxygenation of (-)-citronellonitrile[1] (1) in methanol followed by reduction of the resulting photohydroperoxides with sodium sulfite gave a 55 : 45 mixture of alcohols 2 and 3 in 75% yield.[2] When the mixture of 2 and 3 was heated in acetone-1N sulfuric acid, 2 was dehydrated to give a dieno-nitrile 4, bp 85-86°/3.5mm, which was separated from the recovered 3, bp 114-115°/3.5mm, by fractional distillation. The conversion of 2 into 4 was also observed in a gas-chromatographic column over 160°. The structures of 3 and 4 were assigned from their spectral data[3][3: ν_{max}^{neat} 3480, 2240, 1645, 900cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 1.08d (3H, J=6Hz), 1.27-1.65m (5H), 1.73s (3H), 2.32d (2H, J=6Hz), 2.63s (1H), 4.01t (1H, J=6Hz), 4.87s (broad, 2H). 4: λ_{max}^{EtOH} 228nm (ε 13600); ν_{max}^{neat} 2250, 965, 885cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 1.09d (3H, J=6Hz), 1.29-1.64m (1H), 1.84s (3H), 2.04-2.44m (4H), 4.91m (2H), 5.54 (sextet, 1H, J=7 and 15 Hz), 6.21d (1H, J=15Hz)].

Pyrolysis of 4 at 500° gave a single oily base, bp 63-65°/3.5mm, which formed a crystalline prcrate, mp 180°(decomp.). The mass spectrum of the base showed a strong peak at $[M-1]^+$, characteristic of alkylated pyridines,[4] in addition to M^+ and $[M-15]^+$ peaks. This and other spectral data [λ_{max}^{EtOH} 275nm (ε 26600); ν_{max}^{neat} 1568 (C=N), 871, 715cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 1.20d (3H, J=6Hz), 2.28s (3H), 2.3-3.3m (5H), 7.17s (broad, 1H), 8,05s (broad, 1H)] led us to assign the structure 5 for the base.

The synthesis of pyridine derivatives by the intermolecular cyclization between nitriles and conjugated dienes has been reported.[5] Thus the formation of **5** is reasonably explained by a thermal dehydrogenation of a dihydropyridine intermediate **6** which is formed by an intramolecular Diels-Alder addition of **4**.

In connection with the physiological activity of a structurally related monoterpene alkaloid, actinidine (**7**), for the Feligae animals,[6] the activity of **5** was tested on cats but no significant effect was observed. The present synthesis of **5** implies that pathways involving a nitrile precursor may be possible for the biogenesis of terpene alkaloids for which there seems to be no reliable theory.

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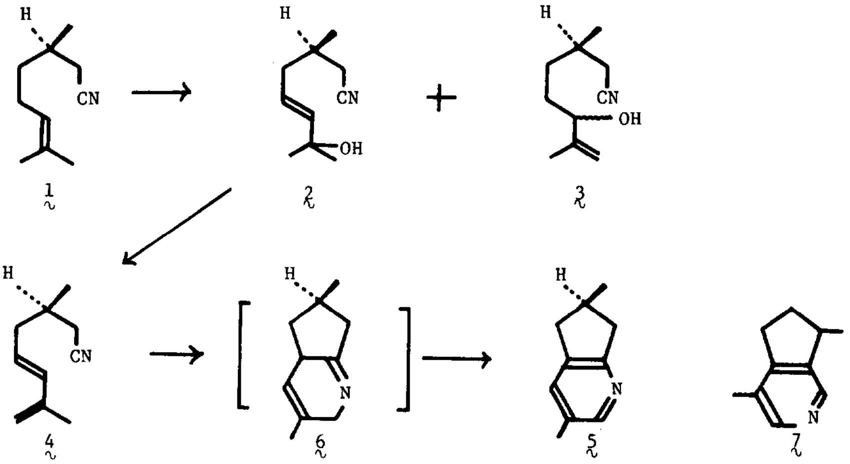

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