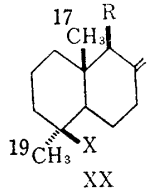
The nuclear magnetic resonance spectra of these compounds, together with those obtained in the degradation investigation of methyl sciadopate seem to deserve a brief comment. The nuclear magnetic resonance spectrum of Ⅳ exhibited an angular methyl signal at a rather high field of 9.52. Spectral analyses of the related compounds enable one to attribute this high-field shift to the anisotropic effects of the carbonyl and the exocyclic methylene groups.

The proton resonance signal on C-17, together with the one on C-19 of methyl sciadopate and those of its related compounds are shown in Table I. Data in Table I indicate that the high field shifts of 0.2 p.p.m. of angular methyl signals are due to the anisotropic shielding of the carbonyl function axially oriented at C-4, and those of 0.15 p.p.m. are due to the exocyclic methylene function, compared to those of the compounds having the axial acetoxymethylene group and methyl group at C-4 and C-8 respectively in XX.



XX

These observations of the angular methyl chemical shifts at C-10 should be useful for stereochemical problems of other diterpenes having the same carbon skeleton as XX.

More detail discussions concerning the anisotropic shielding effects of these functional groups on the angular methyl group will be published elsewhere, together with the complete set of data.

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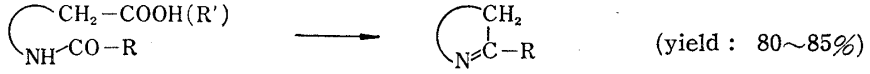
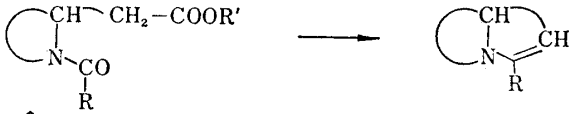
Decahydropyrido[2,1,6-*de*]quinolizine (Decahydrocycl[3.3.3]azine)*[1]

We wish to report the synthesis of 1,2,3,3*a*,4,5,6,6*a*,7,8-decahydropyrido[2,1,6-*de*]-quinolizine (Ⅵ).

In previous reports, we reported a new synthetic method for cyclic nitrogen compounds as shown by the general formulas below.

1. 

(yield : 80~85%)

2. 

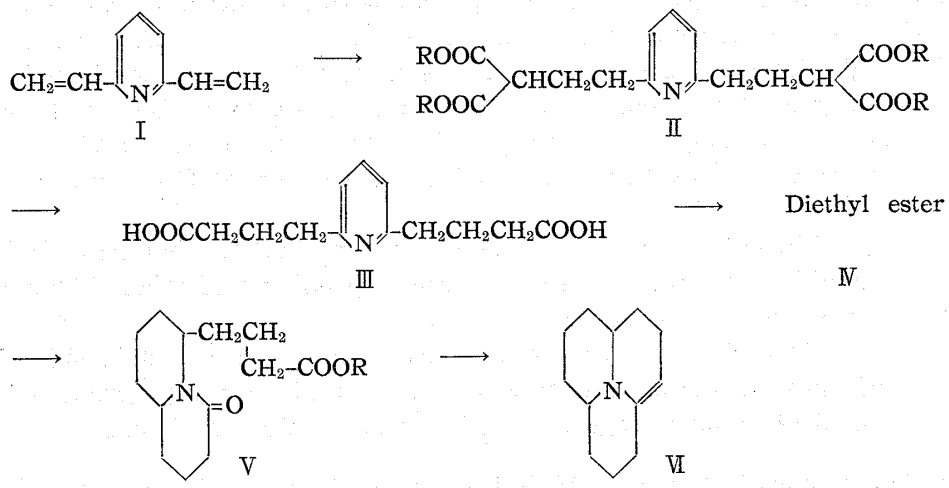
(yield : 90~95%)

3. 

(yield : 40~65%)

*[1] This work is a part of "a new synthetic method of cyclic nitrogen compounds by Isamu Murakoshi."

Accordingly, the following 2-R-3,4,5,6-tetrahydropyridine (R=propyl, γ-coniceine),[1] 2-R-3,4-dihydro-2*H*-pyrrole (R=2-pyridyl, myosmine),[2] 4-R-3,4-dehydroquinolizidine[3] (deoxynupharidine[4]), 3-R-2,3-dehydropyrrolizidine[5], 3-R-2,3-dehydroindolizidine[5], 2-R-indole,[6] 2-R-1,4 or 3,4-dihydroquinoline[6], 3-R-isoquinoline[7] derivatives were synthesized. Type 2 reaction was applied to the synthesis of decahydropyrido[2,1,6-*de*]quinolizine (Ⅵ) as follows.



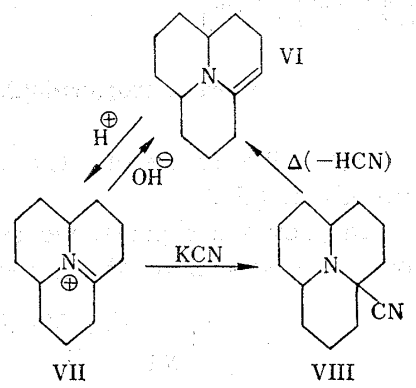
The condesation of 2,6-divinylpyridine (I)[8] was heated with ethyl malonate in the presence of potassium *tert*-butyrate in dimethylformamide for 8 hours afforded a tetraester (Ⅱ) in 32~33% yield: $b.p_{0.03}$ 186~192°.

Heating with 20% hydrochloric acid for 5 hours hydrolyzed Ⅱ into Ⅲ: hydrochloride, prisms, m.p. 156~158° (water-acetone), *Anal.* Calcd. for $C_{13}H_{18}O_4NCl$: C, 54.26; H, 6.30; N, 4.87. Found: C, 54.19; H, 6.48; N, 5.28.

The diacid (Ⅲ) was esterified with abs. ethanol in the presence of dry hydrochloric acid yielding the diester (Ⅳ): $b.p_{0.1}$ 150~156°.

By catalytic reduction (Raney nickel, 150 atm., 150~160°), Ⅳ furnished the cyclic amide (V) in a good yield (85~90%): $b.p_{0.12}$ 117~120°.

When V was dry distilled with the same, or half the amount of soda lime as reported previously, 1,2,3,3*a*,4,5,6,6*a*,7,8-decahydropyrido[2,1,6-*de*]quinolizine (Ⅵ) was obtained in yield of 30% as the perchlorate (Ⅶ): prisms, m.p. 298~304° (decomp.), *Anal.* Calcd. for $C_{12}H_{19}N\cdot HClO_4$: C, 51.89; H, 7.26; N, 5.01. Found: C, 52.13; H, 7.19; N, 4.86, UV: λ_{max}^{EtOH} 266 mμ (ε 242), IR: λ_{max}^{KBr} 1663 cm^{-1} (⟩C=N⟨). The free base (Ⅵ) was isolated, $b.p_{10}$ 120~121°, UV: $\lambda_{max}^{Et_2O}$ 228 mμ (ε 3520), IR λ_{max}^{Liquid} cm^{-1}: 2710, 2740 (shoulder), 2790, 2840 (*trans*-quinolizidine) and 1652 (⟩N-C=), and converted into the



1) I. Murakoshi: Yakugaku Zasshi, **77**, 490 (1957); **79**, 76 (1959).
2) *Idem*: *Ibid.*, **77**, 1062 (1957).
3) *Idem*: *Ibid.*, **78**, 594 (1958).
4) M. Kotake, *et al.*: Bull. Chem. Soc. Japan, **32**, 892 (1959); F. Bohlmann, *et al.*: Chem. Ber., **94**, 3151 (1961).
5) I. Murakoshi: Yakugaku Zasshi, **78**, 598 (1958).
6) *Idem*: *Ibid.*, **79**, 72 (1959).
7) *Idem*: *Ibid.*, **79**, 1578 (1959).
8) J. Michalski, *et al.*: Roczniki Chem., **29**, 1141 (1955) (C. A., **50**, 12044 (1956)).

picrate, yellow prisms, m.p. 128~129° (EtOH). *Anal.* Calcd. for $C_{18}H_{22}O_7N_4$: C, 53.20; H, 5.42; N, 13.79. Found : C, 53.14; H, 5.63; N, 13.96.

In order to demonstrate the α,β-enamine structure in the Ⅵ, to a solution of the perchlorate (Ⅶ) was added conc. potassium cyanide solution dropwise with stirring. In this case the cyano-compound (Ⅷ) was also obtained in a quantitative yield : b.p_3 135~138° (oil bath temp.), IR λ_{max}^{Liquid} cm^{-1} : 2730, 2807 (*trans*-quinolizidine), 2250 (CN) and no band near 1652 due to (>C=C(H)–N<).

Attempted recrystallization of the picrate of Ⅷ from hot ethanol yielded instead the picrate of Ⅵ by elimination of hydrocyanic acid.

The dehydrogeneration of Ⅵ to pyrido[2,1,6-de]quinolizine is now in progress.

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Shihunine : A New Phthalide-Pyrrolidine Alkaloid

A Chinese drug known in Japanese as "Chukanso" (中環草) is sometimes available on the Hong Kong market as a kind of Shih-Hu (Japanese name "Sekkoku") and is derived from the orchidaceous plant, *Dendrobium lohohense* TANG et WANG.*1,1)

We have isolated a crystalline alkaloid from Chukanso, shihunine, m.p. 79°, pKa 3.65,*2 *Anal.* Calcd. for $C_{12}H_{13}O_2N$: C, 70.91; H, 6.45; N, 6.89., mol. wt., 203.23. Found: C, 70.53; H, 6.54; N, 6.59., mol. wt.,*3 200, 209. It formed a picrate, m.p. 163~164°, *Anal.* Calcd. for $C_{12}H_{13}O_2N \cdot C_6H_3O_7N_3$: C, 50.00; H, 3.73; N, 12.96. Found : C, 50.18; H, 3.78; N, 12.74.

Shihunine is racemic ($[\alpha]_{200\sim700\,m\mu}$ 0°) and has a lactone grouping (IR $\nu_{max}^{CCl_4}$ cm^{-1} : 1761; ν_{max}^{Nujol} cm^{-1} : 1743). On permanganate oxidation it yielded phthalic acid identified by comparison of its infrared spectrum with that of authentic sample and by melting point of its anhydride, and mixed m.p. 132~134°.

Shihunine when stirred with Adams catalyst in hydrogen took up one mole of hydrogen and furnished an amino acid, m.p. ca 200°, IR $\nu_{COO^-}^{Nujol}$ cm^{-1} : 1613, pKa 3.3, 10.5, *Anal.* Calcd. for $C_{12}H_{15}O_2N$: C, 70.22; H, 7.37; N, 6.82. Found : C, 69.99; H, 7.45; N, 7.00. It formed a picrate, m.p. 155~156°, IR ν_{COOH}^{Nujol} cm^{-1} : 1684, *Anal.* Calcd. for $C_{12}H_{15}O_2N \cdot C_6H_3O_7N_3$: C, 49.77; H, 4.18; N, 12.90. Found : C, 49.92; H, 4.09; N, 13.09. The

*1 The botanical origin of this drug was authenticated by Dr. S. Takahashi of this Faculty to whom the authors are indebted.

*2 Melting points were measured on a Kofler hot-stage and are given as uncorrected values, and pKa were measured in 50% EtOH-H_2O.

*3 The molecular weight was measured by Rast's method.

1) Zhung-jau-zhi (中葯志), **111**, pp. 39 (1961); T. Tang, F. Wang : Acta Phytotaxonomica, **1**, 82 (1951).