Communications to the Editor

UDC 547.836.7.07

Synthesis of 3-Oxo-10a,1-dihydropyrano[3,4,5-*i,j*]-6-oxoquinolizine

During the course of work on the synthesis of alkaloidal compounds possessing quinolizidine ring, 1,3-bis(ethoxycarbonyl)- and 1-cyano-3-ethoxycarbonyl-8-methoxymethyl-4-oxoquinolizines (Ⅶ) were synthesized by the route shown in Chart 1. On boiling these compounds with hydrochloric acid, a compound (Ⅷ), formed by the saponification of ethoxycarbonyl group in 3-position and decarboxylation, and 3-oxo-10a,1-dihydropyrano[3,4,5-*i,j*]-6-oxoquinolizine (Ⅸ) were obtained. In this case, saponification of ethoxycarbonyl or nitrile group in 1-position is accompanied by the elimination of methanol from that and methoxymethyl group in 9-position and a δ-lactone (Ⅸ) is formed. Formation of a lactone from methoxyl and carboxyl groups has never been found as yet and it is considered that the bonds in 1- and 9-positions are in the same direction in these 4-oxoquinolizine compounds and easily form a six-membered lactone.

2-Methyl-3-hydroxymethylpyridine (Ⅰ) ($b.p_5$ 125～127°; picrate, m.p. 166～168°) was obtained by the reduction of ethyl 2-methylnicotinate[1] with $LiAlH_4$ in ether. (Ⅰ) was chlorinated with $SOCl_2$ and boiled with MeONa in MeOH, affording 2-methyl-3-methoxymethylpyridine (Ⅱ), $b.p_{30}$ 107～110° (picrate, m.p. 140～141°).

Reaction of (Ⅱ) and $CO(OEt)_2$ in the presence of KNH_2 afforded ethyl 3-methoxymethyl-2-pyridylacetate (Ⅲ), $b.p_8$ 148° (picrate, m.p. 116～118°), while application of H_2O_2 to (Ⅱ) in glacial AcOH with warming gave 2-methyl-3-methoxymethylpyridine 1-oxide (Ⅳ), $b.p_2$ 135～138°; m.p. 55～60° (picrate, m.p. 92～95°).

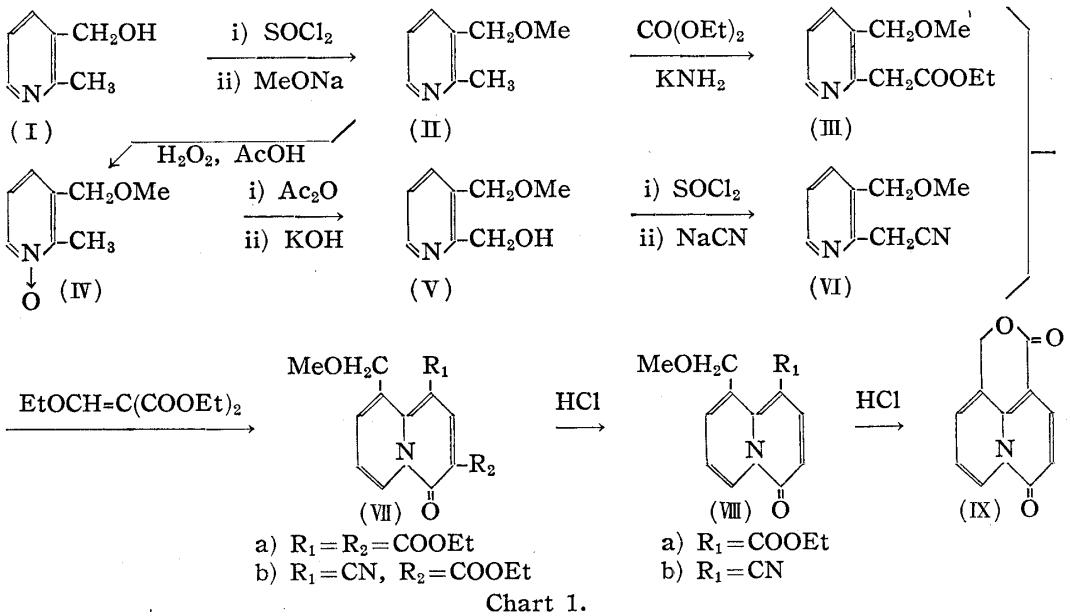

Chart 1.

(Ⅳ) was boiled with Ac_2O to form 2-acetoxymethyl-3-methoxymethylpyridine, $b.p_5$ 135～138° (picrate, m.p. 132～135°), which was saponified by boiling with KOH in EtOH, and 2-hydroxymethyl-3-methoxymethylpyridine (Ⅴ), $b.p_{0.05}$ 120～125° (picrate, m.p. 127～128°), was obtained. Chlorination of (Ⅴ) with $SOCl_2$ afforded 2-chloromethyl-3-methoxymethylpyridine (picrate, m.p. 112～114°) and this was boiled with NaCN in MeOH, affording 2-cyanomethyl-3-methoxymethylpyridine (Ⅵ), b. $p_{0.05}$ 110～115° (picrate, m.p.

1) K. Tsuda, Y. Sato, N. Ikekawa, H. Mishima : J. Org. Chem., **21**, 800(1956).

146~148°) (*Anal.* Calcd. for $C_{15}H_{13}O_6N_5$: C, 46.04; H, 3.35; N, 17.90. Found : C, 46.23; H, 3.67; N, 17.69).

Condensation of (Ⅲ) and diethyl ethoxymethylenemalonate by boiling resulted in the formation of 1,3-diethoxycarbonyl-9-methoxymethyl-4-oxoquinolizine (Ⅶa), m.p. 75~76°. *Anal.* Calcd. for $C_{17}H_{19}O_6N$: C, 61.12; H, 5.7; N, 4.22. Found : C, 61.22; H, 6.52; N, 4.02. U. V. λ_{max}^{MeOH} mμ(log ε) : 263(4.16), 350(3.93), 408(4.24). I. R. $\nu_{max}^{CHCl_3}$ cm^{-1} : 1724(ester C=O), 1700(CON<), 1100, 1110(ether).

On the other hand, condensation of (Ⅵ) and diethyl ethoxymethylenemalonate by boiling afforded 1-cyano-3-ethoxycarbonyl-9-methoxymethyl-4-oxoquinolizine (Ⅶb), m.p. 156~158° *Anal.* Calcd. for $C_{15}H_{14}O_4N_2$: C, 61.31; H, 5.15; N, 10.21. Found : C, 61.07; H, 5.28; N, 9.90. U. V. λ_{max}^{MeOH} mμ(log ε) : 258.5(4.17), 266.5(4.21), 346(3.96). 406(4.28). I. R. $\nu_{max}^{CHCl_3}$ cm^{-1} : 2227(CN), 1745(ester C=O), 1712(CON<), 1105(ether).

On boiling (Ⅶb) with 10% HCl, 1-cyano-9-methoxymethyl-4-oxoquinolizine (Ⅷb), m.p. 150~151°, was obtained. *Anal.* Calcd. for $C_{12}H_{10}O_2N_2$: C, 67.28; H, 4.71; N, 13.08. Found : C, 67.09; H, 5.05; N, 12.73. U. V. λ_{max}^{MeOH} mμ(log ε) : 259(4.13), 272.5(4.08), 380 (4.20). I. R. $\nu_{max}^{CHCl_3}$ cm^{-1} : 2195(CN), 1675(-CON), 1088(ether).

On boiling (Ⅷb) with 20% HCl, a δ-lactone derivative (Ⅸ), m.p. 252~254°, was formed. *Anal.* Calcd. for $C_{11}H_{17}O_3N$: C, 65.67; H, 3.51; N, 6.96. Found : C, 65.96; H. 3.70; N, 6.91. U. V. λ_{max}^{MeOH} mμ(log ε) : 254(3.84), 260.5(3.87), 288.5(3.89), 355(4.18). I. R. ν_{max}^{KBr} cm^{-1} : 1724(lactone), 1684(CON<).

(Ⅶa) forms (Ⅸ) under a milder condition than that for (Ⅶb), with HCl. As an intermediate compound, 1-ethoxycarbonyl-9-methoxymethyl-4-oxoquinolizine (Ⅷa), m.p. 83~84.5°, was obtained. *Anal.* Calcd. for $C_{14}H_{15}O_4N$: N, 5.36. Found : N, 5.24. U. V. λ_{max}^{EtOH} mμ(log ε) : 260(4.14), 381(4.16). I. R. ν_{max}^{KBr} cm^{-1} : 1712(ester C=O), 1680(CON<).

The writer expresses his deep gratitude to Prof. K. Tsuda of the University of Tokyo for his kind and helpful guidance and to Mr. M. Matsui, Director of this Laboratory, for encouragement.

Takamine Research Laboratory
Sankyo Co., Ltd.
Shinagawa-ku, Tokyo

Yoshinobu Sato (佐藤義信)

January 25, 1958.

UDC 547.913.5

Studies on Azulenes : S-Guaiazulene-aldehydes

Although several communications on azulenes having ring-substituted aldehyde group have recently been encountered,[1~5] no detailed report has been made on the synthetic procedure for direct introduction of aldehyde group into azulene rings and properties of the products obtained.

In the course of our studies on azulenes, it was found that an aldehyde group could be substituted directly into S-guaiazulene (Ⅰ) in a good yield by Friedel-Crafts type substitution reaction and the results will be recorded.

A solution of (Ⅰ) in *o*-dichlorobenzene was added dropwise into a mixed solution

1) E. Heilbronner, R. W. Schmid : Helv. Chim. Acta, **37**, 2018(1954).
2) W. H. Stafford, D. H. Reid : Chem. & Ind. (London), **1954**, 277.
3) W. L. Galloway, D. H. Reid, W. H. Stafford : *Ibid.*, **1954**, 724.
4) H. Arnold, K. Pahls : Ber., **87**, 257(1954).
5) W. Treibs : *Ibid.*, **90**, 761(1957).