[Chem. Pharm. Bull. 26(2) 680—681 (1978)]

UDC 547.853.3.04 : 547.836.04

Studies on Quinolizine Derivatives. XIX.[1] The Synthesis of Diazacycl[3.3.3]azine Derivatives. (13)

By the reaction of 4-imino-4H-pyrido[1,2-*a*]pyrimidine derivative (I), and dimethyl acetylenedicarboxylate or methyl acetylenecarboxylate, with 5% Pd-C, 1,4-diazacycl-[3.3.3]azine derivatives (III, V) were obtained respectively. Moreover, the degradation of V was attempted to give a new parent compound, namely 1,4-diazacycl[3.3.3]azine (VIII). VIII may be an antiaromatic compound by the PMR spectrum.

Keywords——cycl[3.3.3]azines; $4n$ ($n=3$)π-electron system; nonbenzenoide aromatic compound; palladium carbon as cataryst; antiaromatic compound; 1,4-diazacycl-[3.3.3]azine; paramagnetic ring current

The cycl[3.3.3]azines which are a well-known $4n$ ($n=3$) π-electron system of a series of nonbenzenoide aromatic compounds are particularly interesting in both chemical and physical properties.[2] Previously we reported a synthetic method of 2-methylthio-1,4-diazacycl-[3.3.3]azine derivative in spite of poor yeild from 2-methylthio-4-imino-4H-pyrido[1,2-*a*]-pyrimidine derivative and dimethyl acetylenedicarboxylate (DMAD).[3]

In this communication, we wish to report an improved synthetic method of 1,4-diazacycl-[3.3.3]azine derivatives (III, V) with palladium carbon (Pd-C) as catalyst, and moreover the degradation of V to obtain a parent compound; 1,4-diazacycl[3.3.3]azine (VIII) which, compared with cycl[3.3.3]azines in chemical shifts of proton magnetic resonance (PMR), may be an antiaromatic compound.

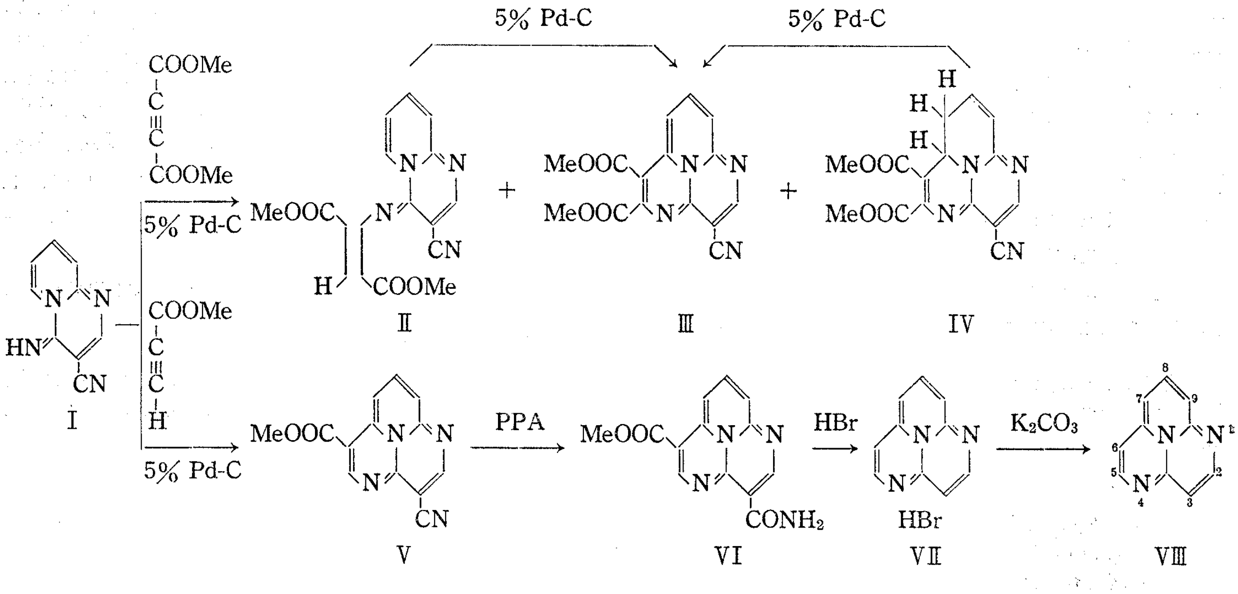

Chart 1

Thus, a xylene solution of 4-imino-4H-pyrido[1,2-*a*]pyrimidine derivative (I), DMAD, and 5% Pd-C was refluxed under nitrogen (N_2) atmosphere for 5 hr. After evaporation under reduced pressure, the residue was chromatographed on Al_2O_3 to give 3-cyano-4-(1,2-

---

1) Part XVIII: K. Kurata, H. Awaya, Y. Tominaga, Y. Matsuda, and G. Kobayashi, *Chem. Pharm. Bull.* (Tokyo), submitted.

2) K. Matsumoto, T. Uchida, and J. Yamauchi, *Yuki Gosei Kagaku Kyokai Shi*, **35** (9), 739 (1977).

3) H. Awaya, C. Maseda, Y. Tominaga, R. Natsuki, Y. Matsuda, and G. Kobayashi, *Yakugaku Zasshi*, **95**, 13 (1975).

dimethoxycarbonylvinyl)imino-4H-pyrido[1,2-*a*]pyrimidine (II), mp 185—186°, mass spectrum (MS) *m*/*e*: 312 (M^+) from benzene elution, dimethyl 3-cyano-1,4-diazacycl[3.3.3]azine-5,6-dicarboxylate (III), mp 238—239°, MS *m*/*e*: 310 (M^+) from benzene: acetone=20: 1 elution, and dimethyl 3-cyano-6a, 7-dihydro-1,4-diazacycl[3.3.3]azine-5,6-dicarboxylate (IV), mp 220—221°, MS *m*/*e*: 312 (M^+) from benzene: acetone=20: 1 elution respectively. By the treatment of II or IV with 5% Pd-C, III was obtained, too.

Furthermore, a xylene solution of I, methyl acetylenecarboxylate, and 5% Pd-C was heated in sealed tube substituted with N_2 atmosphere at 230—250° for 10 hr to afford methyl 3-cyano-1,4-diazacycl[3.3.3]azine-6-carboxylate (V) after Al_2O_3 column chromatography, mp 297—298°, PMR spectrum ($CDCl_3$) ppm: 2.87 (3H, singlet, OMe), 6.87 (1H, doublet, J=8 Hz, C_7–H or C_9–H), 7.42 (1H, singlet, C_2–H or C_5–H), 7.66 (1H, triplet, J=8 Hz, C_8–H), 7.95 (1H, singlet, C_2–H or C_5–H), 8.07 (1H, doublet, J=8 Hz, C_7–H or C_9–H), MS *m*/*e*: 252 (M^+).

Then, the degradation of 1,4-diazacycl[3.3.3]azine derivative (V) was examined to obtain a parent compound, namely 1,4-diazacycl[3.3.3]azine (VIII). Thus, a mixture of V and polyphosphoric acid was heated at 100° for 10 hr to give methyl 3-carbamoyl-1,4-diazacycl-[3.3.3]azine-6-carboxylate (VI) by alkalizing the aqueous solution with K_2CO_3, mp 275—276°, MS *m*/*e*: 270 (M^+).

VI was refluxed in 48% HBr solution for 5 hr to obtain 1,4-diazacycl[3.3.3]azine hydrobromide (VII) as stable salts after evaporation under reduced pressure, mp>300°, MS *m*/*e*: 169 (M^+–HBr), PMR spectrum (DMSO-d_6) ppm: 5.30 (1H, doublet, J=7 Hz, C_3–H or C_6–H), 5.85 (1H, doublet, J=7 Hz, C_3–H or C_6–H), 6.13 (1H, doublet, J=8 Hz, C_7–H or C_9–H), 6.21 (1H, doublet, J=8 Hz, C_7–H or C_9–H), 6.61 (1H, doublet, J=7 Hz, C_2–H or C_5–H), 7.05 (1H, doublet, J=7 Hz, C_2–H or C_5–H), 7.28 (1H, triplet, J=8 Hz, C_8–H).

A parent compound, namely 1,4-diazacycl[3.3.3]azine (VIII), was obtained by the treatment of VII with K_2CO_3, but VII could not be recrystallized due to its instabilty. So, the structure of VIII was only confirmed by the PMR spectrum ($CDCl_3$) ppm: 4.55 (1H, doublet, J=7 Hz, C_3-H or C_6-H), 4.61 (1H, doublet, J=7 Hz, C_3-H or C_6-H), 4.63 (1H, doublet, J=8 Hz, C_7–H or C_9–H), 5.25 (1H, doublet, J=8 Hz, C_7–H or C_9–H), 5.90 (1H, doublet, J=7 Hz, C_2–H or C_5–H), 6.15 (1H, triplet, J=8 Hz, C_8–H), 6.34 (1H, doublet, J=7 Hz, C_2–H or C_5–H). By comparing with other cycl[3.3.3]azines which we had summarized in table of the chemical shifts of PMR in our previous paper,[4] we think of presence of a paramagnetic ring current in 1,4-diazacycl[3.3.3]azine (VIII).

The structure of the products were confirmed by the satisfactory infrared ,ultraviolet, PMR, mass spectra, and elemental analyses.

Acknowledgement The author thanks are due to Mrs. H. Mazume for elemental analyses, to Mr. M. Ohwatari for IR and UV spectra, to Mr. K. Inada for PMR spectra, and to Mr. N. Yamaguchi for mass spectra.

Faculty of Phamaceutical Sciences,
Nagasaki University
1–14, Bunkyo-machi, Nagasaki,
852, Japan

Mayumi Kuya
Keiji Kurata
Hiroyoshi Awaya
Yoshinori Tominaga
Yoshiro Matsuda
Goro Kobayashi

Received December 5, 1977

---

4) K. Kurata, M. Yamada, H. Awaya, Y. Tominaga, Y. Matsuda, and G. Kobayashi, *Yakugaku Zasshi*, submitted.