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Studies on Quinolizine Derivatives. XV.*,[1] Synthesis of Azacycl[3,3,3]azine Derivatives (8)[2]

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From the reaction of 4-imino-6-methyl-4*H*-quinolizine derivatives (I) with acid anhydrides (glutaric anhydride and crotonic anhydride), the corresponding 1-azacycl-[3,3,3]azine derivatives (V, VI) were obtained. 1-Aza-5-oxo-2,3,4,5-tetrahydrobenzo-[*b*]cycl[3,3,3]azine (X) was yielded, as a stable free base, by the decarboxylation of VI. On the other hand, 2-methyl and 2,5-dimethyl-1-azacycl[3,3,3]azine (XVIa, b), which were very unstable free bases, were prepared by the degradation of II and IV. These nuclear magnetic resonance spectral data of XVIa and XVIb may be interpreted in term of a paramagnetic ring current.

Previously, we reported[1] the synthetic methods of 1-azacycl[3,3,3]azine derivatives (II, IV) from 4-imino-6-methyl-4*H*-quinolizine derivatives (I) with acetic anhydride by novel ring-closure. The purpose of the present investigation was to study the extention of our synthetic method of 1-azacycl[3,3,3]azine derivatives (V, VI) and to examine the decarboxylation of such 1-azacycl[3,3,3]azine derivatives (II, IV, VI). Consequently, we obtained the stable salts, 2-methyl- and 2,5-dimethyl-1-azacycl[3,3,3]azine hydrobromides (XVa, b), and their unstable free bases (XVIa, b) by the degradation of II and IV.

The Reaction of 4-Imino-6,8-dimethyl-4*H*-quinolizine Derivative with Acid Anhydrides

In the case of methyl 3-cyano-4-imino-6,8-dimethyl-4*H*-quinolizine-1-carboxylate (Ib) and crotonic anhydride in the presence of pyridine, the good result was obtained by heating at 100° for 10 hr to give methyl 2-allyl-9-cyano-5-methyl-1-azacycl[3,3,3]azine-7-carboxylate (V) as green needles, mp 237—238°. Elemental analysis of V agreed with $C_{18}H_{15}O_2N_3$. The structure of V was determined by the mass spectrum, which showed the expected molecular ion peak at *m/e* 305, and the nuclear magnetic resonance (NMR) spectrum, which showed proton peaks of allyl group at δ: 1.80, 5.70, and 6.68. On the other hand, in the case of Ib with glutaric anhydride in the presence of pyridine, the good result was obtained by heating at 150° for 5 hr. The reaction mixture was chromatographed on alumina to separate methyl 1-aza-11-cyano-7-methyl-5-oxo-2,3,4,5-tetrahydrobenzo[*b*]cycl[3,3,3]azine-9-carboxylate (VI) from benzene elution and methyl 9-cyano-5-methyl-1-azacycl[3,3,3]azine-7-carboxylate (VII) from benzene-acetone(10: 1) elution as a by-product. The structure of VI was determined by the absence of 6-methyl peak of Ib in the NMR spectrum, the mass spectrum which showed the molecular ion peak at *m/e* 333, and elemental analysis, which coincided with $C_{19}H_{15}O_3N_3$. VII was proved to be identical an authentic sample.[1] The above preparation route is seemed to be general and versatile and to permit the ready synthesis of various azacycl[3,3,3]azine derivatives.

* Dedicated to the memory of Prof. Eiji Ochiai.

1) Part XIV: K. Kurata, H. Awaya, C. Maseda, Y. Tominaga, Y. Matsuda, and G. Kobayashi, *Yakugaku Zasshi*, submitted.

2) Preliminary accounts of a part of this work have been published: H. Awaya, C. Maseda, R. Natsuki, Y. Matsuda, and G. Kobayashi, *Chem. Pharm. Bull.* (Tokyo), **22**, 1939 (1974).

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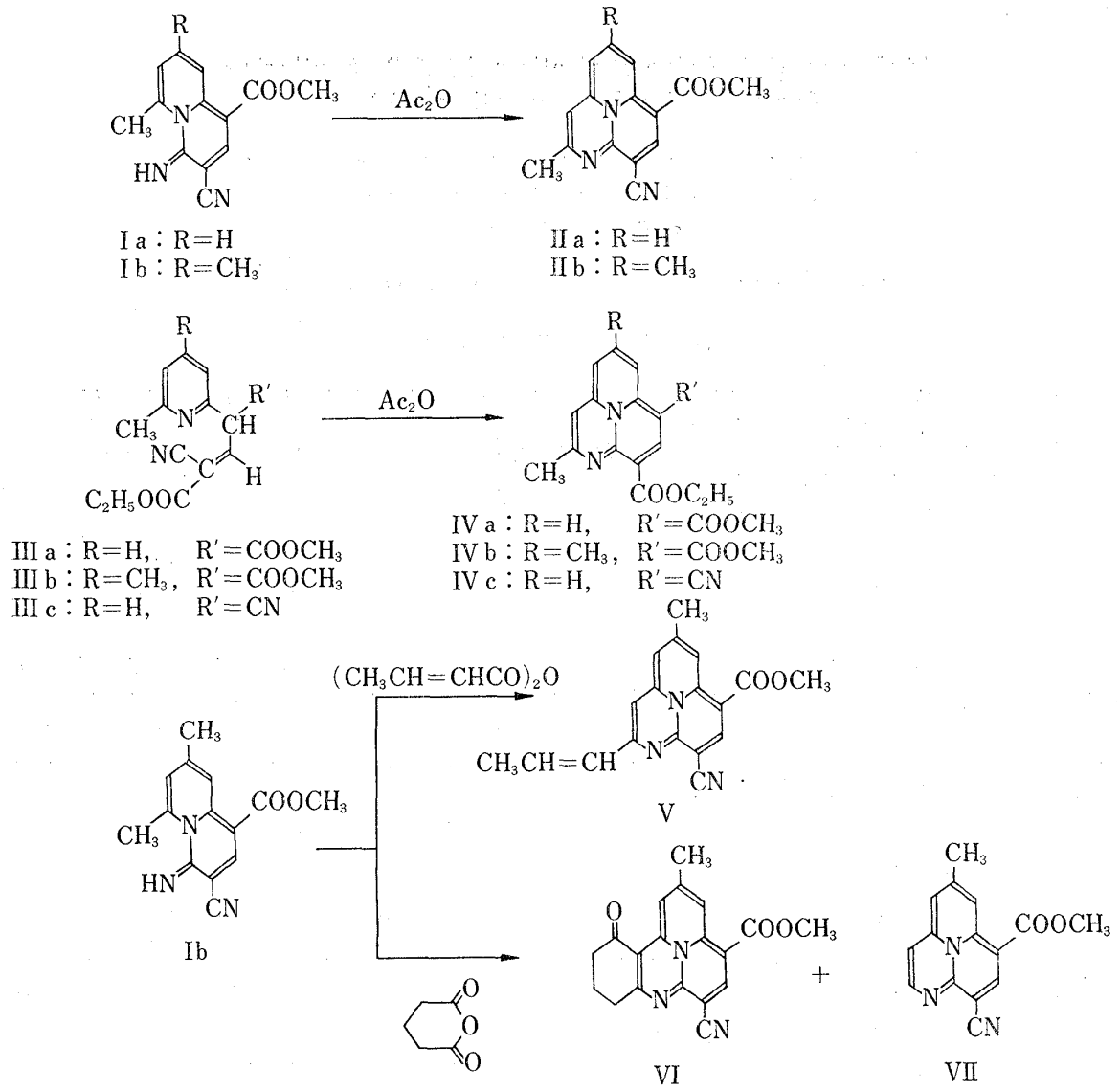

Chart 1

The Degradation of Azacycl[3,3,3]azine Derivatives

At first, we examined the degradation of 1-azacycl[3,3,3] azine derivative (VI) which was regarded as a comparative stable compound. Thus a mixture of VI and polyphosphoric acid (PPA) was heated at 100° for 3 hr to give VIII as green needles, mp 178—179°, $C_{19}H_{17}O_4N_3$. VIII showed the molecular ion peak at *m/e* 351. According to above data and the nuclear magnetic resonance (NMR) spectrum, the structure of VIII was determined methyl 1-aza-11-carbamoyl-7-methyl-5-oxo-2,3,4,5-tetrahydrobenzo[*b*]cycl[3,3,3]azine-9-carboxylate. Then a solution of VIII in 48% hydrobromic acid was refluxed for 3 hr to give IX as red crystals, $C_{16}H_{15}ON_2Br$. According to above data and the NMR spectrum (see Table I), the structure of IX was determined 1-aza-7-methyl-5-oxo-2,3,4,5-tetrahydrobenzo[*b*]cycl[3,3,3]azine hydrobromide, which did not make recyclization to cerunuin skeleton (Xb). By the treatment of IX with potassium carbonate, the stable free base (Xa), mp 123—124° was obtained. X*a* showed an absorption of the carbonyl group at 1625 cm^{-1} in the infrared (IR) spectrum and the molecular ion peak at *m/e* 250 in the mass spectrum. In the NMR spectrum, proton peaks of Xa (see Table I) showed higher magnetic fields than VI, VIII, and IX. We think that

these products are avaiable intermediates for the synthesis of cerunuin (*Lycopodium cernum* L.).[4]

Table I. NMR Spectral Data (ppm) (All Coupling Constants of Ring Protons: *ca.* 8 Hz)

No.	Solvent	H_6 or H_8	H_9	H_{10}	H_{11}	CH_3	H_2, H_3, H_4	
VI	TFAA	8.62(s), 8.72(s)		8.17 (s)		2.55 (s)	2.00—2.30(2H, m) 2.65—2.94(4H, m)	OCH_3:4.03(3H, s)
VIII	TFAA	8.45(s), 8.70(s)		8.50 (s)		2.55 (s)	2.00—2.30(2H, m) 2.65—2.94(4H, m)	OCH_3:4.30(3H, s)
IX	TFAA	6.99(s), 8.18(s)	6.65 (d)	7.46 (t)	6.95 (d)	2.36 (s)	1.95—2.18(2H, m) 2.50—2.90(4H, m)	
Xa	$CDCl_3$	5.70(s), 7.56(s)	5.34 (d)	6.52 (t)	5.75 (d)	2.37 (s)	1.95—2.18(2H, m) 2.50—2.90(4H, m)	

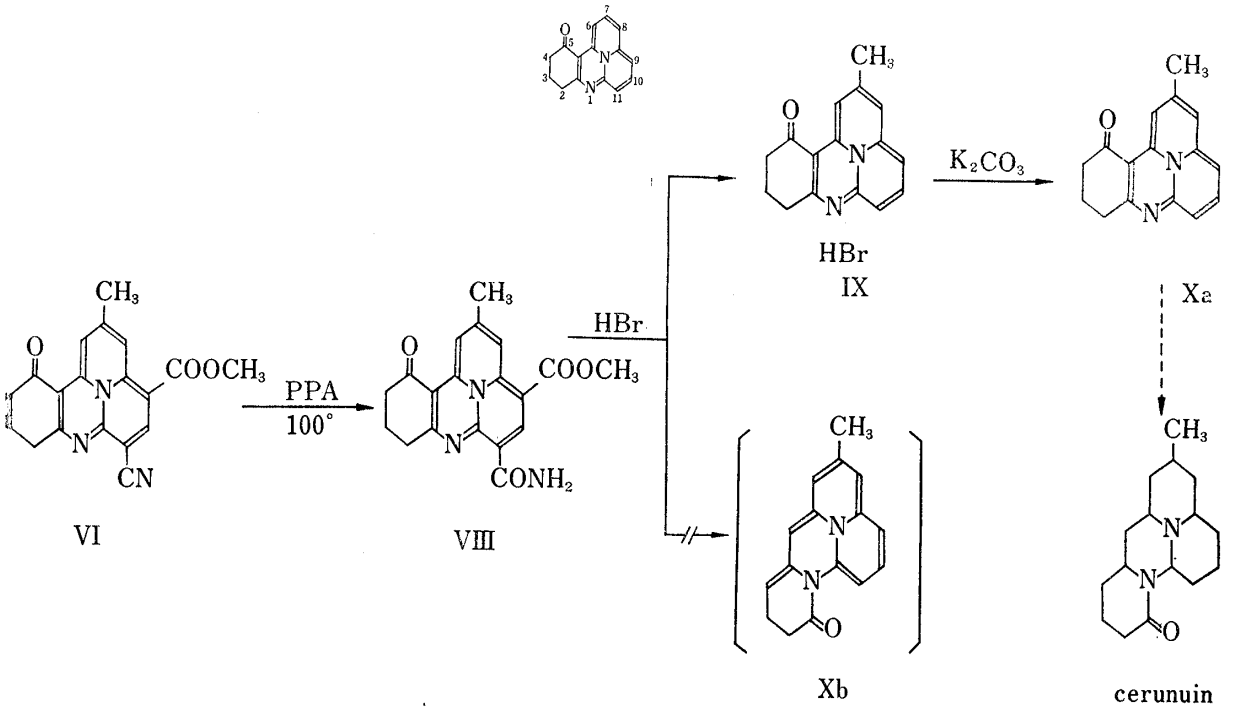

Chart 2

Farquhar[5] reported the synthesis of cycl[3,3,3]azine (XVII) with the existence of a paramagnetic ring current and Dewar[6] pointed out its antiaromaticity. While Ceder[7] reported the synthesis of triazacycl[3,3,3]azine (XVIII) and tetraazacycl[3,3,3]azine (XIX), and then pointed out their aromatic properties. A question, whether the property of a new nitrogen-bridged [12]annulene heterocyclic ring system, 1-azacycl[3,3,3]azine is aromatic or antiaromatic, let us to make following experiments for the synthesis of the parent compound, azacycl-[3,3,3]azine. At first, a mixture of methyl 9-cyano-2-methyl-1-azacycl[3,3,3]azine-7-carboxylate (IIa) with PPA was heated at 100° for 4 hr to give methyl 9-carbamoyl-2-methyl-1-azacycl[3,3,3]azine-7-carboxylate (XIa). On the other hand, the reaction of IIa and PPA at 150° for 5 hr gave XIIa as green crystals, mp 237—238°, $C_{13}H_{11}ON_3$. XIIa showed the

4) *a*) W.A. Ayer, J.K. Jenkins, S. Valvede-Lorenz, and R.H. Burnell, *Can. J. Chem.*, **45**, 433 (1964); *b*) Y. Ban, M. Kimura, and T. Oishi, *Heterocycles*, **2**, 323 (1974).
5) D. Farquhar and D. Leaver, *Chem. Commun.*, **1964**, 24.
6) M.J.S. Dewar and N. Trinajstic, *J. Chem. Soc.* (*A*), **1969**, 1754.
7) O. Ceder and J.E. Andersson, *Acta Chem. Scan.*, **26**, 596 (1972).

molecular ion peak at *m/e* 225 in the mass spectrum. The NMR spectrum of XIIa showed a doublet of C-7 proton due to a proton of C-8 position at δ: 6.20 (J=8 Hz) instead of methoxycarbonyl group of C-7 position. From above data, the structure of XIIa was determined 9-carbamoyl-2-methyl-1-azacycl[3,3,3]azine.

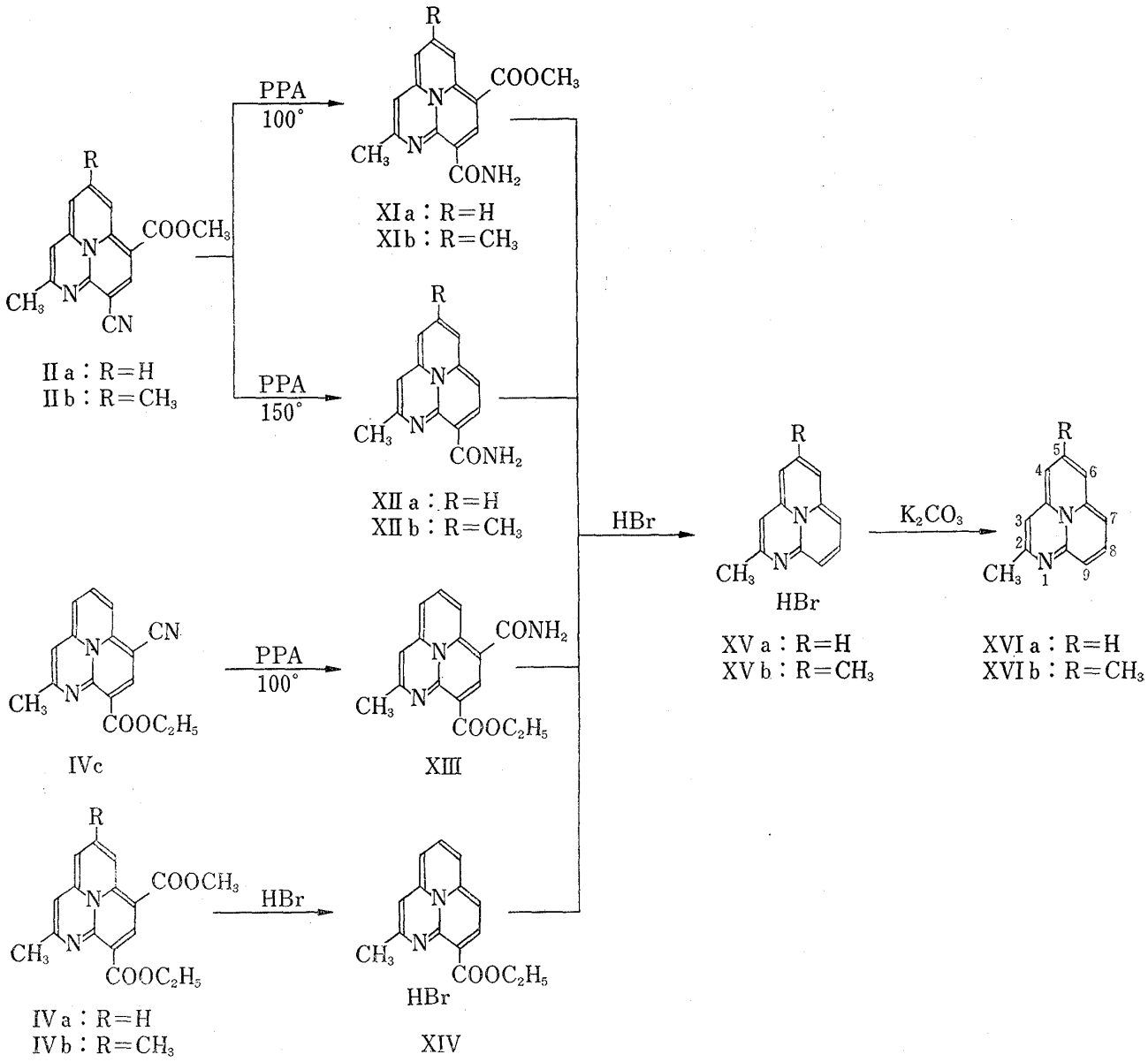

Chart 3

A stable salt, namely 2-methyl-1-azacycl[3,3,3]azine hydrobromide (XVa) was obtained as green crystals by the reaction of XIa or XIIa in 48% hydrobromic acid with refluxing for 3 hr. The structure of XVa was mainly determined by the NMR spectrum (see Fig. 1 and Table II), the mass spectrum, which showed the expected molecular ion peak at *m/e* 182 and no absorption of carbamoyl group in the IR spectrum. By the treatment of XVa with potassium carbonate, 2-methyl-1-azacycl[3,3,3]azine (XVIa) was obtained. XVIa was very unstable yellowish brown crystals, which decomposed on exposure to air within *ca.* 15 min, so the structure of XVIa was only identified by the NMR spectrum (see Fig. 1 and Table II). Under the same reaction condition as giving XIa, XIIa, XVa, and XVIa, methyl 9-cyano-2,5-dimethyl-1-azacycl[3,3,3]azine-7-carboxylate (IIb) was subsequently converted into the corresponding compounds, namely methyl 9-carbamoyl-2,5-dimethyl-1-azacycl[3,3,3]azine-

7-carboxylate (XIb), 9-carbamoyl-2,5-dimethyl-1-azacycl[3,3,3]azine (XIIb), 2,5-dimethyl-1-azacycl[3,3,3]azine hydrobromide (XVb), and 2,5-dimethyl-1-azacycl[3,3,3]azine (XVIb). XVIb, which decomposed on exposure to air within *ca.* 20 min, was a little stabler yellowish brown crystals than XVIa, so the structure of XVIb was identified by the NMR spectrum, too. Then, we examined the degradation of ethyl 7-cyano-2-methyl-1-azacycl[3,3,3]azine-9-carboxylate (IVc). A mixture of IVc and PPA was heated at 100° for 10 hr to give ethyl 7-carbamoyl-2-methyl-1-azacycl[3,3,3]azine-9-carboxylate (XIII). The reaction of XIII with 48% hydrobromic acid by refluxing for 3 hr was obtained green crystals, mp>300°. This was identified with an authentic sample XVa.

Although several attempted to prepare 2-methyl-1-azacycl[3,3,3]azine hydrobromide, the best result was obtained by the route of 9-ethyl 7-methyl 2-methyl-1-azacycl[3,3,3]azine-7,9-dicarboxylate (IVa) as a starting material. Thus a solution of IVa in 48% hydrobromic acid was refluxed for 3 hr to give XIV as green needles. XIV showed the molecular ion peak at *m/e* 230 in the mass spectrum. The NMR spectrum of XIV showed a doublet of C-7 proton due to a proton of C-8 position at δ: 6.44 (J=8 Hz) instead of methoxycarbonyl group of C-7 position and protons of ethoxycarbonyl group of C-9 position at δ: 4.25, 1.25. From above data, the structure of XIV was determined ethyl 2-methyl-1-azacycl[3,3,3]azine-9-carboxylate hydrobromide. Furthermore, by refluxing XIV with 48% hydrobromic acid for 3 hr, XVa was obtained in the good yield. On the similar manner, a solution of IVa or IVb in 48% hydrobromic acid was refluxed for 6 hr to give XVa or XVb respectively, too. This is the best method to prepare 2-methyl- and 2,5-dimethyl-1-azacycl[3,3,3]azine hydrobromides without ammonium bromide which was attributable to carbamoyl group of such 1-azacycl[3,3,3]azine derivataves (XI, XII, XIII).

Table II. NMR Spectral Data (ppm) (All Coupling Constants of Ring Protons: *ca.* 8 Hz)

No.	Solvent	H_3	H_4 or H_6	H_5	H_7	H_8	H_9	CH_3	
IIa[1]	$CDCl_3$	5.03 (s)	5.35(d), 7.15(d)	6.56 (t)		7.10 (s)		1.69	OCH_3:3.63(3H, s)
IVb[1]	$CDCl_3$	5.07 (s)	5.22(s), 7.27(s)			7.63 (s)		1.80, 1.74	OCH_3:3.60(3H, s), OC_2H_5:4.08(2H, q) 1.22(3H, t)
V	$CDCl_3$	5.06 (s)	5.42(s), 7.20(s)			7.26 (s)		1.84	CH=CHCH$_3$:5.70(1H, d), OCH_3:3.62(3H, s) CH=CHCH$_3$:6.68(1H, m) CH=CHCH$_3$:1.80(3H, d)
XIa	TFAA	5.53 (s)	6.42(d), 8.12(d)	7.51 (t)		8.21 (s)		1.94	OCH_3:3.98(3H, s)
XIb	TFAA	5.54 (s)	6.39(s), 8.08(s)			8.25 (s)		2.30, 1.97	OCH_3:3.99(3H, s)
XIIa	TFAA	5.15 (s)	6.08(d), 6.57(d)	7.19 (t)	6.20 (d)	7.23 (d)		1.80	
XIIb	$CDCl_3$	4.18 (s)	4.48(s), 4.90(s)		4.67 (d)	6.96 (d)		1.52, 1.37	
XIII	TFAA	5.42 (s)	6.35(d), 7.53(d)	7.44 (t)		7.83 (s)		1.94	OC_2H_5:4.42(2H, q), 1.40(3H, t)
XIV	DMSO-d_6	5.57 (s)	6.44(d), 6.81(d)	7.38 (t)	6.44 (d)	7.45 (d)		1.78	OC_2H_5:4.25(2H, q), 1.24(3H, t)
XVa	DMSO-d_6	4.64 (s)	5.50(d), 6.17(d)	6.70 (t)	5.50 (d)	6.94 (t)	6.26 (d)	1.40	
XVb	DMSO-d_6	4.64 (s)	5.44(s), 6.16(s)		5.49 (d)	6.90 (t)	6.08 (d)	1.82, 1.44	
XVIa	$CDCl_3$	3.71 (s)	3.84(d), 4.28(d)	5.64 (t)	4.24 (d)	5.60 (t)	4.54 (d)	1.02	
XVIb	$CDCl_3$	3.72 (s)	3.84(s), 4.48(s)		4.36 (d)	5.72 (t)	4.44 (d)	1.28, 1.21	

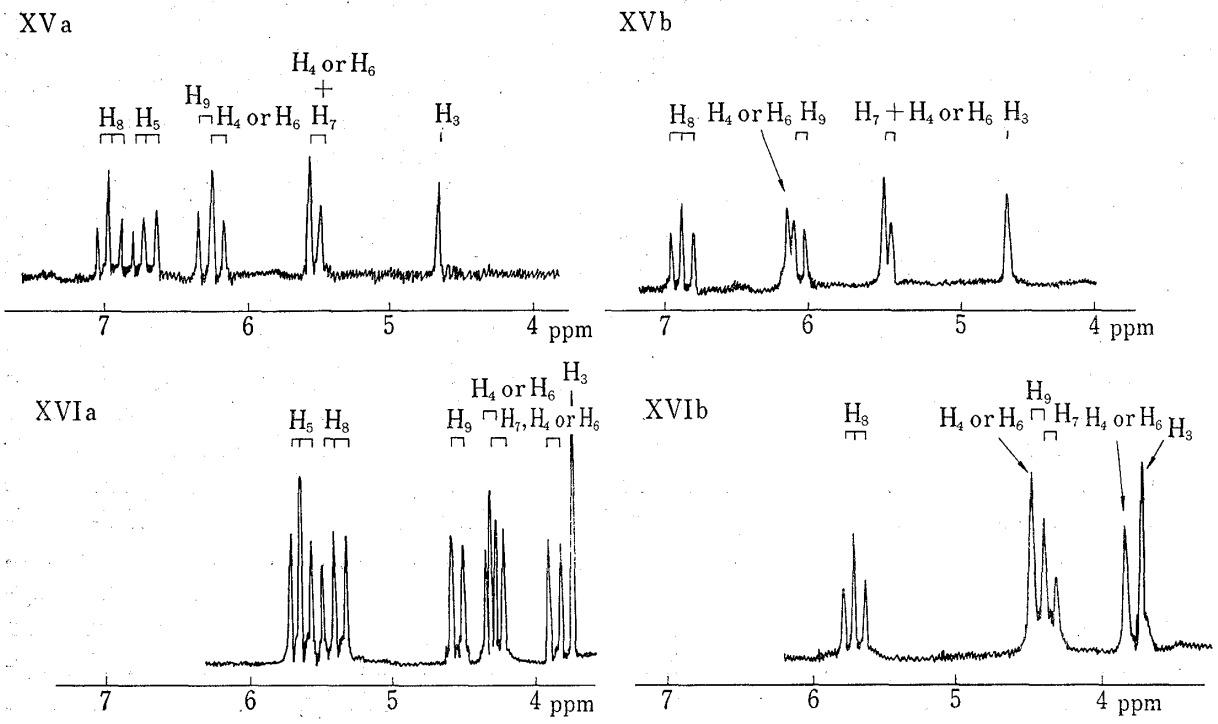

Fig. 1. NMR Spectral Data of XVa,b and XVIa,b

The NMR spectral data for 1-azacycl[3,3,3]azine derivatives are given in Table I, II and Fig. 1. Clearly, the all ring protons of XVIa and XVIb showed at δ: 3.70—5.80 in the exceptionally high magnetic fields. The results clearly established that we do not regard this low degree of deshielding as evidence of an aromatic property in a new [12]annulene heterocyclic ring system, azacyclazine (XVIa, b). Thus XVIa and XVIb are examples of [12]heteromonocyclic system which, based on Dewar's and Breslow's concepts, may be antiaromatic. This antiaromaticity should be reflected in the existence of a paramagnetic ring current in the compounds (XVIa, b), when they are placed into a magnetic field. The C-3 proton in the compound (XVIa), for example, become more shielded by 1.3 ppm in going IIa to XVIa. This dramatic shielding effect, caused by degradation of IIa, can be interpreted as being the result of any one or a combination of the following two factors: an increase in the electron density at the carbon atom, and/or the presence of a paramagnetic ring current. An increase in the electron densities caused by the central nitrogen atom would not be expected to be very significant in view of the fact of diazacyclopent[*fg*]acenaphthylene (XX),[8] and especially in view of quantum chemical calculation (SCF-MO method) done by Dewar[6] and Trost[9] which have shown that there is a very small, if any, contribution to the periphery by the central nitrogen atom in cycl[3,3,3]azine (XVII) and by the central carbon atoms in pyracyclene (XXI). The major factor of the shielding effects in the compounds (XVa, b) is, in all probability, due to their ability to maintain a paramagnetic ring current. We are in the process of preparing other azacyclazine with the hope of expanding our understanding of these interesting compounds.

Experimental

All melting points are uncorrected. The IR spectra were recorded in KBr pelletes on a Nippon-Bunko IRA-2 spectrometer. The ultraviolet (UV) absorption spectra were determined on a Hitachi EP-S-2 spectrometer in 95% EtOH. The NMR spectra were obtained using a JNM-PS-100 (100 MHz) spectrometer with

8) J.L. Atwood, D.C. Hrncir, C. Wong, and W. Paudler, *J. Am. Chem. Soc.*, **96**, 6132 (1974).
9) B.M. Trost, G.M. Bright, C. Frihart, and D. Brittelli, *J. Am. Chem. Soc.*, **93**, 737 (1971).

tetramethylsilane as an internal standard unless otherwise indicated. Mass spectra were recorded on a JEOL-JMS-01SG double focuses mass spectrometer.

Methyl 2-Allyl-9-cyano-5-methyl-1-azacycl[3,3,3]azine-7-carboxylate (V)——A mixture of Ib (0.5 g) excess of crotonic anhydride (5 ml) and a drop of pyridine was heated at 100° for 10 hr. The color of the reaction mixture changed from yellow to dark green. The reaction mixture was poured into ice water. The solution was made basic to litmus with K_2CO_3, and extracted with $CHCl_3$ (3×50 ml). The green exttact was washed with H_2O (50 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was chromatographed on Al_2O_3. Elution with benzene yielded V (60%), which was recrystallized from acetone as green crystals, mp 237—238°. *Anal.* Calcd. for $C_{18}H_{15}O_2N_3$: C, 70.81; H, 4.95; N, 13.76. Found: C, 70.85; H, 4.89; N, 13.65. Mass Spectrum *m/e*: 305 (M^+). IR (KBr) cm^{-1}: 1625 (C=O), 2200 (CN). UV λ_{max}^{EtOH} nm[10]: 316, 415, 438. NMR (see Table II).

Methyl 1-Aza-11-cyano-7-methyl-5-oxo-2,3,4,5-tetrahydrobenzo[*b*]cycl[3,3,3]azine-9-carboxylate (VI)—A mixture of Ib (0.5 g), excess of glutaric anhydride (5 g), and a drop of pyridine was heated at 150° for 5 hr. The color of the reaction mixture changed from yellow to dark green. The reaction mixture was poured into ice water. The solution was made basic to litmus with K_2CO_3, and extracted with $CHCl_3$ (3×50 ml). The green extract was washed with H_2O (50 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was chromatographed on Al_2O_3. Elution with benzene gave VI (70%), which was recrystallized from acetone as green crystals, mp 264—266°. *Anal.* Calcd. for $C_{19}H_{15}O_3N_3$: C, 68.46; H, 4.54; N, 12.61. Found: C, 68.35; H, 4.54; N, 12.61. Mass Spectrum *m/e*: 333 (M^+). IR (KBr) cm^{-1}: 1640, 1700 (C=O), 2200 (CN), UV λ_{max}^{EtOH} nm[10]: 282, 366, 470. NMR (see Table I).

Elution with benzene–acetone (10: 1) gave VII (14%) to be identical an authentic sample,[1] mp 242—244°.

Methyl 1-Aza-11-carbamoyl-7-methyl-5-oxo-2,3,4,5-tetrahydrobenzo[*b*]cycl[3,3,3]azine-9-carboxylate (VIII)——A mixture of VI (0.5 g) and excess of PPA (10 g) was heated at 100° for 3 hr. The greenlish reaction mixture was poured into ice-water. The solution was made basic to litmus with K_2CO_3, and extracted with $CHCl_3$ (3×50 ml). The green extract was washed with H_2O (50 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give crude crystals VIII (60%), which were recrystallized from $CHCl_3$–MeOH as green crystals, mp 178—179°. *Anal.* Calcd. for $C_{19}H_{17}O_4N_3$: C, 64.95; H, 4.88; N, 11.96. Found: C, 64.86; H, 4.77; N, 11.91. Mass Spectrum *m/e*: 351 (M^+). IR (KBr) cm^{-1}: 1620—1660 (broad), 1770 (C=O). UV λ_{max}^{EtOH} nm [10]: 278, 366, 439, 465. NMR (see Table I).

1-Aza-7-methyl-5-oxo-2,3,4,5-tetrahydrobenzo[*b*]cycl[3,3,3]azine Hydrobromide (IX)——A solution of VIII (0.5 g) in 48% HBr (50 ml) was refluxed for 3 hr. The solution was evaporated under reduced pressure to yield crude crystals IX (80%), which were recrystallized from MeOH–EtOAc as red crystals, mp>300°. *Anal.* Calcd. for $C_{16}H_{15}ON_2Br$: C, 58.02; H, 4.57; N, 8.46. Found: C, 57.97; H, 4.59; N, 8.41. Mass Spectrum *m/e*: 250 (M^+−HBr). IR (KBr) cm^{-1}: 1625 (C=O). UV λ_{max}^{EtOH} nm[10]: 277, 365, 428. NMR (see Table I).

Free Base of IX (X)——A solution of IX (0.5 g) in water (50 ml) was made basic to litmus with K_2CO_3, and extracted with $CHCl_3$ (2×30 ml). The extract was then dried (Na_2SO_4) and evaporated under reduced pressure to give crude crystals X (97%), which were recrystallized from acetone as green crystals, mp 123—124°. *Anal.* Calcd. for $C_{16}H_{14}ON_2$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.89; H, 6.00; N, 11.19. Mass Spectrum *m/e*: 250 (M^+). IR (KBr) cm^{-1}: 1625 (C=O). UV λ_{max}^{EtOH} nm [10]: 275, 365, 427. NMR (see Table I).

Methyl 9-Carbamoyl-2-methyl-1-azacycl[3,3,3]azine-7-carboxylate (XIa)——A mixture of IIa (0.5 g) and excess of PPA (10 g) was heated at 100° for 4 hr. The greenlish reaction mixture was poured into ice-water. The solution was made basic to litmus with K_2CO_3, and extracted with $CHCl_3$ (3×50 ml). The greenlish extract was washed with water (50 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give crude crystals XIa (60%), which were recrystallized from $CHCl_3$–MeOH as green needles, mp 277—278°. *Anal.* Calcd. for $C_{15}H_{13}O_3N_3$: C, 63.59; H, 4.63; N, 14.83. Found: C, 63.62. H, 4.49; N, 15.01. Mass Spectrum *m/e*: 283 (M^+). IR (KBr) cm^{-1}: 1670—1690 (broad) (C=O), 3120, 3260 (NH). UV λ_{max}^{EtOH} nm (log ε): 280 (4.57), 340 (4.45), 422 (4.39), 444 (4.49). NMR (see Table II).

Methyl 9-Carbamoyl-2,5-dimethyl-1-azacycl[3,3,3]azine-7-carboxylate (XIb)——A mixture of IIb (0.5 g) and excess of PPA (5 g) was heated at 100° for 4 hr. The resulting mixture was treated as described for XIa. Crude crystals were recrystallized from $CHCl_3$–MeOH to give XIb (60%) as green crystals, mp 270°. *Anal.* Calcd. for $C_{16}H_{15}O_3N_3$: C, 64.64; H, 5.09; N, 14.13. Found: C, 64.65; H, 5.12; N, 14.12. Mass Spectrum *m/e*: 297 (M^+). IR (KBr) cm^{-1}: 1630, 1670 (C=O), 3110, 3250 (NH). UV $\lambda_{max}^{CH_3OCH_2CH_2OH}$ nm (log ε): 283 (4.51), 305 (3.61, shoulder), 384 (4.35), 417 (4.27), 440 (4.41). NMR (see Table II).

9-Carbamoyl-2-methyl-1-azacycl[3,3,3]azine (XIIa)——A mixture of IIa (0.5 g) and excess of PPA (5 g) was heated at 150° for 5 hr. The resulting mixture was treated as described for XIa. Crude crystals were recrystallized from acetone to give XIIa (50%) as green crystals, mp 237—238°. *Anal.* Calcd. for $C_{13}H_{11}ON_3$: C, 69.32; H, 4.92; N, 18.66. Found: C, 69.35; H, 4.89; N, 18.64. Mass Spectrum *m/e*: 225 (M^+). IR (KBr) cm^{-1}: 1630 (C=O), 3240 (NH). UV λ_{max}^{EtOH} nm (log ε): 270 (4.40), 415 (4.42), 430 (4.32). NMR (see Table II).

10) Concentration is unknown because of insufficient solubility.

9-Carbamoyl-2,5-dimethyl-1-azacycl[3,3,3]azine (XIIb)——A mixture of IIb (0.5 g) and excess of PPA (5 g) was heated at 150° for 5 hr. The resulting mixture was treated as described for XIa. Crude crystals were recrystallized from acetone to give XIIb (50%) as green crystals, mp 270°. *Anal.* Calcd. for $C_{14}H_{13}ON_3$: C, 70.27; H, 5.48; N, 17.56. Found: C, 70.32; H, 5.39; N, 17.52. Mass Spectrum *m/e*: 239 (M^+). IR (KBr) cm^{-1}: 1630 (C=O), 3200 (NH). UV λ_{max}^{EtOH} nm (log ε): 276 (4.52), 413 (4.51). NMR (see Table II).

Ethyl 7-Carbamoyl-2-methyl-1-azacycl[3,3,3]azine-9-carboxylate (XIII)——A mixture of IVc (0.5 g) and excess of PPA (5 g) was heated at 100° for 10 hr. The resulting mixture was treated as described for XIa. Crude crystals were recrystallized from $CHCl_3$ to give XIII (80%) as green crystals, mp 277° (decomp.). *Anal.* Calcd. for $C_{16}H_{15}O_3N_3$: C, 64.63; H, 5.09; N, 14.14. Found: C, 64.51; H, 5.02; N, 14.05. Mass Spectrum *m/e*: 297 (M^+). IR (KBr) cm^{-1}: 1650, 1625 (C=O), 3150, 3320 (NH). UV $\lambda_{max}^{CH_3OCH_2CH_2OH}$ nm (log ε): 284 (4.42), 392 (4.27), 422 (4.25), 444 (4.24). NMR (see Table II).

Ethyl 2-Methyl-1-azacycl[3,3,3]azine-9-carboxylate Hydrobromide (XIV)——A solution of IVa (0.5 g) in 48% HBr (20 ml) was refluxed for 3 hr. The green solution was evaporated under reduced pressure to yield crude crystals (90%), which were recrystallized from MeOH as green needles, mp>300°. *Anal.* Calcd. for $C_{15}H_{15}O_2N_2Br$: C, 53.75; H, 4.51; N, 8.36. Found: C, 53.70; H, 4.39; N, 8.40. Mass Spectrum *m/e*: 254 (M^+—HBr). IR (KBr) cm^{-1}: 1670 (C=O). UV λ_{max}^{EtOH} nm (log ε): 236 (4.14), 274 (4.50), 365 (4.22), 386 (4.03, shoulder), 405 (3.90, shoulder), 440 (3.51, shoulder). NMR (see Table II).

2-Methyl-1-azacycl[3,3,3]azine Hydrobromide (XVa)——a) A solution of XIa (0.5 g), XIIa (0.5 g), XIII (0.5 g), or XIVa (0.5 g), in 48% HBr (20 ml) was refluxed for 3 hr. The green solution was evaporated under reduced pressure. The residue was recrystallized from MeOH–EtOAc to give XVa as green crystals in 72%, 70%, 62%, or 80% yields respectively, mp>300°. *Anal.* Calcd. for $C_{12}H_{11}N_2Br$: C, 54.77; H, 4.21; N, 10.65. Found: C, 54.66; H, 4.19; N, 10.62. Mass Spectrum *m/e*: 182 (M^+—HBr). IR ν_{max}^{KBr} cm^{-1}: 2800, 1670, 1640, 1610. UV λ_{max}^{EtOH} nm (log ε): 228 (4.23), 268 (4.43), 350 (4.05), 375 (4.06), 388 (4.05), 428 (2.99). NMR (see Table II).

b) A solution of IVb in 48% HBr (20 ml) was refluxed for 6 hr. The reaction mixture was treated as described for a). Crude crystals were recrystallized from MeOH–EtOAc to give XVa (95%) as green crystals, mp>300°.

2,5-Dimethyl-1-azacycl[3,3,3]azine Hydrobrominde (XVb)——a) A solution of XIb (0.5 g) or XIIb (0.5 g) in 48% HBr (20 ml) was refluxed for 3 hr. The reaction mixture was treated as described for XVa. Crude crystals were recrystallized from MeOH–EtOAc to give XVb as green crystals in 75% or 73% yields respectively, mp>300°. *Anal.* Calcd. for $C_{13}H_{13}N_2Br$: C, 56.34; H, 4.73; N, 10.11. Found: C, 56.26; H, 4.59; N, 10.28. Mass Spectrum *m/e*: 196 (M^+—HBr). IR ν_{max}^{KBr} cm^{-1}: 2770, 1665, 1640, 1615. UV λ_{max}^{EtOH} nm[10]: 228, 265, 271 (shoulder), 347, 374, 387, 420 (shoulder). NMR (see Table II).

b) A solution of IVb in 48% HBr (20 ml) was refluxed for 6 hr. The reaction mixture was treated as described for XVa. Crude crystals were recrystallized from MeOH–EtOAc to give XVb (95%) as green crystals, mp>300°.

Free Base of XVa (XVIa)——A solutfn of XVa (0.5 g) in water (50 ml) was made basic to litmus with K_2CO_3 and instantly extracted with $CHCl_3$ (1×30 ml). The extract was dried (Na_2SO_4) and evaporated under reduced pressure. The residue was dried in vacuumed desiccator (2 mmHg) for 5 min. The NMR spectrum of the crude free base was recorded (see Table II).

Free Base of XVb (XVIb)——A solution of XVb (0.5 g) in water (50 ml) was treated as described for XVIa. The residue was dried in vacuumed desiccator (2 mmHg) for 5 min. The NMR spectrum of crude free base was recorded (see Table II).

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