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Synthesis in the Diazasteroid Group. XX.[1] Synthesis of the 5,14-Diazasteroid System[2]

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trans-2-Quinolizidinone (I) was treated with methyl 2-pyrrolidylacetate (III) to give a mixture of two isomers, 5,14-diaza-1,6-cyclo-1,10-secogon-8-en-11-one (IV) and 5,14-diazagon-8-en-11-one (Va) in 8.6 and 2.7% yields, respectively. 1,2,3,3a,4,5,6,7,8,9-Decahydro-7-benzoylpyrrolo[1,2-*a*]-[1,6]-naphthyridin-5-one (VIb) [prepared from 1-benzoyl-4-piperidone (IIb) and III] was hydrolyzed and then allowed to react with methyl vinyl ketone to give a Michael adduct (VId). It was treated with mercuric acetate to afford regio- and stereoselectively 5,14-diazagon-8-ene-2,11-dione (Vb), whose angular protons at the C_{10} and C_{13} were *anti* to each other. The structure of Vb was determined by X-ray crystallographic analysis. Compound Vb was converted to Va *via* a thioketal (Vc).

Keywords——diazasteroid; 5,14-diazasteroid; oxidative cyclization; mercuric acetate; X-ray crystallographic analysis

In our laboratory, a variety of diazasteroids have been synthesized for examination of their biological activity.[1] In this paper, we will describe a synthesis of the 5,14-diazasteroid system which has not hitherto been synthesized, starting with *trans*-2-quinolizidinone (I) or 1-substituted 4-piperidone (II) and methyl 2-pyrrolidylacetate (III), as shown in Chart 1. Compound I was prepared by the known method[3] in two steps from piperidine and methyl vinyl ketone (MVK). Compound III was synthesized in four steps from 2-pyrrolidone.[4] A solution of I and III in toluene was refluxed in the presence of a catalytic amount of trifluoroacetic acid (TFA), using a Dean–Stark water separator. The reaction mixture showed four spots on thin layer chromatography (TLC), and each product was separated by column chromatography and preparative TLC. The first-eluted product was the starting material, I (34.9%), and the second-eluted product, mp 143—144 °C, was suggested to be 5,14-diaza-1,6-cyclo-1,10-secogon-8-en-11-one (IV), which exhibited characteristic AB-type ($J=14$ Hz) signals at δ 2.72 and 3.74 in the nuclear magnetic resonance (NMR) spectrum due to the C_{10}-protons interposed between the nitrogen atom and carbonyl group. Compound IV exhibited in the mass spectrum (MS) a strong peak at *m/e* 163 due to the fragment produced by retro Diels–Alder reaction (extrusion of piperidene). The third-eluted product, mp 148—151 °C, showed similar physical data to IV and was considered to be a diastereomer of IV. The last-eluted product, which could not be crystallized, showed a strong peak due to M^+ (parent peak) − 1, but a weak fragment peak at *m/e* 163 in the MS. This product was supposed to be a crude 5,14-diazagon-8-en-11-one (Va), which was confirmed later (*vide infra*). The yields of IV, a diastereomer of IV, and Va were 6.3, 2.3, and 2.7%, respectively. The poor yield of Va was ascribed to the formation of 2-(2-methoxycarbonylmethylpyrrolidyl)-*trans*-quinolizidin-2-ene in preference to the corresponding quinolizidin-1-ene as an intermediate. The preferential formation of 2-ene rather than 1-ene has already been found in *trans*-2-decalone.[5]

Because of the preferential formation of IV rather than Va and the poor yields of IV and

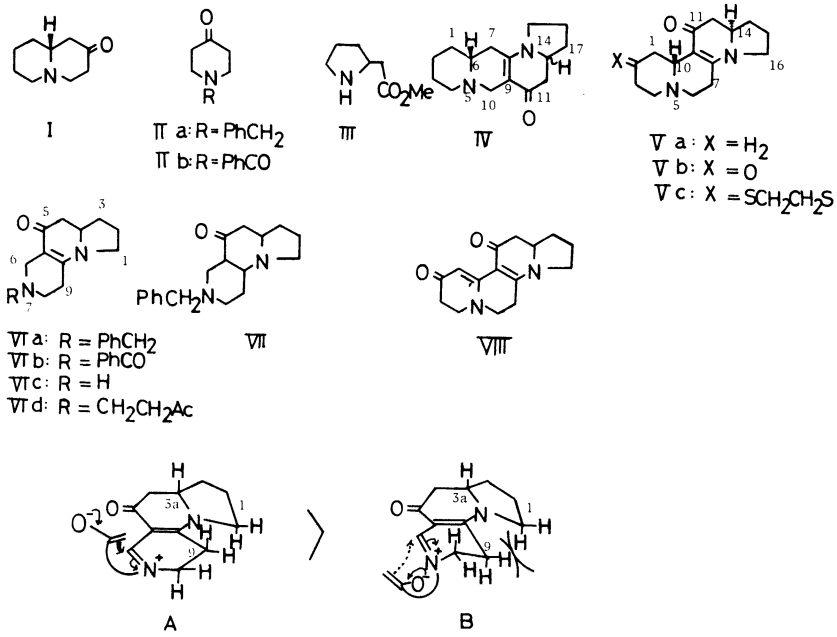

Chart 1

Va, we tried to obtain the 5,14-diazasteroid system from II. 1-Benzyl-4-piperidone (IIa) is commercially available and was treated with III in the presence of TFA as a catalyst in benzene to give 1,2,3,3a,4,5,6,7,8,9-decahydro-7-benzylpyrrolo[1,2-*a*][1,6]naphthyridin-5-one (VIa) in 33.3% yield accompanied with recovery of IIa (49.2%). The NMR spectrum of VIa showed an AB-type signal at δ 2.99 and 3.47 due to the C_6-methylene protons, and a carbonyl band at 1605 cm^{-1} was detected in the infrared (IR) spectrum. When *p*-toluenesulfonic acid(*p*-TsOH) was used as a catalyst, the yield of VIa was 28.4%, and the recovery of IIa was 40.9%. Trials of catalytic debenzylation using Adams' catalyst[6] gave an inseparable mixture and the catalytic reduction of VIa–hydrochloride using palladium–carbon[7] gave a perhydro compound, 7-benzylperhydropyrrolo[1,2-*a*][1,6]naphthyridin-5-one (VII), mp 107—108 °C, which exhibited a carbonyl band at 1705 cm^{-1} in the IR spectrum. The stereochemistry of the ring junctures could not be determined.

As attempts to debenzylate VIa failed, a similar reaction was carried out by using 1-benzoyl-4-piperidone (IIb) instead of IIa. Compound IIb was prepared in five steps starting with ethyl acrylate and liquid ammonia.[8] Compound IIb was treated with III in the presence of a catalytic amount of TFA in benzene to give VIb in 55.6% yield accompanied with recovery of IIb (34.6%). When acetic acid was used as a catalyst, VIb was obtained in better yield in a reasonably pure state without using column chromatography. The NMR spectrum of VIb showed AB-type signals at δ 4.04 and 4.33 due to the C_6-methylene protons and multiplet signals at δ 4.3—4.6 due to the C_{3a} proton. Debenzoylation of VIb was performed with 20% sodium hydroxide–ethanol solution under reflux to give VIc in 98.4% yield. Compound VIc was treated with MVK at room temperature to afford a Michael addition product (VId), which showed a singlet signal at δ 2.17 due to the methyl protons in the NMR spectrum and a carbonyl band at 1705 and 1605 cm^{-1} in the IR spectrum. The cyclization of VId was effected by mercuric acetate in 10% acetic acid followed by treatment with hydrogen sulfide to give a cyclized product, mp 190—191 °C, in 86.4% yield. Analyses using carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectroscopy and high-performance liquid chroma-

tography (HPLC) revealed that the product was diastereomerically pure. The NMR spectrum exhibited an octet-like signal at δ 3.5—3.8 due to the C_{13} proton. This product showed absorptions at 2880—2770, 1710, and 1605 cm^{-1} due to the Bohlmann, carbonyl, and vinylogous lactam bands, respectively, in the IR spectrum. The Bohlmann bands suggested that the fusion of the A/B ring is *trans*. To establish the structure of the cyclized product, dehydrogenation was carried out. When treated with mercuric acetate for a long time, Vb gave a product in 70.5% yield, whose NMR spectrum showed a sharp singlet signal at δ 6.61 due to the vinylic proton. From the above data, the cyclized product and its dehydrogenation product were suggested to be 5,14-diazagon-8-ene-2,11-dione (Vb) and 5,14-diazagona-1(10),8-diene-2,11-dione (VIII), respectively. X-Ray crystallographic analysis of Vb was carried out to determine the stereochemistry, and it was revealed that the angular protons at the C_{10} and C_{13} were *anti* to each other, as shown in Fig. 1. Thus, the cyclization reaction of VId using mercuric acetate proceeded regio- and stereoselectively to afford Vb. We considered that the conformer of the intermediate in the oxidative ring closure on VId is probably A, which may involve less steric repulsion between C_1 and C_9 methylene protons than in B, and the enolate may approach the iminium ion from the sterically less hindered side, or the same side with respect to the C_{3a}-proton, maintaining maximum overlap of the orbitals of the enolate and iminium ion.[9]

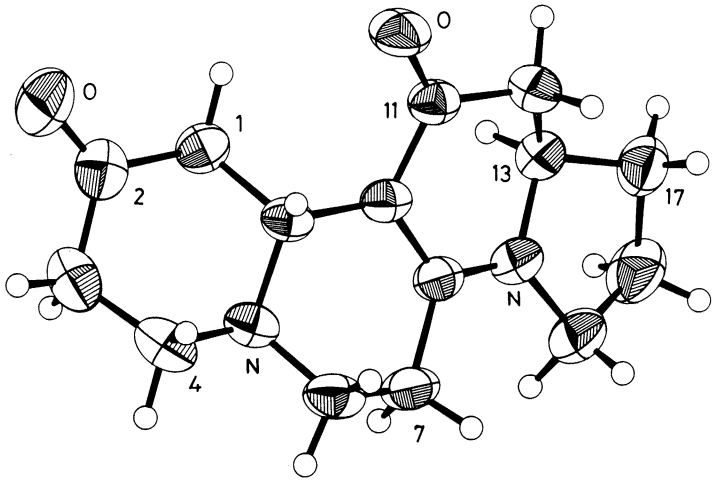

Fig. 1. ORTEP Drawing of Compound V_b

Compound Vb was treated with ethanedithiol and borontrifluoride etherate at 60 °C for 2 h to afford a thioketal (Vc) in 93.4% yield. Compound Vc was then desulfurized with Raney nickel in dry ethanol at 60 °C for 2 h to give Va in 67.3% yield. The product was identified as the target compound on the basis of the elemental analysis, MS, and IR and NMR spectra. These physical data were nearly identical with those of the minor product obtained from I and III.

The biological activities of these synthesized compounds are now being examined.

Experimental

All melting points (taken on a Kofler block) and boiling points (bath temperature) are uncorrected. IR spectra were determined for solutions in $CHCl_3$ by using a JASCO A 102 diffraction grating spectrophotometer; absorption data are given in cm^{-1}. Ultraviolet (UV) spectra were obtained in MeOH with a Hitachi 220 spectrometer, and

absorption maxima are given in nm. HPLC was carried out on a Shimadzu LC-3A apparatus equipped with a column packed with RP-select B and MeOH/0.035 M phosphate buffer (pH 6.9) = 60/40 as the eluent (flow rate: 1.0 ml/min). NMR spectra measured in $CDCl_3$ were recorded on a Varian XL-200 spectrometer with tetramethylsilane as an internal standard. The chemical shifts and coupling constants (J) are given in δ and Hz, respectively. MS were measured with a JEOL D-200 or D-300 (70 eV, direct inlet system) spectrometer. All solvents were removed by evaporation under reduced pressure after drying of the solution over anhydrous K_2CO_3.

Condensation of *trans*-2-Quinolizidinone (I) and Methyl 2-Pyrrolidylacetate (III)——A mixture of I[3] (0.766 g, 5 mmol) and III[4] (0.939 g, 6.6 mmol), TFA (0.086 ml, 1.1 mmol), and toluene (30 ml) was heated to boiling in a flask equipped with a Dean–Stark water separator. After about 4 h, the mixture was cooled and washed with saturated aq. $NaHCO_3$ and brine. The oily product obtained after removal of the solvent was fractionated through an SiO_2 column. I (267 mg, 34.9%), 5,14-diaza-1,6-cyclo-1,10-secogon-8-en-11-one (IV, 77.6 mg, 6.3%), a diastereoisomer of IV (28.2 mg, 2.3%), and 5,14-diazagon-8-en-11-one (Va, 33.5 mg, 2.7%) were eluted with 2, 3, 3, and 5% MeOH–$CHCl_3$, respectively. IV: mp 143—144 °C (recrystallized from isopropyl ether). IR: $\nu_{C=O}$ 1620, 1560. UV λ_{max}: 336. NMR: 1.1—2.8 (17H, m), 2.72 (1H, d, J=14, C_{10}-H), 3.11 (1H, d, J=12), 3.2—3.9 (2H, m, C_6-H and C_{13}-H), 3.74 (1H, d, J=14, C_{10}-H). MS m/e (%): 246 (M^+, 53), 245 (M^+-1, 100), 203 (M^+-1-CH_3CO, 16), 163 (M^+ – piperidene, 29). *Anal.* Calcd for $C_{15}H_{22}N_2O \cdot 2/5H_2O$: C, 71.06; H, 9.06; N, 11.05. Found: C, 71.02; H, 9.11; N, 10.94. High resolution MS, Calcd for $C_{15}H_{22}N_2O$: 246.1731. Found: 246.1718. Diastereomer of IV: mp 148—151 °C (recrystallized from petr. ether). IR: $\nu_{C=O}$ 1625, 1565. UV λ_{max}: 334. NMR: 1.1—2.8 (17H, m), 2.74 (1H, d, J=14, C_{10}-H), 3.11 (1H, d, J=12), 3.3—3.5 (1H, m, C_6-H), 3.4—3.9 (1H, m, C_{13}-H), 3.75 (1H, d, J=14, C_{10}-H). MS m/e (%): 246 (M^+, 53), 245 (M^+-1, 100), 203 (M^+-1-CH_3CO, 20), 163 (M^+ – piperidene, 24). *Anal.* Calcd for $C_{15}H_{22}N_2O \cdot 0.15H_2O$: C, 72.34; H, 9.03; N, 11.25. Found: C, 72.35; H, 8.86; N, 11.06. Va (crude, *vide infra*): IR: ν_{CH} 2810, 2750 (Bohlmann band), $\nu_{C=O}$ 1600. MS m/e (%): 246 (M^+, 53), 245 (M^+-1, 100), 217 (M^+-1-CO, 39), 204 (M^+-CH_3CO, 12), 190 ($M^+-C_4H_9$, 29), 163 (M^+ – piperidene, 4). High-resolution MS, calcd for $C_{15}H_{22}N_2O$: 246.1731. Found: 246.1704.

Condensation of 1-Benzyl-4-piperidone (IIa) and III——A benzene solution of IIa (2.64 g, 14 mmol), III (2 g, 14 mmol), and TFA (0.1 ml, 1.3 mmol) was refluxed in a flask equipped with a Dean–Stark water separator for 20 h. The reaction mixture was cooled and washed with saturated $NaHCO_3$ and brine. The crude product obtained after removal of the solvent was fractionated by SiO_2 column chromatography. IIa (1.30 g, 49.2%) and 1,2,3,3a,4,5,6,7,8,9-decahydro-7-benzylpyrrolo[1,2-*a*][1,6]naphthyridin-5-one (VIa, 1.31 g, 33.3%) were eluted with $CHCl_3$ and 2% MeOH–$CHCl_3$, respectively. VIa: bp 112 °C (1.5 mmHg). IR: $\nu_{C=O}$ 1605. UV λ_{max}: 338. NMR: 1.4—2.8 (10H, m), 2.99 (1H, d, J=13, C_6-H), 3.34 (2H, t, J=8, C_8-H), 3.47 (1H, d, J=13, C_6-H), 3.56 (2H, d like, J=14, $PhCH_2$–), 3.6—3.7 (1H, m, C_{3a}-H), 7.1—7.4 (5H, m, Ph). MS m/e (%): 282 (M^+, 24), 281 (M^+-1, 22), 191 (M^+-PhCH_2, 100), 91 ($PhCH_2^+$, 82). *Anal.* Calcd for $C_{18}H_{22}N_2O \cdot 1/10H_2O$: C, 76.08; H, 7.87; N, 9.86. Found: C, 75.97; H, 7.98; N, 9.90.

Catalytic Reduction of VIa——VIa–hydrochloride, prepared from VIa (200 mg, 0.7 mmol) and HCl gas in Et_2O, was dissolved in dry MeOH. The methanolic solution was stirred in the presence of Pd–C (10%, 0.3 g) at room temperature under high pressure (80 atm) for 14 h. The filtrate was basified with Et_3N and concentrated. The residue was fractionated through an SiO_2 column. 7-Benzylperhydropyrrolo[1,2-*a*][1,6]naphthyridin-5-one (VII) was eluted with 2% MeOH–$CHCl_3$, 43 mg (21.3%), mp 107—108 °C (recrystallized from H_2O). IR: ν_{CH} 2970, 2800, $\nu_{C=O}$ 1705. NMR: 1.4—2.1 (10H, m), 2.2—3.0 (4H, m), 3.0—3.3 (2H, m, C_{9a}-H and C_{5a}-H), 3.4—3.6 (1H, m, C_{3a}-H), 3.50 (2H, d like, J=4, $-CH_2-Ph$), 6.1—6.3 (5H, m, Ph). MS m/e (%): 284 (M^+, 37), 193 (M^+-CH_2-Ph, 63), 91 ($Ph-CH_2$, 100). *Anal.* Calcd for $C_{18}H_{24}N_2O \cdot 1/10H_2O$: C, 75.54; H, 8.52; N, 9.79. Found: C, 75.46; H, 8.36; N, 9.73.

Condensation of 1-Benzoyl-4-piperidone (IIb) with III——A benzene solution (100 ml) of IIb[8] (12.7 g, 89 mmol), III (16 g, 79 mmol), and AcOH (20 ml) was refluxed using the same apparatus as mentioned above for 15 h. The cooled mixture was washed with saturated aq. $NaHCO_3$ and brine. The solid obtained after removal of the organic solvent was recrystallized from acetone to give 7-benzoyl-1,2,3,3a,4,5,6,7,8,9-decahydropyrrolo[1,2-*a*][1,6]-naphthyridin-5-one (VIb). The mother liquor was concentrated and fractionated by SiO_2 column chromatography. IIb (0.94 g, 5.9%) and VIb were eluted with CH_2Cl_2 and 3% MeOH–CH_2Cl_2, respectively. The combined yield of VIb was 17 g (72.9%). mp 144—145 °C (colorless needles). IR: $\nu_{C=O}$ 1605, 1545. NMR: 1.5—2.7 (8H, m), 3.1—3.4 (1H, m, C_4-H), 3.44 (2H, t, J=8, C_8-H), 3.5—3.8 (1H, m, C_4-H), 4.04 and 4.33 (each 1H, d, J=14, C_6-H), 4.3—4.6 (1H, m, C_{3a}-H), 7.38 (5H, br s, aromatic H). MS m/e (%): 296 (M^+, 29), 191 (M^+-PhCO, 63), 149 (m/e 191 $-C_2H_4N$, 100), 105 ($PhCO^+$, 50). *Anal.* Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 72.90; H, 6.79; N, 9.45.

1,2,3,3a,4,5,6,7,8,9-Decahydropyrrolo[1,2-*a*][1,6]naphthyridin-5-one (VIc)——NaOH (20% aq. solution, 20 ml) was added to an ethanolic solution (20 ml) of VIb (4.5 g, 15.3 mmol), and then the mixture was heated under reflux for 2 h. The residue obtained after removal of the solvent was dissolved in CH_2Cl_2, and the solution was washed with water. The residue obtained after removal of the solvent was recrystallized from CH_2Cl_2 to give pure VIc. mp 119—120 °C (colorless needles). The yield was 2.9 g (98.4%). NMR: 1.0—2.8 (9H, m), 2.97 and 3.07 (each 1H, d, J=13, C_6-H), 3.2—4.3 (5H, m). MS m/e (%): 192 (M^+, 61), 191 (M^+-1, 100), 163 (M^+-1-CO, 25).

7-(3-Oxo-1-butyl)-1,2,3,3a,4,5,6,7,8,9-decahydropyrrolo[1,2-*a*][1,6]naphthyridin-5-one (VId)——MVK (1.05 g, 15.1 mmol) was added to a solution of VIc (2.9 g, 15.1 mmol) in CH_2Cl_2 (10 ml), and the mixture was stirred at room

temperature for 12 h. The residue obtained after removal of the solvent was recrystallized from isopropyl alcohol to give VId (2.9 g, 74%). mp 73—75 °C. IR: ν_{CH} 2880, 2810, 2770 (Bohlmann band), $\nu_{C=O}$ 1705, 1605. NMR: 1.5—2.5 (6H, m), 2.17 (3H, s, CH_3CO), 2.47 and 2.74 (each 2H, t, $J=5$, $-COCH_2CH_2N<$), 2.6—2.8 (4H, m, C_4- and C_9-H), 2.96 and 3.47 (each 1H, d, $J=13$, C_6-H), 3.3—3.6 (2H, m, C_8-H), 3.5—3.8 (1H, octet like, C_{3a}-H). MS *m/e* (%): 262 (M^+, 33), 261 (M^+-1, 82), 204 (M^+ − acetone, 84), 192 (VIc, 45), 191 (100). *Anal.* Calcd for $C_{15}H_{22}N_2O_2$: C, 68.07; H, 8.45; N, 10.68. Found: C, 68.61; H, 8.22; N, 10.54.

5,14-Diazagon-8-ene-2,11-dione (Vb)——VId (0.49 g, 1.9 mmol) was added to a solution of Hg $(OAc)_2$ (2.4 g, 7.5 mmol) in 10% AcOH (35 ml). The mixture was heated at 100 °C for 2.5 h. The precipitated $Hg_2(OAc)_2$ was filtered off and then H_2S gas was bubbled into the filtrate. The resulting mixture was filtered through celite and concentrated. The residue was treated with aq. NH_3 and the alkaline solution was extracted with CH_2Cl_2 (20 ml × 3). The combined organic layer was washed with brine and concentrated. The residue was recrystallized from acetone to give Vb (0.42 g, 86.4%). mp 190—191 °C (colorless needles). HPLC: t_R 3.71 min. IR: ν_{CH} 2880, 2820, 2770 (Bohlmann band), $\nu_{C=O}$ 1710, 1605. UV λ_{max} (ε): 332 (16000). NMR: 1.4—3.2 (16H, m), 3.32 and 3.50 (each 1H, dd, $J=15$, 5, C_1-H), 3.46 (1H, m, C_{10}-H), 3.5—3.8 (1H, octet like, C_{13}-H). ^{13}C-NMR: 212.2 (C_2), 188.0 (C_{11}), 157.4 (C_8), 106.1 (C_9), 58.7, 57.4, 53.9, 48.5, 47.1, 46.6, 42.3, 41.0, 32.5, 29.0, 23.8. MS *m/e* (%): 260 (M^+, 51), 259 (M^+-1, 100), 217 (M^+-1-CH_2CO, 31), 190 ($M^+-C_4H_6O$, 86), 175 (41), 163 (M^+ − piperidenone, 4). *Anal.* Calcd for $C_{15}H_{22}N_2O_2$: C, 69.20; H, 7.74; N, 10.76. Found: C, 69.05; H, 7.78; N, 10.61.

5,14-Diazagona-1(10),8-diene-2,11-dione (VIII)——Vb (1 g, 3.9 mmol) was added to a solution of Hg $(OAc)_2$ (4.9 g, 15 mmol) in 10% AcOH (50 ml), and then the mixture was heated at 100 °C for 8.5 h. The resulting mixture was saturated with H_2S and filtered through celite. The filtrate was concentrated and basified with aq. NH_3. The alkaline solution was extracted with CH_2Cl_2 (50 ml × 3). The organic layer was washed with brine and concentrated. The residue was fractionated through an SiO_2 column. Vb (110 mg, 11.1%) and VIII (700 mg, 70.5%) were eluted successively with $CHCl_3$. VIII: mp 223—225 °C (recrystallized from CH_2Cl_2, colorless needles). IR: $\nu_{C=O}$ 1625, 1600. UV λ_{max} (ε): 355 (36000). NMR: 1.7—3.8 (16H, m), 3.7—4.0 (1H, octet like, C_{13}-H), 6.61 (1H, s, C_1-H). MS *m/e* (%): 259 (M^+ + 1, 20), 258 (M^+, 100), 257 (M^+-1, 35), 230 (M^+ − CO, 40), 229 (75), 175 (M^+ − 2-methylenepyrrolidine, 25), 108 (*N*-methylene-4-pyridone, 27). *Anal.* Calcd for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02; N, 10.85. Found: C, 69.47; H, 7.15; N, 10.60.

Vb-2-ethanedithioketal (Vc)——$BF_3 \cdot Et_2O$ (47%, 3.5 ml 32.2 mmol) was added at 0 °C to a mixture of Vb (0.5 g, 1.9 mmol) and ethanedithiol (2 ml, 23.8 mmol), and then the mixture was heated at 60 °C for 2 h. The reaction mixture basified with 5% K_2CO_3 was extracted with CH_2Cl_2 (50 ml × 3). The organic layer was washed with brine and then dried over $CaSO_4$. The viscous syrup obtained after removal of the solvent was fractionated through an SiO_2 column. Vc (0.6 g, 93.4%) was eluted with 1% MeOH–$CHCl_3$ and recrystallized from acetone. mp 230—235 °C (colorless needles). IR: ν_{CH} 2950, 2830, 2770 (Bohlmann band), $\nu_{C=O}$ 1600, 1540. NMR: 3.35 (4H, s like, $-CH_2-S-$). ^{13}C-NMR: 189.2 (C_{11}), 158.4 (C_8), 106.8 (C_9). MS *m/e* (%): 336 (M^+, 33), 275 ($M^+-C_2H_5S$, 63), 243 ($M^+-C_2H_5S_2$, 39), 204 (*m/e* 243 − C_3H_3, 100). *Anal.* Calcd for $C_{17}H_{24}N_2OS_2$: C, 60.68; H, 7.19; N, 8.32. Found: C, 60.38; H, 7.24; N, 8.09.

5,14-Diazagon-8-en-11-one (Va)——An ethanolic solution of Vc (0.49 g, 2.0 mmol) and Raney-Ni (9.8 g) was heated at 50 °C for 9 h. The catalyst was removed and the filtrate was concentrated to give a viscous syrup, which was fractionated through an Al_2O_3 column. Va (238 mg, 67.3%) was eluted with $CHCl_3$ and recrystallized from Et_2O. mp 104—106 °C (colorless needles). IR: ν_{CH} 2810, 2750 (Bohlmann band), $\nu_{C=O}$ 1600. UV λ_{max} (ε): 332 (11000). NMR: 0.9—2.7 (12H, m), 2.78 (2H, t, $J=6$, C_7-H), 2.94 (2H, br s, C_{12}-H), 3.46 (2H, t, $J=6$, C_6-H), 3.4—3.6 (1H, m, C_{10}-H), 3.4—3.8 (1H, octet like, C_{13}-H). ^{13}C-NMR: 188.7 (C_{11}), 158.0 (C_8), 98.8 (C_9), 61.1, 57.2, 56.3, 50.0, 46.5, 42.9, 32.5, 31.3, 29.1, 25.9, 25.2, 23.9. MS *m/e* (%): 246 (M^+, 57), 245 (M^+-1, 100), 217 (M^+-1-CO or $M^+-1-C_2H_4$, 39), 204 (M^+-CH_2CO, 12), 190 ($M^+-C_4H_9$, 25), 163 (M^+ − piperidene, null). *Anal.* Calcd for $C_{15}H_{22}N_2O$: C, 73.13; H, 9.00; N, 11.37. Found: C, 73.07; H, 8.99; N, 11.19.

X-Ray Analysis of Compound Vb——Intensity measurements were performed with a Rigaku AFC 5R automatic

TABLE I. Crystal Data for Compound V_b

Molecular formula		$C_{15}H_{20}N_2O_2$
Molecular weight		260.33
Crystal system		Triclinic
Space group		$P\bar{1}$
Cell dimensions	*a*	11.80 (3) Å
	b	13.56 (9)
	c	8.55 (7)
	v	1332.5 (4) Å
	z	4
	D_x	1.298 g cm^{-3}
Final *R* value		5.1%

TABLE II. Fractional Coordinates of Non-hydrogen Atoms with Estimated Standard Deviations in Parenthesis

Atom	x	y	z	B
C(1)	−0.618 (3)	−0.405 (9)	−0.160 (3)	0.006 (5)
C(2)	−0.707 (0)	−0.381 (8)	−0.059 (4)	0.007 (9)
C(3)	−0.659 (3)	−0.353 (2)	0.113 (6)	0.010 (1)
C(4)	−0.556 (2)	−0.288 (3)	0.136 (8)	0.011 (2)
N(5)	−0.469 (7)	−0.332 (3)	0.050 (5)	0.008 (3)
C(6)	−0.362 (4)	−0.280 (2)	0.089 (7)	0.010 (6)
C(7)	−0.267 (7)	−0.340 (8)	0.028 (2)	0.007 (7)
C(8)	−0.310 (4)	−0.375 (7)	−0.144 (8)	0.006 (7)
C(9)	−0.426 (7)	−0.364 (1)	−0.218 (2)	0.006 (4)
C(10)	−0.518 (4)	−0.334 (5)	−0.123 (2)	0.007 (0)
C(11)	−0.459 (4)	−0.365 (9)	−0.391 (4)	0.007 (0)
C(12)	−0.362 (9)	−0.391 (7)	−0.480 (7)	0.007 (8)
C(13)	−0.270 (6)	−0.460 (1)	−0.387 (3)	0.006 (6)
N(14)	−0.231 (7)	−0.416 (0)	−0.224 (0)	0.005 (7)
C(15)	−0.107 (0)	−0.434 (4)	−0.160 (5)	0.005 (7)
C(16)	−0.069 (2)	−0.503 (0)	−0.289 (8)	0.006 (3)
C(17)	−0.157 (1)	−0.480 (2)	−0.444 (0)	0.007 (4)
O(2)	−0.810 (5)	−0.387 (8)	−0.114 (0)	0.007 (3)
O(10)	−0.558 (3)	−0.342 (0)	−0.466 (2)	0.007 (6)

TABLE III. Bond Distances (Å) for the Non-hydrogen Atoms

C(1)–C(2)	1.505 (3)	C(1)–C(10)	1.538 (2)	C(2)–C(3)	1.497 (3)
C(2)–O(2)	1.214 (2)	C(3)–C(4)	1.515 (3)	C(4)–N(5)	1.462 (3)
N(5)–C(6)	1.450 (3)	N(5)–C(10)	1.471 (2)	C(6)–C(7)	1.513 (3)
C(7)–C(8)	1.508 (2)	C(8)–C(9)	1.383 (2)	C(8)–N(14)	1.337 (2)
C(9)–C(10)	1.511 (3)	C(9)–C(11)	1.446 (2)	C(11)–C(12)	1.516 (3)
C(11)–O(11)	1.238 (2)	C(12)–C(13)	1.511 (2)	C(13)–N(14)	1.469 (2)
C(13)–C(17)	1.525 (3)	N(14)–C(15)	1.466 (2)	C(15)–C(16)	1.520 (4)
C(16)–C(17)	1.526 (3)				

TABLE IV. Valence Angles (°) for the Non-hydrogen Atoms

C(10)–C(1)–C(2)	112.82 (15)	C(1)–C(2)–C(3)	111.43 (19)
C(1)–C(2)–O(2)	122.04 (18)	C(3)–C(2)–O(2)	122.21 (21)
C(2)–C(3)–C(4)	112.43 (19)	C(3)–C(4)–N(5)	110.82 (16)
C(4)–N(5)–C(10)	109.66 (13)	C(4)–N(5)–C(6)	112.23 (14)
C(6)–N(5)–C(10)	110.47 (14)	N(5)–C(6)–C(7)	110.03 (15)
C(6)–C(7)–C(8)	110.51 (14)	C(7)–C(8)–C(9)	120.69 (16)
C(7)–C(8)–N(14)	117.52 (14)	C(9)–C(8)–N(14)	121.77 (14)
C(8)–C(9)–C(10)	121.69 (14)	C(8)–C(9)–C(11)	119.07 (16)
C(10)–C(9)–C(11)	118.60 (14)	C(1)–C(10)–C(9)	111.76 (13)
C(1)–C(10)–N(5)	107.77 (14)	C(9)–C(10)–N(5)	111.60 (13)
C(9)–C(11)–C(12)	116.43 (14)	C(9)–C(11)–O(11)	123.33 (17)
C(12)–C(11)–O(11)	120.08 (15)	C(11)–C(12)–C(13)	111.00 (15)
C(12)–C(13)–C(17)	118.39 (17)	C(12)–C(13)–N(14)	108.84 (15)
N(14)–C(13)–C(17)	102.89 (14)	C(8)–N(14)–C(13)	119.44 (13)
C(8)–N(14)–C(15)	127.40 (15)	C(13)–N(14)–C(15)	112.64 (16)
N(14)–C(15)–C(16)	103.38 (16)	C(15)–C(16)–C(17)	104.86 (19)
C(16)–C(17)–C(13)	103.09 (19)		

4-circle diffractometer using monochromated Cu-K_α radiation. Colorless single crystals of Vb for X-ray study were obtained from acetone. The crystal data for Vb are listed in Table I. Intramolecular bond distances (Å) and valence angles (°) for the non-hydrogen atoms are given in Tables II and III, respectively.

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