  Bull. Chem. Soc. Jpn., 60, 1053—1056 (1987)

Syntheses and Some Reactions of 4*H*-Cyclohepta[4,5]-pyrrolo[1,2-*a*]pyrimidin-4-ones

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(Received September 10, 1986)

The reaction of 2-aminocyclohepta[*b*]pyrroles with ethyl acetoacetate in phoshoryl chloride–polyphosphoric acid gives 2-methyl-4*H*-cyclohepta[4,5]pyrrolo[1,2-*a*]pyrimidin-4-ones. A ring closure of diethyl *N*-(cyclohepta[*b*]pyrrol-2-yl)aminomethylenemalonates gives 4-oxo-4*H*-cyclohepta[4,5]pyrrolo[1,2-*a*]pyrimidine-3-carboxylates (**2**) in phosphoryl chloride–polyphosphoric acid or in hot *t*-butylbenzene, which are deesterified by the treatment with hot hydrobromic acid. Compounds **2** undergo replacement reactions towards some electrophiles at positions C-3, C-11, and C-7 (in that order).

Hetero-annulated azaazulenes are interesting compounds for their physical and chemical properties as well as physiolosical activities. Although some synthetic studies on hetero-annulated azaazulenes are known,[1–4] investigations on azaazulenes fused with a pyrimidine ring are rare,[5,6] in spite of the attractive attention on hetero-annulated pyrimidines.[7,8] In this paper, I wish to report on the syntheses of 4*H*-cyclohepta[4,5]pyrrolo[1,2-*a*]pyrimidin-4-ones by means of the annulation of 2-aminocyclohepta[*b*]-pyrroles (2-amino-1-azaazulenes) in a phosphoryl chloride–polyphosphoric acid mixture ($POCl_3$–PPA), a useful condensing agent.[9]

The treatment of ethyl 2-aminocyclohepta[*b*]pyrrole-3-carboxylate[2,6] (**1a**) with ethyl acetoacetate (EAA) in $POCl_3$–PPA for 1 h at 115 °C yielded ethyl 2-methyl-4-oxo-4*H*-cyclohepta[4,5]pyrrolo[1,2-*a*]pyrimidine-11-carboxylate (**2a**) in 81% yield (which was stimulative). Deesterification of **2a** with hot 48% hydrobromic acid (HBr) gave 2-methyl-4*H*-cyclohepta-[4,5]pyrrolo[1,2-*a*]pyrimidin-4-one (**2b**) in 80% yield together with cyclohepta[*b*]pyrrol-2(1*H*)-one[10] (2%). The structure of **2b** was confirmed from observing the deshielding effects produced by tris(dipivaloylmethanato)europium shift reagent [Eu(dpm)$_3$] on the ^{1}H NMR spectrum. The ^{1}H NMR spectrum of **2b** shows protons at δ 2.45 (s, Me), 6.18 (s, H-3), 6.71 (s, H-11), 6.90—7.35 (m, H-7, 8, and 9), 7.55—7.85 (m, H-10), and 9.50—9.75 (m, H-6). The addition of Eu(dpm)$_3$ produced progressive down-field chemical shifts, and protons were observed at δ 3.47 (s, Me), 7.10—7.60 (m, H-7, 8, and 9), 7.68 (s, H-11), 8.15—8.45 (m, H-10), 9.43 (s, H-3), and 13.85—14.10 (m, H-6). Protons at C-3 and C-6 are most affected, to the extent of 3.25 and 4.35 ppm, respectively; these are much larger than those of H-11 and H-10, 0.97 and 0.60 ppm, respectively. These show that the complexing of the Eu(dpm)$_3$ with amide oxygen at C-4, not at C-2 of **3**, gives rise to a predominant deshilding effect positions C-3 and C-6. If the carbonyl group is present at C-2 as **3**, only the proton of C-3 should be deshilded predominantly.

When 2-aminocyclohepta[*b*]pyrrole[4,11] (**1b**) was treated in a similar manner as for **1a**, the reaction was rather complex and compound **2b** could be isolated only in low yield.

In a similar treatment of **1a** with ethyl benzoate (EBA) in $POCl_3$–PPA, **2c** and **2d** were obtained in moderate yields.

Unsubstituted 4*H*-cyclohepta[4,5]pyrrolo[1,2-*a*]pyrimidin-4-one (**2h**) was synthesized by the reaction of 2-aminocyclohepta[*b*]pyrroles (**1**) with diethyl ethoxymethylenemalonate (DEEM) and a subsequent cyclization and deesterification.

The treatment of **1a—c** with DEEM in hot ethanol or hot 1-butanol gave diethyl *N*-(cyclohepta[*b*]pyrrol-2-yl)aminomethylenemalonates (**4a—c**), respectively, in excellent yields. The ^{1}H NMR spectra of **4a—c** shows low-field resonated olefinic protons at δ 9.1—9.2 which couple (J=13 Hz) with amine protons at δ 11.3—12.5. By adding of D_2O, latter signals were disappeared and former changed to singlets. The results show that the substitution occurred on the amino group at C-2 of **1**, not on the N-1 position. Regarding the reaction of **1b** with DEEM, thermal cyclization partly occurred, and small amount of **2f** was obtained. In the ^{1}H NMR spectrum of **2f**, two signals of singlets can be seen at δ 7.00 (H-11) and 8.97 (H-2), and seven-menbered ring protons at δ 7.25—7.70 (3H, m, H-7, 8, and 9), 7.85—8.20 (1H, m, H-10), and 10.05—10.40 (1H, m, H-6), besides an ethyl ester group. The low-field appearance of the H-6 proton may be due to a shielding effect by the carbonyl group.

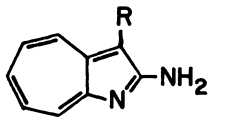
Compound **2f** was easily deesterified by the treatment with a hot 48% HBr–PPA mixture to give **2h** in 75% yield. The ^{1}H NMR spectrum of **2h** shows two 1H doublets (J=6.5 Hz) at δ 6.35 (H-3) and 8.15 (H-2) and low-field resonated 1H multiplet at δ 9.60—9.85 (H-6). The results agree with the report that H-2 protons resonate at δ ca. 8.1 and H-6 protons at lowest field in ^{1}H NMR spectra of 4-oxopyrimido[2,1-*b*]-benzazoles.[12]

The treatment of **2e** with 48% HBr or 48%HBr–PPA gave **2h** in low yields together with cyclohepta[*b*]-pyrrol-2(1*H*)-one[10] and **1b** which should be hydrolyzed products.

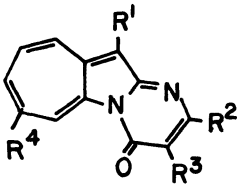
Cyclizations of **4a—c** were achieved by heating in xylene, *t*-butylbenzene, or tetralin, and yielded **2e—g**,

in moderate to excellent yields. Treatment of **4a** with $POCl_3$–PPA at 120 °C for 1h yielded **2e** in 95% yield. Similar treatment of **4b** with $POCl_3$–PPA resulted in complex mixture. From the mixture, **2f** was isolated in 17% yield together with yellow prisms **5** (48%). Compound **5** was assigned as ethyl 1,4-dihydro-4-oxocyclohepta[4,5]pyrrolo[2,3-*b*]pyridine-3-carboxylate. The IR spectra of **5** exhibits a signal at 3370 cm^{-1} assignable to NH. In its ^1H NMR, no signals are seen around δ 7.0; it does exhibit the signals of seven-membered ring protons at δ 7.75—8.15 (3H, m, H-6, 7, and 8), 8.45—8.75 (1H, m, H-9), and 9.75—10.00 (1H, m, H-9). It is known that ethyl 6-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylate transformed thermally to ethyl 7-methyl-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylate.[13] However, an interconversion of **2f** and **5** was not observed under the conditions of boiling *t*-butylbenzene or hot $POCl_3$–PPA. Therefore, **5** would be directly produced from **4b**.

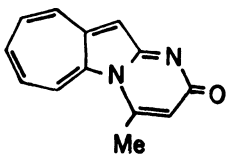
Electrophilic Replacement of 2. Compound **2h** was deuteriated by a treatment with D_3PO_4 or CF_3CO_2D to give 3,11-dideuteriated product **2i**. Bromination of **2h** gave 3,11-dibrominated compound **2j** in excellent yield. Bromination of **2f** gave **2k** in 82% yield. When the positions (C-3 and 11) were blocked, bromination occurred at C-7 position; thus the brominatin of **2e** afforded **21** in 15% yield. When Vilsmeier-Haak reaction of **2h** was carried out at 65 °C, a 3-formylated product **2m** (24%) and a 3,11-diformylated product **2n** (18%) were obtained. Compound **2f** was formylated at C-11 position to give **2o** in 44% yield, but **2e** was not formylated at all. These results show that compounds **2** were reactive towards some electrophiles at the positions of C-3, C-11, and C-7, in the order.



1a: R=CO_2Et
1b: R=H
1c: R=CN



	R¹	R²	R³	R⁴
2a:	CO_2Et	Me	H	H
2b:	H	Me	H	H
2c:	CO_2Et	Ph	H	H
2d:	H	Ph	H	H
2e:	CO_2Et	H	CO_2Et	H
2f:	H	H	CO_2Et	H
2g:	CN	H	CO_2Et	H
2h:	H	H	H	H
2i:	D	H	D	H
2j:	Br	H	Br	H
2k:	Br	H	CO_2Et	H
2l:	CO_2Et	H	CO_2Et	Br
2m:	H	H	CHO	H
2n:	CHO	H	CHO	H
2o:	CHO	H	CO_2Et	H



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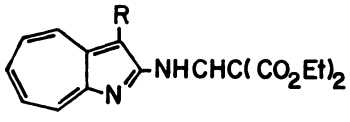
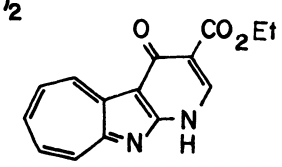


4a: R=CO_2Et
4b: R=H
4c: R=CN



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Experimental

Melting points were uncorrected. ^1H NMR spectra were recorded on a Hitachi R-24B spectrometer and ^{13}C NMR spectra on a JEOL FX-100 spectrometer using deuteriochloroform as a solvent with tetramethylsilane as an internal standard, unless otherwise stated. IR spectra were recorded on a JASCO IR-G spectrometer for Nujol mulls and electronic spectra on a Hitachi 220A spectrophotometer for ethanol solutions. Kieselgel 60 was used for column chromatography.

Reaction of 1 with EAA. A mixture of **1a** (1.729 g, 8.00 mmol), EAA (4.16 g, 32.0 mmol), $POCl_3$ (4.90 g, 32.0 mmol), and PPA (3.0 g) was stirred for 1 h at 115 °C. After hydrogen chloride evolution has ceased, ethanol (10 ml) was added, and the mixture was heated for 10 min at 100 °C. The reaction mixture was poured into ice-water (200 ml), neutralized with Na_2CO_3, extracted with chloroform, dried (Na_2SO_4), and evaporated to dryness. Chromatography of the residue with chloroform gave **2a** (1.826 g, 81%), which, was crystallized from cyclohexane–dichloromethane to give reddish violet prisms (1.170 g, 52%), mp 176—178 °C; λ_{max} 217 nm (log ε 4.40), 236 (4.38), 268 (4.52), 288 (4.29), 297 (4.28, sh), 431 (4.07), and 490 (3.77, sh); ν_{max} 1675 (ester C=O) and 1665 cm^{-1} (amido C=O); ^1H NMR δ=1.48 (3H, t, J=7 Hz, Me), 2.53 (3H, s, Me), 4.48 (2H, q, J=7 Hz, OCH_2), 6.25 (1H, s, H-3), 7.35—7.70 (3H, m, H-7, 8, and 9), 8.95—9.30 (1H, m, H-10), and 10.05—10.30 (1H, m, H-6). Anal. ($C_{16}H_{14}N_2O_3$) C, H, N. Elution with ethyl acetate gave **1a** (0.178 g, 10%).

In a similar manner, **1b** gave **2b** (14%).

2b: Dark violet needles (from cyclohexane–dichloromethane), mp 196—198 °C; λ_{max} 260 nm (log ε 4.54), 289 (4.14), 299 (4.13, sh), 400 (3.99), 425 (4.01), 479 (3.71), 510 (3.67, sh), 545 (3.50, sh); ν_{max} 1675 (amido C=O); ^1H NMR δ=2.45 (3H, s, Me), 6.18 (1H, s, H-3), 6.71 (1H, s, H-11), 6.90—7.35 (3H, m, H-7, 8, and 9), 7.55—7.85 (1H, m, H-10), and 9.50 (1H, m, H-6), δ[$CDCl_3$–Eu(dpm)$_3$]= 3.47 (3H, s, Me), 7.10—7.60 (3H, m, H-7, 8, and 9), 7.68 (1H, s H-11), 8.15—8.45 (1H, m, H-10), 9.43 (1H, s, H-3), and 13.85—14.10 (1H, m, H-6), δ (CF_3CO_2D)=2.68 (3H, s, Me), 6.48 (1H, s, H-3, exch.), 7.33 (1H, s, H-11, exch.), 8.10—8.50 (3H, m, H-7, 8, and 9), 8.65—8.90 (1H, m, H-10), and 10.35—10.70 (1H, m, H-6). Anal. ($C_{13}H_{10}N_2O$) C, H, N.

Deesterification of 2a. a) A solution of **2a** (0.800 g, 2.83 mmol) in 48% HBr (10 ml) was heated under reflux for 2 h, and poured into water (200 ml). The mixture was neutralized with $NaHCO_3$, extracted with chloroform, dried

(Na_2SO_4), and evaporated to dryness. Chromatography of the residue with chloroform gave **2b** (0.481 g, 80%). Elution with ethyl acetate gave cyclohepta[*b*]pyrrol-2(1*H*)-one[10] (0.010 g, 2%).

b) A mixture of **2a** (0.200 g, 0.71 mmol) and PPA (5.0 g) was heated at 150 °C for 3 h, and worked up as above. Chromatography of the residue with chloroform gave **2a** (0.060 g, 30%) and **2b** (0.084 g, 56%), successively.

Reaction of 1a with EBA. a) A mixture of **1a** (0.432 g, 2.00 mmol), EBA (1.54 g, 8.00 mmol), $POCl_3$ (2.46 g, 16.0 mmol), and PPA (3.0 g) was stirred at 120 °C for 3 h. The reaction mixture was treated as for **1a** with EAA. Chromatography of the residue with chloroform gave **2c** (0.347 g, 50%), which was crystallized from cyclohexane–dichloromethane to give reddish violet needles (0.180 g, 26%), mp 201—203 °C; λ_{max} 212 nm (log ε 4.39), 258 (4.48), 273 (4.42, sh), 297 (4.38), 315 (4.36, sh), 353 (3.87, sh), 435 (3.97), and 495 (3.69, sh); ν_{max} 1675 (ester C=O) and 1655 (amido C=O); ^{1}H NMR δ=1.55 (3H, t, J=7 Hz, Me), 4.49 (2H, q, J=7 Hz, OCH_2), 6.82 (1H, s, H-3), 7.10—7.65 (6H, m, H-7, 8, 9, and *m*,*p*-phenyl), 8.00—8.25 (2H, m, H-*o*-phenyl), 9.00—9.40 (1H, m, H-10), and 10.00—10.25 (1H, m, H-6). Anal. ($C_{21}H_{16}N_2O_3$) C, H, N.

b) When the above reaction was carried out under reflux for 1 h and worked up, compound **2d** (0.055 g, 10%) was isolated by chromatography with chloroform; this was crystallized from cyclohexane–dichloromethane to give brown needles (0.030 g, 5%), mp 201—203 °C; λ_{max} 261 nm (log ε 4.50), 288 (4.50), 300 (4.44, sh), 345 (3.88, sh), 403 (3.93), 428 (3.99), 486 (3.72), 510 (3.71, sh), 550 (3.56, sh), and 605 (3.09, sh); ν_{max} 1660 cm^{-1} (amido C=O); ^{1}H NMR δ=6.82 (1H, s, H-3), 6.92 (1H, s, H-11), 7.00—7.30 (3H, m, H-7, 8, and 9), 7.35—7.55 (3H, m, H-*m*,*p*-phenyl), 7.60—7.95 (1H, m, H-10), 8.00-8.20 (2H, m, H-*o*-phenyl), and 9.65—9.90 (1H, m, H-6). Anal. ($C_{18}H_{12}N_2O$), C, H, N.

Reaction of 1 with DEEM. a) A mixture of **1a** (2.60 g, 12.0 mmol) and DEEM (7.80 g, 36.1 mmol) in abs ethanol (100 ml) was heated under reflux for 48 h, then evaporated. Chromatography of the residue with chloroform gave **4a** (4.197 g, 90%), which was crystallized from cyclohexane–dichloromethane to give yellow needles (3.601 g, 77%), mp 158—160 °C; λ_{max} 266 nm (3.96), 311 (4.37), 317 (4.36, sh), 330 (4.31), 386 (4.40), 443 (3.54); ν_{max} 3200 (NH), 1685, 1670, and 1650 cm^{-1} (ester C=O); ^{1}H NMR δ=1.38, 1.41, and 1.53 (each 3H, t, J=7 Hz, Me), 4.28, 4.40, and 4.53 (each 2H, q, J=7 Hz, OCH_2), 7.60—7.95 (3H, m, H-5, 6, and 7), 8.25—8.50 (1H, m, H-8), 9.00—9.30 (1H, m, H-4), 9.20 (1H, d, J=13 Hz, NHC<u>H</u>), 12.53 (1H, bd, J=13 Hz, NH, exch.). Anal. ($C_{20}H_{22}N_2O_6$) C, H, N. Elution with ethyl acetate gave 1a (0.075 g, 3%).

In a similar manner, **1b** gave **4b** (95%) and **2f** (4%).

4b: Reddish orange prisms (from cyclohexane–dichloromethane), mp 129—131 °C; λ_{max} 239 nm (log ε 4.21, sh), 246 (4.22), 253 (4.21), 286 (4.33, sh), 295 (4.41), 328 (4.55), 381 (4.50), 455 (3.89); ν_{max} 3250 (NH), 1690 and 1675 cm^{-1} (ester C=O); ^{1}H NMR δ=1.34 and 1.38 (each 3H, t, J=7 Hz, Me), 4.28 and 4.34 (each 2H, q, J=7 Hz, OCH_2), 6.83 (1H, s, H-3), 7.3—7.85 (3H, m, H-5, 6, and 7), 8.05—8.50 (2H, m, H-4 and 8), 9.10 (1H, d, J=13 Hz, NHC<u>H</u>), 11.35 (1H, bd, J=13 Hz, NH, exch.). Anal. ($C_{17}H_{18}N_2O_4$) C, H, N.

2f: Red needles (from cyclohexane–dichloromethane), mp 179—181 °C; λ_{max} 237 nm (log ε 4.32), 263 (4.48), 305 (4.06), 403 (3.90, sh), 428 (4.04), 480 (3.95, sh), 495 (3.97); ν_{max} 1735 (ester C=O) and 1655 cm^{-1} (amido C=O); ^{1}H NMR δ=1.42 (3H, t, J=7 Hz, Me), 4.40 (2H, q, J=7 Hz, OCH_2), 7.00 (1H, s, H-11), 7.25—7.70 (3H, m, H-7, 8, and 9), 7.85—8.20 (1H, m, H-10), 8.97 (1H, s, H-2), and 10.05—10.40 (1H, m, H-6). Anal. ($C_{15}H_{12}N_2O_3$) C, H, N.

b) When above reaction was carried out in hot 1-butanol, **1a** and **1c** gave **4a** (95%) and **4c** (96%), respectively.

4c: Yellow needles (from cyclohexane–dichloromethane), mp 210—212 °C; λ_{max} 242 nm (log ε 3.94, sh), 262 (4.12), 305 (4.48), 329 (4.48), 382 (4.45), 445 (3.66); ν_{max} 3190 (NH), 2210 (CN), 1700, and 1660 cm^{-1} (ester C=O); ^{1}H NMR δ=1.37 and 1.40 (each 3H, t, J=7 Hz, Me), 4.31 and 4.40 (each 2H, q, J=7 Hz, OCH_2), 7.75—7.95 (3H, m, H-5, 6, and 7), 8.27—8.53 (2H, m, H-4 and 8), 9.10 (1H, d, J=13 Hz, NHC<u>H</u>), and 11.62 (1H, bd, J=13 Hz, exch.). Anal. ($C_{18}H_{17}N_3O_4$) C, H, N.

Cyclization of 4. a) A mixture of **4a** (4.910 g, 12.7 mmol), $POCl_3$(18.0 g), and PPA (4.0 g) was stirred for 1 h at 120 °C. To the mixture, ethanol (20 ml) was added, and the mixture was heated for 10 min at 100 °C. The reaction mixture was poured into ice–water (200 ml), neutralized with Na_2CO_3, extracted with chloroform, dried (Na_2SO_4), and evaporated. Chromatography of the residue with chloroform gave **2e** (4.110 g, 95%), which was crystallized from cyclohexane–dichloromethane to give red needles (3.910 g, 90%), mp 213—215°C; λ_{max} 233 nm (log ε 4.34), 266 (4.50), 299 (4.22), 310 (4.18, sh), 431 (3.98), 475 (4.00); ν_{max} 1725 and 1670 (ester C=O), and 1655 cm^{-1} (amido C=O); ^{1}H NMR δ=1.43, 1.50 (each 3H, t, J=7 Hz, Me) 4.42, 4.55 (each 2H, q, J=7 Hz, OCH_2), 7.65—8.00 (3H, m, H-7, 8, and 9), 9.07(1H, s, H-2), 9.25—9.55 (1H, m, H-10), and 10.35—10.65 (1H, m, H-6). Anal. ($C_{18}H_{16}N_2O_5$) C, H, N.

In a similar treatment, **4b** gave **2f** (17%) and **5** (48%).

5: Yellow prisms (from methanol–ethyl acetate), mp 234—236 °C; λ_{max} 260 nm (log ε 4.12, sh), 282 (4.40), 315 (4.47), 388 (3.89), 435 (2.98, sh); ν_{max}3370 (NH), 1715 (ester C=O), and 1705 (C=O); ^{1}H NMR δ=1.41 (3H, t, J=7 Hz, Me), 4.42 (2H, q, J=7 Hz, OCH_2), 7.75—8.15 (3H, m, H-6, 7, and 8), 8.45—8.75 (1H, m, H-9), 8.4—9.0 (1H, broad, NH), 8.83 (1H, s, H-2), and 9.75—10.00 (1H, m, H-5); MS (70 eV) *m*/*z* (rel intensity) 268 (M^+; 50), 222 (61), 196 (34), 194 (100), 166 (29), 140 (47), 139 (54), and 113 (21). Anal. ($C_{15}H_{12}N_2O_3$) C, H, N.

b) Solutions of **4a** and **4b** (0.795 mmol) in tetralin (3 ml) were heated under reflux for 1 h and evapolated. Chromatography of the residue with chloroform gave **2e** (46%), and **2f** (46%), respectively.

c) A solution of **4b** (0.300 g, 0.954 mmol) in *t*-butylbenzene (5 ml) was heated under reflux for 12 h and evaporated. Chromatography of the residue with chloroform gave **2f** (0.266 g, 88%).

d) A solution of **4c** (0.150 g, 0.442 mmol) in dry xylene (30 ml) was heated under reflux for 48 h and evaporated. The residue was chromatographed. Elution with chloroform gave **4c** (0.014 g, 9%). Further elution gave **2g** (0.117 g, 90%), mp 240—242 °C (dec); λ_{max} 232 nm (log δ 4.40), 267 (4.57), 297 (4.24), 305 (4.21, sh), 435 (4.06), 475 (4.03); ν_{max} 2230 (CN), 1730 (ester C=O), and 1670 cm^{-1} (amido C=O); ^{1}H NMR δ=1.43, (3H, t, J=7 Hz, Me), 4.38 (2H, q, J=7 Hz, OCH_2), 7.70—8.00 (3H, m, H-7, 8, and 9), 8.30—8.60 (1H, m, H-10), 9.00 (1H, s, H-2), 10.40—10.60 (1H, m, H-6). Anal. ($C_{16}H_{11}N_3O_3$) C, H, N.

Deesterifications of 2. A mixture **2f** (0.300 g, 1.19 mmol), PPA (4.0 g), and 48% HBr (15 ml) was heated under reflux for 1 h, then poured into ice-water (200 ml). The mixture was neutralized with Na_2CO_3, extracted with chloroform, dried (Na_2SO_4), and evaporated. The residue was chromatographed with chloroform to give **2h** (0.210 g, 96%), which was crystallized from cyclohexane–dichloromethane to give dark violet needles (0.167 g, 76%), mp 160—162 °C; λ_{max} 225 nm (log ε 4.19), 256 (4.42), 288 (4.03, sh), 397 (3.93), 425 (3.92), 482 (3.64), 505 (3.62); ν_{max} 1660 (amido C=O); ^{1}H NMR δ=6.35 (1H, d, J=6.5 Hz, H-3), 6.83 (1H, s, H-11), 6.95—7.45 (3H, m, H-7, 8, and 9), 7.55—7.90 (1H, m, H-6), 8.15 (1H, d, J=6.5 Hz, H-2), 9.60—9.85 (1H, m, H-10); ^{13}C NMR δ=106.3 (C-11), 108.2 (C-3), 125.9 (C-9), 131.7 (C-7), 132.0 (C-8), 133.8 (C-10), 135.9 (C-6), 141.9 (C-10a), 144.0 (C-5a), 153.4 (C-2), 157.8 (C-11a), 162.2 (C-4). Anal. ($C_{12}H_8N_2O$) C, H, N.

In a similar manner, **2e** gave **2h** (16%) and cyclohepta[*b*]-pyrrol-2(1*H*)-one[10] (5%).

Deutriation of 2h. Compound **2h** (0.090 g, 0.46 mmol) was dissolved in D_3PO_4(1.0 g) and set for 7 d at ambient temperature. The solution was diluted with water (100 ml), neutralized with $NaHCO_3$, extracted with chloroform, and dried (Na_2SO_4). Evaporation of the solution gave **2i** (0.089 g, 98%), which was crystallized from cyclohexane–dichloromethane to give violet needles (0.060 g, 73%), mp 160—161 °C; ^{1}H NMR δ=6.90—7.35 (3H, m, H-7, 8, and 9), 7.55—7.85 (1H, m, H-10), 8.14 (1H, s, H-2), 9.55—9.75 (1H, m, H-6); MS (70 eV) *m/z* (rel intensity) 198 (M^+; 100), 170 (67) 115 (12).

Bromination of 2. A solution of **2h** (0.150 g, 0.76 mmol) and bromine (0.30 g, 1.87 mmol) in acetic acid (4 ml) was stirred for 24 h at ambient temperature. The reaction mixture was diluted with water (100 ml) and neutralized with $NaHCO_3$. The precipitate formed were collected by filtration and washed with water to give **2j** (0.265 g, 98%), which was crystallized from cyclohexane–dichloromethane to give brown needles, (0.176 g, 65%), mp 223 °C (decomp); λ_{max} 221 nm (log ε 4.43), 270 (4.47), 300 (4.06, sh), 418 (4.09), 445 (4.11), 505 (3.74) 534 (3.71), 575 (3.55, sh); ν_{max} 1680 cm^{-1} (amido C=O); ^{1}H NMR δ=7.20—7.50 (3H, m, H-7, 8, and 9), 7.75—8.00 (1H, m, H-10), 8.52 (1H, s, H-2), 9.70—9.85 (1H, m, H-6). Anal. ($C_{12}H_6Br_2N_2O$) C, H, N.

In a similar manner, **2f** and **2e** gave **2k** (82%) and **21** (15%), respectively.

2k: Violet prisms (from cyclohexane–dichloromethane), mp 204—206 °C; λ_{max} 220 nm (log ε 4.43) 238 (4.35), 269 (4.46), 297 (4.04), 303 (4.03), 420 (3.96), 444 (4.11), 490 (3.90), 513 (3.90); ν_{max} 1735 (ester C=O) and 1660 cm^{-1} (amido C=O); ^{1}H NMR δ=1.43 (3H, t, J=7 Hz, Me), 4.43 (2H, q, J=7 Hz, OCH_2), 7.35—7.70 (3H, m, H-7, 8, and 9), 7.95—8.25 (1H, m, H-10), 9.00 (1H, s, H-2), 10.00—10.25 (1H, m, H-6). Anal. ($C_{15}H_{11}BrN_2O_3$) C, H, N.

21: Red needles (from cyclohexane–dichloromethane), mp 210—212 °C; λ_{max} 222 nm (log ε 4.17), 271 (4.46), 299 (4.15), 309 (4.14), 440 (3.93), 485 (3.84); ν_{max} 1735, 1690 (ester C=O), and 1660 cm^{-1} (amido C=O); ^{1}H NMR δ=1.43, 1.48 (each 3H, t, J=7 Hz, Me), 4.42, 4.53 (each 2H, q, OCH_2), 7.48 (1H, dd, J=10 and 9 Hz, H-9), 8.13 (1H, dd, J=9 and 2 Hz, H-8), 9.06 (1H, s, H-2), 9.25 (1H, d, J=10 Hz, H-10), 10.88 (1H, d, J=2 Hz, H-6). Anal. ($C_{18}H_{15}BrN_2O_5$) C, H, N.

Formylation of 2. To a solution of **2h** (0.150 g, 0.76 mmol) in *N,N*-dimethylformamide (DMF) (2 ml), a mixture of DMF (3 ml) and $POCl_3$ (0.5 g) was added drop by drop. The mixture was stirred for 24 h at 65 °C. After addition of NaOAc (0.300 g), the mixture was stirred for 1 h at 65 °C, then poured into water (100 ml), neutralized with $NaHCO_3$, and extracted with chloroform. The extract was dried (Na_2SO_4) and evaporated. Chromatography of the residue with chroloform gave **2h** (0.015 g 10%), **2n** (0.035 g, 18%), and **2m** (0.041 g, 24%), successively. [**2m:** violet needles from cyclohexane–dichloromethane, mp 230 °C (dec); λ_{max} 219 nm (log ε 4.00), 237 (4.08), 264 (4.32), 305 (3.82), 312 (3.82), 405 (3.66, sh), 433 (3.84), 497 (3.89); ν_{max} 1670 cm^{-1} (C=O); ^{1}H NMR δ=7.12 (1H, s, H-11), 7.45—7.85 (3H, m, H-7, 8, and 9), 8.05—8.40 (1H, m, H-10), 8.85 (1H, s, H-2), 10.10—10.35 (1H, m, H-6), 10.42 (1H, s, CHO). Anal. ($C_{13}H_8N_2O_2$) C, H, N. **2n:** red needles (from cyclohxane–dichloromethane), mp >300 °C; λ_{max} 218 nm (log ε 4.26), 237 (4.33), 265 (4.54), 305 (4.07), 314 (4.07), 407 (3.93, sh), 433 (4.08), and 498 (4.13); ν_{max} 1675 and 1660 cm^{-1} (C=O); ^{1}H NMR (DMSO-d_6) δ=8.30—8.55 (3H, m, H-7 , 8, and 9), 8.76 (1H, s, H-2), 9.60—9.80 (1H, m, H-10), 10.23 and 10.58 (each 1H, s, CHO), 10.50-10.65 (1H, m, H-6). Anal. ($C_{14}H_8N_2O_3$) C, H, N. MS *m/z* 252 (M^+)].

In a similar manner, **2f** gave **2o** (44%).

2o: Red needles (from cyclohexane–dichloromethane), mp 229—231 °C; λ_{max} 223 nm (log ε 4.16), 235 (4.09, sh), 269 (4.22), 303 (4.05, sh), 320 (4.09), 450 (3.87), and 465 (3.87); ν_{max} 1735 (ester C=O) and 1660 cm^{-1} (C=O); ^{1}H NMR δ=1.42 (3H, t, J=7 Hz, Me), 4.40 (2H, q, J=7 Hz, OCH_2), 7.80—8.20 (3H, m, H-7, 8, and 9), 9.00 (1H, s, H-2), 9.60—9.85 (1H, m, H-10), 10.73 (1H, s, CHO), 10.55—10.80 (1H, m, H-6). Anal. ($C_{16}H_{12}N_2O_4$) C, H, N.

I am grateful to Dr. Akira Mori, Kyushu University, for the ^{13}C NMR and Mass spectra.

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