Bull. Chem. Soc. Jpn., 63, 1617—1622 (1990)

Synthesis and Some Reactions of 2-(2-Aminoanilino)cyclohepta[*b*]pyrroles: Leading to 5*H*-Cyclohepta[1′,2′:4,5]pyrrolo[2,3-*b*][1,5]benzodiazepine, a Novel 20π Antiaromatic System, and Cyclohepta[1′,2′:4,5]pyrrolo[1,2-*a*]benzimidazoles

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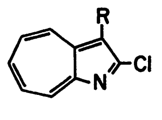
(Received November 18, 1989)

2-Chlorocyclohepta[*b*]pyrroles reacted with *o*-phenylenediamine to give 2-(2-aminoanilino)cyclohepta[*b*]pyrroles (**2a,b**) in good yields. Treatment of **2a** and **2b** with polyphosphoric acid afforded cyclohepta[1′,2′:4,5]pyrrolo[1,2-*a*]benzimidazole (**4a**) in good yields. Treatment of **2b** with acids gave 6-(ethoxycarbonyl) derivatives (**4b**) of **4a** and 12*H*-5,13-dihydrocyclohepta[1′,2′:4,5]pyrrolo[2,3-*b*][1,5]benzodiazepin-12-one (**5**). Compound **5** was methylated with methyl iodide in the presence of DBU to give 5*H*-12-methoxycyclohepta[1′,2′:4,5]pyrrolo[2,3-*b*][1,5]benzodiazepine, a novel 20π antiaromatic system. Treatment of **2b** with sodium ethoxide gave **4b** and 2*H*-1-(cyclohepta[*b*]pyrrol-2-yl)-1,3-dihydrobenzimidazol-2-one (**7a**). Compound **5** rearranged to **7a** in the refluxing sodium ethoxide-ethanol solution. Reactions of **2a** and **2b** with triethyl orthoformate gave corresponding 1-(cyclohepta[*b*]pyrrol-2-yl)benzimidazoles. Reactions of **2a** and **2b** with acetic anhydride are also mentioned.

Chemical and physical properties of azaazulenes are of interest and are being investigated.[1] Although a number of studies on the synthesis of heteroannulated 1-azaazulenes (cyclohepta[*b*]pyrroles) have been made,[2–10] synthetic study of an azepine-annulated system, which would contain antiaromatic π-system, was rare and not successful.[11] In this paper, we wish to report on the syntheses of 5*H*-cyclohepta[1′,2′:4,5]pyrrolo[2,3-*b*][1,5]benzdiazepine, a novel antiaromatic 20π system. It is an isoelectronic system with the unknown non-alternant hydrocarbon, benzo[*f*]cyclohept[*a*]azulenide, the synthesis was achieved by the annulation of ethyl 2-(2-aminoanilino)cyclohepta[*b*]pyrrole-3-carboxylate (**2b**) and successive methylation. Compound **2b** was annulated under acidic conditions to give cyclohepta[1′,2′:4,5]pyrrolo[1,2-*a*]benzimidazoles and 12*H*-5,13-dihydrocyclohepta[1′,2′:4,5]pyrrolo[2,3-*b*][1,5]benzodiazepin-12-one. The latter rearranged under basic conditions to give a benzimidazolone derivative. Reactions of **2a** and **2b** with triethyl orthoformate or acetic anhydride gave the corresponding benzimidazole derivatives.

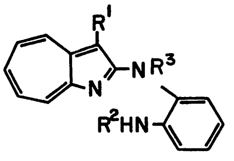
Treatment of 2-chlorocyclohepta[*b*]pyrrole (**1a**) with *o*-phenylenediamine in ethanol under reflux gave 2-(2-aminoanilino)cyclohepta[*b*]pyrrole (**2a**) in an 80% yield. Similar treatment of **1b** with *o*-phenylenediamine gave **2b** in a 69% yield together with diethyl 2,2′-(*o*-phenylenediimino)bis[cyclohepta[*b*]pyrrole-3-carboxylate] (**3**) (29%).

Treatment of **2a** and **2b** with polyphosphoric acid (PPA) at 150 °C gave cyclohepta[1′,2′:4,5]pyrrolo[1,2-*a*]benzimidazole (**4a**) in 81% and 45% yields, respectively. The structure was deduced on the basis of the spectroscopic data as well as elemental analysis and mass spectra. In the ^{1}H NMR spectrum of **4a**, seven-membered proton signals were seen at δ=6.9—7.7. The coupling constants were $J_{7,8}$=11.6 Hz, $J_{8,9}$=8.5 Hz, $J_{9,10}$=11.6 Hz, and $J_{10,11}$=8.6 Hz. Although it is considered that **4a** would be essentially aromatic on the basis of its chemical shifts, the existence of large divergences of the coupling constants, which are almost consistent with those of heptafulvene,[12] suggests that compound **4a** is constructed from a heptafulvene moiety and a benzimidazole moiety and not in a peripheral 18π system.



1a: R=H

1b: R=CO_2Et



2a: $R^1=R^2=R^3$=H

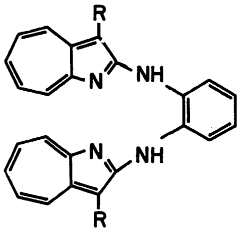
2b: $R^1=CO_2Et$, $R^2=R^3$=H

2c: $R^1=R^2=CO_2Et$, R^3=H

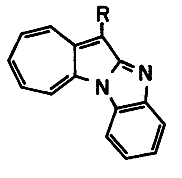
2d: $R^1=R^3$=H, R^2=COMe

2e: $R^1=CO_2Et$, R^2=COMe, R^3=H

2f: $R^1=CO_2Et$, $R^2=R^3$=COMe

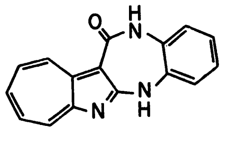


3: R=CO_2Et



4a: R=H

4b: R=CO_2Et



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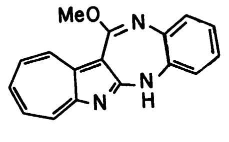

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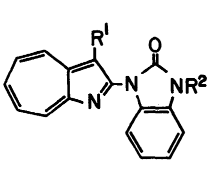
When **2b** was treated with *p*-toluenesulfonic acid (TsOH) in 1-butanol under reflux, **4b** (39%) and 12*H*-5,13-dihydrocyclohepta[1′,2′:4,5]pyrrolo[2,3-*b*][1,5]-benzodiazepin-12-one (**5**) (32%) were obtained. Similar treatments of **2b** with some other acids, such as acetic acid (AcOH), trifluoroacetic acid (TFA), or concd sulfuric acid (H_2SO_4), gave **4b** (22%, 1%, and 15%) and **5** (49%, 96%, and 80%), respectively. The formation of **4a** and **4b** would resemble the reaction of 2,2′-diaminodiphenylether with acid which forms phenoxazine.[13] The reason for the effect of acids on the different proportions of formation of **4** and **5** has remained unclarified.

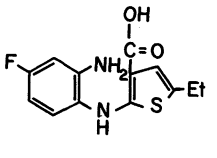
Compound **4b** was deesterified by refluxing with 48% hydrobromic acid to give **4a** in a 60% yield. The ^{1}H NMR spectrum of **5** in DMSO-d_6 shows signals in the normal regions for the benzene ring and the cyclohepta[*b*]pyrrole ring. On the other hand, in the spectrum of **5** in CF_3CO_2D, the protons of the seven-membered ring show down-field shifts of about 0.6 ppm. Those of the benzene ring protons show small shifts (less than 0.2 ppm) compared with those in DMSO-d_6. This suggests that the positive charge of the cation derived from **5** locates on the seven-membered ring.

Enolization and successive methylation of **5** was achieved as follows. Heating of **5** with methyl iodide in the presence of 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) in acetonitrile for 7 h under reflux gave 5*H*-12-methoxycyclohepta[1′,2′:4,5]pyrrolo[2,3-*b*][1,5]-benzodiazepine (**6**) in a 19% yield. Compound **6** was slightly unstable and decomposed on storage. The structure was deduced from its HRMS and spectroscopic behavior. The ^{1}H NMR spectrum of **6** shows signals at δ=3.34 (s, OMe), 6.60 (d, J=9.8 Hz, H-7), 6.62—6.83 (m, H-1, 2, 3, 4, and 9), 7.01 (dd, J=11.0 and 9.8 Hz, H-8), 7.05 (dd, J=11.6 and 9.8 Hz, H-10), 8.57 (d, J=11.6 Hz, H-11), and 9.09 (brs, NH). All the protons of **6** resonated at considerably higher fields than those of **5**, especially at the seven membered ring ($\Delta\delta$>0.5 ppm), even at the benzene ring ($\Delta\delta$>0.2 ppm). This suggests that **6** would behave as a paratropic compound and have a novel peripheral 20π antiaromatic system. Although, the paratropic shifts of **6** were smaller than in the case of annulenes,[14] the fact that the paratropicity is observed in a fused system is interesting.

When **2b** was treated with sodium ethoxide in refluxing ethanol for 4 d, **5** and **7a** were obtained in 1% and 69% yields, respectively. Compound **7a** was identical to the product from the reaction of **2a** with *N,N′*-carbonyldiimidazole, and the structure was established to be 2*H*-1-(cyclohepta[*b*]pyrrol-2-yl)-1,3-dihydrobenzimidazol-2-one on the basis of the spectroscopic data as well as elemental analysis. In the ^{1}H NMR spectrum of **7a**, a signal of a proton at C-3 of cyclohepta[*b*]pyrrole ring resonates at rather low field (δ=8.08). This would be due to the deshielding effect by the carbonyl group of the 2-imidazolone ring. Compound **7a** was acetylated with acetic anhydride to give **7b**. In the ^{1}H NMR spectrum of **7b**, an essential change is not observed on the chemical shifts of cyclohepta[*b*]pyrrole ring, compared with that of **7a**, and this confirms the structure. Compound **5** rearranged to **7a** in a 91% yield by the treatment with sodium ethoxide under reflux in ethanol for 60 h. The reaction was similar to that of compound **8** which afforded **9** under basic conditions at lower temperature but yielded the rearrangement product **10** at higher temperature.[15]



7a: $R^1=R^2=H$
7b: $R^1=H$, $R^2=COMe$
7c: $R^1=CO_2Et$, $R^2=H$
7d: $R^1=CO_2Et$, $R^2=COMe$



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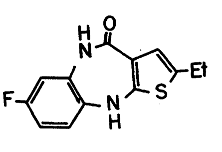

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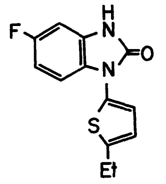
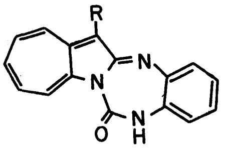


10

The expectation to synthesize the novel triazepinone cyclohepta[1′,2′:4,5]pyrrolo[2,1-*b*][1,3,5]benzotriazepin-6(5*H*)-one (**11**) prompted us to study further reactions. Reaction of **2b** with ethyl chloroformate gave **2c** in a 66% yield along with diethyl *o*-phenylenebis[carbamate].[16] Treatment of **2c** with DBU in refluxing benzene gave **7c** in a 50% yield, and the expected triazepinone **11** was not obtained. Compound **7c** was also obtained by the treatment of **2b** with *N,N′*-carbonyldiimidazole in a 59% yield. Acetylation of **7c** with acetic anhydride gave **7d** in a 90% yield. In the ^{1}H NMR spectrum of **7c**, a proton sig-



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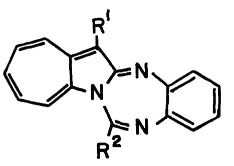

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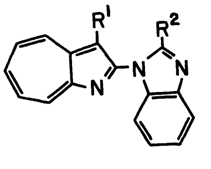

13a: $R^1=R^2=H$
13b: $R^1=CO_2Et$, $R^2=H$
13c: $R^1=H$, $R^2=Me$
13d: $R^1=CO_2Et$, $R^2=Me$

nal at C-4′ is observed at δ=9.56 (d, *J*=10.4 Hz), and at δ=8.84 (d, *J*=9.8 Hz) for C-8′. The low-field resonance of the former would be due to the deshielding effect of the ester group at C-3′.

It was considered that the synthesis of the other novel 20π peripheral antiaromatic compounds, cyclohepta[1′,2′:4,5]pyrrolo[2,1-*b*][1,3,5]benzotriazepines (**12**), could be achieved by the annulation of **2** with trialkyl orthoformate. Therefore, compounds **2a** and **2b** were treated with triethyl orthoformate under reflux in the presence of TsOH. From the reaction mixture, compounds **13a** and **13b** were isolated in 75% and 94% yields, respectively. Compounds **13a** and **13b** were identical with those obtained from the reactions of **1a** and **1b** with benzimidazole. Deesterification of **13b** gave **13a** in a 21% yield together with a small amount of cyclohepta[*b*]pyrrole.[17] From these results, it is deduced that **13a** and **13b** are benzimidazole derivatives, and that no triazepine compound was obtained. In the treatment similar to the formations of **13a** and **13b**, reactions of **2a** and **2b** with triethyl orthoacetate gave **13c** and **13d** in 77% and 94% yield, respectively.

Treatment of **2a** with acetic anhydride at 100 °C for 6 h gave the monoacetylated compound **2d** and the benzimidazole derivative **13c** in 29% and 56% yields, respectively. Similarly, treatment of **2b** with acetic anhydride under reflux for 1 h gave the monoacetylated compound **2e** (8%), the diacetylated compound **2f** (3%), and **13d** (62%). When the reaction was carried out at room temperature, cyclization did not occur and monoacetylated compound **2e** was obtained in a good yield. Treatment of **2e** with PPA-phosphoryl chloride gave **13d** in a good yield. Cyclization of **2d** and **2e** to triazepine derivatives have not yet been successful.

Experimental

Melting points were uncorrected. ^{1}H NMR spectra (250 MHz) and ^{13}C NMR spectra (62.87 MHz) were recorded on a Hitachi R-250H spectrometer using deuteriochloroform as a solvent with tetramethylsilane as an internal standard, unless otherwise stated. IR spectra were recorded on a Hitachi 270-50 infrared spectrophotometer for Nujol mulls. Mass spectra were determined with a JEOL-01SG-2 spectrometer at 70 eV of ionization energy. High-resolution mass spectra (HRMS) were obtained on the same instrument. Kieselgel 60 was used for column chromatography.

Reaction of 1a with *o*-Phenylenediamine. A mixture of **1a**[18] (1.50 g, 9.17 mmol) and *o*-phenylenediamine (1.00 g, 9.25 mmol) in ethanol (50 ml) was heated under reflux for 20 h and evaporated. Water was added to the residue, after which the mixture was neutralized with sodium hydrogen carbonate, and extracted with chloroform. The extract was dried over sodium sulfate (Na_2SO_4) and evaporated. Chromatography of the residue with chloroform gave **2a** (1.723 g, 80%) as orange crystals, which were recrystallized from cyclohexane-dichloromethane to give orange prisms, mp 136—138 °C, IR ν_{max} 3384, 3344, 3192 cm^{-1} (NH); ^{1}H NMR δ=3.97 (2H, brs, exchangeable, NH), 6.52 (1H, s, H-3), 6.85 (1H, dd, *J*=7.9 and 7.3 Hz, H-4′), 6.87 (1H d, *J*=7.3 Hz, H-3′), 7.13 (1H, dd, *J*=7.9 and 7.3 Hz, H-5′), 7.20—7.43 (3H, m, H-5, 6, and 7), 7.45 (1H, d *J*=7.3 Hz, H-6′), 7.84—7.92 (2H, m, H-4 and 8), and 9.35 (1H, brs, exchangeable, NH). Found: C, 76.43; H, 5.48; N, 17.92%. Calcd for $C_{15}H_{13}N_3$: C, 76.57; H, 5.57; N, 17.86%.

Reaction of 1b with *o*-Phenylenediamine. A mixture of **1b**[18] (2.296 g, 9.74 mmol) and *o*-phenylenediamine (1.053 g, 9.74 mmol) in ethanol (100 ml) was heated under reflux for 3 h and worked up as for **1a**. Chromatography of the residue with chloroform gave **2b** (2.06 g, 69%) as yellow crystals, which were recrystallized from cyclohexane-dichloromethane to give yellow needles, mp 134—135 °C, IR ν_{max} 3416, 3300, 3200 (NH), and 1662 cm^{-1} (C=O); ^{1}H NMR δ=1.51 (3H, t, *J*=7.3 Hz, CH_3), 3.55 (2H, brs, exchangeable, NH), 4.50 (2H, q, *J*=7.3 Hz, OCH_2), 6.86 (1H, d, *J*=7,9 Hz, H-3′), 6.90 (1H, dd, *J*=7.9 and 7.3 Hz, H-4′), 7.05 (1H, dd, *J*=7.9 and 7.3 Hz, H-5′), 7.51 (1H, t, *J*=9.8 Hz, H-6), 7.68 (2H, dd, *J*=10.4 and 9.8 Hz, H-5 and 7), 7.83 (1H, d, *J*=7.9 Hz, H-6′), 8.23 (1H, d, *J*=10.4 Hz, H-8), 8.90 (1H, d, *J*=10.4 Hz, H-4), and 9.40 (1H, brs, exchangeable, NH). Found: C, 70.25; H, 5.47; N, 13.75%. Calcd for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58; N, 13.67%. Further elution gave **3** (0.721 g, 29%) as orange crystals, which were recrystallized from cyclohexane-dichloromethane to give orange prisms, mp 178—180 °C, IR ν_{max} 3352 (NH), 1680 and 1668 cm^{-1} (C=O); ^{1}H NMR δ=1.33 (6H, t, *J*=7.3 Hz, 2×CH_3), 4.33 (4H, q, *J*=7.3 Hz, 2×OCH_2), 7.26—7.29 (2H, m, H-4′ and 5′), 7.54 (2H, t, *J*=9.8 Hz, H-6), 7.68 and 7.80 (4H, dd, *J*=10.4 and 9.8 Hz, H-5 and 7), 8.21—8.25 (2H, m, H-3′ and 6′), 8.28 (2H, d, *J*=10.4 Hz, H-8) , 8.95 (2H, d, *J*=10.4 Hz, H-4), and 9.40 (2H, brs, exchangeable, NH). Found: C, 71.20; H, 5.25; N, 11.02%. Calcd for $C_{30}H_{26}N_4O_4$: C, 71.13; H, 5.17; N, 11.06%.

Reaction of 2a with PPA. A mixture of **2a** (0.14 g) and PPA (20 ml) was heated for 1 h at 150 °C, after which water was added to the reaction mixture. The mixture was neutralized with sodium hydrogen carbonate and extracted with chloroform. The extract was dried (Na_2SO_4) and evaporated. Chromatography of the residue with chloroform gave **4a** (0.105 g, 81%) as brown crystals, which were recrystallized from cyclohexane-dichloromethane to give brown needles, mp 188—189 °C, IR ν_{max} no NH; ^{1}H NMR δ=6.76 (1H, s, H-6) , 6.94 (1H, dd, *J*=11.6 and 8.5 Hz, H-8), 7.00 (1H, dd, *J*=11.6 and 8.5 Hz, H-9), 7.07 (1H, dd, *J*=11.6 and 8.6 Hz, H-10), 7.35 (1H, dd, *J*=7.9 and 7.3 Hz, H-3), 7.44 (1H, dd, *J*=7.9 and 7.3 Hz, H-2) , 7.65 (1H, d, *J*=11.6 Hz, H-7), 7.70 (1H, d, *J*=8.6 Hz, H-11), 7.89 (1H, d, *J*=7.3 Hz, H-1), and 7.90 (1H, d, *J*=7.3 Hz, H-4); ^{13}C NMR δ=101.88 (d), 110.73 (d), 114.11 (d), 119.59 (d), 121.15 (d), 123.63 (d), 127.58 (d), 128.07 (d), 128.73 (s) , 130.38 (d), 131.31 (d), 137.85 (s), 144.58 (s), 149.43 (s), and 159.47 (s); MS *m*/*z* (rel intensity) 218 (100, M$^+$), 177 (32), 161 (45), 160 (34), 109 (13), 91 (40), and 57 (85). Found: C, 80.92; H, 4.86; N, 12.55%. Calcd for $C_{15}H_{10}N_2 \cdot 1/4\ H_2O$: C, 80.88; H, 4.75; N, 12.57%. HRMS Found: *m*/*z* 218.0847. Calcd for $C_{15}H_{10}N_2$: M, 218.0843.

Reaction of 2b with PPA: A mixture of **2b** (0.20 g) and PPA (20 ml) was heated for 3 h at 150 °C, after which water was added to the reaction mixture. The mixture was neutralized with sodium hydrogen carbonate and extracted with chloroform. The extract was dried (Na_2SO_4) and evaporated. Chromatography of the residue with chloroform gave **4a** (0.064 g, 45%).

Reaction of 2b with TsOH. A mixture of **2b** (0.300 g) and TsOH (0.01 g) in 1-butanol (20 ml) was refluxed for 3 d and evaporated, and the residue was chromatographed. Elution with benzene-chloroform (1:1) gave recovered **2b** (0.070 g, 23%). Elution with chloroform gave **4b** (0.110 g, 39%) as red crystals, which were recrystallized from cyclohexane-dichloromethane to give red brown needles, mp 213—214 °C, IR $\nu_{\max}$ 1686 cm^{-1} (C=O); ^{1}H NMR δ=1.55 (3H, t, *J*=7.0 Hz, CH$_3$) , 4.62 (2H, q, *J*=7.0 Hz, OCH$_2$), 7.35—7.70 (5H, m, H-2, 3, 8, 9, and 10), 8.01 (1H, d, *J*=7.9 Hz, H-4), 8.06 (1H, d, *J*=7.9 Hz, H-1), 8.27 (1H, d, *J*=8.6 Hz, H-11), and 9.37 (1H, d, *J*=11.0 Hz, H-7); ^{13}C NMR δ=14.77 (q), 60.69 (t), 100.83 (s), 111.06 (d), 118.03 (d), 120.52 (d),121.60 (d), 124.42 (d), 127.99 (s), 131.31 (d), 132.72 (d), 133.26 (d), 133.35 (d), 138.56 (s), 147.57 (s), 149.69 (s), 156.92 (s), and 163.52 (s); MS *m/z* (rel intensity) 290 (55, M$^+$), 245 (11), 219 (21), 218 (100), 169 (11), 109 (6), and 76 (14). Found: C, 74.21; H, 4.95; N, 9.52%. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65%. Elution with ethyl acetate gave **5** (0.081 g, 32%) as red crystals, which were recrystallized from ethanol to give red needles, mp 296—297 °C, IR $\nu_{\max}$ 3300—2800 (NH) and 1644 cm^{-1} (C=O); ^{1}H NMR δ(DMSO-*d*$_6$)=6.80—7.10 (4H, m, H-1, 2, 3, and 4), 7.50 (1H, t, *J*=9.8 Hz, H-9), 7.65 (1H, t, *J*=9.8 Hz, H-8), 7.67 (1H, dd *J*=10.4 and 9.8 Hz, H-10), 7.90 (1H, d, *J*=9.8 Hz, H-7), 9.08 (1H, d, *J*=10.4 Hz, H-11), 9.17 (1H, brs, exchangeable, NH), and 10.08 (1H, brs, exchangeable, NH), δ (CF$_3$CO$_2$D)=6.92—6.96 (2H, m, H-1 and 4), 7.12—7.18 (2H, m, H-2 and 3), 8.05—8.25 (3H, m, H-8, 9, and 10), 8.37 (1H, dm, *J*=9.8 Hz, H-7), and 9.75 (1H, d, *J*=11.0 Hz, H-11); MS *m/z* (rel intensity) 261 (100, M$^+$), 260 (40), 233 (15), 232 (19), 205 (10), 169 (11), 112 (15), 97 (22), 83 (26), 77 (11), 71 (29), 69 (28), and 58 (65). Found: C, 72.20; H, 4.10; N, 15.59%. Calcd for $C_{16}H_{11}N_3N_3O\cdot 1/4\ H_2O$: 72.30; H, 4.36; N, 15.81%.

Reaction of 2b with AcOH. A mixture of **2b** (0.300 g) and AcOH (2 ml) in 1-butanol (30 ml) was refluxed for 4 d. The resulted precipitate was filtered and washed with ethanol to give **5** (0.110 g, 43%) as red needles. The combined filtrate was evaporated. To the residue water was added, and the mixture was neutralized with sodium hydrogen carbonate, then extracted with chloroform. The extract was dried (Na$_2$SO$_4$) and evaporated. The residue was chromatographed. Elution with chloroform gave recovered **2b** (0.057 g, 19%). Further elution gave **4b** (0.063 g, 22%). Elution with ethyl acetate gave **5** (0.015 g, 6%).

Similar treatment of **2b** with TFA and concd H$_2$SO$_4$ gave **2b** (0 and 5%), **4b** (1 and 15%), and **5** (96 and 80%), respectively.

Deesterification of 4b. A mixture of **4b** (0.020 g) and 48% hydrobromic acid (10 ml) was refluxed for 2 h and poured into water. The mixture was neutralized with sodium hydrogen carbonate and extracted with chloroform. The extract was dried (Na$_2$SO$_4$) and evaporated to give **4a** (0.009 g, 60%).

Methylation of 5. A mixture of **5** (0.100 g), DBU (0.30 g), and methyl iodide (1.0 g) in dry acetonitrile (50 ml) was refluxed for 7 h and evaporated, and the residue was chromatographed. Elution with chloroform gave **6** (0.02 g, 19%) as red crystals, which were recrystallized from hexane-dichloromethane to give red needles, mp 188—189 °C, IR $\nu_{\max}$ 3180 cm^{-1} (NH); ^{1}H NMR δ (DMSO-*d*$_6$)=3.34 (3H, s, OMe), 6.60 (1H, d, *J*=9.8 Hz, H-7), 6.62—6.83 (5H, m, H-1, 2, 3, 4, and 9), 7.01 (1H, dd, *J*=11.0 and 9.8 Hz, H-8), 7.05 (1H, dd, *J*=11.6 and 9.8 Hz, H-10), 8.49 (1H, d, *J*=11.6 Hz, H-11), and 9.09 (1H, brs, NH); MS *m/z* (rel intensity) 275 (100, M$^+$), 274 (25), 169 (22), 147 (9), 119 (9), 97 (7), 91 (8), 77 (6), 69 (12), and 57 (14). HRMS Found: *m/z* 275.1069. Calcd for $C_{17}H_{13}N_3O$: M, 275.1058. Elution with ethyl acetate gave recovered **5** (0.071 g, 71%).

Reaction of 2b with Sodium Ethoxide. To the solution of sodium ethoxide, which was prepared from sodium metal (0.150 g, 6.5 mmol) and absolute ethanol (50 ml), **2b** (0.200 g, 0.65 mmol) was added, and the solution was refluxed for 4 d. The resulted precipitate was collected by filtration and washed with ethanol to give **7a** (0.071 g, 42%) as orange crystals. These were recrystallized from ethanol to give orange needles, mp 269—271 °C, IR $\nu_{\max}$ 3148 (NH), 1718 and 1666 cm^{-1} (C=O); ^{1}H NMR δ (DMSO-*d*$_6$)=7.10—7.25 (3H, m, H-4, 5, and 6), 7.71—7.95 (3H, m, H-5′, 6′, and 7′), 8.08 (1H, s, H-3′), 8.60 (1H, d, *J*=9.8 Hz, H-4′), 8.66 (1H, d, *J*=10.4 Hz, H-8′), 8.78—8.83 (1H, m, H-7), and 11.48 (1H, brs, exchangeable, NH), δ (CF$_3$CO$_2$D)=7.50—7.59 (3H, m, H-5, 6, and 3′), 7.85—7.95 (2H, m, H-4 and 7), 8.45—8.69 (3H, m, H-5′, 6′, and 7′), 9.18 (1H, d, *J*=10.4 Hz, H-8′), and 9.24 (1H, d, *J*=9.8 Hz, H-4′); MS *m/z* (rel intensity) 261 (100, M$^+$), 260 (15), 219 (92), 218 (12), 102 (20), 90 (9), 76 (10), 75 (7), and 52 (10). Found: C, 73.80; H, 4.06; N, 15.99%. Calcd for $C_{16}H_{11}N_3O$: C, 73.55; H, 4.24; N, 16.08%. The filtrate was diluted with water, neutralized with dilute hydrochloric acid, and extracted with chloroform. The extract was dried (Na$_2$SO$_4$) and evaporated. The residue was chromatographed. Elution with chloroform-ethyl acetate (1:1) gave **7a** (0.046 g, 27%). Elution with ethyl acetate gave **5** (0.002 g, 1%).

Rearrangement of 5. To the solution of sodium ethoxide, (which was prepared from sodium metal (0.230 g, 1.00 mmol) and absolute ethanol (60 ml)), **5** (0.130 g, 0.50 mmol) was added. The mixture was refluxed for 60 h and evaporated. The residue was dissolved in water, neutralized with dilute hydrochloric acid, and extracted with chloroform. The extract was dried (Na$_2$SO$_4$) and evaporated. The residue was chromatographed. Elution with chloroform gave **7a** (0.109 g, 91%). Elution with ethyl acetate gave recovered **5** (0.002 g, 2%).

Reaction of 2a with *N,N′*-Carbonyldiimidazole. A mixture of **2a** (0.508 g, 2.16 mmol) and *N,N′*-carbonyldiimidazole (0.590 g, 2.26 mmol) in dry tetrahydrofuran (20 ml) was refluxed for 20 h. The precipitate was collected by filtration to give **7a** (0.255 g, 45%). The filtrate was evaporated and chromatographed with chloroform to give **7a** (0.274 g, 49%). The combined crystals of **7a** were recrystallized from ethanol to give orange needles (0.374 g, 66%), mp 269—271 °C.

Acetylation of 7a. A mixture of **7a** (0.100 g), acetic anhydride (10 ml), and 2 drops of concd H$_2$SO$_4$ was heated for 3 h at 100 °C, then poured into water. The mixture was neutralized with sodium hydrogen carbonate, and extracted with chloroform. The extract was dried (Na$_2$SO$_4$) and evaporated. Crystallization of the residue from cyclohexane gave **7b** (0.061 g, 53%) as orange prisms, mp 217—219 °C, IR $\nu_{\max}$ 1754 and 1714 cm^{-1} (C=O); ^{1}H NMR δ=2.87 (3H, s, COCH$_3$), 7.29 (1H, dd, *J*=7.9 and 7.3 Hz, H-5), 7.39 (1H, dd, *J*=7.9 and 7.3 Hz, H-6), 7.63—7.72 (1H, m, H-6′), 7.75—7.90 (2H, m, H-5′ and 7′), 8.05 (1H, s, H-3′), 8.32 (1H, d, *J*=7.9 Hz, H-7), 8.53 (1H, d, *J*=9.8 Hz, H-4′), 8.65 (1H, d, *J*=10.4

Hz, H-8′), and 8.95 (1H, d, J=7.9 Hz, H-4). Found: C, 71.21; H, 4.28; N, 13.87%. Calcd for $\mathrm{C_{18}H_{13}N_3O_2}$: C, 71.28; H, 4.32; N, 13.85%.

Reaction of 2b with Ethyl Chloroformate. A solution of **2b** (0.500 g, 1.63 mmol), ethyl chloroformate (0.354 g, 3.26 mmol), and triethylamine (0.330 g, 3.26 mmol) in dry benzene (50 ml) was refluxed for 3 h. To the solution water was added, and the mixture was extracted with benzene. The benzene layer was dried ($\mathrm{Na_2SO_4}$) and evaporated. The residue was chromatographed. Elution with benzene-chloroform (1:1) gave colorless crystals (0.120 g, 29%), which were recrystallized from cyclohexane-dichloromethane to give diethyl *o*-phenylenebis[carbamate] as colorless needles, mp 87—88 °C (lit.[16] mp 88 °C), IR ν_{max} 3304 (NH), 1754, and 1714 cm^{-1} (C=O); ^{1}H NMR δ=1.31 (6H, t, J=7.0 Hz, 2×CH$_3$), 4.23 (4H, q, J=7.0 Hz, 2×OCH$_2$), 6.94 (2H, brs, 2×NH), 7.11—7.18 (2H, m, H-4 and 5), and 7.45—7.57 (2H, m, H-3 and 6). Found: C, 57.19; H, 6.28; N, 10.87%. Further elution gave **2c** (0.405 g, 66%) as yellow crystals, which were recrystallized from cyclohexane-dichloromethane to give yellow needles, mp 172—173 °C, IR ν_{max} 3172 (NH), 1720, and 1670 cm^{-1} (C=O); ^{1}H NMR δ=1.27 (3H, t, J=7.0 Hz, CH$_3$), 1.47 (3H, t, J=7.3 Hz, CH$_3$), 4.20 (2H, q, J=7.0 Hz, OCH$_2$), 4.42 (2H, q, J=7.3 Hz, OCH$_2$), 7.15—7.25 (2H, m, H-4′ and 5′), 7.58 (1H, t, J=9.8 Hz, H-6), 7.66—7.79 (4H, m, H-3′, 6′, 5, and 7), 8.30 (1H, d, J=9.8 Hz, H-8), 8.43 (1H, brs, NH), 8.91 (1H, d, J=10.4 Hz, H-4), and 9.45 (1H, brs, NH). Found: C, 66.57; H, 5.51; N, 11.15%. Calcd for $\mathrm{C_{21}H_{21}N_3O_4}$: C, 66.48; H, 5.58; N, 11.07%. Elution with chloroform gave recovered **2b** (0.026 g, 5%).

Reaction of 2c with DBU. A mixture of **2c** (0.080 g, 0.21 mmol) and DBU (0.050 g, 0.32 mmol) in dry benzene (30 ml) was refluxed for 16 h and evaporated. The residue was dissolved with water, neutralized with dilute hydrochloric acid, and extracted with chloroform. The extract was dried ($\mathrm{Na_2SO_4}$) and evaporated. Chromatography of the residue with chloroform gave **7c** (0.035 g, 50%), which was recrystallized from cyclohexane to give orange prisms, mp 158 °C (decomp), IR ν_{max} 3176 (NH), 1716, and 1662 cm^{-1} (C=O); ^{1}H NMR δ=1.19 (3H, t, J=7.0 Hz, CH$_3$), 4.32 (2H, q, J=7.0 Hz, OCH$_2$), 7.08—7.19 (3H, m, H-4, 5, and 6), 7.53—7.60 (1H, m, H-7), 7.92—8.10 (3H, m, H-5′, 6′, and 7′), 8.84 (1H, d, J=9.8 Hz, H-8′), 9.34 (1H, brs, NH), and 9.56 (1H, d, J=10.4 Hz, H-4′); MS m/z (rel intensity) 333 (100, M$^+$), 304 (27), 288 (75), 287 (22), 261 (76), 260 (18), 245 (24), 219 (31), 218 (14), 205 (13), 102 (9), 89 (19), and 69 (8). Found: C, 65.02; H, 4.77; N, 11.63%. Calcd for $\mathrm{C_{19}H_{15}N_3O_3 \cdot H_2O}$: C, 64.95; H, 4.88; N, 11.96%.

Reaction of 2b with *N,N′*-Carbonyldiimidazole. A mixture of **2b** (0.400 g, 1.30 mmol) and *N,N′*-carbonyldiimidazole (0.213 g, 1.31 mmol) in dry tetrahydrofuran (20 ml) was refluxed for 24 h, and evaporated. The residue was chromatographed. Elution with chloroform gave **2b** (0.132 g, 33%). Elution with ethyl acetate gave **7c** (0.258 g, 59%). This was recrystallized from ethanol to give orange needles (0.201 g, 46%), mp 157—159 °C.

Acetylation of 7c. A mixture of **7c** (0.098 g), acetic anhydride (10 ml), and 2 drops of concd $\mathrm{H_2SO_4}$ was heated for 3 h at 100 °C, then poured into water. The mixture was neutralized with sodium hydrogen carbonate, and extracted with chloroform. The extract was dried ($\mathrm{Na_2SO_4}$) and evaporated. Crystallization of the residue from cyclohexane gave **7d** (0.099 g, 90%) as orange prisms, mp 184—186 °C, IR ν_{max} 1768, 1722, and 1694 cm^{-1} (C=O); ^{1}H NMR δ=1.17 (3H, t, J=7.0 Hz, CH$_3$), 2.82 (3H, s, COCH$_3$), 4.31 (2H, q, J=7.0 Hz, OCH$_2$), 7.21—7.27 (2H, m, H-5 and 6), 7.37—7.42 (1H, m, H-7), 7.98—8.20 (3H, m, H-5′, 6′, and 7′), 8.28—8.33 (1H, m, H-4), 8.87 (1H, d, J=9.8 Hz, H-4′), and 9.63 (1H, d, J=10.4 Hz, H-8′). Found: C, 67.25; H, 4.66; N, 11.10%. Calcd for $\mathrm{C_{21}H_{17}N_3O_4}$: C, 67.19; H, 4.57; N, 11.19%.

Reaction of 2a with Triethyl Orthoformate. A mixture of **2a** (0.235 g), triethyl orthoformate (5 ml), and TsOH (0.020 g) was refluxed for 1 h, then evaporated. Chromatography of the residue with chloroform gave **13a** (0.184 g, 75%) as orange crystals. These were recrystallized from cyclohexane-dichloromethane to give orange prisms, mp 185—187 °C, IR no NH; ^{1}H NMR δ=7.35—7.51 (2H, m, H-5 and 6), 7.48 (1H, s, H-3′), 7.62—7.74 (1H, m, H-6′), 7.76—7.86 (2H, m, H-5′ and 7′), 7.90 (1H, d, J=7.9 Hz, H-4), 8.42 (1H, d, J=7.3 Hz, H-7), 8.49 (1H, d, J=9.8 Hz, H-4′), 8.57—8.67 (1H, m, H-8′), and 8.89 (1H, s, H-2); MS m/z (rel intensity) 245 (100, M$^+$), 244 (53), 243 (7), 219 (12), 218 (7), 109 (10), 90 (11), 89 (10), 76 (11), 75 (10), and 63 (11). Found: C, 78.46; H, 4.32; N, 17.19%. Calcd for $\mathrm{C_{16}H_{11}N_3}$: C, 78.35; H, 4.52; N, 17.13%.

Reaction of 1a with Benzimidazole. A mixture of **1a** (0.164 g, 1.00 mmol) and benzimidazole (0.237 g, 2.00 mmol) in 1-butanol (15 ml) was refluxed for 19 h and evaporated. The mixture was dissolved with water and chloroform, neutralized with sodium hydrogen carbonate, and extracted with chloroform. The extract was dried ($\mathrm{Na_2SO_4}$) and evaporated. Chromatography with chloroform gave **13a** (0.198 g, 81%) as orange crystals. These were recrystallized from cyclohexane-dichloromethane to give orange prisms, mp 185—187 °C.

Reaction of 2b with Triethyl Orthoformate. A mixture of **2b** (0.277 g), triethyl orthoformate (5 ml), and TsOH (0.020 g) was refluxed for 30 min and worked up as for **2a**. Chromatography of the residue with ethyl acetate gave **13b** (0.269 g, 94%) as yellow crystals, which were recrystallized from cyclohexane-dichloromethane to give yellow needles, mp 137—138 °C, IR ν_{max} 1702 and 1682 cm^{-1} (C=O); ^{1}H NMR δ=1.17 (3H, t, J=7.3 Hz, CH$_3$), 4.34 (2H, q, J=7.3 Hz, OCH$_2$), 7.40—7.44 (2H, m, H-5 and 6), 7.90—8.00 (2H, m, H-4 and H-7), 8.02—8.16 (3H, m, H-5′, 6′ and 7′), 8.73 (1H, s, H-2), 8.86 (1H, d, J=9.8 Hz, H-8′), and 9.71 (1H, d, J=9.8 Hz, H-4′); MS m/z (rel intensity) 317 (100, M$^+$), 245 (74), 244 (51), 243 (39), 127 (39), 115 (38), 102 (49), 90 (35), 89 (60), 76 (41), 75 (64), and 63 (53). Found: C, 71.83; H, 4.64; N, 12.82%. Calcd for $\mathrm{C_{19}H_{15}N_3O_2}$: C, 71.91; H, 4.76; N, 13.24%.

Reaction of 1b with Benzimidazole. A mixture of **1b** (0.300 g, 1.27 mmol) and benzimidazole (0.300 g, 2.54 mmol) in 1-butanol (10 ml) was refluxed for 3 h and worked up as for **1a**. Chromatography of the residue with chloroform gave **13b** (0.320 g, 96%).

Deesterification of 13b. A mixture of **13b** (0.169 g, 0.53 mmol), potassium hydroxide (0.195 g, 3.5 mmol), water (10 ml), and ethanol (30 ml) was refluxed for 2 h, then diluted with water. The mixture was acidified with dilute hydrochloric acid. The resulting precipitate was collected by filtration to give the corresponding carboxylic acid (0.088 g, 57%), mp 190—191 °C. A mixture of the acid (0.085 g) and 48% hydrobromic acid (10 ml) was refluxed for 1 h and poured into water. The mixture was neutralized with sodium hydrogen carbonate and extracted with chloroform. The extract was dried ($\mathrm{Na_2SO_4}$) and evaporated. Chromatography of the residue with chloroform gave **13a** (0.27 g, 37%) as orange crystals, which were recrystallized from cyclohexane-dichloromethane to give orange prisms, mp 186—188 °C. Elution with ethyl acatate gave cyclohepta-[*b*]pyrrole(17) (0.006 g) as yellow crystals, mp 162—163.5 °C (lit.(17) mp 163—164 °C).

Reaction of 2a with Triethyl Orthoacetate. A mixture of **2a** (0.235 g), triethyl orthoacetate (5 ml), and TsOH (0.020 g) was refluxed for 1 h and evaporated. The residue was chromatographed. Elution with chloroform gave **13c** (0.199 g, 77%) as orange crystals. These were recrystallized from cyclohexane to give orange needles, mp 112—114 °C, IR no NH; ^{1}H NMR δ=2.97 (3H, s, CH$_3$), 7.27—7.37 (2H, m, H-5 and 6), 7.47 (1H, s, H-3′), 7.70—7.82 (2H, m, H-7 and 6′), 7.84—7.95 (2H, m, H-5′ and 7′), 8.03—8.09 (1H, m, H-4), 8.59 (1H, d, *J*=10.4 Hz, H-4′), and 8.72 (1H, d, *J*=10.4 Hz, H-8′). Found: C, 78.79; H, 5.16; N, 16.13%. Calcd for $C_{17}H_{13}N_3$: C, 78.74; H, 5.05; N, 16.20%.

Reaction of 2b with Triethyl Orthoacetate. A mixture of **2b** (0.109 g), triethyl orthoacetate (5 ml), and TsOH (0.020 g) was refluxed for 1 h and evaporated. The residue was chromatographed with chloroform to give **13d** (0.110 g, 94%) as yellow crystals. These were recrystallized from cyclohexane to give yellow needles, mp 142—143 °C, IR ν_{max} 1698 cm^{-1} (C=O); ^{1}H NMR δ=0.77 (3H, t, *J*=7.0 Hz, CH$_3$), 2.62 (3H, s, CH$_3$), 4.05 (2H, q, OCH$_2$), 7.15—7.30 (3H, m, H-4, 5, and 6), 7.75 (1H, d, *J*=7.9 Hz, H-7), 8.02—8.25 (3H, m, H-5′, 6′ and 7′), 8.90 (1H, d, *J*=9.8 Hz, H-8′), and 9.79 (1H, d, *J*=10.4 Hz, H-4′). Found: C, 72.21; H, 5.10; N, 12.62%. Calcd for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68%.

Reaction of 2a with Acetic Anhydride. A mixture of **2a** (0.470 g) and acetic anhydride (20 ml) was heated for 6 h at 100 °C and poured into water. The mixture was neutralized with sodium hydrogen carbonate and extracted with chloroform. The extract was washed with 5% aq sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated. The residue was chromatographed. Elution with chloroform gave **2d** (0.160 g, 29%), which was recrystallized from cyclohexane to give orange prisms, mp 150—153 °C, IR ν_{max} 1714 and 1702 cm^{-1} (C=O); ^{1}H NMR δ=2.22 (3H, s, CH$_3$), 7.33 (1H, d, *J*=7.3 Hz, H-7′), 7.40—7.75 (8H, m, H-5, 6, 7, 4′, 5′, 6′, and 2×NH), 8.20 (1H, d, *J*=9.8 Hz, H-8), and 8.39 (1H, d, *J*=9.8 Hz, H-4). Found: C, 73.75; H, 5.42; N, 15.20%. Calcd for $C_{17}H_{15}N_3O$: C, 73.63; H, 5.45; N, 15.15%. Further elution gave **13c** (0.293 g, 56%).

Reaction of 2b with Acetic Anhydride. a) A mixture of **2b** (0.307 g) and acetic anhydride (20 ml) was refluxed for 1 h and worked up as for **2a**. The residue was chromatographed. Elution with chloroform gave **2e** (0.029 g, 8%), which was recrystallized from ethyl acetate to give yellow needles, mp 223—224 °C, IR ν_{max} 3272 (NH) and 1662 cm^{-1} (C=O); ^{1}H NMR δ=1.51 (3H, t, *J*=7.0 Hz, CH$_3$), 2.07 (3H, s, CH$_3$), 4.51 (2H, q, *J*=7.0 Hz, OCH$_2$), 7.16—7.27 (2H, m, H-4′ and 5′), 7.56—7.85 (5H, m, H-5, 6, 7, 3′, and 6′), 8.23 (1H, d, *J*=9.8 Hz, H-8), 8.95 (1H, d, *J*=10.4 Hz, H-4), 9.61 (1H, brs, NH), and 9.66 (1H, brs, NH). Found: C, 68.81; H, 5.53; N, 11.99%. Calcd for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03%. Elution with chloroform-ethyl acetate (1 : 1) gave **2f** (0.010 g, 3%) as yellow crystals, which were recrystallized from cyclohexane-dichloromethane to give yellow needles, mp 165—167 °C, IR ν_{max} 3260 (NH), 1695, 1680, and 1662 cm^{-1} (C=O); ^{1}H NMR δ=1.53 (3H, t, *J*=7.1 Hz, CH$_3$), 2.06 (3H, s, CH$_3$), 2.21 (3H, s, CH$_3$), 4.56 (2H, q, *J*=7.0 Hz, OCH$_2$), 7.22 (1H, dd, *J*=7.9 and 7.2 Hz, H-5′), 7.42 (1H, dd, *J*=7.9 and 7.2 Hz, H-4′), 7.77 (1H, d, *J*=7.9 Hz, H-3′), 7.84—8.05 (3H, m, H-5, 6, and 7), 8.47 (1H, d, *J*=7.9 Hz, H-6′), 8.64 (1H, d, *J*=10.1 Hz, H-8), 9.39 (1H, d, *J*=10.1 Hz, H-4), and 9.66 (1H, brs, NH). Found: C, 67.73; H, 5.60; N, 10.57%. Calcd for $C_{22}H_{21}N_3O_4$: C, 67.51; H, 5.41; N, 10.73%. Elution with ethyl acetate gave **13d** (0.205 g, 62%).

b) A mixture of **2b** (0.620 g) and acetic anhydride (20 ml) was stirred for 4 d at room temperature and worked up as above. The residue was crystallized from ethyl acetate to give **2e** (0.497 g, 71%).

Reaction of 2e with PPA-Phosphoryl Chloride. A mixture of **2e** (0.355 g), PPA (10 ml), and phosphoryl chloride (5 ml) was heated for 30 h at 80 °C. The mixture was dissolved in water and neutralized with sodium hydrogen carbonate, and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was recrystallized from cyclohexane to give **13d** (0.208 g, 61%) as yellow needles, mp 142—143 °C.

We thank Dr. Akira Mori, Kyushu University, for the measurements of the mass spectra and elemental analyses.

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