Preparation and Stereochemistry of Dioxatetraazaperhydroanthracenes and -perylenes from the Reaction of 2-Hydrazinoethanols with Aldehydes and Glutaraldehyde

Tadashi Okawara,* Shuji Ehara, Hideaki Kagotani, Yoshinari Okamoto, Masashi Eto, Kazunobu Harano, Tetsuo Yamasaki, and Mitsuru Furukawa

Faculty of Pharmaceutical Sciences, Kumamoto University, Oe-hon-machi, Kumamoto 862, Japan

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Hydrazinoethanols **1** were reacted with aldehydes **2** and **6** and glutaraldehyde (**14**) in aqueous solution to give dioxatetraazaperhydroanthracenes **3**, **7**, **12**, and **13** and -perylenes **15** in yields of 19−88 and 42−72%, respectively. Compounds **3**, **7**, **12**, and **15** were deduced by ^{13}C-NMR spectra to have two C_2 symmetry axes, while compound **12** was shown to have a symmetry axis by X-ray crystallography. The most favorable stereoisomers were consistent with predictions obtained by the semiempirical molecular orbital method AM1. The structure of compound **15** was confirmed by X-ray crystallography.

Introduction

Recent developments concerning polyazapolycycles,[1−9] including X-ray crystallographic data, have demonstrated that the formation of these compounds is controlled by steric and lone pair−lone pair interactions. Nielsen et al.,[4] Willer et al., [6] and Ferguson et al.[9] emphasized the importance of the relationship between 1,3-steric and peri-electronic interactions of polyazapolycycles. In addition, Crabb and Katritzky reviewed conformational equilibria and lone−pair interactions in nitrogen-containing saturated six-membered rings.[10]

The reaction of hydrazine with formaldehyde and hydrogen peroxide was first reported in 1921.[11] The structure originally reported was modified[12] and was finally determined by X-ray structure analysis to be a tricyclic compound with one six- and two seven-membered rings.[13] Katritzky elucidated why this structure was produced by comparing heats of formation for isomers using a molecular orbital method (AM1).[14] These previous studies seemed relevant to our own work with polyheterocycles[15] which are formed from the reaction of polyfunctionalized compounds with carbonyls. We became interested in the factors which determined why only a few stereoisomers are chosen from among many possible isomers and accordingly attempted to prepare tri- and pentaheterocycles with four nitrogens in a single ring. In this paper, we report the reaction of hydrazinoethanols **1** with aldehydes **2** and **6** and glutaraldehyde (**14**) to provide dioxatetraazaperhydro-anthracenes **3**, **7**, **12**, and **13** and -perylenes **15** and include a prediction of the most likely stereoisomer by AM1. One of these predictions was confirmed by X-ray crystallography.

Results and Discussion

We attempted to react hydrazinoethanols **1** with aldehyde **2** and **6** and glutaraldehyde (**14**). The reaction of **1a**−**d** with 2 equiv of formaldehyde (**2**) was carried out in EtOH at room temperature for 24 h to give dioxatetraazaperhydroanthracenes **3a**−**d** in 29−88% yield (Scheme 1). The mass spectrum of **3a** showed a molecular ion peak at *m*/*z* 200, which represented the loss of four molecules of water from 2 equiv of **1a** and 4 equiv of **2**. No absorptions for hydroxyl, amino, or C=N double bonds were observed in the IR spectrum. The ^{13}C-NMR spectrum showed one-half of the total number of expected carbon signals (8 carbons) at δ 41.82, 63.11, 66.35, and 82.40, which is consistent with a C_2 symmetry axis.

Another plausible structure (**4**) which would have required five carbon signals in the ^{13}C-NMR spectrum was therefore eliminated. In the ^{1}H-NMR spectrum, nonequivalent methylene hydrogens at positions 1, 4, and 9 are indicated at δ 4.28 and 4.62, 2.25 and 4.19, and 3.22 and 4.00, respectively, with assignment based on ^{1}H−^{13}C NMR COSY.

Compound **3a** has three possible stereoisomers, **3aa**, **3ab**, and **3ac**. To determine which of these is the most stable, their heats of formation (ΔH_f) were calculated by a molecular orbital method (AM1).[16] The results are summarized in Figure 1.

Compounds **3ac** and **3aa** had the lowest (12.13 kcal/mol) and highest (23.66 kcal/mol) heats of formation, respectively. This suggests that the trans-trans fused form **3aa** results in repulsion between the lone pairs on nitrogens and oxygens, whereas comparison of the cis-cis fused forms **3ab** and **3ac** indicates that lone pair−

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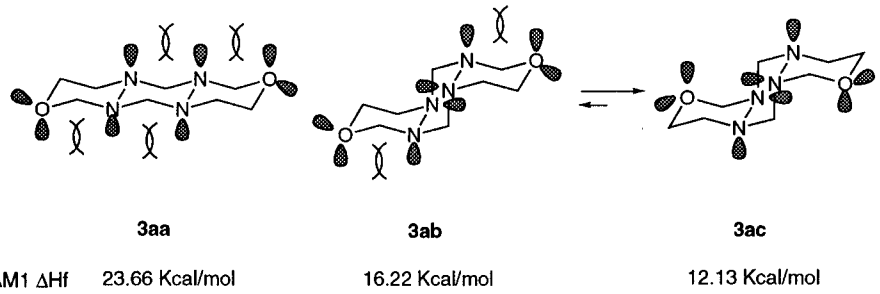
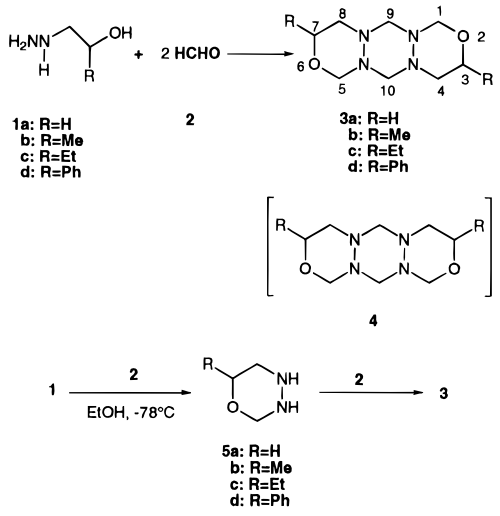
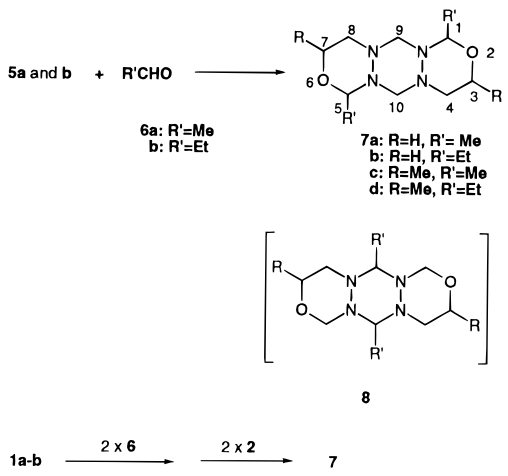


Figure 1.

Scheme 1



Scheme 2



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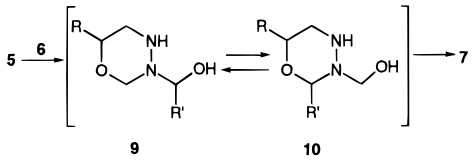
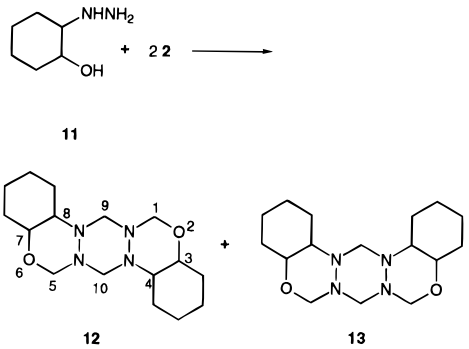


Scheme 4



lone pair repulsion in **3ac** is less than that in **3ab**. Therefore, the stereochemistry of **3a** is most likely given by **3ac**. To elucidate the reaction pathway further, the reaction was performed in EtOH at −78 °C to give 1,3,4-perhydrooxadiazines (**5a**−**d**) in 22−29% yields. Structures **5a**−**d** were confirmed by showing that the molecular ion peak resulted from the loss of a molecule of water from **1** and **2**. In addition, while amino absorption was seen at 3200 cm^{-1}, no C=N double bond absorption was seen in the IR spectra, and the ^{13}C-NMR spectrum showed three methylene carbons at δ 57.82, 60.60, and 71.20 in the case of **5a**. Compound **5** was allowed to react with **2** to give **3** in quantitative yield. Therefore, the deduced reaction pathway to **3** is as follows: Compound **5**, which is derived from **1** and **2**, is presumed to react with a second molecule of **2**, thus avoiding lone pair−lone pair repulsion to produce cis-cis fusion.

Next, the reaction of **5a** and **5b** with aldehyde **6** was attempted, to give 1,5-disubstituted dioxatetraaza-perhydroanthracenes **7a**−**d** in 24−41% yields, but none of the expected 9,10-disubstituted compound **8** (Scheme 2). In the ^{13}C-NMR spectrum of **7a**, the methine carbon (N−C−O) at positions 1 and 5 appeared at δ 87.44 below the expected value in **8**. To ascertain the structure of **7a,** the ^{1}H−^{13}C-NMR long-range correlation was observed, indicating three-bond coupling between the carbon at position 4 and the hydrogen at position 10.

Structure assignment was also supported by another route to **7** which used the reaction of **1** with **6** followed by treatment with **2**. Therefore, the reaction pathway to **7** is as follows: Intermediate **9** derived from **5** and **6** is converted into another intermediate **10**, which then intermolecularly condenses to give **7** (Scheme 3).

Next, the reaction of hydrazinocyclohexanol (**11**) with 2 equiv of **2** was carried out in EtOH to give dioxatetraazaperhydrodibenzoanthracenes **12** and **13** in yields of 33 and 16%, respectively (Scheme 4).

The ^{13}C-NMR spectrum of compound **12** showed eight carbons with a C_2 symmetry axis, while compound **13** showed 16 carbon signals with no symmetry axis. Compound **12** has three possible stereoisomers, **12a**, **12b**, and **12c**. Their heats of formation by AM1 are summarized in Figure 2. The trans-cis-cis-trans forms **12b** and **12c** are more stable than the all-trans fused **12a**. Furthermore, **12c** is presumed to be the most favored stereoisomer due to the lack of lone pair−lone pair repulsion on nitrogen and oxygen.

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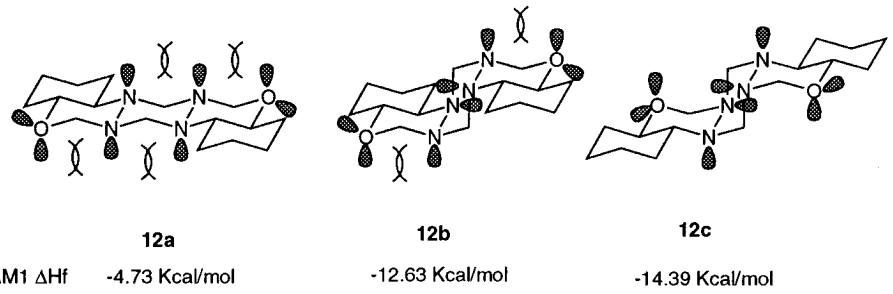


Figure 2.

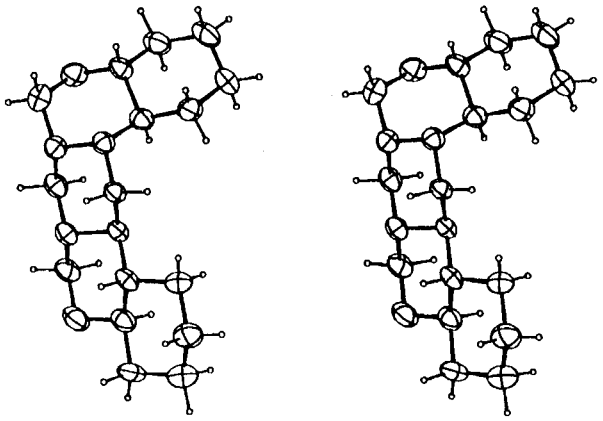
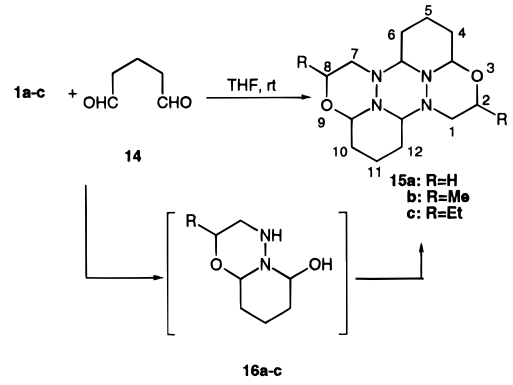


Figure 3. Stereo view of **13**.

Scheme 5



The stereochemistry of compound **13** was not elucidated by $^1H-^{13}C$-NMR COSY. However, the structure of **13** was determined by X-ray crystallography to be the trans-cis-trans-trans fused form **13a** (Figure 3).

As an extension of this method, we attempted to react **1a**−**c** with glutaraldehyde (**14**). A mixture of **1** and **14** in THF was stirred for 15 h at room temperature. Removal of solvent gave an oily residue, which was treated with ether to give the desired products **15** (Scheme 5). The structures of these products were assigned as 3,9-dioxa-3b,6b,9b,12b-tetraazaperhydroperylenes **15** on the basis of the following observations. Product **15a**, derived from **1a** and **14**, showed a molecular ion peak at *m*/*z* 280, which was consistent with the sum of two molecules each of **1a** and **14** after eliminating four molecules of water. The IR spectrum revealed the absence of amino, hydroxy, and carbonyl groups. The DEPT ^{13}C-NMR spectrum indicated five methylene carbons at δ 17.76, 28.17, 30.97, 36.16, and 66.48 and two methine carbons at δ 66.21 and 87.86, which supports a symmetrical structure. The ^1H-NMR spectrum showed C-4, C-5, and C-6 methylene groups at δ 1.22−1.79 and C-3a and C-6a methine protons as a doublet of doublets and a doublet at δ 4.58 and 4.90, respectively. In $^1H-^{13}C$ NMR COSY, the methylene protons at C-2 each appeared as a doublet of doublets at δ 2.50 and 4.03. This shift difference could be attributed to the fact that the hydrogens which are proximal to the lone pairs on oxygen and nitrogen are shifted to lower fields than the hydrogens in the opposite direction.[17] All of the hydrogens and carbons of **15a** could be assigned from $^1H-^1H$- and $^1H-^{13}C$-NMR COSY.

Although several stereoisomers can be formed from the reaction of **1a** with **14**, we estimated that the most favorable stereoisomers were those with an axis of symmetry, giving either the all-trans fused form **15aa** or a form which contained two cis-two trans fused rings, **15ab** and **15ac**. To differentiate among **15aa**, **15ab**, and **15ac**, an NOE difference spectrum of **15a** was measured. Irradiation of the methine proton H−6a (H−12a) at δ 4.58 enhanced the signals of the equatorial protons H−6a (H−12a) and H−1 (H−7) at δ 1.75 and 3.75, and of the axial protons H−5 (H−11) and H−3a (H−9a) at δ 1.65 and 4.89 ppm, respectively. However, these results were not unambiguous and we could not clearly discriminate among the three stereoisomers **15aa**, **15ab**, and **15ac**. Accordingly, the heats of formation were calculated by AM1 as shown in Figure 4. Stereoisomer **15ab** is more stable than **15aa** and **15ac** by 13.55 and 5.68 kcal/mol, respectively. These results show that the lone pairs of stereoisomers **15aa** and **15ac** are repulsed more than those of **15ab**. The lone pairs of isomer **15ab** are arranged so as to minimize this repulsion, as shown in Figure 4. Consequently, isomer **15ab** is assumed to be formed preferentially over **15aa** and **15ac**. Since other structures could also result from this reaction, the structure was unambiguously established as **15a** by X-ray crystallography, as shown in Figure 5.

A comparison of the bond lengths, bond angles, and dihedral angles of the final coordinates obtained from AM1 and X-ray analysis is shown in Table 1.

In conclusion, in the polyheterocycles derived from 2-hydrazinoethanols, the cis-fused isomer is assumed to be formed preferentially to avoid 1,2 and 1,3 lone pair interactions. Heats of formation calculated from AM1 and X-ray structure analyses strongly support these results.

Experimental Section

General Methods. Melting points are uncorrected. ^1H NMR spectra were recorded at 60 and 400 MHz, and ^{13}C NMR spectra were measured at 100 MHz. All spectra were recorded in $CDCl_3$, D_2O, and DMSO-d_6 as solvent, and chemical shifts are reported in δ relative to TMS. Hydrazinoethanols **1b**−**d** were prepared by Gever's method.[18]

General Procedure for 3,7-Disubstituted 2,6-Dioxa-4a, 8a,9a,10a-tetraazaperhydroanthracene (3). A solution of **1** (10 mmol) and **2** (2.3 mL, 30 mmol, 37% w/v in water) in

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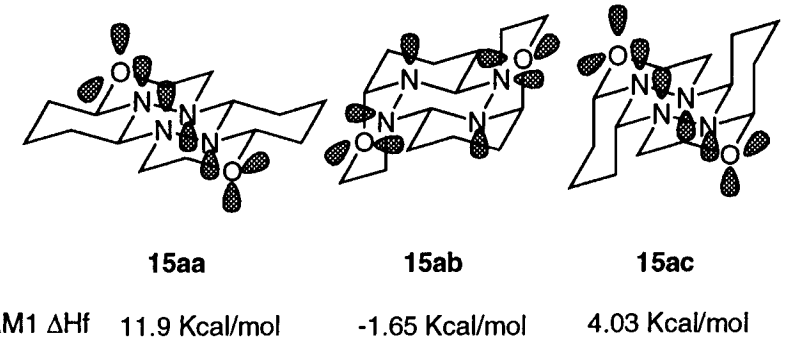

Figure 4.

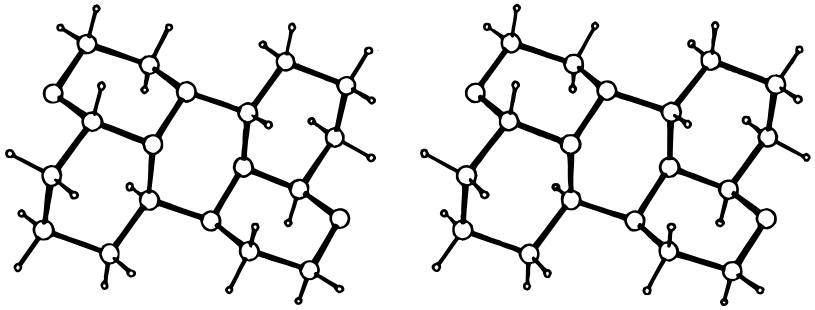

Figure 5. Stereo view of compound **15ab**.

Table 1. Bond Lengths, Bond Angles, and Dihedral Angles of 15a As Obtained from AM1 and X-ray Analysis

	AM1	X-ray
bond length (Å)		
N3b−N12b	1.400	1.450
C3a−N3b	1.486	1.431
O3−C3a	1.443	1.444
C6a−N3b	1.510	1.483
bond angle (deg)		
N3b−C6a−N6b	113.688	109.724
O3−C3a−N3b	112.979	113.158
C6a−N3b−N12b	113.688	111.400
C3a−N3b−N12b	111.289	108.208
dihedral angle (deg)		
N6b−C6a−N3b−N12b	−51.554	−60.517
O3−C3a−N3b−N12b	−55.988	−59.184
C6−C6a−N3b−N12b	−177.998	176.328
N12b−C12a−N10b−C10a	178.483	−175.262
C4−C3a−N3b−N12b	−177.259	−179.000

EtOH (30 mL) was stirred for 24 h. The EtOH was evaporated under reduced pressure. The resulting solid was triturated with isopropyl ether, filtered, and recrystallized.

3a: yield 5.3 g (88%); mp 215−216 °C (recryst from EtOH); ^{1}H NMR ($CDCl_3$) δ 2.25 (d, J = 11.6 Hz, 2H), 3.22 (d, J = 11.9 Hz, 2H), 3.88 (dt, J = 11.4, 3.3 Hz, 2H), 4.00 (dd, J = 11.4, 3.3 Hz, 2H), 4.19 (dd, J = 11.6, 3.3 Hz, 2H), 4.28 (d, J = 10.6 Hz, 2H), 4.62 (d, J = 10.6 Hz, 2H), 5.20 (d, J = 11.9 Hz, 2H); MS-EI m/z 200 (M^+). Anal. Calcd for $C_8H_{16}N_4O_2$: C, 47.99; H, 8.05; N, 27.98. Found: C, 48.01; H, 8.14; N, 27.91.

3b: yield 4.0 g (58%); mp 212−213 °C (recryst from AcOEt); ^{1}H NMR ($CDCl_3$) δ 1.26 (d, J = 5.9 Hz, 6H), 2.32 (d, J = 11.0 Hz, 2H), 3.20 (d, J = 12.1 Hz, 2H), 3.72−3.83 (m, 2H), 3.76 (d, J = 11.0 Hz, 2H), 4.31 (d, J = 10.6 Hz, 2H), 4.61 (d, J = 10.6 Hz, 2H), 5.13 (d, J = 12.1 Hz, 2H); MS-EI m/z 228 (M^+). Anal. Calcd for $C_{10}H_{20}N_4O_2$: C, 52.61; H, 8.83; N, 24.54. Found: C, 52.61; H, 8.87; N, 24.39.

3c: yield 2.0 g (29%); mp 138−139 °C (recryst from AcOEt); ^{1}H NMR ($CDCl_3$) δ 0.96 (t, J = 7.26 Hz, 6H), 1.41−1.68 (m, 4H), 2.34 (dd, J = 11.2, 2.6 Hz, 2H), 3.21 (d, J = 11.6 Hz, 2H), 3.21 (d, J = 11.6 Hz, 2H), 3.55−3.64 (m, 2H), 3.77 (dd, J = 11.2, 10.9 Hz, 2H), 4.33 (d, J = 10.6 Hz, 2H), 4.60 (d, J = 10.6 Hz, 2H), 5.13 (d, J = 11.6 Hz, 2H); MS-EI m/z 228 (M^+). Anal. Calcd for $C_{10}H_{20}N_4O_2$: C, 56.22; H, 9.44; N, 21.86. Found: C, 56.18; H, 9.59; N, 21.95.

3d: yield 4.6 g (44%); mp 259−260 °C (recryst from benzene); ^{1}H NMR (DMSO-d_6) δ 2.56 (dd, J = 12.1, 2.9 Hz, 2H), 3.35 (d, J = 11.7 Hz, 2H), 4.08 (dd, J = 12.1, 11.0 Hz, 2H), 4.48 (d, J = 10.6 Hz, 2H), 4.74 (dd, J = 11.0, 2.9 Hz, 2H), 5.34 (d, J = 11.7 Hz, 2H); MS-EI m/z 352 (M^+). Anal. Calcd for $C_{20}H_{24}N_4O_2$: C, 68.16; H, 6.86; N, 15.90. Found: C, 68.40; H, 7.04; N, 15.76.

General Procedure for 6-Substituted 1,3,4-Perhydrooxadiazine (5). To a solution of **1** (50 mmol) in EtOH (100 mL) was added dropwise **2** (3.8 mL, 50 mmol, 37% w/v in water) at −78 °C. The reaction mixture was then stirred at −78 °C for 4 h and allowed to stand until it reached room temperature. The EtOH was evaporated under reduced pressure, and the residue was recrystallized from solvent.

5a: yield 1.3 g (29%); mp 137−139 °C (recryst from dioxane); ^{1}H NMR (D_2O) δ 2.73 (s, 2H), 3.70−3.73 (m, 4H); IR (KBr) 3180 cm^{-1}; MS-CI m/z 89 ($M + 1^+$). Anal. Calcd for $C_3H_8N_2O$: C, 40.89; H, 9.15; N, 31.79. Found: C, 40.61; H, 8.99; N, 31.51.

5b: yield 1.1 g (22%); mp 106−108 °C (recryst from THF); ^{1}H NMR ($CDCl_3$) δ 1.09 (d, J = 6.3 Hz, 3H), 2.28 (br, 2H), 2.99 (br, 1H), 3.65 (s, 2H), 4.02 (m, 1H), 4.69 (br, 1H); IR (KBr) 3220 cm^{-1}; MS-CI m/z 103 ($M + 1^+$). Anal. Calcd for $C_4H_{10}N_2O$: C, 47.04; H, 9.87; N, 27.43. Found: C, 46.92; H, 9.81; N, 27.46.

5c: yield 1.3 g (23%); mp 123−125 °C (recryst from AcOEt); ^{1}H NMR ($CDCl_3$) δ 0.95 (t, J = 7.6 Hz, 3H), 1.41−1.53 (m, 2H), 2.39 (br, 2H), 3.08 (br, 1H), 3.71 (s, 2H), 3.77−3.86 (m, 1H), 4.78 (br, 1H); IR (KBr) 3220 cm^{-1}; MS-CI m/z 117 ($M + 1^+$). Anal. Calcd for $C_5H_{12}N_2O$: C, 51.69; H, 10.41; N, 24.11. Found: C, 51.60; H, 10.52; N, 24.37.

5d: yield 2.2 g (27%); mp 193−194 °C (recryst from dioxane); ^{1}H NMR (DMSO-d_6) δ 2.59 (br, 2H), 3.68 (s, 2H), 4.48 (t, J = 5.6 Hz, 1H), 5.38 (br, 1H); IR (KBr) 3180 cm^{-1}; MS-CI m/z 165 ($M + 1^+$). Anal. Calcd for $C_9H_{12}N_2O$: C, 65.83; H, 7.37; N, 17.06. Found: C, 65.56; H, 7.22; N, 17.13.

General Procedure for 1,3,5,7-Tetrasubstituted 2,6-Dioxa-4a,8a,9a,10a-tetraazaperhydro-anthracene (7). Method A. A solution of **5a**,**b** (10 mmol) and aldehydes **6a**,**b** (10 mmol) in EtOH (20 mL) was stirred for 24 h at room temperature. The EtOH was evaporated under reduced pressure. The solid was obtained by trituration with Et_2O, filtered by washing with isopropyl ether, and recrystallized from solvent.

Method B. A solution of **1a,b** (10 mmol) and aldehydes **6a**,**b** (10 mmol) in EtOH (20 mL) was stirred for 24 h at room temperature. To the reaction mixture was added **2** (0.75 mL, 10 mmol, 37% w/v in water), and the solution was stirred for

24 h at room temperature. The solution was then treated as described in method A.

7a: method A yield 0.93 g (41%), method B 0.89 g (38%); mp 127−128 °C (recryst from AcOEt); ^{1}H NMR ($CDCl_3$) δ 1.19 (d, J = 6.3 Hz, 6H), 2.17 (dd, J = 11.7, 2.0 Hz, 2H), 3.35 (d, J = 11.9 Hz, 2H), 3.87−3.98 (m, 4H), 4.08 (d, J = 11.9 Hz, 2H), 4.63 (q, J = 6.3 Hz, 2H), 4.90 (d, J = 11.9 Hz, 2H); MS-EI m/z 228 (M^+). Anal. Calcd for $C_{10}H_{20}N_4O_2$: C, 52.61; H, 8.83; N, 24.54. Found: C, 53.10; H, 8.97; N, 24.81.

7b: method A yield 1.22 g (48%), method B 0.50 g (22%); mp 138−139 °C (recryst from EtOH); ^{1}H NMR ($CDCl_3$) δ 0.93 (t, J = 7.6 Hz, 6H), 1.38−1.59 (m, 4H), 2.18 (dd, J =12.2, 2.3 Hz, 2H), 3.35 (d, J = 11.9 Hz, 2H), 3.87−3.98 (m, 2H), 3.28 (d, J = 11.9 Hz, 2H), 3.87−4.05 (m, 4H), 4.35 (t, J = 6.6 Hz, 2H), 4.92 (d, J = 11.9 Hz, 2H); MS-EI m/z 256 (M^+). Anal. Calcd for $C_{12}H_{24}N_4O_2$: C, 56.22; H, 9.44; N, 21.86. Found: C, 55.16; H, 9.39; N, 21.74.

7c: method A yield 0.61 g (24%), Method B 0.36 g (14%); mp 155−157 °C (recryst from EtOH); ^{1}H NMR ($CDCl_3$) δ 1.18 (d, J = 5.6 Hz, 6H), 1.20 (d, J = 5.6 Hz, 6H), 2.22 (dd, J = 11.9, 3.0 Hz, 2H), 3.32 (d, J = 11.9 Hz, 2H), 3.66−3.83 (m, 2H), 4.60 (q, J = 5.9 Hz, 2H), 4.81 (d, J=11.9 Hz, 2H); MS-EI m/z 256 (M^+). Anal. Calcd for $C_{12}H_{24}N_4O_2$: C, 56.22; H, 9.44; N, 21.86. Found: C, 55.92; H, 9.49; N, 21.80.

7d: method A yield 0.97 g (34%), Method B 0.65 g (23%); mp 117−119 °C (recryst from AcOEt); ^{1}H NMR ($CDCl_3$) δ 0.95 (t, J = 7.6 Hz, 6H), 1.21 (d, J = 5.9 Hz, 6H), 1.41−1.62 (m, 4H), 2.50 (dd, J = 11.6, 2.6 Hz, 2H), 3.27 (d, J = 11.9 Hz, 2H), 3.69 (dd, J = 11.6, 10.6 Hz, 2H), 3.79−3.88 (m, 2H), 4.30 (t, J = 6.60 Hz, 2H), 4.85 (d, J = 11.9 Hz, 2H); MS-EI m/z 284 (M^+). Anal. Calcd for $C_{14}H_{28}N_4O_2$: C, 59.13; H, 9.92; N, 19.70. Found: C, 59.06; H, 9.85; N, 19.78.

Hydrazinocyclohexanol (11). Cyclohexene oxide (10.1 mL, 100 mmol) was slowly added to hydrazine hydrate (25 mL, 500 mmol) that had been preheated to 60−70 °C. The reaction mixture was then heated at 100 °C for 2 h. Hydrazine was removed under reduced pressure. The residue was triturated with Et_2O and cooled under ice and water: yield 9.3 g (95%); mp 66−68 °C; IR (KBr) 3200 cm^{-1}.

2,6-Dioxa-4a,8a,9a,10a-tetraazaperhydrodibenz[*c,j*]anthracene (12) and 2,6-Dioxa-4a,8a,9a,10a-tetraazaperhydrodibenz[*c,h*]anthracene (13). A solution of hydrazinocyclohexanol (**11**) (3.9 g, 30 mmol) and **2** (4.5 mL, 60 mmol, 37% w/v in water) in EtOH (30 mL) was stirred for 24 h at rt. The EtOH was then removed under reduced pressure. The residue was subjected to silica gel column chromatography ($CHCl_3$: MeOH = 19:1). The solids **12** and **13** obtained from each fraction were recrystallized from benzene and ethyl acetate, respectively.

12: yield 3.05 g (33%); mp 280−285 °C; MS-EI m/z 308 (M^+); ^{1}H NMR ($CDCl_3$) δ 1.03−1.12 (m, 2H), 1.35−1.50 (m, 6H), 1.76−1.86 (m, 8H), 3.26−3.32 (m, 2H), 3.61−3.68 (m, 2H), 3.62 (d, J = 12.5 Hz, 2H), 4.30 (d, J = 10.6 Hz, 2H), 4.69 (d, J = 10.6 Hz, 2H), 4.99 (d, J = 12.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 24.47, 24.65, 27.08, 30.63, 58.17, 82.51 (CH_2), 52.91, 80.57 (CH). Anal. Calcd for $C_{16}H_{28}O_2N_4$: C, 62.31; H, 9.15; N, 18.17. Found: C, 62.58; H, 9.28; N, 18.20.

13: Yield 1.48 g (16%); mp 231−233°C; MS-EI m/z 308 (M^+); ^{1}H NMR ($CDCl_3$) δ 1.04−1.38 (m, 2H), 1.40−1.44 (m, 6H), 1.75−1.90 (m, 8H), 2.10 (t, J = 8.1 Hz, 1H), 3.28−3.34 (m, 2H), 3.33 (d, J = 9.5 Hz, 1H), 3.51−3.54 (m, 1H), 3.53 (d, J = 11.4 Hz, 1H), 4.12 (d, J = 7.7 Hz, 1H), 4.18−4.24 (m, 1H), 4.23 (d, J = 9.5 Hz, 1H), 4.35 (d, J = 7.7 Hz, 1H), 4.42 (d, J = 10.6 Hz, 1H), 4.81 (d, J = 10.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 24.07, 24.23, 24.38, 24.65, 26.20, 26.69, 30.57, 61.35, 66.39, 82.48, 84.03 (CH_2), 53.50, 66.39, 80.42, 82.48 (CH). Anal. Calcd for $C_{16}H_{28}O_2N_4$: C, 62.31; H, 9.15; N, 18.17. Found: C, 61.74; H, 8.97; N, 17.80.

General Procedure for 2,8-Disubstituted 3,9-Dioxa-3b,6b,9b,12b-tetraazaperhydroperylenes 15. To a vigorously stirred solution of **1** (5 mmol) in THF (15 mL) was gradually added **2** (1 mL, 5 mmol, 50% w/v in water) at room temperature. After the reaction mixture was stirred for 15 h, the solvent was evaporated to dryness under reduced pressure. After the residue was treated with ether (15 mL), the resulting precipitate was collected and recrystallized from EtOH.

15a: yield 1.00 g (72%); mp 225 °C; ^{1}H NMR ($CDCl_3$) δ 1.43−1.75 (m, 6H), 2.37 (dd, J = 2.5, 11.7 Hz, 2H), 3.75 (td, J = 3.7, 11.7 Hz, 2H), 3.90 (td, J = 2.9, 11.7 Hz, 2H), 4.03 (dd, J = 2.9, 11.7 Hz, 2H), 4.58 (d, J = 2.2 Hz, 2H), 4.89 (dd, J = 3.7, 11.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 17.76, 28.17, 30.97, 36.16, 66.21, 66.48, 87.86; IR (KBr) 2950, 1142, 1070, 950, 903, 838 cm^{-1}; MS-EI m/z 280 (M^+), 141, 110, 82, 55. Anal. Calcd for $C_{14}H_{24}O_2N_4$: C, 59.88; H, 8.63; N, 19.98. Found: C, 59.81; H, 8.58; N, 19.80.

15b: yield 0.65 g (42%); mp 234−235 °C; ^{1}H NMR ($CDCl_3$) δ 1.20 (d, J = 6.0 Hz, 6H), 1.47−1.79 (m, 12H), 2.29−2.53 (m, 2H), 3.09−3.98 (m, 4H), 4.46−4.62 (m, 2H), 4.81 (m, 2H); IR (KBr) 2950, 1235, 1165, 1072, 1000, 820 cm^{-1}; MS-EI m/z 308 (M^+), 155, 139, 82, 55. Anal. Calcd for $C_{16}H_{28}O_2N_4$: C, 62.31; H, 9.15; N, 18.17. Found: C, 62.11; H, 9.10; N, 17.74.

15c: yield 0.77 g (46%); mp 183 °C; ^{1}H NMR ($CDCl_3$) δ 0.95 (t, J = 2.0 Hz, 6H), 1.33−1.83 (m, 16H), 2.28−2.56 (m, 2H), 3.11−3.97 (m, 4H), 4.48−4.68 (m, 2H), 4.69−5.03 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 9.29, 17.97, 27.02, 28.26, 30.97, 46.71, 66.24, 76.29, 87.28; IR (KBr) 2900, 1238, 1170, 1038, 940, 862 cm^{-1}; MS-EI m/z 336 (M^+), 169, 153, 82, 55. Anal. Calcd for $C_{18}H_{32}O_2N_4$: C, 64.25; H, 9.59; N, 16.65. Found: C, 64.29; H, 9.43; N, 16.30.

X-ray Analysis[19] of 13 and 15a. Single crystals of $C_{16}H_{28}O_2N_4$ and $C_{14}H_{24}O_2N_4$ corresponding to **13** and **15a**, respectively, were prepared by allowing an ethanol solution of the compound to stand for about 3 weeks. Their crystallographic data are shown in Table 1.

Crystal Data. The cell constants were determined from a least-squares procedure using the Bragg angles of 20 reflections measured on a RIGAKU AFC-6 four-circle autodiffractometer equipped with a graphite monochromatic Mo Kα source, which was interfaced to a PANAFACOM U-1200 minicomputer. The space groups were selected from systematic absences and the number of molecules per unit cell and were later confirmed in subsequent structure refinement. Intensity data were collected in the range of $2\theta < 55°$ using the ω-2θ scan technique. A variable scan rate was adopted. Two reflections were monitored after every measurement of 100 reflections. Of the 3105 and 1548 independent reflections for **13** and **15a**, 1564 and 742 were treated as observed ($F_o > 3.0\sigma F$ and $F_o > 4.0\sigma F$), respectively. The intensities were corrected for Lorentz and polarization effects, but no correction was applied for absorption.

Structure Solution and Refinement. An overall temperature factor obtained from a Wilson plot gave the correct solution. The structure was determined by the direct method using the MULTAN78 programs.[20] An E map calculated using the signed E's (E >1.2) revealed the positions of all of the expected non-hydrogen atoms. Refinements were carried out by the block-diagonal least-squares method. Six cycles of isotropic refinement and six cycles of anisotropic refinement led to an R index. All of the hydrogens were located at the calculated positions. After adding the hydrogens, but keeping their positional and thermal parameters fixed [B(H) = B(C)+1.0], and refining, we obtained a final R. All of the structure-solving programs and the drawing program (ORTEP)[21] were provided by the Computer Center of Kumamoto University, along with the Universal Crystallographic Computation Program System (UNICS III).[22]

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(19) The atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Center, 12 Union Road, Cambridge, CB21EZ, U.K.

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