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7,15-DIOXA-4,8,12,16-TETRAAZA- AND 4,7,8,12,15,16-HEXA-AZAPERHYDROPERYLENES FROM GLYOXAL AND POLYFUNCTIONALIZED COMPOUNDS

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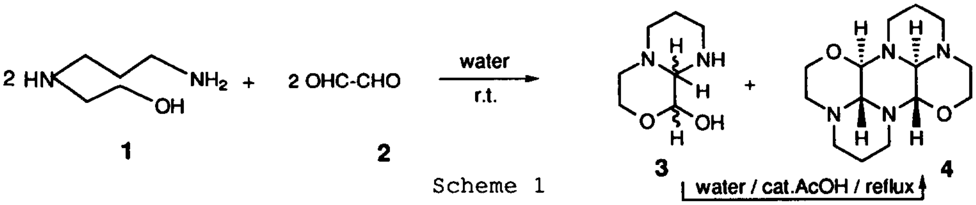
Abstract: The reaction of polyfunctionalized nucleophiles **1** and **5** with glyoxal **2** gave dioxatetraaza- and pentaazaperhydroperylenes, **4** and **6**.

Glyoxal is a useful building block for the direct construction of saturated heterocycles,1) although examples are limited: application to the preparation of the tetraazadioxa-caged polycyclic compound2) by the reaction with 1,2-diaminoethane, the tetraazapentacyclooctadecane3) from 1,1,1-tris(aminomethyl)ethane, and the hexaazatetracyclododecane4) from benzylamine. In continuation of our studies on the preparation of polyheterocycles5), we report herein the one-pot reaction of glyoxal (**2**) with 2-(3-aminopropylamino)ethanol (**1**) and N-(2-aminoethyl)-1,3-propanediamine (**5**) affording unique pentaheterocycles **4** and **6**, respectively. The latter is useful for selective protection and monoalkylation of **5**.

The reaction of **1** with **2** was carried out in water to give the perhydroprimidinomorpholine **3** 6), and **4** (mp 219-220°C) in 38 and 11 % yields, respectively (Scheme 1). Compound **3** was converted into **4** in 36 % yield by refluxing an aqueous solution in the presence of AcOH as a catalyst.



1 **2** **3** **4**

Scheme 1

Structure of **4** was assigned as follows. The mass spectrum indicated the molecular ion at m/z 280. The ^{13}C-nmr spectrum showing seven carbons, five methylene carbons at δ 19.0, 43.9, 49.3, 52.3, and 65.4 and two methine carbons at δ 69.1 and 88.3 ppm indicated the symmetric structure. The ^{13}C-^{1}H and ^{1}H-^{1}H COSY spectra also strongly supported the assigned structure of the 2:2 adduct **4**. The structure was established to be a two cis-two trans fused chair form by X-ray crystallographic analysis (Figure).7)

The reaction is presumed to proceed through coupling of the initially-formed intermediate **3** (Scheme 2).

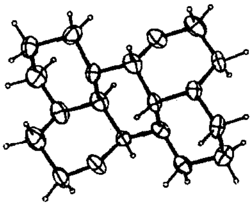
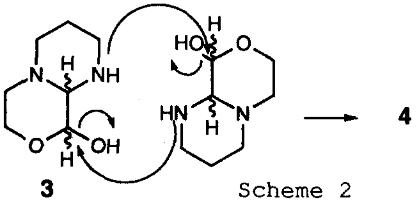
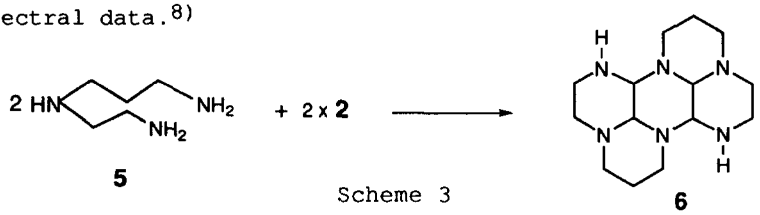


Figure. ORTEP Drawing of **4**



Scheme 2

Similarly, the reaction of **5** with **2** yielded compound **6** in 39% yield (Scheme 3). The structure of **6** was supported by the ^{1}H- and ^{13}C-nmr, ir, and mass spectral data.[8)]



Scheme 3

References and Notes

1. Tisler, M.; Stanovnik, B. "Comprehensive Heterocyclic Chemistry", Vol. 3, Katritzky, A.R.; Rees, C.W. eds, Pergamon Press, Oxford, 1984, p.52.; Bedford, C.T.; Fallah, A.; Mentzer, E.; Williamson, F.A. *J.Chem.Soc.Chem. Commun.* **1992**, 1035; Chaykovsky, M.; Koppes, W.M.; Russell, T.P. *J.Org. Chem.***1992**, *57*, 4295; Contreras, R. *Synthesis*, **1987**, 927; Willer, R.L.; Moore, D.W. *J.Org.Chem.***1985**, *50*, 2365.
2. Edwards, J.M.; Weiss, U.; Gilarde, R.D.; Karle, I.L. *J.Chem.Soc.Chem. Commun.* **1968**, 1649.
3. Craig, D.C.; Kassiou, M.; Read, R.W. *ibid.* **1991**, 607.
4. Nielson, A.T.; Nissan, R.A.; Vanderah, D.J.; Coon, C.L. *J.Org.Chem.* **1990**, *55*, 1459.
5. Okawara, T.; Uchiyama, K.; Okamoto, Y.; Yamasaki, T.; Furukawa, M. *J. Chem.Soc.Chem.Commun.* **1990**, 1385; Okawara, T.; Ehara, S.; Matsumoto, S.; Okamoto, Y.; Furukawa, M. *J.Chem.Soc.Perkin Trans I*, **1990**, 2615.
6. mp 66-68°C; The ^{1}H-NMR spectrum showed **3** to be a 3:1 mixture of cis and trans isomers. ^{1}H-NMR($CDCl_3$) δ cis 2.66(d,J=6.6 Hz,$NC\underline{H}N$),4.56(d,J=6.6 Hz, $OC\underline{H}O$), trans 2.96(d,J=2.2 Hz,$NC\underline{H}N$),4.96(d,J=2.2 Hz,$OC\underline{H}O$); ^{13}C-NMR($CDCl_3$) δ cis 26.44,44.08,53.34,54.55,58.56(CH_2),76.29,89.83(CH), trans 25.05,44.63, 52.70,53.86,63.54(CH_2),79.48,94.96(CH); IR(KBr) 3280(NH),3100(OH)cm^{-1}; MS(EI)m/z 158(M^+),112,84.
7. Fractional atomic coordinates, tables of bond lengths and angles as well as of anisotropic thermal parameters have been deposited with the Cambridge Crystallographic Data Center.
8. mp 265-267°C; ^{1}H-NMR($CDCl_3$) δ 2.12(d,J=7.0 Hz,$NC\underline{H}N$),2.89(d,J=7.0 Hz, $NC\underline{H}N$); ^{13}C-NMR($CDCl_3$) δ 24.04,43.47,48.76,54.61,56.31(CH_2),75.68,85.97(CH); IR(KBr) 3250(NH)cm^{-1}; MS(CI) m/z 279$(M+1)^+$,235,140,112.

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