

The compounds (IV) and (V) were isolated by reaction of their molybdenum complexes with sodium hydroxide and LiAlH_4 and characterized by ^1H and ^{31}P -NMR spectroscopies and mass spectrometry. The ^{31}P -NMR spectra of (IV) and (V) consist, in each case, of one resonance of virtually singlet peak indicating the magnetic equivalence of the phosphine groups. The ^1H and ^{13}C -NMR spectra of (IV) and (V) consist of distinctively characteristic resonances (all complex multiplets) whose assignments were made by considering chemical shift and to the ratio of the intensities. The ^1H -NMR spectrum of each compound shows resonances that are consistent with the magnetic equivalence of the backbone α -protons $\text{PCH}_2\text{CH}_2\text{CH}_2\text{P}$ which are mutually inequivalent to the β -protons ($\text{PCH}_2\text{CH}_2\text{CH}_2\text{P}$). In addition, the remaining substituents of phosphines, P-R ($\text{R}=\text{H}$, Me), were all magnetically equivalent. The compounds (IV) and (V) were studied by mass spectrometry; in both cases, the molecular ions were observed.

Acknowledgement. The present study was supported by a grant from the Basic Science Research Institute Program, Ministry of Education, Korea, 1993.

References

1. Izatt, R. M.; Christensen, J. J. *Synthetic Multidentate Macrocyclic Compounds*; Academic Press: New York, U. S. A., 1978.
2. Lindoy, L. F. *The Chemistry of Macrocyclic Ligand Complexes*; Cambridge Univ. Press: U. K., 1989.
3. Ansell, C. W. G.; Cooper, M. K.; Dancey, K. P.; Duckworth, P. A.; Hevick, K.; McPartin, M.; Tasker, P. A. *J. Chem. Soc. Chem. Comm.* **1985**, 439.
4. Setzer, W. N.; Guo, Q.; Grant, G. J.; Hubbard, J. L.; Glass, R. S.; VanDerveer, D. G. *Heteroatom. Chem.* **1990**, 1, 317.
5. Hornor, L.; Walach, P.; Kunz, H. *Phosphorus and Sulfur* **1979**, 5, 171.
6. (a) Napier, J. R.; Meek, D. W. *J. Chem. Soc. Chem. Comm.* **1974**, 442; (b) Scanlon, I. G.; Tsao, Y. Y.; Cummings, S. C.; Tomao, K.; Meek, D. W. *J. Am. Chem. Soc.* **1980**, 102, 6849.
7. (a) King, R. B.; Kapoor, K. N. *J. Am. Chem. Soc.* **1971**, 93, 4185; (b) King, R. B.; Cloyd, J. C. *Inorg. Chem.* **1975**, 14, 1550.
8. (a) Kyba, E. P.; Hundson, C. W.; Mcpaul, M. J.; John, A. M. *J. Am. Chem. Soc.* **1977**, 99, 8053; (b) Kyba, E. P.; Chou, C. P. *J. Chem. Soc. Chem. Comm.* **1980**, 449; (c) Kyba, E. P.; Brown, S. B. *Inorg. Chem.* **1980**, 19, 2159; (d) Kyba, E. P.; Chou, C. P. *J. Org. Chem.* **1981**, 46, 860.
9. (a) Deldonno, T. A.; Rosen, W. *J. Am. Chem. Soc.* **1977**, 99, 8051; (b) Deldonno, T. A.; Rosen, W. *Inorg. Chem.* **1978**, 17, 3714.
10. (a) Bartsch, R.; Hietkamp, S.; Morton, S.; Peters, H.; Stelzer, O. *Inorg. Chem.* **1983**, 22, 3624; (b) Brauer, R.; Gol, F.; Hietkamp, S.; Peters, H.; Sommer, H.; Stelzer, O.; Sheldrick, W. S. *Chem. Ber.* **1986**, 119, 349.
11. Shriver, D. F.; Drezdson, M. A. *The Manipulation of Air-Sensitive Compounds*, 2nd ed; Wiley: New York, U. S. A., 1986.
12. Diel, B. N.; Brandt, P. F.; Haltiwanger, R. C.; Hackney, M. L. J.; Norman, A. D. *Inorg. Chem.* **1989**, 28, 2811.
13. Angelici, R. J. *J. Chem. Educ.* **1968**, 45, 119.
14. Kim, B. G. unpublished results.

Synthesis of Symmetrically α -N-Functionalized Piperazine-2,5-diones

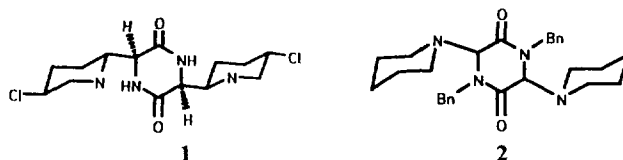
Dong Kyu Park, Jae Wook Lee, Tae Woo Kwon*,
Dai Il Chung†, and Hyo Kyung Jung†

Department of Chemistry, Kyung Sung University,
Pusan 608-736

†Department of Chemistry, Dong-A University,
Pusan, 604-714

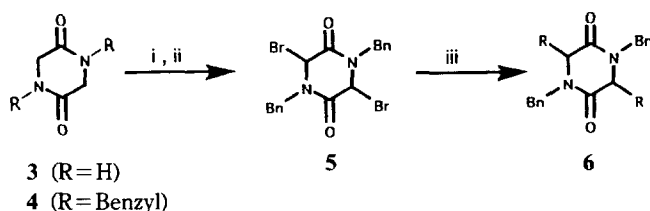
Received December 17, 1993

Piperazine-2,5-diones are one of the most important classes of peptides found in nature¹ and constitute a large class of organic substances that are formally derived by the removed of two molecules of water from two amino acid derivatives.² During the course of our synthetic model studies on the anti-tumour antibiotic agent DKP 593-A, **1**,³ we found that 1,4-dibenzyl-3,6-bis(piperidyl)-piperazine-2,5-dione, **2**, can be easily prepared from glycine anhydride. Surprisingly, this compound was stable as a number of its analogues.



The compound **2** is of particular interest for QSAR (Quantitative Structure-Activity Relationship) study since its structure is quite similar to that of **1**. Synthetic approaches to monoaryl or alkylidene derivatives have been reported for α -carbon⁴, α -oxygen⁵ or α -sulfur⁶ functionalized piperazine-2,5-dione derivatives. However synthetic studies of symmetrically N -functionalized piperazine-2,5-diones have received very little attention. In this paper, we wish to report a facile approach to α - N -functionalized piperazine-2,5-diones that features the nucleophilic reaction of a variety of amines with 1,4-dibenzyl-3,6-bis(bromo)-piperazine-2,5-dione in the presence of NaH.

As shown in Scheme 1, commercially available glycine anhydride, **3**, was treated with NaH/benzylbromide to afford N,N' -dibenzyl piperazine-2,5-dione, **4**. Bromination was accomplished by treating **4** with NBS/benzoyl peroxide.⁷ Treatment of the secondary amines such as piperidine(a), pyrrolidine(b), N -methylpiperazine(c), imidazole(d), and morpholine (e) with 2,2 equiv. of sodium hydride at 0°C generated sodium metallated nitrogen anions which were reacted with dibromide, **5**, to give the corresponding coupled products **6a**-



Scheme 1. Reagents and conditions; (i) NaH, DMF, BnBr, 0°C ; (ii) NBS, CCl_4 , $(\text{PhCOO})_2$, 60°C (iii) amines, NaH, THF.

6e in 52-85% yield.

A stereochemical assignment (*syn/anti*) for the resulting *N*-coupled products could be established through the chemical shift of the C-3 methine proton of the piperazine-2,5-dione ring. It was reported that the C-3 methine protons appear as a sharp singlet for the *syn*-bis(sulfide) while the *anti* diastereomer exhibited C-3 methine protons as two singlets in the symmetrically α -S-functionalized piperazine-2,5-dione and this relationship was also derived from the single-crystal X-ray analysis.⁶ Our results also shows that *N*-substituted C-3 methine protons give one sharp singlet peak as a major peak at 4.16, 4.21 or 6.49 ppm (**6d**). Although X-ray analysis is needed to determine the exact stereochemistry, we believe that the products we have prepared are of *syn* stereochemistry as these have been shown to be thermodynamically more stable by previous authors.⁶

Substituent (R)	C-3 methine yield(%)	mp.
piperidine (6a)	4.16 ppm	79.0 181-182
pyrrolidine (6b)	4.21 ppm	52.0 230(dec.)
<i>N</i> -methylpiperidine (6c)	4.21 ppm	71.8 178-180(dec.)
imidazole (6d)	6.49 ppm	84.6 239(dec.)
morpholine (6e)	4.21 ppm	83.5 150-151

In conclusion, the methodology outlined above, describes a practical approach to α -*N*-functionalized piperazine-2,5-diones. The stereochemical assignment (*syn/anti*) is currently under investigation and will be reported in the full paper.

A typical experimental procedure is as follows. To a stirred suspension of NaH (0.12 g, 4.1 mmol, 2.2 equiv. 80% in oil) in 5 mL THF was added piperidine (0.352 g, 4.1 mmol, 2.2 equiv.) slowly under argon atmosphere. The mixture was stirred for 30 min at room temperature and transferred *via* a syringe into a stirred solution of dibromide, **5**, (0.85 g, 1.9 mmol) in 12 mL THF. The mixture was allowed to stir for 30 min and poured into water and extracted three times with CHCl_3 . The combined organic extracts were dried (MgSO_4), filtered, and purified by column chromatography (SiO_2 , 7 : 1, hexane/ethyl acetate, R_f =0.55). 1,4-dibenzyl-3,6-bis(piperidyl)-piperazine-2,5-dione, **6a** was obtained as a white solid (0.68 g, 79%); mp. 181-182°C; $^1\text{H-NMR}$ (300 MHz, CDCl_3): 7.3-7.2 (10H, m), 5.4-5.2 (2H, d), 4.31-4.14 (2H, d), 4.16 (2H, s), 2.9-2.6 (4H, m), 2.5-2.3 (4H, m), and 1.8-1.3 ppm (12H, m); IR (KBr): 3200, 2910, 1680, 1450, and 1150 cm^{-1} ; Mass spectrum (m/z , rel. intensity): 460 (M^+), 376 (7), 375 (34), 292 (42), 91 (100), and 84 (87).

Acknowledgement. We thank Sir. D. H. R. Barton and Dr. Taylor (Texas A & M University, Chemistry department, U. S. A.) for their helpful discussions and this work was supported by a grant from the Ministry of Education of Korea, 1991.

References

1. Sammes, P. G. *Prog. Chem. Org. Nat. Prod.* **1975**, *32*, 51.
2. Schmidt, U.; Hausler, H.; Ohler, E.; Poisel, H. *Fortschr. Chem. Org. Naturst.* **1980**, *37*, 51.
3. (a) Gitterman, C. O.; Rickes, E. L.; Wolf, D. E.; Madas, J.; Zimmerman, S. B.; Stoudt, T. H.; Demny, T. C. *J. Antibiot.* **1970**, *23*, 305; (b) Arison, B. H.; Beck, J. L. *Tetrahedron* **1973**, *29*, 2743; (c) Pettit, G. R.; Von Dreele, R. B.; Herald, D. L.; Edgar, M. T.; Wood, H. B. *J. Am. Chem.*

Soc. **1976**, *98*, 6472.

4. Gallina, C.; Leberatori, A. *Tetrahedron* **1973**, *30*, 667.
5. Marcuccio, S. M.; Elix, J. A. *Tetrahedron Lett.* **1983**, *24*, No. 13.
6. Williams, R. M.; Armstrong, R. W.; Maruyama, L. K.; Dung, J. S.; Anderson, O. P. *J. Am. Chem. Soc.* **1985**, *107*, 3246.
7. Trown, P. W. *Biochem. Biophys. Res. Commun.* **1968**, *33*, 402.

Infrared Spectrum of Sodium-Benzene Complex in Argon Matrix

Hack Sung Kim and Kwan Kim*

Department of Chemistry, College of Natural Sciences,
Seoul National University, Seoul 151-742

Received December 27, 1993

By cocondensing lithium and sodium atoms with benzene diluted in argon, Manceron and Andrews¹ observed new infrared absorptions attributable to mono- and dibenzene complexes in the case of lithium but nothing with sodium. Based on the UV/VIS spectrum of diluted dispersions of sodium atoms in solid benzene, McCullough and Duley² suggested, on the other hand, that Na atoms in benzene interacted predominantly with one nearby benzene molecule. Its presence has been proposed also by Moore *et al.*³ in their electronic absorption study on dilute thin-film codeposits of potassium or rubidium with benzene.

Considering that the physicochemical properties of alkali metals are generally much the same as one another, the interaction behavior of Na to certain molecules may be expected somewhat similar to that of other alkali metals. In fact, Kunze *et al.*⁴ found the sodium and potassium atoms to interact with UF_4 similarly to the case of lithium. Based on the above informations, it is conjectured that the sodium-benzene complex can be formed even though its interaction strength is not substantial. In this respect, we are currently investigating the possibility of sodium-arene complex formation by using the matrix isolation infrared spectroscopy. In this report, we wish to present the preliminary observation made on the sodium-benzene system in argon matrix.

The reagent grade benzene and the matrix gas (Ar) were mixed in mole ratios varying from 1 : 70 to 1 : 1000 using a standard manometric technique. The gas mixture was sprayed onto a cold CsI window held at 9 K. Sodium metal atoms, prepared by evaporating natural sodium metal inside the deposition line, was also introduced into the cryostat together with C_6H_6 . The sodium concentration was modified by varying the temperature of evaporator, resulting in a 10-fold change in metal pressure. The highest relative proportion of Na and C_6H_6 used here is estimated at 1 : 6.

Experimental setup is nearly the same as that reported previously.⁵ A Janis Model 22 closed cycle helium cryocooler was used to cool the CsI substrate down to 9 K. Appropriate