HETEROCYCLES, Vol. 29, No. 3, 1989

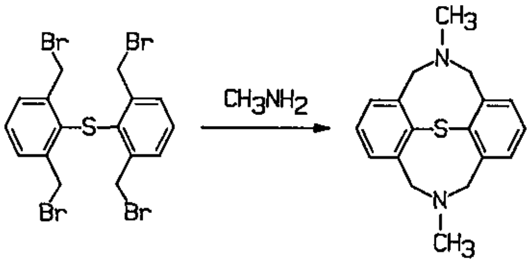
SYNTHESIS, CRYSTAL STRUCTURE, AND CONFORMATIONAL PROPERTY OF N,N'-DIMETHYL-1,11-(METHANOAMINOMETHANO)-5H,7H-DIBENZO[b,g][1,5]-THIAZOCINE: A NEW HETEROCYCLIC SYSTEM

Hisashi Fujihara, Nobuo Oi, Ryouichi Akaishi, Takatoshi Kawai,† and Naomichi Furukawa*

Department of Chemistry, University of Tsukuba, Tsukuba,
Ibaraki 305, Japan
†Tsukuba Research Laboratories, Eisai Co. Ltd., Toyosato,
Tsukuba, Ibaraki 300-26, Japan

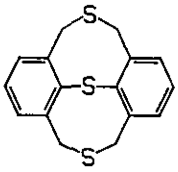
Abstract —— A new heterocyclic compound, N,N'-dimethyl-1,11-(methanoaminomethano)-5H,7H-dibenzo[b,g][1,5]thiazocine has been synthesized; the eight-membered ring is in the rigid chair-chair conformation.

The conformational properties and the reactivities in the heterocyclic analogues of 5,6,7,12-tetrahydrodibenzo[a,d]cyclo-octene are of considerable interest.[1] Recently, we reported the synthesis of a sulfur-bridged dithiametacyclophane, 1,11-(methanothiomethano)-5H,7H-dibenzo[b,g][1,5]dithiocin (3) and the isolation of its dicationic salt.[2] The analogous compound of (3) is expected to exhibit interesting physical and chemical properties on account of their unique arrangement of aromatic rings and heteroatoms in space. We now report the synthesis, the crystal structure, and the conformational property of a new heterocyclic compound, N,N'-dimethyl-1,11-(methanoaminomethano)-5H,7H-dibenzo[b,g][1,5]thiazocine (1).



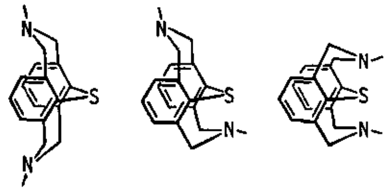
(2) (1)

Scheme 1



(3)

A typical procedure is as follows. Bis[2,6-bis(bromomethy)phenyl]sulfide (2)[2] (3.10 g, 5.6 mmol) was treated with methylamine (0.1 mol) in chloroform (250 ml) using a high dilution technique at room temperature. The whole mixture was stirred at 70 °C for 1.5 h. After usual work-up, the crude products were purified by silica gel column chromatography (eluent; $CHCl_3$-CH_3OH, 10:1) to give the compound (**1**) in 70% yield (see Scheme 1). Recrystallization from chloroform-hexane afforded colorless crystals of (**1**)[3].



Chair-Chair **Chair-Boat** **Boat-Boat**

Chart 1

The mass spectrum (EI) of (1) showed the molecular ion (M^+) at m/z 296 (base peak) and an interestingly doubly charged ion (M^{2+}) at m/z 148. The conformational behaviours in (**1**) concerning eight-membered ring are of interest, because in general, three different conformers, namely, chair-chair, boat-chair, and boat-boat can exist as shown in Chart 1. The 400 MHz ^1H nmr spectrum of (1) in $CDCl_3$ at 30 °C showing the signals at δ 1.95 (s, 6H, CH_3), 3.84 and 5.35 (ABq, J=14 Hz, 8H, CH_2), and 7.03-7.08 (m, 6H, ArH), is assigned to the single chair-chair conformer according to the literature[1]. No other isomers were found in the spectrum at all.

The X-ray crystallographic analysis[4] of (**1**) indicates that the eight-membered thiazocine ring in (**1**) has the chair-chair conformation (see Figure 1). The methyl substituent on N(1) is in a pseudo-axial position as can be seen from the torsional angles C(9)-N(1)-C(7)-C(2) and C(9)-N(1)-C(17)-C(15) which are 51.4 ±0.1°. Also the methyl group on N(2) is the same configuration. Adoption of this pseudo-axial position is necessary to keep the methyl group away from the π-electron cloud of the benzene rings. The distances of S...N are 3.524 and 3.542 Å for S...N(1) and S...N(2), respectively, which are slightly longer than the expected van der Waals contact of 3.35 Å.

The structure of (1) is particularly interesting in view of the conformational isomerism, since inversions both the eight-membered ring and the nitrogen atoms[5] are expected to have energy barriers amenable to study by variable temperature nmr spectroscopy. Compound (**1**) was examined by ^1H nmr spectroscopy at 400 MHz over the temperature range from -60 (in $CDCl_3$) to +150 °C (in DMSO-d_6).

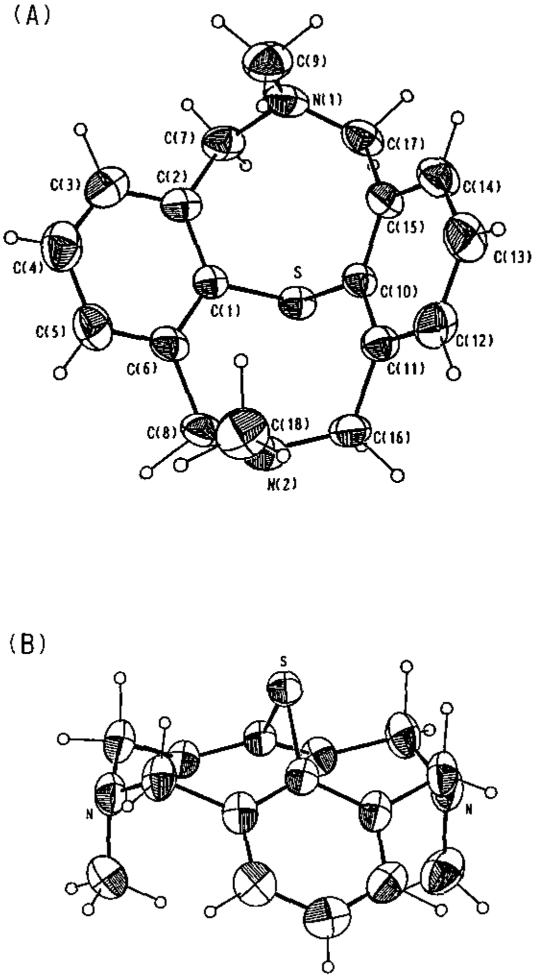


Figure 1. The crystal structure of compound (1).

(A) View from under. Selected bond lengths (Å): S-C(1) 1.790(4); N(1)-C(7) 1.471(6); N(1)-C(9) 1.452(6); N(2)-C(8) 1.480(6); N(2)-C(18) 1.461(6); C(1)-C(2) 1.399(5); C(1)-C(6) 1.402(6); C(2)-C(7) 1.524(7); C(6)-C(8) 1.518(6). Selected bond angles (°): C(1)-S-C(10) 94.6(2); C(7)-N(1)-C(9) 112.9(4); C(7)-N(1)-C(17) 118.3(3); C(8)-N(2)-C(16) 117.5(4); C(8)-N(2)-C(18) 113.1(4): S-C(1)-C(2) 119.0(4); S-C(1)-C(6) 119.1(3); C(2)-C(1)-C(6) 121.9(4); C(1)-C(2)-C(7) 122.8(4); C(1)-C(6)-C(8) 122.4(4); N(1)-C(7)-C(2) 116.6(3); N(2)-C(8)-C(6) 117.4(3).

(B) Side-on view. For clarity, the carbon atoms of C(12), C(13), and C(14) in the one benzene ring have been omitted.

However, surprisingly, the ^{1}H nmr spectra of (**1**) do not change in these temperature ranges, indicating that this compound exists as a single conformer. This result clearly demonstrates that the compound (**1**) is conformationally immobile under the present conditions.

In contrast, N-methyl-5H,7H-dibenzo[b,g][1,5]thiazocine[1a] as an azathiaorthocyclophane analogue of (1) and its related compounds[1b,1c], and a quadruply ortho-substituted diphenyl ether, 1,11-(ethano)-5H,7H-dibenz[b,g][1,5]oxathiocin[6] as a similar class of (1) are conformationally mobile.

The results described herein are of general importantance for the conformational analysis of quadruply ortho-bridged biphenyl compounds containing heteroatoms.

REFERENCES AND NOTES

1. a) S. Tanaka, K. Hashimoto, H. Watanabe, and K. Sakaguchi, *Chem. Pharm. Bull.*, 1973, **21**, 1683.
   b) R. P. Gellatly, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc., Perkin Trans 1*, 1976, 913.
   c) L. E. Brieaddy, B. S. Hurlbert, and N. B. Mehta, *J. Org. Chem.*, 1981, **46**, 1630.
   d) K. Ohkata, K. Okada, and K. Akiba, *Tetrahedron Lett.*, 1985, **26**, 4491.
2. H. Fujihara, J.-J. Chiu, and N. Furukawa, *J. Am. Chem. Soc.*, 1988, **110**, 1280.
3. (**1**): mp 197-198 °C; ^{13}C nmr ($CDCl_3$) δ 37.22, 61.73, 127.3, 130.7, 141.2, and 143.1; exact mass for $C_{18}H_{20}N_2S$: 296.1347. Found: 296.1358. Anal. Calcd for $C_{18}H_{20}N_2S$: C, 72.93; H, 6.80; N, 9.45%. Found: C, 72.81; H, 6.90; N, 9.41%.
4. Crystal data for (**1**): $C_{18}H_{20}N_2S$, monoclinic, space group $P2_1/n$, a=9.268(2), b=14.346(3), c=11.511(2) Å, β=95.77(1)°, U=1522.7 Å^3, Z=4, D_c=1.293 gcm^{-3}, D_m=1.294 gcm^{-3}, Cu-K_α radiation (λ=1.542 Å), F(000)=632, a CAD4 diffractometer, 2822 reflections ($4.0° \leq 2\theta \leq 126°$), 2257 observed with $I_o > 3.0\sigma(I_o)$. The structure was solved by direct methods and refined anisotropically by full-matrix least-squares using the SDP program package. The final R value was 0.055.
5. J. M. Lehn, 'Topics in Current Chemistry', vol. 15, Springer-Verlag, Berlin, 1970, p. 311.
6. A. J. Gordon and J. P. Gallagher, *Tetrahedron Lett.*, 1970, 2541.

Received, 14th November, 1988