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A Conformational Study on Highly Crowded 1,3,5-Tris[bis(trimethylsilyl)methyl]benzene Derivatives

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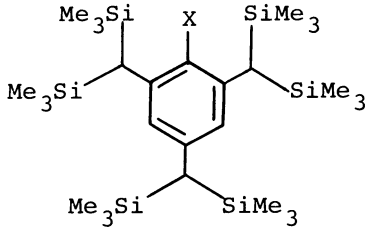
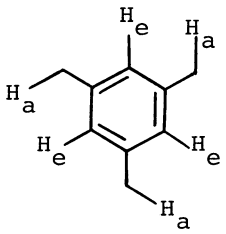
Dynamic NMR and molecular mechanics calculations show that 1-bromo-2,4,6-tris[bis(trimethylsilyl)methyl]benzene exists as a conformer where both o-methine hydrogens are coplanar with the ring and directed toward the bromine. Relevance of this conformation with unique properties of Tb as a steric protection group is also described.

Recently we have reported that 2,4,6-tris[bis(trimethylsilyl)methyl]phenyl (denoted as Tb hereafter in this paper) is a useful protective group for kinetic stabilization of highly reactive species.[1] In view of current interest in the isolation of highly reactive compounds using kinetic stabilization by various kinds of bulky groups,[2] it is important to know structural characteristics of this steric protection group. Since information on the conformational behavior of bis(trimethylsilyl)methyl group (Bsi) is of critical importance to understand the reactivity of compounds containing the Tb group, we have studied their conformations by dynamic NMR spectroscopy and molecular mechanics (MM) calculation. We disclose here preliminary results of such a study on 1,3,5-tris[bis(trimethyl-

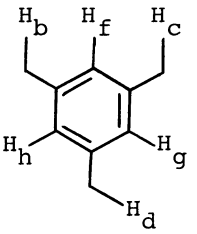


1: X = H

2: X = Br



1a



1b

silyl)methyl]benzene (**1**) and 1-bromo-2,4,6-tris[bis(trimethylsilyl)methyl]benzene (**2**) and their implication to the effectiveness of Tb as a steric protection group.

In order to get information on the conformation of a Bsi group attached to a benzene ring, the ^{1}H NMR spectrum (270 MHz) of p-bromo[bis(trimethylsilyl)methyl]-benzene was taken at -90 °C where internal rotation of the Bsi group is frozen. An ABCD spectrum observed for the aromatic protons indicates that the Bsi group adopts a conformation in which the methine hydrogen is coplanar with the benzene ring on the NMR time scale. This was also supported by the MMP2 study[3] on [bis(trimethylsilyl)methyl]benzene.[4]

In the ^{1}H NMR spectrum of **1** at 20 °C, the methyl, methine, and aromatic protons show a singlet for each,[5] suggesting fast equilibration among conformers. At -54 °C, conformational interconversion is frozen and two isomers are observed in a ratio of 0.76:1 (Fig. 1).[6] The minor isomer is **1a**[7] as judged from a sharp singlet aromatic signal, while the major one is assigned to **1b**,[7] where the three aromatic protons are magnetically nonequivalent to each other. The presence of comparable amounts of isomers suggests that the steric interaction between the Bsi groups meta to each other is rather small.[8]

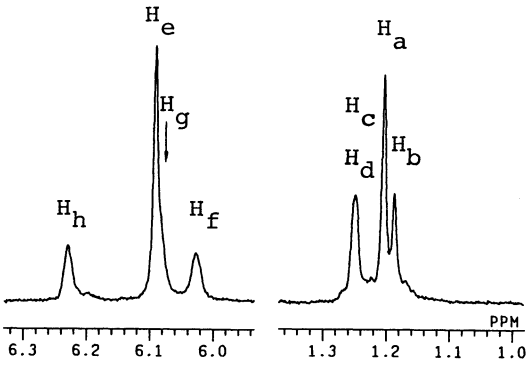


Fig. 1. ^{1}H NMR spectrum (270 MHz) of **1** ($CDCl_3$, -54 °C).

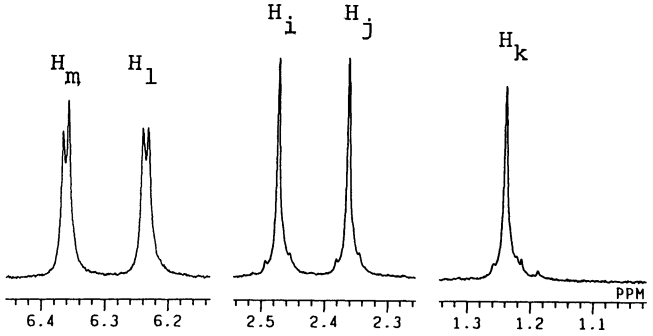
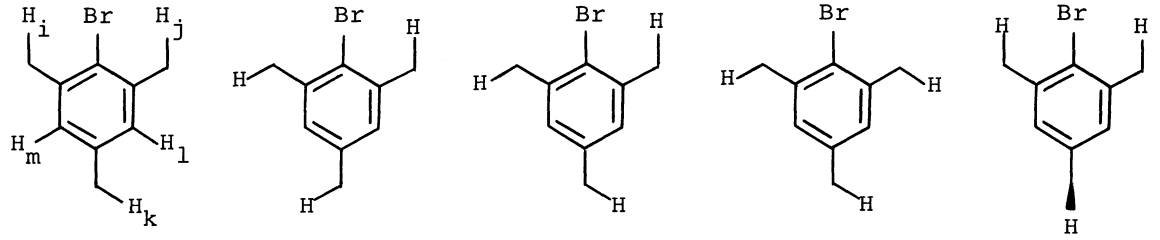


Fig. 2. ^{1}H NMR spectrum (270 MHz) of **2** ($CDCl_3$, -40 °C).

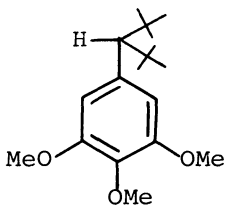
In **2**, the signals due to the methine protons of the o-Bsi groups and aromatic protons appear as broad bands at 20 °C and sharpen into a doublet and an AB quartet, respectively, at -40 °C (Fig. 2), suggesting the presence of a single isomer of unsymmetrical structure. Four conformers **2a-2d**[7] with methine hydrogens coplanar with the benzene ring are possible, in any of which the two o-methine protons are diastereotopic. The MMP2 study shows that the relative steric

energies of **2a-2d** are 0, 4.50, 6.66, and 9.37 kcal mol^{-1}, respectively. It may therefore be reasonable to assume that **2** exists almost exclusively as **2a**. This suggests that the reactions of **2** proceed via conformer **2a** with the benzylic hydrogens directed toward the bromine and hence that functionalization at position 1 are relatively easy in spite of total bulkiness of the Bsi group.[9] Furthermore, the magnetic nonequivalence of the o-methine protons in **2a** seems to suggest that there is some, albeit rather small, interaction between the trimethylsilyl groups of o- and p-Bsi's directly or via m-hydrogens.



2a **2b** **2c** **2d** **2e**

The above-mentioned temperature dependence of ^1H NMR observed for **2** can be interpreted in terms of restricted rotation of the para Bsi group. The lineshapes of the aromatic proton signal were analyzed as a coalescing AB spin system using the DNMR3 program[10] to give the following kinetic parameters: $\Delta H^{\ddagger}$ 11.9±0.3 kcal mol^{-1}, $\Delta S^{\ddagger}$ -10.5±1.0 e.u., $\Delta G^{\ddagger}$ (300 K) 15.0 kcal mol^{-1}. The $\Delta H^{\ddagger}$ value thus obtained is in good agreement with the relative steric energy of 14.2 kcal mol^{-1} calculated for conformer **2e** which corresponds to the transition state for rotation. The $\Delta G^{\ddagger}$ value for **2** is considerably smaller than that reported for **3** (22.3 kcal mol^{-1}).[11] This may be ascribed to the difference in the compactness of Bsi and $CH(t\text{-}Bu)_2$ groups, which is mainly due to the difference in lengths of C-Si and C-C bonds.



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In summary, DNMR and MM studies have indicated that Tb derivatives with a substituent at 1 position have such a conformation that the o-benzylic hydrogens

are coplanar with the benzene ring and directed toward the substituent, and hence the congestion around 1-position is not so severe. This suggests that Tb is a unique protection group for kinetic stabilization in that functionalization at 1-position would be relatively easy although it is very bulky as a whole.

References

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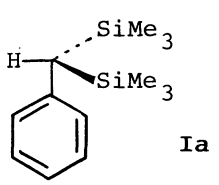
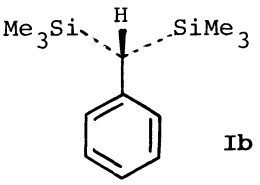
2) For reviews, see, for example, R. West, Angew. Chem., Int. Ed. Engl., 26, 1201 (1987); A. H. Cowley and N. C. Norman, Prog. Inorg. Chem., 34, 1 (1986); N. Inamoto, Yuki Gosei Kagaku Kyokai Shi, 43, 777 (1985); R. Okazaki, ibid., 46, 1149 (1988).
3) N. L. Allinger and H. L. Flanagan, J. Comput. Chem., 4, 399 (1983).
4) The calculations show that conformer **Ia** with its benzyl hydrogen almost coplanar with the ring (H-C-C(sp^2)-C(sp^2) = 5.9°) is the most stable while conformer **Ib** with its benzyl hydrogen perpendicular to the ring corresponds to the transition state for rotation.



Ia



Ib

5) The singlet signal for the methine protons is accompanied by sidebands due to coupling to ^{29}Si nuclei.
6) The assignment of H_a-H_m is tentative and the detail will be discussed in a full paper.
7) For brevity, Me_3Si groups are omitted in **1a**, **1b**, and **2a-e**.
8) The MMP2 steric energy of **1a** is 0.52 kcal mol^{-1} larger than that of **1b**. If it is assumed that the entropy term is determined solely by the symmetry factor, the free energy difference bewteen **1a** and **1b** at -54 °C is calculated to be 1.00 kcal mol^{-1} favoring **1b**, while the experimental value is 0.12 kcal mol^{-1}. This discrepancy may partly be ascribed to the possible inadequacy of parameters for silicon in MMP2 calculations.
9) In some reactions Tb acts as a bulkier group than 2,4,6-tri-t-butylphenyl which has often been used for kinetic stabilization of highly reactive compounds. Nevertheless, TbH can be brominated under much milder conditions than 1,3,5-tri-t-butylbenzene. M. Unno, R. Okazaki, and N. Inamoto, unpublished results.
10) D. A. Kleier and G. Binsch, QCPE, No. 165.
11) A. R. Katritzky, V. J. Becker, and F. M. S. Brito-Palma, J. Chem. Soc., Perkin Trans. 2, 1979, 143.

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