Structure and Dynamic Stereochemistry of Trimesitylmethane. I. Synthesis and Nuclear Magnetic Resonance Studies[1]

Paolo Finocchiaro,[2] Devens Gust, and Kurt Mislow*

Contribution from the Department of Chemistry, Princeton University, Princeton, New Jersey 08540. Received August 16, 1973

Abstract: Trimesitylmethane, a sterically congested molecule, has been synthesized in low yield, and the temperature dependence of its ^{1}H-nmr spectrum has been studied. The molecule assumes a propeller conformation in the ground state, and the barrier for interconversion of enantiomeric propellers by the two-ring flip mechanism is $\Delta G^{\pm}_{167} = 21.9$ kcal/mol. This remarkably high barrier admits the possibility of resolution of **1** under ordinary conditions.

Substituted methanes may exhibit torsional isomerism when one or more of the substituents lacks local conical symmetry on the time scale of measurement. Such torsional isomerism is independent of central chirality, elements of which may or may not be present in a given structure. The present paper deals with the stereochemistry of trimesitylmethane (**1**), a representative of the simplest stereochemical class of triarylmethanes, *i.e.*, that in which all rings are the same and possess local C_{2v} symmetry.[3]

Synthesis. An early attempt to prepare trimesitylmethanol by the reaction of mesityllithium and dimesityl ketone yielded a dibenzocyclooctane derivative instead.[4] Consequently, we employed another route, the direct preparation of **1** from mesityllithium and chlorodimesitylmethane. The desired product was obtained in *ca.* 1% yield, along with numerous unidentified byproducts (see Experimental Section).

Ground-State Conformation. Information bearing on the ground-state structure of **1** is provided by the pioneering nmr investigations of other triarylmethanes carried out by Kessler and coworkers,[5] and by Martin and coworkers.[6] An X-ray diffraction study[6] of dimesityl-1-(2,4,6-trimethoxyphenyl)methane (**2**) showed that this compound adopts a propeller conformation in the ground state. A similar conformation had previously been found for triphenylmethane in the gas phase by electron diffraction.[7] Nmr evidence is also consistent with such a conformation for triarylmethanes in solution.[5,6]

On the basis of these earlier experimental studies, as well as on the basis of empirical force field calculations,[8] we conclude that **1** has a propeller (C_3) conformation in the ground state,[9] in which all three mesityl rings are twisted in the same sense with respect to a *reference plane*, defined by the three carbon atoms attached to the central carbon. Thus, the compound is chiral and may exist in two enantiomeric forms which differ in their sense of twist (helicity). One of the enantiomers is shown in Figure 1. In addition, each of the three equivalent mesityl rings has two diastereotopic *o*-methyl groups: one proximal (a, Figure 1) and one distal (b, Figure 1) to the methine hydrogen. The ^{1}H-nmr spectrum of **1** is therefore expected to feature three methyl resonances of equal intensity in an achiral solvent: two signals arising from the diastereotopic *o*-methyl groups, and a third from the *p*-methyl groups (c, Figure 1). The 60-MHz ^{1}H-nmr spectrum of the methyl region of **1** at 37° (hexachloro-1,3-butadiene solution) does indeed show three resonances of equal intensity (Figure 2), and is therefore consistent with the postulated conformation.

Stereoisomerization of Trimesitylmethane. There are in principle two possible rearrangements[11] of a given isomer of **1**. One of these will convert this isomer directly into itself, whereas the other will result in enantiomerization. These rearrangements may reasonably be interpreted in terms of one or more of five classes of mechanisms: inversion along the central C–H bond, and four rotational "flip" mechanisms.[3a,12] We will couch our discussion of the stereoisomerization of **1** in terms of these five classes. The inversion pathway involves either dissociation into radicals or ions, followed by recombination on the opposite side of the reference plane, or a concerted displacement reaction. In the rotational mechanisms, zero, one, two, or all three of the mesityl groups flip, *i.e.*, rotate through planes perpendicular to the reference plane, while the remaining rings rotate in the opposite direction through

(1) This work was supported by the National Science Foundation (GP-30257).

(2) NATO Fellow, 1972–1973, on leave of absence from the University of Catania, Catania, Italy.

(3) (a) D. Gust and K. Mislow, *J. Amer. Chem. Soc.*, **95**, 1535 (1973). (b) Methyl groups are regarded in the context of the present discussion as possessing conical symmetry on the time scale of observation.

(4) A. C. Faber and W. Th. Nauta, *Recl. Trav. Chim. Pays-Bas*, **62**, 469 (1943).

(5) (a) H. Kessler, A. Moosmayer, and A. Rieker, *Tetrahedron*, **25**, 287 (1969); (b) A. Rieker and H. Kessler, *Tetrahedron Lett.*, 1227 (1969).

(6) M. J. Sabacky, S. M. Johnson, J. C. Martin, and I. C. Paul, *J. Amer. Chem. Soc.*, **91**, 7542 (1969).

(7) P. Andersen, *Acta Chem. Scand.*, **19**, 622 (1965).

(8) J. D. Andose and K. Mislow, *J. Amer. Chem. Soc.*, **96**, 2168 (1974).

(9) A propeller conformation has also been found for trimesitylborane.[10]

(10) J. F. Blount, P. Finocchiaro, D. Gust, and K. Mislow, *J. Amer. Chem. Soc.*, **95**, 7019 (1973).

(11) The term "rearrangement" as used here refers only to the net result of a transformation of starting materials to products. A rearrangement is thus permutational in nature, and implies nothing about the details of the actual physical mechanism involved (*i.e.*, it tells us nothing about transition-state geometries, energy barriers, physical motions of the atoms, etc.).

(12) These flip mechanisms are analogous to those proposed by Kurland, *et al.* (R. J. Kurland, I. I. Schuster, and A. K. Colter, *J. Amer. Chem. Soc.*, **87**, 2279 (1965)), for triarylcarbenium ion isomerizations.
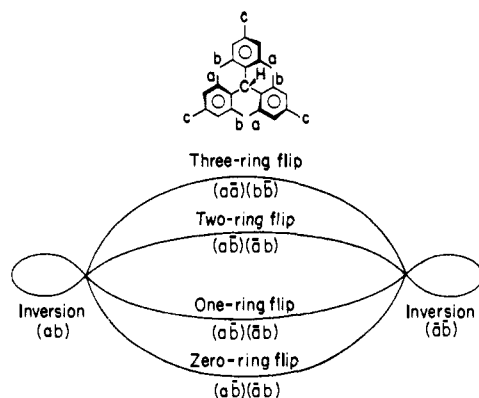
Figure 1. Graph depicting the possible stereoisomerizations of 1. The environments of the methyl groups are labeled with lower case letters. A barred letter labels an enantiomeric environment. Exchanged (permuted) environments are parenthesized.

orientations in which the normal to the ring which passes through the carbon atom bonded to the central atom lies in a plane perpendicular to the reference plane and containing these two atomic centers. The product and starting molecules thus have opposite helicities. In principle, rotational mechanisms which do not involve a reversal of helicity are conceivable. However, empirical force field calculations[8] for 1 indicate that such mechanisms may be disregarded. This conclusion is supported by the observation that isomerizations of the closely related triarylmethyl radicals,[13] triarylcarbenium ions,[14] and triarylamines[15] include reversals of helicity.

Figure 1 gives a topological representation of the results of isomerizations of 1 by means of the five mechanisms. The two vertices represent the two enantiomeric propeller conformations, and the edges denote stereoisomerizations. Each of the four flip mechanisms results in enantiomerization, but inversion alone does not (and hence is strictly a topomerization). Thus, an optically active sample of 1 would be racemized by any of the flip mechanisms, but not by inversion.

Each pathway shown in Figure 1 has been labeled with the environments of the methyl groups which are exchanged by the mechanism in question. Each inversion, zero-, one-, and two-ring flip results in transfer of one or more o-methyl groups from a site proximal to the methine hydrogen to the diastereotopic (distal) site, and vice versa. However, the three-ring flip involves no such transfer, and as a result exchanges only enantiotopic methyl group environments.

When the nmr sample of 1 is warmed, the two upfield methyl signals (corresponding to o-methyl groups) broaden and coalesce to a singlet at 167° (Figure 2). This behavior reflects an exchange of environments of the diastereotopic o-methyl groups which is becoming rapid on the nmr time scale at 167°. The Gutowsky–Holm approximation[16] was used to calculate a rate constant for the exchange process of 37.7 sec⁻¹ at the coalescence temperature (167°).

(13) (a) J. S. Hyde, R. Breslow, and C. DeBoer, *J. Amer. Chem. Soc.*, **88**, 4763 (1966); (b) L. D. Kispert, J. S. Hyde, C. de Boer, D. LaFollette, and R. Breslow, *J. Phys. Chem.*, **72**, 4276 (1968).

(14) J. W. Rakshys, Jr., S. V. McKinley, and H. H. Freedman, *J. Amer. Chem. Soc.*, **93**, 6522 (1971).

(15) D. Hellwinkel, M. Melan, and C. R. Degel, *Tetrahedron*, **29**, 1895 (1973).

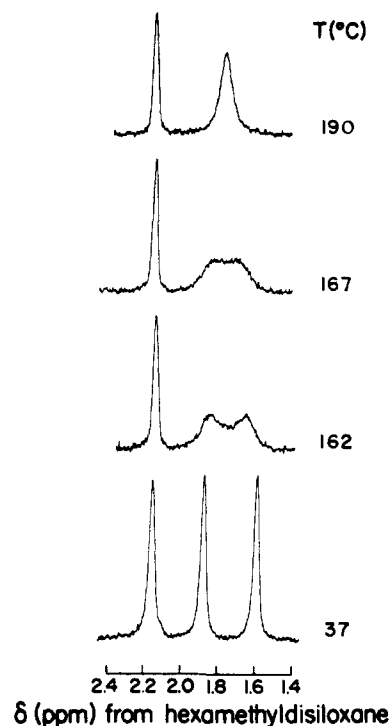(16) H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, **25**, 1228 (1956).

Figure 2. Temperature-dependent 60-MHz ¹H-nmr spectrum (methyl region) of 1.

We will now examine this coalescence behavior in terms of the five stereoisomerization mechanisms described above. Since the three-ring flip does not exchange the proximal and distal methyl groups, it may be immediately ruled out as an explanation of the nmr spectral behavior; its concomitant occurrence cannot be rigorously excluded, since it is undetectable in this experiment. Any one of the remaining four stereoisomerization mechanisms is capable of explaining the spectral results.

Inversion is considered unlikely for 1 since it would involve breaking of the central C–H bond. It might be expected that an inversion pathway could become important in compounds where this hydrogen is replaced by a readily ionizable group such as halogen or hydroxide. However, arguments against this pathway in related compounds have been presented.[5b] Since inversion does not result in enantiomerization, this mechanism could also in principle be ruled out experimentally if the rate of enantiomerization were directly measured, e.g., by racemization of optically active 1 or by use of a suitable diastereotopic probe. Such experiments have not as yet been performed.

Since the zero-ring flip transition state is without a doubt much more sterically congested than the transition states for the one- or two-ring flips, this mechanism may reasonably be eliminated a priori as an interpretation of the spectral results. Thus, the one- and two-ring flips remain as possible explanations for the observed coalescence of the o-methyl group resonances of 1. The results of empirical force field calculations shed some light on the relative barriers for these two processes. These calculations, fully described elsewhere,[8] demonstrate that the two-ring flip pathway is the mechanism of lowest energy for the enantiomerization of 1.

The interpretation of the temperature-dependent ¹H-nmr spectrum of 1 in terms of the two-ring flip

mechanism is in harmony with the results of studies of related compounds. As was pointed out previously,[3a] the "gear meshing" mechanism suggested by Martin and coworkers[6] for the coalescence of the o-methyl group resonances in the nmr spectrum of 2 (corresponding to the two-ring flip mechanism) is the only flip mechanism which is consistent with the experimental results, in the absence of accidental isochrony or fortuitously equivalent rates for two processes. Similar results have been obtained for other triarylmethane systems.[17] The two-ring flip pathway has also been shown to be the mechanism of lowest energy for the stereoisomerization of triarylboranes.[10] Similarly, the stereoisomerizations of triarylcarbenium ions,[3a,14] triarylamines,[15] and triarylsilanes[18] have all been discussed in terms of the two-ring flip mechanism.

Granted that the two-ring flip is the mechanism of lowest energy for the enantiomerization of 1, the free energy of activation for this process may be calculated. The ratio of the rate constant for enantiomerization (k_e) to the rate constant for coalescence of the o-methyl signals (k_c) is dependent upon the isomerization mechanism. The ratio k_e/k_c is 1 for the zero-ring flip, 3/2 for the one-ring flip, 3 for the two-ring flip, and undefined for the three-ring flip. Thus, the rate constant for enantiomerization of 1 by the two-ring flip is $3 \times 37.7 = 113$ sec^{-1}. This result is readily understood when one recalls that each two-ring flip results in the exchange of the o-methyl group environments of only one of the three mesityl rings.[20] The free energy of activation for enantiomerization of 1 by the two-ring flip, calculated from the Eyring equation and assuming a transmission coefficient of unity, is $\Delta G^{\ddagger}_{167} = 21.9$ kcal/mol, in excellent agreement with the value of 20 kcal/mol independently found by force field calculations.[8]

Of the several flip mechanisms by which a given molecule may undergo a reversal in propeller helicity, we designate the one of lowest energy as the *threshold mechanism*, and the associated barrier as the *threshold barrier*. The threshold barrier for 1 is therefore 21.9 kcal/mol. *A threshold barrier of such magnitude for a triarylmethane or similar system is unprecedented.* The highest such barrier previously reported for a methane (2) is only *ca.* $\Delta G^{\ddagger}_{-20} = 12–13$ kcal/mol.[6,21] The analogous barriers thus far reported for triarylboranes are below *ca.* $\Delta G^{\ddagger} = 16$ kcal/mol.[10] Corresponding activation energies reported for triarylcarbenium ions,[14,22] triarylsilanes,[18a] and triarylamines[15]

are even lower. A contributory reason for the high threshold barrier in 1 is the shortness of the C–C bond length of the bond to the methine carbon atom (1.55 Å),[8] relative to that of the C–B bond in trimesitylborane (1.58 Å)[10] or to the C–Si bond (1.86 Å in acetyltriphenylsilane).[23] A similar decrease of activation energy with increasing bond length has been noted in compounds of group Va elements.[5b] An important additional factor is the greatly increased steric bulk[5b] of an o-methyl group as compared to the o-methoxy groups used in previous studies.[5,6] Factors such as differences in conjugation energy, bond angles, and bond stretching force constants, as well as the presence or absence of a fourth ligand to the central atom, must also play a role in determining the relative barrier heights of the systems studied.

An intriguing consequence of the high barrier to enantiomerization is the possibility that 1 may be obtainable in optically active *form*. For example, the half-life for racemization of 1 at 0° should be *ca.* 2 hr, and therefore resolution should be feasible without recourse to excessively low temperatures.

Experimental Section[24]

Trimesitylmethane (1). A solution of 2-bromomesitylene (24.0 g, 0.12 mol) in 200 ml of anhydrous ether was treated with *n*-butyllithium (0.12 mol, 1.9 *M* solution in hexane, Alfa Inorganics) at room temperature with stirring under nitrogen. After 2 hr a snow-white precipitate of mesityllithium had formed. Chlorodimesitylmethane[25] (23.0 g, 0.08 mol) dissolved in 150 ml of dry benzene was added dropwise to the suspension of the organolithium reagent at room temperature with stirring. The mixture was refluxed for 2 hr and then poured onto crushed ice. The organic layer was diluted with chloroform, separated, and dried over anhydrous MgSO$_4$, and the solvent was distilled at reduced pressure. The resulting oil was vacuum distilled (0.1 mm) and two major fractions were collected: fraction I boiling below 160° and fraction II with bp 165–180°. Glpc analysis of fraction I revealed that at least seven products were present (no attempt was made to characterize these substances). There was no appreciable amount of 1 in this fraction. Fraction II was shown by glpc analysis to be a mixture of four products, including 1. Fraction II was redistilled, and the cut with bp 170–180° was collected. Trituration of the distillate with a mixture of acetone and bp 30–60° petroleum ether afforded crude 1 as a microcrystalline white powder (0.48 g, 1.6% yield). The product was recrystallized from an 80–20 mixture of acetone and methanol to yield 0.33 g (1.1%) of white plates, mp 185–187°. The [1]H-nmr spectrum featured resonances at δ_{C_2S}[TMS] 1.55 (9 H, s, CH$_3$), 1.85 (9 H, s, CH$_3$), 2.15 (9 H, s, CH$_3$), 5.64 (1 H, s, CH), 6.53 (3 H, s, aromatic H), and 6.66 (3 H, s, aromatic H). Mass spectra were consistent with the assigned structure; exact mass, 370.226434 (calcd, 370.226038).

Anal. Calcd for C$_{28}$H$_{34}$: C, 90.75; H, 9.25. Found: C, 90.61; H, 9.14.

Dnmr Measurements. [1]H-nmr spectra were recorded on a Varian A-60A spectrometer equipped with variable-temperature accessories. Temperature measurements were based on the chemical shift separation of the protons of an ethylene glycol sample, and utilized the temperature-shift correlation of Van Geet.[26] Temperatures are considered to be accurate to ±2°.

(17) P. Finocchiaro, D. Gust, and K. Mislow, *J. Amer. Chem. Soc.*, 96, 2176 (1974).

(18) (a) R. J. Boettcher, D. Gust, and K. Mislow, *J. Amer. Chem. Soc.*, 95, 7157 (1973). (b) It is obvious that trimesitylsilane[18a] is stereochemically correspondent[19] to trimesitylmethane, and that its possible stereoisomerization pathways may therefore be delineated in the same fashion.

(19) K. Mislow, D. Gust, P. Finocchiaro, and R. J. Boettcher, *Fortschr. Chem. Forsch.*, 47, 1 (1974).

(20) In a study of the temperature-dependent [1]H-nmr spectra of tris(2,6-dimethoxyphenyl)methane, Kessler, *et al.*,[5a] observed a coalescence of the resonances for the diastereotopic (proximal and distal) methoxy groups and calculated a rate constant k_c for this coalescence from the Gutowsky–Holm equation. They then divided the constant obtained by 3, and calculated a free energy of activation based on $k_c/3$. It was stated[5a] that the rate constant $k_c/3$ refers to "die Rotation um eine bestimmte C$_{Ring}$-C$_\alpha$-Bindung." However, the rate constant for the two-ring flip is $3k_c$ (not $k_c/3$), and therefore the constants previously reported by these authors[5a,b] must be multiplied by 9 before they may be compared to those reported here.

(21) Note that the barrier for exchange of methoxy groups reported[6] for 2 ($\Delta G^{\ddagger}_{145} = 22$ kcal/mol) does not correspond to a threshold barrier.[3a] We shall return to this point in a later paper.[17]

(22) (a) I. I. Schuster, A. K. Colter, and R. J. Kurland, *J. Amer. Chem. Soc.*, 90, 4679 (1968); (b) J. W. Rakshys, Jr., S. V. McKinley, and H. H. Freedman, *ibid.*, 92, 3518 (1970).

(23) P. C. Chieh and J. Trotter, *J. Chem. Soc. A*, 1778 (1969).

(24) Elemental analysis was performed by Schwarzkopf Microanalytical Laboratories, Woodside, N. Y. Unless specified otherwise, nmr spectra were recorded on a Varian A-60A spectrometer at ambient temperature (*ca.* 37°) and refer to *ca.* 20% solutions in CS$_2$ containing tetramethylsilane (TMS) as internal reference. Mass spectra were obtained on an AEI MS-9 high-resolution mass spectrometer, with an ionizing voltage of 70 eV. Melting points were measured in a Thomas-Hoover apparatus and are corrected.

(25) J. Coops, W. Th. Nauta, M. J. E. Ernsting, and A. C. Faber, *Recl. Trav. Chim. Pays-Bas*, 59, 1109 (1940).

(26) A. L. Van Geet, *Anal. Chem.*, 42, 679 (1970); 40, 2227 (1968).