Molecular Mechanics Studies (MM3) on the Conformations of Some Derivatives of Triptycene

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Received February 1, 1995[®]

Several derivatives of triptycene have been studied, wherein the substituent at the bridgehead can be directed in or out relative to the benzene rings, or wherein one of the benzene rings is substituted to make it different from the others, and a substituent can take up different conformations, depending on which pair of benzene rings the tails of the substituent chooses to lie between. The equilibria between the different conformations gives one a way to measure interactions between various kinds of substituents. Experimental results of this kind from the literature have been compared with the results of molecular mechanics. In some cases the experimental results are well calculated with MM3, and in some cases they are not. The latter cases are instructive, because they show shortcomings in our molecular model, which again in some cases are understood, but in other cases show a further shortcoming in our knowledge of chemistry.

Introduction

Molecular mechanics is a powerful tool for studying chemistry. If we understood things as well as we would like to, then our molecular modeling procedures would be complete and would always give accurate predictions. When we cannot calculate something correctly, it indicates that our model is incomplete or inaccurate, and thus these calculations are a powerful tool for showing how well we do indeed understand various aspects of chemistry.

In the present work we have made use of the extensive studies of a number of triptycene derivatives reported by Oki and co-workers.[1] As the tritycene skeleton is quite rigid, and a 9-substituted triptycene exhibits a high barrier to rotation about the C_9-to-substituent bond, the 1,9-disubstituted triptycenes are good molecules for conformational analyses using both experimental and computational methods. When the 1-position of triptycene is substituted, a substituent which contains a sufficient number of segments located at the bridgehead (9-position) may orient itself so that these segments fall preferentially between the two unsubstituted benzene rings or between a substituted and an unsubstituted benzene ring. The rotational isomers with respect to the C_9-to-substituent bond can be easily distinguished by NMR due to the high barriers to rotation. Therefore, the population ratios of stable conformers can be measured easily. The conformers where the substituent is between the substituted and unsubstituted rings are named as +sc or −sc (synclinal) forms, and the conformer where the substituent is between the two unsubstituted rings is named as an ap (antiperiplanar) form by the Klyne–Prelog nomenclature.[2] The conformational equilibria are influenced by the repulsion or attraction between the substituents and the ring system.

In addition to conformational studies, 1,9-disubstituted triptycenes are appropriate for the investigation of the interactions between 1- and 9-substituents, because the distance between them is unusually small for a nonbonded distance (ca. 2.7 Å).[3] In the normal case where there are no special interactions between the 1- and 9-substituents, the steric repulsions lead to the ap conformer being more stable than the ±sc conformers. However, the experiments by Oki and co-workers[1] revealed many cases in which the ±sc conformers were favored over the ap. MM2 molecular mechanics calculations were only moderately successful at explaining the experimental facts.[1] As the MM3 force field is more accurate than MM2,[4] it was of interest to see how well MM3 would predict or interpret the conformational equilibria of some 1,9-disubstituted triptycenes.

Calculations

The MM3 calculations were carried out with the full matrix minimization method for 1,4-dimethyl-9-(formylmethyl)triptycene(**A**), 9-(4-substituted benzyl)-8,13-dichloro-1,4 dimethyltriptycenes (**B**), 4-substituted 9-benzyl-8,13-dichloro-1-methyltriptycene (**C**), 9-(acetylmethyl)-1,4-dimethoxytriptycene (**D**), and 9-isobutyl-1,4-dimethoxytriptycene (**E**). The conformational equilibria of these triptycenes determined earlier by experimental methods[1] are summarized in Figure 1.

Results and Discussion

1,4-Dimethyl-9-(formylmethyl)triptycene (A). Let us take as the first example a molecule with a 1,4-dimethyl-substituted benzene ring and two unsubstituted benzene rings in which the substituent at the bridgehead carbon is CH_2CHO (**A**). This formylmethyl group may orient itself so that the carbonyl group falls preferentially

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[®] Abstract published in *Advance ACS Abstracts,* June 1, 1995.

(1) (a) Oki, M. *Acc. Chem. Res.* **1990**, *23*, 351. (b) Oki, M. *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 87. (c) Oki, M. *Top. Stereochem.* **1983**, *14*, 1.

(2) Klyne, W.; Prelog, V. *Experientia* **1960**, *16*, 521.

(3) (a) Mikami, M.; Toriumi, K.; Konno, M.; Saito, Y. *Acta Crystallogr. Sect. B* **1975**, *31*, 2474. (b) Nogami, N., Oki, M.; Sato, S.; Saito, Y. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3580. (c) Oki, M.; Takiguchi, N.; Toyota, S.; Yamamoto, G.; Murata, S. *Bull. Chem. Soc. Jpn.* **1986**, *61*, 4295.

(4) Allinger, N. L.; Yuh, Y. H.; Lii, J.-H. *J. Am. Chem. Soc.* **1989**, *111*, 8551.

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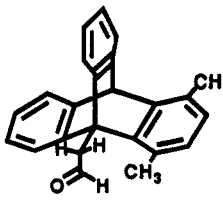
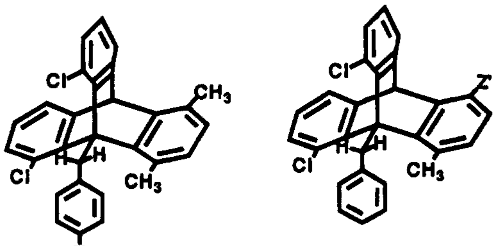
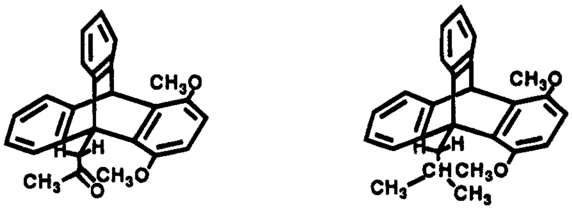


1,4-dimethyl-9-(formylmethyl)triptycene (A)
(ap form exclusively)



9-(4-substitutedbenzyl)-8,13-dichloro-1,4-dimethyltriptycene (B)
K(±sc/ap) = 2~3

4-substituted-9-benzyl-8,13-dichloro-1-methyltriptycene (C)
K(±sc/ap) = 2~4



9-acetylmethyl-1,4-dimethoxytriptycene (D) K(±sc/ap) > 10

9-isobutyl-1,4-dimethoxytriptycene (E) K(±sc/ap) = 2~3

Figure 1. Structures and conformational equilibria of 1,9-disubstituted triptycenes.

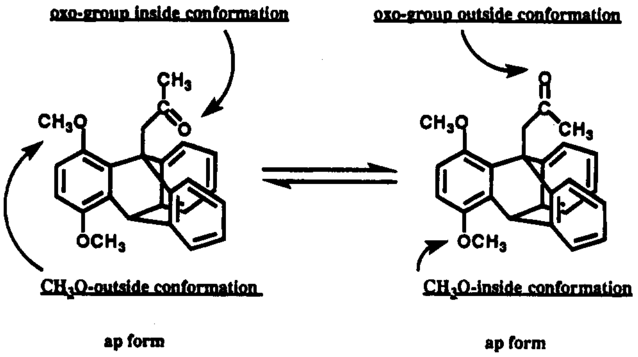


Figure 2. 9-(Acetylmethyl)-1,4-dimethoxytriptycene (D).

Table 1. MM3 Calculations on 1,4-Dimethyl-9-(formylmethyl)triptycene (A) Conformational Energies and Populations of ±sc and a Conformers at 25 °C[a]

conformation[b]	ΔE (kcal)	population (%)	order of stability
±sc(C=O:out)	1.56	9.44	3
±sc(C=O:in)	2.17	3.38	4
ap(C=O:out)	0.00	65.47	1
ap(C=O:in)	0.65	21.71	2

[a] K(±sc/ap) = 0.147, population(Σ±sc) = 12.82, population(Σap) = 87.18, cf. NMR experiments show ap form is present exclusively. [b] (C=O:out) and (C=O:in) stand for the conformations where oxo group was outside and inside of the triptycene skeleton, respectively.

between the two unsubstituted benzene rings (ap conformer) or between a substituted and an unsubstituted benzene ring (+sc or −sc conformers). In addition to these three conformations about the bond at the bridgehead carbon, the conformational analysis of **A** must also take into account the orientation of the formyl group. This particular substituent may orient in such a way that the oxygen is down in between the benzene rings (O-inside conformation), or in the other direction, in which case the aldehyde hydrogen is down between the benzene rings (O-outside conformation). (These orientations are similar to those shown in Figure 2 for a different molecule.) Thus there are two conformations with respect to the rotation about C(carbonyl)−C(methylene) bond and a total of six conformations to be considered for this molecule.

It is reasonable to think that the equilibrium between the ap and ±sc conformations can be understood by considering the steric interactions between the bridghead- and the peri-substituents, as this is a normal case when there are no strong electrostatic or special interactions involved. Hence it is expected that this molecule will be preferentially in the ap conformation. With respect to the orientation of carbonyl group, the equilibrium between the O-inside and O-outside conformations (Figure 2) is indicative of the extent to which oxygen versus hydrogen prefers to be in between the two benzene rings. In this case the atom which is down between the rings is quite close to the benzene carbons, and the van der Waals' repulsion between that atom and those carbons is such as to try to force the atom from that position. The electrostatic interactions appear to be of minor importance. Accordingly, one expects that the hydrogen will be found in the inside position, rather than the oxygen, because of the smaller size of the former. This is indeed what is found experimentally. NMR and X-ray crystallographic studies on this molecule showed that **A** exists exclusively in the ap form.[5] The X-ray structure of **A** showed that the aldehyde hydrogen was down between the benzene rings (O-outside conformation) in the crystal. The MM3 calculations on **A** reproduced correctly the conformational equilibrium which is found by experiment (Table 1). The X-ray structure of **A** indicated that the bond angles were very much opened (C(methylene)−C(9)−C(9a) = 118.0°, C(9a)−C(1)−C(CH_3) = 126.6°) and that the bond lengths become longer (C(9)−C(9a) = 1.5556 Å, C(9)−C(8a) = 1.5443 Å, C(9)−C(12) = 1.5443 Å) than the normal values in an effort to relieve the steric strain caused by the substituents at the 1- and 9-positions. MM3 calculates the conformational energies and geometries reasonably well for this molecule.

9-(4-Substituted benzyl)-8,13-dichloro-1,4-dimethyltriptycenes (B) and 4-Substituted 9-Benzyl-8,13-dichlorotriptycenes (C). When only one hydrogen atom at the peri-position of C(9) bridgehead carbon atom is substituted by a methyl group to give molecule **A**, it is easy to predict that the ap form will be more stable than the ±sc form, based on the steric interactions between the peri-substituent and benzene rings. It is more difficult to predict which conformer will predominate when the hydrogen atoms at C(8)- and C(13)-peri positions are additionally substituted by chlorine atoms as in molecules **B** and **C**, however. The steric congestion around the substituent connected at the bridgehead carbons in **B** and **C** is more severe than that in **A**. Thus it is necessary to consider carefully the van der Waals' repulsion and the special interactions (if any) between the substituents to correctly predict the conformational

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[5] Oki, M.; Izumi, G.; Yamamoto, G.; Nakamura, N. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 159.

Table 2. Conformational Equilibria at 54 °C of 9-(4-Substituted benzyl)-8,13-dichloro-1,4-dimethyltriptycenes (B) and 4-Substituted 9-Benzyl-8,13-dichloro-1-methyltriptycenes (C) Determined by MM3 and NMR

		MM3[a]		
compd	subst (Z, Z′)	$K(\pm sc/ap)$	ΔE[c]	NMR[b] $K(\pm sc/ap)$
B	$N(CH_3)_2$	3.51	0.366	2.87
B	H	3.40	0.345	2.30
B	NO_2	2.94	0.249	1.52
C	H	2.98	0.260	2.20

[a] $K(\pm sc/ap)$ values were calculated from the steric energy (E) using Boltzmann's equation. [b] NMR experiments were carried out in $CDCl_3$ solution. [c] $\Delta E = E_{(ap)} - E_{(sc)}$ (kcal/mol).

equilibria. With the aid of Taft's E_s parameters[6] for evaluation of the bulkiness of the substituents (CH_3: −1.24, Cl: −0.97), we might predict that the ap conformer should be more stable than the ±sc conformers on the basis of steric repulsion between the bridgehead and peri-substituents. The NMR experiments reported that sc/ap ratios for these triptycenes (**B**, **C**) were larger the statistical value of 2, however. Although MM2 calculations were previously carried out on these triptycenes (**B**, **C**),[7] MM2 values did not reproduce the experiments and in fact calculated that the sc isomers were less stable than the ap by about 1 kcal/mol. As these triptycenes (**B**, **C**) are so crowded around the C(9) bridgehead carbon, an accurate evaluation of the van der Waals' repulsions between the substituents is necessary if the conformational equilibrium is to be correctly calculated. Since Taft's E_s values and MM2 both gave incorrect results in these cases, it was of interest to see whether or not MM3 could correctly calculate the preference of the sc over the ap form.

The results of MM3 calculations of **B** and **C** are shown in Table 2. In contrast to MM2, MM3 does reproduce the conformational equilibria of the rotational isomers reasonably well. The small electrostatic effect of the substituents, which was detected by the experiments,[7] was approximately reproduced by the dipole−dipole interaction term with the dielectric constant DE = 1.5 (the default value) in the MM3 force field.[8] Though Oki explained the preference of ±sc forms in molecules **B** and **C** by assuming a special interaction between the CH_3 group bonded at C(1) carbon and aromatic ring of the benzyl substituent,[7] the conformational equilibria of **B** and **C** result from the van der Waals' interactions and dipole−dipole interactions in the MM3 force field.

Why did MM2 not predict that the ±sc form was more stable than the ap form? The reason is that MM2 did not evaluate the dipole−dipole interaction correctly in this case. Investigating the components of MM3 steric energies in detail, it was found that the difference in the relative steric energies between the ±sc and ap forms of **B** and **C** appeared mainly in the dipole−dipole interaction term. The ap form had a more positive dipole−dipole interaction energy than the ±sc form by 0.6 kcal/mol.

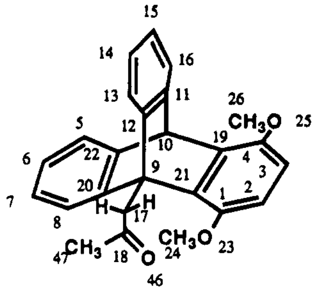

Figure 3. Numbering system of 9-(acetylmethyl)-1,4-dimethoxytriptycene (D).

Table 3. MM3 Calculations on 9-(Acetylmethyl)-1,4-dimethoxytriptycene (D) Conformational Energies and Populations of ±sc and ap Conformers at −30.0 °C[a]

conformation[b]	ΔE (kcal)	population (%)	order of stability
±sc(C=O:in)1	0.53	23.16	2
±sc(C=O:out)1	3.20	0.09	10
ap(C=O:in)1	0.00	34.39	1
ap(C=O:out)1	2.78	0.11	9
±sc(C=O:in)2	0.86	11.72	4
±sc(C=O:out)2	3.50	0.05	11
ap(C=O:in)2	0.44	13.78	3
ap(C=O:out)2	3.21	0.04	12
±sc(C=O:in)3	1.39	3.88	6
±sc(C=O:out)3	3.77	0.03	14
ap(C=O:in)3	0.63	9.21	5
ap(C=O:out)3	3.38	0.03	13
±sc(C=O:in)4	1.87	1.43	8
±sc(C=O:out)4	4.27	0.01	15
ap(C=O:in)4	1.36	2.06	7
ap(C=O:out)4	4.12	0.01	16

[a] $K(\pm sc/ap) = 0.677$, population($\Sigma\pm sc$) = 40.37, population(Σap) = 59.63, cf. $K(\pm sc/ap) > 10$ from NMR experiments. [b] The conformations of **D** are designated as shown in Figure 2, where the conformation numbers are as follows:

conformation	1-CH_3O	4-CH_3O
1	outside	outside
2	outside	inside
3	inside	outside
4	inside	inside

This contributes to the preference of the ±sc form. In the MM2 calculations the C_{sp^2}−H bond dipole was assumed to be zero, and the $C_{sp^2}-C_{sp^3}$ bond moment is therefore much smaller than it should be. This was corrected in MM3, with the resultant change in the dipole−dipole interaction energy difference between the conformations.[9]

The above examples are instructive as to the kinds of calculations that we expect to be able to carry out with MM3 and the kind of accuracy that we can expect to obtain. Thus these systems can be regarded as rather well understood, and MM3 provides a good model of what is observed.

9-(Acetylmethyl)-1,4-dimethoxytriptycene (D). Next we will examine some cases where things are less well understood. The first of these is compound (**D**). Here one benzene ring is substituted with methoxyl groups, and we have a carbonyl substituent as previously in **A**. If the aldehydic hydrogen in molecule **A** is replaced with a methyl group, so that we have a substituent CH_2-

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(6) Gallo, R. *Prog. Phys. Org. Chem.* **1983**, *14*, 115.

(7) Nakai, Y.; Inoue, K.; Yamamoto, G.; Oki, M. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2923.

(8) The population ratios of rotational isomers $K(\pm sc/ap)$ by using the free energies were also calculated. However, the remarkable improvement of agreement with experimental values could not be recognized. When the value of 4 for dielectric constant in the dipole−dipole interaction term was used in MM3 calculations in order to take into account of solvent effect of $CDCl_3$ used in NMR experiments, the agreement with experimental became worse. All compounds took almost identical equilibrium constants ($K(\pm sc/ap) = 2$).

(9) In ref 7, the calculations were carried out with the MM2(77) force field and it was found that sc conformers were less stable by about 1 kcal/mol than ap form. The most recent version of MM2 (MM2(92)) calculated that the sc conformers were less stable than the ap by about 0.3 kcal/mol for both **B** and **C**. Although this is an improvement, MM2-(92) still does not calculate the populations of the conformers correctly.

Table 4. Dihedral Angles Calculated by MM3 to Characterize the Stable Conformations of 9-(Acetylmethyl)-1,4-dimethoxytriptycene (D) (see Figure 3)

conformation	ω(21-9-17-18)	ω(9-17-18-46)	ω(2-1-23-24)	ω(3-4-25-26)
±sc(C=O:in)1	−63.1	−0.4	−14.1	−3.8
±sc(C=O:out)1	−67.8	−163.4	7.5	−9.7
ap(C=O:in)1	180.0	0.0	0.9	−0.5
ap(C=O:out)1	−172.3	154.8	−2.7	−2.1
±sc(C=O:in)2	−62.4	−0.9	−10.9	94.9
±sc(C=O:out)2	−67.8	−161.6	10.3	95.9
ap(C=O:in)2	−179.7	−0.2	7.0	93.0
ap(C=O:out)2	−171.7	153.5	10.2	93.4
±sc(C=O:in)3	−61.9	−3.0	79.6	7.8
±sc(C=O:out)3	−68.2	−161.4	80.8	−0.1
ap(C=O:in)3	−179.6	−1.8	76.2	9.3
ap(C=O:out)3	−171.8	154.2	79.3	8.9
±sc(C=O:in)4	−61.4	−3.2	74.9	93.6
±sc(C=O:out)4	−68.2	−159.8	77.6	94.4
ap(C=O:in)4	−179.4	−2.0	69.3	91.4
ap(C=O:out)4	−171.5	153.0	74.2	91.4

Table 5. MM3 Calculations on 9-(Acetylmethyl)-1,4-dimethoxytriptycene (D) Conformational Energies and Populations of ±sc and ap Conformers at −30.0 °C. Electrophilic Bonding is Assumed to Exist between Atom Type 3 and 6[a,b]

conformation	ΔE (kcal)	population (%)	order of stability
±sc(C=O:in)1	0.00	52.76	1
±sc(C=O:out)1	2.71	0.19	9
ap(C=O:in)1	0.65	6.83	4
ap(C=O:out)1	3.43	0.02	12
±sc(C=O:in)2	0.35	25.76	2
±sc(C=O:out)2	3.15	0.08	10
ap(C=O:in)2	1.09	2.76	5
ap(C=O:out)2	3.87	0.01	13
±sc(C=O:in)3	0.98	6.95	3
±sc(C=O:out)3	3.44	0.04	11
ap(C=O:in)3	1.28	1.85	7
ap(C=O:out)3	4.03	0.01	14
±sc(C=O:in)4	1.51	2.32	6
±sc(C=O:out)4	4.50	0.00	15
ap(C=O:in)4	2.01	0.41	8
ap(C=O:out)4	4.77	0.00	16

[a] K(±sc/ap) = 7.41, Population(Σ±sc) = 88.11, Population(Σap) = 11.89 cf. K(±sc/ap) > 10 from NMR experiments. [b] Parameters for electrophilic bonding: sum of the van der Waals radii 2.82 Å, ε = 0.24 kcal.

$COCH_3$, then we expect the orientation of carbonyl group to be reversed, since the methyl group is larger than the oxygen. As to the orientation of the $-CH_2COCH_3$ group bonded to bridgehead carbon, we can predict the preferred conformation by considering the interaction between the oxygen of the methoxyl and the CH_2COCH_3 group. If that interaction is favorable, that conformation (+sc or −sc) will be favored. If it is unfavorable, then the conformation will be disfavored, and the CH_2COCH_3 group will preferentially be between the two unsubstituted rings (ap form). From steric effects we might conclude that the large methoxyl group will interact sterically in an unfavorable manner with the carbonyl, and therefore the ap conformations should be favored.

The conformational equilibrium of **D** has been investigated carefully by NMR and IR spectroscopy.[5] The results indicated that the acetyl group took an O-inside conformation as expected. The frequency of the carbonyl stretching absorption was reported[5] to be 1742 cm^{-1}, which is slightly high for an aliphatic ketone. This high frequency was considered to be the result of the steric effect. An alternative view is the following. Ordinary simple ketones show their carbonyl stretching frequencies at about 1720 cm^{-1} in the liquid phase or in indifferent solvents.[10] The frequencies in the gas phase are close to 1740 cm^{-1}. The difference appears to stem largely from the fact that the ketones form dimers in condensed phases, and the lower frequencies are probably attributable to these dimers.[11] In this particular molecule (**D**), the carbonyl group is shielded from dimerization by the triptycene ring system in the O-inside conformation, and the observed frequency is more nearly that of a gas phase value. The MM3 calculated frequency is 1722 cm^{-1}, very slightly different from the MM3 value for acetone (1727). Thus the carbonyl frequency appears to be unexceptional, both from theory and by experiment. The NMR spectra of **D** indicated clearly the conformational preference of the ±sc form over the ap form. The ^{1}H-NMR spectra showed that the integrated ±sc/ap ratio of **D** was ≥10 at −30 °C. The preference of ±sc form over the ap is opposite to what would be expected from steric effects alone.

The conformational energies and the populations of the ±sc and ap conformers of **D** (Figure 3) calculated by MM3 are shown in Table 3. In addition to the relative orientation of the acetylmethyl group against the 1-methoxyl substituent (ap or ±sc forms) and the conformation of the oxo group (O-inside or O-outside), the relative orientations of the 1- and 4-methoxyl groups must be taken into account. In total, MM3 found 16 minimum energy conformations. The MM3 calculated dihedral angles that characterize the stable conformers are shown in Table 4. The orientation of the carbonyl group was calculated correctly by MM3 as preferentially O-inside, as was found by the IR experiments. However, MM3 did not reproduce the experimental NMR result that the ±sc conformations strongly predominate over the ap conformation. The most stable ±sc conformer (±sc(C=O:in) 1 in Table 3) was calculated to be less stable by 0.53 kcal/mol than the most stable ap conformer (ap(C=O:in) 1). The summed population for the ap conformers was 59.6%. Indeed, what is calculated with MM3 is what would be expected from just the steric effects around acetylmethyl group. The MM3 program takes into account the van der Waals' interactions, and the electrostatics from the group dipoles, and if that were a complete and accurate description of the molecule, the ap conformation would be favored. Therefore, something important has been left out of our molecular mechanics model at this point. We can understand this as what we might call *Lewis bonding*. The best known example of this type of bonding occurs when a hydrogen (bound to an electronegative

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(10) *The infra-red Spectra of Complex Molecules*; Bellamy, L. J., Ed.; Methuen and Co. Ltd., 1954; p 117.

(11) Allinger, J.; Allinger, N. L. *Tetrahedron* **1958**, *2*, 64.

Table 6. Dihedral Angles Calculated by MM3 to Characterize the Stable Conformations of 9-(Acetylmethyl)-1,4-dimethoxytriptycene (D). Electrophilic Bonding between Atom Type 3 and 6 is Taken into Account

conformation	ω(21-9-17-18)	ω(9-17-18-46)	ω(2-1-23-24)	ω(3-4-25-26)
±sc(C=O:in)1	−61.2	−4.9	−10.9	−1.8
±sc(C=O:out)1	−57.0	−166.9	−1.0	−7.9
ap(C=O:in)1	180.0	0.0	0.9	−0.5
ap(C=O:out)1	−172.3	154.8	−2.7	−2.1
±sc(C=O:in)2	−60.3	−5.5	−3.8	94.2
±sc(C=O:out)2	−56.2	166.2	6.3	94.6
ap(C=O:in)2	−179.6	−0.7	10.7	93.2
ap(C=O:out)2	−171.7	153.5	10.1	93.4
±sc(C=O:in)3	−59.9	−7.0	76.9	8.3
±sc(C=O:out)3	−55.8	165.0	79.6	5.8
ap(C=O:in)3	−179.6	−1.8	76.2	9.2
ap(C=O:out)3	−171.8	154.2	79.3	8.9
±sc(C=O:in)4	−59.5	−7.1	68.5	93.4
±sc(C=O:out)4	−63.4	−171.5	75.5	93.8
ap(C=O:in)4	−179.4	−2.0	69.3	91.4
ap(C=O:out)4	−171.5	153.0	74.2	91.3

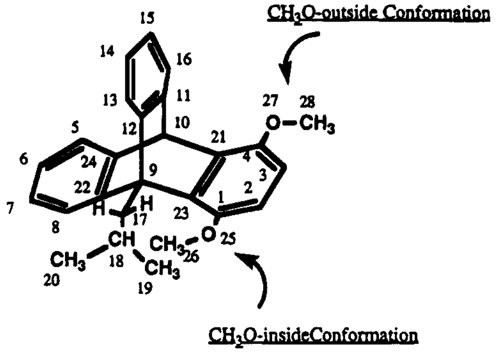

Figure 4. Numbering system of 9-isobutyl-1,4-dimethoxytriptycene (E).

Table 7. MM3 Calculations on 9-Isobutyl-1,4-dimethoxytriptycene (E) Conformational Energies and Populations of ±sc and ap Conformers at −110.6 °C[a]

conformation[b]	ΔE (kcal)	population (%)	order of stability
±sc(+G)1	1.48	0.82	6
±sc(A)1	2.12	0.11	10
ap(+G)1	0.00	40.74	1
ap(A)1	0.04	36.05	2
±sc(+G)2	1.57	0.63	7
±sc(A)2	2.19	0.09	11
ap(+G)2	0.57	6.90	4
ap(A)2	5.08	0.00	14
±sc(+G)3	1.72	0.40	8
±sc(A)3	2.23	0.08	12
ap(+G)3	0.69	4.84	5
ap(A)3	0.48	9.15	3
±sc(+G)4	2.05	0.14	9
±sc(A)4	2.55	0.03	13
ap(+G)4	5.78	0.00	16
ap(A)4	5.54	0.00	15

[a] $K(\pm sc/ap) = 0.024$, population($\Sigma\pm$sc) = 2.32, population(Σap) = 97.68, cf. $K(\pm sc/ap) = 3.0$ from NMR experiments. [b] The conformations of **E** are as in Table 3.

atom) forms a bond to an atom with a lone pair, usually oxygen or nitrogen (hydrogen bonding). Hydrogen bonding can be understood as coming in part from a dipole−dipole interaction and in part from the donation of electrons by a donor atom (usually oxygen or nitrogen) into the σ^* orbital of the H−X bond. Hydrogen bonding is a specific case. Theory says that in general, there should be something that we will call "Lewis bonding", which is analogous to hydrogen bonding, except instead of especially a hydrogen, we may have any electrophilic atom as the source of the σ^* orbital into which the electrons from the nucleophilic atom will be delocalized. (Thus in this view a hydrogen bond is just a special case of a Lewis bond.) A carbonyl carbon is a prime example of such an electrophilic atom, since much of the electron density that normally would be on carbon is displaced out to the carbonyl oxygen. Ordinary hydrogen bonds have two definitive characteristics.[12] The first is that they stabilize the system relative to what it would have been without such bonding, and the second is that the hydrogen approaches the electron donor atom very closely, much more closely than the van der Waals' radii would normally allow. The Lewis bonding here is qualitatively similar. We expect the atoms to approach closely and that stabilization will result. But in this case, we do not have the kind of data available that we have concerning hydrogen bonding. And nothing has been put into the MM3 program to allow for this kind of bonding. Accordingly, MM3 says that the methoxy oxygen and the carbonyl carbon will exert a repulsive interaction, since their van der Waals' radii are too large to let them be as close together as they must be, because of the steric confinements imposed by the triptycene moiety. Allowing this distance to become smaller, and stabilizing the interaction (analogous to hydrogen bonding) can easily explain in a qualitative sense what happens. However, a quantitative explanation is more difficult to arrive at. We can easily estimate approximate parameters for the electrophilic bond. (Two parameters are necessary: the well depth, which is chosen in the form of a parameter epsilon (ϵ), and the bond length of the electrophilic bond at the energy minimum (r^*).) The problem in this case is not that we can't fit what is observed, but rather that we have at least two parameters, and we have only one qualitative piece of energy information at one specific (although uncertain) distance. Hence we cannot uniquely define the parameters needed from the available information.

In order to obtain values for the two parameters for electrophilic bonding in this case, ab initio calculations were carried out for a model system where dimethyl ether and acetone were allowed to interact. The geometry used constrained the ether to come down a line perpendicular to the plane of the carbonyl, to maintain overall C_s symmetry for the complex, and to keep the two molecules oriented with their molecular planes perpendicular. This is an approximation, just so that we can see how the

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(12) Morokuma, K.; Kitaura, K. In *Molecular Interactions*; Ratajczak, H., Orville-Thomas, W. J., Eds.; J. Wiley & Sons: New York, 1980; Vol. 4, p 21.

Table 8. Comparison of Close Nonbonded Distances (<3.5 Å) of 9-Isobutyl-1,4-dimethoxytriptycene (E) Determined by X-ray and MM3

	X-ray	MM3	diff (MM3 − X-ray)
C(1), C(3)	2.4183	2.4389	0.0206
C(1), C(4)	2.7975	2.8258	0.0283
C(1), C(9)	2.6714	2.6633	−0.0081
C(1), C(17)	3.1536	3.1327	−0.0209
C(1), C(19)	3.2615	3.2263	−0.0352
C(1), C(21)	2.3953	2.4149	0.0196
C(1), C(26)	2.3999	2.4218	0.0219
C(2), C(4)	2.3909	2.4183	0.0274
C(2), C(21)	2.7390	2.7589	0.0199
C(2), C(23)	2.4100	2.4273	0.0173
C(2), O(25)	2.4225	2.4109	−0.0116
C(2), C(26)	2.8251	2.8344	0.0093
C(3), C(21)	2.3919	2.3982	0.0063
C(3), C(23)	2.8043	2.8209	0.0166
C(3), O(27)	2.4484	2.4373	−0.0111
C(3), C(28)	2.8095	2.8603	0.0508
C(4), C(10)	2.5740	2.5729	−0.0011
C(4), C(23)	2.4437	2.4636	0.0199
C(4), C(28)	2.3803	2.4101	0.0298
C(5), C(7)	2.3818	2.4116	0.0298
C(5), C(8)	2.7753	2.7942	0.0189
C(5), C(10)	2.5756	2.5777	0.0021
C(5), C(22)	2.4228	2.4483	0.0255
C(6), C(8)	2.4088	2.4255	0.0167
C(6), C(22)	2.7966	2.8227	0.0261
C(6), C(24)	2.3950	2.4087	0.0137
C(7), C(22)	2.4104	2.4330	0.0226
C(7), C(24)	2.7475	2.7702	0.0227
C(8), C(9)	2.6300	2.6437	0.0137
C(8), C(17)	3.0201	3.0145	−0.0056
C(8), C(18)	3.2127	3.2147	0.0020
C(8), C(19)	3.4955	3.5913	0.0958
C(8), C(24)	2.3915	2.4016	0.0101
C(9), C(10)	2.6392	2.5965	−0.0427
C(9), C(11)	2.4730	2.4563	−0.0167
C(9), C(13)	2.6241	2.6299	0.0058
C(9), C(18)	2.6957	2.7092	0.0135
C(9), C(19)	3.1218	3.1324	0.0106
C(9), C(21)	2.4750	2.4611	−0.0139
C(9), C(24)	2.4814	2.4682	−0.0132
C(9), O(25)	3.0138	3.0471	0.0333
C(10), C(12)	2.4510	2.4423	−0.0087
C(10), C(16)	2.5878	2.5929	0.0051
C(10), C(22)	2.4294	2.4189	−0.0105
C(10), C(23)	2.4446	2.4337	−0.0109
C(10), O(27)	2.8513	2.8898	0.0385
C(11), C(13)	2.4132	2.4233	0.0101
C(11), C(14)	2.7607	2.7844	0.0237
C(11), C(15)	2.3983	2.4110	0.0127
C(11), C(21)	2.4141	2.4158	0.0017
C(11), C(22)	2.7788	2.7704	−0.0084
C(11), C(23)	2.7676	2.7652	−0.0024
C(11), C(24)	2.4237	2.4172	−0.0065
C(12), C(14)	2.3996	2.4216	0.0220
C(12), C(15)	2.7794	2.8059	0.0265
C(12), C(16)	2.4194	2.4407	0.0213
C(12), C(17)	2.5630	2.5723	0.0093
C(12), C(21)	2.8018	2.8086	0.0068
C(12), C(22)	2.4194	2.4053	−0.0141
C(12), C(23)	2.4056	2.3869	−0.0187
C(12), C(24)	2.8129	2.8193	0.0064
C(13), C(15)	2.4114	2.4271	0.0157
C(13), C(16)	2.7991	2.8072	0.0081
C(13), C(17)	2.9754	3.0166	0.0412
C(14), C(16)	2.4021	2.4211	0.0190
C(17), C(19)	2.6393	2.6451	0.0058
C(17), C(20)	2.5085	2.5404	0.0319
C(17), C(22)	2.5844	2.5637	−0.0207
C(17), C(23)	2.6429	2.6220	−0.0209
C(17), O(25)	2.7883	2.8107	0.0224
C(18), C(22)	3.2468	3.2106	−0.0362
C(18), C(23)	3.4368	3.4066	−0.0302
C(18), O(25)	3.0803	3.1475	0.0672
C(19), C(20)	2.5157	2.5193	0.0036
C(19), C(22)	3.4200	3.4249	0.0049
C(19), C(23)	3.2560	3.2056	−0.0504
C(19), O(25)	3.0165	3.0651	0.0486
C(20), O(25)	3.3326	3.4182	0.0856
C(21), C(22)	2.8227	2.8333	0.0106
C(21), C(24)	2.4340	2.4283	−0.0057
C(21), O(27)	2.3542	2.3638	0.0096
C(22), C(23)	2.5120	2.5202	0.0082
C(23), C(24)	2.8545	2.8635	0.0090
C(23), O(25)	2.3792	2.3926	0.0134

energy varies as the ether moves along this line with-respect to the acetone. The actual ab initio calculations to search for energy minima were done using the STO-3G basis set with the correction of the basis set superposition error.[13] The real minimum then has to be searched for by allowing one molecule to tilt with respect to another. We have done this only at the minimum distance using a larger basis set (6-31G**). We found from these approximate ab inito calculations that the net attraction is about 1 kcal/mol, and the optimum distance is about 3 Å. Using these preliminary numbers in the MM3 calculation on compound **D**, we found the electrophilic bond made the ±sc form more stable than the ap form by about 0.6 kcal/mol (Tables 5 and 6). This isn't exactly right, but MM3 then is able to calculate approximately what happens with compound **D**, and with further refinement this approach will likely lead to an approximately correct result.

This example is instructive in a different way from the examples given previously. In the first examples **A**–**C**, we have a good model of what is happening, and we can calculate things accurately. In this example, we have a good qualitative understanding of what is happening, but we do not at present have sufficiently good data to be able to carry out the calculation accurately, and this kind of interaction is not presently accounted for in MM3. We feel that these calculations offer convincing proof for Lewis bonding in the present case. The requirements for Lewis bonding are met: The atoms approach each other to well within the sum of their van der Waals' radii, and the system is significantly stabilized in the process. This effect can (and will) be incorporated into MM3, analogous to the present treatment for hydrogen bonding. It can be general for any Lewis acid–Lewis base pair, but parameters will have to be determined for the various possible combinations of interacting groups.

9-Isobutyl-1,4-dimethoxytriptycene (E). Next we come to a case which proves to be rather different from any of those above. In this case we have a methoxyl group on one benzene ring again, but the 9-substituent is an isobutyl group (Figure 4). Accordingly, the isobutyl group may either be sc or ap to the methoxyl. Because the van der Waals' radii are as large as they are and the molecule is as congested as it is, we would guess that the ap conformation should be favored. But experimentally, what is found from NMR and IR is that the sc conformation predominates in solution, and strongly so.[14] An X-ray study revealed that the molecule also exists as the sc conformer in the crystal.[14]

The results of the MM3 energy calculations are shown in Table 7. In order to find the stable conformers, four

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(13) Boys, S. F.; Bernardi, F. *Mol. Phys.* **1970**, *19*, 553.

(14) Oki, M.; Takiguchi, N.; Toyota, S.; Yamamoto, G.; Murata, S. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 4295.

dihedral angles were driven with the dihedral angle driver; ω_1 = C(23)–C(9)–C(17)–C(18) : ±sc or ap, ω_2 = C(9)–C(17)–C(18)–C(19), the conformation of the methyls in the isobutyl group, ω_3 = C(2)–C(1)–O(25)–C(26) and ω_4 = C(3)–C(4)–O(27)–C(28), and the conformations of the 1- and 4-CH_3O groups. MM3 found 16 stable conformations, and the ap conformation was strongly predominant (the summed up population of the ap form was 97.7%). The most stable ap conformation (ap(+G)1 in Table 7) was favored by about 1.5 kcal/mol over the most stable ±sc conformer(±sc(+G)1). A comparison of the X-ray structure with the most stable sc conformer calculated by MM3 showed that the agreement was only fair (Table 8). The standard deviation of the close nonbonded distances (<3.5 Å) between non-hydrogen atoms in compound **E** was 0.0243 Å, which seems a bit large. So MM3 can calculate the geometry of this molecule fairly well, but it fails to evaluate the conformational energies adequately.

The problem in this case is different from the above cases, because here we have no good theory that is telling us even qualitatively what is happening. The hydrogens involved in these repulsions are just ordinary alkane hydrogens on the isobutyl group. The oxygen involved seems to be an ordinary ether oxygen, as we would find in anisole. We believe that we understand the properties of both of these atoms, but clearly something is missing, because the calculation gives the wrong result, by roughly 2 kcal/mol, which is a very large amount considering the kind of accuracy that we expect.

So what is going on in this molecule? We really don't know. We can certainly speculate. Hydrogen bonds involving alkane type hydrogens have been proposed time to time in the past.[15] Or one might imagine that the electron density about oxygen here is delocalized into the benzene ring to a greater extent than we anticipated, making the oxygen effectively smaller. Or maybe the van der Waals' parameters for the O/H or O/C interactions need to be scaled as they were for C/H interactions in alkanes. The fact is that we do not understand this case at present, and it will require further work.

JO9502007

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(15) $CH_3 \cdots O$ hydrogen bond: (a) Tamura, Y.; Yamamoto, G.; Oki, M. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 1781. (b) Tamura, Y.; Yamamoto, G.; Oki, M. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3789. $CH_3 \cdots \pi$ interactions: (c) Nishio, M.; Hirota, M. *Tetrahedron* **1989**, *45*, 7201.