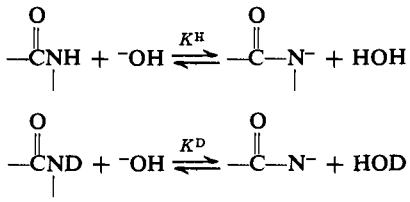
Figure 3) is consistent with the mechanisms of eq 4 and 5.

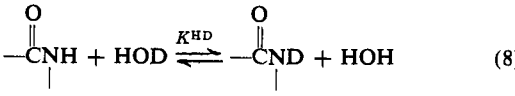
In the mechanism for specific acid catalysis, proton transfer to the amide nitrogen by hydronium ion does not contribute to the rate determining step for exchange which involves the diffusion-limited separation and approach of water and N-protonated amide (eq 4). Secondary kinetic isotope effects, if present, are expected to be small.[32]

For specific base catalysis, a competition for the protium or deuterium exists between the amide nitrogen and the hydroxide ion oxygen (k_{-2}/k_2 in eq 5). If little or no isotope effect is present in the diffusion rate constant, k_1, the isotope effect should be a reflection of the equilibrium constants for amide deprotonation (eq 7). Thus, the ratio of equilibrium constants is



(7)

equal to the equilibrium expression for the binding of deuterium *vs.* protium (eq 8), where $K^{HD} = K^H/K^D$.



(8)

In this regard, an equilibrium isotope effect of 21% has been measured for tritium–hydrogen exchange and of 13% for tritium–deuterium exchange with poly-D,L-alanine by Englander and Poulsen.[23]

An accurate estimate of the isotope effects in the present work is not possible but the results indicate that such effects are within the experimental uncertainty of about 15%.

Comparison of amide hydrogen exchange in H_2O with hydrogen exchange in D_2O[8,10] for *N*-methylacetamide indicates that amide hydrogen exchange is faster in D_2O by approximately a factor of two for both specific acid and specific base catalysis. This inverse kinetic isotope effect is related in part to the difference in basicity of H_2O (K_w = 14.0 at 25°) and D_2O (K_w' = 14.8 at 25°).[33]

Acknowledgment. We wish to extend our appreciation to Dr. S. W. Englander for his active interest, support, and numerous valuable discussions pertinent to this work. We wish also to thank Dr. R. O. Viale and Mr. C. Choi for helpful discussions and assistance.

(32) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969.

(33) H. A. Sober and R. A. Harte, Ed., "Handbook of Biochemistry," 2nd ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1970.

Conformational Properties of Some Ortho-Substituted 1,1-Diphenylethanes

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Abstract: We report here the results of an investigation of the conformational properties of some 1,1-diphenylethanes. Nmr spectra provide a generally applicable method for studying the conformational preference of these compounds through the detection of the ring current shielding effects. In our approach, semiempirical conformational energy calculations have been used to build contour maps of relative conformational energy as a function of the two internal rotation angles of these molecules. Conformations of minimum energy, as detected from the contour maps, have been assumed as the most stable. The theoretical ring current effects corresponding to these conformations have been calculated and the predicted shieldings on the ortho nuclear positions and α-hydrogen atoms have been found in agreement with those experimentally observed. Barriers to internal rotation, as detected from the energy contour maps, have been compared with the experimental barriers but only a semiquantitative agreement has been found.

In previous studies,[1] we have investigated (mainly by nmr) the conformational properties of bridged aromatic compounds of the type Ar–X–Ar (X = CH_2, O, S, SO_2, CO). We report here a similar study on some 1,1-diphenylethanes (compounds I–III). Nmr spectra provide a generally applicable method to detect the conformational preference in compounds of the type Ar–X–Ar.

In fact, due to the proximity of the two aromatic rings, the shielding of the ring current[2] of the adjacent nucleus on the ortho positions of the other ring is a function of the molecular conformation. The presence of a methyl group at the bridge position in 1,1-diphenylethanes (X = $CHCH_3$; DPE) poses steric restraints to

(1) (a) G. Montaudo, S. Caccamese, and P. Finocchiaro, *J. Amer. Chem. Soc.*, **93**, 4202 (1971); (b) G. Montaudo, P. Finocchiaro, S. Caccamese and F. Bottino, *ibid.*, **93**, 4208 (1971); (c) G. Montaudo, P. Finocchiaro, and P. Maravigna, *ibid.*, **93**, 4214 (1971); (d) G. Montaudo, P. Finocchiaro, S. Caccamese, and F. Bottino, *J. Chem. Eng. Data*, **16**, 249 (1971); (e) G. Montaudo, P. Finocchiaro, E. Trivellone, F. Bottino, and P. Maravigna, *Tetrahedron*, **27**, 2125 (1971); (f) G. Montaudo, P. Finocchiaro, and S. Caccamese, *J. Org. Chem.*, **36**, 2860 (1971); (g) G. Montaudo, F. Bottino, and E. Trivellone, *ibid.*, **37**, 504 (1972); (h) G. Montaudo, S. Caccamese, P. Finocchiaro, and F. Bottino, *Bull. Chem. Soc. Jap.*, **44**, 1439 (1971); (i) G. Montaudo, S. Caccamese, P. Finocchiaro, F. Bottino, *Tetrahedr n Lett.*, 877 (1970); (j) G. Montaudo, P. Finocchiaro, F. Bottino, S. Caccamese, P. Maravigna, and E. Trivellone, *Prepr. Macromol. Pap., XXIIIrd Int. Union Pure Appl. Chem.*, 1169 (1971).

(2) C. E. Johnson and F. A. Bovey, *J. Chem. Phys.*, **29**, 1012 (1958).

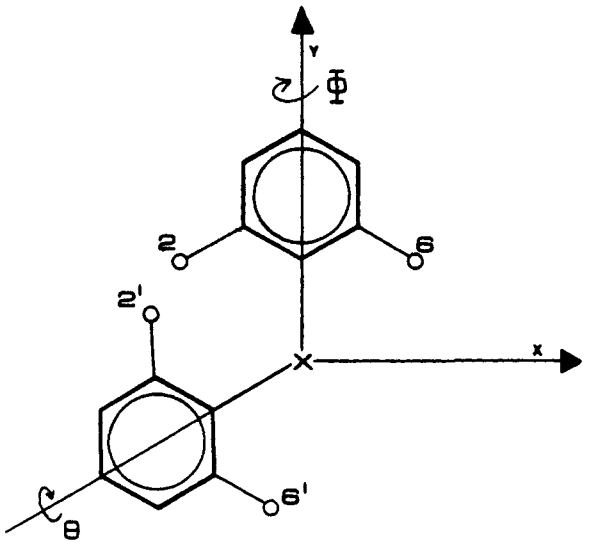
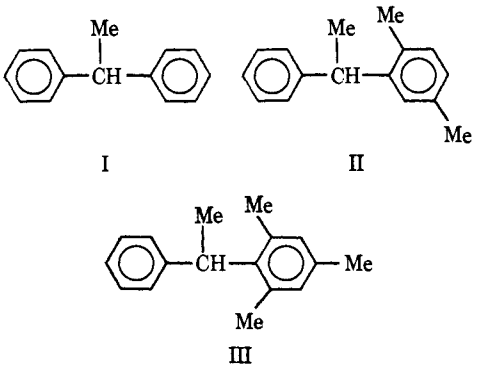


Figure 1. Structural model and internal rotation angles for the Ar–X–Ar type compounds studied. Both phenyl rings lie in the *xy* plane and the *z* axis (omitted in the figure) is directed toward the observer.



maps of relative conformational energy as a function of the two internal rotation angles of these molecules.[5,6] Conformations of minimum energy, as detected from the contour maps, have been assumed as the most stable. The theoretical[2] ring current effects corresponding to these conformations have been calculated, and the predicted shieldings on the ortho nuclear positions and α-hydrogen atoms have been found in agreement with those experimentally observed.

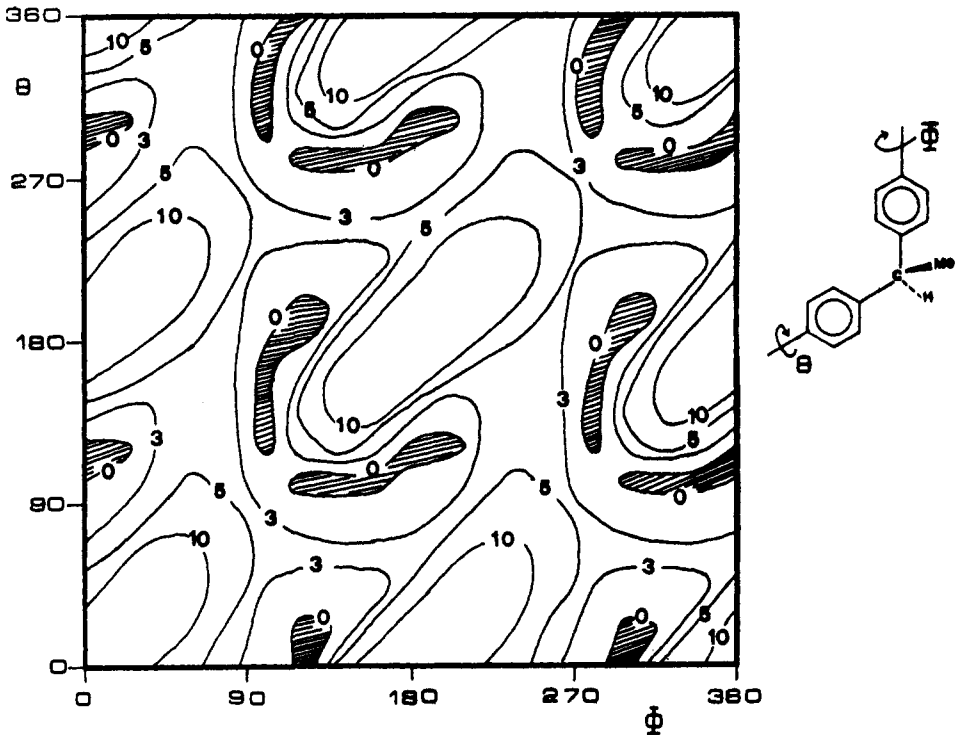


Figure 2. Energy contour map of compound I. The (planar) starting conformation ($\Phi = \theta = 0°$) is represented in the upper right side of the figure.

the internal rotation of the adjacent phenyl groups, and, contrary to the case of diphenylmethanes[1a] (DPM), kinetically restricted rotation has been reported[3,4] for the mesityl derivative III. This implies that a study of the conformational properties of DPE offers the chance to look at the internal rotation mechanism, through the investigation of the activation energies relative to such processes.

In our approach, semiempirical conformational energy calculations have been used to build contour

Barriers to internal rotation, as detected from the energy contour maps, have been compared with the experimental ones but only a semiquantitative agreement has been found.

Experimental Section

General. The compounds used were synthesized according to the literature. ^1H nmr spectra were recorded with an HA-100

(3) A. Hassner and E. G. Nash, *Tetrahedron Lett.*, 525 (1965).
(4) A. Mannschreck and L. Ernst, *ibid.*, 5939 (1968).

(5) Energy contour maps, based on extended Hückel calculations, have been recently reported[6] in a study of the conformational properties of some arylcarbonium ions and related molecules.
(6) R. Hoffmann, R. Bissell, and D. C. Farnum, *J. Chem. Phys.*, 73, 1789 (1969), and references therein.

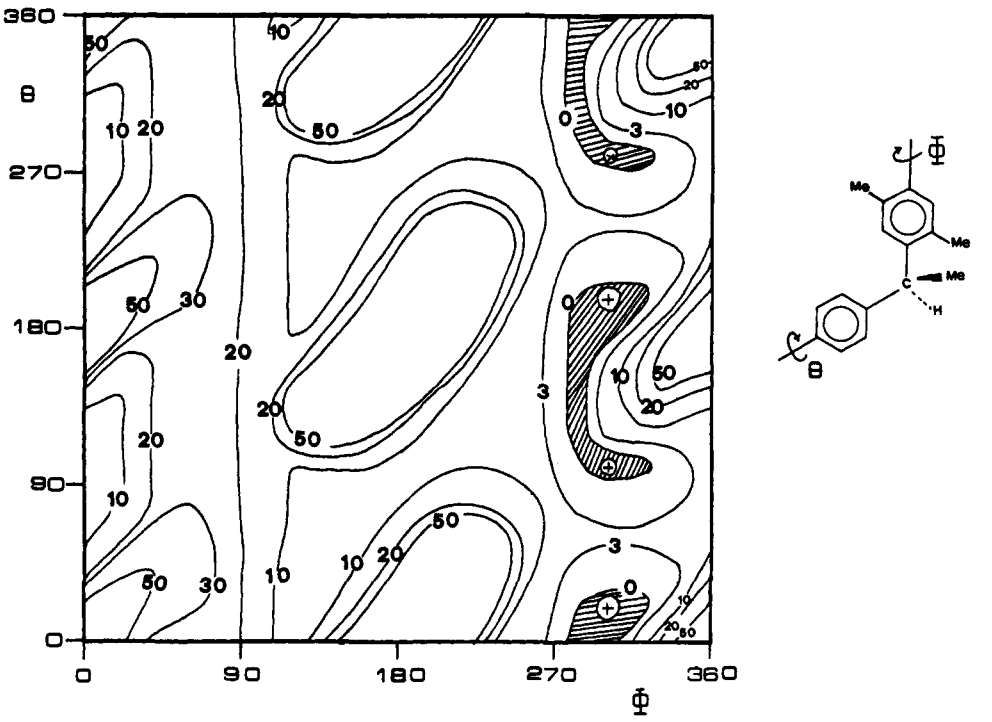


Figure 3. Energy contour map of compound II. The (planar) starting conformation ($\Phi = \theta = 0°$) is represented in the upper right side of the figure.

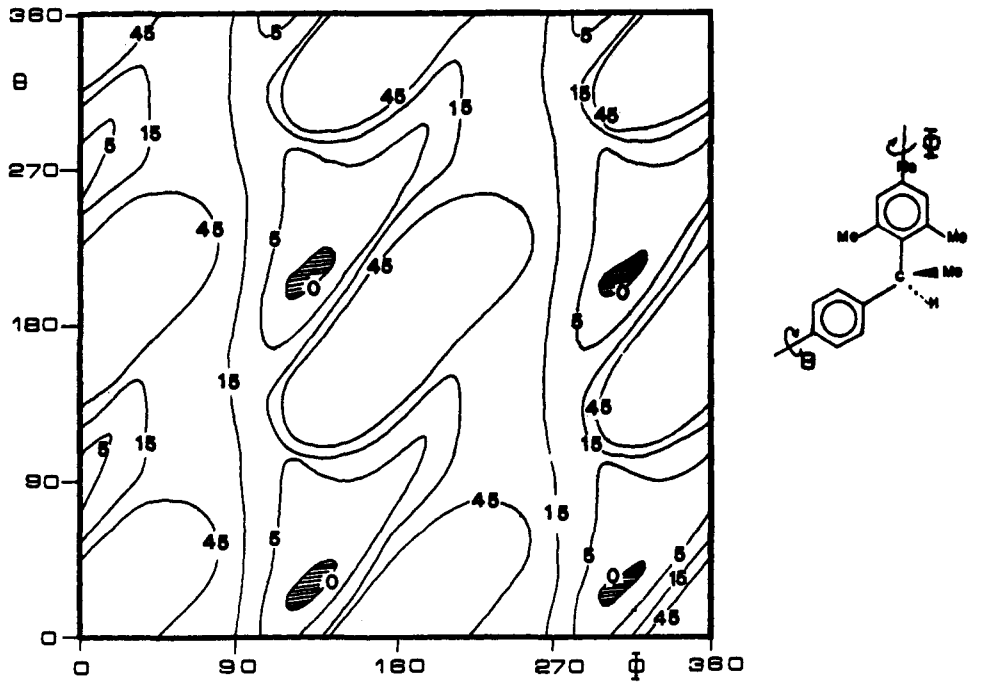


Figure 4. Energy contour map of compound III. The (planar) starting conformation ($\Phi = \theta = 0°$) is represented in the upper side of the figure.

Varian spectrometer. Energy calculations were performed with the help of a microcomputer Hewlett-Packard 9100 B.

Calculations. The starting conformation ($\Phi = \theta = 0°$) for compounds studied was taken with both rings planar, and the origin of the axes was placed at the X atom, as depicted in Figure 1. In the case where X = CHMe, the methyl group was placed above the sheet plane.

Interatomic distances and natural bond angles were taken from pertinent literature data.[7]

Distances among interacting atoms were computed for each pair of Φ and θ values calculating first (trigonometrically) the atomic coordinates for each interacting atom for a fixed conformation and then applying the usual rotational matrix methods.[8]

Nonbonded interactions were obtained from the calculated distances (r) according to the Lennard-Jones[7,9] potential. Torsional

(7) A. Mannschreck and L. Ernst, *Chem. Ber.*, **104**, 228 (1971), and references therein.

(8) H. A. Elliott, K. D. Fryer, J. G. Gardner, and N. J. Hill, "Vectors and Matrices," Holt, Toronto, Canada, 1966, p 254.

(9) R. A. Scott and H. A. Scheraga, *J. Chem. Phys.*, **45**, 2091 (1966); **46**, 4410 (1967); H. A. Scheraga, *Advan. Phys. Org. Chem.*, **6**, 103 (1968).

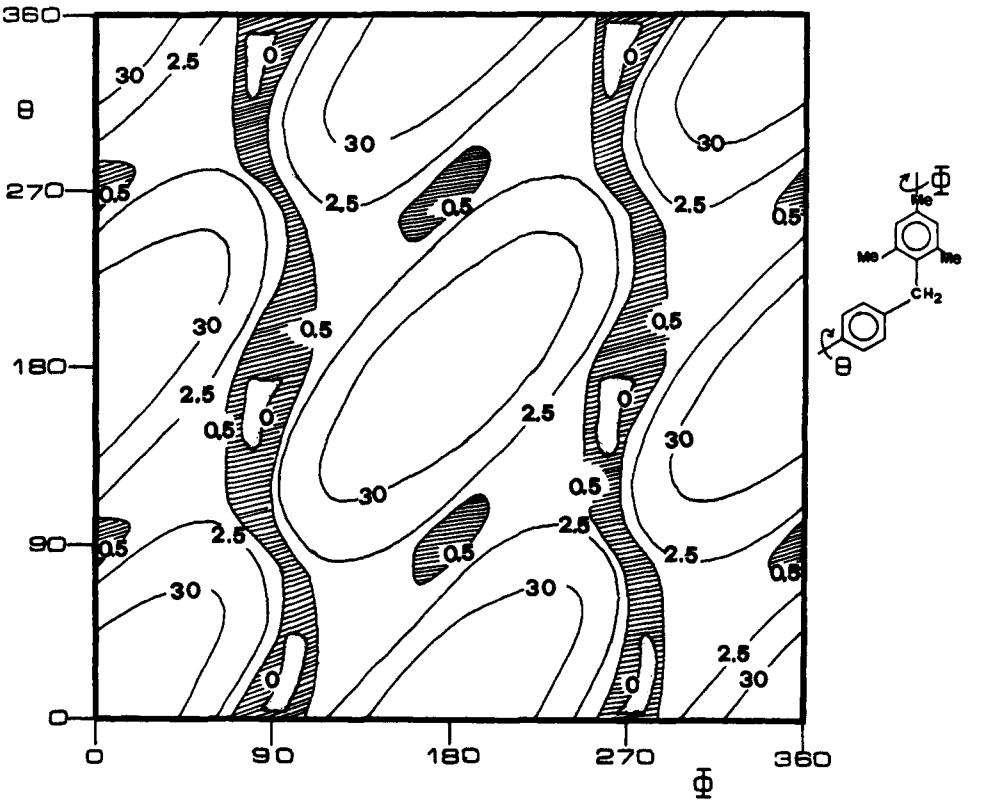


Figure 5. Energy contour map of compound IV. The (planar) starting conformation ($\Phi = \theta = 0°$) is represented in the upper right side of the figure.

energies were not taken into account because they were found to be negligible.[10] Individual energy values for each one of the 24 interacting pairs considered were added together obtaining the total strain energy (unminimized) for each pair of Φ and θ values from 0 to 360°, with a stepwise 10° increment. Appropriate symmetry operations proved useful in reducing the computing work involved.

The strain energies found were minimized through the deformation of the valence angle, of the Ar–Me or Ar–H bond angles, and through the stretching of these bonds. The bending and stretching constants were taken from the literature.[7,11]

In order to simplify the minimization scheme, we have confined ourselves to minimizing only the values of energy exceeding 2–3 kcal/mol by a concomitant 5° widening of the Ar–X–Ar valence angle and 10° deformation of the Ar–Me or Ar–H angles.

Preliminary optimization trials had in fact shown that the strain energy in these molecules is best released through this process. This procedure, although not very rigorous, allows a considerable reduction of the energy barriers to internal rotation leaving unchanged the position and the relative energy of the conformational minima.

Discussion

Contour Maps of Relative Conformational Energy. Semiempirical conformational energy calculations have been performed for the three DPE's investigated (compounds I–III) and for mesitylphenylmethane (IV) (included for comparison).

The results have been used to build contour maps of relative conformational energy as a function of the two internal rotation angles Φ and θ (Figure 1). The contour maps relative to compounds studied are shown in Figures 2–5. The main features of these maps are the location of the stable molecular conformation and the energy barrier to internal rotation.

The energy minima for the three DPE's studied fall roughly in the same conformational area (Figures 2–4) and correspond to a skew conformation with the phenyl rings bent away from coplanarity (the coplanar is, of course, the most hindered conformation).

Ortho substitution restricts rather drastically the "energetically allowed" area (shaded area in Figures 2–5); the latter is relatively wide for the unsubstituted compound I (Figure 2) and for the ortho-substituted compound II (Figure 3), but is reduced to a narrow region in the ortho-disubstituted compound III (Figure 4).

The barrier to internal rotation is low (about 4.0 kcal/mol) in the case of compound I. The presence of an ortho methyl group raises the energy barrier up to 28 kcal/mol (saddle point at about $\Phi = 60°$; $\theta = 100°$) for the substituted ring in compound II, while the barrier to rotation for the unsubstituted ring remains as low (about 4.0 kcal/mol) as in compound I. The interconversion of the two nuclear otho methyls in compound III requires an energy of about 23 kcal/mol (saddle point at about $\Phi = 60°$; $\theta = 120°$), while the barrier to rotation for the unsubstituted ring is here about 10 kcal/mol (saddle point at about $\Phi = 280°$; $\theta = 120°$).

These high barriers disappear in the corresponding ortho-disubstituted DPM (Figure 5), confirming that the presence of the α-methyl group is the main source of steric restraints to internal rotation for the ortho-substituted ring in DPE.

Comparison of *a Priori* and Experimental Data. Assuming that the three DPE's investigated are actually

(10) J. F. Yan, G. Vanderkooi, and H. A. Scheraga, *J. Chem. Phys.*, 49, 2713 (1968).

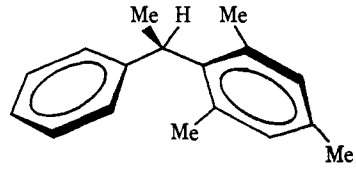
(11) E. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1965, p 447, and references therein.

Table I. ^{1}H Nmr Data[a] of 1,1-Diphenylethanes of General Formula

No.	Position of nuclear methyl groups	Ph	Me_α	H_α	H_2	H_3	H_4	H_5	H_6
1		7.05[b]	*1.53*[c]	4.05[d]	7.05[b]	7.05[b]	7.05[b]	7.05[b]	7.05[b]
		7.05[b]	*1.55*[c]	4.04[d]	7.05[b]	7.05[b]	7.05[b]	7.05[b]	7.05[b]
2	2, 5	7.13[b]	*1.54*[c]	4.24[d]	*2.10*[e]	6.90[f]	6.90[f]	*2.29*[e]	6.90[f]
		7.12[b]	*1.57*[c]	4.20[d]	*2.10*[e]	6.92[f]	6.92[f]	*2.29*[e]	6.92[f]
3	2, 4, 6	7.16[b]	*1.61*[c]	4.58[d]	*2.09*[e]	6.80[e]	*2.24*[e]	6.80[e]	*2.09*[e]
		7.25[b]	*1.69*[c]	4.65[d]	*1.77*[e]	6.82[e]	*2.30*[e]	6.99[e]	*2.49*[e]

[a] Chemical shifts measured in ppm downfield from TMS as internal standard at 100 MHz, in $CDCl_3$. First row values at 30°; second row values at −67°. Values in italics denote the methyl signal. [b] Very narrow complex multiplet. [c] Doublet; J = 7 Hz. [d] Quartet, J = 7 Hz. [e] Singlet. [f] Deceptively simple ABC system.

present in the skew form V predicted by the *a priori* energy calculations, it should be possible to estimate the theoretical[2] shielding on the four ortho positions and to compare it with the experimental values.



V

However, in our cases the experimental shielding value is not directly observable from the room temperature nmr spectra because of the fast interconversion rate of ortho protons (or methyls) which are rapidly interchanged from a deshielded to a shielded position (and vice versa).

Low-temperature spectra (−67°, Table I), while unable to resolve the ortho hydrogen signals, in the case of compound III do succeed in splitting the ortho nuclear methyls into two signals resonating at 1.77 and 2.49 ppm, respectively. Assuming the chemical-shift value of the para methyl group in this molecule (2.30 ppm) is appropriate for an unshielded methyl, the experimental diamagnetic shielding for the methyl group resonating at 1.77 ppm can be computed as 0.53 ppm.

This value compares well with the theoretical[2] shielding value (about 0.5 ppm) computed for compound III, in its minimum energy conformation.

As mentioned above, the shielding effects on the ortho nuclear positions are not experimentally observable for compounds I and II, but we can take advantage of another shielding effect to investigate the preferred conformation in these molecules.

In the case of DPM, DPE, and triphenylmethanes (TPM), a ring current shielding effect should be observed also on the hydrogen at the bridged (α) carbon atom, depending on the relative spatial orientation of the phenyl rings and of the bridged group. This prediction has not been verified in DPM, where such an effect has been found negligible for a number of variously substituted derivatives.[12,1d] However, a sizable paramagnetic shielding, induced by ortho substitution in some TPM, has been correctly ascribed to ring current effects.[12]

(12) H. Kessler, A. Mossmayer, and A. Rieker, *Tetrahedron*, **25**, 287 (1969).

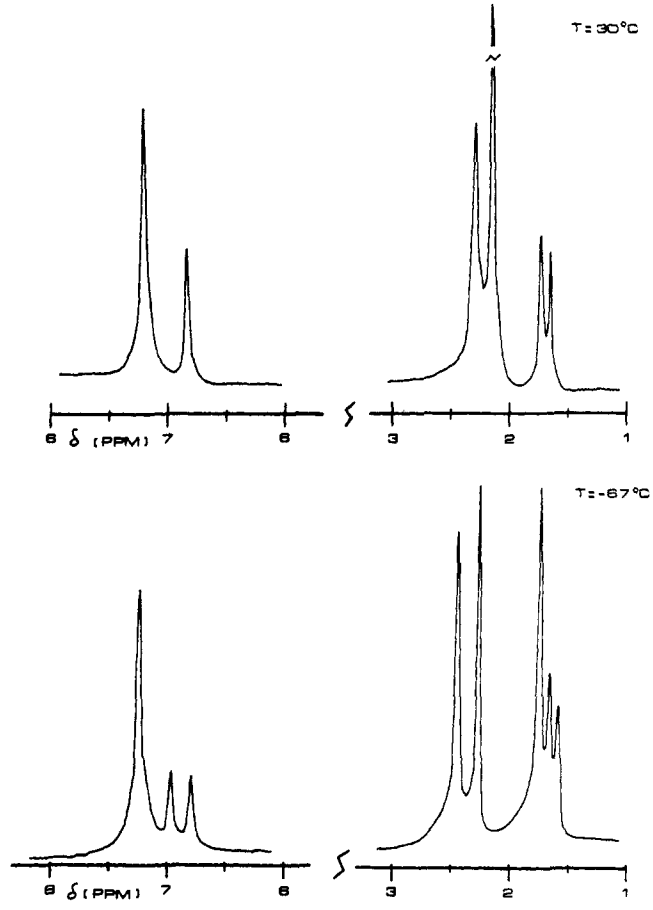
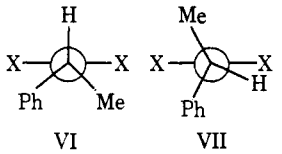


Figure 6. ^{1}H nmr spectra of compound III at two different temperatures in $CDCl_3$ at 100 MHz. Only the portion relative to methyl and aromatic proton signals is represented, and methine absorption is omitted.

In the case of DPE, the theoretical[2] shielding difference between the two limiting spatial arrangements VI and VII is about 0.25 ppm per ring, *i.e.*, about 0.5 ppm in total. Close to this value (0.5 ppm) is the difference between the chemical shifts of the α-hydrogen signals in compounds I and III. Compound II has an intermediate value (Table I).

These data seem to imply that ortho substitution stabilizes form VII, where the α-hydrogen atom experiences a higher paramagnetic shielding from the ad-



VI VII

X = H, Me

jacent phenyl rings, with respect to form VI. This interpretation is in agreement with the results of the *a priori* energy calculations.

In fact, the contour map in Figure 2 shows that both phenyl rings in compound I may experience wide torsional oscillations, so that most of the ring current shielding on the α-hydrogen atom results averaged. On the contrary, for compound III the contour map (Figure 4) shows a very narrow minimum in which both phenyls are held nearly in form VII, so that the paramagnetic shielding on the α-hydrogen atom is here retained. This interpretation also allows one to explain the failure[12,1d] to observe experimentally a similar effect in DPM. In fact, from the analysis of the contour map in Figure 5, it can be inferred that averaging of the ring current shielding on the α-hydrogen atoms is very likely to occur also in this case.

Coming now to the discussion of the energy barriers to internal rotation in these molecules, a comparison between experimental and *a priori* data seems most appropriate in the case of compound III, since for the latter the free-energy barrier to rotation is known[4] (about 11.3 kcal/mol; variable temperature nmr). The contour map in Figure 4 shows a barrier of about 23 kcal/mol to the interconversion of ortho methyls in the substituted ring, and a barrier of about 10 kcal/mol to the interconversion of the ortho hydrogens in the unsubstituted ring. Assuming that the highest barrier (methyl interconversion) corresponds to the process experimentally observed, it is apparent that our calculations overestimate this energy barrier.

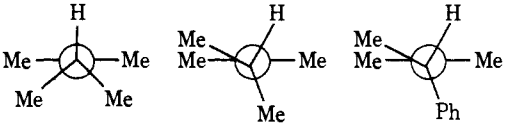
Also, for the other process (*i.e.*, the rotation of the unsubstituted ring), the calculated energy barier (10 kcal/mol) seems overestimated. In fact, the nmr spectrum at $-67°$ (Figure 6) shows kinetically restricted rotation of the substituted ring (split methyls and meta nuclear hydrogens), but the nuclear protons of the unsubstituted ring appear still coalesced, implying that a free-energy barrier lower than 10 kcal/mol is associated with the latter process.

Although we cannot claim here a quantitative agreement between predictions and experimental results, we wish to stress that the agreement is at least semiquantitative.

Accurate prediction of barriers to internal rotation is a major problem, difficult to deal with in the case of semiempirical energy calculations. In fact the equation used to estimate the pairwise nonbonded interactions tends to become progressively unreliable as the internuclear distance decreases.[9] Analogous overestimation problems are reported in calculations of rotation barriers, performed with methods essentially similar to ours, which have appeared quite recently on such systems as isopropylmesitylene[7,13] and halotoluene derivatives.[14]

Acknowledgments. We are indebted to Dr. E. Trivellone (C.N.R. Laboratory, Arco Felice, Naples) for the use of the Varian HA-100 instrument, and to N. Barbagallo for his help in the computing work.

(13) Mannschreck and Ernst[7] find that the barrier to rotation in isopropylmesitylene is represented by form VIII, rather than form IX.



VIII IX X

In our case (compound III), the barrier is represented by form X, equivalent to IX, because the phenyl group (when properly oriented) provides minor strain energy with respect to a methyl group.

(14) B. H. Barber and T. Schaefer, *Can. J. Chem.*, **49**, 789 (1971).