(40) B. R. Malcolm, *Biopolymers*, **9**, 911 (1970).
(41) F. Happey, D. W. Jones, and B. M. Watson, *Biopolymers*, **10**, 2039 (1971).
(42) For the calculations of the rotational entropy contribution to the Helmholtz conformational free energy described here, the lattice constant *c*, which is in the direction of the helix axis, is assumed to be fixed at the observed crystallographic value.
(43) The isolated ω helix is not a minimum-energy backbone conformation. The minimization referred to here is one where the side-chain dihedral angles were allowed to vary, with the backbone conformation held fixed.
(44) Even though 4 residues is only one turn of an ω helix, the dihedral angles resulting from the computation with such a short helix were used only as starting values for a subsequent calculation on a crystalline array of ω helices, in which 12 residues/chain were taken (see section C).
(45) The starting conformation for the ω helix was chosen in this manner because no other data were available, either from a complete theoretical study of the ω helix or from an X-ray conformation of the ω helix of *p*-Cl-PBLA.
(46) Since we are comparing the energy *per residue*, this comparison is almost valid (and would become more so as the chain length increases) even though 18 and 4 residues are used in the computations for the α and ω helices, respectively.
(47) The X-ray results were interpreted[6] in terms of a random distribution of up and down chains. This suggests that, during nucleation, both up and down arrangements are equally probable without any energetic preference for one or the other arrangement. For simplicity in studying the crystal packing, we have thus assumed that all helical chains run in the same direction.
(48) Here, E_{total} refers to $E_{\text{r}\rho}(a, b, \{q_i{}^0\}_{i \neq z_{\text{rot}}}, z_{\text{rot}})$ defined in eq 19.
(49) The Helmholtz conformational free energy per residue was computed only for Rt(−) and not T(R), since Rt(−) is the lower-energy structure. For each a (= b), E_{intra} is a constant since the backbone is the fixed Rt(−) conformation; hence, only E_{inter} varies with z_{rot} (Figure 7).
(50) From infrared dichroism studies of fibers of poly(ethylene suberate),[51] the transition moment of the C=O stretching vibrations is 19° away from the C=O bond (in the direction of the C^{β}—C^{γ} bond) and, from similar studies of crystalline dimethyl oxalate, the transition moment of the C—O—C antisymmetric stretching vibration lies in the COO plane and is nearly perpendicular to the C=O bonds.[52,53]
(51) E. M. Bradbury, A. Elliott, and R. D. B. Fraser, *Trans. Faraday Soc.*, **56**, 1117 (1960).
(52) J. K. Wilmshurst, *J. Mol. Spectrosc.*, **1**, 201 (1957).
(53) T. Miyazawa and K. Kuratani, *Nippon Kagaku Zasshi*, **72**, 804 (1951).
(54) Only selected values of $a = b$ were considered because of limitations on computer time, and because it was our intent here to determine (i) if a minimum-energy conformation would occur with only a small distortion in the α helix, and (ii) whether a distortion in the α-helix conformation favored an expansion or contraction of the lattice.
(55) Since no geometry has been presented for the ω helix, we chose the values of ϕ, ψ, and ω from our minimum-energy conformation[43] for the isolated chain (last line of Table II); these values of ϕ, ψ, and ω reproduce the experimental values of *h* and *t*.
(56) The volume per residue occupied by Rt(−) and Rt(ω) crystals at their minimum-energy conformations are 215 and 238 Å,[3] respectively, calculated as $\pi d^2 h/4$, where *d* is the distance between two neighboring helical chains (13.5 and 15.3 Å for α and ω helices, respectively). This may indicate that structure Rt(ω) has more room for the side chains to move than has Rt(−).

Conformational Analysis of the 1,3,5,7-Tetramethylcyclooctane Stereoisomers

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ABSTRACT: A theoretical conformational analysis of the four stereoisomers of 1,3,5,7-tetramethylcyclooctane has been carried out using Warshel and Lifson's consistent force field. Two nonequivalent stable conformers were found for the *mmrr* isomer, while in the case of the other isomers only equivalent conformers contribute significantly to the equilibrium population at room temperature; the energy paths connecting the minima were also examined. The results of the calculations show the failure of less refined methods, based on geometrical assumptions, in the study of sterically hindered systems. The nmr spectra of the four isomers were measured at 220 MHz in *o*-dichlorobenzene and successfully analyzed. The vicinal proton coupling constants are fairly well correlated with the values calculated from the theoretical conformations using various forms of the Karplus equation, thus supporting the structures elucidated by the energy calculations. On the other hand, there is no simple connection between chemical shifts and conformations or configurations; this result indicates that great caution should be used when correlating chemical shifts and conformations of complex and sterically strained systems.

Rotational isomeric state theory and related methodology have been used for relating molecular properties of polymers to their chemical structure.[1] Such methods however require more and more refined conformational energy evaluations as more detailed correlations are wanted.[2] Therefore it cannot be stated that the literature is lacking in controversies even with regard to such extensively studied and relatively simple polymers as isotactic polypropylene.[2-10] To a certain extent the disagreement may stem from the difficulty of describing a macromolecule precisely, from uncertainties in the determination of physical properties of polymers, and perhaps from the fact that different researchers have examined nonidentical polymers. A related relevant problem, given the importance of nmr spectroscopy as a tool for the configurational and conformational studies of polymers, is to establish to what extent not only the vicinal proton coupling constants, but also the chemical shifts can be reliably correlated to the conformeric populations.[5,11]

In order to clarify the last point, as well as to test the current theoretical methods of analysis, the four stereoisomers of 1,3,5,7-tetramethylcyclooctane (TMCO) have been synthetized as reported elsewhere.[12] For each of these compounds extensive conformational energy calculations have been performed and the results have been checked against the nmr spectra.

Method of Calculation

In recent years the advent of large computers and the development of procedures for finding the minima of many-variable functions have made possible a considerable progress in the prediction of the structure and of other molecular properties of hydrocarbons. Several authors[13-16] have proposed similar methods, which have been verified against a wealth of experimental data; common to all these methods are the assumptions that the Born–Oppenheimer potential energy surface of a molecule can be empirically represented by a sum of terms and

Table I
Low-Energy Conformations of the TMCO Isomers[a]

Isomer	Conformer	χ_1	χ_2	χ_3	χ_4	χ_5	χ_6	χ_7	χ_8	V (kcal/mol)
mmmm	TCC	−84.8	61.9	−85.6	113.4	−84.8	61.9	−85.6	113.4	−34.67
	CC I[b]	−76.8	76.8	−99.3	99.3	−76.8	76.8	−99.3	99.3	−34.03
	CC II[b]	−76.6	99.2	−99.2	76.6	−76.6	99.2	−99.2	76.6	−34.08
	CROWN[c]	−89.1	89.1	−89.1	89.1	−89.1	89.1	−89.1	89.1	−33.76
mmrr	BC (symm)	−102.0	68.2	−68.2	102.0	−43.2	−63.9	63.9	43.2	−35.56
	BC (asymm)	−70.4	69.7	−102.7	46.7	62.4	−63.4	−45.0	103.4	−34.88
	TCC	−115.7	84.0	−60.7	85.5	−112.9	79.0	−55.5	84.9	−32.82
	CC I[b]	−100.2	75.2	−75.2	100.2	−98.7	70.2	−70.2	98.7	−32.40
	CC II	−79.8	73.3	−94.4	104.3	−80.9	68.6	−88.5	100.5	−32.15
	TC	−40.2	105.9	−105.9	40.2	38.6	−105.8	105.8	−33.6	−27.24
mrmr	BC	−70.0	70.0	−102.7	44.5	64.6	−64.6	−44.5	102.7	−34.82
	TBC	−52.0	118.1	−46.5	−47.6	93.4	−92.3	92.7	−45.8	−33.22
	TC	−102.8	35.5	43.4	−108.0	102.8	−35.5	−43.4	108.0	−27.30
	C[c]	−117.8	77.5	0.0	−75.1	117.8	−77.5	0.0	75.1	−26.97
rrrr	BC	−43.4	−63.8	63.8	43.4	−100.7	63.7	−63.7	100.7	−33.96
	S4 I	−39.5	−60.4	39.5	60.4	−39.5	−60.4	39.5	60.4	−31.56
	S4 II	59.3	−44.5	−59.3	44.5	59.3	−44.5	−59.3	44.5	−31.57
	TCC	−85.3	56.4	−78.7	113.2	−85.3	56.4	−78.7	113.2	−30.97
	CC[b]	−98.6	70.7	−70.7	98.6	−98.6	70.7	−70.7	98.6	−30.67

[a] The dihedral angles χ are numbered clockwise, starting from the angle formed by carbon atoms 8–1–2–3 in the sketch of Table VI. [b] Saddle point. [c] Maximum.

that the parameters appearing in these terms of the energy are transferable from the molecules used for fitting the parameters to similar molecules.

The conformations of medium cycloalkane rings, among them cyclooctane, have been studied by Hendrickson,[14] who has also exhaustively examined the path of interconversion between the numerous conformers.[17] In the present study of the conformations of the 1,3,5,7-tetramethylcyclooctane isomers we preferred to use the so-called consistent force field proposed by Warshel and Lifson[16] rather than Hendrickson's potential for two reasons: namely that in Warshel and Lifson's scheme no geometrical restriction is maintained, all bond lengths and bond angles being allowed to vary, and that vibrational frequencies of several alkanes were included in the fitting of the parameters, so that more accurate frequencies should be expected with this method.

Further in the text we shall consider the total potential energy as the sum of four terms

$$V = V_{\text{str}} + V_{\text{bend}} + V_{\text{tor}} + V_{\text{nbd}}$$

where V_{str} is the sum of the bond stretching energies; V_{bend} includes both the bond-angle deformation energies and the 1-3 nonbonded interactions; V_{tor} includes the torsional energies together with a corrective term, which is a function of the torsional angle and of the two bond angles adjacent to the bond around which the torsion occurs; V_{nbd} is the sum of all the nonbonded interactions between atoms separated by at least three bonds, each term being expressed by a 9-6-1 potential.

The reader is referred back to the paper by Warshel and Lifson[16] for the details of the potential functions. A minor difference was introduced in V_{tor} by equally distributing the potential between the nine torsional angles around the same bond. Moreover it should be mentioned that the same parameters were used for the carbon and hydrogen atoms of the methylene and of the methyne groups, since the authors only provide distinct values of some parameters of the methylene and of the methyl groups.

The determination of the minimum energy conformations of the four isomers was done by steps in the following manner. In a preliminary step we assumed constant bond lengths and bond angles; under these conditions the closure of the ring reduces to two the number of degrees of freedom in a cycle of eight bonds, and the energy can be described by a collection of bidimensional surfaces. Gō and Scheraga[18] have shown how the ring closure problem can be treated exactly by solving a set of geometric equations; therefore, by using this method we first calculated all the energy maps (in practice six for each isomer) as a function of two consecutive torsional angles. The differences between the minima of the energy surfaces thus obtained depend very much on the value assumed for the CCC angle and are not realistic; nevertheless, the conformations having low energy are good starting points for the successive refinement.

Then the molecular energy was minimized simultaneously with respect to the $(3N - 6)$ atomic coordinates; unlike Hendrickson, who considered only symmetric conformations, we did not impose any symmetry condition because it could be too restrictive for such crowded molecules. The iterative method originally due to Davidon and revised by Fletcher and Powell[19] was used for finding the minima of the energy; this method requires the calculation of the first partial derivatives of the function (but not the second derivatives), and it proved to be very efficient in previous conformational problems. Starting points for the minimization were chosen randomly in the low-energy regions of the maps; only when it was clear that a conformation was converging toward a symmetric one the proper element of symmetry was introduced in order to reduce the computer time per iteration and to speed up the convergence.

Later with the aim of checking the systematicity of the search we repeated the calculation starting from the symmetric conformations listed by Hendrickson for cyclooctane. During the minimization only the true symmetry of the conformer, if any, was kept. No new low-energy minimum was found in this way; only in the case of symmetric conformations some saddle points having relatively low energy were obtained; of course these false minima could not be found without imposing the symmetry.

Finally, for the most stable conformers of each isomer we calculate the statistical weight $w = e^{-F}/kT$. The $(3N - 6)$ vibrational frequencies ν_i can be obtained straightforwardly by diagonalizing the matrix $M^{-1/2}\, V\, M^{-1/2}$, where V is the matrix of the potential energy second derivatives

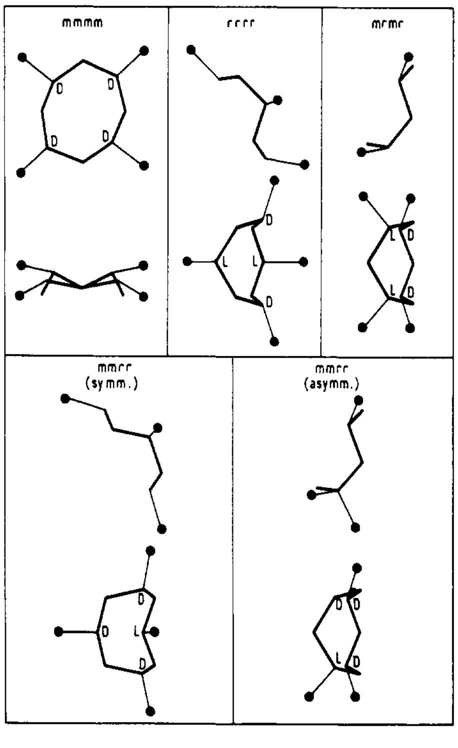


Figure 1. Two orthogonal projections of the most stable conformers of the four stereoisomers of TMCO.

and M is the diagonal matrix of the atomic masses. Then the vibrational zero-point energy is given by

$$E_{\text{vib}}^0 = 1/2h \sum_{i=1}^{3N-6} \nu_i$$

while at temperature T the vibrational and the total free energies (neglecting the rotational free energy) of one conformer are calculated as

$$F_{\text{vib}} = kT \sum_{i=1}^{3N-6} \ln [1 - \exp(-h\nu_i/kT)]$$

$$F = V + E_{\text{vib}}^0 + F_{\text{vib}}$$

Results of the Calculations

The low-energy minima and some significant symmetric conformations are listed in Table I. We use Hendrickson's notation to indicate the types of conformation. Sketches of the most stable conformers are shown in Figure 1.

For the *mmmm* isomer only one region in the conformational space is accessible, namely, one of the two pseudorotational paths TCC-CC. As in cyclooctane the TCC form, with a twofold axis of symmetry, is the conformation of minimum energy. The pseudorotational path connects four equienergetic minima (two identical *dl* pairs), separated by barriers of about 0.6 kcal corresponding to the CC forms, while the crown conformation is a maximum of 0.9 kcal (see the energy profiles in Figure 2). The low values of the barriers allow a considerable flexibility for this isomer.

In the case of the *mmrr* isomer the most stable conformer is the symmetric boat-chair form, which presents a plane of symmetry; the BC-TBC pseudorotational path leads from this unique conformer to two equienergetic (mirror images) asymmetric BC forms, less stable by 0.7 kcal; as shown in Figure 3 a barrier of 4.2 kcal separates the absolute minimum from the higher ones. Also one part of the TCC-CC path is a low energy region for the *mmrr* isomer, but the TCC minima are here less stable than in *mmmm* by about 2 kcal.

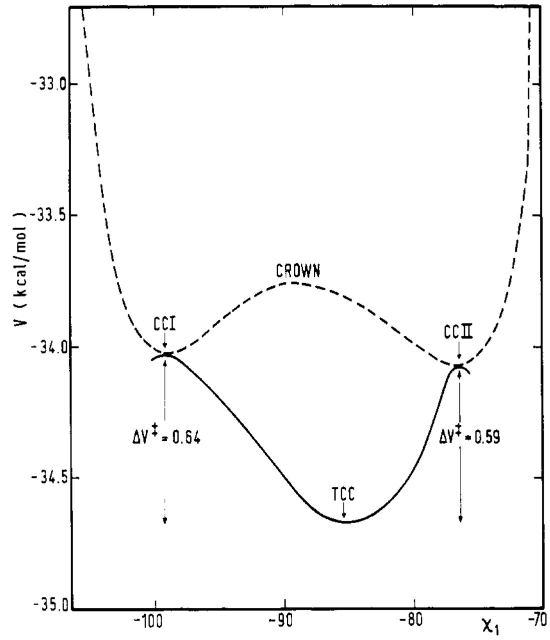


Figure 2. Pseudorotational path (solid line) and symmetrical path (dashed line) connecting two CC conformations of the *mmmm* isomer of TMCO respectively through the absolute minimum TCC and the maximum crown conformation.

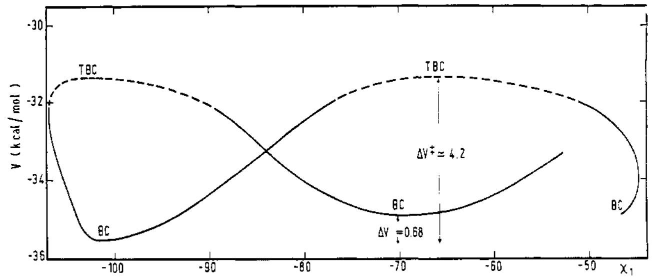


Figure 3. Portion of the pseudorotational BC/TBC energy path of the *mmrr* isomer, connecting the absolute minimum with the two asymmetrical BC forms through the TBC conformations. The dashed parts of the curve have been calculated with less accuracy (~0.1 kcal/mol).

The stable conformer of the *mrmr* isomer is a symmetric BC form in which a plane of symmetry passes through two CH_2 groups. This structure differs from the asymmetric BC form of *mmrr* only for the configuration of one tertiary carbon; the exchange of the positions of H and CH_3 occurs without a significant energy change, leaving the position of the other atoms unaltered. In *mrmr* there are two identical such conformers: the interconversion path joining them (BC → TBC → C → TBC′ → BC′) is shown in Figure 4. The highest barrier of 7.85 kcal should still allow a fast interconversion at room temperature. It should be noted that along this path a higher minimum is found, which does not correspond to any energy minimum in cyclooctane. No other low-energy region exists for *mrmr*.

Also in the case of the *rrrr* isomer the most stable conformer is a symmetric BC form, with a plane of symmetry passing through two tertiary carbons. The structure can be obtained from the absolute minimum *mmrr* by changing the configuration of one carbon; however, this time the H-CH_3 exchange is unfavored by a strong repulsion between the methyl group and two axial methylene hydrogens, so that this isomer is less stable by 1.6 kcal. Again

Table II
Ring CCC Bond Angles in the Stable Conformers of TMCO[a]

Isomer	Conformer	θ_1	θ_2	θ_3	θ_4	θ_5	θ_6	θ_7	θ_8
mmmm	TCC	113.0	116.2	114.3	114.9	113.0	116.2	114.3	114.9
mmrr	BC (symm)	114.3	115.7	116.3	115.7	114.3	118.4	115.4	118.4
mmrr	BC (asymm)	113.5	117.3	113.5	116.1	116.6	119.0	116.0	116.5
mrmr	BC	113.5	117.2	113.5	116.9	116.3	117.5	116.3	116.9
rrrr	BC	114.2	118.3	116.0	118.3	114.2	117.6	116.9	117.6

[a] The bond angles are numbered clockwise, starting from the angle 8–1–2 in the sketch of Table VI.

Table III
Contributions to the Potential Energy of the Stable Conformers of TMCO Referred to the Lowest Minimum of *mmrr* (kcal/mol)

Isomer	Conformer	ΔV_{str}	ΔV_{bend}	ΔV_{tor}	ΔV_{nbd}	ΔV
mmmm	TCC	−0.10	−1.77	3.35	−0.59	0.89
mmrr	BC (asymm)	−0.09	0.12	0.09	0.56	0.68
mrmr	BC	−0.08	−0.14	0.45	0.50	0.73
rrrr	BC	−0.03	0.92	−0.28	0.98	1.59

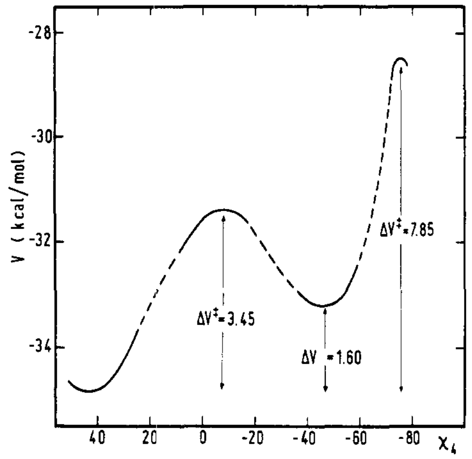


Figure 4. One-half of the energy path BC → TBC → C → TBC′ → BC′ connecting the two equivalent stable conformers of the *mrmr* isomer.

there are four identical minima of the energy. In this case the interconversion cannot occur either along the BC–TBC path (as in *mmrr*) or through the chair conformation (as in *mrmr*). The only viable path of interconversion seems that through the TCC and B conformations, for which a barrier of a least 11 kcal should be expected.[5] This isomer shows other regions of relatively low energy, with minima S_4 and TCC respectively 1.4 and 3.0 kcal higher than the stable conformer.

The ring dihedral angles of the stable conformers differ by no more than 6° from the values calculated by Hendrickson for cyclooctane, *i.e.*, in all the isomers there is at least one way of inserting the four methyl groups without much affecting the ring geometry. The insertion is helped by a further deformation of some bond angles, as shown in Table II.

The various contributions to V are given in Table III. The smaller steric hindrance in the TCC conformer of *mmmm* is indicated by the low values of the bending and nonbonded energies, but this conformation is largely unfavored with respect to the BC form by the torsional term. On the contrary in *rrrr*, the most sterically hindered isomer, V_{nbd} can be reduced only at expense of a considerable increase of V_{bend}. Finally the asymmetric *mmrr* conformer and the similar *mrmr* are mildly destabilized by the nonbonded interactions.

For a comparison of the present method with calculations which assume constant bond angles, we have minimized the energy of some conformers with respect to the torsional angles only and for several values of the ring CCC angles, all taken equal. Figure 5 shows the strong dependence of the relative energies on the value of θ_{CCC}; moreover for no value of this angle are all the relative energies close to those obtained by full minimization.

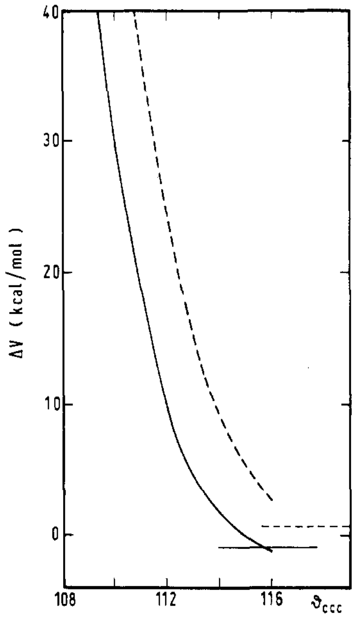


Figure 5. Energy difference between the stable conformers of *mmrr* and *mmmm* (solid line), and between the stable conformers of *rrrr* and *mmmm* (dashed line), calculated assuming rigid bond lengths and bond angles as a function of the ring bond angle. Horizontal lines indicate the corresponding energy difference found by full minimization.

At not very high temperatures the equilibrium population is negligible except for the five most stable conformers, *i.e.*, two conformers of *mmrr* and one of each other isomer. Therefore we proceeded to calculate the statistical weights, including the vibrational energy, only for these five conformers. The results are summarized in Tables IV and V. As already indicated by the energy profiles of Figures 2–4 the *mmmm* isomer is significantly stabilized by the vibrational term; minor differences, roughly proportional to the differences in potential energy, occur between the BC conformers.

Taking the most stable conformer as reference state the partition function of *mmrr* is given by

$$Z = 1 + 2W_a$$

where W_a is the statistical weight of the asymmetric con-

Table IV
Free Energy of the Stable Conformers of TMCO at 50° Referred to the Lowest Minimum of *mmrr* (kcal/mol)

Isomer	Conformer	ΔV	$\Delta E_{\mathrm{vib}}^0$	ΔF_{vib}	∇F
mmmm	TCC	0.887	−0.289	−0.483	0.115
mmrr	BC (asymm)	0.680	0.134	−0.004	0.814
mrmr	BC	0.734	0.131	−0.033	0.832
rrrr	BC	1.595	0.117	0.092	1.804

Table V
Equilibrium Population of the Four Isomers of TMCO at 50°

Isomer	Z	ΔF (kcal/mol)	Equil Pop. (%)	Yield[a] (%)
mmrr	1.566		57.2	53.8
mmmm	0.836	0.40	30.6	32.3
mrmr	0.274	1.12	10.0	11.5
rrrr	0.070	1.99	2.2	2.4

[a] By hydrogenation of 1,3,5,7-tetramethylcyclooctatetraene in the presence of palladium (ref 12).

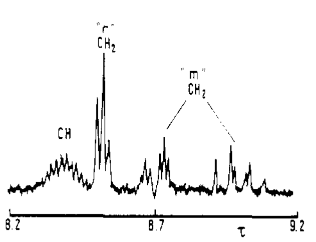


Figure 6. CH and CH_2 nmr spectrum of the *mrmr* isomer at 220 MHz in CS_2 solution at 30°.

former, while the partition function of the other isomers is provided simply by the statistical weight of their only conformer. [The asymmetric conformer of *mmrr* must be taken twice since it is a *dl* pair. The *mmmm* conformer is also a *dl* pair, but is counted once because it has symmetry number $\sigma = 2$ (twofold axis). The other conformers are also taken once since they have one plane of symmetry and $\sigma = 1$.] The resultant equilibrium populations calculated at 50° are close to the yields of the four isomers when they are obtained by hydrogenation of tetramethylcyclooctatetraene in the presence of palladium catalyst.[12] Most probably our calculation underestimates the stabilization of *mmmm* due to the molecular vibrations: in fact the very low barrier separating the four energy minima of this isomer would not allow us to consider the molecular motions as oscillations around one minimum.

Correlation of Calculated Conformations with Nmr Coupling Constants

The nmr spectra of all isomers are fairly straightforward at 220 MHz and the correct number of chemical shifts is observed in all cases. For example, Figure 6 shows the CH and CH_2 region of the *mrmr* isomer spectrum in *o*-dichlorobenzene at 30°. All four methyl groups are equivalent by symmetry and also all four methine protons, but there are two types of methylene groups. In one of these (the "*r*" group) the two protons are identical in chemical shift and form effectively an AA′XX′ system with the adjacent methine protons, but in the other (the "*m*" group) the protons are not identical, and form effectively an ABX_2 system with the adjacent methine protons. In most cases the spectra were almost first order and could be analyzed directly but in some cases spectrum simulations were performed on a trial-and-error basis in order to determine the coupling constants more accurately. This procedure was particularly useful for the *mmrr* isomer which has a strongly overlapping spectrum and for the CH resonances whose structure is not immediately clear because of the large number of couplings to each CH.

The observed coupling constants in *o*-dichlorobenzene at 30° are listed in column 3 of Table VI. Subsequent columns in this table contain coupling constants calculated according to various forms of the Karplus equation

$$\hat{J} = A + B\cos\phi + C\cos 2\phi$$

giving the variation of vicinal H–H coupling constant with the dihedral angle ϕ. The coupling constants are averaged over the conformations which are appreciably populated at 30°. These are *four identical TCC conformations for the mmmm* isomer, and two and four respectively identical BC conformations for the *mrmr* and the *rrrr* isomer. For the *mmrr* isomer the lowest energy conformation is the unique symmetric BC conformation but there are also two identical asymmetric BC conformations 0.8 kcal mol^{-1} higher in energy. The various versions of the Karplus equation are as follows

I (column 4) $A = 7.0$ Hz, $B = -1.0$ Hz, $C = 5.0$ Hz

These parameters have been derived by Bothner-By and Naar-Colin[20] and have been used in a similar correlation[21] of coupling constants and conformation in the dimethylcycloheptanes.

II (column 5) $A = 4.5$ Hz, $B = 0.5$ Hz, $C = 4.5$ Hz

This set was also suggested by Bothner-By and Naar-Colin.

III (column 6) $A = 6.45$ Hz, $B = 0.34$ Hz, $C = 5.37$ Hz

This set was determined by a least-squares fit to the coupling constants for the *mmmm*, *mrmr*, and *rrrr* isomers.

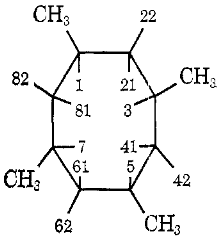
In general there is good qualitative agreement between the experimental and calculated sets of coupling constants. Quantitatively, set I gives reasonable agreement, but most of the values for set II are uniformly too low by 2–3 Hz. As is only to be expected there is very good agreement for set III and the *mmmm*, *mrmr*, and *rrrr* isomers, but the reasonable agreement between predicted and experimental coupling constants in the *mmrr* isomer is satisfactory. The application of the Karplus equation thus supports the conformational state of the tetramethylcyclooctanes elucidated by the conformational energy calculations.

There appears to be no simple connection between the chemical shifts and conformations or configurations. For instance the chemical shift of the methylene groups in the *rrrr* isomer (τ 8.79 in *o*-dichlorobenzene) falls approximately midway between the chemical shifts of the nonequivalent methylene protons in the *mmmm* isomer (τ 8.66 and 9.00). Likewise the methylene shifts in the *mmrr* isomer (τ 8.84 and 8.97 for *m* CH_2's, τ 8.82 and 9.02 for *r* CH_2's). However in the *mrmr* isomer which has a BC conformation very similar to the asymmetric BC form of the

Table VI

Isomer	Coupling Constant[a]	Expt.	Calculated[b] I	II	III
mmmm	1–21	9.5 ± 0.5	11.0	7.3	9.5
	1–22	2.5 ± 0.5	3.0	3.9	2.2
rrrr	1–21	8.7 ± 1.0	9.7	6.2	8.5
	1–22	4.1 ± 1.0	4.3	1.7	4.1
mrmr	1–21	11.5 ± 0.5	13.0	8.0	11.5
	1–22	3.0 ± 0.5	3.2	0.7	2.9
	3–21	4.5 ± 1.0	6.0	3.0	5.0
	3–22	4.5 ± 1.0	4.9	2.3	4.6
mmrr	1–21	12.0 ± 0.5	10.6	6.6	9.1
	1–22	3.0 ± 0.5	3.0	1.0	2.3
	1–81	5.5 ± 0.5	10.1	6.3	8.8
	1–82	6.0 ± 0.5	5.4	3.8	5.5
	3–21	8.5 ± 0.5	12.4	8.0	10.9
	3–22	3.0 ± 0.5	3.0	1.3	2.6
	7–81	5.5 ± 0.5	4.1	2.6	4.0
	7–82	9.5 ± 0.5	11.3	7.3	9.9

[a] The nuclei are numbered thus:



Isomer	Configuration of Methyls 1	3	5	7
mmmm	d	d	d	d
rrrr	d	l	d	l
mrmr	d	d	l	l
mmrr	d	d	d	l

[b] See text for origin of these sets.

mmrr molecule, the *r* chemical shift (τ 8.57) is well to low field of the *m* chemical shifts (τ 8.79 and 9.09). This situation is in constrast to the regular variation of CH_2 chemical shift with configuration observed in polypropylene.[6] The polymer chemical shifts have been successfully interpreted qualitatively but not quantitatively by Ando and Nishioka[22] in terms of the magnetic anisotropy of the C–C bonds. Their method is only partially successful when applied to the methylcyclooctanes investigated here. As for polypropylene, the CH_3, CH_2, and CH shifts calculated for each isomer are in the correct order, although a factor of 3 or so too small, but there are a number of discrepancies within each type of proton. For instance in the *mrmr* isomer, the *r* chemical shift is predicted to occur within the two *m* CH_2 shifts whereas, as noted above, it actually lies well to low field. Also the CH shifts in the *mrmr* and *mmmm* isomers are predicted to be to low field of the CH in *rrrr* whereas the opposite is observed. Thus Ando and Nishioka's model is probably too limited to be applied effectively to compounds with greater conformational stress than that occurring in the unstrained local conformations of polypropylene.

The CH_2 chemical shifts in polypropylene have also been rationalized by Flory and Fujiwara[23] and Peraldo[11] by an empirical relationship between the chemical shifts of units of different tacticity and the relative occurrence of certain conformations within those units. This relationship is not applicable to the present compounds which are much restricted conformationally but it is worth noting that such a simple correlation of chemical shift with conformation does not exist for these compounds, and the model may not be of general application.

Conclusions

The four stereoisomers of TMCO cannot certainly be considered completely satisfactory models of polypropylene. In fact these cyclic molecules undergo strains which have no exact correspondence in polymers. However it appears clear that the presence of strains due to large steric repulsions induce changes in the bond angles, which *must* be taken into account in the evaluation of conformational energy *differences*.

The results of the theoretical analysis of the conformations of TMCO are supported by the observed values of the vicinal proton coupling constants of the nmr spectra. Therefore the method used by us should be applicable also to the study of strained conformations of polymers. Following the same method, although using different potential functions, Boyd and Breitling have obtained a value of E_ω (the so-called pentane interference energy) significantly lower than previous authors.[24]

A second result is that there is no evidence of a straightforward correlation between chemical shifts and conformations. It is superfluous to underline the caution needed in the prediction of chemical shifts relative to polymers.

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