

125. A Dynamic Study of the Stereoisomerization of Pentaphenylethane by Molecular Mechanics Methods

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Summary

Two conformations, **1** and **2**, of pentaphenylethane are compared. The ground state conformation **2** results from an earlier computational work by force fields procedures [1], whereas **1** has been more recently observed in the crystalline state by X-ray diffraction methods. The strain energy of **1** minimizes very close to the value computed for **2**. These conformations belong to two *distinct* minima of the potential energy surface and are at the most separated by a barrier of about 7 kcal/mol. The pathway converting **1** into its enantiomer is shown to run over a barrier of only 1.5 kcal/mol.

Introduction. - Although polyphenylethanes have long been of chemical interest, extensive stereochemical investigations of the highly strained penta- (PPE) and hexaphenylethane (HPE) have only been carried out relatively recently. PPE can be regarded as a true ethane at RT., whereas HPE still remains elusive. Investigating the structure of HPE and related polyaryl compounds, *Mislow et al.* [1] have computed a ground state conformation (**2**, *Table 1*) for PPE by empirical force field methods. More recently the crystal structures of the PPE/tetrahydrofuran [2] and PPE/acetone [3] solvates were reported, confirming the expected major lengthening of the central ethane bond. However the preferred solid state conformation (**1**, *Table 1*) of PPE differs in some respects from that computed in [1].

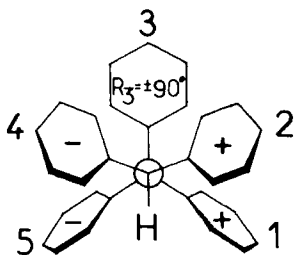


Fig. 1. The molecule of pentaphenylethane viewed down the central C, C-bond axis and the numbering system of the phenyl rings. The reported signs of the twist angles of the rings illustrate the convention used in the text.

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We show here that these conformations belong to distinct *minima* of the potential energy hypersurface and, therefore, that the conformational differences are not simple local distortions due to packing forces.

Stereoisomerization of pentaphenylethane. - It is convenient to view the PPE molecule down the central ethane bond as illustrated by the *Newman* projection in *Figure 1*. The rotational position of a phenyl ring *i* (where *i* refers to the ring label) is described by the torsion angle $R_i(C_{\text{ethane}}-C_{\text{ethane}}-C_{\text{ipso}}-C_{\text{ortho}})$ whose sign is fixed according to the usual convention and whose absolute value will be taken within the limits $0^\circ \leq |R_i| < 90^\circ$, thus precluding any ambiguity as to the choice of the C_{ortho} atom. Furthermore, each PPE conformation is characterized by the set of central dihedral angles $R_i R_j (C_{\text{ipso},i}-C_{\text{ethane}}-C_{\text{ethane}}-C_{\text{ipso},j})$.

In a trityl, or a diphenyl moiety, all the phenyl rings may be twisted in the same sense. By convention, the group with all the $R_i > 0^\circ$ is said to display a helical (*M*)-configuration; in the opposite case it exhibits a helical (*P*)-configuration. Experimental results and molecular mechanics calculations have shown that helical arrangements are in general representative of lower-energy conformations [4]: for instance, a skeleton of D_3 symmetry was calculated for the ground state of the heretofore unreported HPE [1]. In this respect, it is noteworthy that the PPE structure minimized to a non-helical structure. The stereoisomers with one or several $R_i = 0^\circ$ or 90° , generally correspond to states of higher energy arising in stereoisomerization processes. There are $2^3 = 32$ stereoisomeric forms for PPE with all $0^\circ < |R_i| < 90^\circ$ and differing at least by the sign of one phenyl twist angle. These configurations are subdivided into 16 *DL*-pairs among which only two pairs are helical. Both the conformers **1** (solid state) and **2** [1] correspond with the same stereoisomeric form as defined above. Their intrinsic geometry differ from each other mainly in that **1** bears a closer resemblance to a staggered conformation than **2**. Surprisingly, as will be seen, **1** and **2** are separated by a very small steric energy gap. Spurred on by the predicted existence of two practically isoenergetic conformations of which only one has been observed, we decided to explore the potential energy hypersurface in search of a reasonable interconversion mechanism.

Critical evaluation of the force fields employed in the investigation. - For the purpose of comparison several mechanical models were calculated, at the outset, by full relaxation of the input geometry of the X-ray structure (**1**), using the MMI and MMPI programs of *Allinger et al.* [5]. Contrary to the MMI scheme, the MMPI force field includes semi-empirical quantum mechanical calculation (VESCF method) in sequence with the standard FF calculations. The VESCF calculation is undertaken on conjugated π -systems to obtain bond orders that are involved in the assignment of new stretching and torsional parameters till self-consistency is attained. The method has been extensively discussed [5b]. The net effect of the MMPI formulation, originally introduced to handle highly deformed π -systems, is to reduce the 'rigidity' of the phenyl rings. By inspection of the contact distances in our computed models the fact emerged that, as a whole, the original *Allinger* force fields tend to underestimate the non-bonded interactions in a crowded molecule such as PPE. To increase the 'hardness' of the atoms, we selected one of the

parameters sets employed by *Mislow et al.* in the *Buckingham* potential expression²⁾ for the treatment of parent molecules [6]. The selected parameters values *a* are listed below, together with those of the original *Allinger* force field *b*. In conclusion, a

Atom <i>k</i>	<i>a</i>		<i>b</i>	
	<i>r_k</i>	ϵ_k	<i>r_k</i>	ϵ_k
H	1.50	0.060	1.50	0.063
C _{sp³}	1.50	0.116	1.75	0.041
C _{sp²}	1.95	0.060	1.85	0.030

better agreement between the observed **1** and calculated geometries was obtained when the PPE model was rendered more rigid, on the one hand by fixing constant values for the rotational parameters of the aromatic bonds (MMI scheme)³⁾, on the other hand by increasing the *van der Waals* energy by virtue of the parameters *r_k* and ϵ_k . A better concordance was not only reflected in the bond distances but also in the torsional angles and in the geometry of the phenyl rings as expressed by the out-of-plane displacements of the ring atoms. For example the original MMPI force field predicted out-of-plane distortions about 3–4 times larger than those observed for the strained Ph(5). By way of example some relevant bond distances (Å) are reported below to show how sensitive they are to non-bonded interactions as implied by the parameters sets *a* and *b* above.

	X-ray	<i>a</i> (MMI)	<i>b</i> (MMI)	<i>a</i> (MMPI)	<i>b</i> (MMPI)
C _{ethane} -C _{ethane}	1.612 (3)	1.585	1.557	1.597	1.556
⟨C _{ethane} -C _{trityl} ⟩	1.555 (7)	1.556 (6)	1.534 (5)	1.564 (8)	1.533 (4)
⟨C _{ethane} -C _{diph.} ⟩	1.530 (12)	1.541 (1)	1.522 (2)	1.542 (1)	1.521 (1)

Finally the MMI force field, implementing the set *a*, was adopted in preference to the MMPI force field in all the subsequent calculations because of a substantial saving in computing time and no less satisfying overall results with regard to **1**. The X-ray model minimized to the conformation **3** (*Table 1*). For the purpose of comparison the *Mislow* structure **2** was 'optimized' with our force field and yielded the conformation **4** (*Table 1*). The molecular mechanics models are representative of *isolated* molecules preserved from any external influence. Accordingly, the small conformational differences between **1** and **3** may be taken as indicative of a very small contribution of the packing forces to the actual solid state structure. As a matter of fact the geometries of **3** and **4** differ from each other to a larger extent in spite of their vanishing steric energy difference of about 1 kcal/mol in favor of the 'more stable' conformation **4**.

A dynamic approach to the stereoisomerization of 3 into 4. - As already mentioned, the change of sign of a torsional angle *R_i* affords a new stereoisomeric

2) The non-bonded interaction energy is expressed by the equation: $E_{\text{non-bonded}} = \epsilon^* \{ 8.28 \cdot 10^5 \exp(-r/0.0736 \cdot r^*) - 2.25 (r^*/r)^6 \}$; where ϵ^* (kcal/mol) = $(\epsilon_i \epsilon_j)^{1/2}$; r^* (Å) = $r_i + r_j$; r_i , r_j are the atomic *van der Waals* radii, *r* is the effective interatomic distance (Å).

3) Effects due to variations in the π -conjugation, resulting from local distortions, are ignored.

Table 1. *Minimum-energy conformations of pentaphenylethane*

Structural data ^{a)}	1 ^{b)} f)	2 ^{c)}	3 ^{d)}	4 ^{e)}
R_1	2.0	39.3	7.4	28.6
R_2	50.5	25.4	50.3	21.6
R_3	-76.0	-88.0	-74.9	-83.5
R_4	82.9	86.2	84.9	90.0
R_5	-47.3	-20.2	-49.5	-25.3
R_1R_2	51.7	30.0	45.9	35.6
R_2R_3	-71.4	-99.6	-77.0	-90.8
R_3R_4	59.1	41.0	65.0	46.6
R_4R_5	-65.0	-77.4	-58.7	-73.6
R_5H	50.9	33.5	50.2	39.4
R_1H	-61.8	-76.5	-63.3	-73.9
$C_{eth}-C_{eth}$ (Å)	1.612	1.595	1.585	1.602
Steric energy ^{g)}	-	-	71.2	70.0

^{a)} See text for the meaning of the symbols. ^{b)} X-ray structure [3]. ^{c)} Calculated in [1]. ^{d)} ^{e)} Optimization, with our force field, of the input geometry of 1, respectively 2. ^{f)} (°); the standard deviations for the dihedral angles are $\sigma_R \approx \sigma_{RR} \leq 0.26^\circ$ and $\sigma_{RH} = 1.4^\circ$. ^{g)} kcal mol⁻¹.

form. The ring motion may occur *via* the values $R_i = 0^\circ$ or 90° (in the former case it is said that the ring 'flips'). This distinction has proved of great service in the description of the stereoisomerization pathways of *three-bladed* propellers [4] [7]. In the case of PPE, however, this approach is largely obscured by the intricate correlation of ring motions *between* the trityl and diphenyl moieties, and a general dynamic study of PPE would involve a formidable task far beyond the scope of the present investigation.

The isomerization process was most simply interpreted in terms of the constrained incremental rotation (ΔR_i) of *one* selected phenyl ring Ph(*i*), while the rest of the molecule was given full freedom of movement. In the first series of calculations a fixed number of iterations (~ 85) was allocated to each run (one point of the energy diagram)⁴⁾ thus allowing a semi-quantitative estimation of the potential energy profile. At the second stage, the steric energy was minimized at the points of interest of the energy profile. The structural parameters of 3 were arbitrarily used as initial input geometry from which the independent rotational parameters ΔR_i were incremented.

Rotation of Ph(3). With regard to the correlation of motions of the phenyl rings, Ph(3) assumes a unique position in the *quasi-staggered* ethane frame, because it is *directly* coupled with the four other rings, whereas the latter are in *van der Waals* contact with only three congeners and *indirectly* coupled with the fourth. The potential energy diagram is illustrated in *Figure 2* as a function of ΔR_3 . As mentioned previously the steric energies do not correspond to full minimization; nevertheless the energy profile gives a satisfactory representation of the isomerization itinerary with the location of the troughs and barriers (denoted by

⁴⁾ In each structure the driven ring was attributed an average rigid geometry: C_{2v} symmetry with C_2 coaxial with the $C_{ethane}-C_{phenyl}$ bond (of constant length 1.545 Å); the C,C-bonds were as follows: *ipso-ortho* = 1.389, *ortho-meta* = 1.387, *meta-para* = 1.374 Å; $C_{phenyl}-H$ = 1.08 Å; the valence bond angles at the *ipso*, *ortho*, *meta* and *para*-positions were: 116.9, 121.6, 120.4 and 119.1°, respectively.

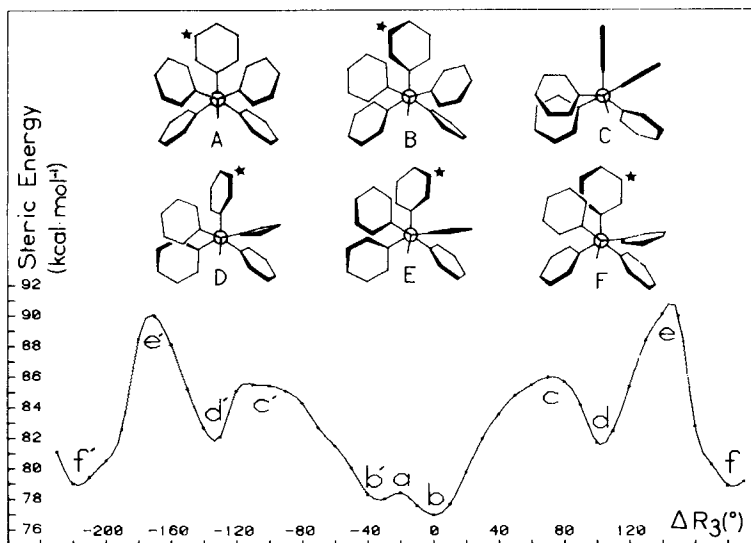


Fig. 2. Potential energy profile and some relevant conformations of PPE as functions of the varying torsion angle R_3 . The direction of motion of the ring is visualized by the aid of a starred atom in *meta* position. The twist angle of Ph(3) in the solid state structure **B** is arbitrarily chosen for the origin ($\Delta R_3 = 0^\circ$) of the incremental rotation. An increase in the value of ΔR_3 corresponds to anti-clockwise rotation.

small letters). The corresponding conformations (labelled with capital letters) were further optimized with the necessary inclusion of a minimum number of geometrical constraints⁵⁾. The conformational parameters and steric energies are listed in Table 2. The bias resulting from the constraints can be evaluated in comparing **B** and **F** (Table 2) with the corresponding fully relaxed structures **3** and **4** (Table 1).

Clockwise⁶⁾ rotation of Ph(3) leads to a vicinal energy minimum **b'** corresponding to the enantiomeric form of the conformer **B**. The pathway connecting **b** to **b'** runs over the turning point **a** that proved to be the transition state of the racemization process⁷⁾. Accordingly, the conformer corresponding to the potential well **f'** minimized to the enantiomeric form of **F**. The conformation **A*** at the top **a** deviates in some respects from the C_s symmetry that might be postulated in the transition state; moreover if this structure is optimized with reflection symmetry constraints, conspicuously short ($C_{\text{ethane}}-C_{\text{ethane}} = 1.561$) and long ($C_{\text{ethane}}-C_{\text{phenyl}} = 1.581 \text{ \AA}$ in the trityl group) bonds ensue in the new model (**A**). In spite of **A** appearing to be less stable than **A*** by 0.5 kcal/mol the occurrence of a symmetrical transition

5) These constraints are dictated by the optimization of conformations at *maxima* of the energy curve. For the sake of comparison they were retained at the *minima* of the curve. The constraints consist of ascribing constant values to the following internal parameters related to the driven ring: the $C_{\text{ethane}}-C_{\text{ipso}}$ and $C_{\text{ipso}}-C_{\text{ortho}}$ bonds, the $C_{\text{ethane}}-C_{\text{ipso}}-C_{\text{ortho}}$ bond angle, and the incremented dihedral angle.

6) The phenyl ring is viewed down a virtual axis passing through $C_{\text{para}} \cdots C_{\text{ipso}}$, with the C_{para} atom close to the observer.

7) In Figure 2, the section **a**→**f'** is not the perfect mirror image of its 'enantiomeric' counterpart **a**→**f** owing to the truncation of the energy minimization.

Table 2. Calculated conformations^{a)} of pentaphenylethane at the minima and maxima of the **B**⇌**F** interconversion pathway^{b)}

Structural data	A [#]	A ^{c)}	B	C	D	E	F
R_1	28	23	9	-25	24	25	21
R_2	71	67	53	4	5	2	11
R_3	-90	-90	-74	0	30	60	-82
R_4	-73	-67	89	-78	-87	-77	90
R_5	-26	-23	-45	-79	82	73	-33
R_1R_2	48	55	49	68	46	41	43
R_2R_3	-75	-69	-75	-60	-79	-84	-85
R_3R_4	68	69	67	89	69	58	52
R_4R_5	-55	-55	-56	-28	-50	-63	-68
R_5H	54	56	54	82	58	50	46
R_1H	-60	-56	-60	-34	-59	-65	-66
$C_{eth.} - C_{eth.}$ (Å)	1.600	1.561	1.600	1.617	1.600	1.606	1.603
Steric energy	72.9	73.4	71.5	76.7	73.8	78.0	71.0

^{a)} The conformations were optimized subject to certain necessary constraints, and are reported with the respective values of their steric energy (kcal mol⁻¹). ^{b)} See Figure 2. ^{c)} C_s symmetrical transition state conformation of the enantiomerization process.

state conformation does not seem unreasonable in view of the symmetrical appearance of the energy profile with respect to the barrier **a**⁸⁾.

Rotation of Ph(3) of half a turn in anti-clockwise direction brings about a favorable correlation of the phenyl motions leading to the sought for conformation **F**. The interconversion itinerary involves two energy barriers **c** and **e** (Fig. 2). The higher barrier corresponds to an activation energy of 6.5–7.0 kcal/mol with respect to the low-energy conformations **B** and **F**. The transition state structure **E** has the trityl group in a (*M*)-helical configuration and the ring Ph(2) eclipses the central ethane bond (ring flip). The latter situation is sterically very unfavorable and recurs for Ph(2) and Ph(3) at the top of the barrier **c**. The correlated torsional motions of the phenyl rings are reported graphically⁹⁾ in Figure 3a for a complete revolution of Ph(3). The symmetry of the interconversion pathway is reflected in the centrosymmetrical lay-out of the curves. Each cross-point of a curve with the horizontal line ($R_i = 0^\circ$) corresponds with a flip of the ring. The ring motions are coupled in no simple way, except along that section of the pathway passing over the racemization barrier (**b**→**b'**; shaded area in Fig. 3) where the values of all the dihedral angles fit fairly well a linear dependance on ΔR_3 , with the sense of the rotations opposite to that of R_3 . Within the same section, the dihedral angles R_iR_j are relatively insensitive to the variation of ΔR_3 and the ethane frame preserves a near- C_s symmetry. Despite the fact that the minimum-energy conformations **B** and **F** are characterized by the same stereoisomeric form, they are interconverted by the

⁸⁾ The existence of another energetically favorable racemization mechanism not involving a C_s symmetrical transition state cannot be excluded. However with due consideration of the effects of the constraints in the minimization procedure we will not aim for a determination of its relative (if any) contribution.

⁹⁾ Emphasis is placed on the fact that the dihedral angles values R_i (Fig. 3a) and R_iR_j (Fig. 3b) results from calculations implying truncated minimizations and therefore differ slightly from those in Table 2.

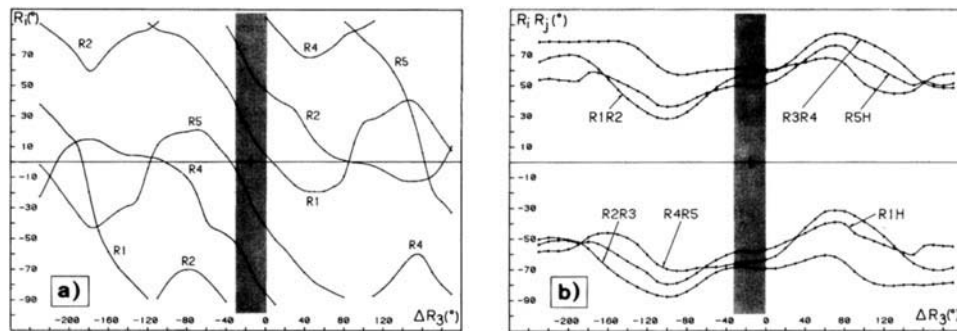


Fig. 3. Deformations of some characteristic dihedral angles (described in the text) resulting from the incremental rotation (ΔR_3) of *Ph*(3). These curves can be regarded as a one-dimensional dynamic illustration of the main conformational changes occurring in the stereoisomerization process.

successive occurrence of no less than eight different intermediate stereoisomeric forms. In contrast to **B** and **F**, all these forms exhibit at least a helical configuration for either the trityl or the diphenyl group (and some for both of them).

Rotation of Ph(2), respectively Ph(1). The constrained clockwise rotation of *Ph*(2) first entails a rapid increase of the strain energy up to a value¹⁰⁾ of about 83 kcal/mol ($\Delta R_2 \approx -30^\circ$), then the potential energy remains approximately constant till the ring flips, after having passed through the position assumed in the conformation **F**. The correlated motions of the four other rings appear to be surprisingly insensitive to the rotation of *Ph*(2) from $R_2 = 53^\circ$ to $R_2 = 0^\circ$; their dihedral angle (as well as the internal $R_i R_j$) all vary by less than 10° . Following these results and since it was necessary to limit our exploration of the potential energy surface the process was not further investigated along this pathway. On the other hand anti-clockwise rotation of either *Ph*(2) or *Ph*(1) yields the transition state conformer **A**. This is not so surprising in consideration of the linear relationships that seem to prevail between the rotational motions of the rings in the vicinity of the racemization barrier.

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¹⁰⁾ This value has to be compared with those of the diagram in *Figure 2*.