Semiempirical Calculations on Phenylcarbene, Cycloheptatrienylidene, and Cycloheptatetraene and Their Benzo-Annelated Derivatives

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Abstract: Theoretical evidence indicating that both cycloheptatrienylidene and cycloheptatetraene may exist in singlet electronic states is presented. The nonplanar allene structure is predicted to be the more stable form. A new, slightly nonplanar, structure is suggested for phenylcarbene. Calculated stabilizing effects of annelation at various sites on phenylcarbene, cycloheptatrienylidene, and cycloheptatetraene, which satisfactorily explain the effect of annelation on carbene–carbene rearrangements, are reported.

In recent years, considerable attention has been given to the chemistry of a number of carbenes in which the p_z orbital of the singlet state is incorporated in a cyclic conjugated system having $4n + 2$ π electrons.[1] These so-called aromatic carbenes have been found to exhibit a number of anomalous chemical properties, most of which are easily understood on the basis of simple theories of aromaticity. However, there have emerged at least two strange phenomena which have not yielded to such a simple approach.

It has been found[2] that annelation apparently shifts the following reaction to the left.

$$(1)$$
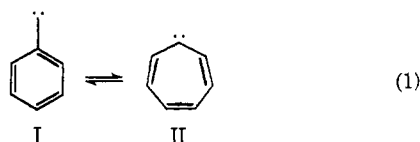
Thus, whereas phenylcarbene (I) (gas phase, 250°)[2] gives a fair yield of the dimer of cycloheptatrienylidene (II), under comparable conditions naphthylcarbene gives only naphthylcarbene products.[3] Furthermore, in contrast to II which gives only its dimer when in solution at room temperature, VI, VIII, and XVI undergo facile rearrangement to give naphthylcarbene and phenanthrylcarbene products (see Figure 6).

A second anomaly has appeared in studies[4] of the chemistry of the β-methanoannulenylidene in eq 2, which have found that some of its behavior can best be explained in terms of an allene form.

$$(2)$$
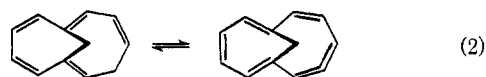
Since detailed molecular orbital calculations could shed light on both the effect of annelation on the position of the equilibrium in eq 1 and the relative stabil-

ities of carbene and allene forms such as those in eq 2, a series of semiempirical calculations using the intermediate neglect of differential overlap (INDO) procedure has been made.

Although some previous semiempirical calculations for similar systems have been reported, based on the extended Hückel[5] and CNDO/2[6] schemes, they have not dealt with possible structural variations in any systematic way.

We thus report the results of a series of calculations on the carbene and allene forms of the seven-membered ring and on the related phenycarbene and on their benzo-annelated derivatives. Geometry variations have been carried out, subject to certain constraints, and results are interpreted with emphasis on the bond structure of the compounds considered.

Calculations

Calculations were carried out using the well-known semiempirical INDO scheme.[7] As the method is now nearly standard, suffice it to say that it is an all-valence electron LCAO–MO–SCF scheme based on a parametrized Fock matrix. Details of the method may be found elsewhere.[8]

Cycloheptatrienylidene. An optimized structure for cycloheptatrienylidene, in a singlet electronic state, was determined on the basis of minimizing the INDO total energy of the molecule. Energies were obtained for various trial geometries, including several with varying degrees of nonplanarity which could have been favorable due to relief of bond angle strain. Lowest total energies resulted for a planar model which allowed the $C_2C_1C_7$ bond angle and C_1–C_2($= C_1$–C_7) bond length to be varied independently (Figure 1). This was accomplished by expanding or contracting the rest of the ring, depending on the resultant C_2–C_7 distance. The remaining atomic coordinates were determined by this distance and the requirements: (1) that (internal) ring angle C_2 equal ring angle C_7 and (2) that ring angles C_3, C_4, C_5, and C_6 be equal. The C–H bonds bisected the external angles at the corresponding carbon

(1) *Cf.* E. E. Waali and W. M. Jones, *J. Org. Chem.*, **38**, 2573 (1973); W. M. Jones and C. L. Ennis, *J. Amer. Chem. Soc.*, **91**, 6391 (1969), and references cited therein.

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(3) T. Mitsuhashi and W. M. Jones, *J. Amer. Chem. Soc.*, **94**, 677 (1972).

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(7) P. A. Dobosh, Program CNINDO, No. 141 from the Quantum Chemistry Program Exchange, Bloomington, Ind.

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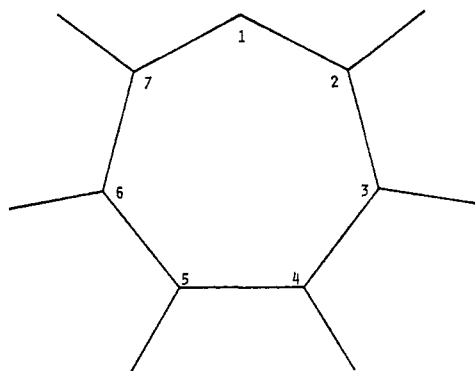
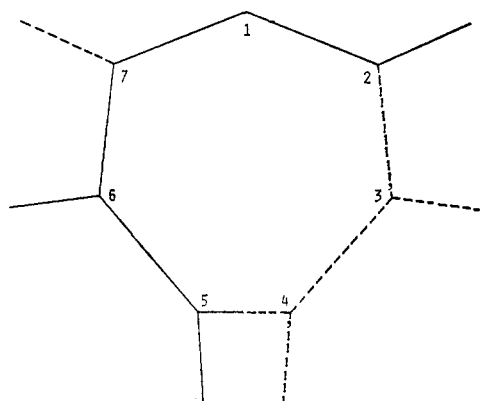Figure 1. Cycloheptatrienylidene geometric model.

Figure 2. Cycloheptatretraene geometric model (Z coordinates suppressed: dotted lines indicate negative Z; solid lines indicate positive Z).

atoms. A minimum total energy of -52.10925 au was obtained, for C_1–C_2 bond length of 1.38 Å and $\angle C_2 C_1 C_7 = 124°$.

This geometry suggested a distorted sp^2 hybridization at C_1. Indeed, orbitals of this type were constructed,[9] and examination of the INDO density matrix elements with respect to the nonbonding orbital of C_1 (pointing outward from the ring and in the plane of the molecule) indicated an occupation number of 1.87 electrons. Hence, this optimal geometric model was adopted for cycloheptatrienylidene. The stability of this structure is attributed to conjugation of the p_z orbital of C_1 with the π cloud (containing six π electrons) of the rest of the ring. INDO calculations indicate that the C_1 orbital has an occupation of 0.64 electron acquired at the expense of all of the other p_z orbitals which consequently have occupation numbers less than unity. This conjugation also explains why the lone pair orbital has, on the average, less than two electrons, in that the charge on C_1 is increased by conjugation and partially balanced by decreased population of the lone pair orbital.

Cycloheptatetraene. As a model for the allene in eq 2, calculations were also carried out on cycloheptatetraene (III),[10] the allene analog to II. The problem

(9) J. C. Schug, "Introductory Quantum Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1972.

(10) Nonplanar cycloheptatetraene, either in equilibrium with or possibly as an alternative to planar cycloheptatrienylidene, was first suggested by K. Untch at the International Symposium on the Chemistry of Nonbenzenoid Aromatic Compounds, Sendai, Japan, August 1970. We are indebted to Dr. Untch for informing us of his work.
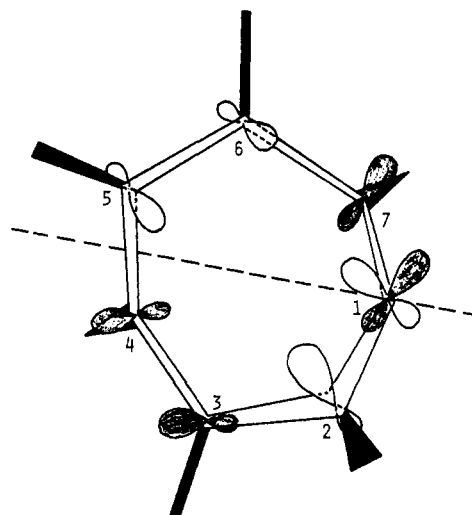
Figure 3. π bonding in cycloheptatetraene (dotted line indicates C_2 symmetry axis).

III

of determining its geometry was approached by calculating total energies for several nonplanar structures which seemed likely to accomodate the characteristic allene bond (i.e., to have hybridized orbitals at C_1 directed so that bonds could form with the p-type orbitals of both neighboring sp^2 hybridized carbon atoms) and to relieve bond angle strain. One configuration was particularly stable (Figure 2). The first energy calculated using the model was for a structure having all C–C bond lengths of 1.4 Å and all ring angles of 120°. The model was then optimized by varying the C_1–C_2 bond length and $C_2 C_1 C_7$ bond angle dependently; i.e., all other atoms were fixed, then C_1 was moved inward along the altitude of the triangle formed by $C_2 C_1 C_7$. The optimum position of C_1 resulted in a C_1–C_2 bond length of 1.30 Å, $\angle C_2 C_1 C_7 = 136.4°$, and a total energy of -52.13123 au. This optimal structure was taken to be a reasonable representation of the allene cycloheptatetraene. The configuration has a C_2 symmetry axis and exists in two enantiomeric forms.

The stability of this structure is attributed to occupancy of an additional bonding orbital and to a lack of a bond angle strain, except for the distorted sp hybridization at C_1 and a slight deviation from perfect sp^2 hybridization at the adjacent carbon atoms. The alignment of the orbitals used for π bonding is shown in Figure 3. The sp hybridization at C_1 leaves two p-type orbitals for π bonding, one to overlap with the p-type orbital (no longer oriented in the z direction) of each neighboring carbon atom. Thus, there is no lone pair as in a carbene.

Phenylcarbene. For purposes of studying the relative energies of phenylcarbenes and cycloheptatrienylidenes, an optimal geometry for phenylcarbene was required. The phenyl group geometry was assumed to be a regular hexagon with C–C bond lengths of 1.40 Å and C–H bond lengths of 1.08 Å. Under the assumption that the C_1–H_1 bond length was also 1.08 Å, the geometric parameters left to be determined by total
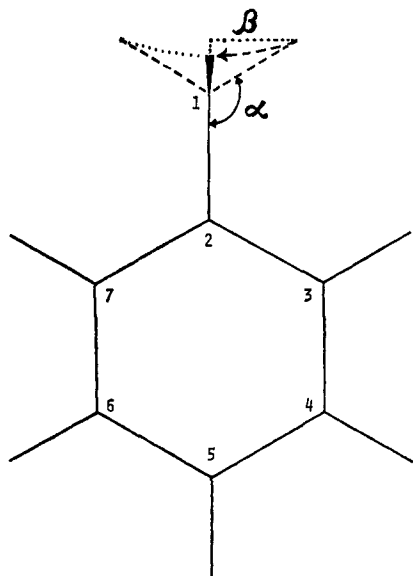
Figure 4. Phenylcarbene geometric model.

Figure 5. Phenylcarbene total energy as a function of out-of-plane rotation (β) for $\alpha = 120°$ and C_1-C_2 bond lengths of (a) 1.54 Å and (b) 1.38 Å.

energy minimization were the C_1-C_2 bond length and the H_1 position with respect to both angle $H_1C_1C_2$ (α) and the out-of-plane rotation angle (β) (Figure 4).

The geometry determined by Gleiter and Hoffmann,[5] using extended Hückel methods, was planar, with the C_1-C_2 bond length of 1.54 Å and with H_1 located in the plane of the phenyl group $(\beta = 0°)$ at an angle (α) of 115–120° (Figure 5). (The C_1-H_1 bond length was 1.1 Å.) INDO calculations using the above bond lengths showed that total energy minimization favored a rotation about the C_1-H_1 bond to a geometry such that H_1 was located in a (symmetry) plane perpendicular to the plane of the phenyl group $(\beta = 90°)$. Varying the C_1-C_2 bond length for $\beta = 90°$ yielded an optimum geometry having a C_1-C_2 bond length of 1.38 Å and $\alpha = 120°$ (α was also varied). The minimum energy was -52.09683 au.

The shortness of the C_1-C_2 bond for the optimum geometry determined herein seems to suggest that a structural representation indicating double bond character at this position may be appropriate. The stability of this structure is attributed to hyperconjugation of the lone pair sp^2 orbital of C_1 with the π cloud of the phenyl group. Compared to the planar geometry, possible steric interference between hydrogen atoms (H_1-H_3, H_1-H_7) is decreased.

Annelation. Figure 6 identifies all of the possible benzo-annelated derivatives of phenylcarbene, cycloheptatrienylidene, and cycloheptatetraene. Table I gives their total energies (hartrees), stabilizations, relative energies, and dipole moments. The stabilization is defined to be the total energy of the derivative minus the total energy of the nonannelated species from which it was derived. The relative energy, given in kilocalories for convenience, is computed with respect to the least stable isomer in a given row of Figure 6, for which the relative energy is defined to be zero.

The structures were assumed to be composed of the nonannelated species with the appropriate hydrogen atoms replaced by a regular hexagon concatenated to the common C–C bond. In the case of cycloheptatetraene, since no two C–H bonds were coplanar with the C–C bond joining them, the plane of the annelating
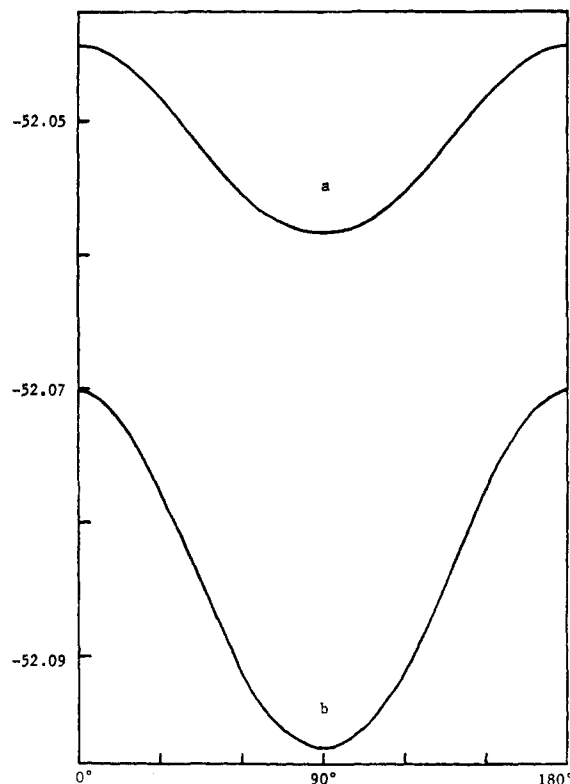
benzene ring was assumed to bisect the dihedral angle between the C–H bonds. Thus, the geometries of the annelated derivatives were not further optimized.

Aromaticity. The molecular orbitals generated by an INDO calculation are not very useful to the chemist for study of specific types of bonding in that the MO's have components from AO's on all of the carbon atoms in the molecule. The localized orbital procedure[11] was designed to transform the occupied INDO molecular orbitals into an equivalent set of orbitals which could often be identified with particular combinations of hybrid orbitals used in classical pictures of bonding.

When this procedure is applied[12] to phenylcarbene, the aromaticity of the phenyl group is apparent as three delocalized π orbitals. Examination of the density matrix shows that the π cloud of the ring contains slightly more than six electrons, due to hyperconjugation with the lone pair of the external carbon atom. The localized orbital technique, when applied to cycloheptatrienylidene, indicates that it too has a delocalized π system (including the p_z orbital of C_1), this time having exactly six π electrons.

The localized orbitals show clearly the drastically different bonding of cycloheptatetraene. Although the nonplanarity of the molecule makes it more difficult to recognize the π orbitals (since the localized orbitals, like the original INDO–MO's, are expressed in terms of AO's directed along fixed x, y, and z axes on the atomic centers), there is no problem seeing that the π electrons are not delocalized. The results show that

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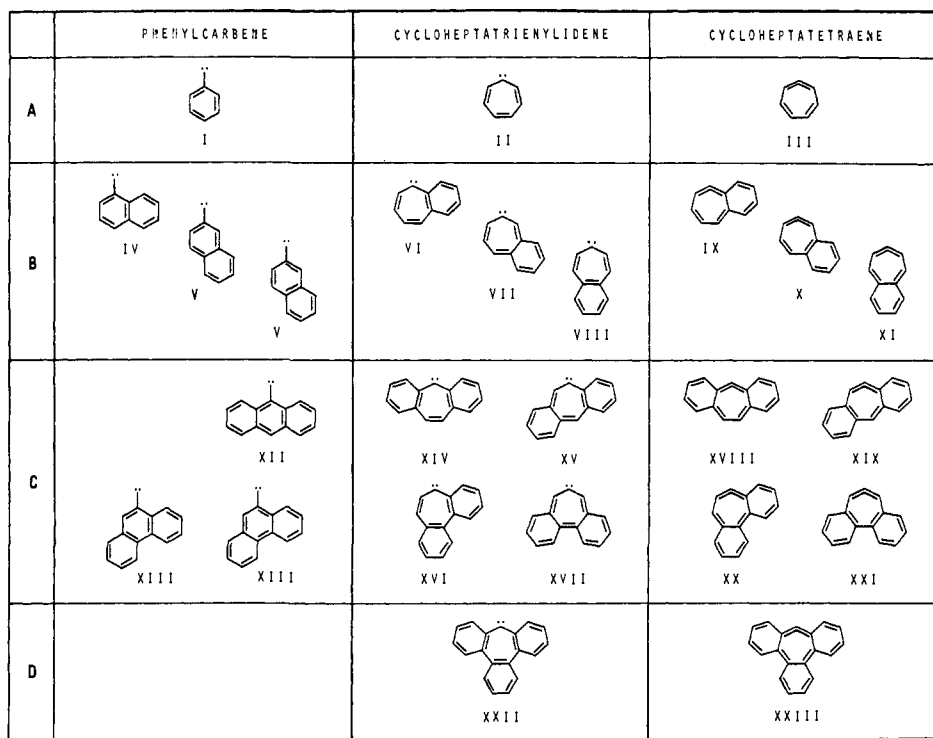
Figure 6. Classification of annelation products.

Table I. Total Energies (hartrees), Stabilizations (hartrees), Relative Total Energies (kcal), and Dipole Moments (D) for Phenylcarbene, Cycloheptatrienylidene, and Cycloheptatetraene and Their Benzo-Annelated Derivatives (Pictured in Figure 6)

	Phenylcarbene		Cycloheptatrienylidene		Cycloheptatetraene
			Total energy, au Stabilization, au Relative energy, kcal Dipole moment, D		
I	−52.09683	II	−52.10925	III	−52.13123
	0.0		−7.7936		−21.5886
	1.8703		5.8213		0.8642
IV	−81.04491	VI	−81.06371	IX	−81.03045
	−28.94808		−28.95446		−28.89922
	−9.0713		−20.8686		0.0
	1.7391		5.1583		1.4181
V	−81.05118	VII	−81.05402	X	−81.12763
	−28.95435		−28.94477		−28.99640
	−13.0090		−14.7895		−60.9821
	1.9037		6.5447		0.6508
V	−81.05118	VIII	−81.06055	XI	−81.07217
	−28.95435		−28.95130		−28.94094
	−13.0090		−18.8869		−26.1794
	1.9037		6.8600		1.2560
		XIV	−110.02983	XVIII	−109.93414
			−57.92058		−57.80290
			−60.0464		0.0
			3.6989		2.4739
XII	−110.00202	XV	−109.99872	XIX	−110.02196
	−57.90519		−57.88947		−57.89073
	−42.5990		−40.5270		−55.1095
	1.6041		6.1960		0.9904
XIII	−110.02195	XVI	−109.98401	XX	−109.98989
	−57.92512		−57.87476		−57.85865
	−55.1014		−31.2935		−34.9848
	1.9203		5.7280		1.5710
XIII	−110.02195	XVII	−109.96918	XXI	−110.12554
	−57.92512		−57.85993		−57.99433
	−55.1014		−21.9881		−120.1267
	1.9203		6.5766		0.3808
		XXII	−138.91549	XXIII	−138.00758
			−86.80624		−86.77635
			−4.9645		0.0
			4.0274		2.3163

the double bonds of the allene are indeed located as indicated in representation III. Thus, the behavior of cycloheptatetraenes should be expected to be different from that of the aromatic carbenes.

Discussion

The calculations satisfactorily account for both the equilibrium anomalies of eq 1 and the unusual chemical properties of the β-methanoannulenylidene in eq 2. Table I gives the total energies, stabilizations, relative total energies, and dipole moments of the molecules in Figure 6. Since different assumptions were made for the geometries of the nonannelated species, caution must be exercised when making quantitative comparisons between energies in different columns of Table I. However, the stabilizations due to annelation are differences in energies calculated under the same basic assumptions, and they may be compared quantitatively with more confidence.

If one compares the total energies and stabilizations of the cycloheptatrienylidene derivatives with their arylcarbene analogs (e.g., IV and VI, V and VII or VIII, in Table I or Figure 6), it can be seen that, with only one exception, annelation has a more pronounced stabilizing effect on the arylcarbenes than on the corresponding isomeric aromatic (planar) carbenes. Thus, the calculated total energies reflect qualitatively the observed experimental equilibria.

Furthermore, the allene form of the methanoannulenylidene in eq 2 becomes eminently reasonable as a possible reactive intermediate since, according to the calculations, even the more highly strained seven-membered ring prefers the tetraene structure. Even though the chemistry of the parent seven-membered system is that expected of a carbene rather than an allene (three-membered ring formation from alkenes, including ethylene, rather than their thermodynam-

ically favored cyclobutane isomers;[1,13] heptafulvalene formation rather than its dimethylenecyclobutane isomer,[4] etc.), these calculations indicate that aromatic carbenes as small as the seven-membered ring system might well be in equilibrium with allene forms. Although it must be recognized that the position of such equilibria would certainly be affected by differences in solvation due to the large difference in dipole moments of the two species, an explanation for the anomalous chemistry of the intermediate in eq 2 would simply require an equilibrium lying far enough toward the allene to allow reactions to dominate those of the carbene.

It is also interesting to compare the effect of the location of the annelating benzene ring on the relative stabilities of the carbene and the allene forms of seven-membered ring systems. As would be expected from

classical resonance forms, monoannelation at the 2,3 or 4,5 positions stabilizes the carbene form relative to its allene isomer. Conversely, annelation in the 3,4 position has a pronounced stabilizing effect on the allene form. As would be expected, these trends are even more pronounced in the diannelated cases. Thus, it would appear from these calculations that the 3,4-diannelated isomer should be a good model system for a study of the chemistry of cycloheptatetraene whereas 2,3- or 4,5-annelated isomers would better represent the carbene.

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A Theoretical Study of Solvent Effects on the Conformational Stability of Acetylcholine

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Abstract: The conformational stability of the chemical neurotransmitter acetylcholine in water and in chloroform is discussed based on quantum theoretical studies of the isolated molecular ion and solvation energies computed from the calculated solute properties and physicochemical properties of the solvent. The solvation energy is partitioned into electrostatic, dispersion, and cavity terms. A comparison of theory and experiment and a discussion of the biological significance of the results are presented.

The development of theoretical methods based on quantum mechanics for treating the electronic structure of large polyatomic molecules has provided widely used techniques for treating conformational stability problems in chemistry and biochemistry. The theoretical calculations are customarily carried out in the "free-space approximation," treating the molecule or molecular ion under consideration as an isolated, independent entity. There has generally been considerable accord between theoretically calculated energetically preferred geometries and the structures observed in the crystalline solid using X-ray or neutron diffraction methods and in the gas phase using microwave spectroscopy. Nevertheless, a number of systems wherein the geometry of a molecule adopted in the solid or gas phase differs significantly from that observed in solution have been experimentally characterized, and it is clear that a general theoretical account of the conformational stability of a molecule in solution requires explicit consideration of environmental effects.

Such problems are clearly evident in structural studies of acetylcholine (Ach), where a detailed knowledge of the structural chemistry is considered a vital prerequisite to the understanding of cholinergic neural transmission systems at a molecular level.[1] Experi-

mental data are available on Ach in solid[2,3] and solution,[4-8] and theoretical studies have been reported for Ach using a variety of models and methods.[1,9-17] The relevance of the calculated results to the conformational

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