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Applications of ab initio molecular orbital theory to large organic molecules

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APPLICATIONS OF AB INITIO MOLECULAR ORBITAL THEORY TO LARGE ORGANIC MOLECULES

by

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A dissertation submitted to the Graduate Faculty in Chemistry in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York.

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GENERAL INTRODUCTION

This thesis, entitled, 'Applications of Ab Initio Molecular Orbital Theory to Large Organic Molecules', consists of research on two diverse chemical projects: thermochemistry, (Project I), and medicinal chemistry, (Project II). In project I, ab initio molecular orbital calculations were used to calculate the heats of reaction, heats of formation and molecular geometries for 16 aromatic molecules ranging in size from benzene to coronene. In project II, theoretical calculations formed the basis of a conformational study of the muscarinic agonist pilocarpine. The potential surface of pilocarpine was studied by molecular mechanics, and semiempirical and ab initio molecular orbital calculations. From the results of these calculations, a possible biologically active conformation of pilocarpine was deduced.

1. A METHOD FOR CONVERTING AB INITIO ENERGIES TO ENTHALPIES OF REACTION AND FORMATION OF AROMATICS

Introduction

Molecular orbital theory can be used in the calculation of thermodynamic properties of molecules. Such theoretical calculations enable the prediction of experimental properties that are as yet unknown. Conversely, for known properties they provide a test of the reliability of the method of calculation. This study involves the theoretical calculation of enthalpies of reaction and formation for aromatic molecules from ab initio molecular orbital energies. Computer programs capable of calculating ab initio molecular energies for large molecules (up to 24 carbons in the present study) make this research possible.

When the ab initio energies are available, heats of reaction and formation can be calculated by construction of hypothetical isodesmic[1] and homodesmic[2] reactions. Both isodesmic and homodesmic reactions balance the numbers of bonds of each type; homodesmic reactions also require equal numbers of bonds between atoms of the same hybridization and chemical group.[3] The determination of reaction enthalpies, however, usually requires the zero-point energies, heat capacities and heats of formation for each reactant and product involved - quantities not always available. By use of the alternative group-equivalent scheme of Wiberg[4] (or the

atom equivalent scheme of Ibrahim and Schleyer[5], heats of formation can be calculated from ab initio molecular energies alone. The group equivalents or atom equivalents are obtained by a least-squares fit of the ab initio molecular energies to known experimental heats of formation, for some training set.

The homodesmic scheme, when carried out at the 6-31G* SCF level, is adequate for most molecules, except those having a high degree of strain energy.[6] Second-order correlation energies are necessary in the case of strained molecules[7], but for an important class of molecules, the aromatics, experimental heats of reaction and formation are not reasonably reproduced even when this is done in the large 6-31G* basis set. Thus the heat of formation of benzene, derived from the homodesmic reaction,

benzene + (3)ethylene ---> (3)butadiene

is in error by 3.7 and 7.9 kcal/mol at the 6-31G* SCF and RMP2 levels, respectively. Moreover, the defect at the 6-31G* RMP2 level is not ameliorated by substantial enlargement of the basis set. Similarly, the atom equivalent scheme furnishes a heat of formation of benzene which is too low by 7.7 kcal/mol.

For naphthalene, the homodesmic reaction

naphthalene + (5)ethylene + (4)propene --->

(6)butadiene+(2)isobutene

furnishes a heat of reaction in error by 6.6 and 14.3 kcal/mol at the 6-31G* SCF and RMP2 levels, respectively. The heat of

formation derived from atom equivalents in the same basis is too low by 8.9 kcal/mol.

The present work offers two improved methods for calculating the heats of reaction and formation of aromatic molecules. It is shown that when both reactants and products in homodesmic reactions are restricted to the class of aromatics, experimental enthalpy changes can be successfully reproduced. The method works best when the aromatics are further restricted to benzenoid hydrocarbons. This strongly suggests a nearly complete cancellation of electron correlation energies when only benzenoid aromatics are contained in the reaction.

In this study we obtain group equivalents which can be used to convert ab initio total molecular energies of aromatics to heats of formation. The procedure is highly accurate and more general than the homodesmic scheme.

Geometries

The geometries of the molecules shown in Figure 1.1 were optimized at the STO-3G level, assuming symmetries of D_{6h}: benzene 1, coronene 15; D_{3h}: triphenylene 9; D_{2h}: naphthalene 2, biphenylene 4, anthracene 6, pyrene 8, tetracene 11, perylene 14; C_{2v}: azulene 3, phenanthrene 7, acenaphthylene 5; C_{2h}: chrysene 10, C_2: 3,4-benzophenanthrene 12; C_s: 1,2-benzanthracene 13. The molecular energies at these geometries were also calculated at the 3-21G and 6-31G* SCF levels. In

addition, the geometries of molecules 1 through 16 excluding 13 were also optimized at the 6-31G* SCF level. AM1 structures and energies for each of these molecules were obtained assuming the same symmetries as above.

The calculated bond lengths at the STO-3G geometry, given in Table 1.1, range from 1.329 to 1.516 Å, the average for 114 bonds being 1.408 Å. The corresponding experimental range and average are 1.338-1.514 and 1.409 Å, respectively. The 6-31G* bond lengths range from 1.339 to 1.508 with an average bond length of 1.404 Å for 93 bonds. (See Supplementary Material in Appendix.) It is shown that the 6-31G* CC bond lengths show a smaller range of variation between the shortest and longest bonds. The rms deviation between 6-31G* calculated bond lengths and experiment is 0.016 Å; the rms error for the same bond lengths at the STO-3G geometry is 0.019 Å. The AM1 semi-empirical molecular orbital calculations[11] and two molecular mechanics methods, MOMM[12] and MMP2[20], which include a molecular orbital calculation for the conjugated pi systems, also produce geometries which agree well with experiment.

Figure 1.1 Aromatic Molecules studied in this research.

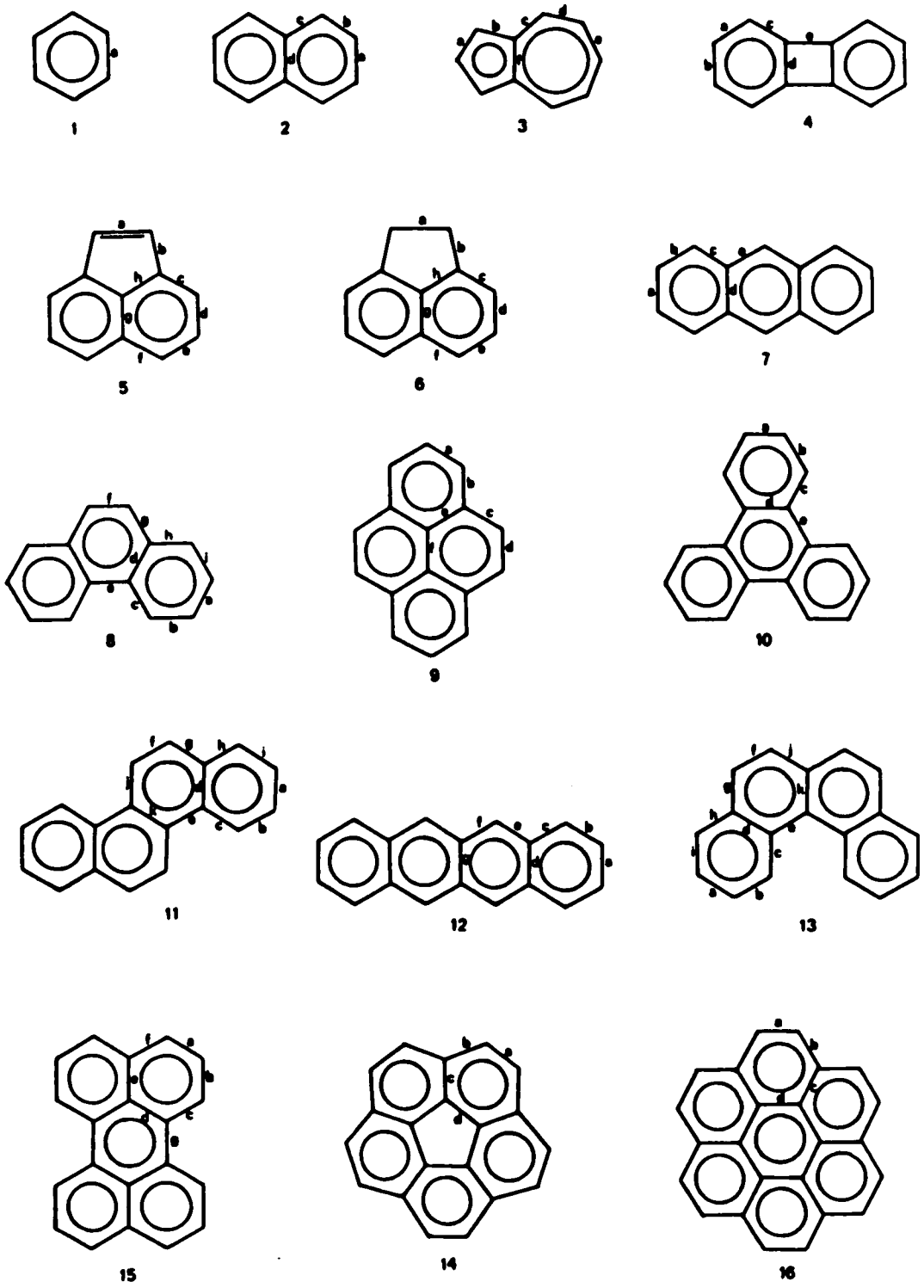


Table 1.1 CC Bond Lengths (Å)

molecule	bond	STO-3G	6-31G*	experiment[a]
benzene	a	1.387	1.386	1.399
naphthalene	a	1.425	1.416	1.412
	b	1.353	1.358	1.371
	c	1.432	1.420	1.422
	d	1.405	1.409	1.420
azulene	a	1.391	1.393	1.399
	b	1.396	1.395	1.418
	c	1.392	1.385	1.383
	d	1.389	1.387	1.406
	e	1.391	1.388	1.403
	f	1.502	1.485	1.501
biphenylene	a	1.426	1.417	1.419
	b	1.367	1.373	1.385
	c	1.353	1.357	1.372
	d	1.426	1.413	1.426
	e	1.516	1.508	1.514
acenaphthylene[b]	a	1.331	1.340	1.395
	b	1.495	1.480	1.466
	c	1.357	1.360	1.381
	d	1.435	1.427	1.424
	e	1.360	1.366	1.382
	f	1.436	1.425	1.433
	g	1.377	1.378	1.386

	h	1.421	1.410	1.441
anthracene	a	1.444	1.432	1.418
	b	1.341	1.347	1.375
	c	1.451	1.436	1.444
	d	1.425	1.424	1.433
	e	1.393	1.389	1.405
phenanthrene	a	1.409	1.402	1.394
	b	1.364	1.367	1.384
	c	1.418	1.411	1.409
	d	1.402	1.404	1.420
	e	1.473	1.461	1.465
	f	1.334	1.339	1.350
	g	1.454	1.440	1.453
	h	1.417	1.409	1.423
	i	1.363	1.365	1.386
pyrene	a	1.385	1.384	1.395
	b	1.395	1.391	1.406
	c	1.462	1.446	1.438
	d	1.333	1.339	1.367
	e	1.413	1.411	1.425
	f	1.446	1.432	1.430
triphenylene	a	1.398	1.392	1.397
	b	1.369	1.369	1.381
	c	1.411	1.407	1.410
	d	1.402	1.401	1.413
	e	1.485	1.472	1.458

chrysene	a	1.414	1.406	1.394
	b	1.360	1.364	1.381
	c	1.425	1.417	1.409
	d	1.402	1.404	1.407
	e	1.464	1.453	1.468
	f	1.340	1.344	1.369
	g	1.442	1.429	1.421
	h	1.422	1.412	1.428
	i	1.358	1.362	1.363
	j	1.446	1.434	1.428
	k	1.390	1.392	1.401
3,4-benzo-phenanthrene	a	1.414	1.406	1.409
	b	1.360	1.365	1.378
	c	1.427	1.419	1.433
	d	1.407	1.409	1.431
	e	1.470	1.459	1.446
	f	1.338	1.342	1.342
	g	1.444	1.431	1.443
	h	1.423	1.412	1.391
	i	1.359	1.363	1.374
	j	1.445	1.432	1.430
	k	1.389	1.391	1.412
tetracene	a	1.454	1.441	1.459
	b	1.336	1.342	1.381
	c	1.460	1.444	1.420
	d	1.442	1.438	1.420

	e	1.371	1.374	1.390
	f	1.416	1.408	1.404
	g	1.427	1.427	1.460
perylene	a	1.353	1.356	1.370
	b	1.417	1.407	1.418
	c	1.367	1.370	1.397
	d	1.440	1.430	1.425
	e	1.410	1.413	1.424
	f	1.427	1.416	1.400
	g	1.499	1.486	1.471
corannulene	a	1.363	1.370	1.402
	b	1.462	1.451	1.440
	c	1.361	1.361	1.391
	d	1.423	1.413	1.413
coronene[c]	a	1.349	1.353	1.362
	b	1.437	1.424	1.444
	c	1.396	1.397	1.381
	d	1.438	1.426	1.438
1,2-benz-anthracene[a]	a	1.438		1.405
	b	1.346		1.358
	c	1.444		1.417
	d	1.414		1.422
	e	1.406		1.408
	f	1.380		1.385
	g	1.430		1.426
	h	1.479		1.466

i	1.409	1.400
j	1.369	1.358
k	1.401	1.387
l	1.369	1.359
m	1.404	1.405
n	1.401	1.407
o	1.465	1.437
p	1.329	1.338
q	1.463	1.439
r	1.382	1.390
s	1.408	1.394
t	1.445	1.423
u	1.346	1.354

[a]Except for acenaphthylene and coronene, the experimental values are given by Kao, J; Allinger, N. L. J. Am. Chem. Soc. 1977, 99, 975. [b]Wood, R. A.; Welberry, T. R.; Rae, A. D. J. Chem. Soc., Perkin Trans. 2, 1985, 451. [d]The experimental values were obtained by X-ray diffraction: Robertson, J. M.; White, J. G. J. Chem. Soc. 1945, 607. The electron-diffraction values of bond lengths a-d are 1.385, 1.415, 1.430 and 1.430 A, respectively: Bastiansen, O.; Skancke, P. N. Adv. Chem. Phys. 1961, 3, 323. [d]The experimental values are averages derived from five methyl-substituted benzanthracenes. Briant, C. E.; Jones, D. W.; Shaw, J. D. J. Mol. Struct. 1985, 130, 167.

There are only a few ab initio calculations on aromatics with which to compare our calculated geometries. The STO-3G geometry and energy of naphthalene agree with those reported by Haddon and Raghavachari[8a]; their 6-31G geometries are in slightly better agreement with experiment than our 6-31G* values. These authors also calculated the energy and geometry of azulene (3) assuming C_s and C_{2v} symmetries. In the STO-3G basis, azulene is more stable in its C_s form by 3.7 kcal/mol. The C_{2v} azulene is the more stable in the 6-31G[8b] basis and is the form observed experimentally. The geometries and energies of azulene employed here were obtained for C_{2v} azulene in both STO-3G and 6-31G* basis sets. The 6-31G* SCF value of its dipole moment is 1.51 D, with the positive end toward the seven-membered ring. Inclusion of the correlation energy in the 6-31G basis reduced the dipole moment by 0.50 D.[8b] Application of this correction to the 6-31G* SCF value, 1.51 D, gives a dipole moment of about 1.0 D, in good agreement with the experimental values of 0.80[9a] and 1.08 D.[9b]

The largest error in a calculated bond length occurs for the C_1C_2 bond of acenaphthylene (5). The STO-3G value is 1.331 Å, vs. 1.395 $\pm$ 0.011 Å is obtained by neutron diffraction.[10] The 6-31G* calculated value, 1.340 Å, is in only slightly better agreement. However, the neutron diffraction C_1H_1 bond length is 1.052 $\pm$ 0.013 Å, much smaller than the STO-3G value, 1.081 Å; the other three experimental CH bond lengths - 1.090, 1.094, and 1.077 Å - are normal. The

6-31G* C_1H_1 bond length, 1.073 Å, is slightly shorter than the typical CH 6-31G* bond length, 1.076 Å. The AM1 C_1C_2 bond length is 1.371 Å and a normal C_1H_1 bond length is found[11].

Triphenylene (9) was assumed to have D_{3h} symmetry although in its X-ray structure there are very slight out-of-plane deformations. Since the MOMM molecular mechanics method shows the planar form to be only 0.1 kcal/mol higher in energy than the out-of-plane form[12], the assumption of planarity therefore introduces a very small error.

The X-ray structure for 3,4-benzophenanthrene ([4]helicene, 12) is decidedly non-planar[13]. There are small distortions from C_2 symmetry, due perhaps to thermal effects or crystal packing forces. The non-planarity of 3,4-benzophenanthrene results partly from steric repulsion of its two inner hydrogens. In the optimized C_2 structure, Figure 1.2, the separation of the inner hydrogens is increased to 1.96 Å (STO-3G) and 1.98 Å (6-31G*), approximately the same distances found for the corresponding hydrogens of phenanthrene.

Calculated values for the seven independent C-C-C-C dihedral angles of benzophenanthrene are given in Table 1.2, along with their average counterparts from the X-ray structure. The agreement of the calculated STO-3G dihedral angles with experiment is good, the largest deviations from experiment being (in degrees): 2.4, 4-4a-5-6; -2.6, 4-4a-12c-12b; -2.2, 4-4a-12c-1; 2.2, 12b-12c-1-2. The errors are

Figure 1.2 Perspective drawing of 3,4-benzophenanthrene optimized in the STO-3G basis.

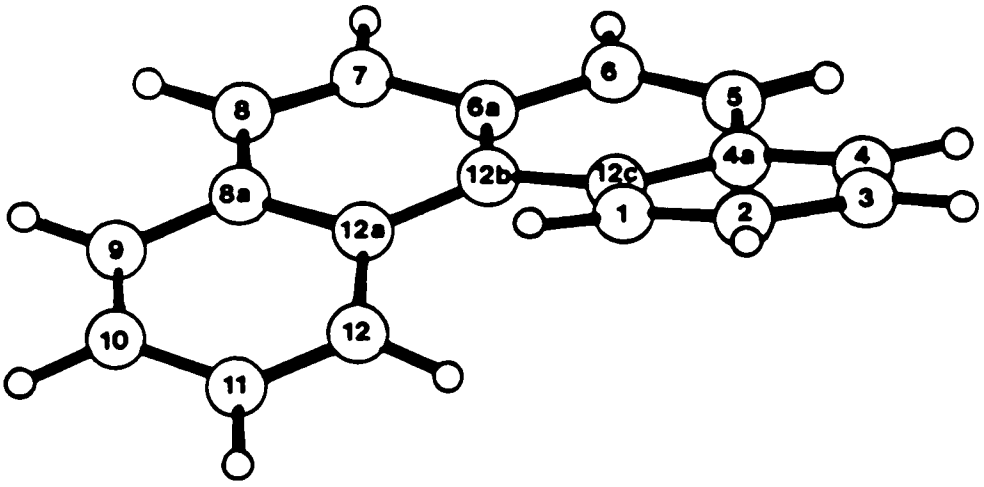


Table 1.2 Dihedral Angles of 3,4-benzophenanthrene (degrees)

angle	STO-3G	6-31G*	experiment[a]
12c-1-2-3	-0.4	-0.1	-0.8
1-2-3-4	-3.3	-3.6	-4.1
2-3-4-4a	1.9	1.5	2.2
3-4-4a-5	-172.7	-172.5	-172.5
6-6a-12b-12c	-11.1	-11.3	-10.0
6a-12b-12c-1	-161.3	-161.2	-161.4
12b-12c-1-2	179.9	-179.8	-177.9

[a]Determined from the cartesian coordinates of Hirshfeld, F. L.; Sandler, S.; Schmidt, G. M. J. J. Chem. Soc. 1963, 2108.

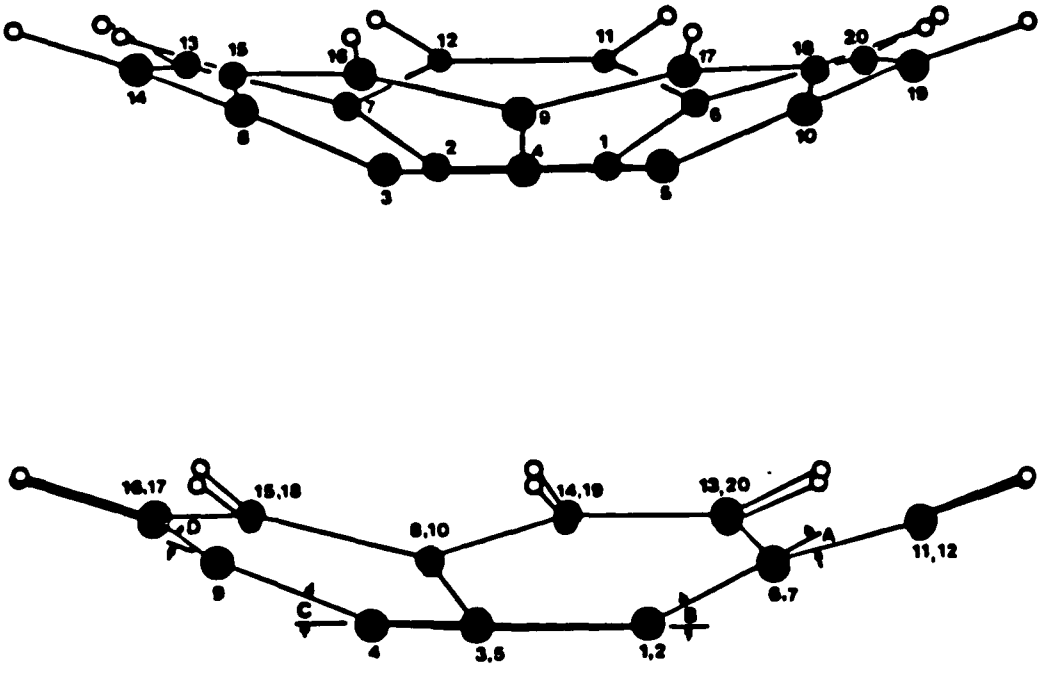
reduced by half at the 6-31G* geometry. The deviations from experiment for these angles found with the AM1 method, are smaller yet: 0.6, 0.0, -0.7, and -0.5, respectively.

The geometry of corannulene (15) was optimized in both D_{5h} and C_{5v} symmetries. The bowl-shaped C_{5v} form, Figure 1.3, is lower in energy than the planar form by 8.8, 10.3, and 8.8 kcal/mol in the STO-3G, 3-21G, and 6-31G* basis sets (at the STO-3G geometries), respectively. The MOMM energy difference is 5.7 kcal/mol.[12] The STO-3G CC bond lengths of corannulene are in fair agreement with their X-ray values[14]; the improvement in the 6-31G* is found primarily in the long bonds b and d, which are overestimated in the STO-3G geometry. Corannulene can be considered to contain a fragment of the icosahedral C_{60} molecule. The STO-3G lengths of the short and long bonds in C_{60} are 1.376 and 1.465 Å;[15a] the STO-3G lengths of their counterparts in corannulene, bonds c and d, are 1.361 and 1.423 Å.

The angles B and C, (Figure 1.3), in the notation of ref. 16 measure the deviation of the carbons from planarity. They are 25.5° and 21.1° in the 6-31G* SCF geometry; the X-ray values are 26.8° and 22.4°.[16]

There have been two experimental studies of the structure of coronene (16). Both the STO-3G and 6-31G* geometries give somewhat better agreement with the X-ray results[17a] than with the electron diffraction values.[17b]

Figure 1.3 Two views of corannulene optimized in the 6-31G* basis.



The difference between the 6-31G* energy of a molecule, when calculated at its own geometry (6-31G*//6-31G*) and its STO-3G geometry (6-31G*//STO-3G), increases with the size of the molecule. For benzene, azulene and acenaphthylene the 6-31G*//6-31G* SCF energies are lower than the 6-31G*//STO-3G values by 0.1, 0.4 and 0.6 kcal/mol, respectively. Differences of 1 kcal/mol are found for both coronene and corannulene. In contrast, the energy difference between an optimized structure - even an STO-3G optimized structure - and a structure with uniform CC bond lengths is much larger. For example, the STO-3G, 3-21G, and 6-31G* energies of

phenanthrene, calculated at a geometry in which the CC bond lengths are fixed at 1.404 Å, are 11.1, 8.1 and 8.1 kcal/mol higher than the corresponding values at the phenanthrene STO-3G geometry. This suggests that standard geometries are not sufficient for the calculation of total energies of condensed benzenoid hydrocarbons. They are useful, however, for comparing the effects of substituents on the same benzenoid skeleton.[18]

Our calculations show that the length of bond C_iC_j correlates well with the product of STO-3G p-pi atomic orbital coefficients and the Mulliken total bond order, n_{ij}[19] (Figure 1.4).

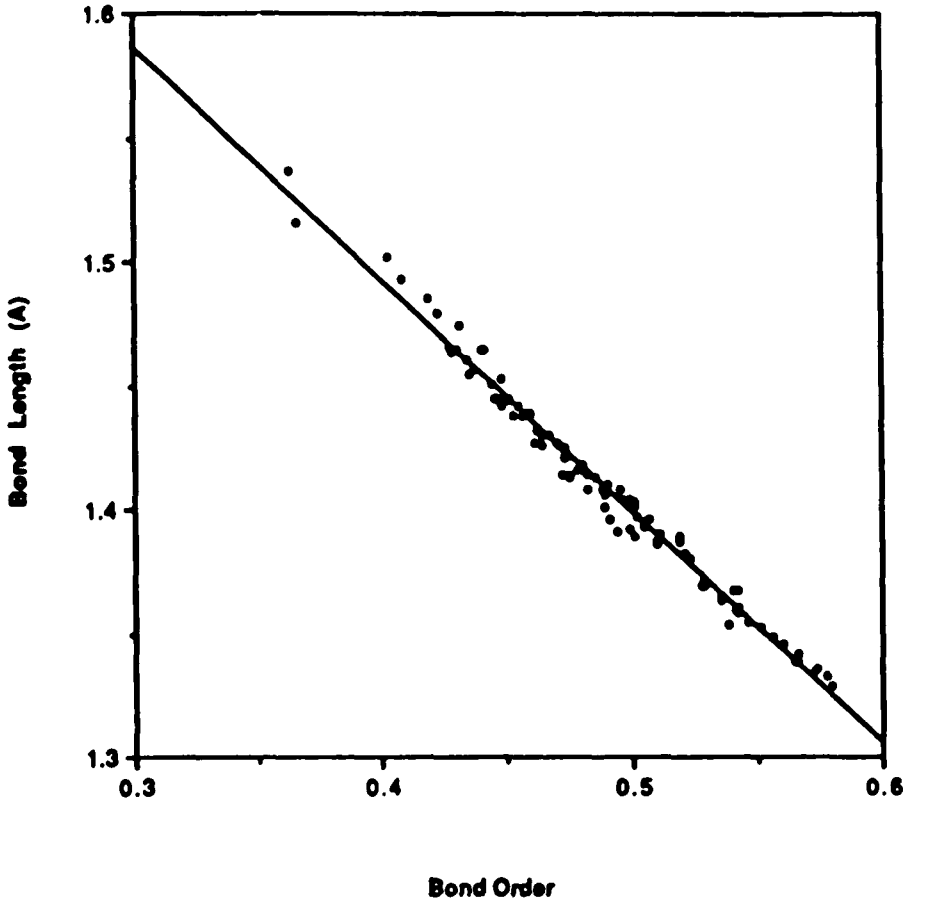


Figure 1.4 Least-squares fit of the STO-3G CC bond lengths to the Mulliken total overlap populations of the bonded carbons. The figure includes the CC bond of ethane, whose length and bond order are 1.538 Å and 0.363, respectively.

Thermochemistry

a. Homodesmic Reactions

The STO-3G, 3-21G, and 6-31G* energies of the 16 aromatic hydrocarbons (Figure 1.1), calculated at their STO-3G geometries, are given in Table 1.3. These energies can be used to obtain accurate heats of reaction for the model homodesmic reactions shown in Figure 1.5. The reactants of reaction I contain 10 and 18 carbons; the calculated ΔH's of reaction, 8.1, 5.8 and 4.6 kcal/mol in the STO-3G, 3-21G and 6-31G* basis sets are in good agreement with experiment, 5.6 kcal/mol. For reaction II, there are 14 and 20 carbons; the calculated values in these same basis sets are 7.2, 8.0, and 7.7 kcal/mol, which compare well with the experimental value, 8.23 kcal/mol. No correction was made for the small zero-point and thermal effects since the experimental error of ca. 4 kcal/mol for each reaction is much larger. Furthermore, it is probable that zero-point energies and thermal contributions are nearly the same per bond for a class of similar molecules such as the aromatics.[4] The energies given in Table 1.4 were calculated at the 6-31G* geometry; the ΔH for the two reactions are essentially the same: for reaction I, the ΔH_r is 4.2 kcal/mol, while for reaction II, the ΔH_r is 7.5 kcal/mol.

The enthalpy changes for these homodesmic reactions are very small compared with the ab initio energies of their reactants and products. The ΔH's of reaction, mentioned

Table 1.3 Total Energies of Aromatic Hydrocarbons (au) at their STO-3G geometries.

molecule	STO-3G	3-21G	6-31G*
benzene (C_6H_6)	-227.8914	-229.4190	-230.7029
naphthalene ($C_{10}H_8$)	-378.6868	-381.2146	-383.3543
azulene ($C_{10}H_8$)	-378.5925	-381.1366	-383.2819
biphenylene ($C_{12}H_8$)	-453.4176	-456.4368	-459.0138
acenaphthylene ($C_{12}H_8$)	-453.4829	-456.5020	-459.0728
anthracene ($C_{14}H_{10}$)	-529.4725	-533.0017	-535.9975
phenanthrene ($C_{14}H_{10}$)	-529.4874	-533.0142	-536.0088
pyrene ($C_{16}H_{10}$)	-604.3253	-608.3439	-611.7667
triphenylene ($C_{18}H_{12}$)	-680.2860	-684.8106	-688.6593
chrysene ($C_{18}H_{12}$)	-680.2838	-684.8096	-688.6595
tetracene ($C_{18}H_{12}$)	-680.2535	-684.7848	-688.6375
3,4-benzo-phenanthrene ($C_{18}H_{12}$)	-680.2702	-684.7983	-688.6480
1,2-benz-anthracene ($C_{18}H_{12}$)	-680.2770	-684.8045	-688.6558
perylene ($C_{20}H_{12}$)	-755.1125	-760.1275	-764.4049
corannulene ($C_{20}H_{10}$)[a]	-753.9035	-758.9051	-763.1871
coronene ($C_{24}H_{12}$)	-904.8227	-910.8177	-915.9503

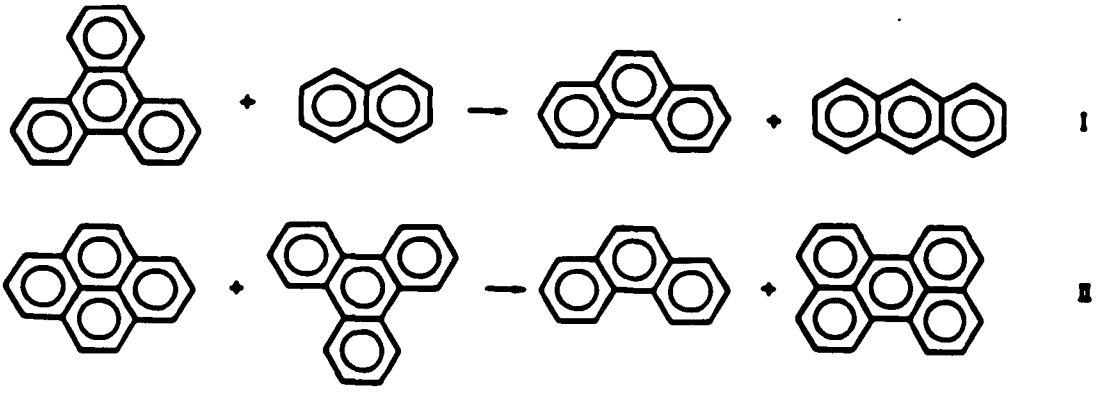
[a]The corresponding total energies for planar corannulene are -753.8893, -758.8887 and -763.1730 au.

Table 1.4 Total Energies of Aromatic Hydrocarbons (au)[a]

molecule	6-31G*
benzene (C_6H_6)	-230.7031
naphthalene ($C_{10}H_8$)	-383.3550
azulene ($C_{10}H_8$)	-383.2826
biphenylene ($C_{12}H_8$)	-459.0146
acenaphthylene ($C_{12}H_8$)	-459.0738
anthracene ($C_{14}H_{10}$)	-535.9988
phenanthrene ($C_{14}H_{10}$)	-536.0098
pyrene ($C_{16}H_{10}$)	-611.7680
triphenylene ($C_{18}H_{12}$)	-688.6603
chrysene ($C_{18}H_{12}$)	-688.6609
tetracene ($C_{18}H_{12}$)	-688.6386
3,4-benzophenanthrene ($C_{18}H_{12}$)	-688.6495
perylene ($C_{20}H_{12}$)	-764.4065
corannulene ($C_{20}H_{10}$)[b]	-763.1893
coronene ($C_{24}H_{12}$)	-915.9526

[a]The 6-31G* SCF energies were calculated at the 6-31G* geometries. [b]The corresponding total energy for planar corannulene is -763.1730 au.

Figure 1.5 Homodesmic reactions I and II.



above, are in kcal/mol whereas the energies of reactants and products are on the order of $-5x10^2$ a.u., (1 a.u. = 627.5 kcal/mol). The agreement with experiment, independent of basis size, suggests that the ab initio energy differences are meaningful.

Several sets of isomers have been considered in the study: naphthalene and azulene; biphenylene and acenaphthylene; anthracene and phenanthrene; the five C18H12 isomers, triphenylene, chrysene, tetracene, 3,4-benzophenanthrene and 1,2-benzanthracene.

For the reaction

phenanthrene ---> anthracene,

which involves two benzenoid aromatics, the calculated isomerization energies (at their STO-3G geometries) are 9.3,

7.8, and 7.1 kcal/mol in the STO-3G, 3-21G and 6-31G* basis sets, in reasonable agreement with experiment, 5.9 kcal/mol. The 6-31G*//6-31G* isomerization energy is 6.9 kcal/mol.

In order of increasing energy, the five $C_{18}H_{12}$ isomers are: chrysene, triphenylene, 1,2-benzanthracene, 3,4-benzophenanthrene, tetracene. The experimental ordering is the same except for tetracene, whose experimental heat of formation, 69.8 kcal/mol, is nearly equal to that of 3,4-benzophenanthrene, 69.6 kcal/mol. We tentatively conclude, as have Kao[12], Sprague et al.[20], and Dewar[21] previously, that the experimental heat of formation of tetracene is too low, perhaps owing to its reactivity. The number of Kekule structures also agrees with the ab initio ordering of energies.

Lesser agreement with experiment for ΔH_r is found at the SCF level for the simple homodesmic isomerization

naphthalene ---> azulene,

which involves a benzenoid reactant and a non-benzenoid product. The calculated isomerization energies are 59.2, 48.9 and 45.4 kcal/mol at the STO-3G, 3-21G and 6-31G* SCF levels, whereas the experimental value is 37.65 $\pm$ 1.15 kcal/mol, based upon 73.5 kcal/mol for the heat of formation of azulene. Haddon and Raghavachari[88] obtained an isomerization energy of 37.7 kcal/mol at the 6-31G RMP2 level, an improvement of 10 kcal/mol over the 6-31G SCF value. In the present study, the isomerization energies are 45.4 and 34.8 kcal/mol at the 6-

31G* SCF and RMP2 levels, respectively. These results suggest that second-order correlation energies per bond in benzenoids and non-benzenoids differ significantly. They must be explicitly calculated since energy differences between benzenoids and non-benzenoids cannot be relied upon to cancel.

For the isomerization

biphenylene ----> acenaphthalene,

neither of which is benzenoid, the agreement with the experimental enthalpy change, 42.8 $\pm$ 2.7 kcal/mol is fair: the calculated values (at the STO-3G geometry) are 41.0, 40.9, and 37.0 kcal/mol in the three basis sets. The 6-31G*//6-31G* isomerization energy is 37.2 kcal/mol. The correlation energies of isomeric non-benzenoids are unequal, unlike the situation in the benzenoids. An RMP2 calculation of ΔH for the above reaction might be of interest.

b. Group equivalents for benzenoid aromatics

Since accurate heats of reaction can be calculated from homodesmic reactions using only ab initio energies, there may exist a characteristic ab initio energy per bond (or per group) for aromatics. That is, the ab initio energy of an aromatic can be considered to be distributed in an additive way among the bonds, atoms or even groups of atoms of that molecule. It is well known that for most molecules, thermal effects on enthalpies and zero-point energies are approximatively additive. It seems reasonable then that these

quantities, along with the ab initio energy, might be combined into constant equivalent energies per atom, group of atoms, or bond, as described below. For a hydrocarbon, C_nH_m, which can also be described as $(CH)_mC_{n-m}$, we employ m CH groups, denoted $=C_bH-$, and (n-m) groups, denoted $=C_b-$ for carbons devoid of hydrogens e.g. C_9 and C_{10} of naphthalene. Following Wiberg[4], the group equivalents for each basis were obtained by a least squares fit of the experimental heats of formation to differences between the ab initio energies E_{SCF} and the sums of the m and (n-m) group equivalents according to the equation

$$\Delta H_f = E_{SCF} - m\ GE[=C_bH-] - (n-m)\ GE[=C_b-] \quad (1)$$

The group equivalents (GE's) were determined at the STO-3G geometry in each basis for a training set of molecules that met the following criteria: 1. they are completely benzenoid, and 2. their heats of formation are reliably known. The training set consisted of ten molecules: the 16 molecules studied, except for the non-benzenoids azulene, biphenylene and acenaphthylene; tetracene, whose experimental heat of formation is in question; and corannulene and coronene, whose heats of formations are unknown. The group equivalents for each basis are given in Table 1.5. Group equivalents at the 6-31G*//6-31G* level were determined using a training set of 9 molecules - all the molecules in the STO-3G training set with the exception of 1,2-benzanthracene for which the optimized geometry was not calculated in the larger basis. The 6-31G*//6-31G* group equivalents are also given in Table

1.5.

Ibrahim and Schleyer[5] employed a Wiberg-type procedure to obtain atom equivalents for olefinic hydrocarbons. The 6-31G*//6-31G* value of GE[=C_b-], -37.88149 au, can be compared with the corresponding Ibrahim-Schleyer olefinic carbon atom equivalent[5], for the group denoted C_d-(C_d)$(C)_2$. The aromatic group (or atom) equivalent is algebraically larger by 0.00222 au. For GE[=C_bH-], the corresponding olefinic =CH- group equivalent derived from the Ibrahim-Schleyer values[5] is smaller than the aromatic value by 0.00222 a.u. Since the differences between the aromatic and olefinic equivalents are nearly identical but of opposite sign, the calculated heats of formation of molecules having equal numbers of =CH- and =C groups, such as corannulene and coronene, have the same value when either olefinic or aromatic group equivalents are employed.

Table 1.5 Group Equivalents for Benzenoid Aromatics (au)

	group equivalent (GE)			
group	STO-3G[a]	3-21G[a]	6-31G*[a]	6-31G*[b]
$=C_bH-$	-37.98722	-38.24198	-38.45600	-38.45605
$=C_b<$	-37.42280	-37.66773	-37.88138	-37.88150

[a]Group equivalents calculated from energies of molecules at their STO-3G geometries. [b]Group equivalents calculated from energies of molecules at their 6-31G* geometries.

The calculated heats of formation of all 16 molecules are given in Table 1.6; the respective rms deviations for the training set at the STO-3G geometries are 1.2, 0.7, and 0.7 kcal/mol in the STO-3G, 3-21G, and 6-31G* bases. (In computing the rms deviations, experimental values closest to the calculated values were selected.) The calculated heats of formation at the 6-31G* geometries are given in Table 1.7. The rms deviation for the training set at the 6-31G*//6-31G* level of calculation is also 0.7 kcal/mol.

Table 1.6 Heats of Formation of Aromatic Hydrocarbons (kcal/mol)

molecule	from group equivalents[a] obtained at the STO-3G geometries				
	STO-3G	3-21G	6-31G[a]	exptl[b]	
benzene (1)	20.0	20.6	20.8	19.81	
naphthalene (2)	35.5	35.6	35.4	35.85	
azulene (3)	94.7	84.5	80.9	69.06,	73.5
biphenylene (4)	107.5	106.6	100.2	104.43,	115.2
acenaphthylene (5)	66.6	65.7	63.2	62.04,	61.6
anthracene (6)	57.0	55.8	55.2	55.44,	55.2
phenanthrene (7)	47.7	48.0	48.2	49.52,	49.5
pyrene (8)	52.5	51.6	51.2	51.59	
triphenylene (9)	61.1	62.5	63.4	63.4	
chrysene (10)	62.5	63.1	63.3	62.8	
tetracene (11)	81.5	78.7	77.0	69.8	
3,4-benzo-phenanthrene (12)	71.1	70.2	70.5	69.6	
1,2-benz-anthracene (13)	66.8	66.3	65.6	69.63,	65.97
perylene (14)	73.1	74.1	74.2	73.7	
corannulene (15)	123.4	120.5	117.2		
coronene (16)	61.2	62.0	61.7		

[a]The group equivalents are given in Table 1.5; 1 au = 627.5 kcal/mol. [b]Experimental values are from Kao.[12]

Table 1.7 Heats of Formation of Aromatic Hydrocarbons (kcal/mol)

molecule	from group equivalents[a] 6-31G[a]	exptl[b]
benzene (1)	20.8	19.81
naphthalene (2)	35.4	35.85
azulene (3)	80.8	69.06, 73.5
biphenylene (4)	100.3	104.43, 115.2
acenaphthylene (5)	63.1	62.04, 61.6
anthracene (6)	55.0	55.44, 55.2
phenanthrene (7)	48.1	49.52, 49.5
pyrene (8)	51.3	51.59
triphenylene (9)	63.6	63.4
chrysene (10)	63.2	62.8
tetracene (11)	77.2	69.8
3,4-benzophenanthrene (12)	70.3	69.6
perylene (14)	74.1	73.7
corannulene (15)	116.8	117.2
coronene (16)	61.5	61.7

[a]The group equivalents are given in Table 1.5; 1 au = 627.5 kcal/mol. [b]Experimental values are from Kao.12

Our calculated 6-31G*//6-31G* tetracene heat of formation, 77.2 kcal/mol, agrees with that obtained by molecular mechanics: 77.58 kcal/mol, MOMM[12] and 76.19 kcal/mol, MM2[20]. As noted above, the experimental value of 69.8 kcal/mol may be in error. According to the ab initio and molecular mechanics methods, tetracene has the highest heat of formation of the $C_{18}H_{12}$ isomers and is less stable by 6-10 kcal than 3,4-benzophenanthrene, even though the latter is non-planar.

The heat of formation of corannulene has not been measured. Our calculated heats of formation, 117.2 kcal/mol and 116.8 kcal/mol, of the 6-31G*//STO-3G and 6-31G*//6-31G* levels, respectively, are close to the MOMM value of 115.2 kcal/mol. The heat of formation of corannulene, which is bowl-shaped and non-benzenoid, has a resonance stabilization and strain energy which are unlike those of the benzenoid aromatics. Its heat of formation is 66 kcal/mol, more than 5/6 of the planar benzenoid, coronene. Both molecules have m/n = 1/2. The planar form of corannulene should have a larger resonance stabilization than the C_{5v} form. It is offset, however, by its larger angle strain. The latter effect appears to predominate since the calculated heat of formation of planar corannulene is higher than that of the bowl-shaped form by ca. 8.8 kcal/mol in 6-31G*//6-31G* (and by 8.3 kcal/mol in 6-31G*//STO-3G). In contrast, 3,4-benzophenanthrene appears not to have lost much of its resonance energy due to non-planarity, since its heat of formation is

similar to those of its planar isomers chrysene and tetracene.

The MMP2 molecular mechanics method[20] generally furnishes heats of formation within 1 kcal/mol of experiment for aromatics. However for perylene, the MMP2 value is 79.0 kcal/mole, compared with 74.1 kcal/mol obtained from the 6-31G*//6-31G* group equivalents. The experimental value, 73.7 kcal/mol, agrees with the ab initio values; the 3-21G and 6-31G* ΔH_f's are 74.1 kcal/mol and 74.2 kcal/mol. The MOMM value, 72.88 kcal/mol is similar to the ab initio result.

The ΔH_f of the non-benzenoid, azulene shows the largest deviation from experiment, ca. 7 kcal. There are, in fact, two experimental values reported for azulene, 69.06 and 73.5 kcal/mol. The experimental heats of formation and vaporization of a molecule can be related to its dipole moment. The two heats of vaporization corresponding to the small and large heats of formation are 18.36 and 22.8 $\pm$ 0.9 kcal/mol, respectively. The heat of vaporization used to obtain the larger heat of formation of azulene is more consistent with its dipole moment of ca. 1 D. The smaller ΔH_f is obtained from a (smaller) ΔH_v which is close to that of naphthalene, a molecule with no dipole moment. That the ab initio result agrees more closely with the larger experimental heat of formation, is consistent with the fact that its dipole moment implies a large ΔH_v for azulene.

There are also two experimental heats of formation of biphenylene, 104.43 and 115.2 kcal/mol, based on two heats of

vaporization. Biphenylene and acenaphthylene should have similar heats of vaporization, since their dipole moments are similar, 0 and 0.1 D, respectively. The heat of vaporization more consistent with its dipole moment furnishes the smaller heat of formation, 104.43 kcal/mol. It is this value with which our calculated heat of formation, 100.3 kcal/mol is in best agreement.

3.Extension of the Group-Equivalent Scheme to Substituted Aromatics

By combining the aromatic group equivalents with the atom equivalents of Ibrahim and Schleyer, the heats of formation of a variety of substituted benzenoid aromatic molecules can be obtained. The calculated values agree well with experiment, as shown by the following examples. The heat of formation of toluene is obtained by combining its 6-31G*//STO-3G energy, -269.7402 au (assumming Cs symmetry) with the Ibrahim-Schleyer methyl group equivalent (-39.59836 au) calculated from its atom equivalents[8], five $=C_bH-$ group equivalents, and one $=C_b-$ group equivalent (Table 1.5). The result is 12.3 kcal/mol, in good agreement with experiment, 11.99 $\pm$ 0.10 kcal/mol.[22]

The heat of formation of fluorobenzene, whose 6-31G*//-STO-3G energy is -329.5530 au, can be obtained from the aromatic group equivalents and a fluorine atom equivalent.[8] The calculated heat of formation, -26.2 kcal/mol, compares

well with the experimental value of -27.76 ± 0.29 kcal/mol.[22]

Aniline has an experimental heat of formation of 20.81 ± 0.18 kcal/mol. Based on its 6-31G*//STO-3G, -285.7280 au, combined with the aromatic group equivalents and an amino equivalent[5], the calculated aniline heat of formation is 21.8 kcal/mol, which differs from the experimental value by ca. 1 kcal/mol.[22]

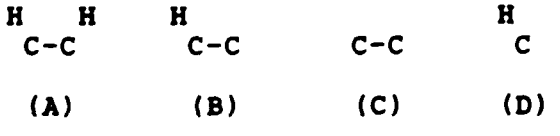
The STO-3G energy of biphenyl was recently reported to be -454.64848 au.[23]. Using the STO-3G group equivalents (Table 1.5), we calculate a heat of formation of 43.5 kcal/mol, in good agreement with the experimental value, 43.5 ± 0.60 kcal/mol.[22]

For C_{60}, use of eq 1 with m=0 and its previously calculated STO-3G//STO-3G energy, -2244.2193 au, gives a heat of formation/C of 12.0 kcal/mol.[15b] This value is an overestimate, since the STO-3G basis lacks polarization functions and cannot adequately represent the strain effects in C_{60}. Assuming a change in energy per carbon in going from the STO-3G//STO-3G to the 6-31G*//6-31G* basis, similar to that found for C_{24},[15b] the 6-31G*//6-31G* energy for C_{60} can be estimated to be -2272.0441 au. Use of eq 1 with m=0 as described above and the GE[=C_b-] 6-31G*//6-31G* group equivalent from Table 1.5, gives a heat of formation/C of 8.85 kcal/mol.[18b] A comparable value, 8.83 kcal/mol, was obtained by Almlöf and Lüthi, who extrapolated their ab initio SCF energies of a variety of carbon clusters and hydrocarbons.[24]

Other Work

Bond energy equivalents for alkanes were first introduced around 1920. It was assumed that the bond-energy equivalent for a given bond type is independent of its environment and hybridization, and that it is additive and transferable between molecules. This approach has several drawbacks. Firstly, large deviations in calculated heats of formation occur for the lower members of a homologous series, e.g. ethane in the alkane series. Secondly, bond-energy terms that are independent of environment cannot furnish different heats of formation for structural isomers[22].

Many refinements of the bond energy scheme have been proposed including the use of steric and bond-interaction energy corrections to the equivalents. Among the most successful is the bond energy scheme of Laidler which takes into account the environment of the bonds.[22] For alkanes, he ascribes different energy values to primary, secondary and tertiary CH bonds. For aromatic hydrocarbons, Tatevskii, Korolov, and Mendzheretskii and McGinn proposed a Laidler-type method[22] using four groups:



(A) (B) (C) (D)

Values for their parameters (in kcal/mol) suggested by Benson, are:

(A) = 119.17

(B) = 114.30

(C) = 112.80

(D) = 100.53

Group methods, such as those of Benson and Buss, were also introduced[21]. These methods give heats of formation and entropies as additive functions of structural-group contributions, which are assumed to be constant and transferable between molecules. Benson applied the group energy scheme to aromatics using the following parameters and values (in kcal/mol):

(A) $C_b - (H) = 3.30$

(B) $C_b - (C_b) = 4.96$

(C) $C_{bf} - (C_b)_2(C_{bf}) = 4.8$

(D) $C_{bf} - (C_b)(C_{bf})_2 = 3.7$

(F) $C_{bf} - (C_{bf})_3 = 1.5$

where bf indicates fused benzenoid carbons[22].

Tables 1.8 and 1.9 contain the heats of formation for the aromatics studied in this work, obtained from the Laidler and Benson methods. Large deviations from experiment occur with both methods. Also, differentiation between the $\triangle H_f$ of structural isomers cannot be made, e.g. for naphthalene vs. azulene, and chrysene vs. 3,4-benzophenanthrene in the Laidler treatment; naphthalene vs. azulene in the Benson method. In contrast, group equivalents procedure developed in this

Table 1.8 Heats of formation calculated with Laidler bond scheme. (kcal/mol)

molecule	ΔH_f expt.	ΔH_f calc.	expt.-calc.
benzene	19.81	19.80	0.01
naphthalene	35.85	36.54	-0.69
azulene	73.5	36.54	36.96
acenaphthalene	62.04	43.31	18.73
biphenylene	104.43	39.94	64.49
anthracene	55.44	53.28	2.16
phenanthrene	49.52	49.91	-0.18
pyrene	51.59	56.68	-5.09
triphenylene	63.4	59.91	3.49
chrysene	62.8	63.28	-0.48
tetracene	69.8	70.02	-0.22
3,4-benzo-phenanthrene	69.6	63.28	6.32
1,2-benz-anthracene	69.63	66.65	2.98
perylene	73.7	66.68	7.02

Table 1.9 Heats of formation calculated with Benson group scheme.(kcal/mol)

molecule	ΔH_f expt.	ΔH_f calc.	expt.-calc.
benzene	19.81	19.80	0.01
naphthalene	35.85	36.00	-0.15
azulene	73.5	36.00	37.50
acenaphthalene	62.04	42.30	19.74
biphenylene	104.43	105.04	-0.61
anthracene	55.44	52.20	3.24
phenanthrene	49.52	50.00	-0.08
pyrene	51.59	55.20	-3.61
triphenylene	63.4	61.80	1.60
chrysene	62.8	64.00	-1.20
tetracene	69.8	68.40	1.40
3,4-benzophenanthrene	69.6	62.90	6.70
1,2-benanthracene	69.63	66.20	3.43
perylene	73.7	67.00	6.70

research is clearly more versatile than the empirical procedure. The deviations from experiment are much smaller and no difficulty is encountered in differentiating structural isomers.

Group equivalents were first obtained from ab initio energies by Wiberg in 1984.[4] In the Wiberg approach, the ab initio energies of a set of molecules are least-squares-fit, to their experimental heats of formation using five structural groups: -CH3, -CH2-, -CH-, =CH2, =CH-. His training set consisted of twenty-one alkane and olefinic molecules. Wiberg's group equivalents, when applied to alkanes and olefinics, furnish heats of formation which differ from experiment by ca. 2 kcal/mol. However for benzene, the large error led him to note that these group equivalents were not applicable to aromatics.

A similar multiple linear regression analysis using ab initio energies was used by Ibrahim and Schleyer[5], who derived atom equivalents for carbon, hydrogen, nitrogen, oxygen and flourine. They took into account the kind of bond (single, double, triple) and the kind of attached atoms; 56 atom equivalents were obtained. Their calculated heats of formation are somewhat better than Wiberg's, probably because of the greater number of parameters; they also do not apply to aromatics, however. The failures of the group and atom-equivalent methods suggest the need to treat the heat of formation of aromatics as a separate problem.

Alternative Structural Groups

Although correlation energies were not calculated in this study, our findings support the idea that they are additive in the same sense as is the thermal correction to the heat of formation, and the vibrational energy. The heats of reaction of homodesmic reactions involving only benzenoid aromatics were calculated accurately at the SCF level, implying the almost complete cancellation of reactant and product correlation energies. Since homodesmic reactions are bond (or group) balancing schemes, the accuracy of the calculated heat of reactions suggests that the correlation energy is regularly distributed among bonds (or groups) in the benzenoid aromatics. A more formal discussion as follows: Assuming that the equation we used to determine the group equivalents

$$(\Delta H_f = E_{SCF}(C_aH_b) - n_I GE_I - n_{II} GE_{II}) \qquad (2)$$

continues to hold as the restricted Hartree-Fock (RHF) limit is approached and also in the limit of 0 K, the heat of formation as calculated above can also be expressed as

$$\Delta H_f = E_{RHF}(C_aH_b) + E_{corr}(C_aH_b) + E_{zpt}(C_aH_b) - mH(C_{graphite}) - (n/2)H(H_{2gas}), \qquad (3)$$

Equating the two expressions results in the correlation energy:

$$E_{corr} = m(H_{(C,graphite)} - GE_{II}) + n(1/2H_{(H2,gas)} - (GE_I - GE_{II})) \qquad (4).$$

$(GE_I - GE_{II})$ can be interpreted as the group equivalent for hydrogen and $1/2H_{H2} - (GE_I - GE_{II})$ as the correlation energy

per H atom. It is evident from the coefficients in the above equation that the correlation energy is simply an additive function of the numbers carbon and hydrogen atoms, m and n, respectively.

A consequence of the additivity of the correlation energy is the existence of alternative group equivalents - the choice of structural groups is not unique. They could also be chosen as; (1) CC and CH bonds, (2) C and H atoms. The aromatic bond equivalents BE[CC] and BE[CH], atom equivalents AE[C] and AE[H], and the group equivalents of this study are all linearly related.

$$BE[CC] = 2/3\ GE[=C_b-],\ BE[CH] = GE[=C_bH-] - 2/3\ GE[=C_b-] \quad (5)$$

$$AE[C] = GE[=C_b-],\ AE[H] = GE[=C_bH-] - GE[=C_b-] \quad (6)$$

Since the number of CC bonds in a C_mH_n aromatic molecule is equal to 1/2(3m-n), the equation to be used for BE's is:

$$\Delta H_f = E_{SCF} - n\ BE[CH] - 1/2(3m-n)\ BE[CC]$$

A linear multiple regression based on either bond equivalents or atom equivalents and ab initio energies fits the experimental data well. If one omits parameter B, Benson's group scheme then becomes equivalent to Laidler's bond energy scheme. (Table 1.10)

Table 1.10 Comparison of Group and Bond Equivalents

Benson Group equivalents		Laidler Bond equivalents
A	=	A + D
C	=	2B + 1/2C - A
D	=	B + C - A/2
F	=	3/2C

Both the Laidler and Benson parameters can be further condensed to the two parameters used in this study:

Benson Group equivalents		Laidler Bond equivalents	
A	=	A + D	= GE_I
C + D + F	=	3B + 3C -3A/2	= GE_{II}

Either the Benson group parameters or the Laidler bond parameters can be substituted into the above expression for the heat of formation. When energy values for Benson group equivalents or Laidler bond equivalents are derived from ab initio energies in a linear multiple regression (using 4 unknowns), they give results which are very similar to our results; the small difference arises from the fact that our scheme defines two group equivalents vs. five in Benson's and four in Laidler's. (See Tables 1.11 and 1.12.) These results show that it is the fitting to ab initio energies that produces accurate enthalpy changes and not the nature of the structural groups.

Table 1.11 Heats of formation calculated with Laidler bond parameters derived from STO-3G energies(au)[a]

molecule	ΔH_fexpt. (kcal/mol)	ΔH_fcalc.	expt.-calc.
benzene	19.81	20.49	-0.68
naphthalene	35.85	35.70	0.15
azulene	73.5	94.94	-21.44
acenaphthalene	62.04	66.80	-4.76
biphenylene	104.43	108.07	-3.64
anthracene	55.44	57.06	-1.62
phenanthrene	49.52	48.01	1.51
pyrene	51.59	52.88	-1.29
triphenylene	63.4	61.91	1.49
chrysene	62.8	63.00	-0.20
tetracene	69.8	81.37	-11.57
3,4-benzophenanthrene	69.6	71.86	-2.26
1,2-benanthracene	69.63	66.95	2.68
perylene	73.7	73.99	-0.29

[a](A)=18.31457 (B)=-3.31681 (C)=-24.94870 (D)=-56.30191 au.

Table 1.12 Heats of formation calculated with Benson group parameters derived from STO-3G energies[a]

molecule	ΔH_f expt. (kcal/mol)	ΔH_f calc.	expt.-calc.
benzene	19.81	19.64	0.17
naphthalene	35.85	35.26	0.59
azulene	73.5	94.50	-21.00
acenaphthalene	62.04	65.84	-3.80
biphenylene	104.43	107.67	-3.24
anthracene	55.44	57.04	-1.60
phenanthrene	49.52	48.31	1.21
pyrene	51.59	51.11	0.48
triphenylene	63.4	63.30	0.10
chrysene	62.8	64.05	-1.25
tetracene	69.8	81.74	-11.94
3,4-benzophenanthrene	69.6	71.36	-1.76
1,2-benanthracene	69.63	67.66	1.97
perylene	73.7	73.30	0.40

[a] (A)=-37.98711 (C)=-37.42308 (D)=-37.42361 (F)=-37.42166

Applications

Carbon clusters which are found experimentally in relatively large abundance are assumed to have unusually stable and often symmetrical structures. It is of interest to be able to identify these structures. Almlöf and Lüthi (AL) studied large clusters of carbon atoms by ab initio SCF calculation using basis sets of double-zeta quality. They considered a sufficient number of structures of a homologous series to enable extrapolation to the energy of a carbon atom in the cluster, E_c. The value of E_c varies with the type of cluster - graphitic, or diamond-like, or a carbon chain system, etc. We discuss here their graphite model.

By fitting the energies of graphite fragments and extrapolating to large clusters, AL calculate a E_c of -37.8366 au. (When they fit the energies of planar clusters with hydrogens on the periphery, a similar E_c of -37.8363 a.u. was obtained.) They concluded that it is possible to model a graphitic sheet with large condensed aromatics, thereby avoiding cumbersome open-shell calculations. Using a similar approach in the present work, the 6-31G*//STO-3G energies per carbon of the C_nH_n hydrocarbons, benzene, naphthalene, phenanthrene, triphenylene, pyrene, perylene, and coronene were plotted against m/n. The linear fit had a standard deviation of 0.0006 au and an intercept of -37.8773 au (similar to the AL E_c but obtained here in a different basis set), which can be taken as the 6-31G* energy of a carbon atom

in a hypothetical gaseous graphitic sheet. Use of this value in our equation for the heat of formation from group equivalents with m = 0 furnishes a 2.5 kcal/mol as the standard heat of formation per mole of carbon of the graphitic sheet. This is equivalent to the standard heat of sublimation per mole of carbon of graphite to graphitic sheets and could be compared with the heats of sublimation per mole of carbon clusters to determine whether they are graphitic or not.

It is also possible to extrapolate the heat of formation per carbon using the heats of formation of the large hydrocarbons studied by Almlöf and Lüthi. Since we have already shown that the validity of group equivalents for benzenoid aromatics is largely independent of basis, we can derive double-zeta group equivalents from the AL ab initio energies of five D_{6h} aromatics. (While the geometries of the AL structures were not fully optimized, they provide the best available estimates for these large hydrocarbons.) Using the experimental heat of formation of benzene, 19.8 kcal/mol, our calculated heat of formation of coronene, 61.5 kcal/mol, and the corresponding ab initio energies, we obtain the following AL group equivalents: GE[=C_bH-]AL = -38.4101 au and GE[=C_b-]AL = -37.8392 au. For $C_{54}H_{18}$, $C_{96}H_{24}$, and $C_{150}H_{30}$, they lead to heats of formation of 126, 212 and 320 kcal/mol. When the calculated heats of formation per carbon for the five D_{6h} hydrocarbons are plotted against the H-C ratio there results a nearly straight line with an intercept of 1.83 kcal/mol, a reasonable

value for the graphitic monolayer, judging from known heats of sublimation of large aromatics.[24] Thus, a graphitic monolayer may be expected to have a heat of formation (or sublimation) in the range of 1.83 to 2.5 kcal/mol/C.

Conclusion

We have shown that ab initio molecular orbital calculations can be used successfully in computing molecular properties. The geometries of 16 aromatic hydrocarbons, ranging in size from 6 to 24 carbons, were optimized in the STO-3G and 6-31G* basis sets. Several of the larger aromatics are non-planar. The calculated geometries agreed well with experiment at the STO-3G level; the rms deviation from experiment improved slightly at the 6-31G* level. A linear relationship between bond order and bond length was found for these molecules.

Accurate heats of reaction were calculated using only SCF ab initio energies for homodesmic reactions with the constraint that all products and reactants were benzenoid aromatics. We therefore conclude that the correlation energies cancel between bonds of reactants and products for benzenoid aromatics. Calculations of ΔH_r for homodesmic reaction involving both benzenoid and non-benzenoid aromatics or only non-benzenoid aromatics were less successful.

Group equivalents that can be used to convert ab initio SCF energies into ΔH_f values were derived by fitting the SCF

energies of a training set of molecules to their experimental heats of formation. Heats of formation were predicted most successfully for benzenoid aromatics. That the more accurate heats of formation were calculated for benzenoid aromatics also suggests the incomplete cancellation of correlation energies between benzenoid and non-benzenoid aromatics. It was also found in this study that the group-equivalent scheme could be extended to yield accurate heats of formation for substituted aromatics. Finally, ab initio group equivalents were shown to be more accurate and more versatile in predicting heats of formation than other group or bond equivalent methods.

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2. CONFORMATIONAL STUDIES OF PILOCARPINE

Introduction

The aim of much current research in molecular pharmacology is a determination of the active site of a receptor (or enzyme). An understanding of the mechanism of interaction of the receptor and its ligand and the ability to design new molecules that will bind to the receptor's active site depend upon such knowledge. The nature of the receptor site is often inferred from natural or synthetic biologically active molecules - agonists and antagonists (or, in the case of enzymes, substrates and inhibitors). The agonist or antagonist structure of most interest is clearly its active conformation. A flexible agonist possesses more possible conformations than a semi-rigid or rigid agonist. Thus rigid and semi-rigid agonists can be used to deduce active conformations of flexible agonists.

This study concerns the active conformation of pilocarpine, which mimics the muscarinic cholinergic agonist acetylcholine (1). The conformational potential energy surface of pilocarpine was determined by several methods, including ab initio molecular orbital calculations. A model for the muscarinic pharmacophore, previously developed for semi-rigid muscarinic agonists[1] was then applied to determine the possible active conformations of pilocarpine.

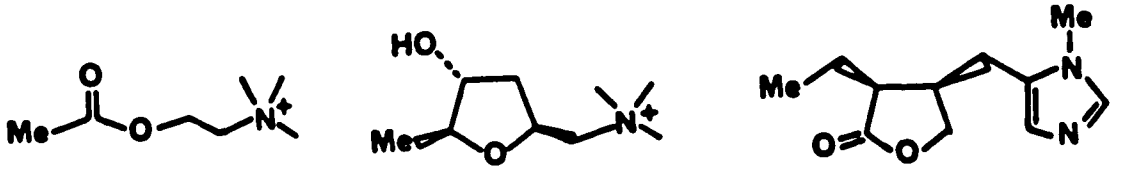
Background

Muscarinic agonists interact with the muscarinic receptor of the parasympathetic and central nervous systems to mimic the effects of acetylcholine. In classical muscarinic agonists such as muscarine (2), an NCCOCC-type linkage forms the backbone of the molecule; and a cationic head group is invariably present, usually a trimethylammonium group. These agonists often contain an ester or ether oxygen. It has been demonstrated that potency is associated with an optimum alkyl chain length.

Pilocarpine (3) is a tertiary amine that lacks the NCCOCC linkage and has no obvious structural similarity to either acetylcholine or muscarine. There is at present no definitive explanation of why it mimics the muscarinic effects of acetylcholine.[2] Structure-activity studies have at most been able to suggest a relationship between the percent protonation of the imine nitrogen and potency relative to acetylcholine.[3,4]

A model previously developed by Schulman et al., based on conformational analyses of semi-rigid agonists, proposed several geometrical parameters and criteria to define the muscarinic pharmacophore[1]. This allowed the active conformations of the classical muscarinic agonists to be deduced. Because pilocarpine is not a classical muscarinic agonist, the model cannot be applied to it directly. However, the active conformation of muscarine provides a template with

Figure 2.1 Structures of acetylcholine (1), muscarine (2) and pilocarpine (3).



(1) (2) (3)

which to determine the active conformation of pilocarpine.

The X-Ray Structure of Pilocarpine

The structure of pilocarpine first proposed by Jowett[5] in 1900 has been confirmed by chemical degradation,[6] synthesis[7] and X-ray analyses.[4,8] The ethyl and imidazolylmethyl groups on C_7 and C_{11} (Figure 2.2) of the dihydrofuranone ring are cis, making the configurations at these carbons S and R, respectively.[6] Pilocarpine is thermodynamically less stable than its (R,R) trans epimer isopilocarpine (4), a much less

active compound.[9]

The conformation of pilocarpine is largely defined by the values of three torsional angles (Figure 2.2): alpha = $C_4-C_5-C_6-C_7$; beta = $C_5-C_6-C_7-C_8$; and gamma = $C_7-C_{11}-C_{13}-C_{14}$.

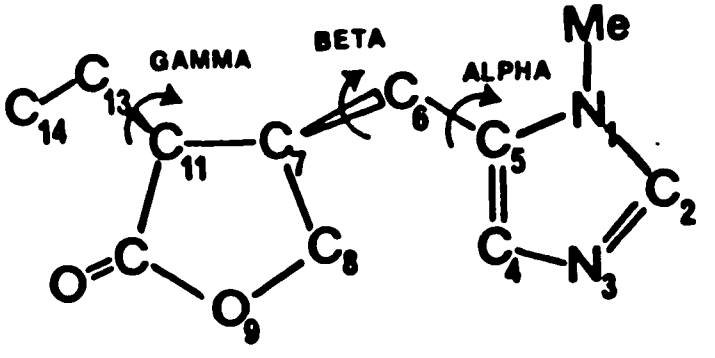


Figure 2.2 The torsional angles of pilocarpine.

The X-ray structure of the trichlorogerminate salt of pilocarpine has been reported by Fregerslev and Rasmussen (FR).[8] Two nearly equivalent forms of pilocarpine are found in each asymmetric unit; the values, in degrees, of the three torsional angles are alpha = 7.4, beta = 71.7, gamma = -64.4; and alpha = 18.2, beta = 72.3, gamma = -58.1. The imidazole ring is nearly planar while the lactone ring has an envelope form with C_7 in the flap position; the two rings are

essentially perpendicular. The trichlorogerminate structures differ from that of the hydrochloride salt studied by Codding and James (CJ),[4] where alpha = -4.2°, beta = 168.4°, gamma = -171.4° and the lactone envelope has its C_7 flap bent in the opposite sense. The envelope-shaped lactone rings of the FR and CJ structures have values of the torsional angle C_6-C_{11}-C_{13}-C_{14} of 39° and -32°, respectively. The existence of two very different structures in the solid state implies either at least two minima or a flat region of the conformational potential energy surface with respect to the torsional angles. Structures found in the solid state need not of course be biologically active forms, as in the case of acetylcholine itself.[1] The relationship of the X-ray structures to the active form of pilocarpine will be described later.

Methods

The conformational energy of pilocarpine was obtained by the MMP2 molecular mechanics method[10a], by semiempirical (AM1[11]), and ab initio (STO-3G[12] and 6-31G*[12]) molecular orbital SCF calculations. The AM1 and MMP2 calculations, in which the 3N - 8 = 85 remaining parameters were relaxed, were performed on a 30° grid of alpha-beta values with alpha ranging from -180 to 180° and beta from 0 to 210°.[3] For all alpha values, beta > 210° leads to large steric repulsions between the imidazole ring and the methylene hydrogens on C_{13}. In the MMP2 and AM1 studies, the FR crystal structure was used

as a starting geometry for beta between 0 and 90°, while for beta > 90° the CJ structure was used.

Some MM2 parameters which involve the pyrrole and imine nitrogens were obtained from Tai and Allinger.[12b] However, thirteen parameters involving a pyrrole-type and/or imine-type nitrogen and an sp^3 carbon were not available. They were taken without change from other known MM2 parameters by assuming the imine- or pyrrole-type nitrogen to be equivalent to an sp^2 carbon.

The ab initio calculations were performed with full optimization of the remaining parameters for several values of alpha and beta using the Queens College Quantum Chemistry Package.

The fitting of pilocarpine to muscarine and generation of the perspective pictures were carried out with the Chem-X molecular modeling package, developed and distributed by Chemical Design, Ltd., Oxford, England.

Application of Muscarinic Model to Pilocarpine

Since the structure of pilocarpine differs from that of a classic muscarinic agonist, the model of the muscarinic pharmacophore proposed by Schulman et al.[1] can only be applied to it in a limited fashion.

Studies of the pilocarpine proton NMR spectrum[4] and pilocarpine-induced contractions of the guinea-pig ileum[13], as a function of pH, infer a pK_a of 7.0; ca. 30% of the molecules

would be N_3-protonated at a physiological pH of 7.4. Point P, corresponds to an anionic site of the receptor that interacts electrostatically with protonated pilocarpine. Recent data derived from the receptor sequences[14] and proteolysis of covalently bound propylbenzilylcholine mustard[15] suggest that the anionic receptor site is a carboxylate oxygen(s) on one of two aspartates in helix 3 of the receptor. We locate point P of the model for pilocarpine 3 A from N1 and colinear with the N_1-C_5 bond.

Point Q of the model is not applicable to pilocarpine. Even though pilocarpine contains an ester group - its ester is a gamma butyrolactone, rather than the more common acyclic ester or reverse ester (as in arecoline and the esters of 4-imidazoleacetic acid) - Dreiding models show that the lactone group of pilocarpine is not in the same position to interact with a receptor proton at point Q as are the dicoordinate oxygens of classical muscarinics.

While the geometrical parameters of the model, dihedral angle PNOQ and distance PQ, are also not directly applicable, the model identifies a distance, PC_t which can be used. This distance describes the length of the agonist and correlates with agonist potency; PC_t values of 8.5 A - 8.9 A are associated with maximum potency among the semi-rigid muscarinic agonists.

Finally, the model assumes a conformation accessible if its energy is within 3-4 kcal/mol of the minimum energy

conformer.

Conformational Energy Surface of Pilocarpine

Application of the energy criterion of the model requires that comprehensive survey be made of the pilocarpine conformational potential energy surface in order to locate conformers of low energy. The AM1 and MMP2 calculational methods were used to scan the potential energy surface of pilocarpine, as a function of its torsional angles alpha and beta. Ab initio calculations were then made at selected points and also used to scan parts of the potential surface. The calculations were carried out primarily for the neutral base, on the grounds that the cationic head group would be largely neutralized by the anionic receptor site. The MMP2 surface of N_3-protonated pilocarpine was calculated and found to have a shape virtually identical to that of the neutral species. It seems unlikely that over the distances involved, the dipole interaction of the head group's salt bridge with the receptor anionic oxygen would profoundly influence the conformational energy surface.

Figures 2.3 and 2.4 depict contours of the AM1 and MMP2 conformational energy surfaces of pilocarpine. Figure 2.5 shows a three-dimensional view of the MMP2 potential energy surface. Values of beta much above 180° are energetically unfavorable owing to strong steric repulsions. For most points on the energy surfaces, gamma is ca. 70°, although for

beta > 90°, gamma values closer to 160° are found. The value of gamma for any point on the energy surface is consistent with that of the crystal structure nearest to that point.

The AM1 and MMP2 surfaces contain four nearly equi-energetic minima, labeled A, B, C and D in Figures 2.3 and 2.4, which surround two local maxima. The torsional angles and energies of the minima are given in Tables 2.1 and 2.2, respectively. (The energy scales in the two cases are different: AM1 ΔH_f values are of the order of -45 kcal/mol, MMP2 steric energies, 19 kcal/mol). The maxima on each surface occur at (alpha,beta) values of (0°,115°) and (180°,115°), where the lactone hydrogen on C_7 is close to an imidazole hydrogen on C_4 or a hydrogen on the N_1-methyl group, respectively. In addition, beta = 115° corresponds to an eclipsed conformation about the C_6 - C_7 bond. The AM1 surface is flatter than the MMP2 surface due partly to the tendency of the AM1 method to underestimate ring-puckering effects. For example, the lactone rings produced by AM1 are flatter than the envelope forms observed in the X-ray structures or calculated by the MMP2 and ab initio methods. Energy values for the maxima relative to the global minima, B, on each surface, are 7.0 and 10.1 kcal/mol (MMP2) and 2.7 and 6.7 kcal/mol (AM1) for (0°,115°) and (180°,115°), respectively. The ab initio STO-3G relative energy for the (0°,115°) maximum is 4.9 kcal/mol.

Figure 2.3 The AM1 potential energy surface of pilocarpine.

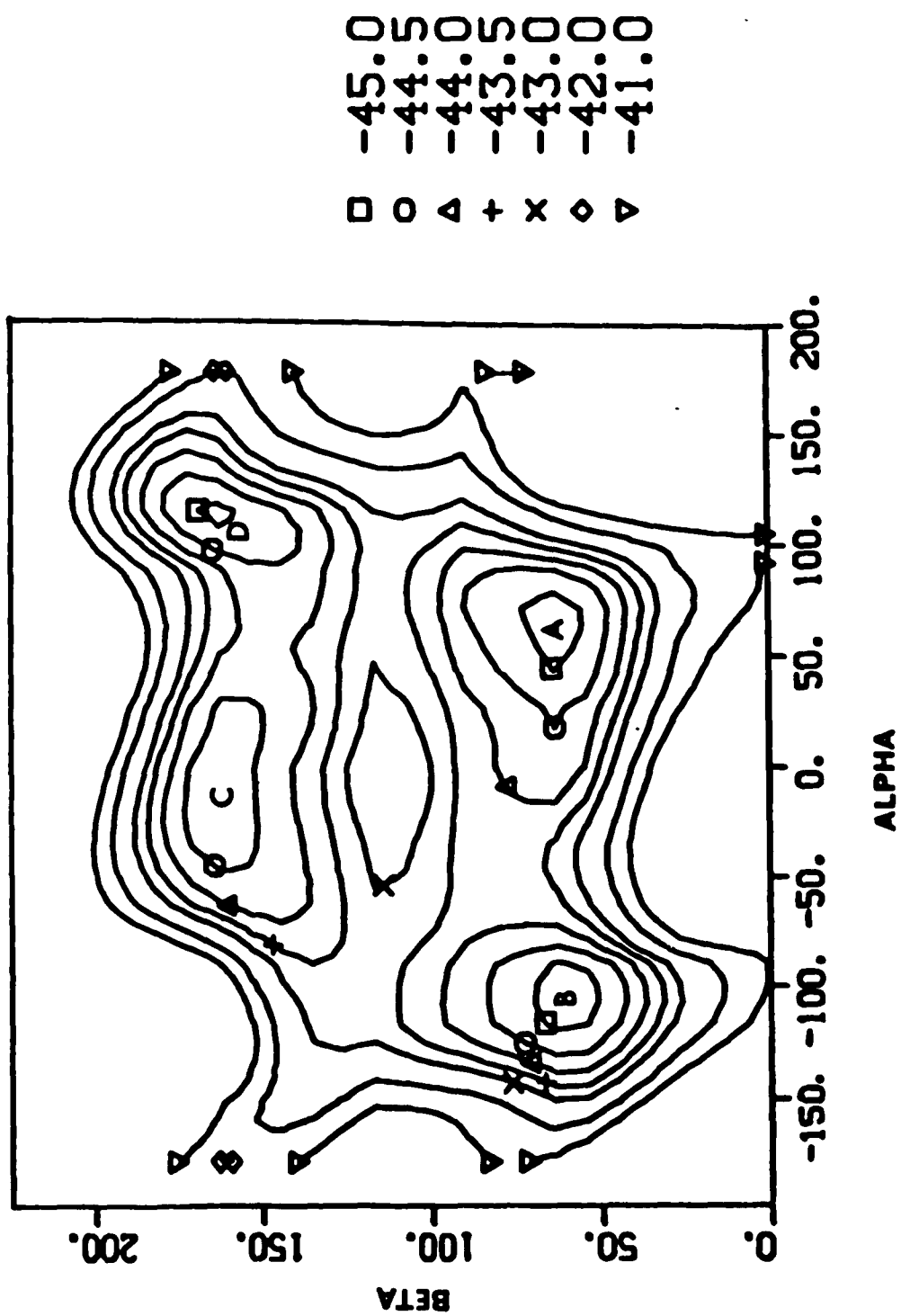


Figure 2.4 The MMP2 potential energy surface of pilocarpine.

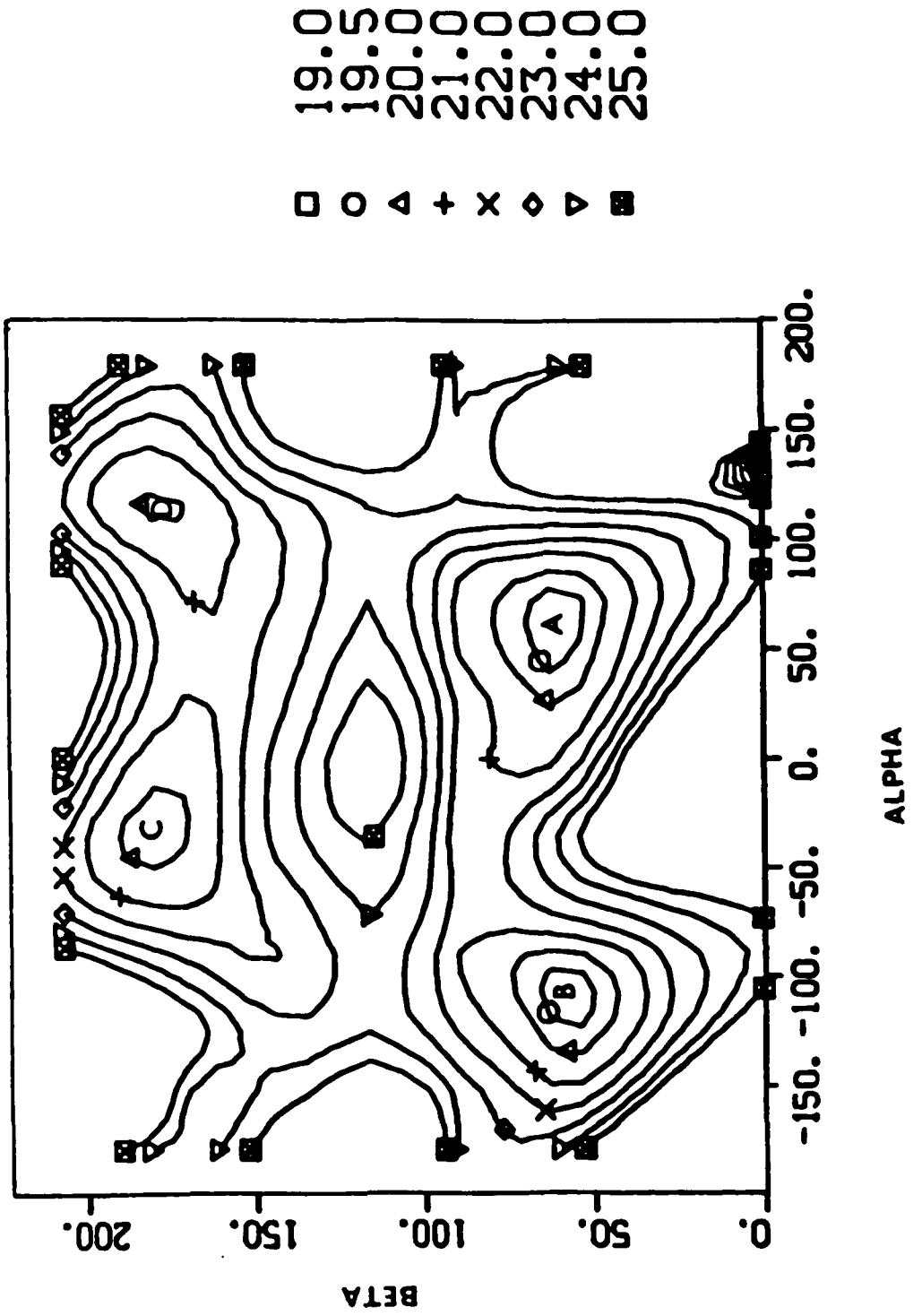
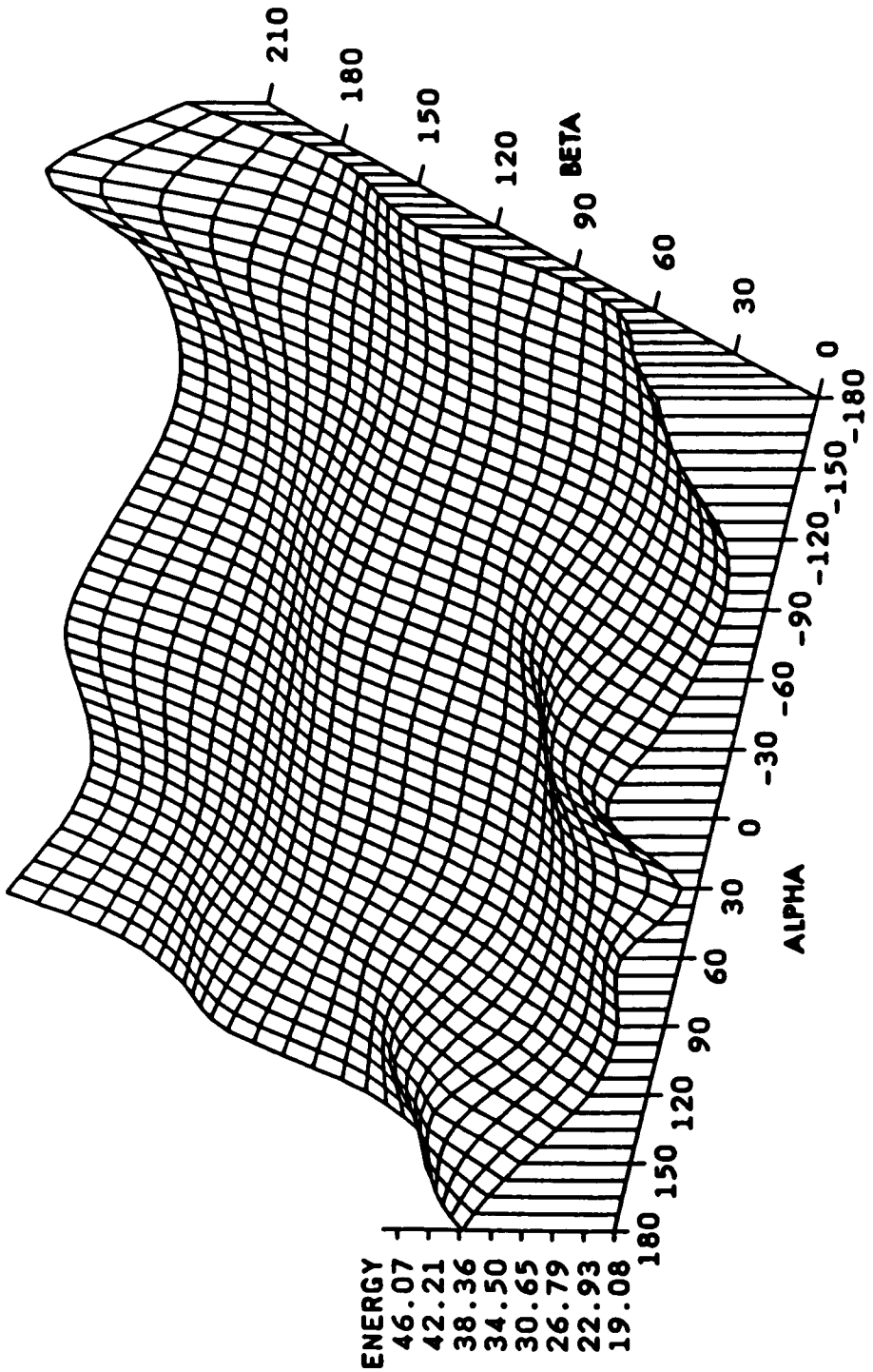


Figure 2.5 The MMP2 potential energy surface of pilocarpine in 3-dimensions.



Points A correspond roughly to the FR trichlorogerminate X-ray structures,[8] although the AM1 and MMP2 alpha values of 64.2 and 60.1° are considerably larger than in the two FR structures, 7.4 and 18.2°. From a scan of alpha with beta held fixed at 72°, ab initio STO-3G calculations suggest that the region around minimum A is more elongated than is predicted by AM1 and MMP2: the conformational energy for beta = 72° remains constant to within 1 kcal/mol for alpha values ranging from 7 to 60°. The energies of minimum A and the FR structures are therefore very similar. Minimum A is the lowest of the four minima according to the STO-3G calculations.

Energy minimum C corresponds to the CJ X-ray structure.[8] The ab initio STO-3G and 6-31G* SCF calculations furnish nearly equal energies for minima A and C, A being slightly lower. This is in agreement with the AM1 and MMP2 results. No X-ray structures corresponding to minima B and D have been observed.

Table 2.1 Torsional Angles of the Pilocarpine Structures (deg)

Description	alpha	beta	gamma
A:			
FR X-ray(1)	7.4	71.7	64.4
STO-3G SCF	7.4	71.0	66.7
FR X-ray(2)	18.2	72.3	58.4
STO-3G SCF	18.2	71.2	61.9
AM1	64.2	68.0	81.1
MMP2	60.1	60.1	65.0
B:			
AM1	-107.0	66.2	81.0
MMP2	-113.5	61.5	64.4
C:			
Codding X-ray	-4.2	168.4	-171.4
STO-3G SCF	-4.2	169.2	-172.0
AM1	3.6	162.4	171.2
MMP2	-32.3	-177.2	-178.3
D:			
AM1	117.2	163.7	172.9
MMP2	119.0	179.8	-177.4
Active Conformation:			
From fitting	60	80	69

Table 2.2 Energies of the Pilocarpine Structures[a]

Description	--- Energy --- AM1	MMP2	STO-3G
A	-45.4	19.2	-675.9923,-675.9924
B	-45.5	19.1	-675.9921
C	-44.8	19.5	-675.9923
D	-45.2	19.9	-675.9917
Active Conformation	-44.7	19.8[b]	-675.9901

[a]Ab initio total energies are in atomic units (1 au = 627.5 kcal/mol). AM1 energies are ΔH_f values in kcal/mol. MMP2 steric energies are in kcal/mol. [b]Represents an upper bound to the steric energy at the active conformation since only two parameters may be held fixed simultaneously by the MMP2 driver.

Active Conformation of Pilocarpine

The ring substituents of pilocarpine and muscarine are ogriented cis in both compounds: pilocarpine has its ethyl group *cis* to an imidazolylmethyl group, muscarine a methyl group *cis* to its trimethylmethammonium group. Based upon these similarities pilocarpine can be related to muscarine as follows: (1) the methyl-containing nitrogen of pilocarpine is equivalent to the muscarine nitrogen; (2) the terminal methyl groups of pilocarpine and muscarine correspond; (3) there is no oxygen in pilocarpine equivalent to the dicoordinate ether oxygen (O_e) of muscarine. This has been the major structural impediment to identifying pilocarpine as a muscarinic agonist; and (4) the lactone oxygens of pilocarpine are analogous to the hydroxyl of muscarine. While the precise role of these oxygens is not clear, they probably have long-range dipole-dipole interactions with the receptor.[16] The wide variety of their positions in muscarinic agonists, however, renders them difficult to model.

Since the lack of the dicoordinate oxygen to interact with receptor point Q precludes a literal application of the model in determining its active conformation, an alternative approach is needed. We therefore used the previously determined active conformation of a classical agonist, such as muscarine (2), as a template (Figure 2.6a). The torsional angles alpha, beta and gamma of pilocarpine can be varied to fit that template. The conformer of muscarine used in the

fitting has an envelope form for its tetrahydrofuran ring with oxygen as the flap. The following atom pairs of each molecule were juxtaposed (the pilocarpine atom is given first), with the resulting interatomic deviations in A: N_1 and N_1, 0.13; C_5 and C_2, 0.18; C_6 and C_3, 0.18; C_7 and C_4, 0.44; C_{11} and C_5, 0.26; C_{13} and C_6, 0.66; C_{14} and C_7, 0.32. The average deviation between corresponding atoms of 1 and 3 is 0.31 A, the largest deviation being found for the methylene of the ethyl group of 3. The fit was undoubtedly more demanding than the receptor itself in requiring the near juxtaposition of seven pairs of atoms.

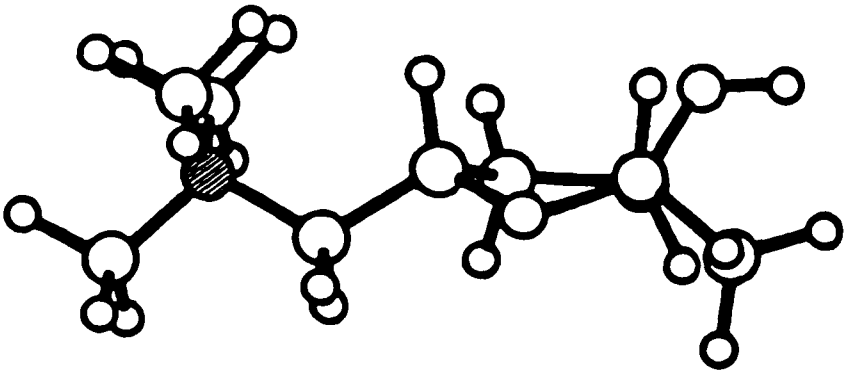
The proposed active conformation of pilocarpine is shown in Figure 2.6b. The values of the torsional angles resulting from the fit are alpha = 60°, beta = 80°, gamma = 69°. The AM1 and MMP2 energies of the structure are each only 0.7 kcal/mol higher than the global minimum, B, on their respective potential energy surfaces (Figures 2.3 and 2.4). Its STO-3G and 6-31G* energies are respectively 1.4 and 1.8 kcal/mol higher than those of the lowest-energy ab initio structure, A. Thus the proposed active conformation of pilocarpine, derived from its juxtaposition with muscarine as a template, should be accessible.

As noted earlier, potent classical muscarinic agonists frequently have a terminal methyl group whose carbon, C_t, lies 8.5 to 8.9 A from P (Figure 2.7). We assume that for pilocarpine, C_t is the terminal methyl carbon atom (C_{14}) of

its ethyl group. This is supported both by the presence of an ethyl, rather than a methyl, group and the requirement that the ethyl group be cis to the imidazolylmethyl group for biological activity, despite adverse steric interactions. In the case of the proposed structure, the P-C_t distance is 8.9 Å.

Figure 2.6 Active conformations of a. muscarine b. pilocarpine.

a



b

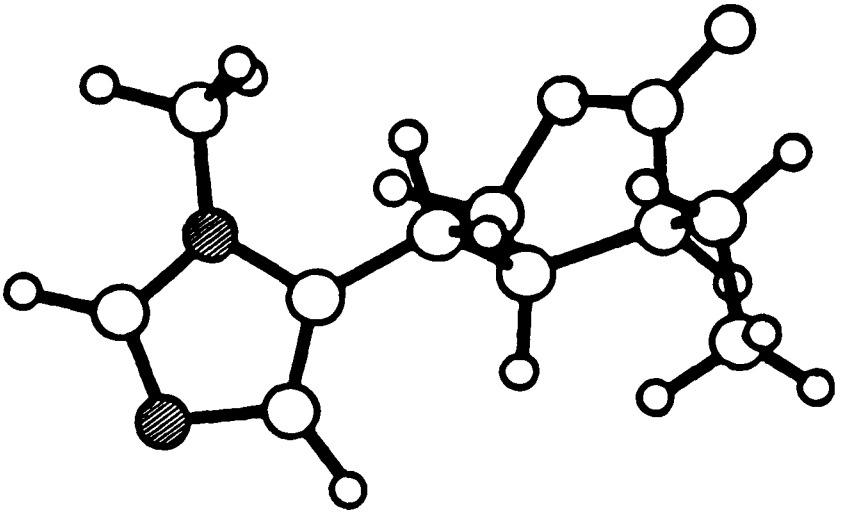
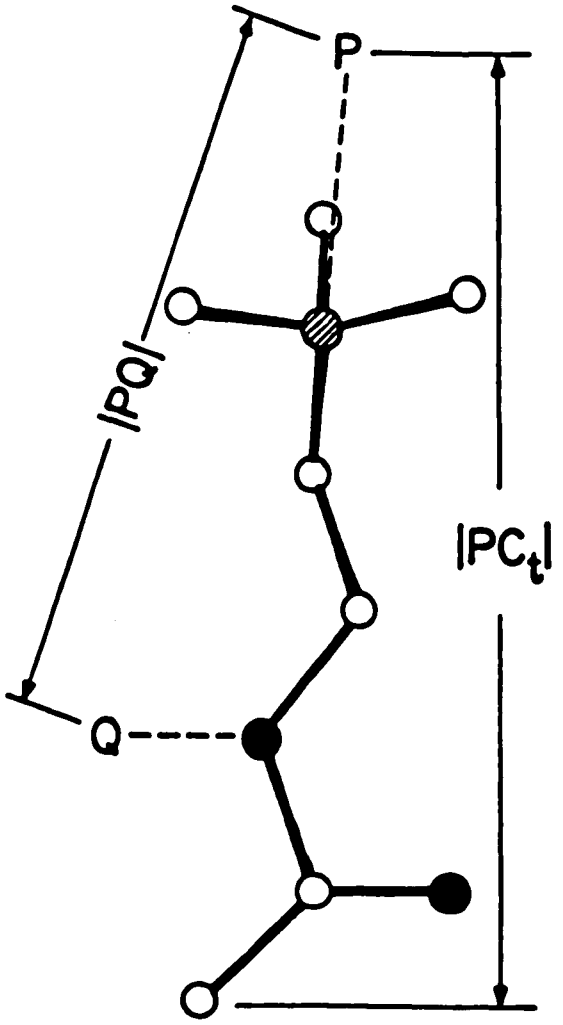


Figure 2.7 PC_t distance shown in acetylcholine.



Alternative Structures

The proposed active structure was determined by fitting pilocarpine to the active conformation of muscarine. However, other pilocarpine conformations cannot be excluded. For example, the fitting employed the previously determined active conformation of muscarine, whose NCCO torsional angle is 143° and whose envelope tetrahydrofuran ring has oxygen in the flap position.[1] Muscarine is a somewhat flexible molecule; in its crystalline form, where C_4 is the flap atom, the value of this angle is considerably smaller, 73°.[17] However, even if this angle were overestimated by the model and the active conformation of muscarine employed an NCCO angle closer to the X-ray value, the fit of pilocarpine to muscarine could still be accommodated: for beta = 80°, a decrease of angle alpha to 15° would involve only a 1 - 2 kcal/mol increase in energy, and would maintain the fit of pilocarpine to the new muscarine template. In fact, the fit is as good as that of the active structure, the average deviation among the seven juxtaposed atoms being 0.33 Å.

An important question is whether it must be concluded that the N_1-methyl group, rather than N_3H, is the site of interaction with the receptor anionic oxygen. The former affords a better fit to the trimethylammonium group of muscarine, and therefore provides a better fit to the receptor: the P-C_1 distance for approach to the methyl-bearing nitrogen N_1 is 8.9 Å, while that for protonated N_3 exceeds 10

A. Only the smaller value is consistent with the PC_t derived for the classical muscarinics. It has been suggested that muscarinic receptors show higher activity for N-methylated than for N-protonated agonists, the reverse of the situation found in the adenoreceptors.[18] It is known, for example, that pilocarpine devoid of its N-methyl (pilocarpidine[6]) has less activity.[19]

Despite this evidence, the possibility that N_3H is the actual site of interaction cannot be entirely ruled out. Since twisting of the imidazole ring of the active structure by 180° puts N_3 in an arrangement similar, though not identical, to the N_1-methyl group of the proposed structure, the use of N_3 could be accommodated by the present approach; the active form would then be close to minimum B. The large $P-C_t$ distance could be reduced if there were a significantly non-linear $N_3-H...O$ hydrogen bond.

"A-Face" vs. "B-Face"

From their X-ray structures of the salts of muscarinic agonists, Gieren and Kokkinidis (GK) proposed a model for muscarinic-receptor interaction based on a so-called "activity triangle" formed from the agonist oxygen and nitrogen (3.2 Å apart) and a receptor oxygen.[20] Since pilocarpine lacks the characteristic ether oxygen used by GK to form an activity triangle, their model does not fully apply to pilocarpine. An attempt to locate the activity triangle by using one of the

two lactone oxygens and either of the imidazolyl nitrogens fails. For all energetically accessible conformations of pilocarpine, the carbonyl oxygen comes no closer to either nitrogen than ca. 4.9 Å. The dicoordinate pilocarpine O_9 is 4.6 and 6.2 Å from N_1 and N_3, respectively, in the active conformation. Only for small values of beta, such as 25°, with alpha = 88°, does the N_1-O_9 distance become as small as 3.3 Å. However, such a conformation is significantly energetic and does not furnish a particularly convincing fit to muscarine since the pilocarpine carbonyl oxygen must play the role of the muscarine C7-methyl group, for which there is no precedent.

The analysis presented in this paper has assumed that the anionic receptor oxygen(s) will contact the protonated pilocarpine imidazolyl head group in the plane of its ring. Most classical muscarinics have a trimethylammonium cationic head group, in which case the approach to the receptor oxygen is likely to be perpendicular to one of the four tetrahedral faces defined by three (of the four) carbons attached to the nitrogen.[20,21] The choice made in our model[6] is the so-called A-face, formed from the three methyl carbons. GK have suggested instead that approach would be perpendicular to one of the two B-type faces, formed from one methylene and two methyl carbons.[21] The agonist conformations deduced from the model by Schulman et al. were found to be essentially consistent with either choice, A- or B-face. But for

pilocarpine, a B-face approach involves an anionic attack perpendicular to the imidazole ring where it would encounter the negative potential of the imidazole pi electron system. To model the interaction of the imidazole ring with a receptor oxygen, we calculated the energy of an imidazole cation with an acetate anion approaching from several directions and scanned over several imidazole-acetate distances: three approaches are in the plane of the imidazole ring and two are perpendicular approaches. The energies obtained indicate that an in-plane approach is clearly preferable to one perpendicular to the imidazole ring.

Another interpretation of the B-face interaction they propose is an approach to the imidazolyl head group in plane as in the A-face approach but with a rotation of alpha such that the head group is in the same position relative to the anion as would be the head group of muscarine in a B-face approach. This required a refitting of pilocarpine to muscarine juxtaposing C_3 of pilocarpine to C_9 of muscarine instead of C_2. The result was a large deviation between atoms of pilocarpine and muscarine, which provides more evidence for an A-face approach in preference to a B-face approach to the anionic receptor for muscarinic agonists in general.

Conclusion

We conclude that the active conformation of pilocarpine proposed in this study is a reasonable possibility because:

1. it meets all the applicable criteria of the model previously deduced for muscarinic agonists, and 2. pilocarpine can be superimposed on the muscarinic template with a remarkably small average deviation of fitted atoms. From our imidazole-acetate calculations we conclude that an in-plane approach to the receptor is the preferred mode of interaction. In addition, the large deviation resulting from a refitting to simulate the B-face approach of muscarine, further argues for an A-face approach to the receptor for all muscarinic agonists.

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APPENDIX

Supplementary Material
6-31G* (SCF) Geometries of Aromatic Hydrocarbons
(Principal-Axis Coordinates in Å)

BENZENE C_6H_6, D_{2h}

C	0.0000	0.0000	1.3861
C	1.2004	0.0000	0.6930
C	1.2004	0.0000	-0.6930
C	0.0000	0.0000	-1.3861
C	-1.2004	0.0000	-0.6930
C	-1.2004	0.0000	0.6930
H	0.0000	0.0000	2.4618
H	2.1320	0.0000	1.2309
H	2.1320	0.0000	-1.2309
H	0.0000	0.0000	-2.4618
H	-2.1320	0.0000	-1.2309
H	-2.1320	0.0000	1.2309

NAPHTHALENE $C_{10}H_8$, D_{2h}

C	0.0000	0.0000	0.7043
C	0.0000	0.0000	-0.7043
C	1.2426	0.0000	1.3923
C	-1.2426	0.0000	1.3923
C	1.2426	0.0000	-1.3923
C	-1.2426	0.0000	-1.3923
C	2.4158	0.0000	0.7081
C	-2.4158	0.0000	0.7081
C	2.4158	0.0000	-0.7081
C	-2.4158	0.0000	-0.7081
H	1.2401	0.0000	2.4683
H	-1.2401	0.0000	2.4683
H	1.2401	0.0000	-2.4683
H	-1.2401	0.0000	-2.4683
H	3.3517	0.0000	1.2376
H	-3.3517	0.0000	1.2376
H	3.3517	0.0000	-1.2376
H	-3.3517	0.0000	-1.2376

BIPHENYLENE $C_{12}H_8$, D_{2h}

C	-0.7538	0.0000	0.7066
C	-0.7538	0.0000	-0.7066
C	0.7538	0.0000	0.7066
C	0.7538	0.0000	-0.7066
C	-1.8992	0.0000	1.4343
C	-1.8992	0.0000	-1.4343

C	1.8992	0.0000	1.4343
C	1.8992	0.0000	-1.4343
C	-3.1029	0.0000	0.6864
C	-3.1029	0.0000	-0.6864
C	3.1029	0.0000	0.6864
C	3.1029	0.0000	-0.6864
H	-1.9193	0.0000	2.5091
H	-1.9193	0.0000	-2.5091
H	1.9193	0.0000	2.5091
H	1.9193	0.0000	-2.5091
H	-4.0419	0.0000	1.2107
H	-4.0419	0.0000	-1.2107
H	4.0419	0.0000	1.2107
H	4.0419	0.0000	-1.2107

AZULENE $C_{10}H_8$, C_{2v}

C	1.1416	0.0000	1.8797
C	-1.1416	0.0000	1.8797
C	0.7423	0.0000	0.5427
C	-0.7423	0.0000	0.5427
C	0.0000	0.0000	2.6777
C	1.5835	0.0000	-0.5580
C	-1.5835	0.0000	-0.5580
C	-1.2587	0.0000	-1.9063
C	1.2587	0.0000	-1.9063
C	0.0000	0.0000	-2.4925
H	2.1579	0.0000	2.2239
H	-2.1579	0.0000	2.2239
H	0.0000	0.0000	3.7520
H	2.6372	0.0000	-0.3317
H	-2.6372	0.0000	-0.3317
H	2.0904	0.0000	-2.5887
H	-2.0904	0.0000	-2.5887
H	0.0000	0.0000	-3.5697

ACENAPHTHYLENE $C_{12}H_8$, C_{2v}

C	0.0000	0.0000	0.1267
C	0.0000	0.0000	-1.2514
C	1.1571	0.0000	0.9330
C	-1.1571	0.0000	0.9330
C	1.2815	0.0000	-1.8741
C	-1.2815	0.0000	-1.8741
C	2.3710	0.0000	0.3191
C	-2.3710	0.0000	0.3191
C	2.4115	0.0000	-1.1072
C	-2.4115	0.0000	-1.1072
C	0.6701	0.0000	2.3307
C	-0.6701	0.0000	2.3307
H	1.3602	0.0000	-2.9474

H	-1.3602	0.0000	-2.9474
H	3.3727	0.0000	-1.5898
H	-3.3727	0.0000	-1.5898
H	3.2940	0.0000	0.8721
H	-3.2940	0.0000	0.8721
H	1.3003	0.0000	3.1995
H	-1.3003	0.0000	3.1995

ANTHRACENE $C_{14}H_{10}$, D_{2h}

C	0.0000	0.0000	1.3908
C	0.0000	0.0000	-1.3908
C	1.2122	0.0000	0.7120
C	1.2122	0.0000	-0.7120
C	-1.2122	0.0000	0.7120
C	-1.2122	0.0000	-0.7120
C	2.4727	0.0000	1.3997
C	2.4727	0.0000	-1.3997
C	-2.4727	0.0000	1.3997
C	-2.4727	0.0000	-1.3997
C	3.6339	0.0000	0.7162
C	3.6339	0.0000	-0.7162
C	-3.6339	0.0000	0.7162
C	-3.6639	0.0000	-0.7162
H	0.0000	0.0000	2.4675
H	0.0000	0.0000	-2.4675
H	2.4704	0.0000	2.4756
H	2.4704	0.0000	-2.4756
H	-2.4704	0.0000	2.4756
H	-2.4704	0.0000	-2.4756
H	4.5730	0.0000	1.2401
H	4.5730	0.0000	-1.2401
H	-4.5730	0.0000	1.2401
H	-4.5730	0.0000	-1.2401

PHENANTHRENE $C_{14}H_{10}$, C_{2v}

C	1.4130	0.0000	0.8473
C	-1.4130	0.0000	0.8473
C	-0.6694	0.0000	2.0806
C	0.6694	0.0000	2.0806
C	-0.7304	0.0000	-0.3793
C	0.7304	0.0000	-0.3793
C	-2.8214	0.0000	0.8663
C	2.8214	0.0000	0.8663
C	-3.5406	0.0000	-0.2944
C	3.5406	0.0000	-0.2944
C	-2.8658	0.0000	-1.5237
C	2.8658	0.0000	-1.5237
C	-1.4989	0.0000	-1.5626

C	1.4989	0.0000	-1.5626
H	-1.2173	0.0000	3.0063
H	1.2173	0.0000	3.0063
H	-3.3261	0.0000	1.8168
H	3.3261	0.0000	1.8168
H	-4.6156	0.0000	-0.2696
H	4.6156	0.0000	-0.2696
H	-3.4260	0.0000	-2.4416
H	3.4260	0.0000	-2.4416
H	-1.0147	0.0000	-2.5194
H	1.0147	0.0000	-2.5194

PYRENE $C_{16}H_{10}$, D_{2h}

C	0.6695	0.0000	2.4563
C	-0.6695	0.0000	2.4563
C	0.6695	0.0000	-2.4563
C	-0.6695	0.0000	-2.4563
C	1.4220	0.0000	1.2216
C	-1.4220	0.0000	1.2216
C	1.4220	0.0000	-1.2216
C	-1.4220	0.0000	-1.2216
C	0.7162	0.0000	0.0000
C	-0.7162	0.0000	0.0000
C	2.8132	0.0000	1.2015
C	-2.8132	0.0000	1.2015
C	2.8132	0.0000	-1.2015
C	-2.8132	0.0000	-1.2015
C	3.4996	0.0000	0.0000
C	-3.4996	0.0000	0.0000
H	1.2150	0.0000	3.3836
H	-1.2150	0.0000	3.3836
H	1.2150	0.0000	-3.3836
H	-1.2150	0.0000	-3.3836
H	4.5751	0.0000	0.0000
H	-4.5751	0.0000	0.0000
H	3.3558	0.0000	-2.1305
H	-3.3558	0.0000	-2.1305
H	3.3558	0.0000	2.1305
H	-3.3558	0.0000	2.1305

TRIPHENYLENE $C_{18}H_{12}$, D_{2h}

C	-0.7003	0.0000	1.2543
C	0.7003	0.0000	1.2543
C	-1.4364	0.0000	-0.0206
C	-0.7361	0.0000	-1.2336
C	0.7361	0.0000	-1.2336
C	1.4364	0.0000	-0.0206
C	-1.4704	0.0000	-2.4338

C	-2.8429	0.0000	-0.0565
C	2.8429	0.0000	-0.0565
C	1.4704	0.0000	-2.4338
C	1.3725	0.0000	2.4903
C	-1.3725	0.0000	2.4903
C	-3.5358	0.0000	-1.2376
C	-2.8397	0.0000	-2.4433
C	3.5358	0.0000	-1.2376
C	2.8397	0.0000	-2.4433
C	0.6961	0.0000	3.6809
C	-0.6961	0.0000	3.6809
H	-1.2404	0.0000	4.6078
H	1.2404	0.0000	4.6078
H	-4.6107	0.0000	-1.2296
H	-3.3702	0.0000	-3.3781
H	4.6107	0.0000	-1.2296
H	3.3702	0.0000	-3.3781
H	-3.4062	0.0000	0.8547
H	-0.9629	0.0000	-3.3772
H	0.9629	0.0000	-3.3772
H	3.4062	0.0000	0.8547
H	2.4433	0.0000	2.5225
H	-2.4433	0.0000	2.5525

CHRYSENE $C_{18}H_{12}$, C_{2h}

C	0.1637	0.0000	1.8651
C	-0.1637	0.0000	-1.8651
C	-0.4202	0.0000	0.5550
C	0.4202	0.0000	-0.5550
C	1.4954	0.0000	2.0435
C	-1.4954	0.0000	-2.0435
C	2.3897	0.0000	0.9292
C	-2.3897	0.0000	-0.9292
C	-1.8619	0.0000	0.3724
C	1.8619	0.0000	-0.3724
C	-3.7879	0.0000	-1.1279
C	3.7879	0.0000	1.1279
C	-2.7803	0.0000	1.4511
C	2.7803	0.0000	-1.4511
C	-4.6455	0.0000	-0.0695
C	4.6455	0.0000	0.0695
C	-4.1280	0.0000	1.2383
C	4.1280	0.0000	-1.2383
H	-0.4694	0.0000	2.7289
H	0.4694	0.0000	-2.7289
H	1.9089	0.0000	3.0365
H	-1.9089	0.0000	-3.0365
H	4.1654	0.0000	2.1360
H	-4.1654	0.0000	-2.1360
H	5.7090	0.0000	0.2271

H	-5.7090	0.0000	-0.2271
H	4.8009	0.0000	-2.0773
H	-4.8009	0.0000	2.0773
H	2.4282	0.0000	-2.4633
H	-2.4282	0.0000	2.4633

TETRACENE $C_{18}H_{12}$, D_{2h}

C	1.2322	0.0000	1.3947
C	-1.2322	0.0000	1.3947
C	1.2322	0.0000	-1.3947
C	-1.2322	0.0000	-1.3947
C	0.0000	0.0000	0.7136
C	0.0000	0.0000	-0.7136
C	2.4279	0.0000	0.7188
C	-2.4279	0.0000	0.7188
C	2.4279	0.0000	-0.7188
C	-2.4279	0.0000	-0.7188
C	3.6990	0.0000	1.4043
C	-3.6990	0.0000	1.4043
C	3.6990	0.0000	-1.4043
C	-3.6990	0.0000	-1.4043
C	4.8538	0.0000	0.7205
C	-4.8538	0.0000	0.7205
C	4.8538	0.0000	-0.7205
C	-4.8538	0.0000	-0.7205
H	1.2307	0.0000	2.4711
H	-1.2307	0.0000	2.4711
H	1.2307	0.0000	-2.4711
H	-1.2307	0.0000	-2.4711
H	3.6975	0.0000	2.4803
H	-3.6975	0.0000	2.4803
H	3.6975	0.0000	-2.4803
H	-3.6975	0.0000	-2.4803
H	5.7950	0.0000	1.2414
H	-5.7950	0.0000	1.2414
H	5.7950	0.0000	-1.2414
H	-5.7950	0.0000	-1.2414

3,4-BENZOPHENANTHRENE $C_{18}H_{12}$, C_2

C	1.2162	0.0000	2.5118
C	-1.2162	0.0000	2.5118
C	0.0000	0.0000	0.3898
C	0.0000	0.0000	1.7812
C	2.3882	0.3516	1.8771
C	-2.3882	-0.3516	1.8771
C	2.4651	0.1884	0.4576
C	-2.4651	-0.1884	0.4576
C	1.2921	-0.0495	-0.2867

C	-1.2921	0.0495	-0.2867
C	3.7241	0.1974	-0.1817
C	-3.7214	-0.1974	-0.1817
C	1.4643	-0.4354	-1.6408
C	-1.4643	0.4354	-1.6408
C	3.8438	-0.1048	-1.5050
C	-3.8438	0.1048	-1.5050
C	2.6943	-0.4614	-2.2313
C	-2.6943	0.4614	-2.2313
H	-2.7842	0.7719	-3.2573
H	2.7842	-0.7719	-3.2573
H	-4.8075	0.1053	-1.9824
H	4.8075	-0.1053	-1.9824
H	-4.5971	-0.4162	0.4085
H	4.5971	0.4162	0.4085
H	-3.2942	-0.5355	2.4273
H	3.2942	0.5355	2.4273
H	-1.1630	-0.2459	3.5852
H	1.1630	0.2459	3.5852
H	-0.6231	0.7703	-2.2103
H	0.6231	-0.7703	-2.2103

PERYLENE $C_{20}H_{12}$, D_{2h}

C	1.2474	0.0000	0.7428
C	-1.2474	0.0000	0.7428
C	1.2474	0.0000	-0.7428
C	-1.2474	0.0000	-0.7428
C	0.0000	0.0000	1.4417
C	0.0000	0.0000	-1.4417
C	2.4072	0.0000	1.4721
C	-2.4072	0.0000	1.4721
C	2.4072	0.0000	-1.4721
C	-2.4072	0.0000	-1.4721
C	0.0000	0.0000	2.8545
C	0.0000	0.0000	-2.8545
C	1.2287	0.0000	3.5582
C	-1.2287	0.0000	3.5582
C	1.2287	0.0000	-3.5582
C	-1.2287	0.0000	-3.5582
C	2.4023	0.0000	2.8793
C	-2.4023	0.0000	2.8793
C	2.4023	0.0000	-2.8793
C	-2.4023	0.0000	-2.8793
H	1.2131	0.0000	4.6337
H	-1.2131	0.0000	4.6337
H	1.2131	0.0000	-4.6337
H	-1.2131	0.0000	-4.6337
H	3.3394	0.0000	3.4067
H	-3.3394	0.0000	3.4067
H	3.3394	0.0000	-3.4067

H	-3.3394	0.0000	-3.4067
H	3.3606	0.0000	0.9828
H	-3.3606	0.0000	0.9828
H	3.3606	0.0000	-0.9828
H	-3.3606	0.0000	-0.9828

CORANNULENE $C_{20}H_{10}$, C_{2v}

C	0.0000	-0.5580	1.2021
C	1.1432	-0.5580	0.3715
C	0.7066	-0.5580	-0.9725
C	-1.1432	-0.5580	0.3715
C	-0.7066	-0.5580	-0.9725
C	-2.3511	-0.0677	0.7639
C	-1.4530	-0.0677	-1.9999
C	1.4530	-0.0677	-1.9999
C	2.3511	-0.0677	0.7639
C	0.0000	-0.0677	2.4721
C	2.4268	0.2634	2.1745
C	1.3182	0.2634	2.9800
C	-1.3182	0.2634	2.9800
C	-2.4268	0.2634	2.1745
C	-3.2414	0.2634	-0.3328
C	-2.8180	0.2634	-1.6361
C	-0.6852	0.2634	-3.1856
C	0.6852	0.2634	-3.1856
C	2.8180	0.2634	-1.6361
C	3.2414	0.2634	-0.3328
H	3.3624	0.5893	2.5935
H	1.4275	0.5893	3.9993
H	-1.4275	0.5893	3.9993
H	-3.3624	0.5893	2.5935
H	-4.2447	0.5893	-0.1218
H	-3.5056	0.5893	-2.3964
H	-1.1958	0.5893	-4.0746
H	1.1958	0.5893	-4.0746
H	3.5056	0.5893	-2.3964
H	4.2447	0.5893	-0.1218

CORANNULENE $C_{20}H_{10}$, D_{5h}

C	0.0000	0.0000	1.1864
C	1.1283	0.0000	0.3666
C	0.6973	0.0000	-0.9598
C	-1.1283	0.0000	0.3666
C	-0.6973	0.0000	-0.9598
C	-2.4078	0.0000	0.7823
C	-1.4881	0.0000	-2.0482
C	1.4881	0.0000	-2.0482
C	2.4078	0.0000	0.7823

C	0.0000	0.0000	2.5317
C	2.4843	0.0000	2.2440
C	1.3665	0.0000	3.0562
C	-1.3665	0.0000	3.0562
C	-2.4843	0.0000	2.2440
C	-3.3289	0.0000	-0.3552
C	-2.9019	0.0000	-1.6693
C	-0.6908	0.0000	-3.2757
C	0.6908	0.0000	-3.2757
C	2.9019	0.0000	-1.6693
C	3.3289	0.0000	-0.3552
H	3.4462	0.0000	2.7280
H	1.5296	0.0000	4.1205
H	-1.5296	0.0000	4.1205
H	-3.4462	0.0000	2.7280
H	-4.3915	0.0000	-0.1814
H	-3.6595	0.0000	-2.4345
H	-1.1845	0.0000	-4.2327
H	1.1845	0.0000	-4.2327
H	3.6595	0.0000	-2.4345
H	4.3915	0.0000	-0.1814

CORONENE $C_{24}H_{12}$, D_{6h}

C	0.0000	0.0000	1.4258
C	1.2348	0.0000	0.7129
C	-1.2348	0.0000	0.7129
C	1.2348	0.0000	-0.7129
C	-1.2348	0.0000	-0.7129
C	0.0000	0.0000	-1.4258
C	0.0000	0.0000	2.8226
C	2.4445	0.0000	1.4113
C	-2.4445	0.0000	1.4113
C	2.4445	0.0000	-1.4113
C	-2.4445	0.0000	-1.4113
C	0.0000	0.0000	-2.8226
C	-1.2459	0.0000	3.5113
C	-2.4179	0.0000	2.8347
C	-3.6639	0.0000	0.6767
C	-3.6639	0.0000	-0.6767
C	-2.4179	0.0000	-2.8347
C	-1.2459	0.0000	-3.5113
C	1.2459	0.0000	-3.5113
C	2.4179	0.0000	-2.8347
C	3.6639	0.0000	-0.6767
C	3.6639	0.0000	0.6767
C	2.4179	0.0000	2.8347
C	1.2459	0.0000	3.5113
H	-1.2424	0.0000	4.5875
H	-3.3517	0.0000	3.3697
H	-4.5941	0.0000	1.2178

H	-4.5941	0.0000	-1.2178
H	-3.3517	0.0000	-3.3697
H	-1.2424	0.0000	-4.5875
H	1.2424	0.0000	-4.5875
H	3.3517	0.0000	-3.3697
H	4.5941	0.0000	-1.2178
H	4.5941	0.0000	1.2178
H	3.3517	0.0000	3.3697
H	1.2424	0.0000	4.5875

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