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Molecular Mechanics Calculations on Conjugated Nitrogen-Containing Heterocycles

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Abstract: The MM2 program has been extended so as to be able to deal with conjugated nitrogen containing molecules (MM2(85)). The simple heterocycles, pyridine and pyrrole and several other molecules with pyridine-type and pyrrole-type nitrogen atoms, were examined and used to parameterize MM2. Calculations were then carried out with about 25 additional and more complicated heterocycles, and the calculated structures are compared with the experimental ones. The agreement is generally good, but problems remain. The source of these problems and their possible future corrections are discussed. The heats of formation were calculated for 11 compounds containing pyridine-type nitrogen atoms. The agreement with the experimental values is fair, at best.

Molecular mechanics has become a standard and widely applicable method for the determination of molecular structures.[1-3] Delocalized electronic systems cause special problems. A method for dealing with these was described earlier[4] and incorporated in the MM1 program. This scheme was only applied to conjugated hydrocarbons and ketones, and it was extended to the MM2 program more recently, in the MM2(82) program.[5] Small additional modifications of the method which are important for nonplanar conjugated systems have also been recorded previously.[6] Both the MM1 and MM2 programs had options for the treatment of molecules which contained heteroatoms in the delocalized part of the system, but the full parameterization was not previously developed. Such a development is reported here for MM2 and is included in MM2(85).

The method used for the molecular mechanics treatment of a conjugated system will be briefly outlined here. In ordinary molecular mechanics of nonconjugated systems, one needs to have a force field (equations which describe the variation of the energy with the structure when the molecule is deformed by stretching, bending, or twisting). When one has a suitable set of equations, and the necessary parameters for these equations are known, one finds the structure of the molecule by minimizing the energy with respect to the geometry. In general, the scheme works quite well.[1-3] If the molecule contains a delocalized system, then it is necessary to determine several specific parameters for each delocalized bond in that system, by a more elaborate method. The method we have used[1,2,4-6] involves carrying out a self-consistent field calculation on the π electronic system of the planar molecule. The off-diagonal elements of the density matrix give the bond orders of the conjugated bonds. From known relationships between the bond orders and the force field parameters of the different bonds, the parameters are deduced individually for the specific bonds as they occur in the molecule at hand. The energy is then minimized as usual. Since the geometry is changed by energy minimization, the self-consistent field calculation and its results no longer apply accurately to the molecule. The whole process is therefore iteratively repeated until complete internal consistency is obtained. At that point one obtains a good structure and also an energy which may be additionally used to deduce the heat of formation for a conjugated hydrocarbon.[5] If the molecule contains a heteroatom in the conjugated system, then some modifications of this method are required in order to deal with the specific heteroatom. A similar calculational method has been reported by Warshel and Lappicirella.[3ℓ]

Table I. π Orbital Parameters[a]

atom type	I (ev)[b]	γ_{11} (ev)	Z	Q[c]
C	11.16	11.134	3.25	1
N(imine)	14.12	12.34	3.90	1
N:(pyrrole)	13.145	17.21	3.90	2

[a] The amine-type nitrogen is type 8 in MM2, and it is attached to a lone pair. The pyrrole nitrogen is type 40, and is not attached to a lone pair. (This type of nitrogen is represented by –N: in this manuscript, the two dots indicating the fact that the N atom contributes two π electrons.) The imine (or pyridine) type nitrogen is type 39 and is attached to a lone pair. [b] I is the first ionization potential. When Q is 2, the second ionization potential is equal to $I + \gamma_{11}$. [c] Q is the number of electrons contributed by the orbital.

Method

The one-center electron repulsion integral γ_{ii} for a π atomic orbital on atom i is taken to be the difference between the ionization potential and the electron affinity of the atom in the appropriate valence state as was originally suggested by Pariser and Parr.[7] The two-center electron repulsion potential over atoms i and j, γ_{ij}, is calculated by using a modified formula by Ohno,[8]

$$\gamma_{ij} = 1\Big/\left(R^2 + \frac{1}{\gamma_{ii}\gamma_{jj}}\right)^{1/2} \qquad (1)$$

where R is the distance between atoms i and j, with the γ's and R in atomic units. The original Ohno formula is

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$$\gamma_{ij} = 1/\left(R^2 + \frac{1}{\gamma_{ii}^2}\right)^{1/2}$$

where atoms i and j are of the same kind. The resonance integral β_{ij} is calculated as

$$\beta_{ij} = \beta_{CC}\,\frac{I_i + I_j}{2I_C}\,\frac{S_{ij}}{S_{CC}} \tag{2}$$

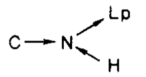
where β_{CC} is the β for a C–C bond of the same distance as the i–j bond calculated by the Lo and Whitehead formula[9] as in the original (MM2(82)) program; I_i and I_j are the ionization potentials of atoms i and j in the appropriate valence states,[10] respectively, the first ionization potential being used if the atomic orbital contributes one electron to the π system and the second ionization potential being used if it contributes two electrons; I_C is the ionization potential of a carbon 2pπ electron, and S_{ij} and S_{CC} are, respectively, overlap integrals of an i–j bond and a C–C bond of the same length. Both overlap integrals are calculated with theoretical formulas for two 2pπ orbitals by using Slater atomic charges. The MMP2 method normally does not include nonbonding β's; however, there is a provision in the program to do this. The nonbonding C–C β's are calculated by using a polynomial as a function of distance.[5] It should be noted that when i = j = C, eq 1 and 2 reduce to those used for C–C bonds in the original program. The values of the parameters used for various π orbitals are given in Table I.

The stretching force constant and natural bond length of the conjugated bond are assumed to be linear functions of the bond order. These and other parameters are chosen to reproduce experimental structural data and relative energies of conformers.

Molecular structures are determined by a variety of techniques, each of which has its own definition(s) of structure built in. The MM2 force field was parameterized to fit r_g structures. These were used because they are accurately determined for a wide variety of simple molecules (usually by electron diffraction on molecules in the gas phase). Most of the structural data in the chemical literature were determined by X-ray crystallography at room temperature.[11] If such an X-ray structure was well determined (esd 0.003 Å in bond lengths, 0.3° in bond angles), the actual probable errors in the structures are 3–5 esds, largely because of the thermal motions of the molecules in the crystal. These molecular thermal motions can often be corrected for to a large extent[12] by the so called "rigid body motion corrections". The error here is always in the same direction, namely the experimental bond length is shorter than the actual bond length. But the amount of shortening may be anywhere from about 0.000 up to about 0.040 Å. When the rigid body motion corrections are applied, perhaps two thirds of this error can be corrected for, although some pretty significant errors are likely to remain. In general, the literature values have not been corrected in this way by the original authors. We can usually carry out these corrections from the data in the original publications; however, they take a good bit of time and effort, and we have not carried out such corrections on the data utilized herein so far. One would prefer to have low-temperature data, where the corrections become much smaller (usually negligible). Such data are few in the existing literature, however.

Since X-rays are scattered by electrons, atoms which have aspherical symmetry with respect to their electron density (oxygen, nitrogen) are found by this technique to be located away from the position of the nucleus, and, worse, the apparent location is a function of the angle of incidence of the X-ray beam. While these things can always be corrected for in principle, and more or less in practice, such corrections have rarely been made in published papers, and they can be laborious or impossible after the fact. We have sometimes made such corrections when there seemed to be good reason to do so. In the present work, however, the quality and quantity of the data are such that we have not made any corrections but have simply taken the published data at face value, recognizing that, excluding hydrogens and special items explicitly mentioned, the probable errors in angles are at least 2–3 esd's and the errors in bond lengths are perhaps 3–5 esds.

Dipole interactions are often sizable in heteromolecules. The π dipole moment is calculated from the diagonal elements of the density matrix (charges) and the atomic positions. σ bond moments are then assigned to reproduce the experimental dipole moments of key molecules. This is analogous to the way σ bond moments are chosen in saturated molecules to fit the experimental dipole moments. The molecular dipole moment is calculated as the sum of the π and σ moments. It is noted that assuming no H–C bond moment, the dipole moment for azulene is calculated by our present method to be 2.2 D, completely from the π-system. The experimental value is 1.08 ± 0.08 D.[13] The SCF method used neglects the induced moments in the σ system and thus overestimates the charge densities on the atomic centers. In view of the poor result for azulene, it is perhaps advisable to scale down the π moments by some factor so that more realistic bond moments may be assigned. For the present, however, full π moments are used, and a bond moment of 0.58 D for the C–N (imine) bond and 0.60 D for the N–Lp moment will reproduce the pyridine dipole moment. By using this value, the dipole moments of pyrimidine, pyridazine, and isoquinoline agree well with the experimental values. For open chain molecules, a bond moment of 0.60 D was assigned to the H–N bond. The calculated dipole moments of the three molecules studied, methanimine, ethanimine, and 2-propen-1-imine, are 2.70, 2.97, and 3.21 D, respectively, while ab initio values reported for methanimine and ethanimine[14] are 2.29 and 2.32 D, respectively, and an experimental value of 2.51 D was reported for 2-propen-1-imine.[15] The diagram below shows the three bond moment contributions. One can see that the calculated dipole moments are very insensitive to the magnitude of the H–N bond moment which increases the y component but decreases the x component of the dipole moment. The calculated moments are affected more by the structures of the molecules, in particular the bond angles involving the N atom, than by the magnitude of the H–N bond. Because of this fact and because of the lack of reliable experimental data both on structure and on dipole moments, no further study on this matter is felt justified at this time, and the value 0.6 D for H–N is tentatively used.



So far molecules containing pyridine-type nitrogen and pyrrole-type nitrogen have been examined. These will be discussed separately in the following paragraphs. A subsequent paper will discuss furan-type oxygen and thiophene-type sulfur.

Pyridine-type nitrogen π orbitals each contribute one electron to the π system. One of the σ orbitals on such a nitrogen carries a lone pair of electrons and this is explicitly included in the calculations in a way described in earlier papers.[16] The same van der Waal's parameters are used as for the amine and amide nitrogen.[16] The natural bond length and stretching force constant for the C–N bond, and their dependence on the bond order, were determined from experimental data on methanimine (bond order 0.96), pyridine (bond order 0.63) and the C–N single bond in *N*-(phenylmethylene)benzenamine (bond order 0.19), and with experimental force constants for methanimine (10.61 mdyn/A)[17] and for pyridine (7.015 mdyn/A).[18] When two N atoms are present, they may be 1,2; 1,3; or 1,4 to each other (no new parameters are required if they are farther away than the 1,4-position). With the 1,2-position the bond properties for an N–N bond are needed. The bond length–bond order relationship was obtained by considering the N–N bond lengths and bond orders in diazene (bond order 1.0), *s*-tetrazine (bond order 0.65), pyridazine (bond order 0.55), and 2,3-diazanaphthalene (bond order 0.41) molecules. The experimental force constant of diazene[19] was used, and the dependence on bond order is taken to be the same as in the case of a C-N bond. Natural bond angles and bending force constants were determined by first taking the values previously determined for similar angles and then modifying them to fit known structures. The twofold torsional barrier about the C=N bond is taken from the theroretical value for methanamine[20] and that about the N=N bond is taken to be the same as in the C=C bond.

The parameters thus developed are given in Table II. All of these parameters are included in the latest version of the program, MM2(85). (The latest parameter set is always available from N. L. Allinger upon request.)

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Table II. Force Field Parameters[a]

van der Waals Constants

atom	r^*, Å	ϵ, kcal/mol
N	0.055	1.820

Natural Bond Lengths and Stretching Force Constants

bond	l_0, Å	slope (l_0)	K_s, mdyn/Å	slope (k_s)
C–N	1.260	0.1956	11.09	10.88
N–LP	0.600		6.10	
H–N	1.022		5.24	
N–N	1.248	0.170	10.72	10.88
C–N:	1.266	0.1956	11.09	10.88
H–N:	1.050		6.10	
N–N:	1.230	0.1956	11.00	10.88

Bond Moment

bond	moment, D	bond	moment, D
C–N	0.583	C–N:	0.87
LP–N	–0.60	H–N:	0.55
H–N	0.60	N–N:	0.30

Natural Bond Angles and Bonding Constants

angle	θ_0 (1), deg	θ_0 (2), deg	k_θ, mdyne Å/rad^2
C–C–N	120.0	123.5	0.43
H–C–N	116.5	120.5	0.36
C–N–C	115.0		0.43
C–N–LP	122.5		0.50
C–N–H	110.0		0.50
LP–N–H	127.5		0.50
C_{sp^3}–C–N	115.1	125.3	0.55
N–C–N	120.0	127.0	0.40
C–N–N	107.5		0.40
LP–N–N	120.0		0.35
H–N–N	103.5		0.40
H–C_{sp^3}–N	107.5		0.48
C–C–N:	120.0	119.0	0.43
H–C–N:	113.5		0.40
C–N:–C	120.0	124.0	0.43
C–N:–H	118.0		0.36
out-of-plane bending			0.050
N–C–N:	126.0		0.40
C–N–N:	115.0		0.43
Lp–N–N:	122.5		0.50
C–N:–N	124.0		0.43
H–N:–N	113.0		0.36

Torsional Constants, kcal/mol

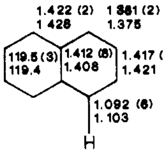
angle	V_1 or V_3	V_2	angle	V_1 or V_3	V_2
A–C–C–N		15	H–C_{sp^3}–C–N	–0.24[c]	
C–C–C–N	1.0[b]	15	H–C–C–N:		15
C–C–N–H	0.75[b]	10	C–C–C–N:		15
C_{sp^3}–C–N–E		10	C–C–N:–M		15
C–C–N–J		10	H–C–N:–M		15
H–C–N–X		10	N–C–N:–M		15
N–C–N–Z		10	N:–C–N–R		10
H–N–N–H	2.4[b]	10	R–N–N:–C		10
C–N–N–C		10	R–N–N:–H		10
Lp–N–N–E		10			

[a] C (C_{sp^2}); Lp (lone pair), N: (pyrrole type nitrogen), N (imine/azo type nitrogen), A (H, C_{sp^3}, N, N:), E (C, Lp, H), J (C, Lp, N, N:), M (C, H, N), X (C, C_{sp^3}, Lp, H, N, N:), Z (C, Lp, N:), R (C, Lp). [b] V_1. [c] V_3.

An attempt was made to calculate the heats of formation of 11 compounds containing pyridine type nitrogen atoms by using a method similar to that described in the earlier paper[5] on hydrocarbons. Because not enough experimental information is available and because preliminary results showed a large standard deviation between calculation and experiment, the details of the calculation will not be presented here.

Results and Discussion

The experimental and calculated geometries of a number of molecules studied are shown. Of particular interest are the diazanaphthalenes. With the exception of 2,3-diazanaphthalene, the calculated bond lengths show a definite pattern. The C–C bonds are to within 0.002 Å the same as those calculated for the corresponding bonds in naphthalene. And just as for naphthalene, there seem to be some systematic errors. The 1–2 and 9–10 bonds are calculated to be too short and the 2–3 and 1–9 bonds too long. A comparison of a recent high quality electron diffraction geometry of naphthalene[21] with our calculated values is given below.



The calculated C–N bond lengths depend on their locations in the molecule and, for a given type of location, are constant within 0.002–0.005 Å. At the 1–2 position, the length is 1.315 Å; at the 2–3 position, 1.370 Å; and at the 1–9 position, 1.375 Å. The calculated C–N bond lengths agree well with experiment, with an average deviation of 0.007 Å. In 2,3-diazanaphthalene, the experimental bond length for the C-N bond is unusually low, 1.297 Å, and the calculation predicts 1.294 Å. In pteridine (1,3,5,8-tetraazanaphthalene) we also correctly predicted two unusually short bonds (1.303 and 1.306) at the 5–6 and 7–8 positions (experimental 1.308 (8) and 1.286 (8)).

A few typical geometries are reproduced in Tables III and IV. The others discussed herein are available as Supplementary Material.

There are no experimental geometries available for quinoline and isoquinoline. Since the crystal structure for 3-methylisoquinoline is known, its structure was calculated and was found to agree quite well with experiment. The calculated quinoline bond lengths coincide almost exactly with those from an ab initio calculation.[22] The bond lengths and angles in 8,8'-biquinolyl are given for comparison with corresponding quantities in quinoline.

The 5-aza(acridine)- and the 5,10-diaza(phenazine)anthracenes were studied. The C–C bond lengths calculated in these molecules were almost identical with those calculated for those in the corresponding positions of anthracene. The C–N bond lengths are correctly calculated.

The calculated CNC angles in the azanaphthalenes and azaanthracenes are found to be 1–2 degrees too large when the nitrogen atom is next to the bridge carbon atom, resulting in a smaller CCN angle (or perhaps because of the low prediction for the CCN angle). When the nitrogen is in the 2- or 3-position, the CNC angle is only 0.2° too big, which is within the experimental error.

It should also be noted that all the above mentioned molecules are calculated to be planar, although experimental data indicate that some of the azanaphthalenes have ring atoms which deviate somewhat from the average molecular plane in the crystal. These deviations are surely a result of crystal packing forces.

The molecules 2,2'-bipyridyl, 2,5-diphenylpyrazine, 1-(1-naphthyl)isoquinoline, and *N*-(phenylmethylene)benzenamine were chosen to study the dihedral angles about bonds connecting six-membered rings. In the first three molecules, that bond is a C–C bond next to a C–N bond. The dihedral angles are 0°, 20°, and 60° for these molecules, respectively, and the calculated and experimental values agree perfectly. In the fourth molecule, the rotation is about a C–N bond which is in an open chain connecting the two rings. There the calculated dihedral angle is 40° compared with the experimental (X-ray) value of 57°, which is surprisingly large considering the fact that the steric hindrance does not appear as severe as in 1-(1-naphthyl)isoquinoline (and may be due in part to crystal-packing forces).

When pyrrole and furan were studied, it was found that the C–C bond lengths in the molecules could not be calculated to equal the experimental values unless the relative bond orders of the bonds change in a certain fashion. This could be accomplished if the ionization potentials for the N and O atoms used in eq 2 are

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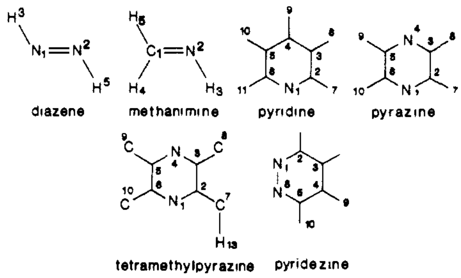
Table III. Calculated and Experimental Structures



	diazene			diazene	
	expt[a]	calcd		expt[a]	calcd
R_{12}	1.252 ± 0.002	1.248	I_a	0.2797	0.2700
R_{13}	1.028 ± 0.005	1.021	I_b	2.1449	2.1428
∠125	106.85 ± 0.47	106.8	I_c	2.4327	2.4129

	methanimine			methanimine	
	expt[b]	calcd		expt[b]	calcd
R_{12}	1.273	1.271	∠215	119.7	120.4
R_{23}	1.021	1.023	∠415	116.9	117.9
R_{14}	1.09	1.103	μ	2.29[c]	2.70
R_{15}	1.09	1.102	I_a	0.4265	0.4329
∠123	110.5	110.9	I_b	2.4153	2.4083
∠214	123.3	121.7	I_c	2.8418	2.8412

	pyridine			pyridine	
	expt[d]	calcd		expt[d]	calcd
R_{12}	1.3376	1.3398	∠216	116.94	117.03
R_{23}	1.3938	1.3976	∠127	116.03	116.18
R_{34}	1.3915	1.3965	∠238	120.11	120.76
R_{27}	1.0856	1.1031	∠349	120.80	120.85
R_{38}	1.0819	1.1029	μ	2.215 ± 0.01	2.216
R_{49}	1.0811	1.1029	I_a	13.899	13.9454
∠123	123.80	123.80	I_b	14.4594	14.5311
∠234	118.53	118.53	I_c	28.3641	28.4765
∠345	118.40	118.31			

	pyrazine			pyrazine	
	expt[e]	calcd		expt[e]	calcd
R_{12}	1.3392 (18)	1.335	∠216	116.3 (0.14)	115.5
R_{23}	1.3931 (26)	1.402	∠123	121.8 (0.16)	122.2
R_{27}	1.08	1.103	∠127	115.9 (1.4)	117.0
R_{38}	1.08	1.103	∠327	122.2 (2.1)	120.8

	tetramethylpyrazine			tetramethylpyrazine	
	expt[f]	calcd		expt[f]	calcd
R_{12}	1.3500 (6)	1.334	∠123	120.8 (0.03)	121.1
R_{23}	1.4088 (6)	1.404	∠127	117.8 (0.03)	116.4
R_{27}	1.5071 (6)	1.506	∠327	121.4 (0.03)	122.5
R_{38}	1.5130 (6)	1.506	∠438	117.6	116.4
∠216	118.3 (0.03)	117.8	1,2,7,13	−4.70	−0.19

	pyridazine			pyridazine	
	expt[g]	calcd		expt[g]	calcd
R_{12}	1.341	1.310	∠234	117.0	116.2
R_{23}	1.393	1.415	∠216	119.3	119.3
R_{34}	1.375	1.374	∠4,5,10	124.6	119.5
R_{16}	1.331	1.340	∠549	122.7	121.9
∠123	123.7	124.5	μ	3.94–4.09[h]	4.24

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increased by 10–15% from their values for free atoms. Since both the pyrrole and furan orbitals contribute two electrons to the π system and thus have a positive charge, using the modified ionization potentials has an effect similar to that which would be obtained by a variable electronegativity SCF treatment[4] on the π system in that it maintains higher electron densities on the heteroatoms.

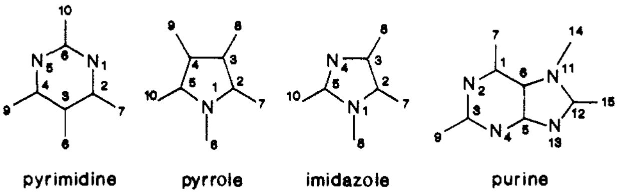
The rotational barrier about the C_{sp^2}–N (pyrrole) bond is unknown, so the values for the C_{sp^2}–C_{sp^2} bond were used. The stretching force constant and its dependence on the bond order were taken to be similar to those of the C_{sp^2}–N (pyridine) bond at equal bond lengths. Natural bond lengths and bond angles involving N (pyrrole) were first determined so as to fit the geometry of the pyrrole molecule and then further optimized to give the best overall fit to all of the molecules studied. There are very few molecules containing only one pyrrole-type nitrogen whose geometries are known. Of the three that were studied, only pyrrole has a reasonably reliable geometry. The reported structures of indole and carbazole are too poor to be of much use in helping determining the parameters. Recent neutron diffraction studies of imidazole and pyrazole were very helpful in this respect. Since the locations of H atoms are determined much more accurately by neutron diffraction, the natural bond length of the N–H bond was chosen to reproduce those bonds in imidazole and pyrazole rather than those found in pyrrole by microwave spectroscopy. With imidazole, the angle type N (pyridine)–C–N (pyrrole) is introduced. With pyrazole, the bond type N (pyridine)–N (pyrrole) and the related angles are introduced. The force field parameters developed are included in Table II. The molecules studied and a comparison of their calculated and experimental structures are shown.

The calculated C–N (pyrrole) bond lengths agree well with the experimental values, usually to within 1–2 standard deviations. The C–N (pyridine) bond lengths in these five-membered rings are not calculated as well. The largest discrepancy occurs in imidazole where one of the C–N (pyridine) bonds is calculated to be 0.023–0.030 Å shorter than the experimental value. Similar shortages were found in benzimidazole and possibly in pyrazole where microwave, X-ray, and neutron diffraction determinations give C–N (pyridine) bond lengths, varying from 1.328 Å (X-ray) to 1.350 Å (neutron). On the contrary, the C–N (pyridine) bond in indazole is calculated to be 0.028 Å too long. The experimental value of 1.288 Å in the latter case is suspiciously small. The prediction for purine is very poor, possibly because of the intermolecular hydrogen bonding in the experimental structure.

When benzene rings are attached to a heterocycle, as in indole, carbazole, benzimidazole, and indazole, the calculated bond lengths and bond angles in the benzene ring are very similar among the molecules. The long bonds tend to be too long and short ones too short, although in most cases the differences are within experimental error. Two opposite C–C–C angles are 117–118°, smaller than the other four angles. This is born out by the experimental values in benzimidazole and indazole, less so in carbazole. The C–N (pyridine)–C angle is calculated about 1° too big when benzene rings are fused to the heterocycle. Similar deviations are found when the angle is in a six-membered heterocycle fused to a benzene ring as was discussed earlier.

The calculated and experimental heats of formation of pyridine-type compounds are presented in Table V. The standard deviation is calculated to be 2.9 kcal/mol. However, it should be noted that pyrimidine and 7,8-benzoquinoline each has a unique structural feature (and a unique parameter), and their heats of formation can thus be fixed to any values. Excluding these two compounds, the standard deviation increases to 3.3 kcal/mol. The calculation of heats of formation is a very tricky exercise. The calculated value is a sum of many terms, some of which are large numbers of opposite signs. In other words, it represents a small difference between large numbers, and the inherent percent error can become very large. Furthermore, almost all of the structural parameters affect the absolute value of the steric energy which constitutes part of the heats of formation. Thus while an alternate set of structural parameters may predict the same geometry, it

Table IV. Calculated and Experimental Structures



	pyrimidine				pyrimidine		
	expt[a]	expt[b]	calcd		expt[a]	expt[b]	calcd
R_{12}	1.340 (2)		1.344	∠612	115.5 (2)	116.1	115.8
R_{16}	1.340 (2)	1.338	1.345	∠123	122.3	122.2	122.1
R_{56}	1.340 (2)	1.340	1.343	∠234	116.8	116.6	116.9
R_{23}	1.393 (2)	1.391	1.398	∠327			120.9
R_{34}	1.393 (2)	1.391	1.397	∠238			121.5
R_{27}	1.099 (7)		1.103	∠127	115.3		117.1
R_{38}	1.099 (7)		1.103	∠1,6,10	115.3		116.3
$R_{6,10}$	1.099 (7)		1.103	μ	2.334[c]		2.321
∠165	127.6 (3)	126.8	127.3				

	pyrrole			pyrrole	
	expt[d]	calcd		expt[d]	calcd
R_{12}	1.3705	1.3707	∠234	107.4	107.5
R_{23}	1.3822	1.3821	∠127	121.5	122.4
R_{34}	1.4167	1.4094	∠216	125.1	125.2
R_{16}	0.996	1.046	∠438	127.1	126.3
R_{27}	1.076	1.102	I_a	9.19558	9.1246
R_{38}	1.077	1.102	I_b	9.32764	9.3600
∠215	109.8	109.6	I_c	18.52599	18.4846
∠123	107.7	107.7	μ	1.74 ± 0.02	1.74

	imidazole				imidazole		
	expt[e]	expt[f]	calcd		expt[e]	expt[f]	calcd
R_{12}	1.378	1.381	1.379	∠215	106.9	107.2	106.9
R_{15}	1.355	1.358	1.353	∠216	126.0	125.7	126.5
R_{16}	1.064	1.053	1.044	∠123	106.3	106.0	105.0
R_{23}	1.369	1.378	1.377	∠127	123.7	123.0	123.7
R_{27}	1.091	1.087	1.102	∠234	109.8	109.8	111.0
R_{34}	1.382	1.389	1.359	∠238	128.2	128.0	126.3
R_{38}	1.084	1.086	1.102	∠345	105.1	105.3	104.9
R_{45}	1.333	1.333	1.328	∠154	111.8	111.8	112.1
$R_{5,10}$	1.088	1.087	1.102	∠1,5,10	123.9	123.7	122.0

	purine			purine	
	expt[g]	calcd		expt	calcd
R_{12}	1.330 (1.336)	1.329	∠216	118.9 (119.)	119.3
R_{16}	1.393 (1.385)	1.406	∠217	118.7 (113.9)	118.8
R_{17}	1.00 (0.93)	1.102	∠123	118.4 (117.5)	116.7
R_{23}	1.349 (1.349)	1.373	∠234	128.5 (127.9)	128.6
R_{34}	1.339 (1.324)	1.326	∠239	121.9 (114.4)	115.6
R_{39}	1.06 (0.97)	1.103	∠345	113.0 (113.4)	115.1
R_{45}	1.337 (1.336)	1.367	∠456	123.9 (123.1)	120.1
R_{56}	1.407 (1.398)	1.410	∠6,5,13	109.6 (109.6)	109.1
$R_{5,13}$	1.379 (1.369)	1.372	∠165	117.9 (118.5)	120.1
$R_{6,11}$	1.373 (1.375)	1.392	∠5,6,11	105.1 (105.5)	105.9
$R_{11,12}$	1.327 (1.337)	1.351	∠6,11,14	118.8 (126.6)	127.0
$R_{11,14}$	0.89 (0.84)	1.044	∠6,11,12	106.5 (106.3)	106.1
$R_{12,13}$	1.311 (1.313)	1.330	∠11,12,13	115.1 (114.1)	113.3
$R_{12,15}$	0.95 (1.06)	1.102	∠11,12,15	123.1 (120.3)	121.5
			∠5,13,12	103.8 (104.6)	105.7

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may give different relative heats of formation for the same group of compounds. However, since the steric energy is usually only a minor contribution and since the contributions from the σ system are usually approximately predictable and adjustable, the difficulty appears to lie in the π energy calculation. The π energy depends on the values of π system parameters, such as the ionization potentials, effective nuclear charges, etc. in a complex way, and because of the charge distribution problem discussed before, we decided to defer the π energy study until a more satisfying scheme for getting the charge distribution is found. There is also some uncertainty regarding the experimental data on the heats of formation of conjugated heterocycles.[23]

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Table V. Heats of Formation of Pyridine-Type Compounds in kcal/mol

compound	ΔH_f, calcd	ΔH_f, expt	difference
pyridine	32.1	34.55	−2.5
pyrazine	47.7	46.90	0.8
pyrimidine	47.0	47.00	0.0
isoquinoline	47.3	48.20	−0.9
quinoline	46.6	51.80	−5.2
quinoxaline	61.2	62.70	−1.5
phenazine	80.9	80.70	0.2
7,8-benzoquinoline	55.2	55.19	0.0
5,6-benzoquinoline	61.1	55.90	5.2
3,4-benzoquinoline	60.2	58.20	2.0
acridine	65.6	69.90	−4.3

Conclusions

While conjugated hydrocarbons were successfully dealt with by molecular mechanics years ago, the introduction of heteroatoms poses special problems. Firstly, information vital to good parameterization, such as, accurate structures, rotational barriers, heats of formation, dipole moments, etc., is very scarce for heterocycles. There are not enough model compounds to allow for unique choices of parameters. Secondly, polarization becomes important, and there is no simple way for dealing with it at present. But since heterocycles are so important, we have taken the first step of providing a scheme to include them in the present framework of MM2. Polarization is not explicitly taken care of. Only heterocycles including nitrogen atoms are reported here, although the same scheme can handle other heteroatoms as well. As we have already shown, the agreement between the calculated structures and the experimental ones is generally good. However, an attempt at predicting the heats of formation yielded disappointing results. We believe that the failure to calculate accurate heats of formation and the dipole moments of azulene and linear conjugated amines is in large part due to our neglect of the polarization in the π system.[23] Preliminary studies employing the variable electronegativity self-consistent field molecular orbitals rather than the self-consistent field molecular orbitals as used here showed great improvement in predicting the dipole moments of azulene and of conjugated ketones.[24] We think that as better and more abundant experimental data on conjugated heterocycles become available, it will be worthwhile to reexamine the method presented in this work.

Acknowledgment. We are indebted to Professor K. N. Trueblood for a copy of his current program for correcting crystallographic bond lengths for rigid body motion. We are also indebted to the National Institutes of Health (5 R24 RR02165) and the National Science Foundation (CHE 8315543) for support of this work.

Supplementary Material Available: Experimental and calculated data and structures for compounds listed in this paper (48 pages). Ordering information is given on any current masthead page.

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(23) Experimental error may also be a problem. We have been advised (personal communication to N.L.A. by W. Steele) that his repeated determinations of the heats of formation of several heterocycles have given values which differ from those reported earlier by more than the quoted error limits would suggest.

(24) A referee has suggested that if nonneighbor resonance integrals are included in the π system calculation, the polarization in the π system will be represented differently, and this may improve the dipole moments. This may well be true, but the whole π system calculation, beginning with hydrocarbons (ref 5) has been parameterized without including these integrals. It is not possible to add them in an ad hoc fashion now. One would have to go back and reparameterize the whole calculation. This was not done originally, because the earlier work on heats of formation was not parameterized in this fashion.

Photophysical Properties of Fluorescent *N*-Purin-6-ylpyridinium Chloride[†]

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Abstract: The absorption and fluorescence spectra and the excited-state lifetimes of *N*-purin-6-ylpyridinium chloride have been studied in polar organic solvents (acetonitrile, methanol, and ethanol) and, as a function of pH, in water. The ground state exhibits a prototropic equilibrium between the cation and the zwitterion with $\mathrm{p}K_a = 6.7$ in H_2O. At $3 < \mathrm{pH} < 6$ in aqueous solutions, excitation of the ground-state cation results in proton transfer to give only the excited zwitterion, on a time scale that is short compared to the lifetime of the excited species. A large Stokes shift in the emission results. The fluorescence quantum yield and lifetime of the excited zwitterion are 0.08 and 1.6 ns, respectively, in aqueous solution and remain constant over the entire $3 < \mathrm{pH} < 9$ range. Diabatic proton transfer to the excited zwitterion at pH <3 results in quenching of the emission with a rate constant of $2 \times 10^9\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$. Proton quenching does not dominate the excited zwitterion decay, however, so that the apparent $\mathrm{p}K_a^*$ values of 0.4 ± 0.3 from the Förster cycle and 0.6 ± 0.1 from fluorescence titration give good approximations to the true excited state $\mathrm{p}K_a^*$. The effects of solvent and temperature have also been examined. The potential application of pyridinium salts of purines as fluorescence probes for biomolecules is discussed.

Purines and related compounds are widely distributed among natural products. In particular, a vast body of information is now available concerning the roles that these molecules play in the chemistry and physics of nucleic acids and other biomolecules.[1] The use of luminescence techniques to probe the structure and dynamic behavior of macromolecules such as these continues to provide some of the most useful data available.[2–4]

The purines form part of the near-UV light-absorbing system in nucleic acids. However, the use of purine moieties as lumi-

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[†] Preliminary results were presented at the 69th Annual Conference of the Chemical Institute of Canada, Saskatoon, June 1986.

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