A Quantitative Molecular-orbital Study of the Structures and Vibrational Spectra of the Hydrogen-bonded Complexes $H_2O{\cdot}NH_3$, $H_2CO{\cdot}NH_3$ and $(H_2O)_n$, n = 2–4.

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Comparison of the calculated structures, interaction enthalpies, and vibrational spectra of water dimer, trimer, and tetramer, and the complexes formed between water/ammonia and NH_3/H_2CO at the OPLS/A molecular mechanics, semi-empirical AM1 and PM3 SCF-MO methods and *ab initio* theory at the SCF and MP2 levels shows the best agreement to occur between the correlated *ab initio* and the PM3 SCF-MO methods. The AM1 method generally predicts bifurcated hydrogen bonds, whilst the molecular mechanics force field does not reproduce the non-planar character of the water trimer and tetramer, nor the trend in the hydrogen-bond lengths as the size of the water cluster increases. Several specific errors in the PM3 method are identified, in particular concerning the interaction between N–H σ bonds and other lone pairs, which results in a calculated geometry and interaction energy for NH_3/H_2CO which is significantly different from the *ab initio* values.

A particularly demanding test of any quantitative theory of molecular structure is the ability to model weak intermolecular interactions. Single configurational *ab initio* self-consistent field molecular-orbital (SCF-MO) theory can be successfully used to study polar interactions such as hydrogen bonding, but subtle effects arising from dispersion (van der Waals) forces are not recovered since they originate from correlated electron motion. For this reason, the MP2 second-order correction for correlation effects together with an adequately large orbital basis set is increasingly used as the starting point for modelling weak complexes.[1] A particularly sensitive test of whether the relatively shallow potentials involved in weak complexes are adequately reproduced is *via* an analysis of the normal vibrational modes and frequencies of the complex, where a correction of the MP2 type together with allowance for basis set superposition errors (BSSE) appears desirable.[1] The importance of modelling weak interactions accurately is illustrated by the ever increasing interest in explicit environmental effects in chemical reactivity, such as solvation by water. Such systems can be modelled by developing analytical potential functions derived from high quality *ab initio* calculations, which can then be used in Monte–Carlo or molecular dynamics simulations for generating statistical solvent configurations about a reacting solute.[2] An alternative is to treat the system as a 'supermolecule' in which all interactions are handled at a self-consistent theoretical level,[3] which has the advantage that subtle stereo–electronic, steric, or polarisation effects for smaller clusters may be recovered. There is indeed much experimental structural information available concerning hydrogen-bonding interactions in organic molecules both in solution[4a] and the gas phase[4b] against which such calculations can be compared.

Such structural calculations require unusually large computational resources at *e.g.* the *ab initio* MP2 level of theory noted above. One traditional solution to this problem of resource has been to apply semi-empirical SCF-MO methods. In the case of weak intermolecular interactions, such methods have not been conspicuously successful in the past. For example, Hamiltonians such as CNDO/2 are well known to grossly over-emphasise the energies of intermolecular interactions and particularly those involving water, whilst the MINDO/3 and MNDO procedures considerably under-estimate *e.g.* hydrogen bonding interactions.[3,5] The more recent AM1 method[5] was developed with this problem in mind, and although the interaction energies of weak complexes are predicted quite accurately, qualitatively incorrect geometries for *e.g.* hydrogen bonding interactions are obtained.[3,6,7] Where geometry is important, such as in steric or stereo–electronic interactions, such errors are undesirable. The most recent semi-empirical method PM3 has been shown[7] to predict a structure for water dimer which is very similar to calculated *ab initio* structures,[8] an encouraging result since it suggests that a parametrisation based on the neglect of three-centre two-electron integrals can indeed reproduce many of the subtle stereo–electronic effects arising from the interaction of lone pairs with bonds. The PM3 method has also been demonstrated to provide a realistic model for solvation of the oxy-anionic intermediates involved in phosphoryl group transfer,[9] and for the solvation of ionic triplet excited states arising from electron transfer between ammonia and oxygen.[10] We considered it important to evaluate in further detail the PM3 method for higher aggregates of water, and for hydrogen bonding between neutral oxygen and nitrogen systems. We report here the energies, structures, and vibrational frequencies for three types of hydrogen-bonded complex, the clusters $(H_2O)_n$, n = 2–4, $H_2O{\cdot}NH_3$ and the hydrogen-bonded complex formed between H_2CO and ammonia. The results are compared with both *ab initio* and molecular-mechanics calculations for the same systems.

Computational Procedure.—The OPLS/A molecular-mechanics calculations[11] were carried out using the MacroModel (V2.5) program system,[12] using a constant relative permittivity of 2.5. Semi-empirical AM1 and PM3 calculations were carried out using the MOPAC program system (V5.0),[13] with full optimisation of geometrical variables within the constraint of any molecular symmetry imposed. Such constraints were checked by carrying out a normal co-ordinate analysis *via* the calculated Hessian matrix, all the calculated frequencies being positive for ground state minima. *ab initio* calculations were carried out using the GAUSSIAN 86[14] and the CADPAC[15] program systems. No correction for BSSE is made in the present

Table 1. Calculated properties for (1).

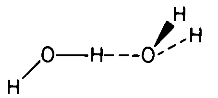
Property	OPLS	AM1	PM3	RHF/6-31G**[a]	MP2/6-31G**[a]
ΔH_{dim}[b]	−2.1	−123.49	−110.35	−152.0561 (−152.0305)	−152.4562 (−52.4103)
$\Delta\Delta H_{dim}$[c]	−2.1	−5.1	−3.5	−5.6 (−5.7)	−7.2 (−7.5)
H • • • O distance[c] [d]	2.035	2.22	1.809	2.039 (2.025)	1.956 (1.954)
H–Ô–H angle	171.6	90	178.8	172.1 (172.2)	166.8 (167.3)
Normal frequencies[e]					
1 A″	35	103	104	117 (120)	97 (97)
2 A′	92	119	151	137 (137)	147 (146)
3 A″	109	219	190	142 (141)	164 (160)
4 A′	123	432	412	177 (182)	204 (213)
5 A′	211	481	338	377 (384)	421 (435)
6 A″	347	678	472	612 (619)	659 (680)
7 A′	1 606	1 869	1 732	1 768 (1 824)	1 681 (1 731)
8 A′	1 616	1 953	1 736	1 797 (1 852)	1 715 (1 767)
9 A′	3 677	3 494	3 999	4 100 (4 028)	3 827 (3 709)
10 A′	3 686	3 503	3 860	4 142 (4 065)	3 884 (3 763)
11 A′	3 731	3 578	3 862	4 239 (4 163)	3 996 (3 885)
12 A″	3 737	3 583	3 988	4 256 (4 179)	4 015 (3 896)

[a] 6-31G* basis set values in parentheses. [b] Energy in kcal mol^{-1} for OPLS, heat of formation in kcal mol^{-1} for AM1 and PM3, total energy in hartree (=627.5 kcal mol^{-1}) for *ab initio* results. [c] $\Delta H_{dim} - 2(\Delta H_{monomer})$, in kcal mol^{-1}. [d] In Å. [e] In cm^{-1}.

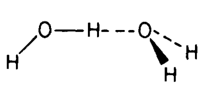
paper in the *ab initio* calculations. Vibrational modes were drawn using the program MOLECULE.[16]

Results and Discussion

Water Dimer.—The structures calculated at various levels for the *anti* water dimer [(**1**), Table 1] reveal essential agreement between all the methods except the AM1 procedure, which predicts a bifurcated structure in which both pairs of hydrogen atoms are equivalent (Figure 1). The PM3 method reproduces closely the O–H hydrogen-bonding distance and the H–O–H bond angle compared with *ab initio* calculations at various levels of theory.[8] An alternative *syn* isomer (**2**) was calculated (PM3) to be 0.7 kcal mol^{-1} higher in energy, but normal co-ordinate analysis revealed this not to be a true minimum, with one negative force constant corresponding to rotation about the O–H–O bond back to (**1**). No true *syn* isomer could be located at any of the *ab initio* levels.



(**1**)



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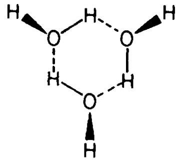

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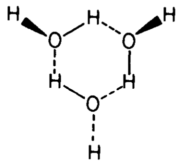

(**4**)

The intermolecular interaction energies reveal wider variation between the various methods. This is underestimated at the PM3 level, approximately correct with AM1 and overestimated at the high level MP2 level. Basis set superposition errors[1b] are indeed well known to account for up to 60% of total calculated interaction energies at the *ab initio* level, and a variety of methods have been proposed to correct for this effect.[1b] In the semi-empirical approach, BSSE is clearly assimilated into the parametric functions intrinsic to the method, and it would clearly be inappropriate to attempt such corrections.

Comparison of the normal co-ordinate analyses reveals greater differences between the various methods. The AM1 normal modes cannot be directly compared with the other methods because of the different symmetry of the equilibrium structures, although the numerical values are not greatly different from the *ab initio* results (Table 1). The OPLS molecular mechanics approach treats intermolecular interactions in terms of relatively simple potential functions, which are not necessarily optimised to reproduce the lower frequency molecular vibrational modes.[11] Thus, these OPLS modes in particular are noticeably smaller numerically than any of the quantum mechanical calculations, whereas as expected, the high wavenumber stretching vibrations are much better reproduced. Of the *ab initio* methods, we note that the difference between the RHF/6-31G* and 6-31G** basis sets, which differ in having *p* type functions associated with the hydrogens, are relatively small for those low-energy modes associated with the intermolecular interaction. The MP2 correlation correction does tend to increase the numerical values of the low-energy modes, and to decrease the high-energy stretching and bending modes. However, correction for basis set superposition errors appears to result in a more shallow intermolecular interaction potential,[1b] and hence, would be expected to decrease the energy of normal modes corresponding to intermolecular stretching. It is not certain, however, if such a conclusion is generally true of all intermolecular modes.

The PM3 method shows the greatest congruence with the MP2/6-31G** calculation (Figure 2). Only two normal modes differ in wavenumber by more than 100 cm^{-1}, v4 (by +208) and v6 (by −187) (Figure 1), both corresponding to weak stretching modes associated with the H • • • O hydrogen bond. It seems probable that for v6 at least, the inclusion of a correction for BSSE at the MP2/6-31G** level would bring the two methods into closer agreement. The ordering of the normal modes is also in agreement, excepting the two pairs v4/v5 and v9/v12, where the PM3 and *ab initio* orderings are transposed. In both cases, the PM3 symmetric (A′) vibration is too high in energy and the anti-symmetric (A″) mode too low. This in fact may be a subtle indication that the closed shell PM3 method does not correctly reproduce molecular polarisabilities and the symmetries of

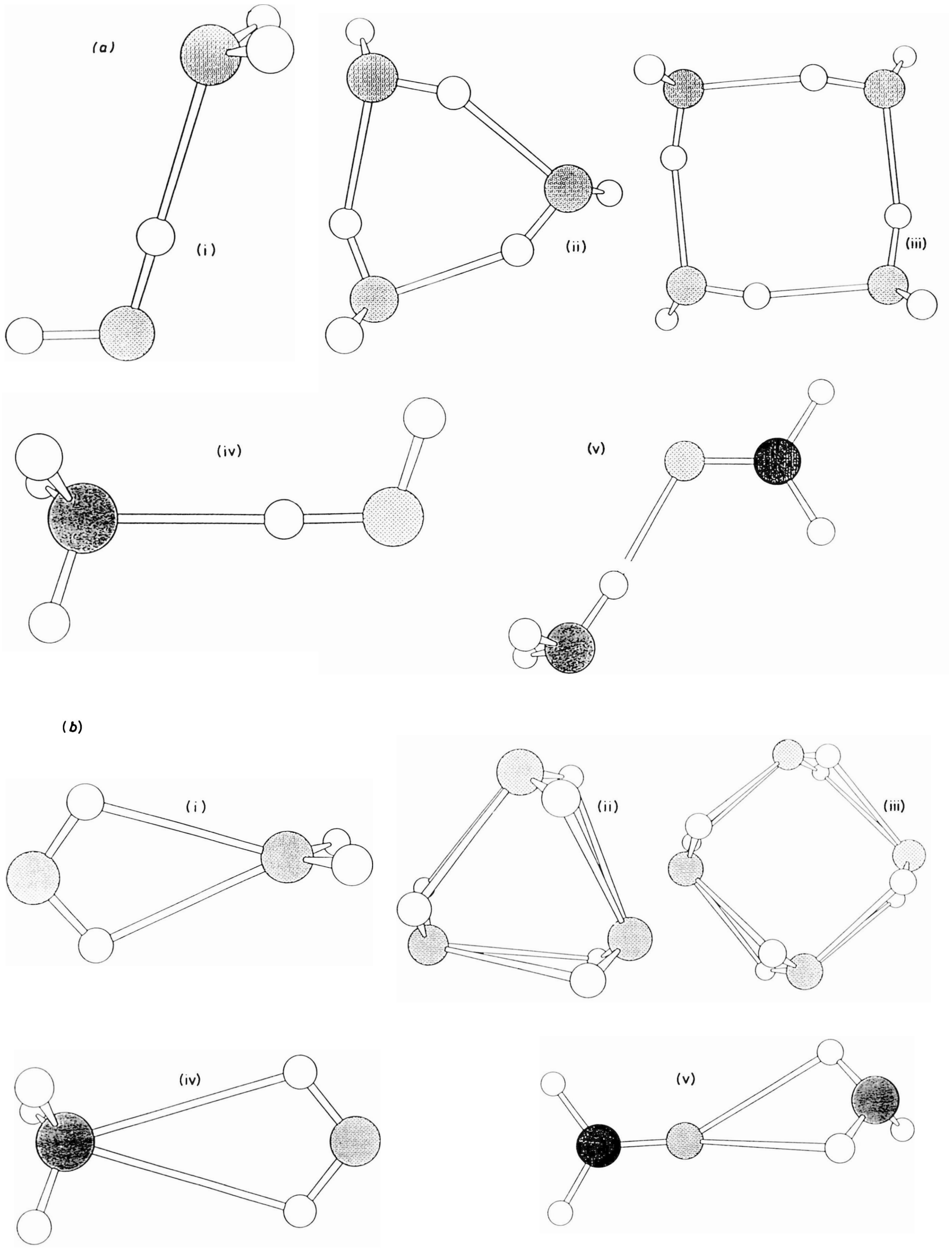

Figure 1. Calculated (*a*) PM3 and (*b*) AM1 structures for (**1**), (**4**), (**6**), (**9**), and (**12**).

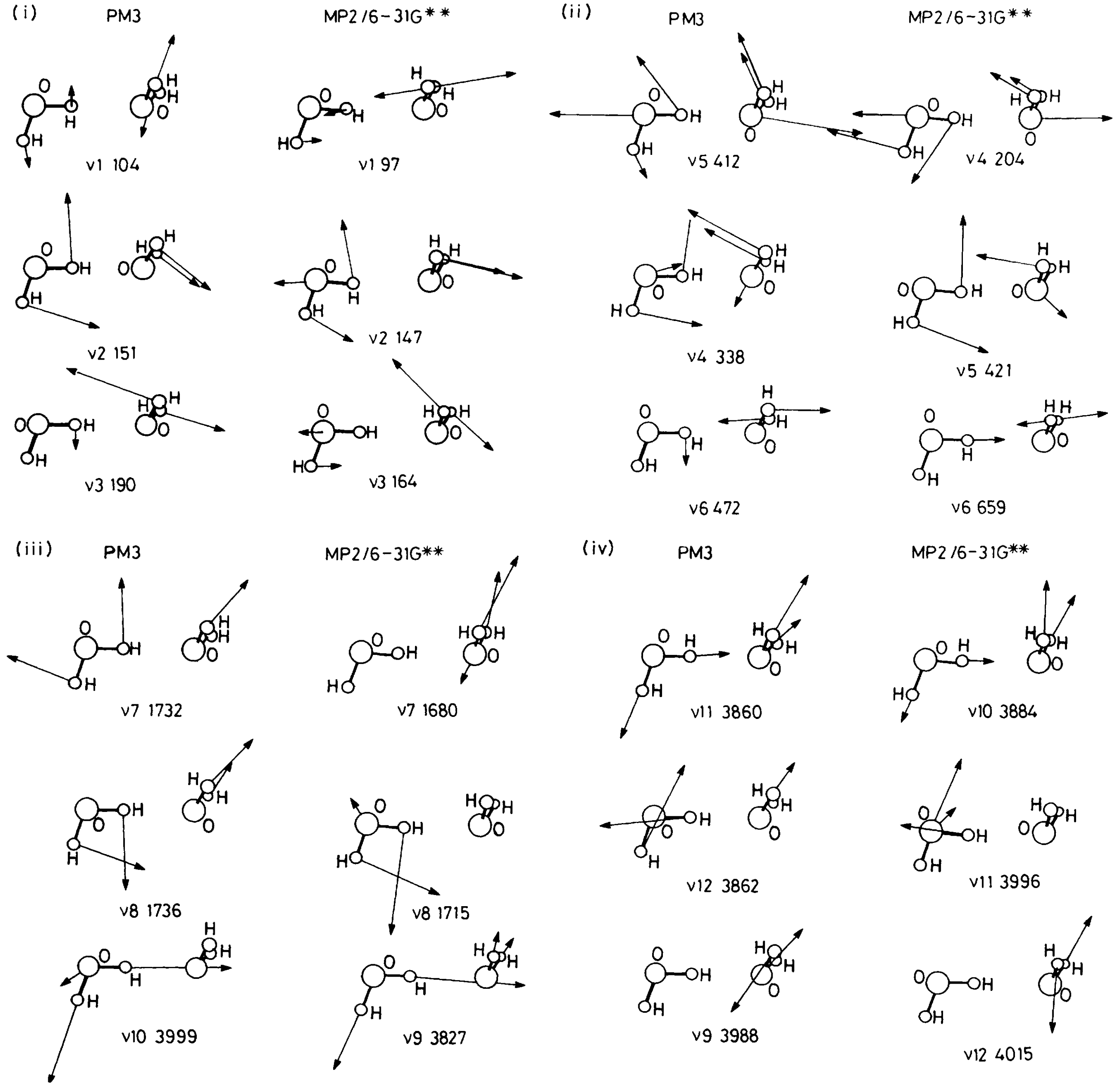

Figure 2. Calculated normal modes for (**1**) at (*a*) the PM3 and (*b*) the MP2/6-31G** levels.

certain transition states.† The close agreement between the parametric PM3 method and the *ab initio* correlated method does, however, suggest that the semi-empirical Hamiltonian must allow for certain types of correlation effect *via* the parameters. These parameters include both attractive and repulsive Gaussian functions as part of the classical core–core repulsion function, the coefficients of which are derived from experimental quantities such as molecular geometries. The PM3 parametrisation therefore includes potential energy information in the region of 2–3 Å, and hence in principle such a parametric single determinant SCF-MO method might be capable of reproducing structural effects that otherwise require the use of correlation and basis set superposition corrections at the *ab initio* level. The PM3 potential surface for the Beckmann rearrangement at O–N distances of *ca.* 2 Å was indeed previously noted[17] as being more similar to a correlated (MP2) than to a RHF level *ab initio* potential surface. However, the ability of PM3 to reproduce the geometries of hydrogen-bonding interactions correctly cannot be due entirely to the use of modified core–core repulsion terms. Such Gaussian functions are purely radial in character, and would not be expected to reproduce the highly anisotropic nature of hydrogen bonds. This effect is particularly manifest in the structures of the higher aggregates of water, which we next considered.

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† Another manifestation of this effect is for potential-energy calculations of six-electron cycloaddition reactions involving charged species (*e.g.* NO_2^+ + HCCH). PM3 predicts the allowed closed shell asynchronous (stepwise) route to be lower in energy than the alternative (equally allowed) closed shell synchronous addition. In contrast, MP2 level *ab initio* calculations of this cycloaddition indicate only the synchronous mechanism, no stepwise route being apparent (H. S. Rzepa, unpublished calculations).

Table 2. Calculated properties of (**4**).

Property[a]	OPLS	AM1	PM3	6-31G**[b]	MP2/6-31G**[b]
ΔH_{trim}	−5.8	−193.095	−170.350	−228.0989 (−227.9948)	−228.7039 (−228.6357)
$\Delta\Delta H_{trim}$	−5.8	−15.5	−10.2	−17.2 (−17.3)	−23.7
HB distance	2.090	2.198	1.796	1.99 (1.94)	1.89 (1.880)
O–$\hat{H}$–O angle	157.6	96.6	148.5	149.6 (150.8)	152.4
Normal frequencies					
1	64	137	197	166 (175)	(212)
2	64	139	199	174 (180)	(215)
3	83	173	227	181 (182)	(223)
4	93	186	230	188 (187)	(233)
5	93	266	235	213 (218)	(250)
6	142	280	314	244 (249)	(283)
7	197	397	346	329 (333)	(398)
8	197	398	383	348 (350)	(421)
9	260	451	436	449 (454)	(520)
10	260	453	743	567 (582)	(686)
11	348	529	769	659 (667)	(753)
12	401	696	789	891 (911)	(1 058)
13	1 616	1 905	1 706	1 788 (1 842)	(1 759)
14	1 616	1 905	1 716	1 797 (1 849)	(1 768)
15	1 628	1 908	1 719	1 809 (1 866)	(1 784)
16	3 671	3 484	3 748	4 014 (3 941)	(3 511)
17	3 683	3 486	3 780	4 058 (3 986)	(3 601)
18	3 683	3 486	3 780	4 061 (3 987)	(3 606)
19	3 731	3 574	3 967	4 224 (4 149)	(3 854)
20	3 731	3 575	3 978	4 227 (4 149)	(3 856)
21	3 734	3 575	3 978	4 229 (4 150)	(3 858)

[a] Units are indicated in the footnotes for Table 1. [b] 6-31G* basis set values in parentheses.

Table 3. Calculated properties of (**6**).

Property[a]	OPLS	AM1	PM3	6-31G*	MP2/6-31G*
ΔH_{tet}	−9.7	−260.89	−232.06	−304.0902	−304.8605
$\Delta\Delta H_{tet}$	−9.7	−24.1	−18.5	−29.5	−39.6
HB distance	1.996	2.17	1.781	1.892	1.770
O–$\hat{H}$–O angle	174.1	99	162.8	167.0	168.6

[a] Units indicated in Table 1.

Water Trimer.—Evidence from isotopic shift and other measurements[18] suggest that water trimer is cyclic, with C_3 symmetry and two distinct environments for the hydrogen atoms. Two non-planar cyclic structures consistent with the spectroscopic evidence have either three-fold symmetry (**3**), or no symmetry (**4**). The various theoretical procedures predict much greater structural variation (Table 2). Only one isomer is predicted at the AM1 level, corresponding to a clearly incorrect bifurcated geometry with a plane of symmetry, in which all six hydrogen atoms are equivalent (Figure 1). At the PM3 and *ab initio* levels, two distinct non-planar structures (**3**) and (**4**) are indeed predicted, with the latter slightly lower in energy than the more symmetric isomer by 1.1, 1.1, and 1.6 kcal mol^{-1} at the PM3, 6-31G** and MP2/6-31G** levels, respectively. Comparison of the calculated normal frequencies at the PM3 and MP2/6-31G* levels suggest that the two sets of results are numerically very similar (Table 2). To allow a more accurate assessment of the accuracy of PM3 would require BSSE corrections at the *ab initio* level, which have not been attempted in the present study. These PM3 frequencies allow the classical entropies of (**3**) and (**4**) to be estimated as 76.61 and 75.72 cal mol^{-1} K^{-1}, which indicates a free-energy difference between (**3**) and (**4**) of 0.8 kcal mol^{-1}, still in favour of (**4**). The OPLS force field predicts a single *planar* cyclic structure for water trimer, as indeed do other molecular-mechanics force fields such as MM2(85) and AMBER. Such a geometry may be the result of using only the monopole term of an atom-centred multipole expansion for the electrostatic interaction,[2b] and hence, treating the electron lone pairs as spherical charge distributions. In this respect, the PM3 method does indeed represent a qualitatively more accurate description of the aggregated structure of water.

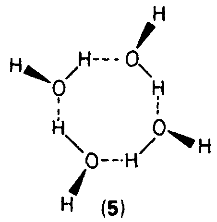
Water Tetramer.—Four cyclic isomers (**5**)–(**8**) are possible for this system, the structure of C_2 symmetry (**6**) being predicted the lowest in energy at both the *ab initio* and PM3 levels (Figure 1, Table 3). Again, the molecular-mechanics force field OPLS predicts an entirely planar structure and AM1 an entirely bifurcated geometry for this system. At this level, an MP2 calculation of the normal modes (together with BSSE corrections) represents a major investment of computational resource, and the level of structural agreement between PM3 and the *ab initio* procedures suggests that the semi-empirical PM3 method may provide a reasonable alternative for the calculation of vibrational properties.

Ammonia–Water Complex.—Two distinct isomers (**9**) and (**10**) are possible for this interaction, each with several possible conformations. The PM3 and *ab initio* calculations agree in predicting (**9**) to have the staggered conformation (Figure 1). There is, however, significantly greater divergence between the two approaches regarding the calculated normal modes (Table

Table 4. Calculated properties of (**9**).

Property[a]	OPLS	AM1	PM3	6-31G**[b]	MP2/6-31G**[b]
Energy	−1.2	−69.43	−59.54	−132.2293 (−132.2056)	−132.6221 (−132.5702)
$\Delta\Delta H_{dim}$		−2.89	−3.01	−6.40 (−6.59)	−8.0 (−8.53)
N ··· H distance	2.208	2.641	1.825	2.099 (2.085)	1.987 (1.987)
O–Ĥ ··· N angle	173.4	111.7	178.3	176.6 (176.4)	175.4 (176.1)
Normal frequencies					
1 A″	16		41	17 (29)	34 (34)
2 A″	70		244	159 (156)	159 (164)
3 A′	70		219	163 (164)	172 (177)
4 A′	92		376	182 (185)	202 (211)
5 A′	152		418	431 (434)	459 (471)
6 A″	249		566	660 (666)	713 (729)
7 A′	929		1 439	1 192 (1 254)	1 158 (1 198)
8 A′	1 201		1 736	1 801 (1 841)	1 715 (1 744)
9 A″	1 201		1 756	1 808 (1 847)	1 724 (1 751)
10 A′	1 610		1 756	1 818 (1 870)	1 743 (1 793)
11 A′	3 240		3 457	3 706 (3 692)	3 568 (3 509)
12 A′	3 331		3 456	3 841 (3 823)	3 722 (3 623)
13 A″	3 331		3 658	3 843 (3 825)	3 723 (3 663)
14 A′	3 681		3 718	4 035 (3 968)	3 729 (3 660)
15 A′	3 733		3 970	4 227 (4 151)	3 989 (3 872)

[a] Units indicated in Table 1. [b] Values for 6-31G* basis in parentheses.



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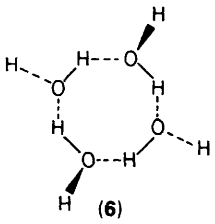

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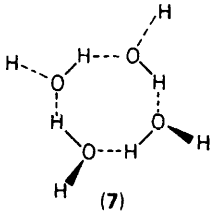

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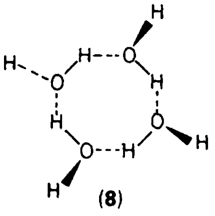


(**8**)

4), compared to the much higher agreement obtained for water dimer. Of the low-frequency modes, the only difference in ordering is for v2/v3 (Table 4). The high frequency modes show the expected switching of symmetric and anti-symmetric vibrations (see footnote †, p. 946). Numerically, three modes differ by more than 100 cm^{-1} (v4 + 174, v6 − 147, and v7 + 281). The v7 mode represents N–H ··· O stretching combined with umbrella inversion at nitrogen (Figure 3). This last result accords with the high inversion barrier for ammonia predicted using PM3 (10.0 *vs.* 5.4 kcal mol^{-1} at the MP3/6-31G* level[19]). A second, possibly related error in the PM3 procedure relates to the calculated charge on the central nitrogen in (**9**) (−0.05/PM3, −1.035/6-31G*) which would affect the dipolar interactions between the two components. A close inspection of the reported[7] PM3 atomic valence ionization potentials U_{ss} and U_{pp} shows the values for nitrogen specifically to be respectively *ca.* 12 and 4 eV less negative than expected from a smooth interpolation of the parameters for boron to fluorine. The calculated charge distribution within a molecule can be expected to be directly related to the values of the U_{ss} and U_{pp} parameters, and these PM3 anomalies for nitrogen would indeed predict a less electronegative nitrogen centre than expected. The different errors in the PM3 (s) and (p) valence-shell ionisation potentials may in turn affect properties where the s/p orbital mixing at nitrogen changes, as for example the v7 mode referred to above, or the inversion barrier in ammonia. It has also been noted[7] that the rotational barrier predicted using PM3 for the C–N peptide bond is far too low, and this again may be related to an anomaly in the PM3 nitrogen U_{ss} and U_{pp} parameters. In comparison, the AM1 atomic parameters show a much smoother progression from C–F, and indeed the calculated AM1 charge distribution in (**9**) is intuitively more reasonable ($N = -0.4$). PM3 is nevertheless far superior to AM1 in correctly predicting the geometry of (**9**), with AM1 predicting a bifurcated geometry (Figure 1). Moreover, the AM1 complexation energy is significantly too low compared to the *ab initio* results (Table 4). An entirely different type of error for the AM1 nitrogen core–core repulsion parameters has in fact been noted previously,[20] the effect of which is to overestimate core repulsions at *ca.* 2.5 Å. This effect is probably responsible for the large difference in OH ··· N bond length between AM1 and the other methods (Table 4) and the low complexation energy. As with water, the OPLS procedure underestimates the low frequency normal modes corresponding to the intermolecular interactions in (**9**), the most prominent discrepancy being for v6, which is in error by 464 cm^{-1} compared to the MP2 *ab initio* result.

Ammonia–Formaldehyde Complex.—This system represents the simplest example of the peptide hydrogen bond, differing from the previous systems in having an N–H ··· O rather than an O–H ··· N interaction. The AM1 complex (Figure 1) displayed the usual bifurcated geometry, whereas three different complexes were located at the PM3 level. Of these, (**11**) corresponds to the reaction pathway for nucleophilic addition to the carbonyl group, whilst two isomers (**12**) and (**13**) were located differing in the H ··· O bond lengths (1.89 and 2.70 Å) the C=O ··· H angles (118.8 and 90.8) and the O ··· H–N angles (185.7 and 218.4°) respectively. The interaction energies of (**12**) and (**13**) compared with isolated components were −0.1 and −1.0 kcal mol^{-1}, indicating little stabilisation at the PM3 level and a barrier of only some 0.2 kcal mol^{-1} separating (**12**) from (**13**). *ab initio* optimisation resulted in a single complex with geometrical values intermediate to the two PM3 results

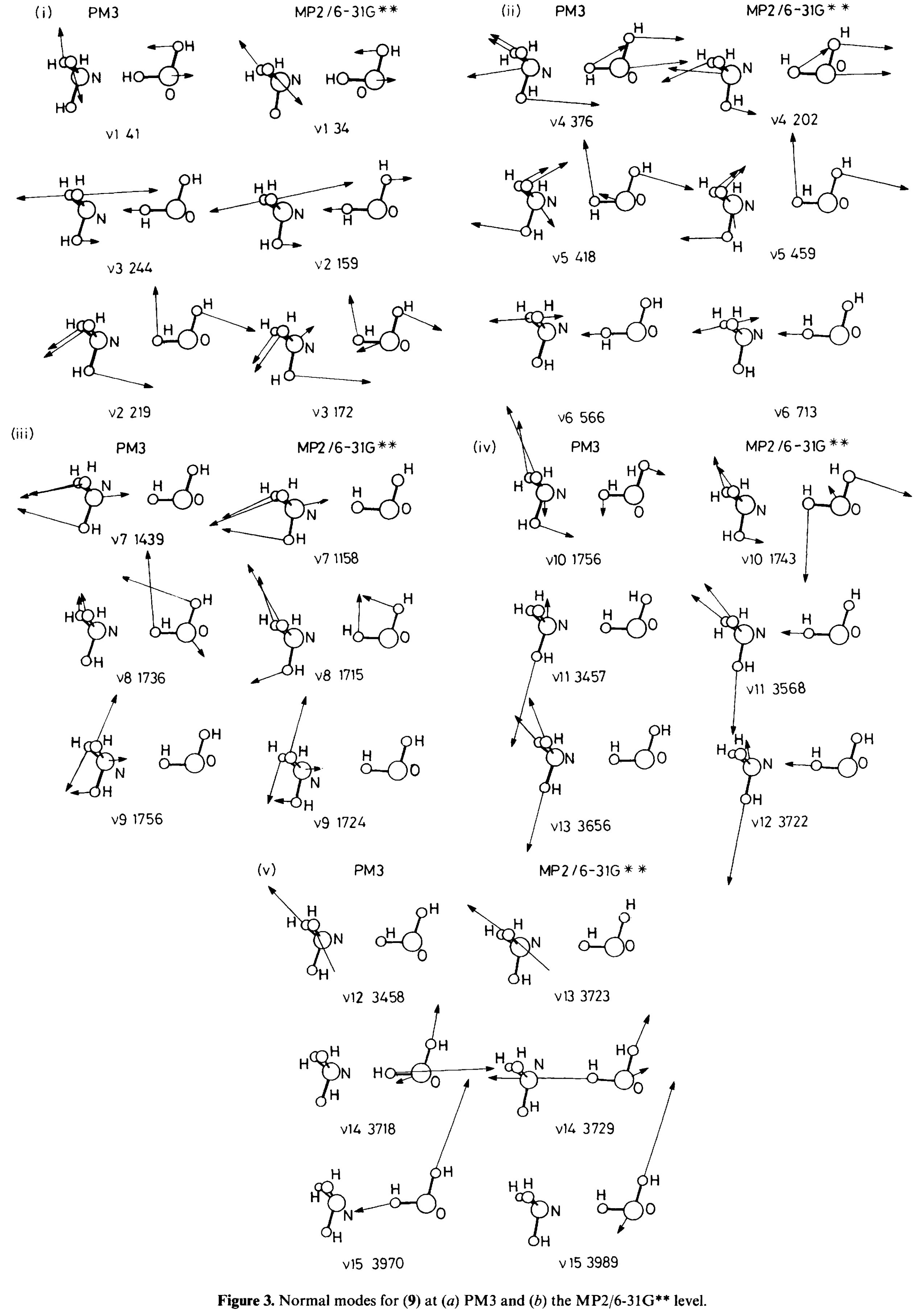
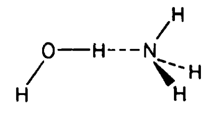


Figure 3. Normal modes for (**9**) at (*a*) PM3 and (*b*) the MP2/6-31G** level.

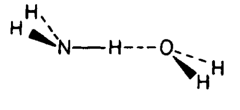
Table 5. Calculated properties of (**12**).

Property[a]	OPLS	AM1	PM3	6-31G**[b]	MP2/6-31G**[b]
Energy	−1.0	−41.5	−37.23	−170.0713 (−0.170.0566)	−170.5863 (−170.5407)
$\Delta\Delta H_{dim}$	−1.0	−2.73	−0.08	−3.77 (−3.70)	−5.27 (−5.21)
O • • • H distance	2.30	2.49	1.882	2.405 (2.403)	2.270 (2.262)
N–H • • • O angle	164.7	104.2	188.0	139.2 (140.3)	143.3 (143.2)
Normal frequencies					
1 A″	30		40	112 (109)	(129)
2 A′	42		239	121 (118)	(146)
3 A′	46		68	139 (135)	(160)
4 A″	75		72	181 (180)	(203)
5 A″	87		206	190 (181)	(236)
6 A′	131		309	332 (327)	(374)
7 A′	544		1 417	1 178 (1 241)	(1 193)
8 A″	930		1 102	1 353 (1 352)	(1 233)
9 A′	988		1 070	1 385 (1 391)	(1 305)
10 A′	1 200		1 282	1 662 (1 674)	(1 575)
11 A′	1 205		1 761	1 809 (1 847)	(1 751)
12 A′	1 280		1 979	2 006 (2 009)	(1 767)
13 A″	1 657		1 747	1 826 (1 864)	(1 776)
14 A′	2 894		3 000	3 132 (3 180)	(3 038)
15 A′	2 998		3 033	3 240 (3 269)	(3 134)
16 A′	3 239		3 410	3 700 (3 687)	(3 495)
17 A′	3 329		3 638	3 837 (3 818)	(3 642)
18 A″	3 331		3 455	3 838 (3 821)	(3 656)

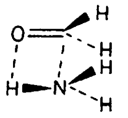
[a] Units indicated in Table 1. [b] Values for 6-31G* basis in parentheses.



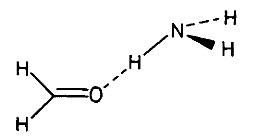
(**9**)



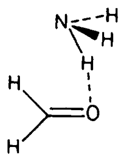
(**10**)



(**11**)



(**12**)



(**13**)

Table 6. PM3 calculated atomic charges and two-centre energy terms for hydrogen bonded complexes.

	qO	qH_{HB}	q$H_{non\text{-}HB}$	Coulombic term[a]	Two-centre energy[b]
H_2O	−0.359	—	0.179		—
NH_3	+0.007[c]	—	−0.002		—
(**1**)	−0.365	0.207	0.176	−0.232	−1.219
(**4**)	−0.422	0.233	0.189	−0.368	−1.477
(**6**)	−0.427	0.236	0.191	−0.369	−1.587
(**9**)	−0.424	0.210	0.169	+0.292	−1 051
(**12**)	−0.320 (−0.050)[c]	0.039	−0.002	+0.196	−0.453

[a] Coulombic (electron–electron repulsion, core-electron attraction and core–core repulsion) two-centre energy (in eV). [b] Total (resonance, exchange, and coulomb) two-centre energy (in eV) of hydrogen bond H • • • X (X = O,N). [c] Charge on N.

(2.27 Å, 143.2 and 93.6° respectively at the MP2/6-31G** level) and a significantly greater stabilisation (Table 5). The OPLS molecular mechanics force field, which was specifically developed for peptides, predicts a complex similar to the *ab initio* result (2.29 Å, 165.8 and 102.5° for the three variables quoted above). A comprehensive analysis of the crystallographically derived geometries of 1 509 C=O • • • H–N hydrogen bonds[21] indicates, however, that the mean value of the C=O • • • H angle (160.3°) is substantially greater than that calculated for formaldehyde/ammonia by any method, indicating that this specific system may be somewhat anomalous compared to more typical hydrogen bonds of this type.

PM3 is clearly at variance with the other theoretical procedures in predicting two separate complexes (**12**) and (**13**). Whilst the method clearly handles hydrogen bonds involving interaction between an O–H σ bond and a nitrogen lone pair [as in (**9**)] reasonably well, the inverse interaction between an N–H σ bond and an oxygen lone pair has a more significant error. This reinforces the suggestion made above that the error in the PM3 U_{ss} atomic parameter is significantly greater than that for U_{pp}, and, therefore, that any weak interaction involving an N–H bond may be incorrectly predicted. Indeed a partitioning of the two-centre energies[13] reveals that the total O • • • H term for (**12**) is significantly less than that for the other complexes (**1**), (**4**), (**6**), and (**9**) (Table 6). This can be traced in part to the positive value of the two-centre coulombic contribution for (**12**) compared to negative values for (**1**), (**4**), and (**6**). In contrast to the neutral complex (**12**), we have established that hydrogen-bonding interactions between charged nitrogen (*e.g.* NH_4^+ and oxygen lone pairs) are much stronger (> 10 kcal mol^{-1}) and that both the geometries and the interaction energies of such systems are more reliably predicted than for (**12**).[10,22]

Finally for this system, we note that the PM3 calculated normal modes for (**12**) show a much larger variation compared to *ab initio* calculations, with the ordering of a number of modes being inverted (Table 5). The lowest energy modes reflect the low PM3 binding energy, while the errors in both v2 and v7 are probably due as noted above to the large PM3 error in the inversion barrier for ammonia. It is generally true that antisymmetric modes tend to be too low in energy compared to the symmetric equivalents. Interestingly, the C=O stretching mode is predicted to be too high in energy at both the PM3 and RHF/*ab initio* levels, and is only correctly reproduced at the correlated MP2 level.

Trends in Hydrogen-bond Strengths.—The series $(H_2O)_n$, n = 1–4 can be used to investigate how hydrogen-bond strengths are influenced by the immediate environment. Table 6 shows an analysis of the PM3 results for (**1**), (**4**), and (**6**) in terms of the calculated atomic charges, and the total two-centre energies.[7] These both show a significant increase in the hydrogen-bond strengths in the trimer compared to the dimer, and a further small increase in the strength of each hydrogen bond in the tetramer. This effect can be traced to the increased polarisation of the water molecule upon hydrogen bond formation, which in turn reinforces the interactions in the adjacent hydrogen bonds. This is also reflected in the increasing two-centre coulombic interaction along the series (**1**)–(**6**).

Structurally, all the SCF-MO methods predict a uniform contraction in the $H \cdots O$ bond lengths for the series $(H_2O)_n$, n = 2–3, and n = 3–4, although the average PM3 contraction (−0.014 Å) is smaller than the RHF or MP2 *ab initio* contractions (*ca.* −0.09 Å). This last value may well be over-estimated because of the lack of corrections for BSSE in the *ab initio* calculations.[8] In contrast, the OPLS molecular-mechanics potential predicts an *increase* in the hydrogen-bond length for $(H_2O)_n$, n = 2–3, and a decrease only for n = 3–4. These effects indicate that the mutual polarisation of water molecules can result in significant structural differences in the solvation structures. At the molecular-mechanics level at least, it has been suggested[2b] that polarisation effects of this type can be treated by using a distance dependent dielectric for the electrostatic interactions, but such an approach could not incorporate differing solvent polarisation along *e.g.* a reaction co-ordinate. A single water potential applied equally to all parts of a potential surface may, therefore, fail to recover subtle changes in the structure and energetics of the solvation. Qualitatively such effects are only handled in a self consistent way at the quantum mechanical level. There is no obvious reason why the specific errors noted in the PM3 nitrogen parametrisation could not be removed in future versions, and the further development of such semi-empirical potentials for use in studying reaction solvation is to be encouraged.

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