Directional Hydrogen Bonding in the MM3 Force Field: II

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ABSTRACT: Extensive calculations on hydrogen bonded systems were carried out using the improved MM3 directional hydrogen bond potential. The resulting total function was reoptimized. Comparisons of the hydrogen bonding potential function from *ab initio* calculations (MP2/6-31G**); the original MM3(89); and the reoptimized MM3 force field MM3(96), for a variety of C, N, O, and Cl systems including the formamide dimer and formamide–water complex, are described herein. Hydrogen bonding is shown to be a far more complicated and ubiquitous phenomenon than is generally recognized.   © 1998 John Wiley & Sons, Inc.   J Comput Chem 19: 1001−1016, 1998

Keywords: *ab initio*; molecular mechanics; hydrogen bond

Introduction

This is the second of two articles concerning calculations of the hydrogen bond potential using an improved MM3 hydrogen bond potential.[1] As described in the previous article,[2] a directional term has been added to the original MM3 hydrogen bonding function to improve the accuracy.

This explicit MM3 hydrogen bonding potential function is:

$$E_{HB} = \varepsilon_{HB} * \left(184000 * \exp(-12.0 * (R_{YH}/r)) \right.$$
$$\left. - F(\beta, R_{X-H}) \times 2.25 * (r/R_{YH})^6 \right)/D$$
$$F(\beta, R_{X-H}) = \cos\beta * (R_{X-H}/R_{X-H}^0) \quad (2)$$

where ε_{HB} is the hydrogen bonding energy parameter; r is the equilibrium hydrogen bonding distance; R_{YH} is hydrogen bonding distance $Y \cdots H$; $\cos\beta$ is the cosine of angle $\angle H-X \cdots Y$; R_{X-H} is the bond length of bond X—H; and R_{X-H} is the natural bond length of bond X—H; and D is the dielectric constant. These relationships are summarized in Figure 1.

In this article, we compare the results obtained with hydrogen bonding potential functions from
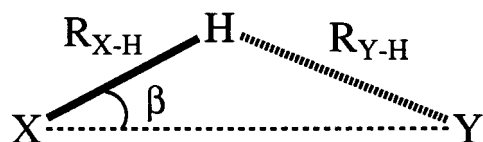
FIGURE 1. Relationship among parameters used in MM3 hydrogen bonding potential function.

ab initio calculation (MP2/6-31G**), the original MM3, and the reoptimized MM3 force field MM3(96) for a variety of C, N, O, and Cl systems. The calculations include the ethylene–ammonia complex, ethylene–acetylene complex, water–acetylene complex, ammonia–acetylene complex, formaldehyde–acetylene complex, acetylene dimer, formamide–water complex, formamide–methanol complex, formamide–formaldehyde complex, formamide dimer, guanidinum ion–water complex, formate ion–water complex, ammonium ion–water complex, methyl chloride–water complex, 4-chloro-1-butanol, cyclopropane–water complex, 2-cyclopropyl ethanol, and acetaldehyde–methanol complex.

Computational Method

As in the previous article, *ab initio* calculations at the 6-31G** MP2 level with counterpoise BSSE corrections[3] were carried out for all the aforementioned complexes. The MM3 hydrogen bonding parameters were then reoptimized to fit to the *ab initio* results. In what follows, we provide a discussion of the overall results calculated with optimized parameters (shown in Table I) and compared them with *ab initio* and experimental results (Tables II–VII and Supplemental Material[4]). Finally, the hydrogen donors and acceptors used in the studies are summarized in Table VIII.

TABLE I.
MM3(96) Force Field for Directional Hydrogen Bonding.[a]

		MM3(96)		MM3(89)	
		ε_{HB}	r	ε_{HB}	r
Hydrogen bonding parameters					
Hydrogen bond type					
=C $\cdots$ H(N)	(2...23)	0.100	3.00	0.750	3.00
=C $\cdots$ H(—C≡C)	(2...124)	0.250	2.96	None	
≡C $\cdots$ H(O)	(4...21)	0.510	2.60	None	
≡C $\cdots$ H(N)	(4...23)	0.260	2.87	None	
≡C $\cdots$ H(—C≡C)	(4...124)	0.340	2.82	None	
—O $\cdots$ H(N amide)	(6...28)	5.140	2.03	3.150	2.25
—O $\cdots$ H(N ammonium)[b]	(6...48)	13.800	1.72	4.200	1.88
—O $\cdots$ H(—C≡C)	(6...124)	1.700	2.30	None	
C=O $\cdots$ H(O)	(7...21)	2.550	2.07	3.975	2.14
C=O $\cdots$ H(N amide)	(7...28)	4.440	2.07	5.100	2.03
C=O $\cdots$ H(—C≡C)	(7...124)	1.390	2.33	None	
C[c] $\cdots$ H(O)	(22...21)	0.950	2.38	None	
(—)O—C=O $\cdots$ H(O)	(47...21)	5.000	2.07	3.150	2.15
N—C=O $\cdots$ H(O)	(79...21)	3.460	1.95	3.975	2.14
N—C=O $\cdots$ H(N amide)	(79...28)	5.240	1.96	5.100	2.03
N $\cdots$ H(—C≡C)	(8...124)	3.530	2.30	None	
Cl $\cdots$ H(O)	(12...21)	1.100	2.80	4.500	2.43
Bond moment parameters					

Bond type		Bond moments	
N(+)—H[b]	(39–48)	− 1.9219 Debye	

[a] ε_{HB} is the well-depth parameter in the hydrogen bond equation (kcal/mol), and r is the distance between the atoms at the energy minimum (Å).
[b] These parameters are not in MM3(96).
[c] C is cyclopropane carbon.

Results and Discussion

ETHYLENE–AMMONIA AND ETHYLENE–ACETYLENE COMPLEXES

Two conformations of the ethylene–ammonia complex, Cs (**1**) and Cl (**2**), and the T-shaped ethylene–acetylene complex (**3**) were studied by first carrying out *ab initio* calculations. The results show that both ethylene–ammonia conformations have similar and weak binding energies, 0.75 and 0.74 kcal/mol, respectively, whereas the ethylene–acetylene complex has a slightly stronger binding energy, 1.10 kcal/mol (Table II). These values suggest that ethylene is a poor hydrogen acceptor, as one would expect, and acetylene is a better hydrogen donor than ammonia, although it is not as good as water (ethylene–water binding energy 1.71 kcal/mol).[2]

The binding energies of the ethylene–ammonia complexes are well calculated by both MM3 and MM3(96). The geometries of the ethylene complexes are calculated poorly by MM3, but they are, with the help of the directional function, improved significantly with MM3(96) (Table III). Although the acetylene hydrogen is not treated explicitly as a hydrogen bond proton donor in MM3, the T-shaped ethylene–acetylene complex is fairly well calculated with respect to both binding energy and geometry. Note that the T-shaped ethylene–acetylene complex is not on a ''hill-top'' on the MM3(96) potential surface as was the case earlier.

WATER–ACETYLENE, AMMONIA–ACETYLENE, AND FORMALDEHYDE–ACETYLENE COMPLEXES AND ACETYLENE DIMER

The acetylene hydrogen is known to be acidic enough to be a hydrogen donor, but what about

TABLE II.
Binding Energies of Selected Hydrogen Bonded Complexes.[a]

No.	Complex	MP2/6-31G**	MM3	MM396	Reference[l]
1	Ethylene–ammonia (1), C_s	0.75	0.76	0.78	Table S-1, Fig. S-1.1
2	Ethylene–ammonia (2), C_1	0.74	0.71	0.79	Table S-1, Fig. S-1.2
3	Ethylene–acetylene, T-shape	1.10	0.46	1.08	Table S-2, Fig. S-1.3
4	Water–acetylene (1)[b]	2.45	0.82	2.48	Table S-3, Fig. S-1.4
5	Water–acetylene (2)[c]	1.60	0.96	1.62	Table S-3, Fig. S-1.5
6	Ammonia–acetylene (1), C_{3v}[d]	3.80	0.83	3.79	Table S-4, Fig. S-1.6
7	Ammonia–acetylene (2)[e]	0.73	0.50	0.73	Table S-4, Fig. S-1.7
8	Formaldehyde–acetylene (1), C_{2v}	1.91	0.60	2.01	Table S-5, Fig. S-1.8
9	Formaldehyde–acetylene (2), Cyclic	2.13	0.94	2.05	Table S-5, Fig. S-1.9
10	Acetylene–dimer, T-shape	1.03	0.49	1.03	Table S-6, Fig. S-1.10
11	Formamide–water (1), cyclic	8.45	8.85	8.47	Table S-7, Fig. S-1.11
12	Formamide–water (2)[f]	5.02	N/A	5.02	Table S-7, Fig. S-1.12
13	Formamide–methanol (1), cyclic	8.51	9.16	8.43	Table S-8, Fig. S-1.13
14	Formamide–methanol (2)[g]	5.22	5.44	5.25	Table S-8, Fig. S-1.14
15	Formamide–formaldehyde (1), cyclic	6.37	7.25	6.37	Table S-9, Fig. S-1.15
16	Formamide–Formaldehyde (2)[h]	3.76	N/A	5.84	Table S-9, Fig. S-1.16
17	Formamide dimer, cyclic	13.36	13.78	13.36	Table S-10, Fig. S-1.17
18	Guanidinium ion–water, bifurcated	19.38	14.48	16.32	Table S-11, Fig. S-1.18
19	Formate ion–water, bifurcated	19.65	19.52	19.62	Table S-12, Fig. S-1.19
20	Ammonium ion–water, linear	23.28	14.06	22.63	Table S-13, Fig. S-1.20
21	Ammonium ion–water, bifurcated	18.92	17.62	19.60	Table S-13, Fig. S-1.21
22	Methylchloride–water, cyclic	2.04	7.15	2.04 (2.15)[k]	Table 4, Fig. S-1.22
34	Cyclopropane–water	1.41	0.56	1.42	Table 6, Fig. S-1.34
39	Acetaldehyde–methanol (1)[i]	4.44	5.56	4.46	Table S-14, Fig. S-1.39
40	Acetaldehyde–methanol (2)[j]	2.11	0.86	0.83	Table S-14, Fig. S-1.40

[a] All energies in kcal/mol; [b] O is H acceptor; [c] C≡C is H acceptor; [d] N is H acceptor; [e] C≡C is H acceptor; [f] only C=O is H acceptor; [g] only C=O is H acceptor; [h] N is H donor; [i] C=O is H acceptor; [j] C=O is H acceptor; [k] using modified van der Waals parameter for $C_{(\alpha)}$—H⋯O interaction (ε: 0.85 kcal/mol; r^*: 2.40 Å); [l] Table S-Xs and Figure S-Xs are available in Supplementary Material.

TABLE III.
Geometries and Dipole Moments of Selected Hydrogen Bonded Complexes.[a]

No.	Complex	MP2/6-31G**	MM3	MM3(96)	Reference[m]
1	Ethylene–ammonia (1), C_s				Table S-1, Fig. S-1.1
	C=C $\cdots$ N dist. (Å)	3.715	3.687	3.723	
	C=C $\cdots$ H dist. (Å)	2.734	3.153	2.710	
	$\angle$(C=)C $\cdots$ N—H (deg.)	12.1	51.2	2.9	
	Dipole moment (Debye)	1.981	1.511	1.500	
2	Ethylene–ammonia (2), C_1				Table S-1, Fig. S-1.2
	C=C $\cdots$ N dist. (Å)	3.817	3.845	3.719	
	C=C $\cdots$ H dist. (Å)	2.826	3.029	2.763	
	$\angle$(C=)C $\cdots$ N—H (deg.)	10.1	31.7	16.9	
	Dipole moment (Debye)	2.040	1.502	1.500	
3	Ethylene–acetylene, T-shape				Table S-2, Fig. S-1.3
	C=C $\cdots$ C dist. (Å)	3.807	3.810	3.819	
	C=C $\cdots$ H dist. (Å)	2.766	2.754	2.760	
	$\angle$(C=)C $\cdots$ C—H(deg.)	10.1	10.1	10.1	
	Dipole moment (Debye)	0.503	0.003	0.000	
4	Water–acetylene (1)[b]				Table S-3, Fig. S-1.4
	O $\cdots$ C≡C dist. (Å)	3.254	3.747	3.262	
	O $\cdots$ H—C≡C dist. (Å)	2.195	2.666	2.178	
	$\angle$O $\cdots$ C—H (deg.)	5.9	0.0	0.0	
	Dipole moment (Debye)	2.424	2.036	2.037	
5	Water–acetylene (2)[c]				Table S-3, Fig. S-1.5
	C≡C $\cdots$ O dist. (Å)	3.411	3.601	3.404	
	C≡C $\cdots$ H dist. (Å)	2.481	3.124	2.515	
	$\angle$(C≡)C $\cdots$ O—H (deg.)	12.2	53.0	17.4	
	Dipole moment (Debye)	2.545	2.057	2.052	
6	Ammonia–acetylene (1), C_{3v}[d]				Table S4, Fig. S-1.6
	N $\cdots$ C≡C dist. (Å)	3.291	3.781	3.293	
	N $\cdots$ H—C≡C dist. (Å)	2.218	2.700	2.206	
	$\angle$N $\cdots$ C—H(deg.)	0.0	0.0	0.0	
	Dipole moment (Debye)	2.726	1.496	1.504	
7	Ammonia–acetylene (2)[e]				Table S-4, Fig. S-1.7
	C≡C $\cdots$ N dist. (Å)	3.709	4.025	3.711	
	C≡C $\cdots$ H dist. (Å)	2.716	3.025	2.714	
	$\angle$(C≡)C $\cdots$ N—H (deg.)	9.4	8.7	9.4	
	Dipole moment (Debye)	1.991	1.495	1.494	
8	Formaldehyde–acetylene (1), C_{2v}				Table S-5, Fig. S-1.8
	C=O $\cdots$ C dist.(Å)	3.292	3.854	3.293	
	C=O $\cdots$ H dist. (Å)	2.228	2.773	2.209	
	$\angle$(C=)O $\cdots$ C—H (deg.)	0.0	0.0	0.0	
	Dipole moment (Debye)	3.510	2.485	2.480	
9	Formaldehyde–acetylene (2), cyclic				Table S-5 Fig. S-1.9
	C=O $\cdots$ C dist. (Å)	3.206	3.561	3.289	
	C=O $\cdots$ H dist. (Å)	2.211	2.950	2.217	
	O=C $\cdots$ H—C dist. (Å)	2.695	3.433	3.110	
	O=C—H $\cdots$ H—C dist. (Å)	2.498	3.123	3.248	
	$\angle$(C=)O $\cdots$ C—H (deg.)	17.3	48.1	7.1	
	Dipole moment (Debye)	2.990	2.483	2.480	

TABLE III.
Continued.

No.	Complex	MP2/6-31G**	MM3	MM3(96)	Reference[m]
10	Acetylene dimer, T-shape				Table S-6 Fig. S-1.10
	C≡C ··· C≡C dist.(Å)	3.743	4.119	3.748	
	C≡C ··· H—C dist. (Å)	2.699	3.054	2.685	
	∠(C≡)C ··· C—H (deg.)	9.4	8.5	9.3	
	Dipole moment (Debye)	0.464	0.006	0.007	
11	Formamide−water (1), cyclic				Table S-7, Fig. S-1.11
	C=O ··· O dist. (Å)	2.829	2.830	2.822	
	C=O ··· H dist. (Å)	1.936	2.093	1.982	
	N ··· O—H dist. (Å)	2.875	2.981	2.887	
	N—H ··· O—H dist. (Å)	2.018	2.168	2.021	
	∠C=O ··· O(—H) (deg.)	96.2	98.6	96.7	
	∠C—N ··· O(—H) (deg.)	91.4	88.3	90.2	
	∠C=O ··· H(—O) (deg.)	105.5	N/A	107.7	
	Dipole moment (Debye)	3.570	2.727	1.634	
12	Formamide−water (2)[f]				Table S-7, Fig. S-1.12
	C=O ··· O dist. (Å)	2.847	N/A	2.819	
	C=O ··· H dist. (Å)	1.953	N/A	1.878	
	O=C ··· O—H dist. (Å)	3.067	N/A	3.711	
	O=C—H ··· O—H dist. (Å)	2.581	N/A	3.878	
	∠C=O ··· O(—H) (deg.)	88.3	N/A	129.4	
	∠C=O ··· H(—O) (deg.)	97.1	N/A	126.2	
	Dipole moment (Debye)	4.569	N/A	4.547	
13	Formamide−methanol (1), cyclic				Table S-8, Fig. S-1.13
	C=O ··· O dist. (Å)	2.805	2.853	2.795	
	C=O ··· H dist. (Å)	1.913	2.092	1.971	
	N ··· O—H dist. (Å)	2.857	3.011	2.894	
	N—H ··· O—H dist. (Å)	2.004	2.179	2.037	
	∠C=O ··· O(—H) (deg.)	96.2	99.4	97.4	
	∠C—N ··· O(—H) (deg.)	91.2	88.6	89.4	
	∠C=O ··· H(—O) (deg.)	105.4	112.4	109.1	
	Dipole moment (Debye)	3.704	2.517	2.501	
14	Formamide−methanol (2)[g]				Table S-8, Fig. S-1.14
	C=O ··· O dist. (Å)	2.813	2.983	2.821	
	C=O ··· H dist. (Å)	1.923	2.051	1.869	
	O=C ··· O—H dist. (Å)	3.038	3.506	3.724	
	O=C—H ··· O—H dist. (Å)	2.550	3.454	3.810	
	∠C=O ··· O(—H) (deg.)	88.4	170.2	130.3	
	∠C=O ··· H(—O) (deg.)	97.3	167.1	130.9	
	Dipole moment (Debye)	4.715	5.363	4.819	
15	Formamide−formaldehyde (1), cyclic				Table S-9, Fig. S-1.15
	C=O ··· N dist. (Å)	2.991	2.959	3.010	
	C=O ··· H—N dist. (Å)	1.996	1.939	1.981	
	O=C ··· O=C dist. (Å)	3.231	3.584	3.632	
	C—H ··· O=C dist. (Å)	2.276	2.774	2.802	
	∠(C=)O ··· N—C (deg.)	110.8	112.8	113.5	
	∠(O=)C ··· O=C (deg.)	104.3	101.5	101.2	
	∠C=O ··· H(—N) (deg.)	106.8	118.2	116.2	
	Dipole moment (Debye)	1.316	1.469	1.448	

TABLE III.
Continued.

No.	Complex	MP2/6-31G**	MM3	MM3(96)	Reference[m]
16	Formamide–formaldehyde (2)[h]				Table S-9, Fig. S-1.16
	C=O ⋯ N dist. (Å)	3.007	N/A	3.007	
	C=O ⋯ H—N dist. (Å)	2.055	N/A	1.971	
	O=C ⋯ O=C dist. (Å)	4.055	N/A	4.669	
	∠C=O ⋯ H(—N) (deg.)	102.5	N/A	145.5	
	Dipole moment (Debye)	5.205	N/A	5.300	
17	Formamide dimer, cyclic				Table S-10 Fig. S-1.17
	C=O ⋯ N dist. (Å)	2.900	2.956	2.907	
	C=O ⋯ H—N dist. (Å)	1.882	1.932	1.873	
	∠(C=)O ⋯ N—H (deg.)	3.3	3.8	3.4	
	∠(C=)O ⋯ N—C (deg.)	117.3	114.9	115.1	
	Dipole moment (Debye)	0.005	0.000	0.000	
18	Guanidinium ion–water, bifurcated				Table S-11, Fig. S-1.18
	O ⋯ C(+)dist. (Å)	3.326	3.463	3.337	
	O ⋯ N dist. (Å)	2.888	3.033	2.902	
	O ⋯ H—N dist. (Å)	1.982	2.116	1.970	
	∠O ⋯ N—H (deg.)	21.7	21.9	20.9	
	Dipole moment (Debye)	0.196	2.090	2.128	
19	Formate ion–water, bifurcated				Table S-12, Fig. S-1.19
	O=C ⋯ O dist. (Å)	3.132	3.133	3.137	
	C=O ⋯ O dist. (Å)	2.843	2.821	2.826	
	C=O ⋯ H—O dist. (Å)	1.989	2.015	2.004	
	∠C=O ⋯ O(—H) (deg.)	91.0	92.4	92.3	
	Dipole moment (Debye)	1.700	4.428	4.464	
20	Ammonium ion–water, linear				Table S-13, Fig. S-1.20
	N(+) ⋯ O dist. (Å)	2.673	2.718	2.668	
	N(+)—H ⋯ O dist. (Å)	1.614	1.732	1.616	
	∠H—N ⋯ O (deg.)	0.0	0.0	0.0	
	Dipole moment (Debye)	2.668	2.160	2.155	
21	Ammonium ion–water, bifurcated				Table S-13, Fig. S-1.21
	N(+) ⋯ O dist. (Å)	2.664	2.477	2.350	
	N(+)—H ⋯ O dist. (Å)	2.184	2.000	1.862	
	∠H—N ⋯ O (deg.)	51.8	51.5	50.1	
	Dipole moment (Debye)	3.123	2.291	2.427	
22	Methylchloride–water, cyclic				Table 4, Fig. S-1.22
	Cl ⋯ O dist. (Å)	3.431	2.939	3.589 (3.549)[k]	
	Cl ⋯ H—O dist. (Å)	2.708	2.474	2.684 (2.803)	
	C(α) ⋯ O dist. (Å)	3.304	3.781	3.768 (3.433)	
	C(α)—H ⋯ O dist. (Å)	2.418	3.375	3.551 (2.533)	
	∠Cl ⋯ O—H (deg.)	35.8	52.2	15.0 (33.1)	
	∠H—C(α) ⋯ O(—H) (deg.)	29.2	60.4	70.3 (29.7)	
	Dipole moment (Debye)	1.370	2.944	0.515 (0.502)	

TABLE III.
Continued.

No.	Complex	MP2/6-31G**	MM3	MM3(96)	Reference[m]
34	Cyclopropane–water				Table 6, Fig. S-1.34
	C $\cdots$ O dist. (Å)	3.307	3.781	3.425	
	C $\cdots$ H—O dist. (Å)	2.396 (2.342)[l]	3.305	2.513	
	C—H $\cdots$ O—H dist. (Å)	3.085	3.753	3.405	
	Dipole moment (Debye)	2.379	2.033	2.036	
39	Acetaldehyde–methanol (1)[i]				Table S-14, Fig. S-1.39
	C=O $\cdots$ O dist. (Å)	2.903	2.958	2.918	
	C=O $\cdots$ H dist. (Å)	1.975	2.058	1.976	
	C $\cdots$ O—H dist. (Å)	3.318	3.881	3.987	
	C—H $\cdots$ O—H dist. (Å)	2.407	3.169	3.223	
	$\angle$(C=)O $\cdots$ O—H (deg.)	13.8	15.2	7.1	
	$\angle$H—C $\cdots$ O(—H)	27.4	43.5	40.3	
	Dipole moment (Debye)	3.607	3.029	3.449	
40	Acetaldehyde–methanol (2)[j]				Table S-14, Fig. S-1.40
	C=O $\cdots$ CH$_3$ dist. (Å)	3.499	4.107	4.139	
	C=O $\cdots$ H—CH$_2$ dist. (Å)	2.452	3.011	3.043	
	H$_3$C $\cdots$ O—H dist. (Å)	3.397	4.007	4.013	
	H$_2$C—H $\cdots$ O—H dist. (Å)	2.319	2.896	2.907	
	$\angle$(C=)O $\cdots$ C—H (deg.)	12.5	7.5	7.4	
	$\angle$H—C $\cdots$ O(—H) (deg.)	5.4	1.8	2.5	
	Dipole moment (Debye)	1.949	1.889	1.914	

[a] Details are available in Supplementary Material; [b] O is H acceptor; [c] C≡C is H acceptor; [d] N is H acceptor; [e] C≡C is H acceptor; [f] only C=O is H acceptor; [g] only C=O is H acceptor; [h] N is H donor; [i] C=O is H acceptor; [j] C=O is H acceptor; [k] using modified van der Waals parameter for C$_{(\alpha)}$—H $\cdots$ O interaction (ε: 0.85 kcal/mol; r^*: 2.40 Å); [l] MW value, see Andrews et al., *J. Am. Chem. Soc.* **114**, 6765 (1992); [m] Table S-Xs and Fig. S-Xs are available in Supplementary Material.

the acetylene carbon? Is it a good hydrogen acceptor? In this section, intensive studies of interactions between acetylene and other molecules, such as water, ammonia, formaldehyde, and acetylene itself, are described. Two water–acetylene complexes, one with water oxygen as hydrogen acceptor (**4**) and the other with acetylene carbon as hydrogen acceptor (**5**), are examined. According to our MP2/6-31G** results, complex **4** has a stronger binding energy than complex **5** (2.45 vs. 1.60 kcal/mol, Table II), as expected. The significant binding energy of complex **5** suggests that acetylene carbon is indeed a hydrogen acceptor, and is similar to ethylene (the ethylene–water complex binding energy is 1.71 kcal/mol).[2] The MM3 and MM3(96) results also show significant improvements of binding energies and geometries, due to the treatment of acetylene as both a hydrogen donor and acceptor, and the angle of C≡C $\cdots$ O—H in complex **5** (Tables II and III) is improved dramatically in MM3(96).

Two ammonia–acetylene complexes were investigated. The MP2/6-31G** results show that complex **6**, with the ammonia nitrogen as a hydrogen acceptor, has a much stronger binding energy than the water–acetylene complex (**4**) (3.80 vs. 2.45 kcal/mol, Table II). This is consistent with the fact that ammonia is a better hydrogen acceptor than water. The very weak binding energy of complex **7** (0.73 kcal/mol, Table II), with acetylene carbon as hydrogen acceptor, also confirms that ammonia and acetylene are a poor hydrogen donor and acceptor, respectively. Again, the MM3 and MM3(96) results show that the treatment of acetylene as both hydrogen donor and acceptor is the key element of improvement in these cases.

Two formaldehyde–acetylene complexes, the linear conformation (**8**) and the cyclic conformation (**9**), were studied. The carbonyl oxygens are hydrogen acceptors in both cases. According to our MP2/6-31G** results, the linear and cyclic conformations have similar binding energies, 1.91

kcal/mol and 2.13 kcal/mol, respectively (Table II). They are weaker than those of water–acetylene and ammonia–acetylene. The results suggest that carbonyl oxygen (in the aldehyde) is not as good as water and ammonia as a hydrogen acceptor. There is an important point to be discussed here. In the cyclic conformation, the distance between the formaldehyde hydrogen and the acetylene carbon is much shorter than their van der Waals distance (2.498 vs. 3.680 Å). This fact strongly suggests that something is going on between the aldehyde hydrogen and the acetylene carbon. Is it possible that it is another hydrogen bond-like interaction? We know the acetylene carbon is a poor hydrogen acceptor, but what about the aldehyde hydrogen? Is it acidic enough to be a hydrogen donor? This issue will be discussed later in more detail. Both binding energies and geometries, except the distance between the aldehyde hydrogen and acetylene carbon in the complex **9**, are calculated well using MM3(96). That distance, compared with the *ab initio* value, is calculated to be too long (3.248 vs. 2.498 Å, Table III), as expected.

The next acetylene complex examined was the T-shaped acetylene dimer (**10**). Our MP2/6-31G** results show the complex has a weak binding energy, 1.03 kcal/mol (Table II). The binding energy and C ⋯ C distance are about the same as those of the ethylene–acetylene complex (**3**), consistent with the acetylene being a rather poor hydrogen acceptor. The treatment of acetylene as both a hydrogen donor and acceptor indeed helps the improvement of acetylene dimer geometry in MM3(96). Also, the inclusion of the directional hydrogen bonding function changes the T-shaped acetylene dimer potential surface dramatically for the better, and the dimer is no longer on a "hilltop" on the MM3(96) potential surface (no imaginary frequencies).

FORMAMIDE–WATER, FORMAMIDE–METHANOL, AND FORMAMIDE–FORMALDEHYDE COMPLEXES AND THE FORMAMIDE DIMER

Hydrogen bonding plays a very important role in biological structures. Although hydrogen bonds are weak, they are the single most important interaction determining the three-dimensional folding of proteins. In this and the next sections, we focus on several fundamental hydrogen bonds that commonly occur in peptides and proteins. First, the cyclic formamide–water complex (**11**), with water serving as a hydrogen acceptor on one side and

hydrogen donor on the other side, is examined. Two types of hydrogen bonds are involved in this cyclic complex. One is $O_{(w)} \cdots H_{(amide)}$ and the other is $C=O_{(amide)} \cdots H_{(w)}$. The second formamide–water complex (**12**) has only one type of hydrogen bond, $C=O_{(amide)} \cdots H_{(w)}$, involved, because the other is too far away to be significant. According to our MP2/6-31G** results, the binding energy of complex **11**, 8.45 kcal/mol,[5] is only 1.5 times of that of complex **12**, 5.02 kcal/mol (Table II). This suggests that the $C=O_{(amide)} \cdots H_{(w)}$ interaction is somewhat stronger than the $O_{(w)} \cdots H_{(amide)}$ interaction here.[6] Binding energies of both complexes, as well as the geometry of complex **11** are well calculated using MM3(96), but the geometry of complex **12** is far from the MP2/6-31G** result (Table III).

When we took a close look at the *ab initio* result, we found that the water oxygen was unusually close to the carbonyl carbon and the hydrogen attached to it. The $O=C \cdots O$ and $O=C—H \cdots O$ distances were 3.067 and 2.581 Å respectively. These close contacts appeared to be due to the tendency of oxygen to acquire electrons, which provides a site for nucleophilic addition to the carbonyl carbon, and increases the acidity of the hydrogen attached to it. This finding is consistent with the result described in the formaldehyde–acetylene complex (**9**). $O=C \cdots O$ bonding has been observed previously experimentally, and has been studied by molecular mechanics.[7] It is an example of "Lewis bonding," a more general situation in which hydrogen bonding is a special case. (In Lewis bonding, the proton of a hydrogen bond is replaced by a Lewis acid; i.e., carbonyl carbon in this example.) When water was replaced by methanol in complexes **11** and **12**, very similar results were found in both *ab initio* and MM3(96) calculations. Binding energies of complexes **13** and **14** were 8.51 and 5.22 kcal/mol, respectively, in our MP2/6-31G** calculations, and 8.43 and 5.25 kcal/mol in MM3(96) (Table II). The close contacts of $O=C \cdots O$ and $O=C—H \cdots O$, 3.038 and 2.550 Å, respectively, also were found from the *ab initio* calculations of complex **14**.

Two conformations of formamide–formaldehyde, cyclic complex **15** and complex **16**, were examined to study the interaction between functional groups of $C=O_{(aldehyde)}$ and $H_{(amide)}$. According to the MP2/6-31G** results, cyclic complex **15** has 2.6 kcal mol more binding energy than complex **16** (6.37 vs. 3.76 kcal/mol, Table II). Because there is only one conventional hydrogen bond,

$C=O_{(aldehyde)} \cdots H_{(amide)}$, involved in both complexes, the large difference in the binding energies of the two complexes might not have been expected. The apparent explanation is that there is a hydrogen bond between the aldehyde hydrogen and the amide oxygen in **15**.[8] The close contact of $O=C-H_{(aldehyde)} \cdots O=C_{(amide)}$ is 2.276 Å in the MP2/6-31G** calculation and 2.802 Å in the MM3(96) calculation (where hydrogen bonding is not yet allowed for). Again, this short distance is consistent with what we found in the cyclic formaldehyde–acetylene complex (**9**) and the formamide–water complex (**12**).

Next, the cyclic formamide dimer (**17**) was chosen to study the interaction between $C=O_{(amide)}$ and $H_{(amide)}$. This is the major type of intramolecular hydrogen bond found in proteins that holds the peptide chains together to form an α-helix or a β-sheet structure. Our MP2/6-31G** result shows that the interaction is the strongest one among those neutral complexes we have studied so far. The binding energy is calculated to be 13.36 kcal/mol (see Dory et al.[9]) and the $C=O_{(amide)} \cdots H_{(amide)}$ distance is calculated to be 1.882 Å (Tables II and III), shorter than that in the formamide-formaldehyde complexes. The strong binding energy and the short $C=O \cdots H$ distance suggest that the amide $C=O$ group is a better hydrogen acceptor than the aldehyde $C=O$ group. This can be rationalized by the fact that resonance between the lone pair on the amide nitrogen and the carbonyl group results in more electron density on the carbonyl oxygen (see Fig. 2). The binding energy and the $C=O \cdots H$ distance are very well calculated by MM3(96): 13.36 kcal/mol and 1.873 Å, respectively (Tables II and III).

GUANIDINUM–WATER, FORMATE ION–WATER AND AMMONIUM ION–WATER COMPLEXES

To parameterize the hydrogen bonding interactions between water and five charged protein residues, Asp, Glu, Hip, Lys, and Arg, and termi-
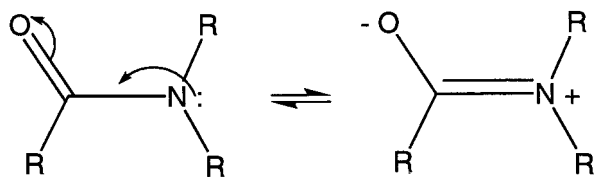

FIGURE 2. The resonance between the lone pair on the amide nitrogen and the carbonyl group.

nal carboxylate and ammonium groups, we investigated the bifurcated guanidinum ion–water complex (**18**), bifurcated formate ion–water complex (**19**), and linear and bifurcated ammonium ion–water complexes (**20**, **21**). The MP2/6-31G** results show that the binding energy and $C \cdots O$ distance for the bifurcated guanidinum ion–water complex are 19.38 kcal/mol and 3.326 Å, which are very close to reported values.[10] The geometry is calculated well by MM3(96), but the binding energy is insufficient by almost 3 kcal/mol (Table II). Because MM3 uses the same atom type (type 28) for both amide hydrogen and guanidinum hydrogen, the binding energy cannot be improved here without sacrificing the accuracy of the binding energy of amide–water complexes. We chose to leave the error in the guanidinum ion–water complex, because we believe the amide–water interaction to be more important. Of course, if necessary, we could use a different atom type for guanidinum hydrogen to correct the discrepancy. Because two important effects, dipole-induced dipole and lone-pair directionality, are still not taken into account in our hydrogen bonding formulation, we are not sure whether or not a new atom type is necessary in this case. For the time being, we decided to keep the force field as simple as possible and not to use a new atom type.

Next, the bifurcated formate ion–water complex (**19**) with water serving as the hydrogen donor was studied. The binding energy and the $C \cdots O$ distance are calculated to be 19.65 kcal/mol and 3.132 Å by *ab initio* methods (Tables II and III). The binding energy is lower than Jorgensen and Gao's RHF/6-31G** value of 22 kcal,/mol.[11] Both the binding energy and $C \cdots O$ distance are very well calculated by MM3(96): 19.62 kcal/mol and 3.137 Å, respectively.

Finally, the linear and bifurcated ammonium ion–water complexes with water as the hydrogen acceptor were examined. According to our MP2/6-31G** results, both complexes have very strong binding energies, 23.28 (see Lukovitz et al.[12]) and 18.92 kcal/mol, respectively. Although the bifurcated complex (**21**) has two close $N-H \cdots O$ contacts, 2.184 Å, the linear complex (**20**) has 4.5 kcal/mol more binding energy (Tables II and III). The $N-H \cdots O$ distance in the linear complex is 1.614 Å, which is the shortest $H \cdots O$ distance we have come across so far. There is no question that the ammonium ion is the best hydrogen donor among the species we have studied. MM3 calculations give fair geometries for both complexes, but not binding energies. Unlike the *ab initio* results,

MM3 calculations favor the bifurcated complex, 17.62 kcal/mol, over the linear complex, 14.06 kcal/mol. However, MM3(96), with the directional hydrogen bonding, gives more reasonable results. MM3(96) now calculates the linear complex as the most stable conformation with no imaginary frequencies. Compared with the *ab initio* results, MM3(96) still overestimates the hydrogen bonding interaction for the bifurcated complex. A further improvement might be possible when the lone-pair directionality is taken into account.

MM3MOD	2.533 Å
MM3(96)	3.551 Å
MP2/6-31G**	2.418 Å

FIGURE 3. The close contact of methyl chloride alpha hydrogen and water oxygen.

METHYL CHLORIDE–WATER COMPLEX AND 4-CHLORO-1-BUTANOL

Internal hydrogen bonding is generally believed to occur in the free molecules of substances that have suitable, properly oriented, donor and acceptor groups. The evidence for the existence of such bonds is found in the structures of many molecules in which internal rotation plays a role, such as ethylene glycol and glycerol.[13] In this section, as well as the next, we focus on two cases known to have internal hydrogen bonding. The first case is 4-chloro-1-butanol. Bastiansen et al.[14] reported electron diffraction evidence for internal hydrogen bonding in their conformational studies of 4-chloro-1-butanol. According to their findings, conformer **32**, which affords a reasonable opportunity for O—H···Cl bonding, is predominant in the mixture (28.5%, Table V), followed by conformer **26** (21%) and conformer **25** (20.8%). However, their original MM2 calculations showed otherwise. MM2 calculated conformer **24** to be the most stable (20%), followed by conformer **25** (19%) and conformer **23** (17%). Conformer **32** was present to the extent of only 2% in their MM2 calculations. They concluded that the lack of hydrogen bonding between O—H and Cl in the MM2 calculation was responsible for the error. Hydrogen bonding for O—H···Cl was subsequently added into the MM2 force field, MM2(87).[15] This change improved these results significantly.

To gain a better understanding of the interaction between O—H and Cl, we examined the cyclic methyl chloride–water complex (**22**). The binding energy and the O—H···Cl distance of the complex are calculated to be 2.04 kcal/mol and 2.708 Å by *ab initio*. Note that there is a close contact of an alpha hydrogen $C_{(\alpha)}$—H···O, 2.418 Å (see Fig. 3), in our MP2/6-31G** calculation. The distance is much shorter than the corresponding van der Waals distance, 3.440 Å. But MM3 overestimates
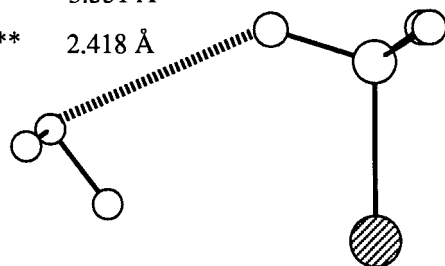
the binding energy (7.15 kcal/mol, Tables II and IV), because it uses very strong hydrogen bonding for the O—H···Cl interaction inherited from the MM2 force field. MM2 used a very deep hydrogen bonding potential[15] to fit the 4-chloro-1-butanol results. Obviously, both the MM2 and MM3 hydrogen bonding parameters for the O—H···Cl interaction are inadequate, and they need to be adjusted. The binding energy and the O—H···Cl distance are now well calculated by MM3(96): 2.04 kcal/mol and 2.684 Å, respectively. However, the $C_{(\alpha)}$—H···O distance is still calculated to be much too long (3.551 vs. 2.418 Å) in MM3(96).

Ab initio calculations at the RHF and MP2 levels with a 6-31G** basis set as well as a single point MP4/6-31G** calculation using the MP2/6-31G** structure were next carried out for 11 conformers of 4-chloro-1-butanol (**23**–**33**). The RHF calculations show that conformer **26** is the most stable (26%), followed by conformers **24** (21%), **23** (13%), and **32** (11%). MP2-optimized calculations show somewhat different results; MP4 energies (single-point calculations on the MP2-optimized structure) differ from the MP2 energies by no more than 0.2 kcal/mol. The MP4 results show (Table V) that conformer **32** is most stable (45%), followed by **30** (19%) and **26** (13%). Although RHF, MP2, and MP4 calculations show mixed results, they more or less support the electron diffraction results. All of them show that conformer **32** contributes significantly to the composition of the mixture. The quantum mechanical calculations are, of course, for equilibrium energies, and the experiment gives free energies.

MM3 calculates conformer **32** to be more stable (33%) than conformer **26** (10%) and conformer **25** (9%), but it also incorrectly lowers the energy of conformer **33** by too much (see Table V). Con-

former **33** has very high energy in the *ab initio* calculations and was not found in the electron diffraction analysis. It is not surprising that MM3(96) gives poorer results for the 4-chloro-1-butanol conformational analysis than MM3, because we cut down the hydrogen bonding interaction between O—H ⋯ Cl, based on the methyl chloride–water result, by about 75% from the original MM3 parameters. The MM3(96) results are similar to Bastiansen's MM2 results. This suggests that the hydrogen bonding between O—H ⋯ Cl is in fact not that important in the conformational analysis of 4-chloro-1-butanol. There must be some other forces that make conformer **32** so stable. The question is what are they? When we carefully examined the structure of conformer **32**, we found that there are several possible stabilizing forces. (1) The hydrogen bonding interaction between O—H ⋯ Cl (It is understandable that the hydrogen bonding contribution is small in this case, because the relative orientation of the O—H and C—Cl groups is not adequate for charge transfer to occur.) (2) The dipole-dipole interactions between the O—H and C—Cl dipoles, which are anti parallel to each other (see Fig. 4). The dipole–dipole interaction is very strong and is well handled in the MM2/MM3 force field. The only things that have not been taken into account are polarization effects, especially (3) the dipole-induced dipole interactions. Because the C–Cl bond is highly polarizable, the dipole-induced dipole interaction may be significant in this case. The dipole-induced dipole energy was calculated to be −0.2 kcal/mol by the IDME program.[16, 17] Thus, it contributes, but not much, to the observed stability.
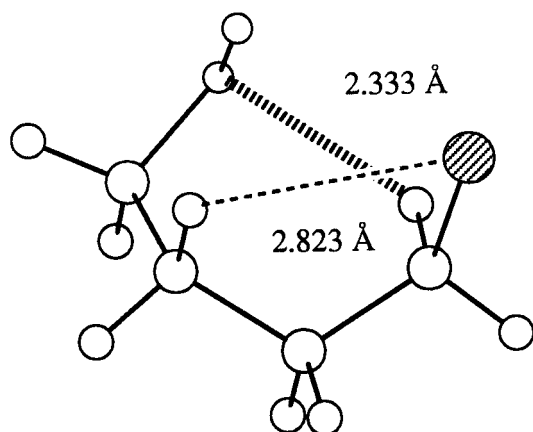

FIGURE 4. The close contacts of $C_{(\alpha)}$ — H ⋯ O and $C_{(\beta)}$ — H ⋯ Cl in the most stable 4-chloro-1-butanol conformation (conformer **32**).

Next, we focused on possible repulsive forces existing in conformer **32** (maybe the stabilization of **32** results not from an attraction but from the absence of a repulsion), because these may be modified by polarization. There are two close contacts, $C_{(\alpha)}$—H ⋯ O and $C_{(\beta)}$—H ⋯ Cl, found in conformers **32**, **31**, and **41**, but not in the other conformers. The $C_{(\alpha)}$—H ⋯ O distance, 2.333 Å (see Fig. 4), is very similar to what we found in the methyl chloride–water complex, and it is very short compared with the van der Waals distance. The $C_{(\beta)}$—H ⋯ Cl distance (2.823 Å) is also much shorter than its van der Waals distance (3.69 Å) as well. The MM3 repulsive energy from these close contacts is estimated to be around 0.9 kcal/mol, which is sufficient to make conformer **32** noticeably less stable. It is not certain that these close contacts and the dipole-induced dipole interaction are the key sources of error, but this seems likely. Using reasonable hydrogen bonding parameters for the $C_{(\alpha)}$—H ⋯ O interaction (ε: 0.85 kcal/mol; r^*: 2.40 Å, but omitting the directionality), we were able to fit the methyl chloride–water complex (**22**) better (see Table IV), and lower the conformational energies of conformations **31**, **32**, and **41** significantly (see Table V). We know that when we attach an electronegative atom (in this case, chlorine) to a carbon, the electronegativity effect[18] causes hydrogens attached to the same carbon to have their bonds shortened, and they become more acidic—in this case, the hydrogen on the same carbon as chlorine, then hydrogen bonds to the oxygen. This $C_{(\alpha)}$—H ⋯ O hydrogen bonding accounts for both the short H ⋯ O distance in the *ab initio* calculations and the stabilization of the conformations where such a hydrogen bond is possible. Note that, in this case, it is not so much that the hydrogen bond lowers the energy by hydrogen bonding attraction, rather it relieves the repulsion by converting it to a (small) attraction. The $C_{(\beta)}$—H ⋯ Cl repulsion is similarly converted to a small attraction by the β-electronegativity effect.[19] We know, qualitatively, that the β-electronegativity effect will cause a weak $C_{(\beta)}$—H ⋯ Cl bonding, but the details of these β H-bonding effects have not yet been worked out, and will be reported later. There is an important conclusion to be drawn at this point, however, because C—H hydrogens can become acidic enough to form weak hydrogen bonds (< 1 kcal/mol) when an electronegative group is attached to the carbon, and accurate molecular mechanics calculations on organic molecules (excluding saturated hydrocar-

TABLE IV.
Binding Energies and Geometries for Methylchloride–Water Complex.

I. CH_3Cl—H_2O, cyclic (22) (Cl is hydrogen acceptor)	MP2/6-31g**	MM3	MM3(96)	MM3MOD[a]
E (binding)	−4.64			
BSSE	−2.60			
E (corrected)	−2.04	−7.15	−2.04	−2.15
Dipole moment	1.370	2.944	0.515	0.502
Imaginary freq.	0	1	0	0
Cl $\cdots$ O dist	3.431	2.939	3.589	3.549
Cl $\cdots$ H—O dist.	2.708	2.474	2.684	2.803
H3C $\cdots$ O dist.	3.304	3.781	3.768	3.433
C—H $\cdots$ O dist.	2.418	3.375	3.551	2.533
O—H bond length	0.963	0.948	0.949	0.949
< Cl $\cdots$ O—H	35.8	52.2	15.0	33.1
< H—C $\cdots$ O(—H)	29.2	60.4	70.3	29.7

[a] Using modified van der Waals parameter for $C_{(\alpha)}$—H $\cdots$ O interaction (ε: 0.85 kcal/mol; r^*: 2.40 Å).

bons) are generally going to require that this effect be taken into account. Electronegative groups are pervasive in organic molecules, so this effect is everywhere. Energies of the order of 1 kcal/mol can dramatically change a conformational distribution. And, conformational energy changes much larger than that will often occur because of the relief of repulsion, which may outweigh the actual attraction in congested systems, and because multiple effects may occur, such as in this case.

CYCLOPROPANE–WATER COMPLEX AND 2-CYCLOPROPYL ETHANOL

It is well known that a hydrogen bonding interaction exists between the hydrogen atom of a hydrogen donor and the pseudo-π electrons of the cyclopropane ring.[20] Although the interaction is very weak, it plays very important role in conformational analysis of many compounds like α-hydroxyl-,[21–24] α-amino-,[25] and α-mercapto-[26] cyclopropanes. Andrews et al.[27] reported that the cyclopropane–water complex (**34**) with one water hydrogen bonded to the center of an edge of cyclopropane was observed in their Fourier-transform microwave spectroscopy experiments. The C $\cdots$ H —O distance and the distance between the centers of mass of water and cyclopropane, R_{cm}, were determined to be approximately 2.34 and 3.71 Å (Table VI). However, the position of the free hydrogen is uncertain. A nearly free rotation of the water about the hydrogen bond is postulated to

explain the anomalous dipole moment and nuclear quadrupole coupling results. Both their RHF/6-31G* and our MP2/6-31G** calculations are in a fair agreement with experiment. Our MP2/6-31G** results show that the binding energy, the C $\cdots$ H—O, and the R_{cm} distance of the complex are 1.41 kcal/mol, 2.396 Å, and 3.658 Å, respectively (Table VI).

MM3 gives very poor results for the cylopropane–water complex, because it does not treat a cyclopropane ring as a hydrogen acceptor. The binding energy and geometries are now well calculated by MM3(96). They are 1.42 kcal/mol, 2.513 Å, and 3.777 Å, respectively (Table VI).

It is well established by means of microwave spectroscopy that the most stable conformation of α-hydroxyl cyclopropane is stabilized by intramolecular hydrogen bonds.[21–24] However, there is little known about the conformational preference when the hydroxy group is in the β position. Hopf et al.[28] reported gas-phase electron diffraction (GED), microwave (MW) spectroscopy, and *ab initio* studies of 2-cyclopropyl ethanol. Their GED and MW results showed that conformer **35**, which allows an intramolecular hydrogen bond to be formed, predominates in the mixture (49%), followed by conformer **38** (32%) and conformer **37** (20%). Their observed conformational composition was in satisfactory agreement with that deduced from the energies of the conformers studied by their RHF/6-31G** calculations. MM3 calculated conformer **35** to be less stable than the others,

TABLE V.
Conformational Energies and Dipole Moments for 4-Chloro-1-butanol.[a]

		Relative energies (kcal/mol)				
		MP2/6-31G**	MP4/6-31G**[b]	MM3	MM3(96)	MM3MOD[c]
tTtt	(23)	1.067	0.945	−0.443	−0.308	−0.266
tTgt	(24)	0.362	0.300	−0.130	0.022	0.080
gTtt	(25)	1.423	1.332	0.048	0.084	0.068
gTg′t	(26)	0.000	0.000	0.000	0.000	0.000
gTgt	(27)	0.648	0.616	0.330	0.382	0.381
tGtt	(28)	1.909	1.765	0.610	0.764	0.844
tGgt	(29)	0.702	0.682	0.722	0.905	0.946
gGgt	(30)	−0.316	−0.200	0.682	0.722	0.667
gGg′t	(31)	0.820	0.804	1.286	1.460	0.385
gGg′s	(32)	−0.597	−0.672	−0.700	1.215	0.235
g′Gg′g	(33)	1.605	1.474	−0.827	2.908	2.796
tGg′s	(41)	0.507	0.310	1.273	1.453	0.641

		Dipole (Debye)/population(%)				
		MP4/6-31G**[b]	ED[d]	MM3	MM3(96)	MM3MOD[c]
tTtt	(23)	2.393/2.7	0.6	2.113/20.7	2.208/27.8	2.202/22.9
tTgt	(24)	3.821/8.1	8.8	3.197/12.2	3.330/15.9	3.327/12.8
gTtt	(25)	3.512/1.4	20.8	3.167/9.0	3.305/14.4	3.308/13.1
gTg′t	(26)	2.554/13.4	21.0	2.163/9.8	2.260/16.5	3.260/14.6
gTgt	(27)	3.756/4.7	3.7	3.333/5.6	3.461/8.7	3.460/7.7
tGtt	(28)	2.247/0.7	1.7	2.254/3.5	2.351/4.6	2.353/3.5
tGgt	(29)	3.892/4.2	10.1	3.369/2.9	3.616/3.6	3.532/3.0
gGgt	(30)	1.986/18.7	4.8	2.002/3.1	2.117/4.9	2.071/4.8
gGg′t	(31)	3.964		3.338	3.476	3.458
gGg′s	(32)	2.384/45.0[e]	28.5	1.834/33.1	1.631/3.5	1.575/17.4
g′Gg′g	(33)	2.702/NA	NA	1.930/NA	1.769/NA	1.397/NA
tGg′s	(41)	3.866/NA[f]	NA	3.349/NA	3.512/NA	3.578/NA

[a] The four dihedral angles are Cl—C—C—C, C—C—C—C, C—C—C—O and C—C—O—H, respectively.
[b] Single-point MP4 calculation using the optimized MP2/6-31G** structure.
[c] Using hydrogen bond parameter for $C_{(\alpha)}$—H $\cdots$ O interaction (ε: 0.85 kcal/mol; r^*: 2.40 Å).
[d] O. Bastiansen, L. Fernholt, K. Hedberg, and R. Seip, *J. Am. Chem Soc.*, **107**, 7836 (1985).
[e] The population here is the sum of populations of gGg′t (**31**) and gGg′s (**32**).
[f] For comparison, this comformer is not included in the population calculation.

mainly due to the lack of hydrogen bonding between the hydroxy group and the cyclopropane ring. The MM3(96) result is now in a fair agreement with experiment. Conformer **35** was calculated to be most stable (45%), followed by conformer **38** (34%) and conformer **37** (21%) by MM3(96) (see Table VII).

ACETALDEHYDE–METHANOL COMPLEX

As mentioned earlier, the hydrogen attached to the carbonyl carbon has a significant interaction with hydrogen acceptors, but what about the hydrogen attached to the α-carbon? We know the

carbonyl group strengthens the acidity of the α-hydrogen (α-H) through the resonance. Therefore, the interactions between the α-H and the hydrogen acceptors are expected to be significant as well. To acquire a better understanding of these kinds of interactions, two cyclic acetaldehyde–methanol complexes, which have close contacts of methanol oxygen and aldehyde α-H, were investigated. Complex **39**, with the hydroxyl hydrogen of the methanol bonded to the carbonyl oxygen, was calculated to be most stable by the *ab initio* method. The MP2/6-31G** results show that the binding energy, C=O $\cdots$ H$_{(methanol)}$ and α-H $\cdots$ O$_{(methanol)}$ distances for complex **39** are 4.44 kcal/mol, 1.975

TABLE VI.
Binding Energies and Geometries for Cyclopropane–Water Complex.

C_3H_6—H_2O, (34)

(C is hydrogen acceptor)	MP2/6-31g**	MW[a]	MM3	MM3(96)
E (binding)	−3.11			
BSSE	−1.70			
E (corrected)	−1.41		−0.56	−1.42
Dipole moment	2.379	1.209[b] 1.241[c]	2.033	2.036
Imaginary freq.	NA		1	1
R_{cm} dist.	3.658	3.712	4.140	3.777
C ··· O dist.	3.307		3.781	3.425
C ··· H—O dist.	2.396	2.342	3.305	2.513
C—H ··· O—H dist.	3.085		3.753	3.405
O—H bond length	0.963		0.947	0.949
Ia	4.3898	4.2066[b]	4.3753	4.3343
		4.2076[c]		
Ib	31.8952	33.3173[b]	39.2606	33.6494
		33.3173[c]		
Ic	34.1884	35.8588[b]	41.5571	35.9939
		35.8503[c]		

[a] A. M. Andrews, K. W. Hillig, and R. L. Kuczkowski, *J. Am. Chem. Soc.*, **114**, 6765 (1992).
[b] Values for strong state.
[c] Values for weak state.

TABLE VII.
Conformational Energies, Moments of Inertia, and Dipole Moments for 2-Cyclopropylethanol.[a]

		E_{rel} (kcal/mol)/population (%)			
		6-31G**[b]	GED/MW[b]	MM3	MM3(96)
gGg' (I)	(35)	0.000/41.2	—/48.6	0.000/17.9	0.000/45.3
gGt (II)	(36)	1.052/—	NA	−0.415/—	0.445/—
gG't(III)	(37)	0.143/26.4	—/19.7	−0.368/33.4	0.455/21.0
gTt (IV)	(38)	0.263/32.4	—/31.7	−0.591/48.7	0.175/33.7

		Moments of inertia for gGg' (35) (in 10^{-39} g(cm^2))			
		6-31G**[b]	MW[b]	MM3	MM3(96)
	Ia	11.2122	11.4244	11.3251	11.4144
	Ib	37.8244	37.5171	38.3464	37.7910
	Ic	44.6697	44.5110	44.8481	44.6997

		Dipole moments (Debye)		
		6-31G**[b]	MM3	MM3(96)
gGg' (I)	(35)	1.891	1.596	1.604
gGt (II)	(36)	1.653	1.800	1.802
gG't (III)	(37)	1.778	1.800	1.802
gTt (IV)	(38)	1.655	1.670	1.674

[a] The three dihedral angles are C'—C'—C—C, C'—C—C—O, and C—C—O—H, respectively, where C' is the cyclopropane carbon.
[b] H. Hopf, K.-M. Marstokk, A. de Meijere, C. Mlynek, H. Møllendal, A. Sveiczer, Y. Stenstrøm, and M. Trœtteberg, *Acta Chem. Scand.*, **47**, 739 (1993).

Å, and 2.407 Å, respectively (Tables II and III). Complex **40**, with the alkane hydrogen of the methanol bonded to the carbonyl oxygen, was calculated to be 2.32 kcal/mol less stable than complex **39** by the *ab initio* method. Its C=O···H—O$_{(methanol)}$ and α-H···O$_{(methanol)}$ distances were calculated to be 2.452 and 2.319 Å, respectively. These distances are also much shorter than the corresponding van der Waals distances.

The binding energy and the hydrogen bond distance, C=O···H$_{(methanol)}$, for complex **39**, were well calculated by MM3(96): 4.46 kcal/mol and 1.976 Å, respectively. However, the binding energy for complex **40** and the α-H···O$_{(methanol)}$ distances for both complexes were poorly calculated by MM3(96). These distances were calculated to be 0.7 Å too long in both complexes (see Fig. 5 and Table III).

Conclusions

So far, our MM3 studies of hydrogen bonded systems have included a variety of C, N, O, and Cl systems.[2] The hydrogen donors and acceptors used are summarized in Table VIII. Based on our studies, we conclude that the relative acidities of the listed hydrogen donors can be represented in the following order:
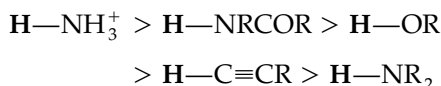
$$H—NH_3^+ > H—NRCOR > H—OR$$
$$> H—C\equiv CR > H—NR_2$$

2.407 Å
(3.223 Å)

2.319 Å
(2.907 Å)

2.452 Å
(3.043 Å)

MP2/6-31G** (MM3(96))

FIGURE 5. The close contacts of C$_{(\alpha)}$—H$_{(acetaldehyde)}$···O$_{(methanol)}$ and C=O···H—C$_{(methanol)}$ in acetaldehyde–methanol complex **39** (left) and **40** (right).

and the relative basicities of the listed hydrogen acceptors are of the order:

$$RCOO^- > R3N > R2NC(R)=O$$
$$> R2O > R2C—O > RCl$$
$$> cyclopropane\ ring > R—C—C\equiv R$$
$$\geq R2C=CR2$$
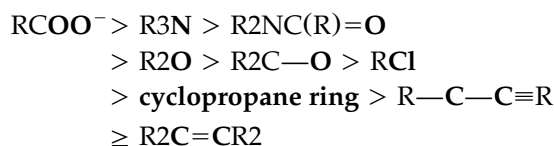
According to Table VII, of the compounds studied, the ammonia–ethylene complex has the weakest hydrogen bond (binding energy of 0.8 kcal/mol), and the ammonium ion–water complex has the strongest (binding energy of 23.3 kcal/mol). (Note that the values in Table VIII give the energy of the hydrogen bond between the two atoms involved only, whereas the binding energy is a total energy that also includes van der Waals and electrostatic interactions). These results are consistent with what we already know.

The overall MM3(96) results are, for the most part, in satisfactory agreement with the experi-

TABLE VIII.
MM3 Hydrogen Bonding Parameter Chart.[a,b]

	Hydrogen donors				
H acceptors	(48) H—N(+)H3	(28) H—NRCOR	(21) H—OR	(124) H—C∫CR	(23) H—NR2
RCO(O—) (47)		—	5.000/2.07	—	—
R3(N) (8)		—	4.700/2.15	3.530/2.30	2.280/2.40
R2NC(=O)R (79)		5.240/1.96	3.460/1.95	—	—
R2(O) (6)	13.800/1.72	5.140/2.03	3.000/2.11	1.700/2.30	1.300/2.38
R2C(=O) (7)		4.440/2.07	2.550/2.07	1.390/2.33	—
R(Cl) (12)		—	1.100/2.80	—	—
Cyclopropane (22)			0.950/2.38	—	—
R(C∫C)R (4)		—	0.510/2.60	0.340/2.82	0.260/2.87
R2(C=C)R2 (2)		—	0.550/2.65	0.250/2.96	0.100/3.00

[a] MM3 atom type in parentheses.
[b] Entries are the results of the MM3 hydrogen bonding parameters (HB energy depth [kcal/mol]/HB distance [Å]) used to reproduce binding energies and structures of interested complexes calculated by the ab initio method.
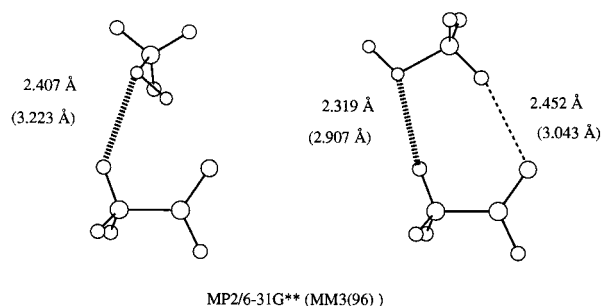
mental and *ab initio* results, and are much better than MM3 results. It is clear to us that the inclusion of the linearity function in the hydrogen bond formulation is the key element in the improvement with MM3(96). It is a better, but still not perfect, description of hydrogen bonding. A better model (currently under development) will have to include lone-pair directionality and dipole-induced dipole interactions in the hydrogen bond formulation as well, and will, in addition, clearly have to recognize the existence of C—H hydrogen bonding (both α and β) as induced by the electronegativity effect.

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