Consistent Force Field Studies of Intermolecular Forces in Hydrogen-Bonded Crystals. 3. The C=O···H—O Hydrogen Bond and the Analysis of the Energetics and Packing of Carboxylic Acids

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Abstract: The detailed structures of 14 crystals of mono- and dicarboxylic acids and 2 gas-phase dimers are studied by the 12-6-1 and 9-6-1 force fields of the preceding papers. The energy of packing of the crystal lattice is partitioned in various ways and the different contributions are compared, with special emphasis on the energetics of the "secondary structure", i.e., the hydrogen-bonded arrays. The electrostatic energy in a homologous series of acids is almost constant, arising from interactions of neighboring carboxylic groups, while the van der Waals energy contribution increases with alkyl chain length. The interaction between the hydrogen-bonded molecules is a balance between an electrostatic attraction and a van der Waals repulsion between the carbonyl and hydroxyl oxygens. A comparison of the alternative secondary structures reveals that for small monocarboxylic molecules the electrostatic interactions stabilize the catamer motif relative to the cyclic dimer motif. For the dicarboxylic acids the analysis shows that the shortening of the alkyl chain reduces the intermolecular electrostatic interaction. This interaction is even smaller in the α form of oxalic acid (catamer motif) where stability of the secondary structure is due to favorable dispersion interactions. The analysis of the secondary structure in terms of group interactions also indicates the reasons for the larger deviations from experiment in some of the crystals. For example, the larger a axis of acetic acid emerges from the short $=O\cdots H_{CH_3}$ distance which is too repulsive in this potential.

Introduction

In the previous two papers[1] two alternative carboxylic acid force fields were derived. It was shown that a good fit to a large set of structural and energetic observables could be obtained by transferring all parameters from the corresponding previously studied amide force fields[2] and optimizing only a single additional adjustable parameter, the charge on the hydroxyl proton. In the second paper the construction of an extensive data base consisting of both amides and carboxylic acids was initiated in order to provide an objective evaluation of various potential functions proposed in the literature.

In the present paper we apply the new carboxylic acid force field to the further study of the energetics of packing of the carboxylic acid crystals.[3] The energetics of the alternative secondary structures are investigated at the molecular level. By secondary structure we refer to hydrogen-bonded arrays (either one or two dimensional), while tertiary structure refers to the way in which these arrays are related to each other to form a three-dimensional lattice.[4] The factors underlying the stability of the different modes are discussed in terms of interactions between the relevant individual molecules. The intermolecular energies are further partitioned into group contributions[5] to better understand the difference between the various hydrogen-bonded motifs. It is shown that this method provides a tool for quantitative analysis which enables us to attain a better understanding of the factors governing crystal packing. Because of the central role of hydrogen bonding and its importance we focus mainly on this interaction.

All crystal structures are minimized with respect to all crystal degrees of freedom, the only constraint being the number of molecules per unit cell. The detailed structural and energetic results are presented and compared with the experimental values (as opposed to the results presented in the second paper where only the average root mean square deviations of each crystal were presented to study the validity of the force fields). The contributions to the overall lattice energy of each crystal, van der Waals and electrostatic, are presented and their relative importance is evaluated. Finally, where large deviations in structural observables such as unit cell vectors are found, these are further discussed at the molecular level. Here also partitioning into group and atomic contributions[5] can shed light on the resultant deviations.

Method

The lattice energies were minimized using both the 9-6-1 and 12-6-1 potentials derived in the first paper by transferring all amide parameters and optimizing only a single additional parameter (the charge on the hydroxyl hydrogen). The energies were minimized with respect to all degrees of freedom in the unit cell, keeping the internal coordinates of the molecules and their number per unit cell fixed, as described previously.[2b] A Cartesian system was constructed (with x along **a** and y in the **ab** plane). One of the molecules was kept fixed in this system (the degrees of freedom corresponding to rotation and translation of the whole crystal). The variables minimized were the 9 Cartesian components of the unit cell vectors and the $3(z - 1)$ translations and $3(z - 1)$ rotations of the remaining molecules in the unit cell (z being the number of molecules per unit cell). In this way the symmetry is not imposed, but rather derived (again within the constraint of the number of molecules per unit cell). However, in all cases in the amides, and all but one (butyric acid) in the acids, the observed symmetry is maintained. Thus, as noted elsewhere,[1b,4a] the relaxation of symmetry is not a sensitive test of potentials, and in general is not necessary except when studying hypothetical crystal structures.[4a] For this reason we report the minimized results consistent with the observed symmetry—i.e., the unit cell parameters, and the translations and rotations of the asymmetric unit (about the center of mass).

Cutoff. The minimization was carried out with lattice sums extended over 125 unit cells and cutoff criteria of 12 Å, which corresponds to an interaction of about 100 molecules with every molecule in the central unit cell. The cutoff is applied such that, if *any* atom of a molecule is within 12 Å of a molecule in the central unit cell, the entire molecule is included. Thus the effective cutoff is significantly larger than 12 Å. (This is done to avoid the "creation" of spurious charges or dipoles.)

Group Contributions and Partial Atomic Energies. One of the major advantages that computer simulations have over experiment is that the contributions to the energy and their

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Table I. Lattice Energies of the Calculated Structures (kcal/mol)

	initial			final		
	elec	vdW	total	elec	vdW	total
			9-6-1 Potential			
formic acid	−10.83	−2.00	−12.83	−9.61	−3.65	−13.26
acetic acid	−9.97	−4.44	−14.41	−9.27	−5.91	−15.19
propionic acid	−9.80	−7.08	−16.88	−9.41	−8.23	−17.64
butyric acid	−9.02	−8.75	−17.77	−8.10	−10.79	−18.89
valeric acid	−9.04	−11.23	−20.24	−9.01	−12.32	−21.33
α-oxalic acid	−18.40	−6.77	−25.17	−17.84	−9.55	−27.39
β-oxalic acid	−18.50	−6.66	−25.15	−18.11	−8.74	−26.85
malonic acid	−19.00	−7.62	−26.62	−18.45	−10.11	−28.56
methylmalonic acid	−17.55	−9.99	−27.54	−18.05	−11.58	−29.64
succinic acid	−19.42	−11.87	−31.20	−19.73	−12.31	−32.04
glutaric acid	−15.53	−13.82	−29.34	−17.26	−13.85	−31.11
adipic acid	−17.17	−15.06	−32.23	−17.34	−17.11	−34.45
suberic acid	−15.74	−19.53	−35.27	−16.80	−20.76	−37.56
sebacic acid	−16.32	−23.01	−39.33	−17.22	−24.66	−41.88
			12-6-1 Potential			
formic acid	−7.56	−6.56	−14.12	−7.47	−7.06	−14.54
acetic acid	−6.95	−8.15	−15.10	−7.33	−8.70	−16.01
propionic acid	−6.84	−10.07	−16.90	−7.22	−10.30	−17.51
butyric acid	−6.35	−11.67	−17.92	−6.36	−12.40	−18.76
valeric acid	−6.29	−13.60	−19.89	−6.90	−13.79	−20.68
α-oxalic acid	−12.70	−10.24	−22.94	−14.31	−14.71	−29.02
β-oxalic acid	−12.73	−11.42	−24.16	−13.89	−14.71	−28.60
malonic acid	−13.21	−14.46	−27.67	−14.06	−15.51	−29.56
methylmalonic acid	−12.22	−15.39	−27.61	−14.13	−15.83	−29.96
succinic acid	−13.48	−18.30	−31.78	−15.55	−17.39	−32.94
glutaric acid	−10.72	−19.32	−30.09	−13.52	−18.50	−32.01
adipic acid	−11.86	−19.94	−31.80	−13.65	−20.38	−34.03
suberic acid	−10.87	−23.61	−34.48	−13.30	−23.72	−37.12
sebacic acid	−11.30	−26.93	−38.93	−13.46	−27.63	−41.09

[a] The energy of butyric acid was calculated here with the structure constrained to maintain the observed monoclinic symmetry. It is slightly higher than the energy of the triclinic form (see discussion below).

variations as a function of structure may be computed at the molecular and submolecular level. The use of partial atomic energies, in which the energy is partitioned into the contribution from each of the atoms in the asymmetric unit, was shown to be useful in understanding the difference in energetic environments of equivalent atoms in conformational polymorphs.[5] Here we use this technique as applied to group contributions. We partition the energy into its contributions from various functional groups in the asymmetric unit such as C=O or O—H by summing the interactions of these groups with the relevant neighboring molecules. In this way the difference in the energetic environment of a given functional group in various secondary structures may be investigated and the origin of the relative stabilities of the various secondary structures elucidated.[4,5]

Results

Lattice Energies. The lattice energies of the minimized crystal structure and the van der Waals (vdW) and electrostatic (elec) components of the energies are given in Table I. The lattice energies do not change much on minimization (~1–2 kcal), although in some cases there are quite large changes in the structural parameters as seen below. This "shallowness" of the crystal energy surface had been noted previously in the study of amide crystals[1b] as well. For the monocarboxylic acids the minimized energies are only 0.5–1.5 kcal/mol lower than the energies at the experimental structures, both for the 6-9 and the 6-12 potentials. The minimum energy structures of the dicarboxylic acids are about 2 kcal/mol more stable than the experimental structures. In the 6-12 potential, the two crystal forms of oxalic acid undergo a large energy change during the minimization. It is of interest that both derived force fields account for the relative stability of the two polymorphs of oxalic acid. Experimentally it was found that the energy of the α form is 1.3 kcal/mol more stable than the β form.[6] More recently a smaller difference (0.3 kcal/mol) has been reported.[7] The result of the minimization with both potentials considered in part 1[1] yielded the α form more stable than the β by approximately 0.5 kcal/mol, in reasonable agreement with the experimental results. It should be noted that, if the structure is not allowed to relax, i.e., the experimental coordinates are used, the calculated stability is reversed for the 12-6-1 potential. This illustrates the need for minimization, as even one "bad" contact, which may be significantly reduced by even a small movement, may lead to a reversal of stability if not allowed to relax.

Analysis of the contributions of the van der Waals and electrostatic interactions to the total energy yields insight into the role of these interactions in stabilizing the crystal structure. The 9-6-1 and 12-6-1 potentials differ in the relative contributions of the electrostatic and van der Waals contributions (Table I). Nevertheless, the two functional forms account almost equally well for the sublimation energies, and the relative validity of the two cannot be distinguished solely on the basis of these observables.[1b] It is clear, however, that neither the van der Waals nor the electrostatic terms can be ignored in describing the energetics of crystal packing. As pointed out by Smit et al.,[8] the electrostatic contribution to the lattice energy of these polar molecules is not insignificant as concluded by Kitaigorodskii.[9] As noted in the first paper,[1a] the charge distribution, which accounts for the observed sublimation energy within 1 or 2 kcal/mol, is also in agreement with observed dipole moments. Thus it would appear that the approximate magnitude of the electrostatic contribution is reasonably represented (i.e., within ~2–3 kcal/mol). The importance of the electrostatic contribution in hydrogen-bonded systems is

Table II. Dimerization Energies[a] (kcal/mol of dimer)

	initial			final		
	elec	vdW	total	elec	vdW	total
			9-6-1 Potential			
formic acid	−17.26	4.02	−13.24	−17.47	3.69	−13.79
acetic acid	−17.39	4.17	−13.23	−17.30	3.36	−13.94
			12-6-1 Potential			
formic acid	−11.98	−0.12	−12.10	−13.57	0.99	−12.58
acetic acid	−12.06	−0.15	−12.21	−13.52	0.77	−12.75

[a] Experimental values:[13] formic acid, −14.1 ± 1.5; acetic acid, −14.2 ± 0.7.

also substantiated by molecular orbital calculations, albeit on smaller systems.[10] On the other hand, it is clear that the van der Waals forces cannot be ignored in a complete description of crystal packing. Even for formic acid the latter contribution amounts to ~30–50% of the total energy, and where large or bulky alkyl groups are encountered this contribution may be dominant. Thus, although much information as to directionality and mutual orientations of molecules in polar crystals may be obtained with an electrostatic model,[8] these properties can clearly be affected by steric interactions. The van der Waals interactions may even be the decisive factor in choosing between alternative low-energy hydrogen-bonding modes,[4a] resulting in a structure which does not have the lowest possible electrostatic energy. This has in fact been shown to occur in the observed packing of adipamide.[4b] Thus a general and consistent description of a large set of molecules including both polar and nonpolar groups must include a representation of both types of interactions.

Dimerization Energies. The dimerization energies of formic and acetic acids are given in Table II. The dimerization of these acids in the gas phase has been the subject of thermodynamic[11] and spectroscopic[12] studies for many years. Mathews and Sheets[13] critically examined the enthalpies of dimerization, and obtained −14.1 ± 1.5 and −14.2 ± 0.7 kcal/mol for formic and acetic acids, respectively. In comparing these values with our results, the contributions of vibrations, rotations, translations, and pV to the enthalpy of dimerization must be considered. These are estimated to be $6RT$, $-1.5RT$, $-1.5RT$, and $-RT$, respectively, totaling $\sim 2RT$, which should be added to the calculated energy. A similar correction was introduced in comparing lattice energies and enthalpies of sublimation.[1,2] With this correction, the difference between the calculated and experimental values is ~1.5 kcal/mol for formic and acetic acid dimers in the 9-6-1 potential (i.e., 0.75 kcal/mol of monomer, which may be compared with the corresponding differences for heats of sublimation, 1.8 and 1.1 kcal/mol for the same acids, respectively[1]). In the 12-6-1 potential the difference is ~2.7 kcal/mol of dimers.

Further insight into the relation between gas-phase dimerization and crystal packing energies is obtained by comparing Tables I and II. Formic acid in the 9-6-1 potential, for example, has a total lattice energy of −13.3 kcal/mol of monomer, while the dimerization energy is −6.9 kcal/mol of monomer. The electrostatic and van der Waals contributions are −9.6 and −3.7 kcal to the lattice energy, as compared with −8.7 and +1.8 kcal for the dimerization energy, respectively. The corresponding differences, about −1 kcal/mol for the electrostatic contribution and −5.5 kcal/mol van der Waals, are mainly due to the long-range lattice interactions which are missing in the gas-phase dimers.

It is of interest to compare the dimerization energies of the empirical consistent force field with those derived by quantum mechanical ab initio calculations. Recently Del Bene and Kochenour[14] have calculated the dimerization energy of formic acid to be −15.2 kcal/mol using a minimal basis set and optimizing both monomer and dimer geometries. Clementi et al.[15] obtained a value of −16.2 kcal/mol using a large (9,5,1;4,1) uncontracted basis set but without geometry optimization (except for the proton position). This result is larger (more negative) by about −2.5 kcal/mol than the result obtained by our 9-6-1 potential, and ~−1 kcal/mol below the experimental value (including the $2RT$ correction). Considering the range of experimental error on the one hand, and the simplifying assumptions inherent in the CFF as well as the ab initio methods on the other hand, the present degree of agreement (or disagreement) between the experimental, empirical, and ab initio evaluations of the dimerization energy of carboxylic acids seems to be reasonably satisfactory.

Electrostatic Energy. The electrostatic energy is almost constant within a homologous series in each of the potentials. The electrostatic stabilization energies in monocarboxylic acids (formic acid through valeric acid) are ~−9 and −7 kcal/mol in the 9-6-1 and 12-6-1 potentials, respectively. The electrostatic energy of the dicarboxylic acids (oxalic through sebacic) is essentially twice that in the monocarboxylic acids. Although overall this contribution is independent of molecular size and packing within a homologous series, there are some small, but apparently significant, deviations. For example, succinic acid has a particularly large electrostatic stabilization in both potentials (−19.7 kcal/mol compared with an average of ~−18 kcal/mol for dicarboxylics in the 9-6-1 and −15.6 vs. −14 kcal/mol in the 12-6-1). At the other "extreme" suberic acid has an electrostatic stabilization energy of only −16.8 and −13.3 kcal/mol, respectively.

van der Waals Energy. The trends in the van der Waals energy are, not unexpectedly, very different from those of the electrostatic energies. This contribution to the energy depends on the length of the alkyl chain, and within the homologous series it increases by about 2 kcal/mol for each additional CH_2 group. It is interesting to note that this is in rough agreement with "empirical" rules for estimation of sublimation energies from "group energies".[16] It should be noted, however, that this is only a rough rule and deviations of as much as 1 kcal can occur, especially in going from even- to odd-numbered alkyl chains. Furthermore, partitioning of the energy into group contributions shows that even within one molecule the energetic contributions of symmetrically unrelated CH_2 groups to the lattice energy may vary within a range of 0.6 kcal/mol.

To summarize, the constancy of the electrostatic energy indicates that it arises mainly from interactions between neighboring carboxylic groups. This is also borne out by the dimerization energies and analysis of individual energetic contributions presented below. The alkyl chains contribute mainly to the van der Waals energy, and their varying length (and topology), along with packing modes, accounts for the variation in sublimation energies within a family of acids.

Hydrogen Bond Energies. A detailed analysis of the individual contributions to the total energy shows that the largest interaction between adjacent molecules in all of the crystals is the interaction of hydrogen-bonded molecules. These interactions are summarized in Table III. The hydrogen bond interaction in this representation is composed mainly of a

Table III. Interaction Energies of Hydrogen-Bonded Molecules

acid	C=O···HO elec	C=O···HO vdW	C=O···HO total	(RCOOH)···(RCOOH)[a] elec	(RCOOH)···(RCOOH)[a] vdW	(RCOOH)···(RCOOH)[a] total
			9-6-1 Potential			
formic[b]	−7.64	2.04	−5.60	−9.24	1.62	−7.62
acetic[b]	−6.98	2.31	−4.67	−9.01	1.51	−7.50
propionic	−6.86	2.11	−4.75	−8.56	1.66	−6.90
butyric	−6.84	2.14	−4.70	−8.35	1.57	−6.78
valeric	−6.93	2.19	−4.74	−8.26	1.72	−6.54
α-oxalic[b]	−6.30	1.89	−4.41	−7.24	0.44	−6.80
β-oxalic	−6.64	1.90	−4.74	−7.70	1.50	−6.20
malonic[c]	−6.50	1.63	−4.87	−8.45	1.19	−7.26
	−6.61	1.95	−4.66	−8.66	1.32	−7.34
methylmalonic[c]	−6.94	2.14	−4.80	−8.31	1.54	−6.77
	−6.82	2.00	−4.82	−8.64	1.33	−7.31
succinic	−7.70	2.37	−5.33	−9.21	1.88	−7.34
glutaric	−6.73	2.04	−4.69	−8.22	1.56	−6.66
adipic	−6.92	2.13	−4.79	−8.49	1.65	−6.84
suberic	−6.73	2.05	−4.68	−8.24	1.55	−6.69
sebacic	−6.68	2.04	−4.64	−8.26	1.52	−6.74
			12-6-1 Potential			
formic[b]	−6.11	0.92	−5.19	−7.29	0.01	−7.28
acetic[b]	−5.76	1.21	−4.55	−7.16	−0.08	−7.24
propionic	−5.36	0.88	−4.48	−6.67	0.36	−6.32
butyric	−5.34	0.84	−4.50	−6.57	0.34	−6.23
valeric	−5.34	0.90	−4.45	−6.37	0.29	−6.08
α-oxalic[b]	−5.42	1.02	−4.40	−5.71	−1.06	−6.77
β-oxalic	−5.26	0.72	−4.54	−6.08	0.26	−5.82
malonic[c]	−4.95	0.65	−4.30	−6.50	0.00	−6.50
	−4.89	0.44	−4.45	−6.31	0.00	−6.31
methylmalonic[c]	−5.52	0.94	−4.58	−6.57	0.26	−6.31
	−5.25	0.76	−4.49	−5.90	0.42	−5.48
succinic	−6.05	1.05	−5.00	−7.20	0.51	−6.69
glutaric	−5.25	0.85	−4.40	−6.38	0.27	−6.11
adipic	−5.52	0.89	−4.65	−6.72	0.38	−6.34
suberic	−5.40	0.84	−4.56	−6.55	0.30	−6.25
sebacic	−5.29	0.78	−4.52	−6.50	0.23	−6.27

[a] Energy, in kcal/mol, is given per hydrogen bond. In the catamer motif it includes all the RCOOH···RCOOH intermolecular interactions with a single hydrogen bond; in the cyclic dimer it is half the RCOOH···RCOOH interactions, i.e., the energy per molecule. [b] Catamer motif. [c] The two values given here correspond to the two symmetry-*unrelated* hydrogen bonds in these crystals.

strong electrostatic attraction opposed by the inverse 9- or 12-power term representing the exchange repulsion.

The total electrostatic interaction energies between hydrogen-bonded molecules containing cyclic dimers are ~−8.5 kcal/mol of hydrogen bond in the 9-6-1 potential and ~−6.5 kcal/mol in the 12-6-1 potential. The electrostatic interactions of the isolated -OH···O=C- groups, given in the first column of Table III, are ~−7 and ~−5 kcal/mol in the 9-6-1 and 12-6-1 potentials, respectively. The difference between these values and the respective dimer energies is due to the electrostatic interaction between the non-hydrogen-bonded -O-H and O=C- groups in the dimer. These additional interactions can play a significant role in influencing the relative stability of the cyclic dimer and the catamer chain modes of hydrogen bonding in acid crystals.

The van der Waals repulsion in the hydrogen bond interaction arises mainly from the O···O interaction in this representation, and is one of the primary factors in determining this distance. The repulsive energy corresponds to ~1 kcal/mol of O···O in the case of the 9-6-1 potential and 0.5 in the 12-6-1. The dispersion contribution from the other groups which are not in contact tends to reduce this repulsion slightly, but still the total van der Waals interaction between the hydrogen-bonded molecules is in general repulsive.

Relative Contribution of Secondary and Tertiary Structure to Sublimation Energy. By comparing the energies given in Tables I and III it becomes apparent that the electrostatic interactions between hydrogen-bonded molecules (secondary structure) account for the major portion of the total electrostatic contribution. Essentially all of the dispersion energy, however, arises from the tertiary structure, i.e., the interaction of the hydrogen-bonded arrays. This contribution is less specific, arising from a large number of small van der Waals interactions and not from a small number of large interactions as in the electrostatic term. Thus to a large degree the electrostatic interaction determines the secondary structures and their geometry while the van der Waals interactions govern the way in which these pack, i.e., form tertiary structure, and, to some extent, which of the possible secondary structures will form.[4]

Structural Properties

Lattice Constants. In examining the adequacy of the various potentials in part 2 we presented average deviations of structural parameters. In Table IV we present the minimized lattice constants a, b, c, α, β, and γ, the unit cell volume, the translations of the center of mass t_a, t_b, and t_c (in fractional units), and the rotations of the asymmetric unit around the Cartesian axis at the center of mass θ_z, θ_x, and θ_y (i.e., θ_z is the rotation in the ab plane; see Methods section). The corresponding experimental values[17-30] are included in the table for comparison. We also include the experimental and calculated structures of formic and acetic acid dimers.[31,32] (In the initial structure the two carbonyl carbon atoms lie on the x axis and the carboxyl groups are in the xy plane.) As indicated by the average deviations,[1b] most of the minimized structures are in reasonable agreement with the observed structures. Nevertheless, there are some outstanding deviations of as much as 1 Å in the

unit cell vectors of acetic, oxalic, and butyric acids, and these deviations will be discussed below. Butyric acid is also an exceptional case in that it is the only crystal, out of the 27 acid and amide crystals we have minimized, whose symmetry was reduced when the minimization was carried out without imposing symmetry (although starting from the observed symmetry).

It should be noted that there is a problem associated with presenting deviations in unit cell vectors in this way. Thus the deviations from experiment in this table are sometimes "overestimated", since they do not always correspond to a "deviation per molecule". For example, it is obvious that, if one would refer to a unit cell of a monoclinic structure (P_1) which contains two translationally related molecules instead of one, the "doubled unit cell vector" would have an associated, artificially *doubled* deviation. In an analogous way a unit cell vector along which there are two molecules related by other symmetry (nontranslational) will also result in an apparently large deviation relative to deviations of cell parameters which correspond to one molecule. Essentially these deviations correspond to twice the deviations of the intermolecular distances of interest. The energy depends only on the relative orientations and positions of the molecules and it is for these reasons that the additional criteria of fit involving root mean square deviations of interatomic distances were introduced in the preceding paper.[1b]

Secondary Structure Motifs. An analysis of the energetics of the secondary structure motifs was carried out in order to better understand the underlying interactions responsible for the observed packing modes. In all crystals the molecules are interlinked by hydrogen bonds. The interactions between the hydrogen-bonded molecules are large (~−7 kcal/hydrogen bond; see Table III) and thus they play a major role in determining the crystal packing. Most of the crystals contain cyclic hydrogen-bonded dimers, but a catamer motif[3] is encountered in acetic acid, formic acid, and α-oxalic acid, where the carboxylic group is linked to two other molecules by a single hydrogen bond to each as depicted in Figure 1.

In order to understand why, and under what circumstances, one motif is preferred over the other we will compare first the interaction of hydrogen-bonded molecules in acetic and formic acid with propionic and valeric acids. In acetic acid the hydrogen-bonded molecules form a chain along the (0,1,1) diagonal as may be seen in stereo in Figure 1B in the first of the two preceding papers.[1a] Each molecule (1) in this chain is related to the neighboring molecules in the chain (2) and (3) by an "*n*" glide (Figure 1A). The dimers in propionic and valeric acid can also be considered as links of a chain along (1,1,0). A molecule in this chain (1) is related through a center near the carboxyl group to another (2), forming two hydrogen bonds, and by another center near the alkyl end to a third molecule (3) with no hydrogen bonds between them (Figure 1B, Figure 1C in ref 1a).

The group interactions of one molecule with the two neighbors in the chain for both motifs are given in Table V. From these interactions it appears that the catamer form is slightly more stable, the total intermolecular energies in the 9-6-1 potential being −7.62 and −7.50 (for formic and acetic acids) in the catamer arrangement and −7.22 and −7.28 (for propionic and valeric acids) in the cyclic dimer arrangement despite the larger size of the latter molecules. Focusing for a moment on the *total* energies it is seen that the van der Waals repulsion is larger in the catamer but the larger total electrostatic attraction more than compensates for the larger repulsion.

The source of the van der Waals repulsion is seen easily from the details of the group interactions in Table V. The OH···O=C van der Waals repulsion is almost equal in all the molecules, but, while in propionic and valeric acid there is a significant attraction between the alkyl groups (especially the R···R interaction of molecules (1) and (3)), the attraction is much smaller in acetic and formic acid since the alkyl groups are both smaller and farther from one another in this motif.

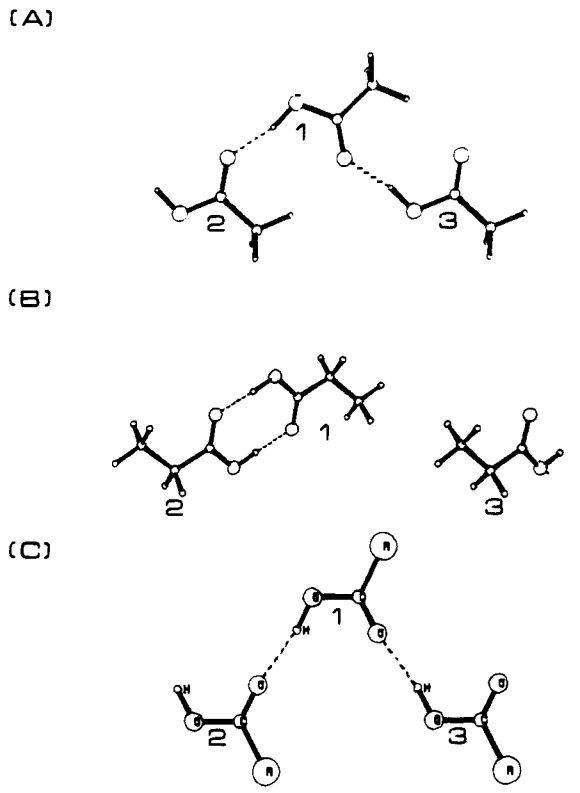

Figure 1. Hydrogen bond arrangement in monocarboxylic acids. (A) Catamer motif in acetic acid crystal with the C=O···H angle ~130° (catamer motif *c* in ref 3). (B) Cyclic dimer motif in propionic acid crystal. (C) Catamer motif with the C=O···H angle ~180° (catamer motif *b* in ref 3).

The interaction in the catamer motif between the carbonyl group of molecule 1 and the R group of molecule 2 (see Figure 1) is of particular interest. It is calculated by the 9-6-1 potential to be +0.34 kcal/mol in the experimental structure of acetic acid, and is presumably the reason why this motif does not appear in the higher homologues; it is relieved in the minimization by opening the -H···O=C- angle (see discussion on deviations of calculated structures below). The corresponding R···O=C interaction in the cyclic dimer is favorable. In the breakdown of the total electrostatic interaction into group interactions we do not discuss those of formic acid since this molecule is an exception in that the COOH group is not neutral (as in the other molecules). The comparison of the electrostatic group interaction brings out several differences. The *total* hydrogen bond attraction by itself (C=O···H-O) does not differ in energy significantly between the dimer and catamer forms, but in acetic acid the small C=O···C=O, OH···OH, and CH_3···O=C attractions combined are significantly larger than in the dimer and these interactions serve to stabilize the catamer motif. The first two contribute to the stability of the catamer motif not because they are more favorable in this motif but rather due to the fact that in the cyclic dimer there is only one such interaction within the dimer while in the catamer motif each CO or OH group interacts with the CO and OH in *two* neighboring molecules, thus yielding a larger contribution (Figure 1). We may conclude that the electrostatic interactions stabilize the catamer motif, but when a large R group is encountered there will be an R···O=C clash in the catamer motif[3] thus destabilizing it. Another small molecule which crystallizes in a catamer motif is tetrolic acid ($CH_3C{\equiv}C$-

Table IV. Minimized Crystal and Dimer Structures (Distances in Å, Angles in deg, and Volume in Å^3)

	exptl	9-6-1 potential	12-6-1 potential
	Formic Acid ($Pna2_1$)[17,18]		
a	10.24	10.56 (0.32)	9.99 (−0.26)
b	3.54	3.59 (0.04)	3.67 (0.12)
c	5.36	5.52 (0.16)	5.37 (0.02)
V	194.39	208.94 (14.55)	196.83 (2.43)
t_a		0.00	−0.01
t_b		0.00	−0.01
θ_z		2.38	−0.95
θ_x		0.89	−0.98
θ_y		−0.26	−3.58
	Acetic Acid ($Pna2_1$)[19]		
a	13.23	14.22 (0.99)	14.61 (1.39)
b	3.96	3.88 (−0.08)	4.01 (0.05)
c	5.76	5.50 (−0.26)	5.01 (−0.75)
V	301.99	303.39 (1.40)	293.82 (−8.17)
t_a		0.00	0.01
t_b		−0.03	−0.13
θ_z		0.7	2.23
θ_x		−1.5	−5.47
θ_y		−1.5	−1.79
	Propionic Acid ($P2_1/c$)[20]		
a	4.04	3.90 (−0.14)	4.03 (−0.01)
b	9.06	9.02 (−0.04)	9.02 (−0.04)
c	11.00	11.02 (0.02)	10.72 (−0.27)
β	91.25	90.85 (−0.40)	90.99 (−0.26)
V	402.52	387.47 (−15.05)	390.07 (−12.45)
t_a		0.07	0.07
t_b		0.00	−0.01
t_c		0.00	0.03
θ_z		6.69	5.43
θ_x		−1.64	1.17
θ_y		−0.14	0.33
	Butyric Acid ($C2/m$)[21]		
a	8.01	8.51 (0.50)	8.52 (0.52)
b	6.82	6.68 (−0.14)	6.69 (−0.13)
c	10.14	9.18 (−0.96)	9.33 (−0.81)
β	111.45	113.83 (2.38)	113.38 (1.93)
V	514.99	477.25 (−37.74)	488.42 (−26.57)
t_a		−0.18	−0.18
t_c		0.03	0.03
θ_y		−1.87	−2.13
	Valeric Acid ($P2_1/c$)[22]		
a	5.55	5.55 (0.00)	5.67 (0.12)
b	9.06	9.37 (−0.29)	9.37 (−0.30)
c	11.34	11.26 (−0.08)	11.27 (0.08)
β	101.81	102.48 (0.67)	100.57 (−1.24)
V	595.40	571.66 (−23.75)	588.51 (−6.89)
t_a		0.01	0.03
t_b		−0.01	−0.01
t_c		0.00	0.00
θ_z		2.59	2.50
θ_x		0.86	−0.28
θ_y		−0.78	−0.16
	α-Oxalic Acid ($Pcab$)[23]		
a	6.55	6.73 (0.18)	6.62 (0.08)
b	7.84	7.09 (−0.75)	6.35 (−1.48)
c	6.09	6.97 (0.88)	7.23 (1.14)
V	312.59	332.54 (19.95)	304.70 (−7.89)
θ_z		2.89	3.22
θ_x		−0.67	1.26
θ_y		−0.71	2.06
	β-Oxalic Acid ($P2_1/c$)[23]		
a	5.33	5.36 (0.03)	5.27 (−0.06)
b	6.01	6.41 (0.40)	7.23 (1.22)
c	5.44	5.46 (0.02)	4.65 (−0.79)
β	115.83	117.81 (1.98)	122.05 (6.22)
V	157.00	166.07 (9.17)	150.23 (−6.66)
θ_z		−1.99	−3.37
θ_x		0.46	14.21
θ_y		−3.30	−1.85
	Malonic Acid ($P\bar{1}$)[24]		
a	5.33	5.48 (0.15)	5.57 (0.24)
b	5.14	5.36 (0.22)	5.10 (−0.04)
c	11.25	11.24 (−0.01)	11.30 (0.05)
α	102.70	107.25 (4.55)	106.11 (3.40)
β	135.17	136.27 (1.10)	139.28 (4.11)
γ	85.16	83.12 (−2.04)	83.09 (−2.06)
V	210.86	215.57 (4.71)	199.34 (−11.51)
t_a		0.14	0.10
t_b		0.02	0.02
t_c		−0.02	−0.04
θ_z		1.90	2.23
θ_x		5.34	4.48
θ_y		0.95	−3.31
	Methylmalonic Acid ($P\bar{1}$)[25]		
a	5.63	5.42 (−0.21)	5.44 (−0.19)
b	5.24	5.34 (0.10)	5.14 (−0.10)
c	11.39	11.35 (−0.04)	11.14 (−0.25)
α	117.00	118.52 (1.52)	118.56 (1.56)
β	76.00	77.35 (1.35)	78.53 (2.53)
γ	114.00	115.83 (1.82)	114.34 (0.34)
V	272.83	259.83 (−13.00)	249.25 (−23.58)
t_a		0.09	−0.08
t_b		0.16	0.15
t_c		0.00	−0.01
θ_z		0.26	−1.41
θ_x		1.51	1.21
θ_y		2.83	2.23
	Succinic Acid ($P2_1/a$)[26]		
a	5.13	5.08 (−0.05)	5.05 (−0.07)
b	8.88	9.12 (0.24)	8.61 (−0.27)
c	7.62	7.58 (−0.04)	7.49 (−0.13)
β	133.00	134.06 (0.46)	132.54 (−1.06)
V	251.15	252.20 (1.05)	240.28 (−10.87)
θ_z		−0.36	−2.50
θ_x		2.36	−0.22
θ_y		−0.10	1.32
	Glutaric Acid ($12/a$)[27]		
a	10.06	10.04 (−0.03)	9.84 (−0.21)
b	4.87	4.95 (0.08)	4.74 (−0.13)
c	17.40	17.06 (−0.33)	16.97 (−0.43)
β	132.60	132.44 (−0.16)	131.07 (−1.53)
V	627.50	625.86 (−1.63)	596.96 (−30.53)
t_a		−0.23	−0.23
t_b		0.03	0.03
θ_z		0.00	0.00
θ_x		0.00	0.00
θ_y		1.18	2.07
	Adipic Acid ($P2_1/c$)[28]		
a	10.00	9.92 (−0.08)	9.85 (−0.15)
b	5.15	5.03 (−0.12)	4.93 (−0.22)
c	10.06	10.13 (0.07)	10.51 (0.45)
β	136.75	137.22 (0.47)	137.89 (1.14)
V	355.02	343.30 (−11.72)	342.61 (−12.42)
θ_z		−2.38	−1.76
θ_x		7.29	12.22
θ_y		−0.45	−1.13
	Suberic Acid ($P2_1/c$)[29]		
a	8.98	8.83 (−0.15)	8.91 (−0.07)
b	5.06	4.98 (−0.08)	4.88 (−0.18)
c	10.12	10.07 (−0.05)	10.30 (0.18)
β	97.83	97.59 (−0.24)	99.97 (2.14)
V	455.55	439.23 (−16.32)	441.47 (−14.08)
θ_z		6.61	10.45
θ_x		2.93	6.04
θ_y		0.34	−1.05

Table IV (*Continued*)

	exptl	9-6-1 potential	12-6-1 potential		exptl	9-6-1 potential	12-6-1 potential
	Sebacic Acid ($P2_1/c$)[30]				Formic Acid Dimer[31]		
a	15.04	14.97 (−0.07)	14.88 (−0.16)	t_x		0.02	0.07
b	5.00	4.87 (−0.13)	4.80 (−0.20)	t_y		−0.24	−0.19
c	10.07	10.09 (0.02)	10.29 (0.22)	θ_z		0.18	0.13
β	133.13	134.02 (0.89)	133.35 (0.22)				
V	552.66	528.33 (−24.32)	534.41 (−18.25)		Acetic Acid Dimer[32]		
θ_z		−1.20	−0.77	t_x		0.03	0.06
θ_x		6.45	11.15	t_y		−0.28	−0.24
θ_y		−0.69	−1.21	θ_z		0.00	0.0

Table V. Group Interactions between Hydrogen-Bonded Monocarboxylic Acid Molecules in Catamer and Cyclic Dimer Motifs (kcal/mol)[a]

	electrostatic			van der Waals			total[b]		
molecule 1/(2 + 3)[c]	C=O	OH	R	C=O	OH	R	C=O	OH	R
				9-6-1 Potential					
				Formic Acid					
C=O	−0.74	−3.30	−1.44	−0.28	0.97	0.05	−1.02	−2.33	−1.39
OH	−3.30	−0.30	0.17	0.97	−0.08	0.00	−2.33	−0.38	0.16
R	−1.44	0.17	0.88	0.05	0.00	0.00	−1.39	0.16	0.88
total		−9.30			1.68			−7.62	
				Acetic Acid					
C=O	−1.40	−3.30	−0.14	−0.34	1.11	−0.04	−1.74	−2.19	−0.18
OH	−3.30	−0.30	−0.22	1.11	−0.08	−0.08	−2.19	−0.38	−0.30
R	−0.14	−0.22	0.00	−0.04	−0.08	−0.04	−0.18	−0.30	−0.04
total		−9.00			1.50			−7.50	
				Propionic Acid					
C=O	−1.22	−3.45	0.03	−0.05	1.05	−0.11	−1.26	−2.40	−0.08
OH	−3.45	−0.13	−0.24	1.05	−0.09	−0.07	−2.40	−0.22	−0.31
R	0.03	−0.24	0.04	−0.11	−0.07	−0.18	−0.08	−0.31	−0.15
total		−8.63			1.41			−7.22	
				Valeric Acid					
C=O	−1.07	−3.48	0.04	−0.06	1.09	−0.12	−1.13	−2.39	−0.08
OH	−3.48	0.02	−0.19	1.09	−0.09	−0.07	−2.39	−0.07	−0.26
R	0.04	−0.19	−0.03	−0.12	−0.07	−0.56	−0.08	−0.26	−0.59
total		−8.34			1.06			−7.28	
				12-6-1 Potential					
				Formic Acid					
C=O	−0.40	−3.45	−1.22	−0.56	0.42	−0.08	−0.96	−2.25	−1.30
OH	−3.45	−0.24	0.19	0.42	−0.04	−0.03	−2.25	−0.28	0.16
R	−1.22	0.19	0.74	−0.08	−0.03	0.00	1.30	0.16	0.74
total		−7.28			0.02			−7.26	
				Acetic Acid					
C=O	−0.98	−2.74	−0.09	−0.62	0.57	−0.18	−1.60	−2.17	−0.27
OH	−2.74	−0.20	−0.17	0.57	−0.04	−0.07	−2.17	−0.24	−0.25
R	−0.09	−0.17	0.01	−0.18	−0.07	−0.04	−0.27	−0.25	−0.03
total		−7.17			−0.06			−7.23	
				Propionic Acid					
C=O	−0.91	−2.68	0.02	−0.20	0.44	−0.12	−1.12	−2.24	−0.05
OH	−2.68	−0.12	−0.19	0.44	−0.07	−0.045	−2.24	−0.20	−0.235
R	0.02	−0.19	0.03	−0.12	−0.045	−0.20	−0.05	−0.235	−0.17
total		−6.72			+0.08			−6.63	
				Valeric Acid					
C=O	−0.79	−2.68	0.04	−0.29	0.45	−0.12	−1.08	−2.23	−0.08
OH	−2.68	−0.01	−0.15	0.45	−0.07	−0.05	−2.23	−0.08	−0.20
R	0.04	−0.15	0.06	−0.12	−0.05	−0.61	−0.08	−0.20	−0.63
total		−6.43			−0.40			−6.83	

[a] Energies are presented per mol of monomer, namely, half the group-group interaction. [b] Note that totals are obtained before individual interactions are rounded so that total may differ from the sum of these in the second place. [c] For definition of molecules 1, 2, and 3 see Figure 3A,B.

COOH) in its β form.[33] The additional acetylenic group, -C≡C-, is linear and does not cause the alkyl hydrogens to get closer to the neighboring carbonyl as would occur in a higher member of the aliphatic acids. The higher members of the aliphatic series could theoretically fit into the catamer motif by change of the molecular conformation (i.e., by rotation about the carbonyl-α-carbon bond). In order to understand the preference for the cyclic dimer motif the interplay between

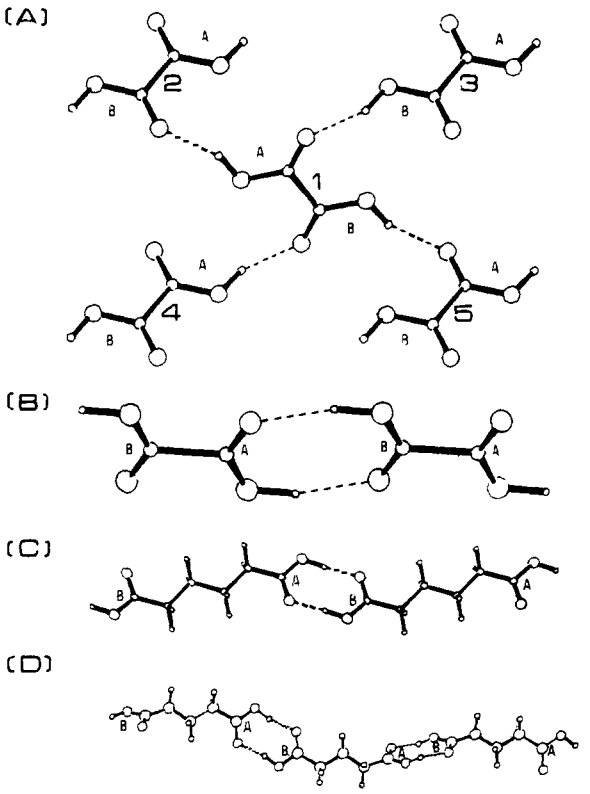

Figure 2. Hydrogen bond arrangement in dicarboxylic acids. (A) Catamer motif in α-oxalic acid crystal. (B) Linear chains of cyclic dimers in β-oxalic acid crystal. (C) Linear chains of cyclic dimers in adipic acid crystal. (D) Twisted chains of cyclic dimers in glutaric acid crystals.

the inter- and intramolecular forces must be studied (see, e.g., ref 5).

Another way in which large molecules can be inserted into a catamer motif is by opening the C=O···H angle from ~120 up to ~180°[3] (the "linear" motif). The opening of this angle is in fact observed to occur even in going from formic (122°)[18] to acetic (133°)[19] and tetrolic acid (137°).[33] The "linear" catamer motif (Figure 1C) is observed in chiral acids[3,34] (which cannot form centrosymmetric cyclic dimers). The hydrogen bonding involved in a linear C=O···H angle is not as favorable as the hydrogen bonding in catamers of the small molecules.

The main reason for the stability of the catamer motif compared to the dimer motif, namely, the electrostatic attraction of CH_3···O=C, OH···OH, and C=O···C=O, is reduced by opening the C=O···H angle, as can be seen by comparing Figures 1A and 1C. The facts that the corresponding racemates exist as dimers[34c] and that enantiomers with very bulky residues (e.g., levopimaric acid, $C_{20}H_{30}O_2$)[35] also prefer the dimer form[3] suggest that there is fine balance between the secondary and tertiary structure. This coupling between secondary and tertiary structure in acids is a subject of further study (see, e.g., ref 4a for a discussion of such coupling in the case of adipamide).

Dicarboxylic Acids. The secondary structure in the dicarboxylic acids consists of a cyclic dimer motif in all the crystals considered here except in α-oxalic acid. But while in the monocarboxylic acids the dimer motif forms linear arrays containing distinct dimers, in the dicarboxylic acids there are carboxyl groups on both sides of the molecule and thus hydrogen-bonded ribbons or chains are generated (Figure 2). Likewise, in α-oxalic acid the catamer motif leads to a two-dimensional hydrogen-bonded array (Figure 2A; see also stereo Figure 1F in ref 1a), as opposed to the linear array generated by this secondary structure in the monocarboxylic acids. Thus we will compare the energetics of the dimer motif in β-oxalic acid and adipic acid to find the effect of the larger alkyl chain and also compare the two different motifs in α- and β-oxalic acids. The group interactions in the hydrogen bond motifs of these molecules are given in Table VI (see also Figure 2). The dimer of adipic acid is more stable than the dimer of β-oxalic acid by 0.64 kcal in the 9-6-1 potential. The hydrogen-bond interactions themselves are almost equal in the two acids; thus the stabilization of the dimer in adipic acid originates from other interactions. There is a repulsion between OH_A···CO_A (and CO_B···OH_B), mainly electrostatic, of ~0.5 kcal in β-oxalic acid, while in adipic acid it is less than 0.05 kcal. This repulsion is negligible in adipic acid since a long alkyl chain separates the two carboxyl groups, but is important in β-oxalic acid, where the OH of one molecule is close enough to be repelled by the carbonyl at the other end of the second molecule. This is analogous to the situation prevailing in oxamide, discussed in ref 2b (see Figure 1 of ref 2b). In adipic acid there is also a contribution to the energy from the attraction of the alkyl chain and the OH group (~0.24 kcal) which does not exist in oxalic acid. The unfavorable interactions in β-oxalic acid are somewhat compensated by an electrostatic attraction of ~0.4 kcal of the OH_A···OH_A groups which are too far to interact in adipic acid. Thus we conclude that the absence of an alkyl chain in oxalic acid destabilizes the cyclic dimer motif. It may be because of the disadvantages of the dimer motif for a small molecule that the second polymorphic form (α) is encountered in oxalic acid. Here every molecule is linked to four other molecules by a single hydrogen bond (Figure 2A). In order to compare the stability of this motif with the stability of a dimer in β-oxalic acid, we sum the interactions of a molecule (1) with the carboxylic groups $COOH_B$ of two other molecules (2 and 3) which are hydrogen bonded to $COOH_A$ of (1). The hydrogen bonds (OH···O=C interaction) are slightly more stable in β-oxalic acid (by ~0.1 kcal). The total electrostatic interaction is also more favorable in β- than in α-oxalic acid (by ~0.5 kcal), but the van der Waals interaction is less favorable also by ~0.5 kcal.

The different interaction pattern in the two forms reflects the different relative orientation of the molecules. As noted above, in the β form the molecules are arranged in a linear chain while in the α form the hydrogen-bonded molecules form "zigzag" chains in a nonplanar layer so that the molecules are packed more efficiently in the layer (see also Figure 1F of part 1a). This closer packing results in better contacts between the hydrogen-bonded molecules in the α form leading to the favorable nonbonded interactions. Thus it seems that the oxalic acid molecule can be accommodated equally well in the two types of secondary structures and the relative stability of the two polymorphs is determined by the tertiary structure.

The detailed features of the hydrogen bond chain motif depend on the relation between the two carboxyl groups in the molecule. The even members of the dicarboxylic acids are essentially planar, having a center of symmetry in the middle of the central C-C bond. The carboxylic groups are antiparallel and thus the linear chain of hydrogen-bonded molecules is formed by translation. This motif appears in β-oxalic, succinic, adipic, suberic, and sebacic acids, and is also found in the higher homologue which was not included in our calculations.[36] The odd members of the dicarboxylic acids are not planar, the carboxyl groups are not antiparallel, and thus the hydrogen-bonded chain of cyclic dimers cannot be formed by translational symmetry. In glutaric acid and also in the higher (odd) homologues (not included in the calculation[37]) the two carboxyl groups are rotated in opposite directions and are related by a twofold axis at the central carbon atom (Figures 2D and 1J of ref 1a). The hydrogen bond is formed by a glide perpendicular to the twofold axis. Thus instead of a linear chain of dimers a twisted chain is formed. Although the structure of

Table VI. Group Interactions of Hydrogen-Bonded Molecules (Dicarboxylic Acid)[a]

molecule 1[b]	electrostatic interactions					van der Waals interactions					total interactions				
	C=O$_A$[c]	C=O$_B$	OH$_A$	OH$_B$	R	C=O$_A$[c]	C=O$_B$	OH$_A$	OH$_B$	R	C=O$_A$[c]	C=O$_B$	OH$_A$	OH$_B$	R
							9-6-1 potential								
							α-Oxalic Acid[b]								
C=O$_A$		−0.46		−3.16			−0.37		0.92			−0.83		−2.24	
C=O$_B$		−0.11		0.60			−0.12		−0.08			−0.24		0.53	
OH$_A$		−3.16		−0.29			0.92		−0.10			−2.24		−0.39	
OH$_B$		0.09		−0.69			−0.07		−0.09			0.02		0.	
total			−7.18					1.01					−6.17		
							β-Oxalic Acid								
C=O$_A$	0.40	−1.25	−0.03	−3.32		−0.06	−0.03	−0.03	0.95		0.04	−1.28	0.06	−2.37	
C=O$_B$	0.15	0.10	−0.17	0.52		−0.01	−0.06	0.00	−0.03		0.15	0.04	−0.17	0.49	
OH$_A$	0.52	−3.32	−0.39	−0.19		−0.03	0.95	−0.02	−0.09		0.49	−2.37	−0.41	−0.28	
OH$_B$	−0.17	−0.03	0.17	−0.39		−0.00	−0.03	−0.00	−0.02		−0.17	0.06	0.17	−0.41	
total			−7.70					1.50					−6.20		
							Adipic Acid								
C=O$_A$	0.07	−1.18	−0.04	−3.46	0.05	0.00	−0.02	0.00	1.06	−0.09	0.07	−1.20	−0.04	−2.40	−0.04
C=O$_B$	0.02	0.07	−0.03	0.03	−0.01	0.00	0.00	0.00	0.00	0.00	0.02	0.07	−0.03	0.03	−0.01
OH$_A$	0.03	−3.46	−0.03	−0.22	−0.17	0.00	1.06	0.00	−0.09	−0.07	0.03	−2.40	−0.03	−0.32	−0.24
OH$_B$	−0.03	−0.04	0.04	−0.32	0.01	0.00	0.00	0.00	0.00	0.00	−0.03	0.04	0.04	0.03	0.01
R	0.00	0.04	0.01	−0.17	0.01	0.00	−0.09	0.00	−0.07	−0.03	0.00	−0.05	−0.01	−0.24	−0.02
total			−8.49					1.65					−6.84		
							Glutaric Acid								
C=O$_A$	−0.02	−1.15	0.00	−3.36	0.02	0.00	−0.05	0.00	1.02	−0.08	0.02	−1.20	0.00	−2.34	−0.06
C=O$_B$	0.00	−0.02	−0.02	0.04	−0.01	0.00	0.00	0.00	0.00	0.00	0.00	−0.03	−0.02	0.04	−0.01
OH$_A$	0.04	−3.36	−0.05	−0.03	−0.15	0.00	1.02	0.00	0.10	−0.06	0.04	−2.34	−0.05	−0.12	−0.21
OH$_B$	−0.02	0.00	0.04	−0.05	0.01	0.00	0.00	0.00	0.00	0.00	−0.02	0.00	0.04	−0.05	0.01
R	−0.01	0.02	0.01	−0.15	0.01	0.00	−0.80	0.00	−0.06	−0.02	−0.01	−0.06	0.01	−0.21	−0.01
total			−8.23					1.57					−6.66		
							12-6-1 Potential								
							α-Oxalic Acid								
C=O$_A$		−0.34		−2.67			−0.56		0.48			−0.90		−2.19	
C=O$_B$		−0.21		0.37			−0.25		−0.09			−0.46		0.28	
OH$_A$		−2.67		−0.14			0.48		−0.06			−2.19		−0.20	
OH$_B$		0.27		−0.37			−0.17		−0.08			0.10		−0.45	
total			−5.76					−0.25					−6.01		
							β-Oxalic Acid								
C=O$_A$	0.06	−0.92	−0.02	−2.63		−0.08	−0.09	−0.02	0.36		−0.02	−1.00	−0.04	−2.27	
C=O$_B$	0.10	0.06	−0.11	0.39		−0.01	−0.08	−0.00	−0.03		0.09	−0.02	−0.11	0.35	
OH$_A$	0.39	−2.63	−0.29	−0.16		−0.03	0.36	−0.01	−0.07		0.35	−2.27	−0.30	−0.23	
OH$_B$	−0.11	−0.02	0.11	−0.29		0.00	−0.02	0.00	−0.01		−0.11	−0.04	0.11	−0.30	
total			−6.08					0.96					−5.82		
							Adipic Acid								
C=O$_A$	0.04	−0.86	−0.03	−2.76	0.04	0.00	−0.15	0.00	0.44	−0.09	0.04	−1.01	−0.03	−2.32	−0.05
C=O$_B$	−0.01	0.04	−0.02	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.04	−0.02	0.02	0.00
OH$_A$	0.03	−2.76	−0.03	−0.18	−0.14	0.00	0.44	0.00	−0.07	−0.04	0.02	−2.32	−0.03	−0.26	−0.18
OH$_B$	−0.02	−0.03	0.02	−0.03	0.01	0.00	0.00	0.00	0.00	0.00	−0.03	−0.03	0.02	−0.03	0.00
R	0.00	0.04	0.00	−0.14	0.01	0.00	−0.09	0.00	−0.04	−0.02	0.00	−0.05	0.00	−0.18	−0.01
total			−6.72					0.38					−6.34		
							Glutaric Acid								
C=O$_A$	−0.02	−0.85	0.00	−2.62	0.02	0.00	−0.22	0.00	0.42	−0.08	−0.02	−1.07	0.00	−2.20	−0.06
C=O$_B$	0.00	−0.02	−0.01	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	−0.02	−0.01	0.03	−0.00
OH$_A$	0.03	−2.62	−0.04	−0.02	−0.13	0.00	0.42	0.00	−0.08	−0.04	0.03	−2.20	−0.04	−0.40	−0.17
OH$_B$	−0.01	0.00	0.02	−0.04	0.01	0.00	0.00	0.00	0.00	0.00	−0.01	0.00	0.02	−0.04	0.01
R	0.00	0.02	0.00	−0.13	0.01	0.00	−0.08	0.00	−0.04	−0.02	0.00	−0.06	0.00	−0.17	−0.01
total			6.38					0.28					−6.10		

[a] Energies are presented per monomer mole, namely, half the group-group interaction. [b] Interactions between molecule 1 to COOH$_B$ of molecules 2 and 3 are given for α-oxalic acid. See Figure 2 for definition of molecules. [c] Molecule 2.

the chain in odd and even members is very different, the interactions *in* the dimers are almost identical, as seen from the comparison of the group interactions in glutaric and adipic acids. The different shape of the chains of hydrogen-bonded dimers affects only the tertiary structure (i.e., the packing of the chains to form a three-dimensional structure). The first member of the odd dicarboxylic acids, malonic acid, has a unique packing. The two carboxyl groups are not symmetry related, and thus there are two types of hydrogen bonding in the chain. (This is also true in the amide family, where malonamide also packs in a structure in which the molecule has no twofold symmetry. Here there are two molecules per asymmetric unit.[2b]) It should be pointed out that, although in the discussions in this section we referred mainly to the results obtained with the 9-6-1 potential, the same trends are observed in the 12-6-1 potential and the same conclusions would be drawn.

Deviations in Calculated Crystal Structures. The analysis of the secondary structure in terms of the group contributions can yield insight into the factors underlying some of the larger deviations between the calculated and observed structural parameters. Understanding the basis for these deviations, in terms of the relevant intermolecular interactions, can in turn help us to pinpoint problems with the analytical representation and directions to further improving this representation.

Acetic Acid. The fact that the catamer motif can accommodate only small molecules is related to the reason for the relatively large deviations between the minimized and experimental structure of acetic acid. One of the most significant changes in intermolecular structure occurs between two hy-

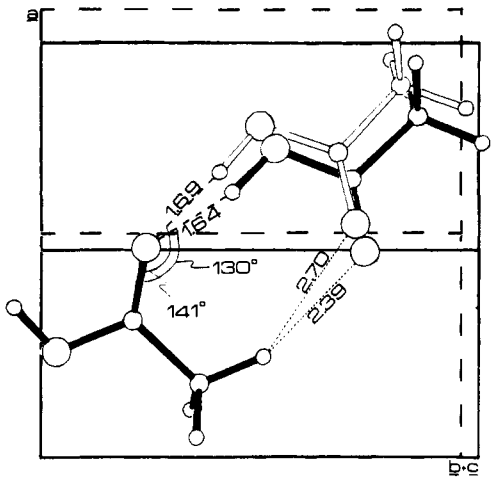

Figure 3. Comparison of the observed and calculated crystal structure of acetic acid. The horizontal lines are in the $b + c$ direction (solid for experimental and dashed for calculated) and the vertical ones in the a direction. The horizontal line at $\frac{1}{4}a$ represents the glide plane. The bonds in the observed structure are solid, while the bonds of molecules in the minimized structure are open. Hydrogen bonds are shown by dashed lines.

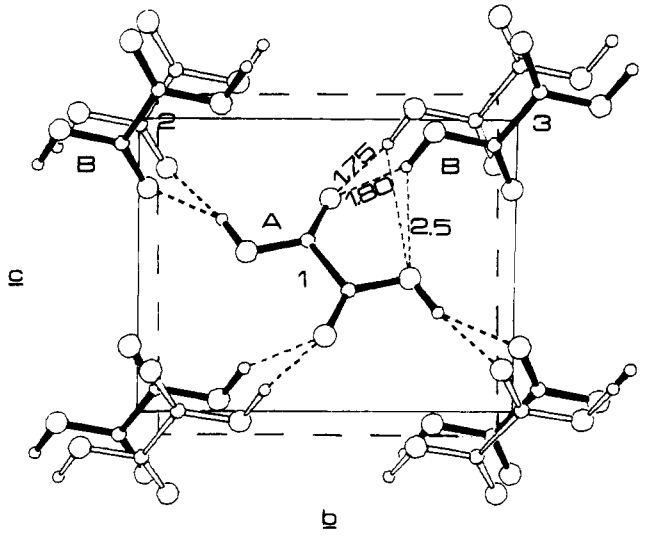

Figure 4. Comparison of the observed and calculated crystal structure of α-oxalic acid viewed down the a^* axis (b is horizontal). The molecules in the observed and minimized structure have solid and open bonds, respectively. Hydrogen bonds are shown by dashed lines. The observed and calculated unit cell boundaries are indicated by solid and dashed lines, respectively.

drogen-bonded molecules. As seen in Figure 3 the HOC angle opens up from 130 to 141° and the O···H distance increases slightly by 0.05 Å. At the same time there is a large increase in the H_{CH_3}···O distance, which is 2.4 Å in the observed crystal and increases to 2.7 Å in the minimized structure. In fact it is this latter interaction which leads to the discrepancy between observed and minimized structures in all potentials used. These potentials do not account for this close O···H_{CH_3} distance, which is too repulsive. (The van der Waals H_{CH_3}···O interaction decreases from 0.97 kcal/mol in the observed structure to 0.32 kcal/mol in the minimized). This leads to the opening of the OH···O=C angle. The change in structure may be thought of as arising from a shift in the n-glide along the a axis by ~0.25 Å as depicted in Figure 3. Thus, the unit cell vector (**a**) increases in the minimized structure in order to maintain orthorhombic symmetry. It should be noted that the deviation

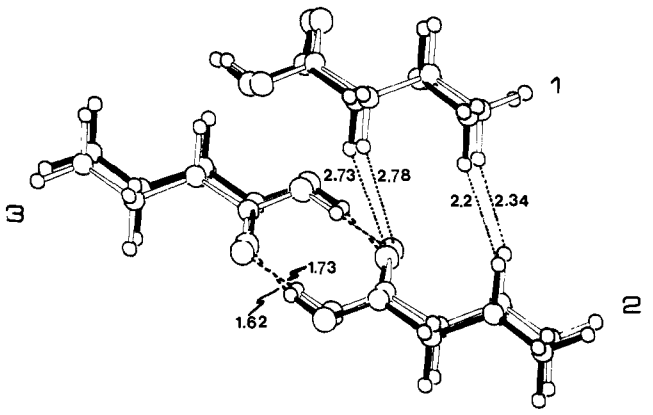

Figure 5. Comparison of the observed butyric acid crystal structure with that calculated with symmetry constraints. Molecules 2 and 3 are related by an inversion and are in the mirror plane ac. Molecule 1 is at ($\frac{1}{2} + x$, $\frac{1}{2} + y$, z). The molecules in the observed and minimized structure have solid and open bonds, respectively. Hydrogen bonds are shown by dashed lines. Other short distances are indicated by dotted lines.

in **a** is essentially amplified by a factor of 4 since the glide lies, by definition, at $\frac{1}{4}$ in **a**. This is a case where the deviations in unit cell vectors do not reflect a "deviation per molecule" as discussed above.

α-Oxalic Acid. Significant deviations of the calculated structure from the experimental one arise in this case too, within the array of hydrogen-bonded molecules (molecules 1, 2, and 3 in Figure 4). The experimental structure is characterized by a bifurcated hydrogen bond, i.e., OH_B of molecule 3 "hydrogen bonding" to both the carbonyl oxygen ($C{=}O_A$) and the hydroxyl oxygen (OH_B) of molecule 1.[23] The H···O distances in the initial structure are 1.8 and 2.5 Å, respectively. In the minimized structure stabilization is obtained (~0.7 kcal/mol including van der Waals interactions) by making the O–H···O=C bond more linear (a deviation from linearity of 15° instead of 30°) and decreasing the H···O distance by ~0.05 Å. This occurs at the expense of the "hydrogen bond" to the hydroxylic oxygen (where the $O{-}H_B{\cdots}O{-}H_B$ interaction increases by 0.25 kcal). As can be seen from Figure 4, these structural changes demand a longer unit cell vector in the c direction and a shortening of the b axis as observed in the minimized structure (Table IV). The shortening of the b axis also results in a more favorable interaction between the hydroxyl groups of molecules 2 and 3 (OH_A and OH_B), respectively (~0.43 kcal/mol).

Butyric Acid. The third structure which exhibits large deviations on minimization is butyric acid. As noted above, this structure is of particular interest because it is the only crystal minimized to date whose symmetry is reduced (monoclinic → triclinic), if symmetry constraints are not imposed when starting from the observed structure. In this connection it is worthwhile pointing out that there is some question as to the presence of a mirror plane in the butyric acid structure.[21] Furthermore, there seems to be no doubt that even if this symmetry plane exists there is considerable displacement of the alkyl chain atoms from it due to thermal motion, especially the methyl.[21] Since this methyl group is involved in one of the interactions which is calculated to destabilize the observed structure, these uncertainties in the experimental structure may be the cause of the resultant discrepancies in the calculated structure.

A comparison of the minimized (with symmetry constraints) and experimental structures of butyric acid is given in Figure 5. As can be seen from this figure two of the closest contacts in the observed structure involve the methyl hydrogen of molecule 1 with a methylene hydrogen of molecule 2 (2.2 Å), and a methylene hydrogen of molecule 1 with the carbonyl

Table VII. Energy and Lattice Constants of Triclinic Butyric Acid Structure

	9-6-1	12-6-1
a	8.27 (0.26)	8.18 (0.18)
b	6.82 (0.00)	6.81 (−0.01)
c	9.45 (−0.69)	9.69 (−0.45)
α	98.9 (8.9)	98.5 (8.5)
β	113.4 (2.0)	112.7 (1.2)
γ	92.3 (2.3)	91.3 (1.3)
E_{tot}	−19.13	−18.94
E_{vdW}	−10.63	−12.29
E_{elec}	−8.50	−6.65

oxygen of molecule 2 (2.73 Å). The van der Waals energies corresponding to these interactions are repulsive, 0.23 and 0.18 kcal/mol, respectively. On minimization both interactions are relaxed, as can be seen in the figure. The relaxation of these interactions is independent of whether or not the structure is constrained to have monoclinic symmetry. In the minimized monoclinic structure these two distances are relaxed to 2.34 and 2.78 Å. In the minimized triclinic structure the H···H distance is 2.32 Å, while two symmetry-unrelated O···H distances arise, one relaxed to 2.96 Å while the other is essentially unchanged at 2.70 Å.

The fact that these interactions are relaxed both in the minimized monoclinic and triclinic structures indicates that they are not the reason for the breakdown of symmetry (nor are they the sole reason for the discrepancies in observed and calculated structure as seen from consideration of the initial and final energies, Table I). The lattice parameters and minimized energy for the minimized triclinic structure are given in Table VII. As can be seen by comparison with Table IV, the deviations in unit cell vector lengths are smaller in the triclinic structure, indicating that in this crystal the symmetry constraint makes it "difficult" to achieve an efficient packing. The total energies of the triclinic and monoclinic structures, on the other hand (see Table I), are almost equal, especially when compared with the initial energy. Both minimum energy structures (triclinic and monoclinic) are characterized by significantly better van der Waals interactions than the observed packing at the expense of slightly less favorable electrostatic energies. This observation holds for both the 12-6-1 and 9-6-1 potentials. The triclinic structure sacrifices less of the electrostatic contribution, and, although its van der Waals energy is slightly less favorable, it is the electrostatic contribution which makes it the (slightly) more stable calculated form.

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