Cubanecarboxylic Acids. Crystal Engineering Considerations and the Role of C−H···O Hydrogen Bonds in Determining O−H···O Networks

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Abstract: A family of 4-substituted-1-cubanecarboxylic acids have been synthesized and their X-ray crystal structures analyzed. The rare *syn-anti* O−H···O catemer **6** is a recurring pattern in this series of compounds. Catemer **6** is observed in the crystal structures of 4-chloro-1-cubanecarboxylic acid (**10**), 4-bromo-1-cubanecarboxylic acid (**11**), 4-iodo-1-cubanecarboxylic acid (**12**), and 4-(methoxycarbonyl)-1-cubanecarboxylic acid (**13**). The ready occurrence of catemer **6** in this family is ascribed to its stabilization by auxiliary C−H···O hydrogen bonds formed by the relatively acidic cubyl C−H groups. The frequency of occurrence of **6** also facilitates its definition as a useful supramolecular synthon. As is true in many catemers, the formation of **6** is sensitive to steric factors. Therefore, the robustness of this synthon may be assessed by analyzing the crystal structures of molecules wherein the 4-substituent is too small (R = H, **14**), too large (R = Ph, **15**), or has a specific hydrogen bonding preference of its own (R = $CONH_2$, **16**). In these structures, either dimer **3** (in **14** and **15**) or heterodimer **22** (in **16**) is observed. Powder diffraction shows that the previously noted structure of 1,4-cubanedicarboxylic acid (**7**) that contains catemer **6** is characteristic of the bulk material. In summary, the *syn-anti* catemer is the dominant supramolecular synthon in this family of cubanecarboxylic acids.

Introduction

The physical and chemical properties of an organic crystal are determined by the nature of the constituent molecules as well as by the mutual orientation and interactions between these molecules.[1] Crystal engineering is the design and construction of crystal structures from molecular components.[2] A crystal structure may be analyzed in terms of supramolecular synthons,[3] defined as structural units within supermolecules which can be formed and/or assembled by known or conceivable intermolecular interactions. Crystal engineering then is carried out by the identification of a molecular skeleton with specific functional groups that will predictably and persistently lead to robust synthons and therefore to the target crystal structure. Hydrogen bonds and other intermolecular interactions have been studied in depth because they provide viable approaches toward the design of molecular solids with specific supramolecular architectures and functions.[4,5] Hydrogen bonds are formed with strong donor−acceptor functionalities (OH, NH_2, CO_2H, $CONH_2$) and with weak donors (C≡C−H, C_6H_5, C═C−H, C(sp^3)-H) and acceptors (CN, NO_2, halogen, π).[6] Because crystal structures are the results of interplay between strong and weak intermolecular interactions,[7] a consideration of supramolecular synthons constructed with strong and weak hydrogen bonds generally provides a more complete understanding of crystal packing.

Hydrogen bond patterns in carboxylic acid crystal structures have been described in detail by Leiserowitz and co-workers.[8] The carboxylic acid group occurs in two distinct conformations,

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(1) (a) Desiraju, G. R. *Science* **1997**, *278*, 404. (b) Desiraju, G. R. *Curr. Opin. Solid State Mater. Sci.* **1997**, *2*, 451. (c) Bryce, M. R., Ed. *J. Mater. Chem.* **1997**, *7*, 1069 (special issue on molecular assemblies and nanochemistry). (d) Hosseini, M. W., Ed. *New J. Chem.* **1998**, *22*, 87 (special issue on molecular networks).

(2) (a) Desiraju, G. R. *Crystal Engineering: The Design of Organic Solids*; Elsevier: Amsterdam, 1989. (b) Anthony, A.; Desiraju, G. R.; Jetti, R. K. R.; Kuduva, S. S.; Madhavi, N. N. L.; Nangia, A.; Thaimattam, R.; Thalladi, V. R. *Cryst. Eng.* **1998**, *1*, 1.

(3) Desiraju, G. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2311.

(4) Selected examples on the use of strong and weak hydrogen bonding in crystal engineering strategies: (a) Schwiebert, K. E.; Chin, D. N.; MacDonald J. C.; Whitesides, G. M. *J. Am. Chem. Soc.* **1996**, *118*, 4018. (b) Lewis, F. D.; Yang, J.; Charlotte, L. S. *J. Am. Chem. Soc.* **1996**, *118*, 12029. (c) Coe, S.; Kane, J. J.; Nguyen, T. L.; Toledo, L. M.; Wininger, E.; Fowler, F. W.; Lauher, J. W. *J. Am. Chem. Soc.* **1997**, *119*, 86. (d) Bhyrappa, P.; Wilson, S. R.; Suslick, K. S. *J. Am. Chem. Soc.* **1997**, *119*, 8492. (e) MacGillivray, L. R.; Atwood, J. L. *Nature* **1997**, *389*, 469. (f) Endo, K.; Ezuhara, T.; Koyanagi, M.; Masuda, H.; Aoyama, Y. *J. Am. Chem. Soc.* **1997**, *119*, 499. (g) Karle, I. L.; Ranganathan, D.; Haridas, V. *J. Am. Chem. Soc.* **1997**, *119*, 2777. (h) Thalladi, V. R.; Brasselet, S.; Weiss, H.-C.; Bläser, D.; Katz, A. K.; Carrell, H. L.; Boese, R.; Zyss, J.; Nangia, A.; Desiraju, G. R. *J. Am. Chem. Soc.* **1998**, *120*, 2563.

(5) Selected recent reviews on hydrogen bonding in crystal engineering: (a) Fyfe, M. C. T.; Stoddart, J. F. *Acc. Chem. Res.* **1997**, *30*, 393. (b) Desiraju, G. R. *Chem. Commun.* **1997**, 1475. (c) Aakeröy, C. B. *Acta Crystallogr.* **1997**, *B53*, 569. (d) Hosseini, M. W.; Cian, A. D. *Chem. Commun.* **1998**, 727. (e) Nangia, A.; Desiraju, G. R. *Acta Crystallogr.* **1998**, *A54*, 934.

(6) Selected reviews on hydrogen bonding: (a) Jeffrey, G. A.; Saenger, W. *Hydrogen Bonding in Biological Structures*; Springer-Verlag: Berlin, 1991. (b) Aakeröy, C. B.; Seddon, K. R. *Chem. Soc. Rev.* **1993**, *22*, 397. (c) MacDonald, J. C.; Whitesides, G. M. *Chem. Rev.* **1994**, *94*, 2383. (d) Desiraju, G. R. *Acc. Chem. Res.* **1996**, *29*, 441. (e) Steiner, T. *Chem. Commun.* **1997**, 727. (f) Jeffrey, G. A. *An Introduction to Hydrogen Bonding*; Oxford University Press: New York, 1997.

(7) (a) Dunitz, J. D. *The Crystal as a Supramolecular Entity, Perspectives in Supramolecular Chemistry*; Desiraju, G. R., Ed.; Wiley: Chichester, U.K., 1996; Vol. 2, pp 1−30. (b) Desiraju, G. R. Sharma, C. V. K. *The Crystal as a Supramolecular Entity, Perspectives in Supramolecular Chemistry*; Desiraju, G. R., Ed.; Wiley: Chichester, U.K., 1996; Vol. 2, pp 31−61.

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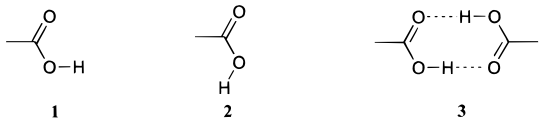
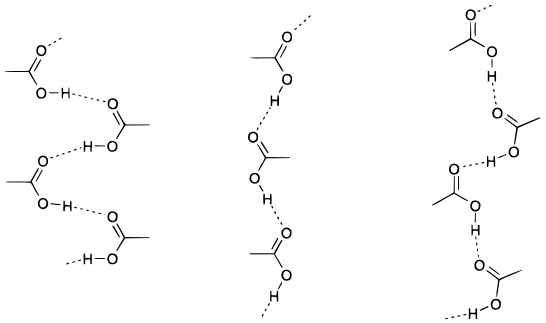
synplanar **1** and antiplanar **2**. The *syn* conformation is more stable (by ca. 2 kcal/mol) and is thus preferred. The most frequent and indeed dominant interlink adopted by carboxylic acids is the *syn-syn* centrosymmetric dimer **3**. In addition,



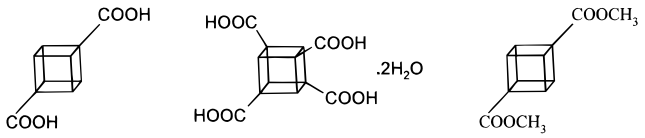
1 **2** **3**



4 **5** **6**

however, catemers of the types **4** (*syn-syn*) and **5** (*anti-anti*) are formed.[9] A third catemer, pattern **6** with alternating *syn* and *anti* carboxylic acid groups has also been observed. A search of the Cambridge Structural Database[10] (CSD, version 5.15) was carried out on these four distinct hydrogen bond patterns.[11] Of the three catemeric arrangements, the *syn-syn* is the most common. The *anti-anti* catemer **5** and the *syn-anti* variant **6** are, however, extremely rare with only two and three occurrences, respectively, in the CSD.

Given this background, the crystal structures of 1,4-cubanedicarboxylic acid (**7**) and 1,3,5,7-cubanetetracarboxylic acid dihydrate (**8**) are of note.[12,13] Diacid **7** is one of the three structures in the CSD that contain catemer **6**. Interestingly, the *syn* and *anti* conformations are present in different (and centrosymmetric) molecules rather than in the same diacid molecule. In tetraacid **8**, three of the four carboxylic groups are in the *syn* conformation while one is in the *anti* conformation. Two of the *syn* carboxylic H atoms are hydrogen bonded to different water molecules. The prominent feature in this abstruse crystal structure is again hydrogen bonding between *syn* and *anti* carboxylic acid groups, though it is interrupted by water molecules. The carboxylic acid is a strong hydrogen bonding functional group that is associated with robust and reliable patterns for solid-state supramolecular aggregation,[14] and yet instead of the usually observed *syn-syn* dimer **3**, the rare catemer **6** or its hydrated variant are found in the only two reported crystal structures of cubanecarboxylic acids. It is this enigmatic and unexplained behavior of **7** and **8** that, in part, led to the present study.



7 **8** **9**

The cubane skeleton is a rigid framework on which functional groups can be attached in specific orientations. Cubanes have potential applications in pharmaceuticals, polymers, explosives, and materials chemistry.[15] Cubanecarboxylic acids are excellent core units for derivatization with amino acids in combinatorial chemistry.[16] Thus, the molecular chemistry of the cubane skeleton is well-developed and advances in the synthesis of highly functionalized cubanes continue to be reported.[17] However, the supramolecular behavior of cubanes in the solid state has not been systematically examined and this is surprising, given the relatively high acidity of the cubyl H atom.[18] The acidity of an unactivated cubyl-H is comparable to NH_3 ($pK_a \sim 38$), while that of a doubly activated cubyl-H, as in 1,3,5,7-tetranitrocubane, is even higher ($pK_a \sim 21$).[19] Cubyl H atoms are at least 10^5-10^6 times more acidic than vinyl and phenyl hydrogens. The active role of C−H···O hydrogen bonds in determining O−H···O networks in the crystal structures of terephthalic acid, fumaric acid, acrylic acid, 2,5-furandicarboxylic acid, and other acids is well-documented.[2a,8a,14a] All of this prompted us to synthesize some selected and related cubanecarboxylic acids[20] (**10**−**16**) and to explore their crystal chemistry.[21] The objective of this study was three-fold: (i) to confirm if cubane derivatives form C−H···O hydrogen bonds and if so to clarify their specific structural role, (ii) to rationalize the supposedly exotic crystal structure of diacid **7**, and (iii) to identify robust supramolecular synthons in crystalline cubane

(8) (a) Leiserowitz, L. *Acta Crystallogr.* **1976**, *B32*, 775. (b) Berkovitch-Yellin, Z.; Leiserowitz, L. *J. Am. Chem. Soc.* **1982**, *104*, 4052.

(9) By "catemer" is meant an infinite or finite noncyclic hydrogen bonded pattern in which each carboxylic group is linked to two neighbours via single O−H···O (carbonyl) bonds. See ref 8a.

(10) (a) Allen, F. H.; Davies, J. E.; Galloy, J. J.; Johnson, O.; Kennard, O.; Macrae, C. F.; Mitchell, E. M.; Mitchell, G. F.; Smith, J. M.; Watson, D. G. *J. Chem. Inf. Comput. Sci.* **1991**, *31*, 187. (b) Allen, F. H.; Kennard, O. *Chem. Des. Autom. News* **1993**, *8*, 1.

(11) The CSD (April 1998 version, 181 309 entries) contains 2067 metal-atom free, nonionic, single-residue organic carboxylic acids. Of these, 1082 contain the *syn-syn* dimer and these could be automatically searched. A manual search of the remaining 985 compounds revealed 67, 2, and 4 hits for the *syn-syn*, *anti-anti*, and the *syn-anti* catemers, respectively. The refcodes for the four *syn-anti* structures are CILDOQ, FIGMAJ, JUKVIU, and SUHSET. Of these, CILDOQ is excluded from further discussion because the *syn* and *anti* carboxylic acid groups are involved in numerous other N−H···O and C−H···O hydrogen bonds. The number of *syn-anti* catemeric structures that are of direct interest here is therefore three. The report of the *anti-anti* catemer in the crystal structure of $HCO_2H{\cdot}HF$ is too recent to be included in the April 1998 version of the CSD. See: Wiechert, D.; Mootz, D.; Dahlems, T. *J. Am. Chem. Soc.* **1997**, *119*, 12665. In the remaining 912 hits, the carboxylic group is hydrogen bonded to other basic groups or is exclusively intramolecularly hydrogen bonded or forms closed *n*-mers ($n \neq 2$). For another recent search of carboxylic acid hydrogen bond patterns, see: Kolotuchin, S. V.; Fenlon, E. E.; Wilson, S. R.; Loweth, C. J.; Zimmerman, S. C. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2654.

(12) Ermer, O.; Lex, J. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 447.

(13) Butcher, R. J.; Bashir-Hashemi, A.; Gilardi, R. D. *J. Chem. Crystallogr.* **1997**, *27*, 99.

(14) (a) Bernstein, J.; Etter, M. C.; Leiserowitz, L. *Structure Correlation*; Bürgi, H.-B., Dunitz, J. D., Eds.; VCH: Weinheim, Germany, 1994; pp 431−507. (b) Herbstein, F. H. *Comprehensive Supramolecular Chemistry*; MacNicol, D. D., Toda, F., Bishop, R., Eds.; Pergamon: Oxford, U.K., 1996; Vol. 6, pp 61−83.

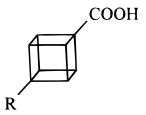
(15) (a) Eaton, P. E. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1421. (b) Bashir-Hashemi, A.; Iyer, S.; Alster, J.; Slagg, N. *Chem. Ind.* **1995**, 551. (c) Marchand, A. P. *Chem. Intelligencer* **1995**, *1*, 8. (d) Hormann, R. E. *Aldrichim. Acta* **1996**, *29*, 31.

(16) (a) Carell, T.; Wintner, E. A.; Bashir-Hashemi, A.; Rebek, J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2059. (b) Carell, T.; Wintner, E. A.; Rebek, J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2061.

(17) (a) Higuchi, H.; Ueda, I. *Carbocyclic Cage Compounds*; Osawa, E., Yonemitsu, O., Eds.; VCH: New York, 1992; pp 217−247. (b) Eaton, P. E.; Xiong, Y.; Gilardi, R. *J. Am. Chem. Soc.* **1993**, *115*, 10195. (c) Bashir-Hashemi, A.; Hardee, J. R.; Gelber, N.; Qi, L.; Axenrod, T. *J. Org. Chem.* **1994**, *59*, 2132. (d) Head, N. J.; Rasul, G.; Mitra, A.; Bashir-Hashmi, A.; Surya Prakash, G. K.; Olah, G. A. *J. Am. Chem. Soc.* **1995**, *117*, 12107. (e) Bashir-Hashemi, A.; Li, J.; Gelber, N.; Ammon, H. *J. Org. Chem.* **1995**, *60*, 698. (f) Lukin, K. A.; Li, J.; Eaton, P. E.; Kanomara, N.; Hain, J.; Punzalan, E.; Gilardi, R. *J. Am. Chem. Soc.* **1997**, *119*, 9591.

(18) Pedireddi, V. R.; Desiraju, G. R. *J. Chem. Soc., Chem. Commun.* **1992**, 988.

(19) Hare, M.; Emrick, T.; Eaton, P. E.; Kass, S. R. *J. Am. Chem. Soc.* **1997**, *119*, 9591.



R = Cl	**10**
Br	**11**
I	**12**
$COOCH_3$	**13**
H	**14**
C_6H_5	**15**
$CONH_2$	**16**

acids as a prerequisite for future crystal engineering investigations.

Experimental Section

In the early stages of this work, 1,4-bis(methoxycarbonyl)cubane (**9**), a common starting material for 4-substituted-1-cubanecarboxylic acids, was synthesized using the well-established Eaton and Cole[22] procedure, while later on, the commercial material (Aldrich)[23] was used. The cubanecarboxylic acids were characterized with NMR and IR spectra and by the comparison of their spectral data with those of the corresponding methyl esters.[21c] ^{1}H NMR and ^{13}C NMR were recorded at 200 and 50 MHz on a Bruker ACF instrument. IR spectra were recorded on a Jasco 5300 spectrophotometer. All reactions were carried out in an inert atmosphere of dry nitrogen using standard syringe-septum techniques with magnetic stirring. Workup means drying of the combined organic extracts with $MgSO_4$, filtration, and concentration of the crude residue in vacuo. All reagents and solvents were dried and distilled prior to use. The synthesis of those acids from **10**−**16** is detailed here, whenever there was a significant variation from the published procedures.

4-(Methoxycarbonyl)-1-cubanecarboxylic Acid (13)[20f] was prepared in 80% yield according to the published procedure.

4-Chloro-1-cubanecarboxylic Acid (10).[20d] The acid chloride of **13** (110 mg, 0.5 mmol), prepared by the treatment of acid **13** (110 mg, 0.5 mmol) with $SOCl_2$, in dry CCl_4 (2.5 mL), was added dropwise to an irradiated (300 W tungsten lamp) suspension of the anhydrous sodium salt of *N*-hydroxypyridine-2-thione (90 mg, 0.6 mmol) and a catalytic amount of DMAP in CCl_4 (5 mL) and refluxed for 3 h. The mixture was cooled and then poured into a separatory funnel, diluted with Et_2O (5 mL), and washed with H_2O (3 × 3 mL). The aqueous layer was extracted with Et_2O (3 × 3 mL). Workup afforded the methyl ester whose saponification with methanolic NaOH yielded 50 mg (55%) of chloro acid **10**. IR (cm^{-1}): 1682, 1622. ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.20−4.25 (m, 6H, cubyl H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 45.9 and 54.0 (cubyl CH), 56.0 and 70.8 (cubyl C), 177.0 (C═O).

4-Bromo-1-cubanecarboxylic Acid (11).[20b] To a solution of 1-bromopentacyclo[4.3.0.0^{2,5}0^{3,8}0^{4,7}]nonan-9-one-4-carboxylic acid ethylene ketal (1.0 g, 3.3 mmol), prepared in 70% yield as described previously,[20a] in boiling CH_2Br_2 (25 mL) containing red HgO (0.8 g, 3.7 mmol) was added dropwise a solution of Br_2 (0.80 g, 0.3 mL, 5 mmol) in CH_2Br_2 (10 mL). When the addition was complete, the mixture was heated at reflux for 3 h, cooled to room temperature, and filtered. The CH_2Br_2 was removed in vacuo to give a brown solid which was extracted with hexane. Evaporation of hexane afforded 700 mg (75%) of 1,4-dibromopentacyclo[4.3.0.0^{2,5}0^{3,8}0^{4,7}]nonan-9-one ethylene ketal. This ketal was hydrolyzed with 80% H_2SO_4 followed by Favorskii rearrangement with 50% KOH to yield 375 mg (50%) of bromo acid **11**. IR (cm^{-1}): 1684, 1623. ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.29−4.34 (m, 6H, cubyl H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 47.7 and 54.6 (cubyl CH), 56.0 and 62.8 (cubyl C), 176.8 (C═O).

4-Iodo-1-cubanecarboxylic Acid (12).[20g] To a degassed solution of the acid ester **13** (56 mg, 0.25 mmol) in benzene (12 mL) were added $Pb(OAc)_4$ (140 mg, 0.32 mmol) and I_2 (152 mg, 0.6 mmol). The resultant mixture was brought to reflux and irradiated with a 300 W tungsten lamp. After 3 h, the solution was cooled, filtered, washed with aqueous $NaHSO_3$ solution (3 × 10 mL), and dried ($MgSO_4$) and the bulk of the benzene was removed. The methyl ester was hydrolyzed to yield 55 mg (80%) of iodo acid **12**. IR (cm^{-1}): 1670, 1636. ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.30−4.50 (m, 6H, cubyl H).

Cubanecarboxylic Acid (14)[20f] was prepared in 50% yield from acid ester **13**.

4-Phenyl-1-cubanecarboxylic Acid (15).[20g] To a degassed solution of the acid ester **13** (112 mg, 0.5 mmol) in dry deoxygenated benzene (12 mL) was added $Pb(OAc)_4$ (280 mg, 0.625 mmol). The resultant mixture was brought to reflux and irradiated with a 300 W tungsten lamp. After 3 h, the solution was cooled, filtered, washed with $NaHSO_3$ solution (3 × 10 mL), and dried ($MgSO_4$) and the bulk of the benzene removed to yield the methyl ester which was saponified to give 34 mg (30%) of phenylcubanecarboxylic acid (**15**). IR (cm^{-1}): 1680. ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.21−4.41 (m, 6H, cubyl H), 7.22−7.48 (m, 5H, phenyl H).

4-(Carboxamido)-1-cubanecarboxylic Acid (16). To a solution of acid ester **13** (56 mg, 0.25 mmol) in dry ether was added aqueous ammonia solution (2 mL, 30%), and the mixture was stirred for 1 h to yield 43 mg (90%) of acid amide **16**. IR (cm^{-1}): 1660, 1610. ^{1}H NMR (200 MHz, DMSO-d_6): δ 4.00−4.10 (m, 6H, cubyl H).

X-ray Data Collection and Crystal Structure Determinations. X-ray data for acids **10**−**16** were collected on an Enraf-Nonius CAD-4 single-crystal diffractometer in the $\theta/2\theta$ scan mode using graphite monochromatized Cu Kα radiation at room temperature. Structure solution was performed by SIR92, and the RAELS program was used for the refinement.[24] A DEC Alpha-AXP workstation was used for these calculations. All interatomic distance and related calculations were carried out with Platon97.[25] The acidic H atom positions were revealed in the ordered acids **10** and **13,** but only calculated positions were used in the refinements because of irregularities that occurred when these positions were refined. For the disordered acids, half H atoms were placed in calculated positions.

Calculations. All calculations were carried out on Indigo Solid Impact and Indy workstations from Silicon Graphics. In the Crystal Packer and Diffraction Crystal (Cerius^2)[26] calculations, the Dreiding 2.21 force field was used.

Results and Discussion

Cubane acids **10**−**16** were synthesized as described above.[20,21c] Crystallization was attempted from a variety of organic solvents (acetonitrile, benzene, chloroform, dichloromethane, dioxane, ethyl acetate, formic acid, tetrahydrofuran, and mixtures of these solvents). X-ray quality crystals were obtained from the solvents listed in Table 1. The crystal structures of acids **7** and **10**−**16** are now described. The three halogenated cubanecarboxylic acids **10**−**12**, the acid ester **13**, and the diacid **7** contain catemer **6** and are discussed first. In the mono- and phenyl-substituted acids **14** and **15** described next, the common carboxy dimer **3** is present. Finally, we note that the acid amide **16** forms the heterodimer **22**. Computational results provide a better understanding of why different packing arrangements are adopted in this family of cubanecarboxylic acids.

(20) (a) Chapman, N. B.; Key, J. M.; Toyne, K. J. *J. Org. Chem.* **1970**, *35*, 3860. (b) Klunder, A. J. H.; Zwanenburg, B. *Tetrahedron* **1972**, *28*, 4131. (c) Edward, J. T.; Farrell, P. G.; Langford, G. E. *J. Am. Chem. Soc.* **1976**, *98*, 3075. (d) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901. (e) Moriarty, R. M.; Khosrowshahi, J. S. *J. Am. Chem. Soc.* **1989**, *111*, 8943. (f) Eaton, P. E.; Nordari, N.; Tsanaktsidis, J.; Upadhyaya, S. P. *Synthesis* **1995**, 501. (g) Della, E. W.; Head, N. J. *J. Org. Chem.* **1995**, *60*, 5303.

(21) It may be noted that the crystal structures of some cubanecarboxylic esters have been reported: (a) Cristiano, D.; Gable, R. W.; Lowe, D. A.; Tsanaktsidis, J. *Acta Crystallogr.* **1995**, *C51*, 1658. (b) Butcher, R. J.; Bashir-Hashemi, A.; Gilardi, R. D. *J. Chem. Crystallogr.* **1995**, *25*, 661. (c) Irngartinger, H.; Strack, S.; Gredel, F. *Liebigs. Ann.* **1996**, *311*, 315.

(22) (a) Eaton, P. E.; Cole, T. W. *J. Am. Chem. Soc.* **1964**, *86*, 962. (b) Eaton, P. E.; Cole, T. W. *J. Am. Chem. Soc.* **1964**, *86*, 3157.

(23) Aldrich Chemical Co., Milwaukee, WI, 42,124-3, $88/g.

(24) (a) SIR92: Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Polidori, G. *J. Appl. Crystallogr.* **1994**, *27*, 435. (b) RAELS: Rae, A. D. A Comprehensive Constrained Least Squares Refinement Program, University of New South Wales, 1989.

(25) Platon97: Spek, A. L. Bijvoet Center for Biomolecular Research, Vakgroep Kristal-en Structure-chemie, University of Utrecht.

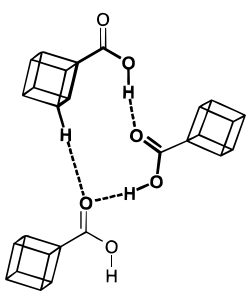
(26) Cerius^2 Program: Molecular Simulations, 9685 Scranton Road, San Diego, CA 92121-3752, and 240/250 The Quorum, Barnwell Road, Cambridge CB5 8RE, U.K.

Table 1. Crystallographic Data of 4-Substituted-1-cubanecarboxylic Acids

acid	space group	*a* (Å)	*b* (Å)	*c* (Å)	*β* (deg)	*Z*	R^b	$R_w{}^c$	density (g/cm^3)^d	solvent used for crystallization	melting point (°C)	$C_k{}^{*e}$
7[a]	$P2_1/n$	7.2512(6)	12.9050(12)	8.3031(5)	90.993(6)	4	0.042	0.051	1.64	formic acid	226	76.8
10	$P2_1/n$	7.175(4)	25.233(8)	8.394(4)	90.60(2)	8	0.045	0.057	1.60	formic acid	197 (dec)	73.0
11	$P2_1/c$	8.306(3)	7.261(2)	14.269(6)	113.13(2)	4	0.032	0.043	1.91	chloroform	178−183	72.3
12	$P2_1/c$	8.304(4)	7.341(2)	14.701(7)	113.11(2)	4	0.023	0.034	2.21	ethyl acetate	228 (dec)	72.5
13	$P2_1/n$	7.260(1)	30.507(3)	8.252(2)	90.724(9)	8	0.047	0.067	1.50	chloroform−ethyl acetate	154	73.6
14	$P2_1/c$	8.599(2)	11.131(2)	14.588(4)	94.68(1)	8	0.039	0.054	1.41	chloroform	120−123	71.5
15	$P2_1/c$	8.998(2)	13.605(2)	11.056(2)	123.448(9)	4	0.048	0.066	1.32	ethyl acetate−hexane	166−168	68.8
16	$Pca2_1$	9.944(1)	7.127(1)	12.723(2)	90	4	0.039	0.064	1.41	formic acid	215 (dec)	67.5

[a] From ref 12. [b] Crystallographic reliability index, $R = \sum|F_o - F_c|/\sum F_o$ for $F_o > 3\sigma(F_o)$. [c] Weighted residual $R_w = (\sum w\Delta^2/\sum wF_o^2)^{1/2}$. [d] Calculated with the program BLOCKLS. [e] Packing fraction $C_k{}^* = N(V_m/V_c)$, where N is the number of molecules is the unit cell, V_m is the volume of a single molecule, and V_c is the total volume of the unit cell (calculated with the program Platon97).[25]

Catemer Synthon 6 as a Recurring Pattern. The four carboxylic acids—chloro acid **10**, bromo acid **11**, iodo acid **12**, and acid ester **13**—are related in that they contain catemer **6** as the common hydrogen bond pattern. In 4-chloro-1-cubanecarboxylic acid (**10**), the alternating, symmetry-independent *syn* and *anti* carboxylic acid groups form the O−H···O catemer along [100]. Additionally, there are C−H···O hydrogen bonds between translation related molecules. These may be taken along with catemer **6**, to derive zigzag tapes that are constructed with two nearly identical patterns, **17** and **18**. Effectively, the larger



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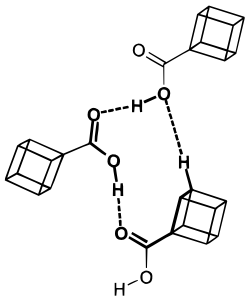

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patterns **17** and **18** contain within them the smaller **6**. In **17**, the C3−H of an *anti* molecule donates to the C═O group, while in **18**, the C3−H of a *syn* molecule donates to the carboxylic OH group (Figure 1, Table 2). This subtle difference between **17** and **18** arises from the fact that the patterns contain both *syn* and *anti* conformations and further because all carboxyl groups are ordered. The Cl atoms fill the centrosymmetric voids (Cl···Cl: 3.668(3) and 4.028(3) Å)[27] created by the rest of the packing and, in this manner, stabilize the overall crystal structure ($C_k{}^*$ = 73%, Table 1). Successive (001) layers are linked through C−H···O hydrogen bonds (2.65−2.88 Å), not shown in Figure 1b for clarity.

4-Bromo-1-cubanecarboxylic acid (**11**) (Figure 2) and 4-iodo-1-cubanecarboxylic acid (**12**) (Table 2) are isostructural and also adopt the catemer structure **6**, but here, the carboxylic acid groups are disordered (Table 3).[28] Since the C═O and the C−OH groups are now indistinguishable, **17** and **18** merge into a single pattern. The view down [100] in bromo acid **11** and iodo acid **12** (not shown) is identical to that down [001] in chloro acid **10**, with the minor difference that, while in **10** the carboxy groups stack on themselves (Figure 1b), they lie on the close-packed Br···Br and I···I atoms[27] of the next layer in **11** and **12** (Figure 2b). In addition to the hydrogen bonds shown in Figure 2, there are C−H···O bonds between the cubyl C3−H and the carboxyl O-atom and a long C−H···Br (3.108 Å, 169.5°) and

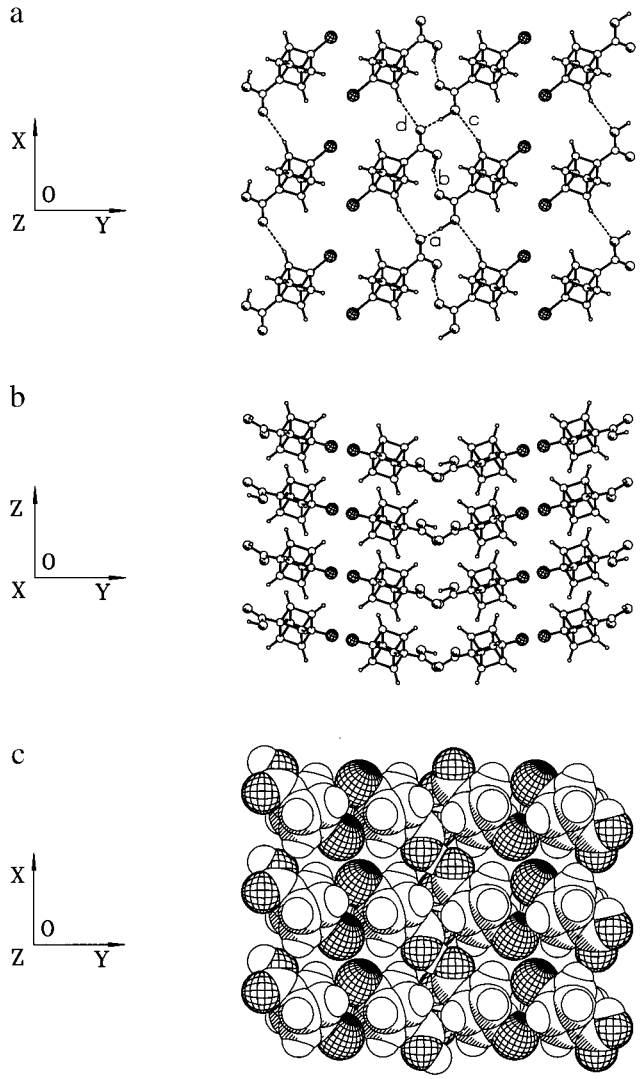


Figure 1. Crystal structure of 4-chloro-1-cubanecarboxylic acid (**10**). (a) View down [001] showing the layer with the zigzag arrangement of synthons **17** and **18**. Notice the type-I contact between the Cl atoms of inversion-related molecules. (b) View down [100] showing the packing of layers. (c) Space-filling diagram of the layer adjacent to that shown in (a) with atoms drawn acccording to their van der Waals radii. Notice that the Cl atoms fill the voids created by the catemer structure.

(27) In the type-I centrosymmetric geometry, it is possible that the inversion-related halogen atoms merely close pack rather than participate in specific polarization-driven interactions. (a) Pedireddi, V. R.; Reddy, D. S.; Goud, B. S.; Craig, D. C.; Rae, A. D.; Desiraju, G. R. *J. Chem. Soc., Perkin Trans. 2* **1994**, 2353. (b) Navon, O.; Bernstein, J.; Khodorkovsky, V. *Angew. Chem., Int. Ed. Eng.* **1997,** *36*, 601.

(28) (a) Diederich, D. A.; Paul, I. C.; Curtin, D. Y. *J. Am. Chem. Soc.* **1974**, *96*, 6372. (b) Goud, B. S.; Pathaneni, S. S.; Desiraju, G. R. *Acta Crystallogr.* **1993**, *C49*, 1107.

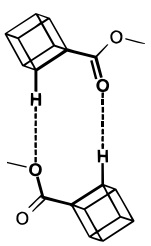
Table 2. Geometry of O−H···O and C−H···O Interactions in the Crystal Structures of Acids **10**−**16**

acid		interaction	d (Å)[a]	D (Å)[a]	θ (deg)[a]
10	a	O−H···O	1.664	2.623	164.2
	b	O−H···O	1.714	2.629	153.2
	c	C−H···O	2.373	3.40	157.4
	d	C−H···O	2.526	3.52	152.1
11	a	O−H···O[b]		2.698	
	b	O−H···O[b]		2.573	
	c	C−H···O	2.547	3.565	156.4
12	a	O−H···O[b]		2.696	
	b	O−H···O[b]		2.591	
	c	C−H···O	2.647	3.66	155.6
13	a	O−H···O	1.665	2.639	170.4
	b	O−H···O	1.670	2.616	160.1
	c	C−H···O	2.596	3.591	152.5
	d	C−H···O	2.447	3.478	158.7
	e	C−H···O	2.61	3.624	155.6
	f	C−H···O	2.514	3.554	160.7
	g	C−H···O	2.746	3.612	136.8
	h	C−H···O	2.747	3.594	134.9
	k	C−H···O	2.646	3.605	147.2
	l	C−H···O	2.697	3.634	144.5
14	a	O−H···O[b]		2.614	
	b	O−H···O[b]		2.645	
	c	C−H···O	2.789	3.784	152.7
	d	C−H···O	2.891	3.894	154.2
	e	C−H···O	2.830	3.747	142.4
15	a	O−H···O	1.660	2.643	179.2
	b	C−H···O	2.819	3.873	164.5
	c	C−H···O	2.826	3.638	131.8
	d	C−H···π	2.679	3.611	143.0
	e	C−H···O	2.944	3.972	158.6
16	a	O−H···O	1.627	2.604	171.9
	b	N−H···O	1.865	2.854	166.0
	c	N−H···O	1.994	2.922	151.7
	d	C−H···O	2.754	3.692	144.9
	e	C−H···O	2.482	3.484	153.3

[a] For the definitions of d, D, and θ, see ref 6d. All H atom positions are normalized (Rowland, R. S.; Taylor, R. *J. Phys. Chem.* **1996**, *100*, 7384). [b] The carboxylic acid groups are disordered.

C−H···I (3.157 Å, 169.6°) contact between the cubyl C2−H group and the halogen atoms of the next layer.

The carboxylic acid group in 4-(methoxycarbonyl)-1-cubanecarboxylic acid (**13**) (Figure 3) is ordered and **17** and **18** run along [100], as in chloro acid **10** (Table 2). Further, because of the carbomethoxy C═O group, translation related *syn* and *anti* molecules are connected by cyclic patterns **19** and **20** formed solely with cubyl C−H···O hydrogen bonds. So, one may analyze the hydrogen bonded layer parallel to (001) as constituted with different synthons depending on how one dissects the structure: (i) synthons **17** and **18** and zigzag C−H···O chains (interactions e and f) or (ii) synthon **6** accompanied by **19** and **20** (Figure 3a). Thus, there is an element of subjectivity



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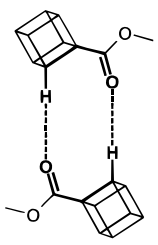

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in deciding which set of interactions constitutes the primary structural motif. This is generally true in complex crystal structures wherein a given interaction may form a part of several

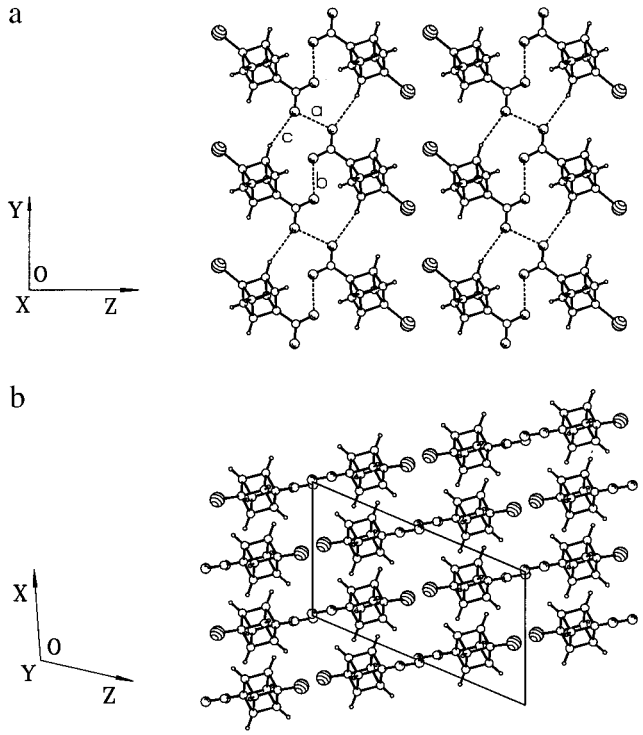


Figure 2. Crystal structure of 4-bromo-1-cubanecarboxylic acid (**11**). (a) Layer containing synthons **17** and **18** and the inversion-related Br···Br contacts. Notice the similarity with Figure 1a. (b) View down [010] to show the stacking of Br atoms and carboxylic acid groups in successive layers. Contrast this with Figure 1b where the stacking is Cl···Cl and CO_2H···CO_2H.

Table 3. Order−Disorder in Acids **7**−**16**

acid	Δd (Å)[a]	$\Delta\theta$ (deg)[b]	acid	Δd (Å)[a]	$\Delta\theta$ (deg)[b]
7	0.095	3.4	**13**	0.085	0.7
	0.089	9.0		0.089	4.2
10	0.088	3.3	**14**	0.002	1.8
	0.076	8.0		0.006	1.0
11	0.020	0.8	**15**	0.046	3.5
12	0.008	1.1	**16**	0.100	10.0

[a] $\Delta d = d_1 - d_2$. [b] $\Delta\theta = \theta_1 - \theta_2$. For more details, see ref 28.

overlapping synthons. However, one may state that synthons **17** and **18** combine compactness in size with completeness of structural information, and in this sense, they may be regarded as effective descriptors of the crystal structure.

It may be noted that the carboxylic acid group is ordered in acids **10** and **13** while it is disordered in **11** and **12**. It is unlikely that there is dynamic disorder along individual catemers since this would involve cooperative proton transfer. A more plausible explanation for the disorder is that it is static in nature and involves translationally related catemers.[29] The crystal structures of the ordered acids **10** and **13** and the disordered acids **11** and **12** offer a clue to the cause of order/disorder. In the former cases, catemer **6** is nonplanar and is stacked along [001] without offset (Figures 1b and 3b). In the latter, the catemer is planar and is stacked between the Br and I atoms of adjacent layers (Figure 2b).[8a] It should be noted here that the assignment of structures as ordered/disordered is not based on the H atom positions but on the particular intramolecular C−O distances

(29) This was verified with lattice energy calculations (Cerius[2]). Pairs of catemers were constructed with opposite senses, for the ordered and disordered acids. The difference in hydrogen bond energy between the two alternative catemer pair arrangements (parallel versus antiparallel) is large (∼10 kcal/mol) for the ordered acids, while it is very small for the disordered acids (<0.1 kcal/mol).

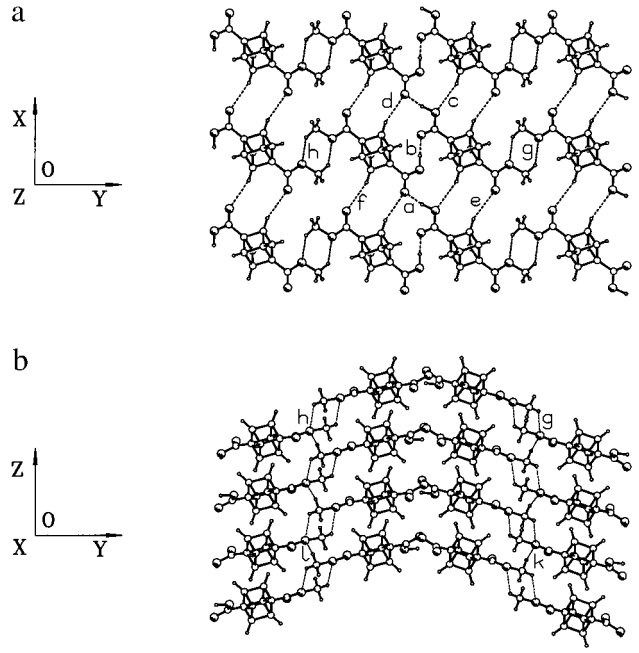
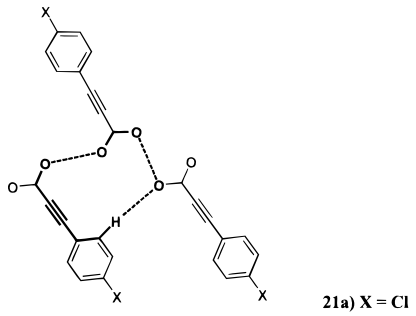


Figure 3. Crystal structure of 4-(methoxycarbonyl)-1-cubanecarboxylic acid (**13**). (a) View down [001] to show the zigzag arrangement of synthons **17** and **18**. Notice that the inversion-related CO_2Me groups play a space-filling role similar to that of the halogen atoms in **10**−**12**. (b) Stacking of the carboxylic acid and ester groups in successive (001) layers.

and angles (Table 3). The classical work of Paul and Curtin[28a] on carboxylic acid disorder justifies such a procedure.

The repeated occurrence of the otherwise rare synthon **6** in the family of carboxylic acids under study here is quite likely the result of fortification of the catemer by a weak hydrogen bond formed by the acidic cubyl C−H group. According to such an argument, if such a favorable C−H···O bond were absent, the catemer structure might not have been observed. In this connection, the crystal structures of 4-chlorophenylpropiolic acid (**21a**) and 4-bromophenylpropiolic acid (**21b**), reported earlier



21 **21a) X = Cl** **21b) X = Br**

by our group,[30] are also of interest (Figure 4a). These are the two other acids in the literature that show the *syn-anti* catemer **6** and here too the catemer is strengthened by a C−H···O bond, but now from a phenyl C(sp^2)−H group.

The efficacy of a supramolecular synthon as an indicator of crystal packing arises from its frequency of occurrence. However, another criterion that should be used while assessing the usefulness of synthons is that of size. Synthons represent a carryover of structural information between crystal structures, and as their size increases, so does their information content. So, larger synthons are potentially more useful than smaller ones (**17** and **18** as opposed to **6**). But, as synthon size increases, occurrence becomes less frequent and, in this sense, the twin criteria for identifying useful synthons seem to be contradictory. Despite this, it should be noted that, between these extremes of small size and numerous occurrences and large size and infrequent occurrences, *there lies an optimal region wherein the maximum structural information is contained in a synthon of minimum size*. It is in this domain then that the visualization of supramolecular synthons and comparison of crystal structures is most effectively accomplished.

To summarize, the primary structural motifs, synthons **17** and **18**, are characterized by a combination of the alternating *syn* and *anti* CO_2H groups and support from the enhanced acidity of the cubyl C−H donors. In this light, the crystal structure of diacid **7** also stands rationalized. It may simply be accounted for in terms of the symmetrical occurrence of synthons **17** and **18** on either side of the cubyl skeleton (Figure 4b). The recurring catemer synthon also determines the repeat distance of ca. 7.2 Å between successive cubane molecules in the five monoclinic crystal structures (**7**, $a = 7.2512(6)$ Å; **10**, $a = 7.175(4)$ Å; **11**, $b = 7.261(1)$ Å; **12**, $b = 7.341(2)$ Å; **13**, $a = 7.260(1)$ Å; Table 1). From the above results, it appears that this structure type is insensitive to substitution changes at the 4-position as long as the groups are of a similar bulk (R = Cl, Br, I, CO_2Me) or have an identical hydrogen bond pattern (R = CO_2H). This led us to examine the crystal structure of cubanecarboxylic acids with very small (R = H, **14**) and very large (R = Ph, **15**) substituents.

The assignment of the monoclinic space group $P2_1/n$ for acids **7**, **10**, and **13** may also be noted. In these cases, there are two independent molecules in the asymmetric unit and the β angles are 90.993(6)°, 90.60(2)°, and 90.724(9)°, respectively (Table 1). These symmetry-independent molecules are related by pseudo-2-fold symmetry along [001] with the pseudo-2-fold axes lying halfway between the inversion centers. These crystal structures thus have pseudo orthorhombic symmetry {$P2_1/c$, $P2_1/n$, $P2_1/b$} or simply *Pcnb*.

Carboxy Dimer Synthon 3 in Acids 14 and 15. Cubanecarboxylic acid **14** adopts the normal dimer **3**. The CO_2H group is disordered,[28] and there are two molecules, A and B, in the asymmetric unit (Figure 5). Unusually, the dimers are of the A···B type (O···O: 2.614, 2.645 Å, Table 2). The dimers are staggered so that a cubyl group lies above an adjacent dimer. Layers parallel to (100) are linked through C−H···O hydrogen bonds between inversion-related dimers. The symmetry-independent A and B molecules form different types of C−H···O bonds.[31]

In 4-phenyl-1-cubanecarboxylic acid (**15**), the dimers lie on inversion centers (Figure 6a). The participation of phenyl and cubyl C−H donors in C−H···O bonding with the carboxy O atom leads to a bifurcated pattern. The (010) layers are formed with cubyl C−H···O and C−H···π(Ph)[32] hydrogen bonds (Figure 6b, Table 2). Consideration of the crystal structures of **14** and **15** suggests that there is a limit to which the catemer structure will manifest itself in this family of acids. As long as the steric requirements of the 4-substituent group are compatible with the O−H···O catemer **6**, it is observed. However, when the substituent group is too small or too large, the dimer is adopted because its formation is largely independent of the size

(30) (a) Desiraju, G. R.; Murty, B. N.; Kishan, K. V. R. *Chem. Mater.* **1990**, *2*, 447. (b) Goud, B. S.; Desiraju, G. R. *Acta Crystallogr.* **1993**, *C49*, 292.

(31) The packing features in acid **14** show some resemblance to those found in 1,4-dicubyl-1,3-butadiyne. Eaton, P. E.; Galoppini, E.; Gilardi, R. *J. Am. Chem. Soc.* **1994**, *116*, 7588.

(32) Madhavi, N. N. L.; Katz, A. K.; Carrell, H. L.; Nangia, A.; Desiraju, G. R. *Chem. Commun.* **1997**, 1953.

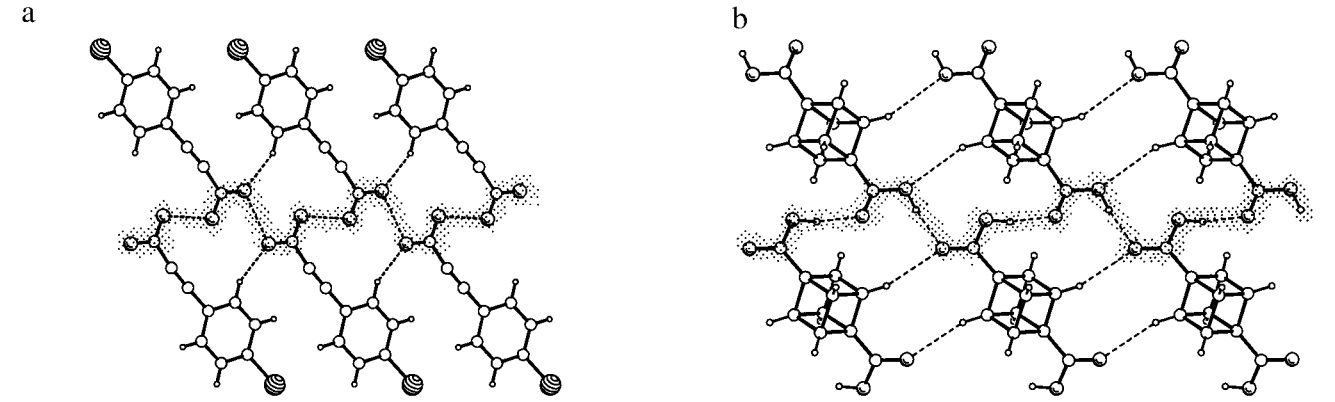


Figure 4. (a) Crystal structure of 4-(bromophenyl)propiolic acid **21b** to show the supportive role of the C(sp^2)-H···O hydrogen bond to the catemer synthon **6**. (b) Crystal structure of 1,4-cubanedicarboxylic acid (**7**) showing the symmetrical arrangement of synthons **17** and **18** on both sides of the cubyl residue. Compare the two figures.

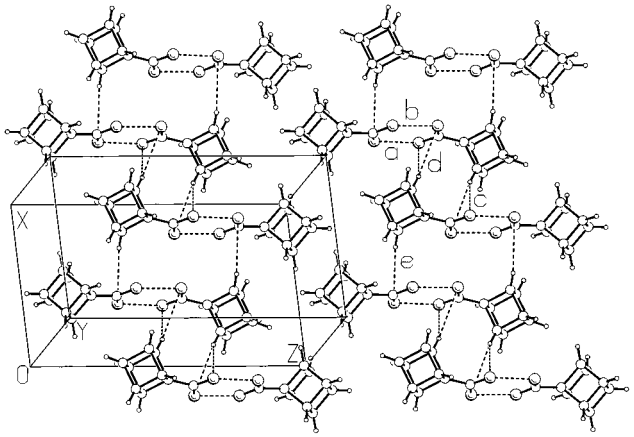


Figure 5. Packing diagram of the crystal structure of cubanecarboxylic acid **14** to show O−H···O and C−H···O hydrogen bonds. The dimers are formed by symmetry-independent molecules. Notice that one of the cubyl C−H atoms forms a bifurcated hydrogen bond (sum of angles at the donor atom = 353.1°).

and shape of the substituent group.[8a] In addition to the supportive role of the C−H···O hydrogen bonds in **10**−**13**, the formation of the catemer in these structures also depends on size complementarity of the hydrophobic groups that enables them to fill the voids in the structure.

The nonformation of the catemer structure in cubanecarboxylic acid **14** was next investigated computationally. The Cl atoms in the observed crystal structure of chloro acid **10** were replaced by H atoms, and the structure was minimized (Crystal Packer, Cerius^2)[26] to obtain a putative catemer structure. The calculated structure contains voids in the hydrophobic region because the rigid cubyl groups are unable to close pack efficiently. Similarly, if phenylcubanecarboxylic acid (**15**) were to have a catemer structure with a translational repeat distance of ca. 7.2 Å, the bulky phenyl groups will approach too close to one another, resulting in unfavorable repulsions.[33] Having examined the role of size- and shape-related features that favor specific

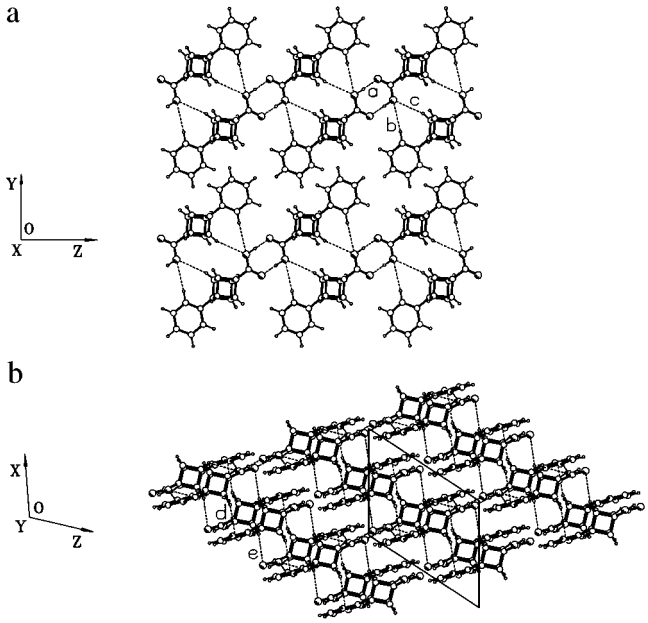
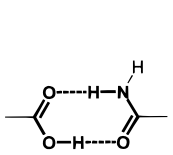


Figure 6. Crystal structure of 4-phenyl-1-cubanecarboxylic acid (**15**). (a) Formation of the centrosymmetric carboxy dimer **3** fortified by auxiliary cubyl and phenyl C−H···O hydrogen bonds. (b) View down [010] showing the connections through C−H···O and C−H···π interactions between the (100) layers.

O−H···O and C−H···O hydrogen bond patterns in cubanecarboxylic acids, we decided to introduce a functional group that has a strong and distinct hydrogen bonding capability of its own. Thus, the 4-carboxamide derivative (R = $CONH_2$, **16**) was examined finally.

NbO-Type Network in the Crystal Structure of Acid Amide 16. The crystal structure of 4-(carboxamido)-1-cubanecarboxylic acid (**16**) is non-centrosymmetric ($Pca2_1$) (Table 1). The dominant hydrogen bond pattern is the heterodimer



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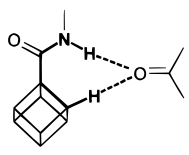

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between the carboxylic acid and carboxamide groups. Heterodimer **22** is commonly found in acid−amide complexes as well as in molecules containing both these functional groups.[34]

(33) Interestingly, it was found that when syn and anti conformers were input together in the Polymorph Predictor program (Cerius^2), the unobserved catemer structure was not generated for either **14** or **15**. This computation provides some corroboration for the occurrence of dimer structure in **14** and **15**. For details on generating structures using the Polymorph Predictor, see: (a) Leusen, F. J. J. *J. Cryst. Growth* **1996**, *166*, 900. (b) Payne, R. S., Roberts, R. J., Rowe, R. C.; Docherty, R. *J. Comput. Chem.* **1998**, *19*, 1. (c) Mooij, W. T. M.; van Eijck, B. P.; Price, S. L.; Verwer, P.; Kroon, J. *J. Comput. Chem.* **1998**, *19*, 459. For an early computational study on the "nonexistence" of a proposed structure, see: Hagler, A. T.; Bernstein, J. *J. Am. Chem. Soc.* **1978**, *100*, 6349.

The formation of such a heterodimer as opposed to acid···acid and amide···amide homodimers may be argued on the following grounds: (i) The principle that a good hydrogen bond donor will seek out the best acceptor atom.[35] Thus, the strongest donor (acid OH) hydrogen bonds to the strongest acceptor (amide C═O) while the slightly weaker donor (amide NH) bonds to the weaker acceptor group (acid C═O). (ii) To avoid intermolecular lone-pair repulsion between the hydroxyl and carbonyl O atoms that occurs in hydrogen bonded chains built from homodimers and connected through N−H···O hydrogen bonds. In the heterodimer arrangement, the distance between neighboring N−H groups hydrogen bonded to the same amide O atom increases and consequently the lone-pair repulsion is minimized.[8a,36]

In acid amide **16**, heterodimers **22** are formed between 2_1 related molecules to produce ribbons along [012] and [01$\bar{2}$]. The amide groups of these heterodimers are in turn connected through N−H···O and C−H···O hydrogen bonds with the *a*-glide related molecules, as shown in **23**.[37,38] Visualizing the crystal structure of **16** in terms of networks,[1d,5b] with the molecules represented as nodes and the supramolecular synthons as node connectors, one can discern the similarity between the four-connected three-dimensional architecture of **16** and the NbO network.[39] This is illustrated as a stereoview in Figure 7. To our knowledge, acid amide **16** is the first all-organic molecule whose crystal structure has been reported to contain the NbO network. Coordination polymers have been recently found that exhibit the NbO architecture.[40] In **16**, however, there is two-fold interpenetration with the networks being linked through a C−H···O hydrogen bond (2.482 Å, 153.3°).

A pertinent issue is the extent to which the abovementioned arguments are valid if polymorphism were to be widespread in the family of structures studied here, especially if the same acid crystallizes in both dimer and catemer forms. The powder X-ray diffraction pattern of 1,4-cubanedicarboxylic acid (**7**) recrystallized from formic acid was recorded. The powder pattern closely matches the pattern simulated from the observed crystal structure using Diffraction Crystal (Cerius^2),[26] confirming that the crystals of diacid **7** that were analyzed by X-ray diffraction represent the bulk sample. Interestingly, when diacid **7** was recrystallized from a mixture of ethyl acetate and hexane, a solvent system very different from formic acid, the crystals still have the same structure. These experiments suggest that the observed catemer structure is the dominant form in these cases. Solubility considerations prevented further recrystallization experiments from other solvents.

Conclusions

Some selected 4-substituted-1-cubanecarboxylic acids have been synthesized and their packing characteristics examined.

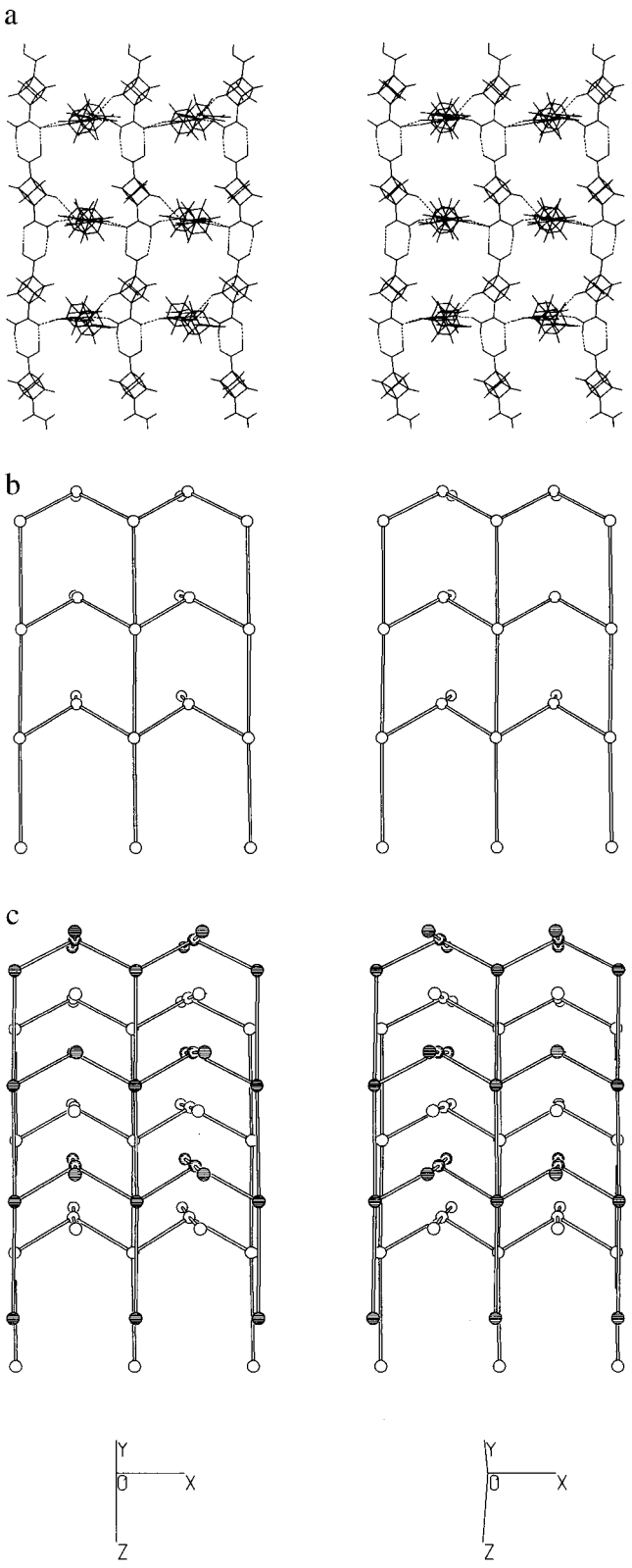

Figure 7. Stereoviews of the crystal structure of 4-(carboxamido)-1-cubanecarboxylic acid (**16**). (a) Actual structure showing heterodimer **22**, N−H···O and C−H···O hydrogen bonds. The heterodimer ribbons along [012] and [01$\bar{2}$] are identical. The N−H···O and C−H···O interactions run along [001]. (b) Structure depicted as a four-connected NbO network. The molecules are reduced to spheres and the supramolecular synthons to double lines. (c) Two-fold interpenetration of networks. The two networks are connected through C−H···O hydrogen bonds (not shown for clarity). The spheres in the two networks are shaded differently.

(34) (a) Leiserowitz, L.; Nader, F. *Acta Crystallogr.* **1977**, *B33*, 2719. (b) Chang, Y.-L.; West, M.-A.; Fowler, F. W.; Lauher, J. W. *J. Am. Chem. Soc.* **1993**, *115*, 5991. (c) Wash, P. L.; Maverick, E.; Chiefari, J.; Lightner, D. A. *J. Am. Chem. Soc.* **1997**, *119*, 3802.

(35) Etter, M. C. *Acc. Chem. Res.* **1990**, *23*, 120.

(36) Leiserowitz, L.; Hagler, A. T. *Proc. R. Soc. London* **1983**, *A388*, 133.

(37) For the crystal structure of *N*,*N*′-dibenzyl-1,4-cubanedicarboxamide, see ref 2b.

(38) This and other synthons may also be represented in the graph set notation (Bernstein, J.; Davis, R. E.; Shimoni, L.; Chang, N.-L. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1555): **4**−**6** as C(4), **3** and **22** as $R_2^2(8)$, **17** and **18** as $R_3^3(12)$, **19** and **20** as $R_2^2(10)$, and **23** as $R_2^1(7)$.

(39) Wells, A. F. *Structural Inorganic Chemistry*, 4th ed.; Clarendon Press: Oxford, U.K., 1975.

(40) (a) Power, K. N.; Hennigar, T. L.; Zaworotko, M. J. *Chem. Commun.* **1998**, 595. (b) Carlucci, L.; Ciano, G.; Macchi, P.; Proserpio, D. M. *Chem. Commun.* **1998**, 1837.

Of the seven crystal structures analyzed, four contain the unusual *syn-anti* O−H···O catemer **6**. This pattern is extremely rare in general (3 out of 2067 carboxylic acids, of which one is diacid **7**) but is found to be the dominant pattern in the particular family of acids studies here. The formation of synthon **6** is attributed to its stabilization from C−H···O hydrogen bonds formed by the acidic cubyl C−H donors and the carboxyl O-acceptor atoms. This study shows that two new synthons, **17** and **18** constructed with a combination of strong and weak hydrogen bonds are the primary structural motifs that determine the supramolecular architecture in these acids. The identification of these synthons is a prerequisite for the crystal engineering of cubanecarboxylic acids toward nanostructures with well-defined architectures and functions.

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Supporting Information Available: ORTEP diagrams and tables giving crystal data and structure refinement, atomic coordinates, isotropic and anisotropic displacement parameters, and bond lengths and angles for **10**−**16** (PDF). An X-ray crystallographic file, in CIF format, is also available. This material is available free of charge via the Internet at http://pubs.acs.org.

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