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Crystallographic Evidence for the Existence of C–H···O, C–H···N, and C–H···Cl Hydrogen Bonds

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Abstract: A survey of 113 published neutron diffraction crystal structures is described. The major results are as follows. Hydrogen atoms that are covalently bonded to carbon have a statistically significant tendency to form short intermolecular contacts to oxygen atoms rather than to carbon or hydrogen atoms. This phenomenon is probably due to electrostatic stabilization of the short C—H···O contacts. The proton in the majority of short C—H···O contacts lies within 30° of the plane containing the lone-pair orbitals of the oxygen atom. C–H groups that are adjacent to nitrogen atoms are particularly likely to participate in short C—H···O interactions, but the environment of the oxygen atom is unimportant. The crystal structures also contain several short, intermolecular C—H···N and C—H···Cl contacts. It is concluded that the C—H···O, C—H···N, and C—H···Cl interactions are more likely to be attractive than repulsive and can reasonably be described as hydrogen bonds.

The ability of carbon atoms to act as proton donors in hydrogen bonds has been the subject of controversy for many years. Spectroscopic studies[2-4] indicate that C—H···X hydrogen bonds occur in many systems, a conclusion that is supported by quantum mechanical[5-8] and empirical potential energy calculations.[9] (The symbol X is used throughout the text to denote a hydrogen bond acceptor atom, i.e., O, N, Cl, or S). However, the crystallographic evidence for C—H···X hydrogen bonding is sparse and circumstantial. A survey of crystal structures containing short C—H···O contacts was conducted by Sutor in 1963.[10] She concluded that the short contacts could best be described as hydrogen bonds, but this interpretation was later challenged by Donohue.[11] In the last 10 years, C—H···X (especially C—H···O) hydrogen bonds have been postulated in many crystal structures, particularly those of nucleosides[12] and amino acids.[13] However, to the best of our knowledge, no further systematic survey of the crystallographic data has been carried out. We have therefore conducted such a survey, with a view to answering the following questions: (1) What crystallographic evidence is there for the existence of C—H···X hydrogen bonds? (2) In what types of crystal structures are they likely to occur?

Crystallographic Data

The crystallographic data used in the survey were retrieved from the Cambridge Structural Database.[14] A total of 113 organic crystal structures were used (Table I). They contain 661 crystallographically independent (C–)H atoms (the symbol (C–)H is used throughout the text to denote a hydrogen atom that is covalently bonded to carbon). The criteria used to select the structures were as follows: (1) All of the structures were determined by neutron diffraction, since the survey depends on an accurate knowledge of the (C–)H atomic positions. (2) Each structure contains at least one (C–)H atom and at least one potential hydrogen bond acceptor atom (O, N, Cl, S). (3) Structures with R factors greater than 0.10, or which were determined from very limited data, or which exhibit disorder, were excluded. (4) Structures which were determined at low temperatures, or which contain deuterated species, were included in the survey. Both factors might have a slight effect on the observed (C–)H atom geometries.[15] However, the number of structures involved is small (about 15% of the total sample), and they were considered to be of sufficient chemical interest to warrant their inclusion.

Crystallographic Evidence for the Existence of C—H···O Hydrogen Bonds

We consider first the crystallographic evidence for the C—H···O hydrogen bond. C—H···N, C—H···Cl, and C—H···S interactions are discussed in the following section.

Nearest-Neighbor Contacts of (C–)H Atoms. The most important geometrical characteristic of hydrogen bonds is that the distance between the proton and the acceptor atom is shorter than the sum of their van der Waals radii.[16] We therefore began our investigation by calculating the "nearest-neighbor contact" of each (C–)H atom in the sample. The "nearest-neighbor contact", (C–)H···Y, is defined here as the shortest contact formed by the (C–)H atom, relative to the sum of the corresponding van der Waals radii, i.e., the contact for which the value of d in the following equation is a maximum:

$$d = v(\mathrm{H}) + v(\mathrm{Y}) - r(\mathrm{H}\cdots\mathrm{Y}) \qquad (1)$$

(v(H) = van der Waals radius of (C–)H; v(Y) = van der Waals radius of Y; r(H···Y) = (C–)H···Y interatomic distance). Only intermolecular contacts were considered at this stage, because short intramolecular interactions may sometimes be due to geometrical constraints within the molecule. Contacts with C—H···Y angles of less than 90° were ignored, as it is generally accepted that the donor–proton–acceptor angle in a hydrogen bond must be at least 90°. The van der Waals radii used were as follows: C = 1.75, H = 1.20,[17] Br = 1.85, Cl = 1.75, N = 1.55, O = 1.50, P = 1.80, S = 1.80 Å. They are based on the values given by Bondi[18] and Kitaigorodsky.[19] In view of the difficulty of assigning reliable van der Waals radii to metal ions,[18] contacts to Li$^+$, Na$^+$, K$^+$, Rb$^+$, Ca^{2+}, and Ba^{2+} were ignored.

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(1) External staff, Medical Research Council.

(2) Green, R. D. "Hydrogen Bonding by C—H groups"; Wiley Interscience: New York, 1974.

(3) Ts'o, P. O. P.; Kondo, N. S.; Schweizer, M. P.; Hollis, D. P. *Biochemistry* **1969**, *8*, 997–1029.

(4) Harmon, K. M.; Gennick, I.; Madeira, S. L. *J. Phys. Chem.* **1974**, *78*, 2585–2591.

(5) Kollman, P.; McKelvey, J.; Johansson, A.; Rothenberg, S. *J. Am. Chem. Soc.* **1975**, *97*, 955–965.

(6) Umeyama, H.; Morokuma, K. *J. Am. Chem. Soc.* **1977**, *99*, 1316–1332.

(7) Vishveshwara, S. *Chem. Phys. Lett.* **1978**, *59*, 26–29.

(8) Gay, R.; Vanderkooi, G. *J. Chem. Phys.* **1981**, *75*, 2281–2289.

(9) Leiserowitz, L., private communication.

(10) Sutor, D. J. *J. Chem. Soc.* **1963**, 1105–1110.

(11) Donohue, J. In "Structural Chemistry and Molecular Biology"; Rich, A., Davidson, N., Eds.; W. H. Freeman: San Francisco, 1968; pp 459–463.

(12) Saenger, W. *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 591–601.

(13) Jeffrey, G. A.; Maluszynska, H. *Int. J. Biol. Macromol.* **1982**, *4*, 173–185.

(14) Allen, F. H.; Bellard, S.; Brice, M. D.; Cartwright, B. A.; Doubleday, A.; Higgs, H.; Hummelink, T.; Hummelink-Peters, B. G.; Kennard, O.; Motherwell, W. D. S.; Rodgers, J. R.; Watson, D. G. *Acta Crystallogr., Sect. B* **1979**, *B35*, 2331–2339.

(15) Takusagawa, F.; Koetzle, T. F. *Acta Crystallogr., Sect. B* **1979**, *B35*, 2126–2135.

(16) Hamilton, W. C.; Ibers, J. A. "Hydrogen Bonding in Solids"; W. A. Benjamin: New York, 1968.

(17) One of the referees has pointed out that Baur (Baur, W. H. *Acta Crystallogr., Sect. B* **1972**, *B28*, 1456–1465) gives a value of 1.0 Å for the van der Waals radius of hydrogen. However, this value was derived for hydrogen atoms that are covalently bonded to electronegative elements such as oxygen. Molecular mechanics calculations[34] suggest that a larger radius should be used for (C–)H atoms that for (O–)H or (N–)H atoms.

(18) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441–451.

(19) Kitaigorodsky, A. I. "Molecular Crystals and Molecules"; Academic Press: London, 1973.

Table I. Bibliography

1	beta-D,L-Arabinopyranose (ABINOR01)	S.Takagi,S.Nordenson,G.A.Jeffrey,Acta Cryst.,B35,991,1979.
2	beta-L-Arabinose (ABINOS01)	S.Takagi,G.A.Jeffrey,Acta Cryst.,B33,3033,1977.
3	Acetamide (ACEMID03)	G.A.Jeffrey,J.R.Ruble,R.K.McMullan,D.J.DeFrees,J.S.Binkley,J.A.Pople, Acta Cryst.,B36,2292,1980.
4	Acetic acid (ACETAC03)	P.-G.Jonsson,Acta Cryst.,B27,893,1971.
5	Chloroacetiminium chloride (ACNITR20)	J.M.Williams,S.W.Peterson,G.M.Brown,Inorg.Chem.,7,2577,1968.
6	N-Acetylglycine (ACYGLY11)	M.F.Mackay,Cryst.Struct.Comm.,4,225,1975.
7	Ammonium glycinium sulfate (AGLYSL01)	S.Vilminot,E.Philippot,M.Lehmann,Acta Cryst.,B32,1817,1976.
8	3-Amino-1,6-anhydro-3-deoxy-beta-D-glucopyranose (AHXGLP)	J.H.Noordik,G.A.Jeffrey,Acta Cryst.,B33,403,1977.
9	2-Amino-5-chloropyridine (AMCLPY11)	A.Kvick,R.Thomas,T.F.Koetzle,Acta Cryst.,B32,224,1976.
10	Ammonium tartrate (AMTART11)	V.S.Yadava,V.M.Padmanabhan,Pramana,6,94,1976.
11	2,4-Diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine (AMXBPM10)	T.F.Koetzle,G.J.B.Williams,J.Am.Chem.Soc.,98,2074,1976.
12	L-Arginine dihydrate (ARGIND11)	M.S.Lehmann,J.J.Verbist,W.C.Hamilton,T.F.Koetzle,J.Chem.Soc.,Perkin 2, 133,1973.
13	L-Asparagine monohydrate (ASPARM02)	J.J.Verbist,M.S.Lehmann,T.F.Koetzle,W.C.Hamilton,Acta Cryst.,B28,3006, 1972.
14	Barium methacrylate monohydrate (BAMACR)	N.W.Isaacs,J.J.van der Zee,K.G.Shields,J.V.Tillack,D.H.Wheeler, F.H.Moore,C.H.L.Kennard,Cryst.Struct.Comm.,1,193,1972.
15	Barbituric acid dihydrate (BARBAD01)	A.R.Al-Karaghouli,B.Abdul-Wahab,E.Ajaj,S.Al-Asaff,Acta Cryst.,B33,1655, 1977.
16	Calcium formate (CAFORM07)	M.O.Bargouth,G.Will,Cryst.Struct.Comm.,9,605,1980.
17	Calcium malonate dihydrate (CAMALD03)	J.Albertsson,A.Oskarsson,C.Svensson,Acta Cryst.,B34,2737,1978.
18	2,5-Dichlorobenzenesulfonic acid trihydrate (CBZSUL01)	J.Roziere,J.M.Williams,J.Chem.Phys.,68,2896,1978.
19	Cyclodecane-1,6-trans-diol (CDECOL11)	O.Ermer,J.D.Dunitz,I.Bernal,Acta Cryst.,B29,2278,1973.
20	N-(2-Chloroethyl)-D-gluconamide (CEGLCA01)	A.C.Sindt,M.F.Mackay,Acta Cryst.,B33,2659,1977.
21	Chloral hydrate (CHORLH01)	G.M.Brown,H.A.Levy,Cryst.Struct.Comm.,2,107,1973.
22	L-Cysteic acid monohydrate (CYSTAC01)	M.Ramanadham,S.K.Sikka,R.Chidambaram,Acta Cryst.,B29,1167,1973.
23	L-Cystine dihydrochloride (CYSTCL02)	D.D.Jones,I.Bernal,M.N.Frey,T.F.Koetzle,Acta Cryst.,B30,1220,1974.
24	Cytosine monohydrate (CYTOSH)	H.P.Weber,B.M.Craven,R.K.McMullan,Acta Cryst.,B36,645,1980.
25	1,3-Diphenyl-1-propenol-3-one (DBEZLM02)	R.D.G.Jones,Acta Cryst.,B32,1807,1976.
26	N,N-Dimethyl-nitramine (DDMNTM)	A.Filhol,G.Bravic,M.Rey-Lafon,M.Thomas,Acta Cryst.,B36,575,1980.
27	5,5-Diethylbarbituric acid (DETBAA04)	R.K.McMullan,R.O.Fox Junior,B.M.Craven,Acta Cryst.,B34,3719,1978.
28	1,3-Diethyl-2-thiobarbituric acid (DETSBR01)	J.-P.Bideau,G.Bravic,A.Filhol,Acta Cryst.,B33,3847,1977.
29	DL-Serine (DLSERN11)	M.N.Frey,M.S.Lehmann,T.F.Koetzle,W.C.Hamilton,Acta Cryst.,B29,876,1973.
30	Dimethylammonium hydrogen oxalate (DMAHOX01)	J.O.Thomas,Acta Cryst.,B33,2867,1977.
31	Dimethylsulfone di-imine (DMSDIM01)	E.Prince,Acta Cryst.,B31,2536,1975.
32	5-Sulfosalicylic acid dideuterate (DSSALD10)	R.Attig,J.M.Williams,J.Chem.Phys.,66,1389,1977.
33	Di-t-butylphosphinic acid (DTBUPA01)	A.H.Reis Junior,S.W.Peterson,M.E.Druyan,E.Gebert,G.W.Mason,D.F.Peppard, Inorg.Chem.,15,2748,1976.
34	Ethylenediammonium D-tartrate (EDATAR01)	C.K.Fair,E.O.Schlemper,Acta Cryst.,B33,1337,1977.
35	beta-D-Fructopyranose (FRUCTO02)	S.Takagi,G.A.Jeffrey,Acta Cryst.,B33,3510,1977.
36	Glycylglycine hydrochloride monohydrate (GLCICH01)	T.F.Koetzle,W.C.Hamilton,R.Parthasarathy,Acta Cryst.,B28,2083,1972.
37	Glycollic acid (GLICAC10)	R.D.Ellison,C.K.Johnson,H.A.Levy,Acta Cryst.,B27,333,1971.
38	alpha-D-Glucose (GLUCSA01)	G.M.Brown,H.A.Levy,Acta Cryst.,B35,656,1979.
39	L-Glutamine (GLUTAM01)	T.F.Koetzle,M.N.Frey,M.S.Lehmann,W.C.Hamilton,Acta Cryst.,B29,2571, 1973.
40	Glycine (GLYCIN03)	P.-G.Jonsson,A.Kvick,Acta Cryst.,B28,1827,1972.
41	Glycine (GLYCIN16)	A.Kvick,W.M.Canning,T.F.Koetzle,G.J.B.Williams,Acta Cryst.,B36,115, 1980.
42	Glycylglycine (GLYGLY04)	A.Kvick,A.R.Al-Karaghouli,T.F.Koetzle,Acta Cryst.,B33,3796,1977.
43	Glycine hydrochloride (GLYHCL)	A.R.Al-Karaghouli,F.E.Cole,M.S.Lehmann,C.F.Miskell,J.J.Verbist, T.F.Koetzle,J.Chem.Phys.,63,1360,1975.
44	6-Hydroxy-1-fulvenecarbaldehyde (HFULCA01)	H.Fuess,H.J.Lindner,Chem.Ber.,108,3096,1975.
45	Hippuric acid (HIPPAC02)	M.Currie,A.L.Macdonald,J.Chem.Soc.,Perkin 2,784,1974.
46	L-Histidine hydrochloride monohydrate (HISTCM12)	H.Fuess,D.Hohlwein,S.A.Mason,Acta Cryst.,B33,654,1977.
47	4-Hydroxy-L-proline (HOPROL12)	T.F.Koetzle,M.S.Lehmann,W.C.Hamilton,Acta Cryst.,B29,231,1973.
48	Imidazole (IMAZOL13)	B.M.Craven,R.K.McMullan,J.D.Bell,H.C.Freeman,Acta Cryst.,B33,2585,1977.
49	Iminodiacetic acid hydrobromide (IMDACB11)	A.Oskarsson,Acta Cryst.,B32,2163,1976.
50	Imidazolium hydrogen maleate (IMZMAL11)	B.Hsu,E.O.Schlemper,Acta Cryst.,B36,3017,1980.
51	Potassium hydrogen oxydiacetate (KAOXYA01)	J.Albertsson,I.Grenthe,Acta Cryst.,B29,2751,1973.
52	Potassium D-gluconate monohydrate (KDGLUM01)	N.C.Panagiotopoulos,G.A.Jeffrey,S.J.La Placa,W.C.Hamilton,Acta Cryst., B30,1421,1974.
53	Potassium D-gluconate monohydrate (KDGLUM02)	N.C.Panagiotopoulos,G.A.Jeffrey,S.J.La Placa,W.C.Hamilton,Acta Cryst., B30,1421,1974.
54	Potassium hydrogen dicrotonate (KHCROT01)	D.R.McGregor,J.C.Speakman,M.S.Lehmann,J.Chem.Soc.,Perkin 2,1740,1977.
55	Potassium hydrogen bis(acetylsalicylate) (KHDASL01)	A.Sequeira,C.A.Berkebile,W.C.Hamilton,J.Mol.Struct.,1,283,1968.
56	Potassium hydrogen bis(dichloroacetate) (KHDCAC10)	D.Hadzi,I.Leban,B.Orel,M.Iwata,J.M.Williams,J.Cryst.Mol.Struct.,9,117, 1979.
57	Potassium hydrogen mesotartrate (KHMTAR01)	M.Currie,J.C.Speakman,J.A.Kanters,J.Kroon,J.Chem.Soc.,Perkin 2,1549, 1975.
58	Potassium trihydrogen disuccinate (KTHSUC)	R.S.Dunlop,J.C.Speakman,Z.Krist.,138,100,1973.
59	L-Alanine (LALNIN12)	M.S.Lehmann,T.F.Koetzle,W.C.Hamilton,J.Am.Chem.Soc.,94,2657,1972.
60	L-Glutamic acid (LGLUAC03)	M.S.Lehmann,A.C.Nunes,Acta Cryst.,B36,1621,1980.
61	L-Glutamic acid (LGLUAC11)	M.S.Lehmann,T.F.Koetzle,W.C.Hamilton,J.Cryst.Mol.Struct.,2,225,1972.
62	L-Glutamic acid hydrochloride (LGLUTA)	A.Sequeira,H.Rajagopal,R.Chidambaram,Acta Cryst.,B28,2514,1972.
63	L-Histidine (LHISTD13)	M.S.Lehmann,T.F.Koetzle,W.C.Hamilton,Int.J.Pept.Protein Res.,4,229, 1972.
64	Lithium formate monohydrate (LIFORM02)	J.O.Thomas,R.Tellgren,J.Almlof,Acta Cryst.,B31,1946,1975.
65	L-Serine monohydrate (LSERMH10)	M.N.Frey,M.S.Lehmann,T.F.Koetzle,W.C.Hamilton,Acta Cryst.,B29,876, 1973.
66	L-Threonine (LTHREO01)	M.Ramanadham,S.K.Sikka,R.Chidambaram,Pramana,1,247,1973.
67	L-Tyrosine hydrochloride (LTYRHC10)	M.N.Frey,T.F.Koetzle,M.S.Lehmann,W.C.Hamilton,J.Chem.Phys.,58,2547, 1973.
68	L-Tyrosine (LTYROS11)	M.N.Frey,T.F.Koetzle,M.S.Lehmann,W.C.Hamilton,J.Chem.Phys.,58,2547, 1973.
69	L-Lysine monohydrochloride dihydrate (LYSCLH11)	T.F.Koetzle,M.S.Lehmann,J.J.Verbist,W.C.Hamilton,Acta Cryst.,B28,3207, 1972.
70	beta-L-Lyxopyranose (LYXOSE01)	S.Nordenson,S.Takagi,G.A.Jeffrey,Acta Cryst.,B34,3809,1978.
71	beta-Maltose monohydrate (MALTOS11)	M.E.Gress,G.A.Jeffrey,Acta Cryst.,B33,2490,1977.
72	Methyl alpha-D-altropyranoside (MALTPY01)	B.J.Poppleton,G.A.Jeffrey,G.J.B.Williams,Acta Cryst.,B31,2400,1975.
73	Methyl beta-D-galactopyranoside (MBDGAL02)	S.Takagi,G.A.Jeffrey,Acta Cryst.,B35,902,1979.
74	3-Mercapto-1,3-diphenylprop-2-en-1-one (MCPROP01)	L.F.Power,K.E.Turner,F.H.Moore,J.Chem.Soc.,Perkin 2,249,1976.
75	Methyl beta-D-ribopyranoside (MDRIBP02)	V.J.James,J.D.Stevens,F.H.Moore,Acta Cryst.,B34,188,1978.
76	9-Methyl-adenine (MEADEN02)	R.K.McMullan,P.Benci,B.M.Craven,Acta Cryst.,B36,1424,1980.
77	Melampodin (MELAMP11)	S.F.Watkins,N.H.Fischer,I.Bernal,Proc.Nat.Acad.Sci.U.S.A.,70,2434, 1973.
78	Methyl-D-mannopyranoside (MEMANP11)	G.A.Jeffrey,R.K.McMullan,S.Takagi,Acta Cryst.,B33,728,1977.
79	1-Methylthymine (METHYM01)	A.Kvick,T.F.Koetzle,R.Thomas,J.Chem.Phys.,61,2711,1974.
80	N,N-Dimethyl-nitramine (METNAM07)	A.Filhol,G.Bravic,M.Rey-Lafon,M.Thomas,Acta Cryst.,B36,575,1980.
81	Methyl alpha-D-galactopyranoside monohydrate (MGALPY01)	S.Takagi,G.A.Jeffrey,Acta Cryst.,B35,902,1979.
82	Methyl alpha-D-glucopyranoside (MGLUCP11)	G.A.Jeffrey,R.K.McMullan,S.Takagi,Acta Cryst.,B33,728,1977.
83	Sodium hydrogen diacetate (NAHACE01)	M.J.Barrow,M.Currie,K.W.Muir,J.C.Speakman,D.N.J.White,J.Chem.Soc., Perkin 2,15,1975.
84	2-Nitro-1,3-indandione dihydrate (NINDOD01)	C.-O.Selenius,J.-O.Lundgren,Acta Cryst.,B36,3172,1980.
85	5-Nitro-1-(beta-D-ribosyluronic acid)-uracil monohydrate (NRURAM11)	F.Takusagawa,T.F.Koetzle,T.Srikrishnan,R.Parthasarathy,Acta Cryst., B35,1388,1979.
86	4-Nitropyridine N-oxide (NTPYRO12)	P.Coppens,M.S.Lehmann,Acta Cryst.,B32,1777,1976.
87	1,3,5,7-Tetranitro-1,3,5,7-tetra-azacyclo-octane (OCHTET12)	C.S.Choi,H.P.Boutin,Acta Cryst.,B26,1235,1970.
88	1,2-Diaminobenzene monohydrochloride (OPHDAH01)	C.Stalhandske,Acta Cryst.,B32,2806,1976.
89	Perdeutero-formic acid (PDEFOR01)	A.Albinati,K.D.Rouse,M.W.Thomas,Acta Cryst.,B34,2188,1978.
90	L-Phenylalanine hydrochloride (PHALNC01)	A.R.Al-Karaghouli,T.F.Koetzle,Acta Cryst.,B31,2461,1975.
91	Putrescine diphosphate (PUTRDP11)	F.Takusagawa,T.F.Koetzle,Acta Cryst.,B35,867,1979.
92	Pyridinium-1-dicyanomethylide (PYRCYM02)	L.Devos,F.Baert,R.Fouret,M.Thomas,Acta Cryst.,B36,1807,1980.
93	Pyridoxinium chloride (PYRXCL01)	G.E.Bacon,J.S.Plant,Acta Cryst.,B36,1130,1980.
94	Pyrazole (PYRZOL02)	F.K.Larsen,M.S.Lehmann,I.Sotofte,S.E.Rasmussen,Acta Chem.Scand.,24, 3248,1970.
95	Quinolinic acid (QUICNA02)	F.Takusagawa,T.F.Koetzle,Acta Cryst.,B34,1149,1978.
96	Rubidium hydrogen oxydiacetate (RBHOXY01)	J.Albertsson,I.Grenthe,Acta Cryst.,B29,2751,1973.
97	Resorcinol (RESORA13)	G.E.Bacon,R.J.Jude,Z.Krist.,138,19,1973.
98	alpha-L-Rhamnose monohydrate (RHAMAH12)	S.Takagi,G.A.Jeffrey,Acta Cryst.,B34,2552,1978.
99	Salicylic acid (SALIAC12)	G.E.Bacon,R.J.Jude,Z.Krist.,138,19,1973.
100	o-Sulfobenzoic acid trihydrate (SLBZAC01)	R.Attig,J.M.Williams,Inorg.Chem.,15,3057,1976.
101	Sucrose (SUCROS04)	G.M.Brown,H.A.Levy,Acta Cryst.,B29,790,1973.
102	1,3,5-Triacetylbenzene (TACBEN01)	B.H.O'Connor,F.H.Moore,Acta Cryst.,B29,1903,1973.
103	Tetra-acetylethane (TACETA01)	L.F.Power,K.E.Turner,F.H.Moore,J.Cryst.Mol.Struct.,5,59,1975.
104	D-Tartaric acid (TARTAC01)	Y.Okaya,N.R.Stemple,M.I.Kay,Acta Cryst.,21,237,1966.
105	9-Thiabicyclo(3.3.1)nonane-2,6-dione (TBCNOD01)	M.J.Bovill,P.J.Cox,H.P.Flitman,M.H.P.Guy,A.D.U.Hardy,P.H.McCabe, M.A.Macdonald,G.A.Sim,D.N.J.White,Acta Cryst.,B35,669,1979.
106	7,7,8,8-Tetracyanoquinodimethane-deutero-p-terphenyl complex (TCQDTP10)	G.C.Lisensky,C.K.Johnson,H.A.Levy,Acta Cryst.,B32,2188,1976.
107	Triglycine sulfate (TGLYSU11)	M.I.Kay,R.Kleinberg,Ferroelectrics,5,45,1973.
108	1,3,5-Trinitrobenzene (TNBENZ10)	C.S.Choi,J.E.Abel,Acta Cryst.,B28,193,1972.
109	p-Toluenesulfonic acid monohydrate (TOLSAM12)	J.-O.Lundgren,J.M.Williams,J.Chem.Phys.,58,788,1973.
110	s-Triazine (TRIZIN02)	P.Coppens,Science,158,1577,1967.
111	L-Valine hydrochloride (VALEHC11)	T.F.Koetzle,L.Golic,M.S.Lehmann,J.J.Verbist,W.C.Hamilton,J.Chem.Phys., 60,4690,1974.
112	Methyl beta-D-xylopyranoside (XYLOBM01)	S.Takagi,G.A.Jeffrey,Acta Cryst.,B33,3033,1977.
113	alpha-L-Xylopyranose (XYLOSE01)	S.Takagi,G.A.Jeffrey,Acta Cryst.,B35,1482,1979.

The Cambridge Structural Database reference code is given in parentheses after each compound name.

The results are summarized in Figure 1, which shows the distribution of d for all 661 nearest-neighbor contacts (the symbol d is used throughout the text to denote the parameter defined in eq 1). The mean value ($\bar{d}$ = 0.030 Å) is close to zero, which suggests that the van der Waals radii given above are reasonably accurate. There are 46 nearest-neighbor contacts with $d > 0.3$ Å, i.e., appreciably shorter than the sum of the van der Waals radii. However, before concluding that these contacts are hydrogen

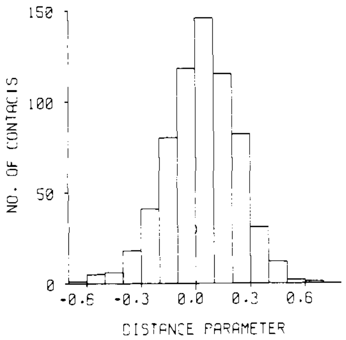

Figure 1. Distribution of the distance parameter d (eq 1; units are angstroms) for the (C–)H atom nearest-neighbor contacts. Three contacts with $d < -0.65$ Å are omitted.

Table II. Atom Types Involved in (C–)H Atom Nearest-Neighbor Contacts[a]

atom type	predicted distbn[b]	obsd distbn[c]: all contacts	contacts with $d > 0.0$ Å	contacts with $d > 0.3$ Å
C	0.30	0.18 (122)	0.16 (63)	0.04 (2)
H	0.47	0.30 (197)	0.23 (90)	0.02 (1)
Br	0.00	0.00 (0)	0.00 (0)	0.00 (0)
Cl	0.01	0.05 (31)	0.03 (13)	0.02 (1)
N	0.04	0.03 (18)	0.03 (11)	0.00 (0)
O	0.18	0.44 (289)	0.54 (211)	0.91 (42)
P	0.00	0.00 (0)	0.00 (0)	0.00 (0)
S	0.00	0.01 (4)	0.00 (1)	0.00 (0)
total	1.00	1.00 (661)	1.00 (389)	1.00 (46)

[a] Results obtained with an oxygen van der Waals radius of 1.50 Å. [b] Normalized to unity. [c] Normalized to unity. Figures in parentheses are the actual numbers of contacts observed.

bonds, it is necessary to determine whether they involve hydrogen bond acceptor atoms. The distribution of atom types involved in the nearest-neighbor contacts is therefore given in Table II for (1) all contacts, (2) contacts that are shorter than the sum of the van der Waals radii, i.e. with $d > 0.0$ Å, and (3) contacts with $d > 0.3$ Å. Also given in Table II is the expected distribution of atom types. This is based on the assumption that the probability of a particular (C–)H atom forming its nearest-neighbor contact to an atom of a given type depends only on the stoichiometry of the crystal structure, e.g.,

$$P(\mathrm{Y{=}C}) = N_c/N \qquad (2)$$

where $P(\mathrm{Y{=}C})$ is the probability that the nearest-neighbor contact is to a carbon atom, N_c is the number of carbon atoms in the asymmetric unit, and N is the total number of atoms in the asymmetric unit.[20] The expected distribution was calculated numerically by a Monte Carlo simulation. It should be compared with the observed distribution for all 661 nearest-neighbor contacts because all of the (C–)H atoms in the sample were included in the simulation.

Two major results emerge from the figures given in Table II. The first is that (C–)H···C and (C–)H···H contacts with $d > 0.3$ Å are uncommon but do exist.[21] This shows that the occurrence of a (C–)H···O contact with $d > 0.3$ Å is not, in itself, conclusive proof of hydrogen bond formation. The second result is that the proportion of nearest-neighbor contacts that involve oxygen atoms is far higher than would be expected from the stoichiometries of the crystal structures studied. The proportion is even larger when only the short nearest-neighbor contacts are considered. Thus, of the 46 contacts with $d > 0.3$ Å, 42 are of the type (C–)H···O. This is reflected by the fact that the mean value of d for the 289 nearest-neighbor contacts involving oxygen is 0.105 Å, compared with a value of 0.030 Å for the complete sample.

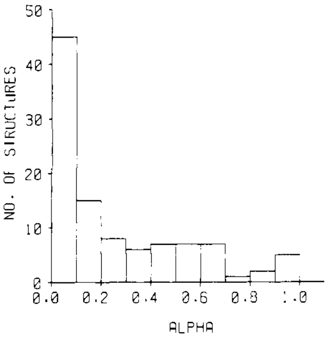

Figure 2. Distribution of α_i (eq 3; oxygen van der Waals radius = 1.50 Å).

Table III. Atom Types Involved in (C–)H Atom Nearest-Neighbor Contacts[a]

atom type	predicted distbn[b]	obsd distbn[c]: all contacts	contacts with $d > 0.0$ Å	contacts with $d > 0.3$ Å
C	0.30	0.21 (136)	0.20 (67)	0.11 (2)
H	0.47	0.35 (233)	0.30 (100)	0.05 (1)
Br	0.00	0.00 (0)	0.00 (0)	0.00 (0)
Cl	0.01	0.05 (31)	0.04 (13)	0.05 (1)
N	0.04	0.03 (18)	0.03 (11)	0.00 (0)
O	0.18	0.36 (239)	0.43 (145)	0.79 (15)
P	0.00	0.00 (0)	0.00 (0)	0.00 (0)
S	0.00	0.01 (4)	0.00 (1)	0.00 (0)
total	1.00	1.00 (661)	1.00 (337)	1.00 (19)

[a] Results obtained with an oxygen van der Waals radius of 1.40 Å. [b] Normalized to unity. [c] Normalized to unity. Figures in parentheses are the actual numbers of contacts observed.

At this stage, it was necessary to eliminate two possibilities: (1) The difference between the observed number of (C–)H···O contacts and that predicted from the stoichiometries of the crystal structures may not be statistically significant. (2) The van der Waals radius used for oxygen may be incorrect. These possibilities are discussed in turn below.

(1) Statistical Significance. Consider the ith crystal structure in the sample, and let N_i = total number of atoms in the asymmetric unit,[20] X_i = number of oxygen atoms in the asymmetric unit, H_i = number of (C–)H atoms in the asymmetric unit, m_i = number of (C–)H atoms in the asymmetric unit that form nearest-neighbor contacts to oxygen atoms. Under the null hypothesis that the (C–)H atoms do not show any preference for forming short intermolecular contacts to oxygen atoms, the probability (α_i) that m_i or $>m_i$ of the nearest-neighbor contacts are of the type (C–)H···O is[22]

$$\alpha_i = \sum_{j=m_i}^{j=H_i} (H_i!/j![H_i - j]!)(X_i/N_i)^j([N_i - X_i]/N_i)^{H_i-j} \qquad (3)$$

The distribution of the α_i values for 103 of the crystal structures is shown in Figure 2 (the remaining 10 structures do not contain any oxygen atoms). If the null hypothesis were correct, we would expect a rectangular distribution in the range 0–1. However, it is obvious that the observed distribution is not rectangular, but that the α_i values tend to cluster in the range 0–0.1. The statistical significance of the departure of the observed distribution from the "ideal" rectangular distribution, estimated by standard statistical techniques,[23] is >99.9%. Accordingly, we reject the null

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(20) Excluding metal ions. Metal ions were ignored in the calculations because they were also ignored when the observed distribution was derived.

(21) The (C–)H···C and (C–)H···H contacts with $d > 0.3$ Å are H^{γ^2}···C in L-glutamine (Table I, 39; note that there is a printing error in this paper: the z coordinate of C should be 0.7250, not 0.7520), H(5)···C(4) in 2-nitro-1,3-indandione dihydrate (Table I, 84), and H(20)···H(14) in potassium hydrogen mesotartrate (Table I, 57).

(22) Siegel, S. "Nonparametric Statistics for the Behavioral Sciences"; International Student Edition; McGraw-Hill Kogakusha: Tokyo, 1956.

(23) Fisher, R. A. "Statistical Methods for Research Workers", 6th ed.; Oliver and Boyd: Edinburgh, 1936; pp 104–106.

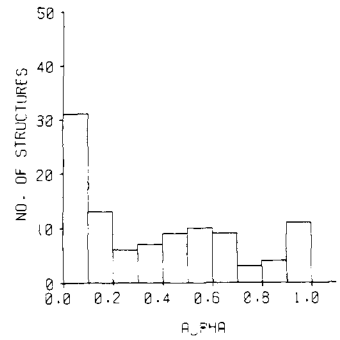

Figure 3. Distribution of α_i (eq 3; oxygen van der Waals radius = 1.40 Å).

hypothesis and conclude that (C–)H atoms have a significant tendency to form short intermolecular contacts to oxygen atoms.

(2) van der Waals Radius of Oxygen. All calculations described so far were based on an oxygen van der Waals radius of 1.50 Å. We believe this to be the most reliable value, but in order to ensure that it was not biasing the results, we repeated the calculations using the value quoted by Pauling[24] (i.e., 1.40 Å; all other van der Waals radii were kept unchanged). The revised distribution of atom types involved in the (C–)H atom nearest-neighbor contacts is given in Table III. The proportion of (C–)H···O contacts is still appreciably higher than would be expected from the stoichiometries of the crystal structures, and the statistical significance, as calculated above, is still >99.9%. The revised distribution of the α_i values is shown in Figure 3.

The van der Waals radius of oxygen was assumed to be 1.50 Å throughout the remainder of the study.

Steric Effects. Many of the carbon atoms in the crystal structures studied are tetrahedrally coordinated and therefore relatively inaccessible to an approaching (C–)H atom. This suggests that steric effects may be important in determining the types of short intermolecular contacts formed by the (C–)H atoms. We therefore recalculated the expected distribution of atom types involved in the (C–)H atom nearest-neighbor contacts. The same Monte Carlo procedure as before was used, except that we now assumed it to be impossible for a nearest-neighbor contact to involve an atom that was more than three-coordinate. For example, the probability that a given (C–)H atom forms its nearest-neighbor contact to a carbon atom was assumed to be as follows:

$$P(\mathrm{Y{=}C}) = N_c'/N' \qquad (4)$$

where N_c' is the number of carbon atoms in the asymmetric unit, excluding tetrahedrally coordinated atoms, and N' is the total number of atoms in the asymmetric unit, excluding metal ions and atoms that are more than three-coordinate.

The resulting predicted distribution was C:H:Br:Cl:N:O:P:S, 0.16:0.58:0.00:0.01:0.04:0.21:0.00:0.00. The predicted proportion of (C–)H···C nearest-neighbor contacts is now close to the observed value,[25] but the expected proportion of (C–)H···H contacts is far higher than that observed. Consequently, the predicted number of (C–)H···O nearest-neighbor contacts is still much smaller than the observed value. We conclude that steric effects do not account for the observed tendency of (C–)H atoms to form short intermolecular contacts to oxygen atoms; apparently, short (C–)H···O contacts are inherently more favorable than (C–)H···C or (C–)H···H contacts.

The Geometry of (C–)H···O Contacts. Ab initio energy decomposition analyses show that the energy of a (C–)H···Y interaction can be expressed as the sum of the following terms: (1) van der Waals energy (i.e., exchange repulsion plus dispersion); (2) electrostatic energy; (3) charge-transfer energy; (4) polarization energy.[6,26] It is unlikely that the charge-transfer or polarization terms are sufficiently important to have a significant effect on the types of intermolecular contacts formed by (C–)H atoms.[27] Consequently, the unexpectedly large number of (C–)H···O nearest-neighbor contacts must be due to one, or both, of the other terms.

Table IV. Calculated van der Waals Interactions for the Atom Pairs (C–)H···O, (C–)H···C, and (C–)H···H

	atom pair		
potential[a]	(C–)H···O	(C–)H···C	(C–)H···H
	d = 0.0 Å		
CHW	0.14	0.10	0.18
HHL, 6-9	0.22	0.04	0.09
HHL, 6-12	−0.04	0.06	0.02
mean	0.11	0.07	0.10
	d = 0.1 Å		
CHW	0.25	0.19	0.29
HHL, 6-9	0.36	0.08	0.15
HHL, 6-12	0.05	0.15	0.10
mean	0.22	0.14	0.18
	d = 0.2 Å		
CHW	0.44	0.33	0.46
HHL, 6-9	0.59	0.15	0.24
HHL, 6-12	0.22	0.30	0.27
mean	0.42	0.26	0.32
	d = 0.3 Å		
CHW	0.71	0.54	0.70
HHL, 6-9	0.95	0.25	0.39
HHL, 6-12	0.54	0.57	0.59
mean	0.73	0.45	0.56

[a] CHW = potential of Cox, Hsu, and Williams;[28] HHL, 6-9 = 6-9 potential of Hagler, Huler, and Lifson;[29] HHL, 6-12 = 6-12 potential of Hagler, Huler, and Lifson.[29] Energies in kcal/mol.

We calculated the van der Waals repulsion between the atom pairs (C–)H···O, (C–)H···C, and (C–)H···H at various values of d. Three different sets of empirical nonbonded parameters were used.[28-30] The results are summarized in Table IV. They show that the (C–)H···O van der Waals repulsion is, if anything, slightly larger than the (C–)H···C and (C–)H···H repulsions at the same value of d. We conclude that the observed preference for short (C–)H···O contacts cannot be explained by the van der Waals repulsion energies.

The determining factor must therefore be the electrostatic energy, i.e., the electrostatic interaction between the permanent electron distribution of the species which contains the Y atom and that of the species which contains the (C–)H atom. Electrostatic forces are relatively long range. Consequently, the sign and magnitude of the electrostatic term will depend not only on the charges borne by the (C–)H and Y atoms but also on the charges of the surrounding atoms. However, the single most important contribution may be expected to arise from the Coulombic interaction between (C–)H and Y. Calculation of atomic point charges by quantum mechanical methods shows that when Y is a carbon or hydrogen atom this interaction will usually be repulsive, but when Y is an oxygen atom, it will almost always be

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[24] Pauling, L. "The Nature of the Chemical Bond", 3rd ed.; Cornell University Press: Ithaca, NY, 1960.

[25] However, it is unlikely that the low proportion of (C–)H···C nearest-neighbor contacts can be entirely attributed to steric effects. A total of 35 of the nearest-neighbor contacts (Table II) involve tetrahedrally coordinated carbon atoms. Thus, the assumption made in the calculation of the expected distribution (i.e., that nearest-neighbor contacts to atoms that are more than three-coordinate are impossible) is actually too conservative.

[26] Schuster, P. In "The Hydrogen Bond—Recent Developments in Theory and Experiments"; Schuster, P., Zundel, G., Sandorfy, C., Eds.; North-Holland: Amsterdam, 1976; Vol. I., p 71.

[27] This statement is based on the results of ab initio energy decomposition studies (e.g., ref 6), which show that the polarization term is usually very small and that "CT (charge transfer) does not depend much on the proton acceptor and depends only weakly on the proton donor".[6]

[28] Cox, S. R.; Hsu, L.-Y.; Williams, D. E. *Acta Crystallogr., Sect. A* **1981**, *A37*, 293–301.

[29] Hagler, A. T.; Huler, E.; Lifson, S. *J. Am. Chem. Soc.* **1974**, *96*, 5319–5327.

[30] Note that only the nonbonded parts of the empirical functions were used, not the Coulombic parts.

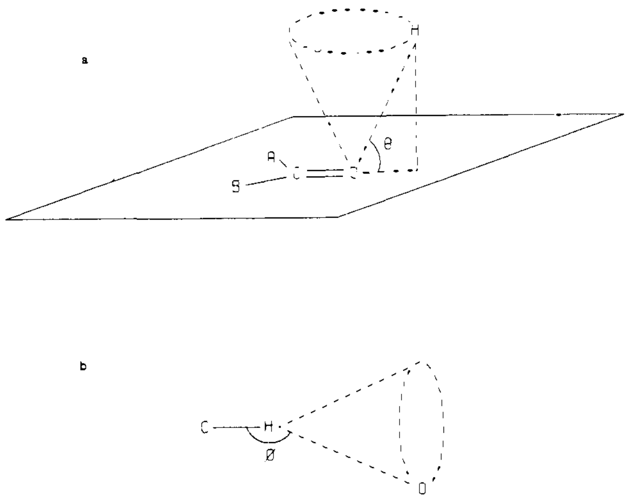

Figure 4. (a) Variation of number of possible C—H···O configurations with angle of elevation θ (see text). (b) Variation of number of possible C—H···O configurations with C—H···O angle ϕ.

attractive.[31-33] Thus, the electrostatic energy will tend to destabilize short (C–)H···C and (C–)H···H contacts and stabilize short (C–)H···O contacts. This is consistent with, and the probable explanation of, the observed tendency of (C–)H atoms to form short contacts to oxygen rather than to carbon or hydrogen atoms.

If the electrostatic stabilization of a short (C–)H···O contact outweighs the (C–)H···O van der Waals repulsion, the contact will be attractive rather than repulsive. The relative importance of the electrostatic and van der Waals terms cannot be inferred with certainty from the crystallographic data. However, a study of the geometries of short (C–)H···O contacts is suggestive. If the van der Waals interaction is dominant, we would expect the (C–)H atom to avoid the lone-pair orbitals of the oxygen atom. Molecular mechanics calculations suggest that the van der Waals repulsion between an oxygen and a hydrogen atom is greatest when the hydrogen atom approaches along the direction of one of the lone pairs.[34] Conversely, if the electrostatic interaction is more important, we would expect the (C–)H atom to be attracted toward the oxygen lone pairs. Recent work suggests that the proton in O—H···O< and O—H···O=C hydrogen bonds prefers to lie in or near the plane containing the lone-pair orbitals of the acceptor atom.[35-37] In addition, there is some evidence that the H···O=C angle in O—H···O=C hydrogen bonds tends to be about 120°,[37] i.e., the value expected on the basis of the sp^2 lone-pair directions. These conclusions are based on the geometries of over 200 hydrogen bonds, many of which were determined by neutron diffraction.

Table V. Short (C–)H···O Contacts

structure[a]	contact[b]	(C–)H···O distance[c]	d[c]	C–H···O angle[d]
79	H2···O8	2.045	0.655	170.9
85	H6···O5'[e,f]	2.080	0.620	155.7
86	H2···O1	2.145	0.555	176.7
87	H2···O1[e]	2.192	0.508	103.0
29	H4···O1	2.196	0.504	174.1
28	H102···O60[e]	2.225	0.475	100.1
47	H8···O3	2.225	0.475	151.7
50	H5···O3	2.225	0.475	154.9
68	H4···O1	2.243	0.457	151.3
108	H2···O8[f]	2.246	0.454	168.3
85	H4'···O2	2.248	0.452	145.7
28	H302···O40[e]	2.251	0.449	98.6
85	H1'···O2[e]	2.257	0.443	107.2
34	H23···O7	2.260	0.440	166.4
101	H1···O6[f]	2.268	0.432	165.8
77	H7···O8[e,f]	2.270	0.430	103.1
95	H2···O3[f]	2.275	0.425	142.2
108	H6···O1	2.281	0.419	154.3
60	H20···O11	2.287	0.413	162.9
77	H1···O6[e]	2.287	0.413	100.4
38	H2···O1	2.291	0.409	147.6
98	H2···O3	2.291	0.409	154.1
100	H3···O22[e]	2.291	0.409	106.2
42	H4···O1	2.301	0.399	155.5
57	H21···O5	2.306	0.394	127.3
107	H2···O12	2.309	0.391	164.9
85	H20'···O4	2.310	0.390	167.7
95	H1···O4[e]	2.317	0.383	98.6
23	H4···O1	2.321	0.379	150.1
90	H5···O1	2.327	0.373	141.0
93	H2···O3[f]	2.330	0.370	155.2
22	H3···O4	2.331	0.369	146.9
32	H6···O71[e,f]	2.334	0.366	98.0
85	H30'···O52[f]	2.334	0.366	132.4
42	H5···O1	2.335	0.365	135.1
86	H1···O2	2.336	0.364	173.1
87	H3···O3[e]	2.337	0.363	90.7
18	H16···O1[e]	2.342	0.358	104.1
74	H1···O1[e]	2.343	0.357	98.4
108	H1···O2[e]	2.345	0.355	94.3
66	H4···O3	2.354	0.346	160.0
87	H4···O2	2.360	0.340	152.6
24	H6···O3	2.362	0.338	154.8
24	H5···O3	2.365	0.335	134.9
50	H2···O2[f]	2.365	0.335	118.8
111	H6···O1	2.368	0.332	151.8
61	H5···O4	2.372	0.328	149.0
58	H5···O6	2.373	0.327	157.5
30	H7···O1	2.375	0.325	171.6
20	H8···O1[e]	2.378	0.322	102.0
107	H8···O13'	2.378	0.322	153.2
95	H3···O2	2.382	0.318	145.5
40	H4···O2	2.390	0.310	137.4
55	H5···O2	2.391	0.309	172.9
71	H14···O6'	2.392	0.308	138.1
25	H23···O17[e]	2.394	0.306	96.7
99	H6···O1[e]	2.394	0.306	98.8
77	H9···O4	2.397	0.303	126.1
108	H4···O9[e]	2.399	0.301	94.3

[a] See Table I. [b] Atom labels are those used in the Cambridge Structural Database.[14] They are not always identical with those used in the original literature. [c] In angstroms. [d] In degrees. [e] Intramolecular contact. [f] (C–)H atom forms two contacts with $d > 0.3$ Å and C–H···O > 90°. Only the shorter contact is given.[40]

We therefore studied the geometries of all the (C–)H···O contacts in our sample with $d > 0.3$ Å. Both intermolecular and intramolecular contacts were now included,[38] but contacts with C—H···O angles of less than 90° were ignored, as before. When a (C–)H atom was found to form two contacts with $d > 0.3$ Å, only the shorter interaction was used. We found 59 contacts that satisfy these conditions. (C–)H···O contacts with $d > 0.3$ Å are therefore relatively common in the crystal structures studied, which in itself suggests that they are attractive interactions. The (C–)H···O distances and C—H···O angles are given in Table V. A total of 14 of the contacts involve carbonyl oxygen atoms (**1**),

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(31) Scheraga, H. A. *Adv. Phys. Org. Chem.* **1968**, *6*, 103–184.

(32) Lifson, S.; Hagler, A. T.; Dauber, P. *J. Am. Chem. Soc.* **1979**, *101*, 5111–5121.

(33) Derissen, J. L.; Smit, P. H. *Acta Crystallogr., Sect. A* **1978**, *A34*, 842–853.

(34) Allinger, N. L.; Chung, D. Y. *J. Am. Chem. Soc.* **1976**, *98*, 6798–6803.

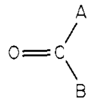
(35) Kroon, J.; Kanters, J. A.; Van Duijneveldt-Van de Rijdt, J. G. C. M.; Van Duijneveldt, F. B.; Vliegenthart, J. A. *J. Mol. Struct.* **1975**, *24*, 109–129.

(36) Ceccarelli, C.; Jeffrey, G. A.; Taylor, R. *J. Mol. Struct.* **1981**, *70*, 255–271.

(37) Olovsson, I.; Jönsson, P.-G. In "The Hydrogen Bond—Recent Developments in Theory and Experiments"; Schuster, P., Zundel, G., Sandorfy, C., Eds.; North-Holland: Amsterdam, 1976; Vol. II, pp 413–420.

(38) Our investigation of (C–)H atom nearest-neighbor contacts establishes that short ($d > 0.3$ Å) *intermolecular* (C–)H···O interactions are relatively common. This shows that short *intramolecular* contacts are not necessarily due to internal geometrical constraints and should therefore be included in the remainder of the study. However, the geometry of an intramolecular contact is more likely to be influenced by its environment than that of an intermolecular interaction. We have therefore marked all intramolecular contacts in Tables V–VII.

and 19 involve ether, alcohol, or water oxygen atoms (**2**). For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each of these contacts, we calculated the angle of elevation of the (C–)H···O vector above the lone-pair plane of the oxygen atom (θ, in Figure 4a). The lone-pair plane of the carbonyl oxygen atoms was assumed to be the least-squares mean plane of the O, C, A, and B atoms. The lone-pair plane of the ether/alcohol/water oxygen atoms was assumed to be the plane bisecting the A–O–B angle and perpendicular to the A,O,B plane.

The calculated values of θ are given in Table VI, and the θ distribution is shown as a histogram in Figure 5. The number of possible (C–)H···O configurations with angles of elevation between $\theta - \delta\theta$ and $\theta + \delta\theta$ is proportional to cos θ (Figure 4a). Thus, if the energy of the (C–)H···O interaction were independent of θ, we would expect as many contacts with $\theta < 30°$ as with $\theta > 30°$. In fact, there are 19 contacts with $\theta < 30°$ and 14 with $\theta > 30°$. This suggests that the (C–)H atom is more likely to be attracted to the oxygen lone-pair plane than repelled by it, though the evidence is obviously not conclusive.

Also given in Table VI are the (C–)H···O=C angles of the contacts that involve carbonyl oxygen atoms. Four of the angles are less than 90°, but they all correspond to intramolecular contacts. The geometries of these contacts may well be influenced by the internal features of the molecules. Eight of the remaining 10 angles are within 22° of the value expected on the basis of the lone-pair directions (i.e., 120°).

Figure 6a shows the distribution of the 59 C—H···O angles listed in Table V. All of the angles that are less than 110° correspond to intramolecular interactions. The distribution for the 41 intermolecular contacts is shown in Figure 6b. The mean value of this distribution, 152.7°, is somewhat smaller than the mean O—H···O hydrogen bond angle in carbohydrates (167.1°[36]). This may be ascribed to the fact that the O—H···O hydrogen bonds are shorter than the (C–)H···O contacts. Consequently, the O···O van der Waals repulsion is likely to be larger than the C···O repulsion at a given value of the O—H···O (C—H···O) angle. The distribution shown in Figure 6b is influenced by the fact that the number of possible C—H···O configurations with a C—H···O angle of ϕ is proportional to sin ϕ (Figure 4b).[35] Correction for this geometrical factor[39] produces the histogram shown in Figure 6c, which is clearly consistent with an energetic preference for the linear C—H···O arrangement.[40]

Conclusions. The principal results may be summarized as follows: (*1*) (C–)H atoms have a tendency to form short intermolecular contacts to oxygen atoms rather than to carbon or hydrogen atoms. This observation is statistically significant at the 99.9% level. The phenomenon is not a steric effect, but is probably due to electrostatic stabilization of the short (C–)H···O contacts. (2) (C–)H···O contacts with $d > 0.3$ Å occur frequently in the crystal structures studied. (3) The proton in the majority of short (C–)H···O contacts lies within 30° of the plane containing the oxygen lone-pair orbitals. The optimum C—H···O arrangement is probably linear.

On the basis of these observations, we conclude that the short (C–)H···O contacts are more likely to be attractive than repulsive. Whether or not they should be described as hydrogen bonds is somewhat arbitrary, but we note the following: (1) The frequency with which they occur suggests that they play a significant role in determining the packing arrangements of some organic crystal structures. (2) The geometrical characteristics of short (C–)H···O contacts are similar to those of O—H···O hydrogen bonds. (3) The results of spectroscopic and ab initio studies[2–8] are consistent with the concept of a C—H···O hydrogen bond. We therefore suggest that it is reasonable to use the terminology "C—H···O hydrogen bond" in crystallographic studies.

Table VI. Geometries of Short (C–)H···O Contacts

carbonyl acceptors				ether/alcohol/water acceptors		
structure[a]	contact[b]	θ[c,d]	(C–)H··· O=C[d]	structure[a]	contact[b]	θ[c,d]
79	H2···O8	2.2	177.0	85	H6···O5′[e]	2.2
85	H4′···O2	31.4	141.4	28	H102···O60[e]	36.1
28	H302···O40[e]	13.1	86.7	47	H8···O3	10.8
85	H1′···O2[e]	2.5	85.0	34	H23···O7	9.4
77	H7···O8[e]	9.8	83.5	101	H1···O6	9.4
60	H20···O11	41.0	125.1	77	H1···O6[e]	34.2
42	H4···O1	56.2	121.9	38	H2···O1	28.1
85	H20′···O4	25.9	131.3	98	H2···O3	22.7
23	H4···O1	37.2	136.9	93	H2···O3	37.4
90	H5···O1	23.8	146.1	32	H6···O71[e]	33.7
42	H5···O1	16.1	137.8	74	H1···O1[e]	36.8
111	H6···O1	30.9	141.0	66	H4···O3	46.7
58	H5···O6	27.9	112.6	24	H6···O3	2.3
20	H8···O1[e]	5.7	81.7	24	H5···O3	41.6
				61	H5···O4	27.1
				107	H8···O13′	24.0
				71	H14···O6′	26.2
				99	H6···O1[e]	36.4
				77	H9···O4	45.1

[a] See Table I. [b] Contacts are listed in order of increasing (C–)H···O distance. Atom labels are those used in the Cambridge Structural Database.[14] [c] See Figure 4a. [d] In degrees. [e] Intramolecular contact.

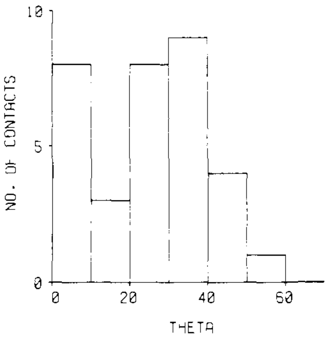

Figure 5. Distribution of θ (in degrees) for contacts listed in Table VI.

Crystallographic Evidence for the Existence of C—H···S, C—H···N, and C—H···Cl Hydrogen Bonds

(C–)H···S, (C–)H···N, and (C–)H···Cl contacts with $d > 0.0$ Å are listed in Table VII. Both intermolecular and intramolecular contacts are included, but contacts with C—H···X angles of less than 90° are omitted. The different interactions are discussed in turn below:

(1) (C–)H···S. Three of the short (C–)H···S contacts are intramolecular. It is difficult to assess all of the factors that might influence the conformation of a particular molecule in the crystalline state (compare, for example, the different interpretations of Sutor and Donohue in ref 10 and 11). We are therefore unsure whether these contacts are attractive or repulsive and are unable to make any conclusion regarding the nature of the (C–)H···S interaction.

(2) (C–)H···N. All of the short (C–)H···N contacts are intermolecular, and three of them are appreciably shorter ($d > 0.2$ Å) than the sum of the (C–)H and N van der Waals radii. In view of the limited amount of data, it is not possible to make any firm statement about the nature of these contacts. However, the electronegativities of oxygen and nitrogen are comparable,[24] and if the majority of short (C–)H···O contacts are attractive, it is reasonable to conclude that at least some of the short (C–)H···N contacts are also attractive.

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(39) The histogram was corrected by multiplying each bar by $N/\sin\bar{\phi}$, where $\bar{\phi}$ is the average of the upper and lower limits of the bar and N is a normalization constant, chosen so that the area under the corrected histogram is equal to the area under the uncorrected histogram.

(40) We could not detect any significant difference between the C—H···O angles of linear and bifurcated (C–)H···O contacts.

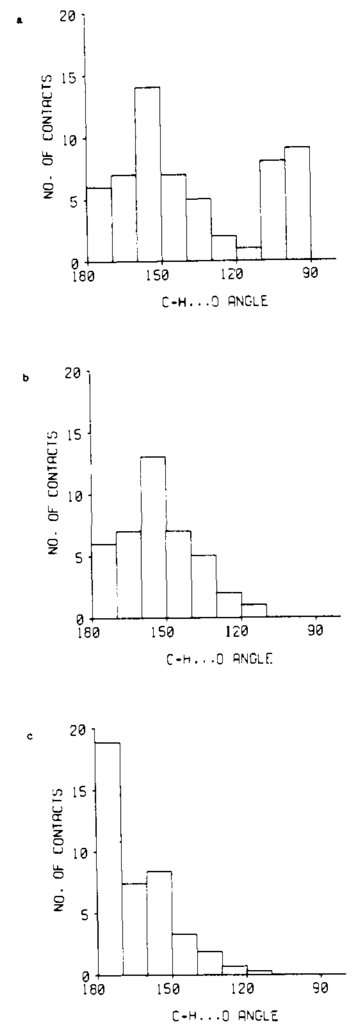

Figure 6. (a) Distribution of C—H···O angle (in degrees) for all contacts listed in Table V. (b) Distribution of C—H···O angle (in degrees) for all intermolecular contacts listed in Table V. (c) As (b), corrected for geometrical factor shown in Figure 4b.[39]

(3) (C–)H···Cl. The interesting feature of the (C–)H···Cl contacts is that all but two of them involve chloride ions rather than covalently bonded chlorine atoms. To some extent, this reflects the stoichiometries of the crystal structures studied: 12 of them contain chloride ions, but only 6 contain covalently bonded chlorine atoms. However, there does seem to be a tendency for (C–)H atoms to form short contacts of the type $(C–)H···Cl^-$ rather than (C–)H···Cl–R. This strongly suggests that the dominant term in the $(C–)H···Cl^-$ interaction is the attractive electrostatic term rather than the repulsive van der Waals term. Furthermore, the chloride ion is small and should be relatively easy to pack into an organic crystal structure. It therefore seems unlikely that very short $(C–)H···Cl^-$ contacts would occur if they were energetically unfavorable. We conclude that the short $(C–)H···Cl^-$ interactions are almost certainly attractive and can reasonably be described as hydrogen bonds.

Occurrence of C—H···X Hydrogen Bonds

The probability of a C—H···X hydrogen bond occurring in a given crystal structure is influenced by three factors: (1) the availability of suitable proton donors; (2) the availability of suitable proton acceptors; (3) the stoichiometry of the crystal structure. These factors are discussed in turn below:

(1) Proton Donor. The (C–)H atoms involved in the ten shortest (C–)H···O contacts in our sample are underlined in Figure 7. All but two are immediately adjacent to neutral or positively charged nitrogen atoms. The remaining contacts involve a (C–)H atom that is part of a pyridinium cation and a (C–)H atom that is part of a trinitrobenzene ring. Apparently, the inductive effect of nitrogen decreases the electron density at nearby (C–)H atoms, thereby enhancing the facility with which they participate in C—H···X hydrogen bonds.[13] In order to confirm this, we studied the environments of the 64 (C–)H atoms in our sample which are immediately adjacent to N^+ atoms (**3**). We found that 56 of these

$$N^+—C—H$$

3

atoms form at least one contact to a hydrogen-bond acceptor (O, N, Cl) with $d > 0.0$ Å and C—H···X > 90°. In contrast, only 293 of the remaining 597 (C–)H atoms form contacts of this type. The statistical significance of the difference between these proportions, estimated by a χ^2 test,[22] is >99.9%. Twenty one of the $(N^+–C–)H$ atoms form at least one contact to a hydrogen-bond acceptor with $d > 0.3$ Å and C—H···X > 90°, compared with only 41 of the remaining (C–)H atoms. Again, these proportions are significantly different at the 99.9% level. We therefore

Table VII. Short (C–)H···S, (C–)H···N, and (C–)H···Cl Contacts

structure[a]	contact[b]	(C–)H···X distance[c]	d[c]	C–H···X angle[d]
		(C–)H···S		
28	H301···S20[e]	2.496	0.504	107.1
28	H101···S20[e]	2.511	0.489	105.8
74	H15···S1[e]	2.743	0.257	98.6
74	H13···S1	2.916	0.084	163.9
		(C–)H···N		
31	H3···N1	2.522	0.228	138.7
76	H111···N3	2.524	0.226	133.3
92	D3···N2	2.530	0.220	136.2
106	H3···N2	2.644	0.106	140.0
76	H113···N1	2.663	0.087	151.8
48	H2···N3	2.665	0.085	138.3
106	D1···N1	2.691	0.059	157.3
106	D9···N2	2.694	0.056	124.6
106	D5···N1	2.698	0.052	130.3
94	H6···N1[f]	2.704	0.046	142.7
110	H1···N1[f]	2.721	0.029	132.1
		(C–)H···Cl		
46	H4···Cl(1)	2.569	0.381	157.9
67	H11···Cl(1)	2.658	0.292	146.1
43	H32···Cl(1)	2.661	0.289	150.8
69	H19···Cl(1)	2.661	0.289	152.9
46	H5···Cl(1)	2.723	0.227	119.3
93	H1···Cl(1)	2.818	0.132	150.4
5	H2···Cl(2)	2.823	0.127	143.6
93	H3···Cl(1)	2.841	0.109	141.2
111	H4···Cl(1)	2.875	0.075	143.6
9	H4···Cl(1)	2.904	0.046	169.2
111	H11···Cl(1)	2.910	0.040	151.8
56	H1···Cl(2)	2.926	0.024	130.8
93	H6···Cl(1)	2.944	0.006	149.7

[a] See Table I. [b] Atom labels are those used in the Cambridge Structural Database.[14] [c] In angstroms. [d] In degrees. [e] Intramolecular contact. [f] (C–)H atom is involved in symmetrically bifurcated interaction. Only one of the contacts is included in the table.

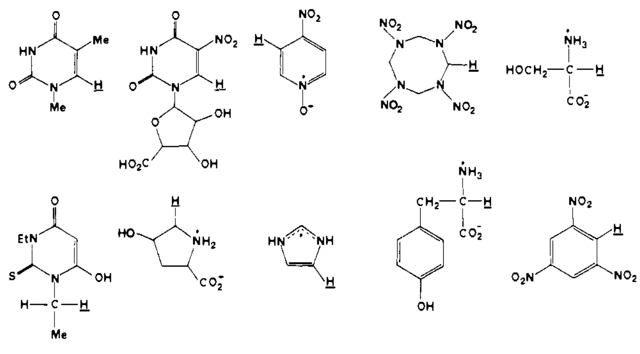

Figure 7. (C–)H atoms involved in the 10 shortest (C–)H···O contacts in Table V.

conclude that an organic molecule that contains a (C–)H atom adjacent to a nitrogen atom is especially likely to form C—H···X hydrogen bonds. This is of interest because two classes of biologically important molecules fall into this category: the amino acids,[41] and the nucleosides and nucleotides. The importance of C—H···O and C—H···Cl hydrogen bonds in the crystal structures of these compounds has been recognized in the literature.[12,13]

The above observations suggest that (C–)H atoms that are not adjacent to electron-withdrawing groups are unlikely to form C—H···X hydrogen bonds and may even be incapable of doing so. Thus, some of the short contacts listed in Tables V and VII may actually be repulsive interactions, which occur only because of crystal packing forces. However, the results outlined in the preceding sections indicate that the majority of the contacts are likely to be attractive.

(2) Proton Acceptor. The (C–)H···O contacts listed in Table V involve a wide variety of acceptor groups—sulfonate, carboxylate, nitro, carbonyl, ether, etc. Apparently, almost any type of oxygen atom is inherently capable of participating in a C—H···O hydrogen bond. We therefore conclude that the energy of the C—H···O hydrogen bond is very sensitive to the nature of the (C–)H atom, but insensitive to the nature of the oxygen atom. This may be rationalized as follows. The electrostatic energy, E, due to the Coulombic interaction between (C–)H and O can be approximated by

$$E = (q_H q_O)/r \tag{5}$$

where q_H is the partial charge on the (C–)H atom, q_O is the partial charge on the O atom, and r is the interatomic distance.[42] The absolute value of q_H will invariably be smaller than that of q_O. Consequently, a change in q_H will have a greater effect on E than an equal change in q_O.

(3) Stoichiometry of the Crystal Structure. Nine of the 59 short (C–)H···O contacts listed in Table V occur in crystal structures that contain oxygen atoms but no O–H or N–H groups. This is a surprisingly large number, because there are only eight such structures in our sample. Furthermore, the α_i values (see eq 3) of seven of these structures fall in the range 0.0–0.075; the eighth is 0.250. These are somewhat lower than would be expected by comparison with the α_i values of the remaining structures. It seems that short (C–)H···O contacts are particularly likely to occur in crystal structures that contain a large number of oxygen atoms, but relatively few proton donor groups (i.e., O–H or N–H). One possible explanation is that oxygen atoms which are not involved in O—H···O or N—H···O hydrogen bonds are more accessible to (C–)H atoms than they would otherwise be.

Summary

We conclude that the majority of short C—H···O, C—H···N, and C—H···Cl contacts are attractive interactions, which can reasonably be described as hydrogen bonds. Our conclusion is based on a survey of 113 published crystal structures, which have been determined very precisely by neutron diffraction. It is consistent with the results of spectroscopic and theoretical studies. The C—H···X hydrogen bond may be a significant factor in determining the minimum energy packing arrangements of small organic molecules that contain nitrogen, e.g., the amino acids and nucleosides.

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[41] A total of 37 of the 47 amino acid (C_α–)H atoms in our sample form at least one contact to a hydrogen bond acceptor atom with $d > 0.0$ Å and C—H···X > 90°.

[42] Dauber, P.; Hagler, A. T. *Acc. Chem. Res.* **1980**, *13*, 105–112.

Kinetics and Mechanism of Oxidation of Aromatic Hydrocarbons by Ru(trpy)(bpy)O^{2+}

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Abstract: The kinetics of oxidation of p-$^-O_2CC_6H_4CH(CH_3)_2$, p-$^-O_2CC_6H_4CH_2CH_3$, and p-$^-O_2CC_6H_4CH_3$ by Ru(trpy)(bpy)O^{2+} (trpy is 2,2′,2″-terpyridine; bpy is 2,2′-bipyridine) to the corresponding α alcohols in water and of $C_6H_5CH(CH_3)_2$ and $C_6H_5CH_3$ by Ru$(bpy)_2$(py)O^{2+} in acetonitrile have been studied. The following conclusions are drawn from kinetics data obtained spectrophotometrically: (1) Rate constants increase with increasing alkyl substitution; for the carboxylates in water at 24.3 °C, $k = 12.2 \pm 1.2$, 3.4 ± 0.3, and 0.43 ± 0.04 $M^{-1}\,s^{-1}$ in the order shown above. (2) Rate constants decrease dramatically for the reactions in acetonitrile; $k(24.3\ °C) = 0.026 \pm 0.003$ $M^{-1}\,s^{-1}$ for isopropylbenzene. (3) In water, rate constants are independent of added O_2 or of changes in ionic strength. (4) In acetonitrile the added nucleophiles water, *tert*-butyl alcohol, or bromide ion enter the rate law directly in terms first order in added nucleophile. From the temperature dependence of k for the oxidation of p-$^-O_2CC_6H_4CH(CH_3)_2$, $\Delta H^\ddagger = 7 \pm 1$ kcal/mol and $\Delta S^\ddagger = -32 \pm 4$ eu. It is concluded that the redox step for the reactions involves a two-electron, hydride ion transfer step. The reactions occur by a template mechanism in that oxo group transfer from Ru to the substrate does not occur and the added oxygen atom must come from the solvent, p-$^-O_2CC_6H_4CH(CH_3)_2$ $(-H{:}^-; +H_2O) \rightarrow$ p-$^-O_2CC_6H_4C(OH)(CH_3)_2$. The solvent or added nucleophile (in acetonitrile) is directly involved in the redox step, apparently by assisting the loss of the hydride ion by electron pair donation.

Functionalized aromatic hydrocarbons are used as starting materials in a variety of syntheses, and their oxidations have been widely studied[1-3] both synthetically and mechanistically.[2,3] We have reported that the Ru(IV)–oxo complex Ru(trpy)(bpy)O^{2+} (bpy is 2,2′-bipyridine; trpy is 2,2′2″-terpyridine) is capable of

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[1] Ross, S. D.; Finkelstein, M.; Rudd, E. F. "Anodic Oxidation"; Academic Press: New York, 1975.

[2] Benson, D. "Mechanisms of Oxidation by Metal Ions"; Elsevier: New York, 1976.

[3] Wiberg, K. B., Ed. "Oxidation in Organic Chemistry"; Academic Press: New York, 1965.

[4] (a) Thompson, M. S. Ph.D. Dissertation, University of North Carolina, Chapel Hill, NC, 1981. (b) Moyer, B. A.; Thompson, M. S.; Meyer, T. J. *J. Am. Chem. Soc.* **1980**, *102*, 2310.