Organic Chlorine as a Hydrogen-Bridge Acceptor O–H···Cl–C

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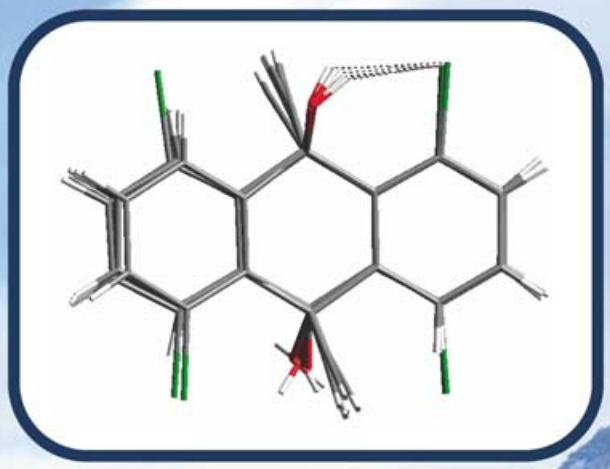

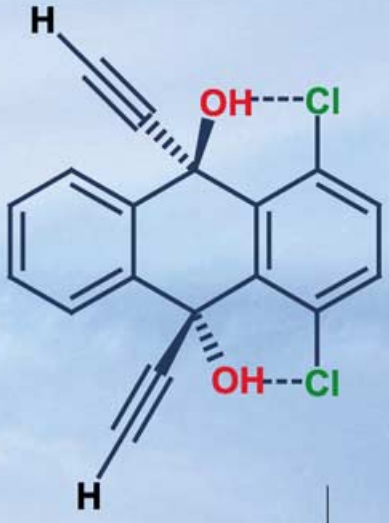

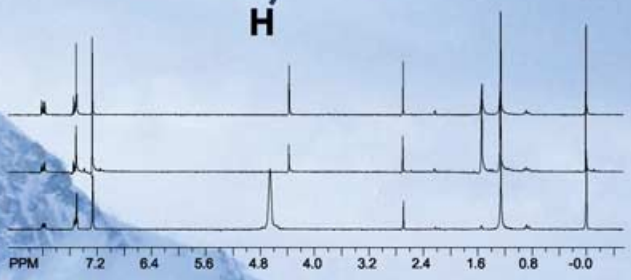

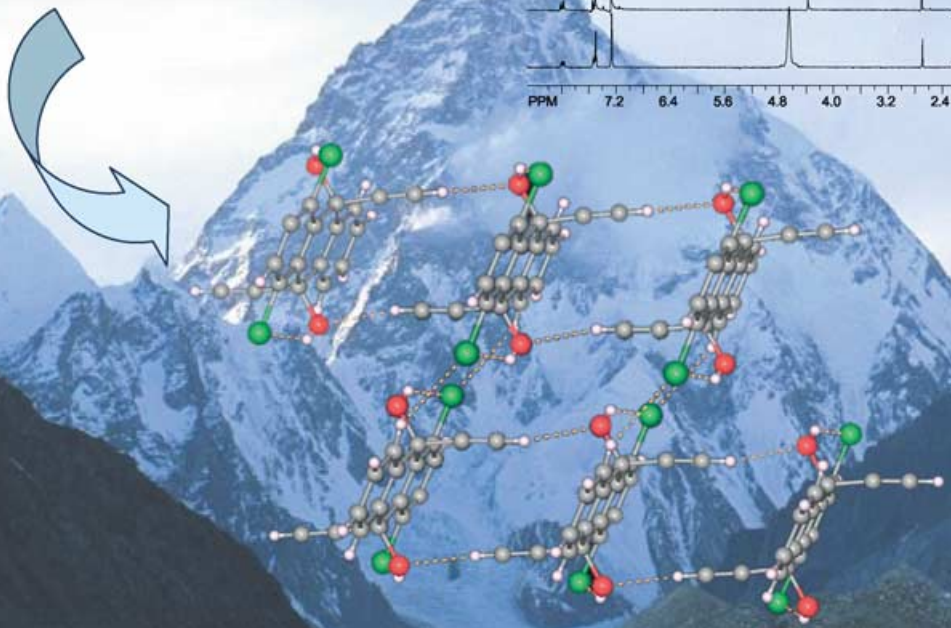

Supramolecular synthons Bridging molecules and crystals

The frontispiece was repared by Venu R. Vangala.

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Organic Chlorine as a Hydrogen-Bridge Acceptor: Evidence for the Existence of Intramolecular O−H···Cl−C Interactions in Some *gem*-Alkynols

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Abstract: The acceptor capabilities of "organic" halogen, CX (X = F, Cl, Br, I), with respect to hydrogen bonding are controversial, and unactivated organic chlorine is generally deemed to be a poor acceptor. Hydrogen bridges of the type O−H···Cl−C are uncommon and occur mainly in an intramolecular situation when the donor group is sterically hindered, so that the formation of intermolecular interactions is difficult. In this paper, intramolecular O−H···Cl−C interactions in a series of chloro-substituted *gem*-alkynols are studied. We describe various features of this interaction using crystallographic, spectroscopic and computational methods. The O−H···Cl−C interaction occurs in five of the six compounds under consideration here (CDDA, 14DDDA, 15DDDA, 18DDDA, 15MKA). Solution ^{1}H NMR spectroscopy shows that the interaction is intramolecular and that it is a true hydrogen bond. DFT calculations give a stabilisation energy around 4.0 kcal mol^{-1}. In the crystal structures of the compounds studied, the intramolecular O−H···Cl−C interactions fit into the overall scheme of cooperative interactions. These structures may be derived from that of the unsubstituted compound DDA by means of synthon exchange and the O−H···Cl−C interaction fares surprisingly well in the presence of competing stronger acceptors. The crystal structures show an unusual degree of modularity for compounds that generally form interactions that are weak and variable. It is noteworthy that the so-called "weak" acceptor, organic chlorine, is able to sustain a good intramolecular hydrogen bridge that is of an attractive and stabilizing nature and which is of potential importance in crystal engineering and supramolecular chemistry.

Keywords: chlorine · crystal engineering · hydrogen bonds · interaction energy · supramolecular chemistry

Introduction

In view of the growing importance of supramolecular chemistry and crystal engineering, there has been continued critical assessment of the weaker intermolecular interactions, which although not individually strong (less than 5 kcal mol^{-1}) may exert a substantial effect when added together.[1] The hydrogen bridge is a typical example.[2] Initial studies of molecular recognition in organic systems focused on strong O−H···O, O−H···N and N···H−O interactions (energy 5 to 15 kcal mol^{-1}) and supramolecular synthons based on these interactions are well documented.[3] More recently, weaker hydrogen bridges like C−H···O have also attracted attention.[4] In this context, the acceptor capabilities of "organic" halogen, C−X (X = F, Cl, Br, I) are controversial and noteworthy.[5]

Hydrogen bridges of the type O−H···Cl−C occur very rarely, and even when they do, they are generally in an intramolecular situation in which the donor group is sterically hindered so that the formation of intermolecular interactions is difficult. Classical studies in solution include the work of Hantzsch on dimethyl 3,6-dichloro-2,5-dihydroxyterephthalate[6] and of Wulf et al. on the *ortho*-halogenated phenols.[7,8] In the crystalline diterpenoid briarein A, a hydroxyl group forms an O−H···Cl−C interaction (d = 2.30, D = 3.11 Å, θ = 139° wherein d = H···A, D = X···A, θ = ∢X−H···A) located roughly at the bottom of the bowl-shaped molecule, and thus inaccessible to a number of strong carbonyl acceptors for the formation of any intermolecular O−H···O hydrogen bridges.[9] Toda et al. reported an unusual O−H···O−H···Cl−C cooperative network (d_{Cl} = 2.30, D_{Cl} = 3.09 Å, θ = 139°) in a ferrocene derivative.[10] The hydroxy groups are tertiary and, because of the awkward molecular shape, intermolecular hydrogen bonding is not favourable.[11]

The issue of organic halogen as a hydrogen bridge acceptor moved from the individual descriptive study to a more

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phenomenological one with a number of attempts that assess this particular capability. The accepting property of organic fluorine was studied by Taylor and Dunitz,[12] by Howard et al.[13] and by Boese, Desiraju and co-workers.[14] While there is no doubt that C–F is a very weak acceptor indeed, there is also convincing recent evidence that C–H···F–C is a necessary interaction in phenomena as disparate as transition-metal-catalysed alkene polymerisation, ligand–enzyme binding and molecular conformation.[15] As for the X–H···Cl–Y interactions, CSD studies by Seddon and Aakeröy,[5e] by Brammer and co-workers[5b] and by Thallapally and Nangia[5a] show that the interaction is viable if the Cl atom is activated, whether as Cl–M (M = transition metal), as Cl^- (chloride ion) or as organic chlorine with suitable activating groups present. Organic halogen as an acceptor may also be considered within the rubric of "halogen bonding" as outlined by Resnati, Metrangolo and co-workers.[16] The overall picture that emerges is mixed. On the one hand, unactivated organic chlorine is deemed to be a poor acceptor.[17] On the other, O–H···Cl–C interactions have been invoked even in solution, for example, to explain the appearance of polymorphs of 2,6-dihydroxybenzoic acid during recrystallisation from $CHCl_3$.[18]

The present study was prompted by the appearance of intramolecular O–H···Cl–C interactions in not just one, but in a series of chloro-substituted *gem*-alkynols that were prepared for other crystal engineering studies. Since the chloro substituents in this group of compounds may hardly be considered to be activated hydrogen-bond acceptors, it was felt that a more detailed study would be useful. In this paper we describe various features of the O–H···Cl–C hydrogen bridges in this set of compounds using crystallographic, spectroscopic and computational methods.

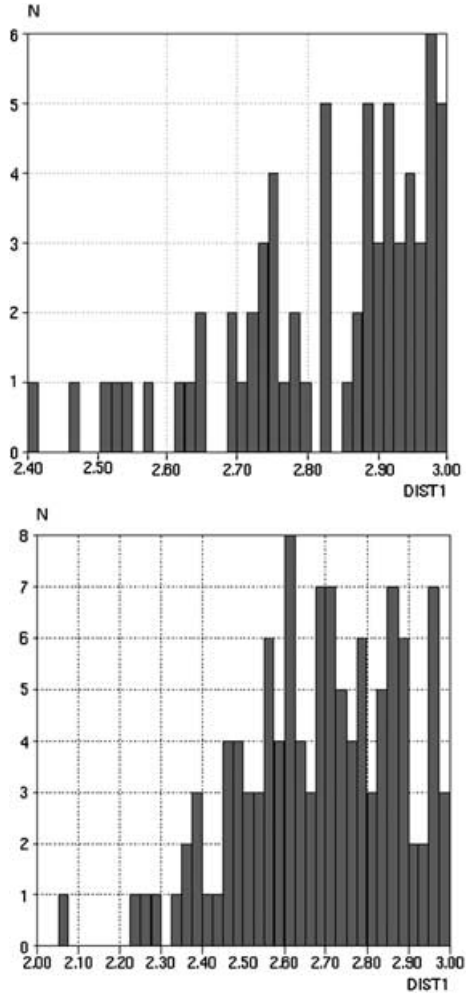
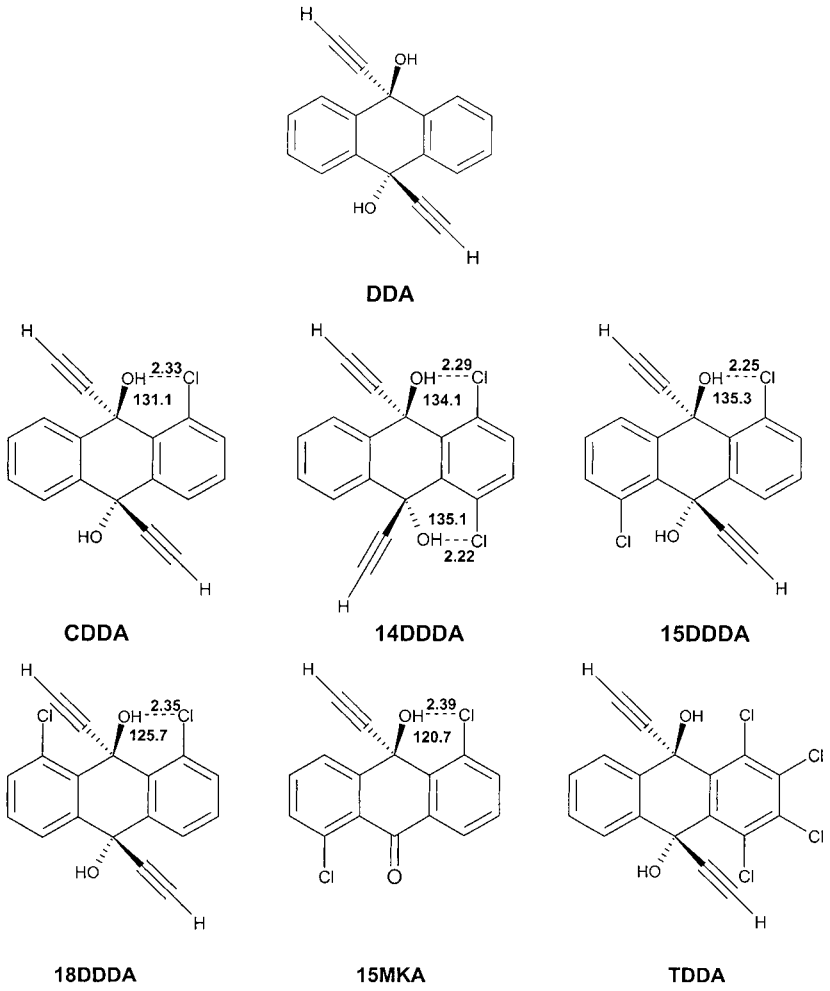


Figure 1. Histograms of intermolecular (top) and intramolecular (bottom) O–H···Cl–C interactions.

Results and Discussion

CSD study: A brief statistical study will place the experimental results in perspective. A search of the CSD (Version 5.25, November 2003) showed that of the 1277 crystal structures that contain both C–Cl and C–O–H functional groups, only 148 contain one or more O–H···Cl–C interactions.[19] Of these interactions, 68 are intermolecular, while 115 are intramolecular. Not only is the interaction observed infrequently but it is also reported to be weak. Rowland and Taylor mention that while values of d(H···A) for (O,N)–H···N(O) interactions are markedly smaller than those for C–H···O(N), these preferences are actually inverted when organic chlorine is an acceptor; in effect, values of d for (O,N)–H···Cl(Br) are larger than those for C–H···Cl(Br). Histograms for the intermolecular and intramolecular situations are given in Figure 1. This inversion is rationalised by the fact that interactions like O–H···Cl are often minor components in a bifurcated hydrogen bond,[20] while the C–H···Cl are stand-alone interactions. Still, this is an intriguing observation.

Molecular structures: Scheme 1 gives the structural formulae of the six *gem*-alkynols in this study; the intramolecular O–H···Cl–C interactions that occur in the solid state are shown in Figure 2. The parent compound *trans*-9,10-diethynyl-9,10-dihydroanthracene-9,10-diol is labelled DDA and the other compounds are given convenient related acronyms. Several previous joint publications from the Hyderabad and Durham groups have dealt with the *gem*-alkynols, and it is a general feature in these compounds that the combination of two hydrogen-bond donors and two acceptors in close proximity and in a sterically hindered situation results in a wide variety of hydrogen-bond patterns. This is because in a sterically demanding situation, the two donors (O–H and C≡C–H) become comparable, as do the two acceptors (–O– and C≡C). Consequently it is extremely difficult to predict in advance what the hydrogen-bond pattern will be for a particular compound.[21] Nonetheless, we noted that five of the six chloro derivatives under consideration (CDDA, 14DDDA, 15DDDA, 18DDDA, 15MKA) have an intramolecular O–H···Cl–C interaction, and in 15DDDA only one of the two Cl atoms does so. TDDA does not show an intramolecular O–H···Cl–C interaction in the solid state. The H···Cl distances (d) and the hydrogen-bond angles (θ) are also indicated in Scheme 1, and these distances are short (see Figure 1). That these interactions are also highly conserved is seen



Scheme 1. Compounds in this study with the geometric data of the solid state O–H···Cl–C interactions marked.

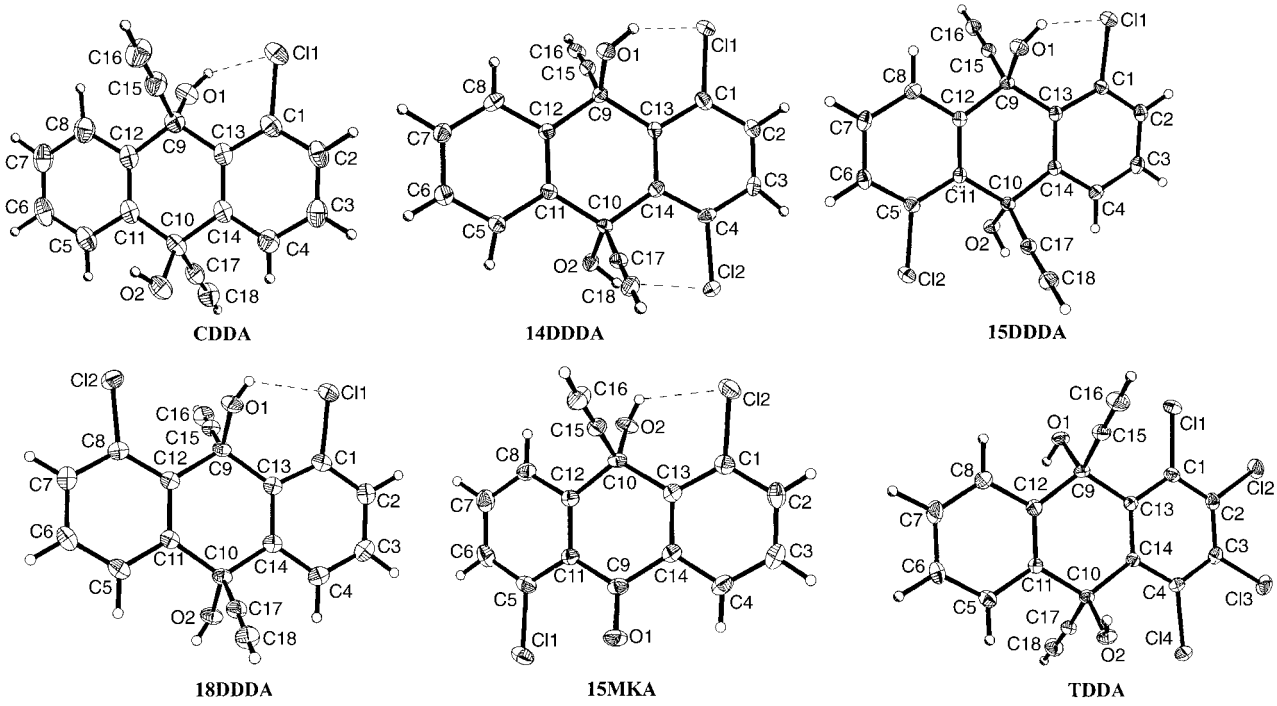


Figure 2. Single-molecule ORTEP drawings of the molecules studied. The O–H···Cl–C interactions are shown as dotted lines. Note that the symmetrical 15DDDA does not sit on an inversion centre in the crystal, and that TDDA and one of the two symmetry independent molecules in CDDA do not form O–H···Cl–C interactions

from an inspection of Figure 3, which is an overlap diagram of CDDA, 14DDDA, 15DDDA, 18DDDA and 15MKA. The approach of the hydroxyl group toward the Cl atom is very nearly the same in all five structures. Clearly this is a geometry that is sustained well within this set of compounds.

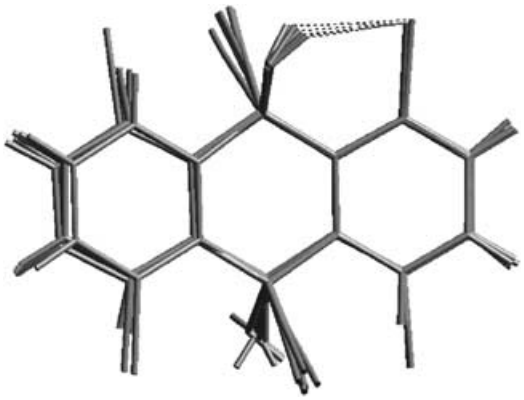


Figure 3. Overlay diagram of CDDA, 14DDDA, 15DDDA, 18DDDA and 15MKA. 14DDDA has been superimposed twice to show the intramolecular O–H···Cl–C interaction for each of the symmetry-independent hydroxyl groups.

NMR spectroscopy: Solution NMR data ($CDCl_3$) of the five molecules studied (Table 1) further reinforce the notion of an intramolecular O–H···Cl–C interaction. Unlike in the solid state, all O–H groups that can participate in intramolecular O–H···Cl–C interactions (both groups in 15DDDA and TDDA) do so in solution. The hydroxyl H atom shifts routinely from $\delta = 2.6$ ppm in *gem*-alkynols that lack a neighbouring Cl-group to around $\delta = 4.5$ ppm. This downfield shift is surprisingly large, but it is consistent and there is some precedent.[17b,22] The lack of further change in intensity or position of the peaks on dilution confirms the intramolecular nature of the interaction (Figure 4) and D_2O exchange confirms the assignment of the $\delta = 4.5$ ppm peak to the hydroxyl H atom.

Table 1. ^{1}H NMR chemical shifts of hydroxyl H atoms in *gem*-alkynols showing the existence of intramolecular O–H···Cl–C interactions.

Compound	δ(O–H···Cl–C) [ppm][a]	δ (free O–H) [ppm]
DDA	–	2.80
CDDA	4.61	2.78
14DDDA	4.39	–
15DDDA	4.46	–
18DDDA	4.51	2.79
TDDA	4.40	–
15MKA	4.71	–

[a] Hydrogen-bonded hydroxyl proton.

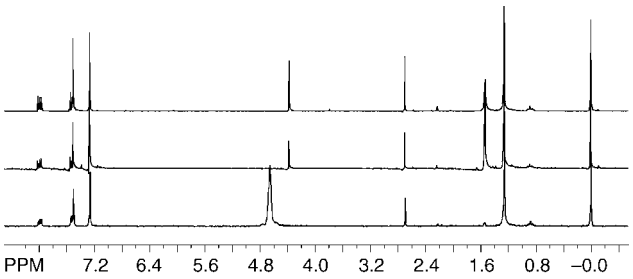


Figure 4. ^{1}H NMR spectra of 14DDDA ($CDCl_3$). Top: Initial spectrum. Middle: twice diluted. Bottom: D_2O added.

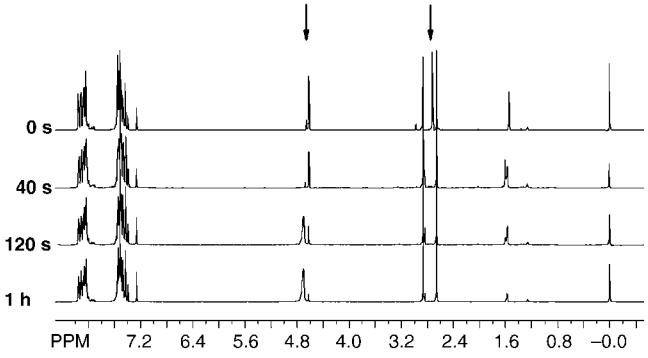


Figure 5. Time-resolved D_2O exchange NMR spectra of CDDA. Note that the intramolecular O–H···Cl hydrogen-bonded proton ($\delta = 4.61$ ppm) exchanges slowly relative to the "free" hydroxyl proton at $\delta = 2.78$ ppm, which exchanges immediately.

A further experiment with CDDA provides very clear evidence of the hydrogen-bond nature of this intramolecular interaction (Figure 5). In this compound, there are two nonequivalent O–H groups, with only one able to form an O–H···Cl–C interaction. Addition of D_2O showed that while the "free" O–H group exchanges immediately, the hydrogen bonded O–H requires one hour for complete exchange. Inspection of Figure 3 shows that the O–H groups in CDDA lie out of the mean plane of the three six-membered rings. Therefore both O–H groups in CDDA are sterically accessible to D_2O. So the difference in exchange rates cannot be attributed to a different steric situation for the O–H groups on the chlorine-rich and chlorine-poor faces of the molecule. The difference in exchange rates is therefore a direct consequence of the O–H···Cl–C interaction. In any discussion of weak interactions, nagging doubts (and rhetorical objections) have been expressed that observed geometries in crystals could well arise from forced contacts (intramolecular) or simple close packing considerations (intermolecular). Our observation on the slow exchange of the $\delta = 4.5$ ppm peak indicates that this particular so-called "weak" acceptor, namely organic chlorine, is well able to sustain a decent intramolecular hydrogen bridge, which is of an attractive and stabilizing nature.

As for 15DDDA and TDDA, intramolecular hydrogen bonds are formed by one and neither of the hydroxyl groups, respectively, in the solid state. In solution, however, both hydroxyl groups are available for hydrogen-bond formation and this is the consistent outcome. In summary, the NMR data show that the intramolecular O–H···Cl–C interaction is the preferred mode of association in appropriately chloro-substituted *gem*-alkynols, and further that it is attractive and of the hydrogen-bond type. It is not a fortuitous forced contact.

Theoretical calculations: The above observations show that organic chlorine is a respectable acceptor of hydrogen bonds. We therefore calculated the energy of the O–H···Cl– interaction using the work of Kovács et al. on the blue shifting of C–H···X (X = O, halogen) dimers of formaldehyde,[23] and taking other work on intramolecular hydrogen-bond energies as background.[24] The results in Table 2 pertain to both the Hartree–Fock ab initio method (PC Spartan; 6–31G*) and to DFT (GAMESS; B3LYP/6–31G*).[25] The Hartree–Fock optimised structure corresponds quite well with that obtained crystallographically, even though we note that the low-level basis set used may overestimate the energetics.[24c] The hydroxyl group H atom(s) of the trial molecule were rotated *anti* relative to the Cl–C bond, so that the O–H···Cl–C interaction is excluded.[26] The hydroxyl H atoms were fixed in their new positions and the structure was optimised at the 6–31G* level. The difference in the total energy of both the optimised conformational isomers gives the O–H···Cl–C bond energy. A similar strategy was employed for the DFT calculations. The respective trial molecules with and without O–H···Cl–C hydrogen bridges were optimised at the AM1 level. These geometries were then input into GAMESS for DFT calculations. The results show that the stabilisation energy for the interaction in question is surprisingly high (as is that for an intramolecular interaction), and that it occurs at the upper limit for weak hydrogen bonding. For example, Desiraju and Steiner have quoted an energy range of 0.5 to 4.0 kcal mol^{-1} for a weak hydrogen bridge.[1]

Table 2. O–H···Cl–C hydrogen-bond energies in the simulated structures.

Compound	Hartree–Fock level [kcal mol^{-1}]	DFT level [kcal mol^{-1}]
CDDA	4.446	4.320
14DDDA	3.558	4.384
15DDDA	4.150	4.681
18DDDA	3.662	2.889

Crystal structures: The crystal structures of the four molecules of interest (14DDDA, 15DDDA, 18DDDA, CDDA) may be considered in terms of: 1) how the intramolecular O–H···Cl–C interactions fit into the overall hydrogen bridge scheme, 2) how these structures may be derived from that of the unsubstituted compound DDA through synthon exchange and 3) how the O–H···Cl–C interaction fares in the presence of competing acceptors. All these descriptions are useful.

We recapitulate also that crystalline TDDA does not form an intramolecular hydrogen bond. Why this is the case is a matter of debate. Perhaps the extent of chlorination is so high and the O–H groups consequently so activated that O–H···O hydrogen-bridge formation competes favourably. In any event, the packing of the TDDA molecules is reminiscent of the packing of one of the CDDA molecules that does not form an intramolecular O–H···Cl–C bridge, in that a cooperative O–H···O–H···π arrangement is seen. Further details of this interesting structure will be published elsewhere.[27]

Table 3 gives pertinent crystallographic data and Table 4 gives the geometric data of the hydrogen bridges in these structures.

Hydrogen-bridge patterns: Figure 6 shows the packing of 14DDDA. The most notable structural feature is the absence of O–H···O hydrogen bonds. There is cooperative assistance to the O–H···Cl–C interaction from a C–H···O interaction and the O–H···Cl–C distance (d = 2.22 Å; θ = 135.1°) is the shortest in the series.

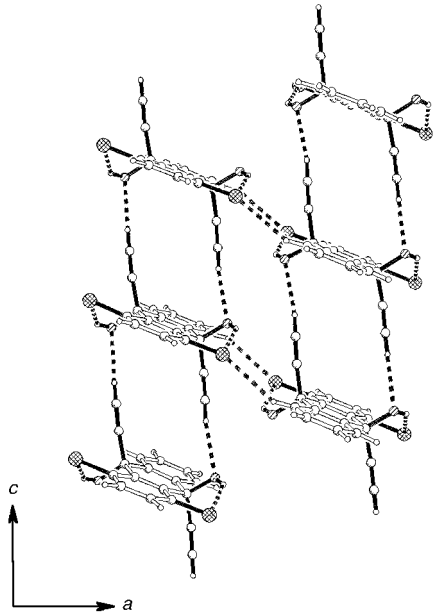


Figure 6. Packing diagram of 14DDDA. Notice the intramolecular O–H···Cl–C interaction. The planar C–H···O dimer synthon and intermolecular C–H···Cl hydrogen bridge are also shown.

Figure 7 shows the packing of 15DDDA. The dominant interaction pattern here is a cooperative arrangement of three hydrogen bridges, an intermolecular C–H···O bridge from the ethynyl group (d = 2.22 Å; θ = 160.5°), an intermolecular O–H···O bridge between hydroxyl groups (d, 1.83 Å; θ, 173.8°) and an intramolecular O–H···Cl–C bridge (d, 2.25 Å; θ, 135.3°).

Figure 8 shows the packing of 18DDDA. Once again there is a cooperative arrangement of the type C–H···O–H···O–H···Cl–C (intermolecular, intermolecular, intramolecular). To summarise, we note that in all three cases (14DDDA, 15DDDA and 18DDDA), the intramolecular O–H···Cl–C interaction gets cooperative assistance from other hydrogen bridges. Whatever the situation in solution (and the NMR results show that the interaction is far from negligible there), this cooperative assistance can only further stabilise the interaction in the solid state. The appearance of a C–H···O dimer synthon in all three structures results in a general similarity in the overall packing.

Table 3. Crystallographic data and structure refinement parameters.

	CDDA	14DDDA	18DDDA	15MKA	TDDA
solvent	EtOH/benzene (1:1)	EtOH/benzene (1:1)	$CHCl_3$/benzene (1:1)	$CHCl_3$/benzene (1:1)	$CHCl_3$/benzene (1:1)
formula	$C_{18}H_{11}O_2Cl$	$C_{18}H_{10}O_2Cl_2$	$C_{18}H_{10}O_2Cl_2$	$C_{16}H_8O_2Cl_2$	$C_{18}H_8O_2Cl_4$
M_r	294.72	329.16	329.16	303.12	398.04
crystal system	triclinic	triclinic	monoclinic	monoclinic	monoclinic
space group	$P\bar{1}$	$P\bar{1}$	$C2/c$	$P2_1/n$	$P2_1$
a [Å]	8.4500(17)	6.7496(4)	27.597(6)	7.2693(2)	9.3730(5)
b [Å]	9.2334(18)	7.2021(4)	6.8419(14)	11.5276(3)	9.5301(5)
c [Å]	14.108(3)	15.5160(8)	15.099(3)	15.4191(4)	10.3102(5)
α [°]	84.52(3)	76.992(2)	90	90	90
β [°]	89.85(3)	87.075(2)	101.48(3)	98.775(1)	114.559(2)
γ [°]	73.53(3)	74.353(2)	90	90	90
Z'	1.5	1	1	1	1
V [Å^3]	1050.4(4)	707.63(7)	2793.8(10)	1276.96(6)	837.65(7)
λ [Å]	0.71073	0.71073	0.71073	0.71073	0.71073
ρ_{calc} [g cm^{-3}]	1.398	1.545	1.565	1.577	1.578
μ [mm^{-1}]	0.273	0.462	0.468	0.504	0.714
2θ [°]	4.62–54.94	2.70–58.10	5.50–54.99	5.34–55.00	4.34–57.97
index range	$-10 \le h \le 10$	$-9 \le h \le 9$	$-35 \le h \le 35$	$-9 \le h \le 9$	$-12 \le h \le 12$
	$-11 \le k \le 11$	$-9 \le k \le 9$	$-8 \le k \le 8$	$-14 \le k \le 13$	$-13 \le k \le 13$
	$-18 \le l \le 18$	$-21 \le l \le 21$	$-19 \le l \le 19$	$-19 \le l \le 20$	$-14 \le l \le 13$
reflns. collected	12642	8590	15923	12801	10227
unique reflns.	4803	3693	3211	2925	4398
observed reflns.	3970	3175	2886	2436	4344
R_1 [$I > 2\sigma(I)$]	0.0408	0.0969	0.0350	0.0348	0.0283
wR_2	0.1025	0.2786	0.0999	0.0912	0.0748
goodness-of-fit	1.028	1.238	1.058	1.052	1.057
T [K]	120(2)	120(2)	120(2)	100(2)	120(2)
CCDC number	224902	224905	224903	224904	224901
crystal size [mm^3]	$0.44 \times 0.32 \times 0.08$	$0.34 \times 0.28 \times 0.08$	$0.32 \times 0.22 \times 0.16$	$0.22 \times 0.18 \times 0.06$	$0.58 \times 0.28 \times 0.12$

Table 4. Hydrogen-bridge geometric data for the crystal structures in this study.

Compound	Hydrogen bridge	d [Å^{-1}] (H···A)	D [Å^{-1}] (X···A)	θ [°] ∢X–H···A
CDDA	O1–H1···Cl1	2.33	3.071(1)	131.1
	O1′–H1′···O2	1.87	2.819(8)	162.3
	C16–H16···O1′	2.03	3.106(1)	174.1
	C18–H18···O1	2.35	3.376(2)	158.3
14DDDA	O1–H1···Cl1	2.29	3.055(5)	134.1
	O2–H2···Cl2	2.22	3.000(5)	135.1
	C16–H16···O1	2.40	3.436(9)	160.1
	C18–H18···O2	2.44	3.453(9)	156.0
15DDDA	O1–H9···Cl1	2.25	3.025(1)	135.3
	O2–H10···O1	1.83	2.814(2)	173.8
	C10–H5···O2	2.44	3.501(1)	164.7
	C16–H7···O2	2.22	3.021(1)	160.5
18DDDA	O1–H1A···Cl1	2.35	3.021(1)	124.4
	O2–H2A···O1	2.14	2.894(2)	132.2
15MKA	O2–H1···Cl2	2.39	3.017(1)	120.7
	O2–H1···O1	2.06	2.801(2)	130.2
	C16–H16···O2	2.44	3.254(2)	131.1
	C16–H16···O1	2.42	3.331(2)	140.4

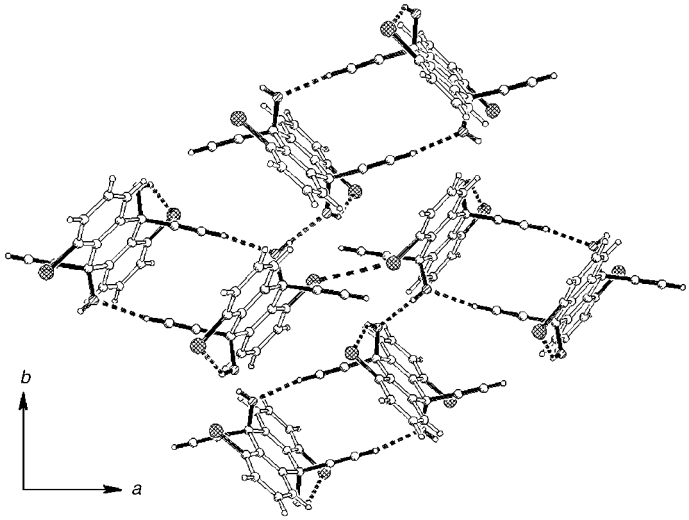
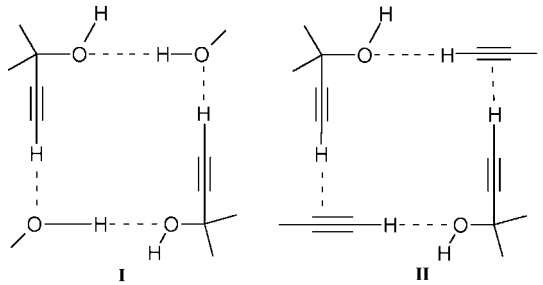


Figure 7. Packing diagram of 15DDDA to show the intramolecular O–H···Cl–C interaction. Notice again the C–H···O dimer synthon.

Synthon distortion and replacement: The representative synthons in DDA are **I** and **II**. Synthon **I** is composed of alternating strong (O–H···O) and weak (C–H···O) bridges, while **II** is made up of a loop of alternating C–H···O and C–H···π hydrogen bridges. It is found that the structure of DDA is related to those of 14DDDA, 15DDDA and 18DDDA via that of the monochloro derivative CDDA. It is therefore useful to discuss this last named compound in detail.

The CDDA molecule exposes a chlorine-rich face (**A**) and a hydrogen-rich face (**B**) in its self-assembly to the crys-



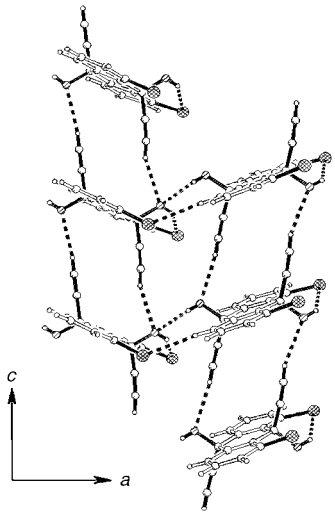
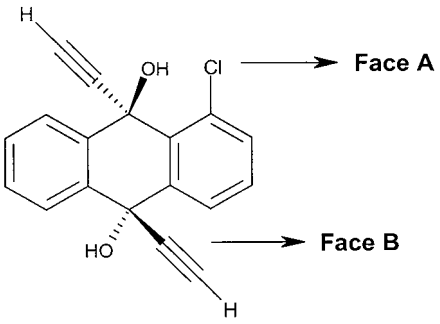
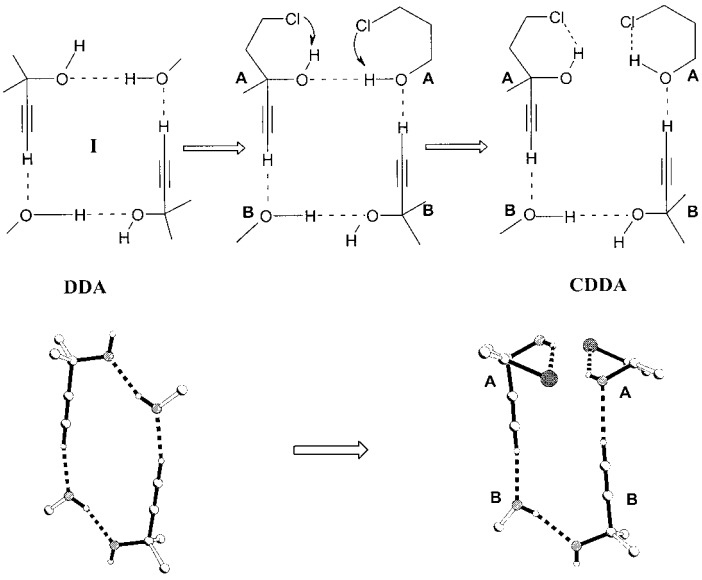


Figure 8. Packing diagram of 18DDDA to show the hydrogen bridges.



tal ($P\bar{1}$, $Z'=1.5$). The packing of CDDA is shown in Figure 9. There are two symmetry-independent molecules. The one which lies on a general position forms an intramolecular O–H···Cl–C interaction while that which lies on the special position does not.[28] Further it may be seen that face **B** forms synthon **II**, characteristic of the unsubstituted DDA, while on face **A** the formation of the intramolecular O–H···Cl–C bond disturbs the formation of synthon **I**, in part, leading to the C–H···O dimer already seen in the three dichloro derivatives, 14DDDA, 15DDDA and 18DDDA. In effect, the crystal packing of CDDA is a composite of the crystal structures of DDA and of the dichloro compounds. This is shown in Scheme 2. Compound CDDA may be therefore be considered as a supramolecular intermediate between DDA and the dichloro derivatives.



Scheme 2. Supramolecular distortion of synthon **I** by the Cl atom through intramolecular hydrogen bonding. Note how the vestigial synthon on the hydrogen rich side **B** of the molecule retains its original identity.

When there are two Cl atoms as in 14DDDA, both faces become chlorine-rich and, therefore, synthon **I** and the O–H···O hydrogen bonding vanish completely (Scheme 3).

In 18DDDA, there are again chlorine-rich and hydrogen-rich faces and an orderly shuffling of hydrogen-bonded synthons leads to the observed packing (Scheme 4). Once again O–H···Cl–C hydrogen bonding modifies the prototype DDA structure in an understandable way.

In 15DDDA the crystal packing is unusual (Figure 7) as has been described elsewhere.[29] The major structural feature is the Cl_4 supramolecular synthon, which is composed of two Cl atoms that are intramolecularly hydrogen bonded to O–H groups and two which are not. However the feature of note again is the absence of synthons **I** and **II** and this may be ascribed to presence of intramolecular O–H···Cl–C bridges.

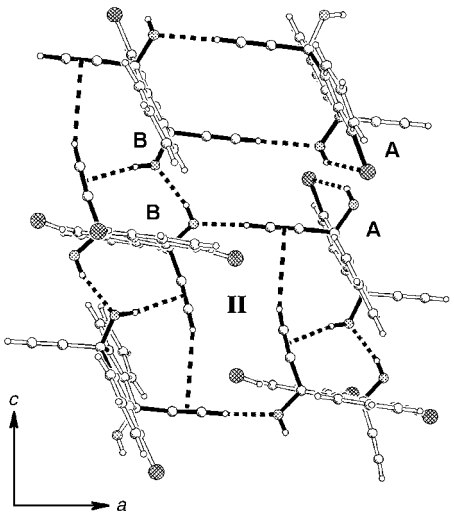
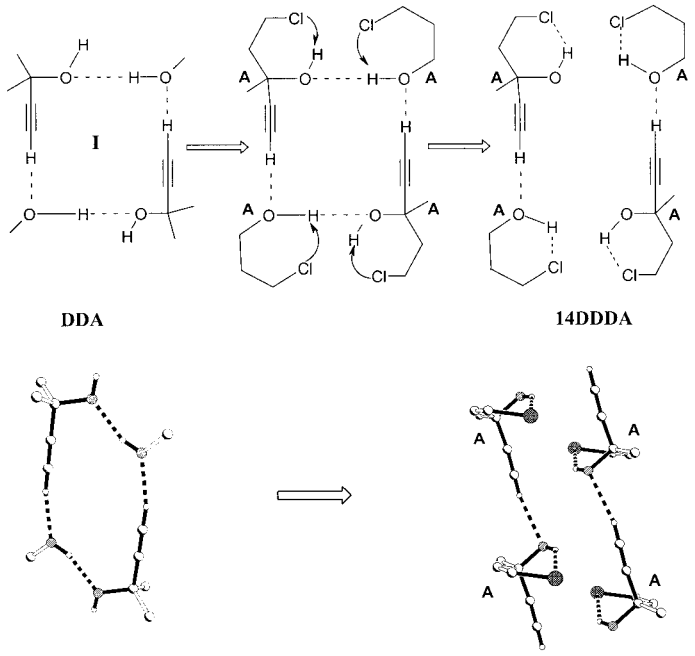


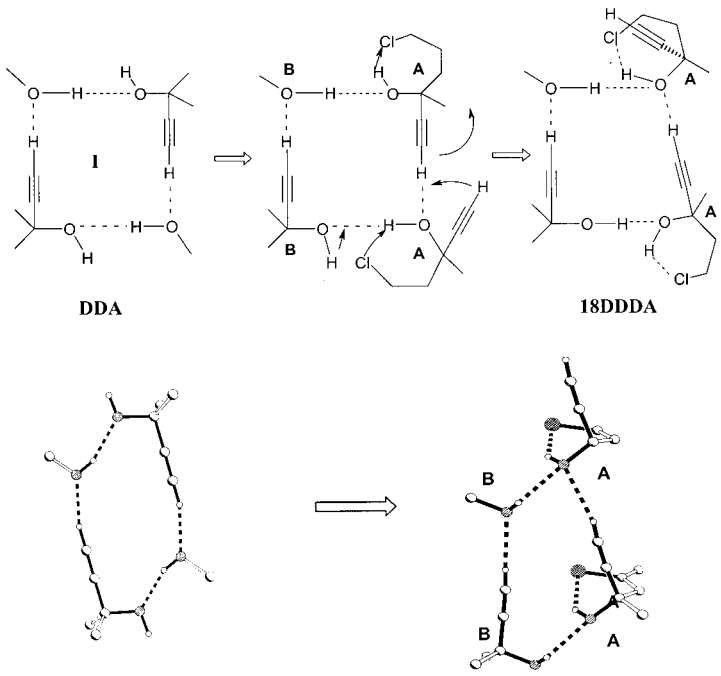
Figure 9. Packing diagram of CDDA. Notice the planar C–H···O dimer synthon, seen in all three dichloro isomers, and synthon **II** seen in DDA.

Competition between organic chlorine and a stronger acceptor: To assess the effectiveness of the intramolecular O–H···Cl–C interaction, we studied the keto-alcohol 15MKA, in which a much stronger acceptor (C=O) is present in a sterically unhindered situation.

If interaction hierarchy is to be followed, one would expect a strong O–H···O=C interaction. The actual crystal structure is most instructive (Figure 10). While there is an



Scheme 3. Supramolecular distortion of synthon **I** by two Cl atoms in 14DDDA.



Scheme 4. Supramolecular relationship between DDA and 18DDDA.

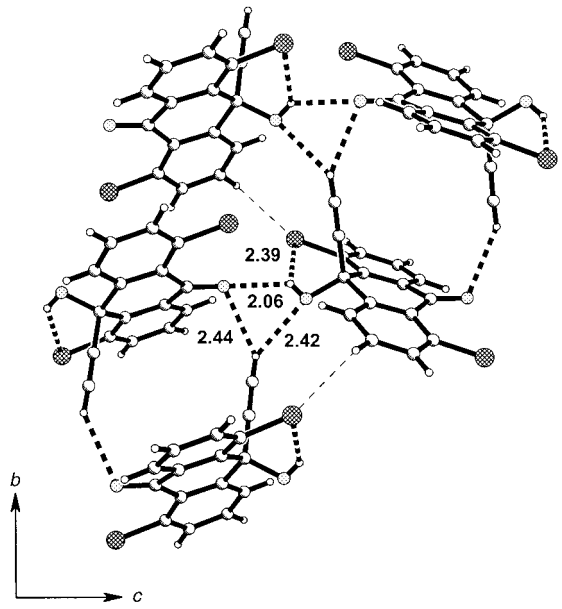


Figure 10. Packing diagram of 15MKA. Cl and O atoms are shaded. Notice the four distinct hydrogen bridges.

O–H···O=C interaction ($d = 2.06$ Å; $\theta = 130.2°$), it is long because the donor is bifurcated, participating also in an intramolecular O–H···Cl–C hydrogen bridge ($d = 2.39$ Å; $\theta = 120.7°$), which is short by the standards of this interaction. As if to "make up" for its "unfulfilled" acceptor capability, the C=O group accepts a weak hydrogen bridge from an ethynyl hydrogen atom ($d = 2.44$ Å; $\theta = 131.1°$); this H atom is also bifurcated and forms a bridge to an hydroxyl oxygen atom ($d = 2.42$ Å; $\theta = 140.4°$). In this interesting pattern of four interactions, it is indeed difficult to say which is more important and which is less important. Each is probably important for the viability of the overall synthon, and it is examples such as this that argue for the use of the term "hydrogen bridge" rather than "hydrogen bond" in describing the phenomenon.

Conclusion

This work shows that the O–H···Cl–C interaction is a notable example of a hydrogen bridge. Despite the fact that unactivated organic chlorine is not considered to be a good acceptor and the interaction is of the hard-donor/soft-acceptor type, it makes its appearance in a whole series of related compounds. Its significance is estimated by that fact that its effects on intra- and intermolecular structure are steady and consistent. The NMR results argue in favour of an attractive interaction and theoretical studies show that it is stabilizing to the extent of ~4.0 kcal mol^{-1}. These interactions are hardly forced contacts caused by functional groups that are merely juxtaposed.

The crystal structures in this paper show a surprising degree of modularity that one would not usually associate with these *gem*-alkynols, compounds that form a variety of hydrogen-bond patterns, because all the interactions are weak and variable. The perturbation that the adjacent Cl atom is able to make on the hydrogen-bond pattern of the parent *gem*-alkynol can be easily understood if the intramolecular O–H···Cl–C interaction is of more importance than a competing intermolecular O–H···O–H interaction. We conclude that O–H···Cl–C hydrogen bridges are of more significance than has been previously thought, and we believe that their potential importance in crystal engineering

and supramolecular chemistry has been somewhat underestimated.

Experimental Section

Solvents were purified by standard methods and dried if necessary. Reagents used were of commercial quality. All these compounds were characterised with NMR and IR spectra. The ^{1}H NMR spectra were recorded at 200 MHz on a Bruker ACF instrument. IR spectra were recorded on a Jasco 5300 spectrometer. All melting points were measured in a Fisher–Jones melting point instrument.

All operations were carried out in a dry N_2 atmosphere. CDDA, 14DDDA, 15DDDA, 18DDDA and TDDA were prepared from 1-chloro-9,10-anthraquinone, 1,4-dichloro-9,10-anthraquinone, 1,5-dichloro-9,10-anthraquinone, 1,8-dichloro-9,10-anthraquinone and 1,2,3,4-tetrachloro-9,10-anthraquinone, respectively. A solution of trimethylsilylacetylene (4.4 mmol) in THF (15 ml) was mixed with *n*-butyllithium (4.2 mmol) at 195 K. After stirring for 15 minutes, a solution of the respective quinone in THF (15 ml) was added dropwise and stirring was continued for 30 minutes at 195 K and for a further 1 h at room temperature. The solid product recovered after workup was treated with methanolic KOH to yield the desired compound. Crystals for X-ray analysis were obtained by purification of the crude material (column chromatography 30% EtOAc/hexane) followed by recrystallisation from 1:1 $CHCl_3$/benzene or 1:1 EtOH/benzene.

1-Chloro-*trans*-9,10-diethynyl-9,10-dihydroanthracene-9,10-diol (CDDA): Yield 65%; ^{1}H NMR (200 MHz $CDCl_3$): $\delta = 8.15$ (m, 3H), 7.58 (m, 4H), 4.61 (s, 1H), 2.87 (s, 1H), 2.78 (s, 1H), 2.68 ppm (s, 1H); IR: $\tilde{\nu} = 3508$, 3387, 3252, 3215, 2108, 1591, 1568, 1489, 1435, 1356,1286, 1248, 1228, 1149, 1111, 1026 cm^{-1}.

1,4-Dichloro-*trans*-9,10-diethynyl-9,10-dihydroanthracene-9,10-diol (14DDDA): Yield 68%; ^{1}H NMR (200 MHz $CDCl_3$): $\delta = 8.01$ (s, 2H), 7.58 (m, 2H), 7.51 (m, 2H), 4.39 (s, 2H), 2.70 ppm (s, 2H); IR: $\tilde{\nu} = 3530$, 3248, 2100, 1435, 1336, 1219, 1151, 1026 cm^{-1}; m.p. 554 K (with decomposition).

1,5-Dichloro-*trans*-9,10-diethynyl-9,10-dihydroanthracene-9,10-diol (15DDDA): Yield 60%; ^{1}H NMR (200 MHz $CDCl_3$): $\delta = 8.10$ (dd, $J = 8$, 3 Hz, peri 2H), 7.51 (m, 4H), 4.46 (s, 2H) 2.70 ppm (s, 2H); IR: $\tilde{\nu} = 3312$, 3288, 3177, 3001, 2881, 2116, 1973, 1811, 1595, 1562, 1456, 1300, 1205, 1039 cm^{-1}; m.p. 553 K (with decomposition).

1,8-Dichloro-*trans*-9,10-diethynyl-9,10-dihydroanthracene-9,10-diol (18DDDA): Yield 50%; ^{1}H NMR (200 MHz $CDCl_3$): $\delta = 8.08$ (m, peri 2H), 7.60 (m, 2H), 7.48 (m, 2H), 4.51 (s, 1H), 2.85 (s, 1H), 2.79 (s, 1H), 2.68 ppm (s, 1H); IR: $\tilde{\nu} = 3530$, 3256, 3048, 2106, 1591, 1562, 1437, 1340, 1222, 1176, 1149, 1024 cm^{-1}; m.p. 501 K.

1,2,3,4-Tetrachloro-*trans*-9,10-diethynyl-9,10-dihydroanthracene-9,10-diol (TDDA): Yield 55%; ^{1}H NMR (200 MHz $CDCl_3$): $\delta = 8.01$ (dd, $J = 8$, 3 Hz, 2H), 7.58 (dd, $J = 8$, 3 Hz, 4H), 4.40 (s, 2H), 2.70 ppm (s, 2H); IR: $\tilde{\nu} = 3485$, 3414, 3271, 3229, 2110, 1444, 1396, 1356, 1249, 1165, 1116 cm^{-1}; m.p. 506 K.

1,5-Dichloro-10-ethynyl-10-hydroxymonohydroanthracene-9-one (15MKA): This compound was obtained as a side product during the preparation of 15DDDA and separated by column chromatography. Yield 35%; ^{1}H NMR (200 MHz $CDCl_3$): $\delta = 8.27$ (dd, $J = 8$, 3 Hz, 1H), 8.15 (dd, $J = 8$, 3 Hz, 1H), 7.73 (m, 4H), 4.71 (s, 1H), 2.66 ppm (s, 1H); IR: $\tilde{\nu} = 3518$, 3271, 2926, 1168, 1585, 1442, 1278, 1138 cm^{-1}; m.p. 470 K.

Crystal structure analysis: X-ray diffraction intensities for all molecules were collected at 120 K (Oxford Cryosystems cryostat) on a Bruker SMART CCD diffractometer (Bruker Systems Inc., 1999a) by using $Mo_{K\alpha}$ radiation. Data were processed by using the Bruker SAINT package (Bruker Systems Inc., 1999b), with structure solution and refinement by using SHELX97 (Sheldrick, 1997).[30] The structures of all the compounds were solved by direct methods and refined by full-matrix least-squares on F^2. Hydrogen atoms were located in all six structures and refined freely with isotropic displacement parameters. The hydrogen atom positions were neutron normalised for all geometrical calculations. Crystal data and details of data collections, structure solutions and refinements are summarised in Table 3. We note that the disorder model for compound CDDA as well as the location of one of the symmetry independent molecules on a special position necessitates that the crystal contain both enantiomers of the molecule. This is not surprising given the method of synthesis. CCDC-224901 to CCDC-224905 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.uk).

Calculations: All calculations were carried out on Indigo Solid Impact and Indy workstations from Silicon Graphics.[31] All interatomic distances and related calculations were carried out with the PLATON programme.[32] Details of the ab initio calculations are given in the results section.

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[1] G. R. Desiraju, T. Steiner, *The Weak Hydrogen Bond in Structural Chemistry and Biology*, Oxford University Press, Oxford, **1999**.

[2] a) G. R. Desiraju, *Acc. Chem. Res.* **2002**, *35*, 565–573; b) T. Steiner, *Angew. Chem.* **2002**, *114*, 50–80; *Angew. Chem. Int. Ed.* **2002**, *41*, 48–76; c) T. W. Martin, Z. S. Derewenda, *Nat. Struct. Biol.* **1999**, *6*, 403–405.

[3] Selected recent references include: a) A. D. Bond, *New J. Chem.* **2004**, *28*, 104–114; b) V. S. S. Kumar, A. Nangia, M. T. Kirchner, R. Boese, *New J. Chem.* **2003**, *27*, 224–226; c) K. K. Arora, V. R. Pedireddi, *J. Org. Chem.* **2003**, *68*, 9177–9185; d) R. D. B. Walsh, M. W. Bradner, S. Fleischman, L. A. Morales, B. Moulton, N. Rodriguez-Hornedo, M. J. Zaworotko, *Chem. Commun.* **2003**, 186–187; e) P. Vishweshwar, A. Nangia, V. M. Lynch, *Cryst. Growth Des.* **2003**, *3*, 783–790; f) B. Olenik, T. Smolka, R. Boese, R. Sustmann, *Cryst. Growth Des.* **2003**, *3*, 183–188; g) J.-H. Fournier, T. Maris, J. D. Wuest, W. Guo, E. Galoppini, *J. Am. Chem. Soc.* **2003**, *125*, 1002–1006; h) C. B. Aakeröy, A. M. Beatty, B. A. Helfrich, *J. Am. Chem. Soc.* **2002**, *124*, 14425–14432; i) J. N. Moorthy, R. Natarajan, P. Mal, P. Venugopalan, *J. Am. Chem. Soc.* **2002**, *124*, 6530–6531; j) P. W. Baures, J. R. Rush, A. V. Wiznycia, J. Desper, B. A. Helfrich, A. M. Beatty, *Cryst. Growth Des.* **2002**, *2*, 653–664; k) V. S. S. Kumar, A. Nangia, A. K. Katz, H. L. Carrell, *Cryst. Growth Des.* **2002**, *2*, 313–318; l) L. R. MacGillivray, *CrystEngComm.* **2002**, *4*, 37–41; m) P. Gilli, V. Bertolasi, L. Pretto, A. Lyæka, G. Gilli, *J. Am. Chem. Soc.* **2002**, *124*, 13554–13567; n) R. K. R. Jetti, F. Xue, T. C. W. Mak, A. Nangia, *J. Chem. Soc. Perkin Trans. 2*, **2000**, 1223–1232; o) G. T. R. Palmore, J. C. MacDonald, *The Amide Linkage: Selected Structural Aspects in Chemistry, Biochemistry, and Materials Science* (Eds.: A. Greenberg, C. M. Breneman, J. F. Liebman), Wiley. New York, **2000**, pp. 291–336; p) F. H. Allen, W. D. S. Motherwell, P. R. Raithby, G. P. Shields, R. Taylor, *New J. Chem.* **1999**, *23*, 25–34; q) R. E. Meléndez, A. D. Hamilton, *Top. Curr. Chem.* **1998**, *198*, 97–130; r) A. Nangia, G. R. Desiraju, *Top. Curr. Chem.* **1998**, *198*, 57–95; s) V. A. Russell, C. C. Evans, W. Li, M. D. Ward, *Science* **1997**, *276*, 575–579.

[4] Selected recent references include: a) Y. Nishiyama, J. Sugiyama, H. Chanzy, P. Langan, *J. Am. Chem. Soc.* **2003**, *125*, 14300–14306; b) M. Jarvis, *Nature*, **2003**, *426*, 611–612; c) R. Boese, M. T. Kirchner, W. E. Billups, L. R. Norman, *Angew. Chem.* **2003**, *115*, 1921–1923; *Angew. Chem. Int. Ed.* **2003**, *42*, 1961–1963; d) D. Das, R. K. R. Jetti, R. Boese, G. R. Desiraju, *Cryst. Growth Des.* **2003**, *3*, 675–681; e) J. N. Moorthy, P. Venkatakrishnan, P. Mal, S. Dixit, P. Venugopalan, *Cryst. Growth Des.* **2003**, *3*, 581–585; f) S. Sarkhel, G. R. Desiraju, *Proteins* **2003**, *54*, 247–259; g) A. C. Pierce, K. L. Sandretto, G. W. Bemis, *Proteins* **2002**, *49*, 567–576; h) P. Raveen-

dran, S. L. Wallen, *J. Am. Chem. Soc.* **2002**, *124*, 12590–12599; i) B. P. Klaholz, D. Moras, *Structure* **2002**, *10*, 1197–1204; j) S. Scheiner, T. Kar, J. Pattanayak, *J. Am. Chem. Soc.* **2002**, *124*, 13257–13264; k) A. K. Chamberlain, J. U. Bowie, *J. Mol. Biol.* **2002**, *322*, 497–503; l) L. Jiang, L. Lai, *J. Biol. Chem.* **2002**, *277*, 37732–37740; m) M. M. Babu, S. K. Singh, P. Balaram, *J. Mol. Biol.* **2002**, *322*, 871–880; n) A. Senes, I. U. Belandia, D. M. Engelman, *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 9056–9061; o) F. M. Raymo, M. D. Bartberger, K. N. Houk, J. F. Stoddart, *J. Am. Chem. Soc.* **2001**, *123*, 9264–9267; p) R. Vargas, J. Garza, D. A. Dixon, B. P. Hay, *J. Am. Chem. Soc.* **2000**, *122*, 4750–4755; q) K. N. Houk; S. Menzer, S. P. Newton, F. M. Raymo, J. F. Stoddart, D. J. Williams, *J. Am. Chem. Soc.* **1999**, *121*, 1479–1487; r) S. S. Kuduva, D. C. Craig, A. Nangia, G. R. Desiraju, *J. Am. Chem. Soc.* **1999**, *121*, 1936–1944; s) S. Harder, *Chem. Eur. J.* **1999**, *5*, 1852–1861; t) T. Steiner, *Chem. Commun.* **1997**, 727–734; u) K. Biradha, A. Nangia, G. R. Desiraju, C. J. Carrell, H. L. Carrell, *J. Mater. Chem.* **1997**, 1111–1122.

[5] C–H···halogen interactions have been the topic of recent papers: a) P. K. Thallapally, A. Nangia, *Cryst. Eng. Comm.* **2001**, *27*, 1–6; b) L. Brammer, E. A. Bruton, P. Sherwood, *Cryst. Growth Des.* **2001**, *1*, 277–290; c) F. Neve, A. Crispini, *Cryst. Growth Des.* **2001**, *1*, 387–393; d) S. L. James, G. Verspui, A. L. Spek, G. van Koten, *Chem. Commun.* **1996**, 1309–1310; e) C. B. Aakeröy, T. A. Evans, K. R. Seddon, I. Pálinkó. *New J. Chem.* **1999**, *23*, 145–152; f) G. Aullón, D. Bellamy, L. Brammer, E. A. Bruton, A. G. Orpen, *Chem. Commun.* **1998**, 653–654.

[6] A. Hantzsch, *Chem. Ber.* **1915**, *48*, 797–816.

[7] O. R. Wulf, U. Liddel, S. B. Hendricks, *J. Am. Chem. Soc.* **1936**, *58*, 2287–2293.

[8] More than 50 years after Hantzsch's work, Curtin, Paul and Byrn (and later Dunitz and Richardson) showed this material to be polymorphic and associated the O–H···Cl–C interaction with only one of the trimorphs of the compound: a) D. Y. Curtin, S. R. Byrn, *J. Am. Chem. Soc.* **1969**, *91*, 1865–1866; b) D. Y. Curtin, S. R. Byrn, *J. Am. Chem. Soc.* **1969**, *91*, 6102–6106; c) S. R. Byrn, D. Y. Curtin, I. C. Paul, *J. Am. Chem. Soc.* **1972**, *94*, 890–898; d) Q.-C. Yang, M. F. Richardson, J. D. Dunitz, *J. Am. Chem. Soc.* **1985**, *107*, 5535–5537; e) Q.-C. Yang, M. F. Richardson, J. D. Dunitz, *Acta Crystallogr.* **1989**, *45*, 312–323; f) M. F. Richardson, Q.-C. Yang, E. N. Bregger, J. D. Dunitz, *Acta Crystallogr.* **1990**, *46*, 653–660.

[9] J. E. Burks, D. van der Helm, C. Y. Chang, L. S. Ciereszko, *Acta Crystallogr.* **1977**, *33*, 704–709.

[10] F. Toda, H. Liu, I. Miyahara, K. Hirotsu, *J. Chem. Soc.*, *Perkin Trans. 2* **1997**, *218*, 85–88.

[11] Although most examples of O–H···Cl–C hydrogen bonding involve sterically hindered donors, crystalline chloramphenicol shows an unexpected intra- cum intermolecular O–H···O–H···Cl–C pattern that would confound most current efforts at crystal structure prediction: K. R. Acharya, D. S. S. Gowda, M. Post, *Acta Crystallogr.* **1979**, *35*, 1360–1363.

[12] J. D. Dunitz, R. Taylor, *Chem. Eur. J.* **1997**, *3*, 89–98.

[13] J. A. K. Howard, V. J. Hoy, D. O'Hagan, G. T. Smith, *Tetrahedron*, **1996**, *52*, 12613–12622.

[14] V. R. Thalladi, H.-C. Weiss, D. Bläser, R. Boese, A. Nangia, G. R. Desiraju, *J. Am. Chem. Soc.* **1998**, *120*, 8702–8710.

[15] a) J. A. Olsen, D. W. Banner, P. Seiler, U. O. Sander, A. D'Arcy, M. Stihle, K. Müller, F. Diederich, *Angew. Chem.* **2003**, *115*, 2611–2615; *Angew. Chem. Int. Ed.* **2003**, *42*, 2507–2511; b) S. C. F. Kui, N. Zhu, M. C. W. Chan, *Angew. Chem.* **2003**, *115*, 1666–1670; *Angew. Chem. Int. Ed.* **2003**, *42*,1628–1632; c) T. J. Barbarich, C. D. Rithner, S. M. Miller, O. P. Anderson, S. H. Strauss, *J. Am. Chem. Soc.* **1999**, *121*, 4280–4281.

[16] A. D. Santis, A. Forni, R. Liantonio, P. Metrangolo, T. Pilati, G. Resnati, *Chem. Eur. J.* **2003**, *9*, 3974–3983.

[17] a) R. Taylor, O. Kennard, *J. Am. Chem. Soc.* **1982**, *104*, 5063–5070; b) T. Spaniel, H. Görls, J. Scholz, *Angew. Chem.* **1998**, *110*, 1962–1966; *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 1862–1865.

[18] R. J. Davey, N. Blagden, S. Righini, H. Alison, M. J. Quayle, S. Fuller, *Cryst. Growth Des.* **2001**, *1*, 59–65.

[19] Distances in the range 2.00–3.00 Å have been considered. We have been very liberal in the cut-offs used so that the readers may draw their own conclusions as to what is and what is not an O–H···Cl–C interaction.

[20] R. S. Rowland, R. Taylor, *J. Phys. Chem.* **1996**, *100*, 7384–7391.

[21] a) N. N. L. Madhavi, G. R. Desiraju, C. Bilton, J. A. K. Howard, F. H. Allen, *Acta Crystallogr.* **2000**, *56*, 1063–1070; b) C. Bilton, J. A. K. Howard, N. N. L. Madhavi, A. Nangia, G. R. Desiraju, F. H. Allen, *Acta Crystallogr.* **2000**, *56*, 1071–1079; c) N. N. L. Madhavi, C. Bilton, J. A. K. Howard, F. H. Allen, A. Nangia, G. R. Desiraju, *New J. Chem.* **2000**, *24*, 1–4; d) F. H. Allen, J. A. K. Howard, V. J. Hoy, G. R. Desiraju, D. S. Reddy, C. C. Wilson, *J. Am. Chem. Soc.* **1996**, *118*, 4081–4084.

[22] E. Engeldinger, D. Armspach, D. Matt, P. G. Jones, *Chem. Eur. J.* **2003**, *9*, 3091–3105.

[23] A. Kovács, A. Szabó, D. Nemcsok, I. Hargittai, *J. Phys. Chem.* **2002**, *106*, 5671–5678.

[24] A. Kovács, A. Szabó, I. Hargittai, *Acc. Chem. Res.* **2002**, *35*, 887–894; b) H. Y. Liao, S. Y. Chu, *New J. Chem.* **2003**, *27*, 421–424; c) S. Scheiner, *Hydrogen Bonding. A Theoretical Prespective*, Oxford University Press, Oxford, **1997**.

[25] M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. J. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. Su, T. L. Windus, M. Dupuis, J. A. Montgomery, *J. Comput. Chem.* **1993**, *14*, 1347–1363.

[26] The fact that the energy in 18DDDA is significantly less (Table 2) could be an artefact of this procedure. Only in this compound is the O–H group kept perpendicular to the ring.

[27] R. Banerjee, G. R. Desiraju, R. Mondal, J. A. K. Howard, unpublished results.

[28] Both molecules exhibit a positional disorder with respect to the site occupancy of the Cl atoms at different substitution sites on the benzene rings. The first shows a disorder between two orientations, with the Cl atom occupying positions Cl(1) and Cl(1A) in a 9:1 ratio. The second is effectively disordered between four sites, arising from the overall crystallographic molecular site symmetry, whereby the Cl atoms at positions Cl′and Cl″ are in an ~2:1 ratio (33%: 17%). The elongated displacement ellipsoids of C atoms indicate that the disorder is not confined to Cl atoms, but involves also the dihydroanthracene core. However the displacement between the two orientations is too small to refine them separately and, as a result, the refinement in an averaged, "*pseudo-ordered*" model gives an apparently shortened C–Cl bond for the minor orientation.

[29] R. Banerjee, G. R. Desiraju, R. Mondal, A. S. Batsanov, C. K. Broder, J. A. K. Howard, *Helv. Chim. Acta* **2003**, *86*, 1339–1351.

[30] G. M. Sheldrick, SHELX97, University of Göttingen (Germany), **1997**.

[31] Cerius^2 Program Molecular Simulations, 9685 Scranton Road, San Diego.

[32] A. L. Spek, PLATON, Bijvoet Centre for Biomedical Research, Vakgroep Kristal-en Structure-Chemie, University of Utrecht (The Netherlands).

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