



Supramolecular equivalence of halogen, ethynyl and hydroxy groups. A comparison of the crystal structures of some 4-substituted anilines

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Paper

Chloro, bromo and ethynyl substituents play exactly the same role in the crystal structures of the corresponding 4-substituted anilines and this is related to their similar polarisations. The iodo derivative is, however, distinct and this may be related to its greater size.

Introduction

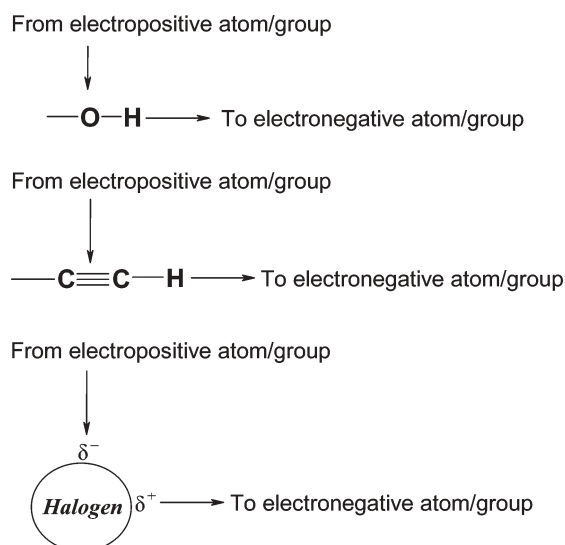
An important goal of crystal engineering is the ability to manipulate crystal packing *via* functional group transformations.¹ Unlike in molecular chemistry, crystal structures cannot be explicitly related to molecular functionality. The relationship is implicit and observed crystal structures arise from a complex convolution of the recognition properties of molecular functional groups.² Given this difficulty, a promising strategy to incorporate the functional group approach into crystal engineering is to examine topology and interaction similarities between selected groups. Consider, for example, Scheme 1.

Groups such as $-\text{OH}$, $-\text{C}\equiv\text{C}-\text{H}$ and $-\text{X}$ ($\text{X} = \text{Cl}, \text{Br}, \text{I}$) have similar supramolecular characteristics, and this similarity whether it be geometrical or chemical has been explored by several workers. That the $-\text{OH}$ and $-\text{C}\equiv\text{C}-\text{H}$ groups play similar roles has been pointed out by Steiner.³ The relationship between ethynyl and halogen groups has been documented by the Boese,⁴ Harris⁵ and Gilardi⁶ groups. Specifically, the $\text{X}\cdots\text{X}$ contacts in these cases are type-II and this is in keeping with the electrophile–nucleophile model.⁷ Accordingly, the crystal structures of the α -form of 1,4-dichlorobenzene, 1,4-diethynylbenzene and γ -hydroquinone are topologically identical and

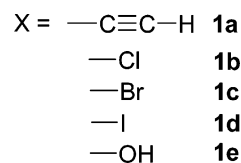
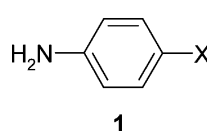
supramolecularly equivalent.⁸ The equivalence of hydroxy and halogen groups has not been discussed *per se* but there are obvious similarities, for example between supramolecular synthons of the type $(\text{OH})_3$ and X_3 , or $(\text{OH})_4$ and X_4 .⁹

In almost all the above studies, compounds were considered that contain $-\text{OH}$, $-\text{C}\equiv\text{C}-\text{H}$ or $-\text{X}$ groups or some combination of these groups. In a particularly detailed work, Philp, Harris and co-workers have examined the occurrence of crystallographic disorder in di- and tri-substituted benzenes, where the substituents are $-\text{C}\equiv\text{C}-\text{H}$ and $-\text{X}$.⁵ Similarly, Boese and co-workers have examined the series of 4-ethynylhalogenobenzenes wherein they found that $-\text{F}$ was distinct from $-\text{Cl}$, $-\text{Br}$ and $-\text{I}$.⁴ The recurring theme in these studies is that replacement of the halogen substituents in a molecule by ethynyl causes no change in the crystal structure. Such behaviour is taken to be evidence of the similarity between ethynyl and halogen groups in determining crystal packing. Halogen–ethynyl exchange can be taken as far as the replacement of elemental Br_2 by C_2H_2 . For instance, bromine in the molecular complexes of Br_2 with benzene and toluene¹⁰ may be substituted by acetylene.¹¹ A further extension of this work is the corresponding $\text{Br}_2/\text{C}_2\text{H}_2$ exchange in the complexes with dioxane.¹¹

In this work, we have extended these arguments by studying a series of compounds where $-\text{X}$, $-\text{C}\equiv\text{C}-\text{H}$ and $-\text{OH}$ are introduced in a molecule in the presence of another group that is not supramolecularly equivalent to the above mentioned groups. In particular, we discuss the crystal packing features of the series of 4-substituted anilines, **1a** through **1e**.



Scheme 1



Experimental

1 Synthesis

Compound **1a** was prepared according to the published procedure.¹² **1c** and **1d** were purchased from Lancaster. Crystals suitable for X-ray investigation were prepared by slow evaporation of solvent. We used 1 : 1 EtOAc–hexane as

Table 1 Crystallographic data for **1a–1d**

Compound	1a	1b ^a	1c	1d
Chemical formula	C ₈ H ₇ N	C ₆ H ₆ NCl	C ₆ H ₆ NBr	C ₆ H ₆ NI
Formula weight	117.15	127.57	172.01	219.02
Crystal system	Orthorhombic	Orthorhombic	Orthorhombic	Monoclinic
Space group	<i>Pnma</i>	<i>Pnma</i>	<i>Pnma</i>	<i>P2₁</i>
<i>a</i> /Å	10.423(4)	8.594	8.594(2)	8.422(7)
<i>b</i> /Å	7.033(3)	7.244	7.6166(19)	4.965(4)
<i>c</i> /Å	8.951(4)	9.191	9.469(2)	8.645(7)
α /°	90	90	90	90
β /°	90	90	90	109.790(13)
γ /°	90	90	90	90
<i>Z</i>	4	4	4	2
<i>V</i> /Å ³	656.2(5)	572.2	619.8(3)	340.2(5)
<i>D_c</i> /Mg m ⁻³	1.186		1.833	2.138
<i>F</i> (000)	248		336	204
μ /mm ⁻¹	0.071		6.513	4.599
<i>R</i> _{int}	0.0356		0.1079	0.0334
θ Range/°	3.00–28.53		3.20–28.42	2.50–28.63
Reflections collected	4811		4777	2964
Unique reflections	866		837	1630
Reflections with <i>I</i> > 2 σ (<i>I</i>)	753		656	1463
<i>R</i> ₁ [<i>I</i> > 2 σ (<i>I</i>)]	0.0544		0.0370	0.0391
<i>wR</i> ₂	0.1528		0.0929	0.0958

^a Data for **1b** is given for comparison.

the recrystallising solvent for **1a** and **1c**, and 2 : 1 EtOAc–CHCl₃ for **1d**.

2 X-Ray crystallography

X-Ray data for compounds **1a**, **1c** and **1d** were collected on a SMART diffractometer using Mo-K α radiation. Structure solution and refinement were carried out using SHELXL programs built in with the SHELXTL (Version 6.12) package.¹³ The positions of the H atoms bound to C and N atoms in **1a**, **1c** and **1d** (only H atoms bound to N) were located in difference Fourier maps and these H atoms were also refined as riding, with $U_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}(\text{N})$ or $1.2 U_{\text{eq}}(\text{C})$, while the phenyl H atoms in **1d** were generated by a riding model on idealized geometries with $U_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}(\text{C})$. See Table 1 for crystallographic data for compounds **1a–1d**.

CCDC reference numbers 209451–209453.

See <http://www.rsc.org/suppdata/ce/b3/b304785g/> for crystallographic data in CIF or other electronic format.

Results and discussion

The crystal structure of 4-ethynylaniline, **1a** was determined earlier by Hogarth, Orpen and co-workers.¹⁴ The earlier work has an *R*-value of 0.14 and no 3-D coordinates are available in the CSD. We redetermined the structure to obtain good parameters. Fig. 1a shows the atom-numbering scheme and Fig. 2a shows the packing. The ethynyl group is hexa-coordinated. In addition to its covalent linkage, it accepts four hydrogen bridges, two N–H $\cdots\pi$ and two C–H $\cdots\pi$, while it donates one to the adjacent phenyl ring, a particularly short C–H $\cdots\pi$ interaction¹⁵ (Table 2). We note that the orientation of the five hydrogen bridges is in conformity with the polarisation of the ethynyl group. Notably, the –NH₂ group favours the formation of N–H $\cdots\pi$ rather than N–H $\cdots\text{N}$ bridges. The geometry of this interaction is very similar to that of the Cl–H $\cdots\pi$ interaction in the 2-butyne–HCl crystal, studied by Mootz and Deeg.¹⁶ Other features of the crystal packing of **1a** have been detailed by Hogarth, Orpen and co-workers¹⁴ and are therefore not discussed again. The importance of the N–H $\cdots\pi$ interactions is hinted at by the melting points of the compounds: **1a** (373 K); **1b** (343 K); **1c** (337 K); **1d** (364 K); *p*-toluidine (315 K).

The crystal structure of 4-chloroaniline, **1b** has been determined several times¹⁷ and our analysis is based on the most recent and accurate data obtained by Takazawa, Ohba and Saito. Fig. 1b gives the atom-numbering scheme and Fig. 2b the packing. The structure is isostructural with **1a** and the Cl-group is likewise hexa-coordinate. Although the Cl-group forms as many as five intermolecular interactions (two N–H $\cdots\text{Cl}$, two C–H $\cdots\text{Cl}$ and one C–Cl $\cdots\pi$), the orientation preferences of these interactions is in keeping with the electrophile–nucleophile model,⁷ in that the contacts towards the pole (electrophilic end) are those where –Cl acts as an electron deficient moiety while contacts towards the equatorial (nucleophilic end) are those where the same –Cl acts as an electron rich moiety (Table 2). The polarisation of the –Cl atom in **1b** is therefore the same as that of the –C=C–H group in **1a**. The two groups –Cl and –C=C–H behave in exactly the same way supramolecularly and replacement of one by the other causes no change in the crystal structure.

We redetermined the crystal structure of 4-bromoaniline, **1c**, because the earlier structure determination is of limited precision¹⁸ with 3-D coordinates unavailable in the CSD. The structure is the same as that of the ethynyl and chloro derivatives (Fig. 1c and 2c; Table 2). The supramolecular equivalence of –C=C–H and –Cl may therefore be extended to –Br.

In contrast, the crystal structure of 4-iodoaniline, **1d** is distinct and now a more conventional packing is obtained with N–H $\cdots\text{N}$, N–H $\cdots\text{I}$, I $\cdots\text{I}$ and C–H $\cdots\pi$ interactions. Fig. 1d gives the atom-numbering scheme and Fig. 3 shows the crystal structure. Table 2 gives the salient intermolecular interactions. The N–H $\cdots\text{N}$, N–H $\cdots\text{I}$, I $\cdots\text{I}$ and C–H $\cdots\pi$ interactions occur within the accepted distance and angle ranges.⁸

A notable question is why iodoaniline, **1d** is not isostructural with the ethynyl, chloro and bromo derivatives, **1a**, **1b** and **1c**. Isostructurality among the non-fluorine halogens is a well-documented phenomenon; for example C₆Cl₆, C₆Br₆ and C₆I₆ are isostructural. Further, *p*-chloro-, *p*-bromo- and *p*-iodoethynylbenzene are isostructural.⁴ However, there are limits to this kind of halogen equivalence. While *p*-C₆H₄Cl₂ and *p*-C₆H₄Br₂ are isostructural, *p*-C₆H₄I₂ is distinct.⁴ Rationalisation of the crystal packing of organic molecular solids may be difficult when strong hydrogen bonding is not involved. Some reasons why the packing of **1d** is hard to understand are: (1) all

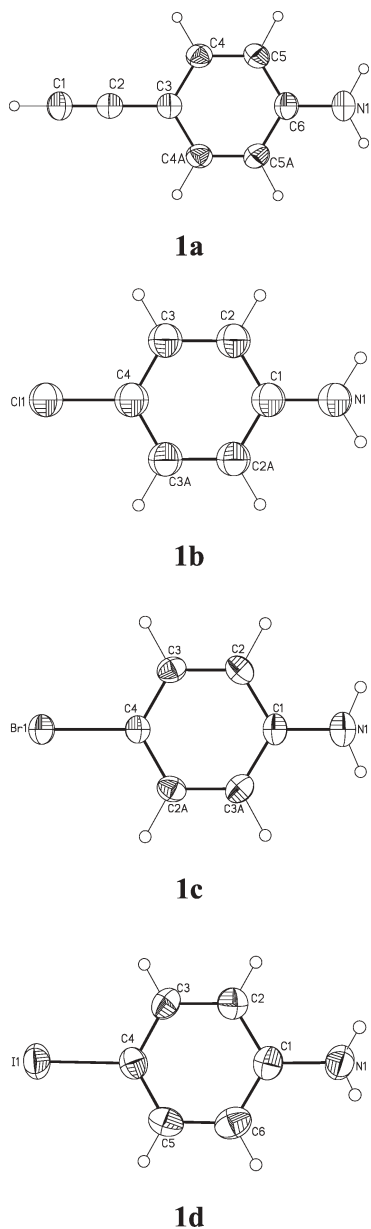


Fig. 1 Atom labelling scheme in the molecules in this study.

the intermolecular interactions are weak; (2) the halogen and/or ethynyl groups could exert effects on the crystal packing that arise from both geometrical and chemical effects; (3) the possibility of polymorphism may have to be considered. With reference to compound **1d** in relation to **1a–1c**, does the iodo group behave like a group of a certain shape and size or like a group with a certain directional polarisation? Such a question is hard to answer because the N–H \cdots N, N–H \cdots π , N–H \cdots I and I \cdots I interactions are equienergetic. Shape and volume effects (close packing arguments) also need not be overriding.¹⁹ In the series of 1,3,5-trisubstituted benzenes, Philp, Harris and co-workers⁵ have noted that 1,3,5-trichlorobenzene is isostructural with 1,3,5-tribromobenzene, 1,3-dibromo-5-ethynylbenzene, 1-bromo-3,5-diethynylbenzene and also 1-fluoro-3,5-diethynylbenzene. However 1,3,5-triethynylbenzene has a different crystal structure. Likewise, Boese and co-workers have noted that 4-fluoro-1-ethynylbenzene has a different packing with respect to the corresponding chloro, bromo and iodo derivatives.⁴ This would suggest that there are subtle chemical differences between the –C \equiv C–H group on the one hand and the –Cl and –Br groups on the other.

Now let us consider the geometrical differences. The volumes

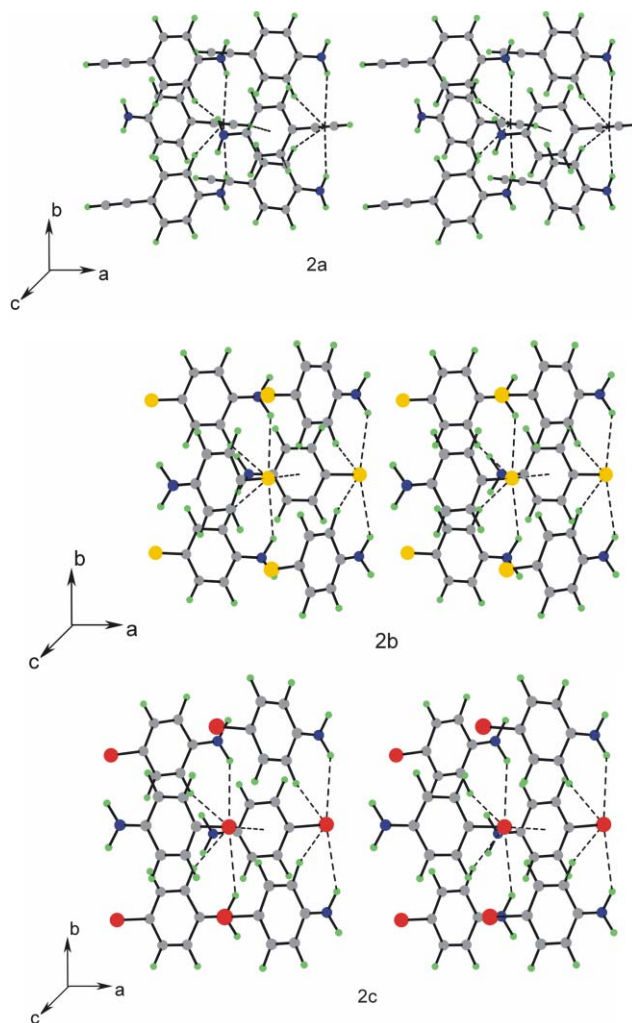


Fig. 2 Stereoviews of the crystal structures of the ethynyl-, chloro- and bromo-anilines. Carbon atoms are grey, nitrogen atoms are blue, chlorine atoms are yellow, bromine atoms are red and all hydrogens light green. Click here to access a 3D representation of chloroaniline. Click here to access a 3D representation of bromoaniline.

of the four groups under consideration are: –Cl (18.1 Å³), –Br (24.4 Å³), –C \equiv C–H (28.8 Å³) and –I (32.96 Å³). When chemically similar groups with differing volumes lead to the same crystal structure, one may conclude that chemical factors are important. When different crystal structures are obtained, geometrical factors possibly play a more dominant role. Accordingly, we may ascribe a geometrical role to the –I group in **1d**. In effect, the formation of the I \cdots I interaction may be a favoured event because the iodo substituent is the largest moiety present. Volume differences between –Cl and –C \equiv C–H may be small enough such that chemical arguments hold sway but the volume of –I may have crossed a threshold value so that a transition to another structure type occurs. This may also be the reason why *p*-diiodobenzene is different from *p*-dichlorobenzene and *p*-dibromobenzene. All this aside, one should also consider the possibility of polymorphism. While no polymorphs of compounds **1a–1d** were found, it must be admitted that they were not searched for in an exhaustive manner.

Finally, it is pertinent to comment on the –OH group which also has a similar polarisation (Scheme 1). However, the crystal structure of 4-aminophenol, **1e** is entirely different from that of **1a–1d** and both O–H \cdots N and N–H \cdots O hydrogen bonds are involved to generate the so-called saturated β -As type hydrogen bonded sheet.²⁰ Curiously, there is a topological similarity between the β -As sheet in **1e** and the 2-dimensional pattern of I \cdots I, N–H \cdots I and N–H \cdots N interactions in **1d**

Table 2 Geometrical parameters of interactions in the crystal structures of **1a–1d**

Compound	Interactions	$D/\text{\AA}$	$d/\text{\AA}$	$\theta/^\circ$
1a	N–H \cdots triple (M) ^a	3.67	2.72	156
	N–H \cdots triple (C ₁)	3.65	2.67	162
	N–H \cdots triple (C ₂)	3.79	2.90	147
	^b C–H \cdots triple (M)	3.72	2.77	146
	^b C–H \cdots triple (C ₁)	3.83	2.88	146
	^b C–H \cdots triple (C ₂)	3.71	2.79	142
	^c C–H \cdots ring (M)	3.35	2.43	142
	^c C–H \cdots ring (C ₃)	3.62	2.54	175
	1b	N–H \cdots Cl	3.72	2.88
^b C–H \cdots Cl		3.75	2.76	152
Cl \cdots ring (M)		3.33		162
Cl \cdots ring (C ₄)		3.48		174
1c	N–H \cdots Br	3.91	3.02	146
	^b C–H \cdots Br	3.91	2.91	152
	Br \cdots ring (M)	3.39		160
	Br \cdots ring (C ₄)	3.46		176
1d	N–H \cdots N	3.13	2.13	169
	N–H \cdots I	3.98	3.12	143
	^b C–H \cdots ring (M)	3.85	2.96	139
	^b C–H \cdots ring (C ₃)	3.67	2.61	165
	I \cdots I	4.02		153/122

^a M = Centre of the π system. ^b C = Phenyl carbon atom. ^c C = Ethynyl carbon atom, triple = bond to the π system of triple bond, ring = bond to π system of the phenyl group. All C–H and N–H distances are neutron normalised to 1.083 and 1.009 Å.

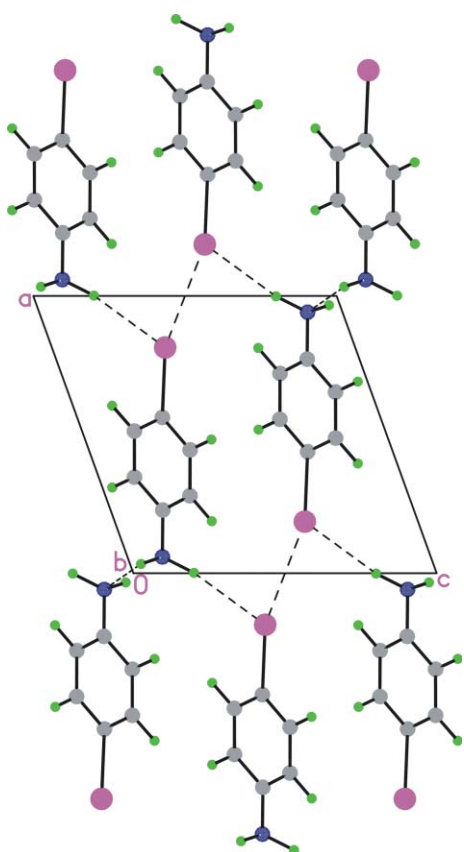


Fig. 3 Crystal structure of 4-iodoaniline. Carbon atoms are grey, nitrogen atoms are blue, iodines magenta and hydrogens light green. Click here to access a 3D representation.

(Fig. 4a and 4b) and in both cases there is the formation of a ‘supramolecular chair form cyclohexane’ synthon.

Conclusions

This study confirms the supramolecular similarity of $-\text{C}\equiv\text{C}-\text{H}$, $-\text{Cl}$, $-\text{Br}$, $-\text{I}$ and $-\text{OH}$ groups and extends their scope in crystal engineering studies. Chloro, bromo and ethynyl substituents play exactly the same role in the crystal structures of **1a–1c** and

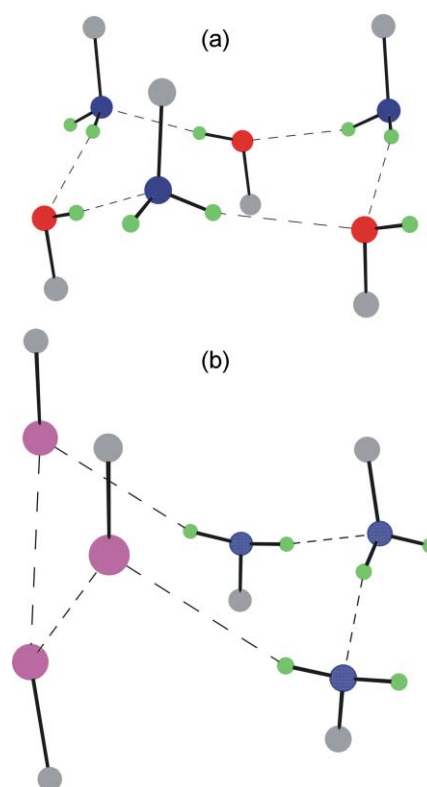


Fig. 4 (a) Supramolecular cyclohexane in **1e**. The phenyl groups are omitted for simplicity. Carbon atoms are grey, nitrogen atoms are blue, oxygen atoms are red and hydrogens light green. (b) Supramolecular cyclohexane in **1d**. The phenyl groups are omitted for simplicity. Carbon atoms are grey, nitrogen atoms are blue, iodines magenta and hydrogens light green.

this is related to their similar polarisations. These functional groups exert generally similar effects on crystal packing even for molecules that contain a ‘different’ type of substituent, such as $-\text{NH}_2$ in the present case. This is encouraging and means that ethynyl and halogen substituents may be exchanged in a wider variety of molecules without deep-seated changes in the crystal packing. However, this behaviour is not completely modular as is seen by the distinct packing of iodoaniline, **1d** and this may be related to its greater size.

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