

Substituent effects on aromatic interactions in the solid state

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A systematic series of structural studies has led to an understanding of how to use hydrogen-bonding and steric interactions to control two aromatic rings to interact in a well-defined and predictable manner in the solid state.

The study of non-covalent interactions in the solid state can be a rather hit or miss pursuit, as subtle changes in molecular structure can have dramatic effects on the way in which molecules organise in the crystal.¹ Indeed, the arrangement of molecules observed in a crystal structure is governed by maximising favourable intermolecular interactions and minimising unfavourable intermolecular interactions throughout the whole crystal, and the fact that the molecular packing arrangement arises from the interplay of several different factors calls for considerable caution in attempting to interpret, to rationalize and even to identify specific intermolecular interactions simply on the basis of inspecting known crystal structures. For example, there is an unfortunate tendency to attribute as a favourable interaction any situation in which two functionalities happen to be found close to each other in a crystal structure—however, the two groups involved may be unwillingly forced into close contact as the result of a stronger interaction involving neighbouring groups. To make progress in understanding and controlling specific interactions in the solid state requires investigations on families of materials designed such that the effects of different factors on the resultant structural properties may be systematically delineated. In this communication, we describe systematic studies of this type, which have led to an understanding of how to use hydrogen-bonding and steric interactions to control two aromatic rings to interact in a well-defined and predictable manner.^{2†}

Using a combination of edge-to-face aromatic interactions and H-bonds to assemble double-stranded 'zipper' complexes from oligomeric amides, we have been able to quantify the magnitudes of a range of aromatic interactions in solution.³ The key non-covalent structural motif is shown in Fig. 1(a). Simple aromatic amides of this general structure are self-complementary on both faces and should therefore self-assemble to give linear hydrogen bonded chains in the solid state (Fig. 1(b)).^{3a,4} This system provides an interesting framework for probing the properties of aromatic interactions in the solid state, and so we have investigated the degree of control that can be achieved over the geometry of the interactions between the aromatic rings and the sensitivity of these interactions to the nature of the substituents on these rings.⁵

We synthesised the fifteen compounds shown in Fig. 2(a).⁶ This series allows us to probe the influence of the size of the aniline *ortho* substituents (R^1 and R^2) and the effects of strongly polarising substituents (X and Y) on the edge-to-face aromatic interaction. For all but one of these compounds, crystals of appropriate size and quality for single crystal X-ray diffraction studies were obtained. It is found that, when there are no aniline

ortho substituents (*i.e.* $R^1 = R^2 = H$), the molecules are more planar, and although linear H-bonded chains are formed, the molecules are arranged in a head-to-head fashion with stacking interactions between like aromatic rings (not shown). All of the other compounds except **12** adopt a conformation in which the benzoyl and aniline groups are orthogonal (in an intramolecular sense), and the crystal structures contain H-bonded chains with head-to-tail dimers of the type depicted in Fig. 1(a)—*i.e.* with

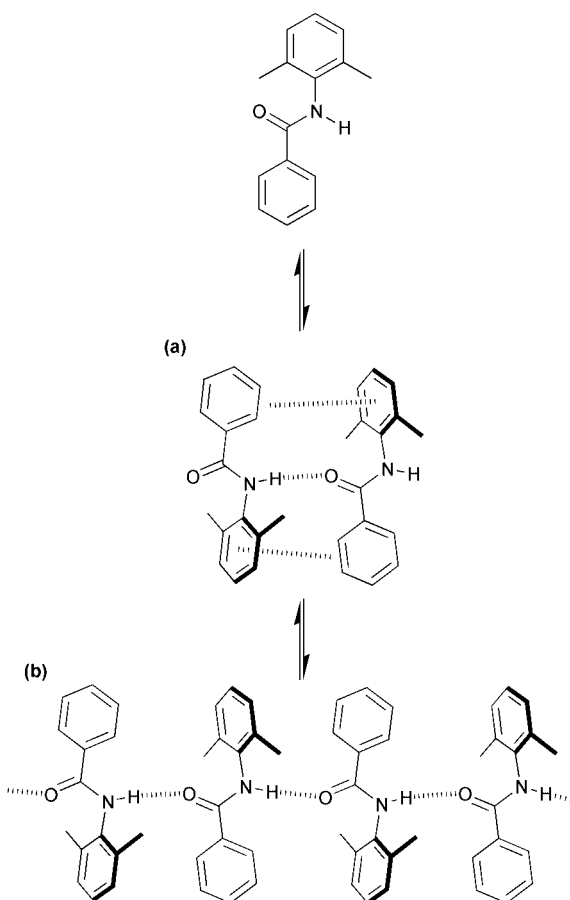


Fig. 1 (a) The key non-covalent structural motif used to assemble oligomeric zipper complexes in solution. (b) Extending this motif yields linear H-bonded chains for aromatic amides of the general structure shown. The term 'head-to-tail dimer' is used to refer to the situation shown, in which the aniline ring of one molecule is adjacent to the benzoyl ring of the neighbouring molecule along the chain (and *vice versa*). In the alternative situation (not shown), the aniline ring of one molecule is adjacent to the aniline ring of the neighbouring molecule along the chain, which is described as a 'head-to-head dimer'.

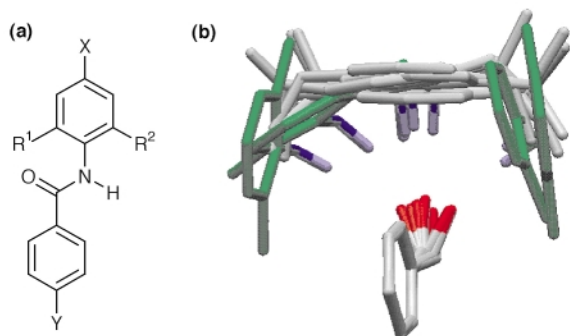


Fig. 2 (a) Compounds used to probe the influence of the aniline *ortho* substituents on the geometry of the aromatic interactions in the solid state.

X	Y	R ¹ =	H	H	Me	Et	iPr
		R ² =	H	Me	Me	Et	iPr
H	^t Bu		1	2	3	4	5
H	NO ₂		6	7	8	9	10
NO ₂	^t Bu		11	12	13	14	15

(b) The aromatic interactions in the head-to-tail dimers found in the crystal structures of **2–5**, **8–10**, **13–15** are shown, with the benzoyl rings superimposed and the *para* substituents deleted for clarity.⁵ Aniline rings with ethyl and isopropyl substituents are coloured grey, and anilines with methyl substituents are coloured green. The H-bonded chains in the crystal structures of **1**, **6**, **11** and **12** contain head-to-head dimers and are not shown. We have not yet been able to obtain a crystal structure of **7**.

interactions between the benzoyl and aniline rings of adjacent molecules.

Fig. 2(b) shows an overlay of the aromatic interactions in all of the crystal structures that contain head-to-tail dimers. The behaviour of the aniline rings with *ortho* methyl groups is clearly different from those with *ortho* ethyl and *ortho* isopropyl groups. The bulkier substituents strictly enforce edge-to-face interactions between the two π -systems, such that the geometry of these interactions is essentially identical for all of the structures with ethyl and isopropyl groups. As shown in Fig. 2(b) (grey structures), the benzoyl group fits into a groove which runs along the face of the aniline ring, sandwiched between the two alkyl substituents which project above the plane of the aniline π -system.

For the smaller *ortho* methyl groups, the molecules still adopt a conformation in which the benzoyl and aniline rings are orthogonal to each other, but the intermolecular interactions are significantly different. Now the geometric relation between adjacent molecules is distorted such that intermolecular aromatic stacking interactions are observed (Fig. 2(b), green structures). The major distortion concerns the geometry of the H-bonding interaction which allows the two π -systems to become parallel, improving the packing efficiency of the dimer.

For X = NO₂, alternating head-to-tail and head-to-head dimers are found within the H-bonded chain for the dimethyl and diethyl aniline derivatives, and for the mono-methyl derivative only head-to-head dimers are found. There appears to be a strong driving force for the nitroanilines to stack with themselves, and this is only prevented in the presence of bulky isopropyl groups which disrupt stacking of the aniline groups.

These results suggest that we can rigorously control the geometry of the aromatic interactions in this system by using isopropyl aniline derivatives, and that the packing, at least within a chain, is insensitive to the nature of the terminal substituents (X and Y). It should therefore be possible to use this system as a scaffold to set up geometrically well-defined intermolecular aromatic interactions with a variety of different substituents. To explore this potential, we have synthesised the wider series of compounds containing isopropyl substituents

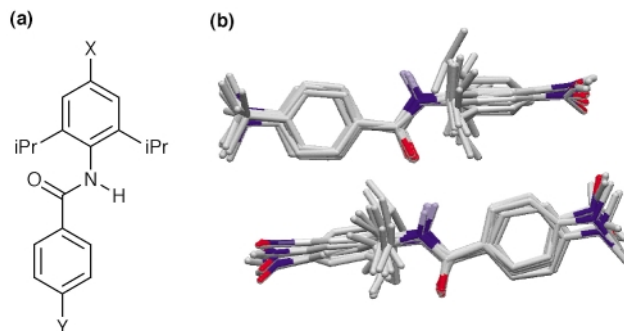


Fig. 3 (a) Compounds used to probe the influence of the polarising substituents on the geometry of the aromatic interactions in the solid state.

X	Y =	NMe ₂	^t Bu	NO ₂
NMe ₂		16	17	18
H		19	5	10
NO ₂		20	15	21

(b) The head-to-tail dimers found in the crystal structures of **16**, **17**, **19**, **5**, **10**, **20**, and **15** are shown as a least squares overlay of the amide group (C, N and O), the aniline ring (six C atoms) and benzoyl ring (six C atoms).⁵ We have not yet been able to obtain the crystal structures of **18** and **21**.

shown in Fig. 3(a), and crystal structures have been obtained for seven of these compounds (three structures were available from our studies of the series shown in Fig. 2(a) and four additional structures were obtained). In all cases, the crystals contain H-bonded chains containing the expected head-to-tail dimers of the type shown in Fig. 1(a).⁷ Fig. 3(b) shows an overlay of the aromatic interactions in the head-to-tail dimers found in these crystal structures. These structures are essentially identical, supporting the view that the H-bonded motif in Fig. 1 represents a robust framework for the study of edge-to-face aromatic interactions in the solid state.

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Notes and references

† CCDC 158573–158589. See <http://www.rsc.org/suppdata/cc/b1/b101575n/> for crystallographic data in CIF or other electronic format for compounds **1–4**, **6**, **8–17**, **19** and **20**. The crystal structure of **5** was reported previously.^{2a}

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- We emphasize that some of the measured diffraction data were of intrinsically poor quality as a consequence of comparatively poor crystal quality. In spite of this fact, significant new structural insights have been obtained, and the structural results are discussed at a level compatible with the quality of the data. Disorder is a factor in structures **12**, **13**, **15** and **16**, and a serious factor in the latter two, where it leads to alternative orientations for the H-bonded chains. These factors do not affect the overall findings reported here and will be fully discussed in a full paper on this topic.
- All new compounds gave satisfactory spectroscopic data.
- For compound **16** (X = Y = NMe₂), head-to-head dimers were also found within the H-bonded chain.