



Practical crystal engineering using halogen bonding: A hierarchy based on calculated molecular electrostatic potential surfaces



Christer B. Aakeröy*, Tharanga K. Wijethunga, John Desper

Department of Chemistry, Kansas State University, Manhattan, KS 66506, USA

HIGHLIGHTS

- 36 co-crystallizations on compounds with two different acceptors were performed.
- An interaction hierarchy was established using calculated electrostatic potentials.
- All 10 structures obtained display best donor/acceptor halogen bonds.
- Halogen bonds with iodine are more effective than the bromo-analogues.

ARTICLE INFO

Article history:

Available online 20 February 2014

Keywords:

Halogen bond
Crystal engineering
Molecular recognition
Electrostatic potential
Co-crystallization
Hierarchy

ABSTRACT

A series of co-crystallization experiments were performed using four multi-topic N-heterocyclic acceptor molecules and nine aromatic halogen-bond donors in order to establish how effectively a ranking of bond strength based on calculated molecular electrostatic potential surfaces translates into predictable primary interactions in the solid state. A total of ten new crystal structures were obtained, and in each case, the observed interaction took place between the best acceptor (with the larger negative electrostatic potential) on the N-heterocycle and the halogen-bond donor. The supramolecular yield (number of successful co-crystallizations) is 70% for iodine-donors whereas none of the bromo-substituted donors produced a co-crystal which underscores the importance of the magnitude of the electrostatic potential and of the polarizability of the halogen-bond donor in the context of successful practical crystal engineering.

© 2014 Elsevier B.V. All rights reserved.

1. Introduction

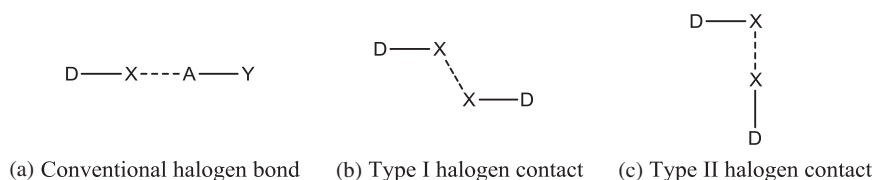
Intermolecular interactions are responsible for all molecular recognition events, and as such represent the primary tools in supramolecular chemistry and crystal engineering [1]. Consequently, it is essential to have solid understanding of the fundamental nature of these interactions in order to successfully design complex supramolecules in a predetermined and effective manner [2–4]. Halogen bonds represent a relatively recent addition to the tool box of supramolecular chemistry and still receive considerable attention [5]. According to IUPAC, “A halogen bond $R-X \cdots Y-Z$ occurs when there is evidence of a net attractive interaction between an electrophilic region on a halogen atom X belonging to a molecule or a molecular fragment $R-X$ (where R can be another atom, including X, or a group of atoms) and a nucleophilic region of a molecule, or molecular fragment, $Y-Z$ ” [6]. According to this definition the halogen-bond donor is accepting

electrons, a convention which is adopted to align it with the generally accepted definition of the hydrogen bond [7,8] where the electropositive hydrogen atom is recognized as the hydrogen-bond donor, accepting electrons from an electronegative atom [9]. The halogen bonding ability of donor atoms increase in the order of $F \ll Cl \ll Br < I$ depending on the polarizability [10], and conventional halogen bonds are highly directional [11]. Generally the bond distance between acceptor and donor atoms in a halogen bond is significantly shorter than the sum of van der Waals radii [12]. In addition to conventional stabilizing halogen bonds, two additional halogen-halogen contacts, classified as type I and type II (depending on the geometry) are frequently encountered in crystal structures of halogen-substituted molecules, Scheme 1 [13]. Factors that influence the strength of a halogen-bond include the presence of electron-withdrawing substituents that serve to ‘activate’ the halogen-bond donor atom by depleting it of electron density thereby increasing its partial positive potential [14,15].

In order to develop reliable and transferable synthetic guidelines for the assembly of molecular solids using multiple intermolecular interactions, Etter [16] and others [17–19] have

* Corresponding author. Tel.: +1 785 532 6096; fax: +1 785 532 6666.

E-mail address: aakeroy@ksu.edu (C.B. Aakeröy).



Scheme 1. (a) Conventional halogen bond (b) Type I halogen···halogen contact (c) Type II halogen···halogen contact; (D & Y-connected atoms, X-halogen bond donor atom, Y-halogen bond acceptor).

demonstrated that in hydrogen-bond based systems, there is a tendency for the best-donors to bind to the best-acceptors, and the second-best donor to bind to the second-best acceptor. If the molecules carry the same functionality, a relative ranking can be established reasonably well using pK_a/pK_b values [20–22] but if different functionalities are employed, an approach to ranking based on calculated molecular electrostatic potential surfaces is required [23–25].

At this point, it is not clear how effectively an electrostatic potential-based ranking of halogen-bond acceptors can be translated directly into strategies for practical crystal engineering, although a halogen bond donor based hierarchy [26], a basicity scale [27], ^{19}F NMR based studies [28], theoretical electrostatic based studies [5,29] and solution based models [30] have been used to explain halogen-bond interactions. In order to establish to what extent halogen bonds follow best-donor/best-acceptor guidelines, we decided to carry out systematic co-crystallizations on a series of N-heterocyclic halogen-bond acceptors, each with two binding sites with different electrostatic potential, Scheme 2, **A1–A3**. In addition, to ensure that the imidazole nitrogen atom was not inaccessible due to some steric hindrance, we also included ligand **A4**, with essentially the same shape, but with only one type of acceptor site. These four compounds have been co-crystallized with six iodo-substituted halogen-bond donors, **D5–D10**, (all but one of them ‘activated’ with fluorine groups) and three bromo-substituted halogen-bond donors, **D11–D13**, all of which are activated by a fluorinated aromatic backbone, Scheme 2. The study is undertaken in response to two hypotheses; (i) if a halogen-bond donor has a choice of two accessible halogen-bond acceptors, it will preferentially select the best-acceptor as determined by molecular electrostatic potentials surfaces (MEPS) and (ii) a bromo-substituted halogen-bond donor will be less successful at forming co-crystals than the corresponding iodo-analogues. The reactants were combined using solvent-assisted grinding, and the products were characterized using infrared spectroscopy. Successful experiments were then subjected to a variety of crystal-growth experiments and a total of ten samples produced crystals suitable for single-crystal diffraction.

2. Experimental

All the reagents, solvents, and donors **D1–D9** and **D11–D13** were purchased from commercial sources and used as received. 2,2'-Biimidazole was synthesized according to previously reported methods [31]. Donor **D10** was prepared according to the synthetic methods reported [32]. A Fisher-Johns melting point apparatus was used to determine melting points. Infrared spectra were recorded with a Nicolet 380 FT-IR. ^1H NMR spectra were recorded using a Varian Unity plus 400 MHz spectrometer.

2.1. Synthesis of 1,1'-bis(pyridin-4-ylmethyl)-2,2'-biimidazole, A1

2,2'-Biimidazole (0.27 g, 2 mmol) and NaOH (0.32 g, 8 mmol) were placed in a 100 mL round bottomed flask with 20 mL of acetonitrile. The mixture was stirred at room temperature for two hours. 4-Picolyl chloride hydrochloride (0.65 g, 4 mmol) in acetonitrile (20 mL) was added to the mixture and refluxed for 24 h at 50–60 °C. The reaction was monitored with TLC and upon completion the solvent was removed by rotary evaporation. The residue was dissolved in water (50 mL) and extracted with methylene chloride (30 mL \times 3). Organic layers were combined, dried over anhydrous MgSO_4 and rotary evaporated to obtain the yellow color powder as the product. Yield: 0.69 g (89%); mp 144–146 °C; ^1H NMR (δ_{H} ;

trile (20 mL) was added to the mixture and refluxed for 24 h at 50–60 °C. The reaction was monitored with TLC and after completion the solvent was removed by rotary evaporation. The residue was dissolved in water (50 mL) and extracted with methylene chloride (30 mL \times 3). Organic layers were combined, dried over anhydrous MgSO_4 and rotary evaporated to obtain the dark brown color powder as the product. Yield: 0.35 g (56%); mp 157–160 °C; ^1H NMR (δ_{H} ; CDCl_3 , 400 MHz): 8.49 (d, 4H), 7.11 (d, 2H), 6.94 (d, 2H), 6.91 (d, 4H), 5.84 (s, 4H).

2.2. Synthesis of 1,1'-bis(pyridin-3-ylmethyl)-2,2'-biimidazole, A2

2,2'-Biimidazole (0.27 g, 2 mmol) and NaOH (0.32 g, 8 mmol) were placed in a 100 mL round bottomed flask with 20 mL of acetonitrile. The mixture was stirred at room temperature for two hours. 3-Picolyl chloride hydrochloride (0.65 g, 4 mmol) in acetonitrile (20 mL) was added to the mixture and refluxed for 24 h at 50–60 °C. The reaction was monitored with TLC and upon completion the solvent was removed by rotary evaporation. The residue was dissolved in water (50 mL) and extracted with methylene chloride (30 mL \times 3). Organic layers were combined, dried over anhydrous MgSO_4 and rotary evaporated to obtain the brown color powder as the product. Yield: 0.45 g (71%); mp 112–115 °C; ^1H NMR (δ_{H} ; CDCl_3 , 400 MHz): 8.46 (d, 2H), 8.45 (s, 2H), 7.39 (d, 2H), 7.17 (m, 2H), 7.11 (d, 2H), 6.95 (d, 2H), 5.78 (s, 4H).

2.3. Synthesis of 1,1'-bis(pyridin-2-ylmethyl)-2,2'-biimidazole, A3

2,2'-Biimidazole (0.27 g, 2 mmol) and NaOH (0.32 g, 8 mmol) were placed in a 100 mL round bottomed flask with 20 mL of acetonitrile. The mixture was stirred at room temperature for two hours. 2-Picolyl chloride hydrochloride (0.65 g, 4 mmol) in acetonitrile (20 mL) was added to the mixture and refluxed for 24 h at 50–60 °C. The reaction was monitored with TLC and upon completion the solvent was removed by rotary evaporation. The residue was dissolved in water (50 mL) and extracted with methylene chloride (30 mL \times 3). Organic layers were combined, dried over anhydrous MgSO_4 and rotary evaporated to obtain the pale brown color powder as the product. Yield: 0.25 g (40%); mp 180–183 °C; ^1H NMR (δ_{H} ; CDCl_3 , 400 MHz): 8.53 (d, 2H), 7.53 (t, 2H), 7.15 (t, 2H), 7.12 (s, 2H), 7.07 (s, 2H), 7.05 (d, 2H), 5.87 (s, 4H).

2.4. Synthesis of 1,1'-dibenzyl-2,2'-biimidazole, A4

2,2'-Biimidazole (0.33 g, 2.48 mmol) and NaOH (0.39 g, 9.92 mmol) were placed in a 100 mL round bottomed flask with 20 mL of acetonitrile. The mixture was stirred at room temperature for two hours. Benzyl bromide (0.63 g, 5 mmol) in acetonitrile (20 mL) was added to the mixture and refluxed for 24 h at 50–60 °C. The reaction was monitored with TLC and after completion the solvent was removed by rotary evaporation. The residue was dissolved in water (50 mL) and extracted with methylene chloride (30 mL \times 3). Organic layers were combined, dried over anhydrous MgSO_4 and rotary evaporated to obtain the yellow color powder as the product. Yield: 0.69 g (89%); mp 144–146 °C; ^1H NMR (δ_{H} ;

Download English Version:

<https://daneshyari.com/en/article/1405019>

Download Persian Version:

<https://daneshyari.com/article/1405019>

[Daneshyari.com](https://daneshyari.com)