Modulation of halogen, chalcogen and pnictogen bonds by σ-hole tuning

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Propertios of halogen (X), chalcogen (E) and pnictogen (Pn) bonds can be modulated by changing *(i)* the nature of the X, E and Pn, *(ii)* the chemical environment of the X, E and Pn, and *(iii)* properties of the electron donor. Apart from small molecular complexes [1], this has been demonstrated in protein-ligand complexes, e.g. on a series of aldose reductase inhibitors [2]. The counterintuitive ability of heteroboranes to form strong σ-hole interactions was found and attributed to the multicenter bonding [3]. It breaks the classical electronegativity concept and results highly positive σ-holes on heterovetices that are incorporated into the skeleton via multicenter type of bonding [3]. X, E and Pn elements in neutral heteroboranes can thus have highly positive σ-holes that are responsible for strong σ-hole interactions. The E···π [4], X···π [5], Pn···π [6] and Pn···H-B [7] types of σ-hole interactions of heteroboranes have been observed in the corresponding crystal packings. σ-Hole interactions can be used for designing protein-ligand interactions as well as for crystal engineering.

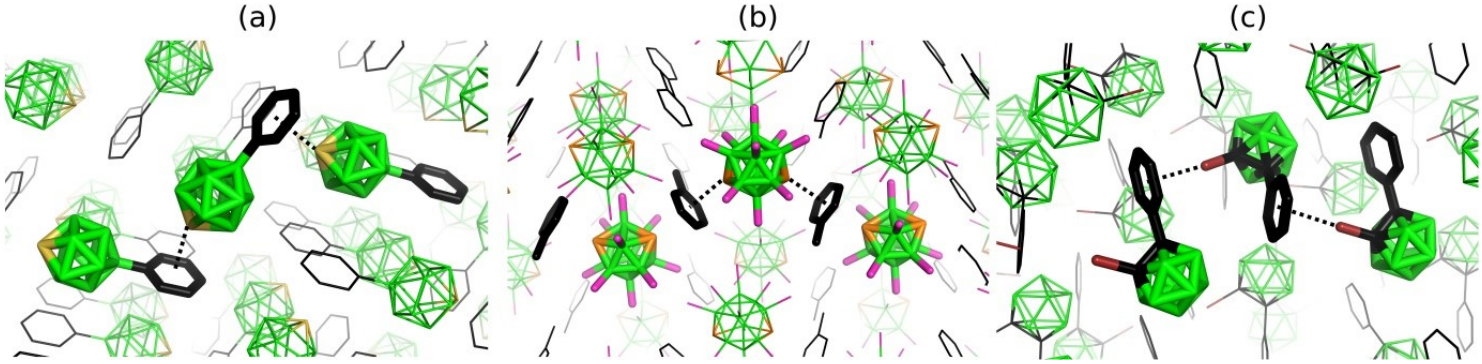

Figure 1. Chalcogen (a), pnictogen (b) and halogen (c) bonding found in heteroborane crystal structures [4-6]. Color coding: black – carbon, yellow – sulfur, orange – phosphorus, pink – boron, dark red – bromine, magenta – chlorine. Hydrogen atom not shown.

[1] Riley, K. E., Murray, J. S., Fanfrlík, J., Řezáč, J., Solá, R. J., Concha, M. C., Ramos, F. M., & Politzer, P. (2011) *J. Mol. Model.* **17**, 3309.

[2] Fanfrlík, J., Kolář, M., Kamlar, M., Hurny, D., Ruiz, F. X., Cousido-Siah, A., Mitschler, A., Řezáč, J., Munusamy, E., Lepšík, M., Matějíček, P., Velselý, J., Podjarny, A., & Hobza, P. (2013) *ACS Chem. Biol.* **8**, 2484.

[3] Melichar, P., Hnyk, D., & Fanfrlík, J. (2018) *Phys. Chem. Chem. Phys.* **20,** 4666.

[4] Fanfrlík, J., Prada, A., Padělková, Z., Pecina, A., Macháček, J., Lepšík, M., Holub, J., Růžička, A., Hnyk, D., & Hobza, P. (2014) *Angew. Chem. Int. Ed.* **58**, 10139.

[5] Fanrlík, J., Holub, J., Růžičková, Z., Řezáč, J., Lade, P. D., Wand, D. A., Hnyk, D., Růžička, A., & Hobza, P. (2016) *ChemPhysChem* **17**, 3373.

[6] Fanfrlík, J. & Hnyk, D. (2018) *Crystals*, **8**, 390.

[7] Holub, J., Melichar, P., Růžičková, Z., Vrána, A., Wann, D. A., Fanfrlík, J., Hnyk, D., & Růžička, A. (2017) *Dalton Trans.* **46**, 137140.

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