Experimental investigation of halogen-bond hard–soft acid–base complementarity

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The halogen bond (XB) is a topical noncovalent interaction of rapidly increasing importance. The XB employs a ‘soft’ donor atom in comparison to the ‘hard’ proton of the hydrogen bond (HB). This difference has led to the hypothesis that XBs can form more favorable interactions with ‘soft’ bases than HBs. While computational studies have supported this suggestion, solution and solid-state data are lacking. Here, XB soft–soft complementarity is investigated with a bidentate receptor that shows similar associations with neutral carbonyls and heavy chalcogen analogs. The solution speciation and XB soft–soft complementarity is supported by four crystal structures containing neutral and anionic soft Lewis bases.

1. Introduction

Refined understanding of the halogen bond (XB) has enabled it to become a useful supramolecular tool over the last two decades (Cavallo *et al.*, 2016; Beale *et al.*, 2013; Mukherjee *et al.*, 2014; Auffinger *et al.*, 2004; Rissanen, 2008; Massena *et al.*, 2016; Carlsson *et al.*, 2015). XB and hydrogen bond (HB) strengths are frequently compared (Mukherjee *et al.*, 2014; Metrangola *et al.*, 2005), yet the XB is unique in that it is more directional and employs a larger, polarizable donor atom. In this regard, the potential for XB complementarity with ‘soft’ (low electronegativity and high polarizability) Lewis basic acceptors is intriguing (Ho, 1977). The strength of the XB has only recently been explored in relation to the chemical hardness of the XB acceptor (Laurence *et al.*, 2011; Beale *et al.*, 2013). Preliminary XB hard–soft acid–base (HSAB) studies have given rise to the question; do soft XB acceptors form relatively favorable XBs compared with HB interactions?

HSAB theory has traditionally been used to rationalize the reactivity of substrates in organic and inorganic chemistry (Pearson, 1963). However, alternative explanations such as Marcus theory have also been considered (Mayr *et al.*, 2011; Breugst *et al.*, 2010). Recently, HSAB theory has also been applied to understand HBs (Sennikov, 1994; Politzer & Murray, 2013; Platts *et al.*, 1996). Studies have shown that HB strength decreases as the electronegativity of the acceptor decreases (descending a group). Therefore, hydrogen bonding between soft Lewis basic acceptors and hard proton donors is weaker in solution (Robertson *et al.*, 2014; Michielsen *et al.*, 2012). In contrast, the XB employs a soft Lewis acidic halogen as the electrophile; thus, HSAB theory would suggest that soft Lewis base acceptors should form more favorable interactions with soft XB donors. Several computational (Pinter *et al.*, 2013; Nagels *et al.*, 2014) and experimental solid-state accounts (Ouvrard *et al.*, 2003; Le Gal *et al.*, 2016; Arman *et al.*, 2010)

Table 1

Association constants and change in NMR shift (Ha and Hb) for titrations of receptors (1) and (3) with Lewis bases.

Lewis base	Receptor (1) [†] K_{11} (M ⁻¹)	Receptor (1) [†] K_{12} (M ⁻¹)	Receptor (3) [†] K_{11} (M ⁻¹)	Receptor (1) [‡] $\Delta\delta$ Ha (p.p.m.)	Receptor (1) [‡] $\Delta\delta$ Hb (p.p.m.)
T ϕ PO	8.9	–	8.0	1.2215	1.0956
T ϕ PS	3.7	–	2.0	0.2608	0.3546
T ϕ PSe	3.3	–	2.2	0.1575	0.2265
TMU	4.1	–	–	0.9242	0.4195
TMTU	3.4	–	–	–	–
DMF	4.6	–	–	0.8280	0.9219
TDMF	2.7	–	–	–	–
TBA ⁺ SCN ⁻	1.1×10^5	1.6×10^2	–	0.2406	0.3626
TBA ⁺ I ₃ ⁻	1.2×10^5	2.8×10^2	–	0.0947	0.2238

[†] All anion titrations were conducted using tetra-*n*-butylammonium (TBA) salts. All binding constants for neutral species were determined in CDCl₃. All anion binding data were obtained in 10% CD₃CN/CDCl₃. All titrations were completed in triplicate and the average value is reported. Errors are estimated at 10%. [‡] The $\Delta\delta$ is the difference in chemical shift between the free host and the saturation point in the NMR titration.

justify this hypothesis. However, few investigations studying this phenomenon in solution have been reported (Sarwar *et al.*, 2010; Robertson *et al.*, 2014; Chudzinski & Taylor, 2012), thus motivating the present study. Herein, we quantify halogen bonding between an organic XB donor and soft carbonyl derivatives and anions.

To study halogen bonding in solution, a charged bidentate XB receptor was developed (Fig. 1, top). The bisethynyl benzene scaffolds (1) and (3) were previously found to XB and HB to perrhenate in solution and solid phases (Massena *et al.*, 2015). In the present study, we quantify halogen bonding between receptor (1), and neutral or anionic Lewis bases of

varying softness (*e.g.* carbonyl, thio-carbonyl and selenocarbonyl). The data suggests minimal attenuation in the binding affinity with soft acceptors which contrasts observations of hydrogen bonding to soft Lewis bases. Additional crystallographic data of receptor (2) with neutral and anionic acceptors complement the solution data.

2. Results and discussion

¹H NMR spectroscopic titrations involving receptor (1) were conducted to assess the XB HSAB complementarity in solution. Titrating neutral or anionic Lewis bases into receptor (1) resulted in significant downfield shifting (Cametti *et al.*, 2012) of the pyridinium protons (Fig. 1, Ha and Hb). Measuring weak interactions in solution necessitated many guest equivalents to reach the endpoints of the titrations for the neutral Lewis bases. HypNMR 2008 (Frassinetti *et al.*, 1995) was used to fit changes in ¹H NMR shift to an association model. Continuous refinement of multiple isotherms provided association constants for neutral and anionic species with receptor (1). A 1:1 host–guest binding ratio was established for all neutral species. However, anions were fit to both 1:1 and 1:2 host–guest binding models. Job plots were conducted to confirm dominant solution binding stoichiometry (see the supporting information). A Job plot of receptor (1) and triphenylphosphine oxide indicated 1:1 host–guest binding stoichiometry. In contrast, a Job plot of receptor (1) and tetra-*n*-butyl ammonium thiocyanate (TBA⁺SCN⁻) also displayed 1:2 host–guest association. These Job plots were used to establish the stoichiometry for all solution complexes.

The obtained association constants for all neutral and anionic species with receptor (1) are displayed in Table 1. Measurable, albeit weak, association constants were determined for neutral XB acceptors ranging from 2.7 to 8.9 M⁻¹. The triphenylphosphine series (oxide, sulfide and selenide) produced the largest K_a values for the neutral acceptors – likely a result of the increased electron density on the chalcogen. Only marginal decreases in binding affinity between carbonyl and thiocarbonyl substrates are observed. Not surprisingly, the XB interactions with neutral acceptors in solution are weak. However, the association constants with the carbonyls are slightly stronger than with the thiocarbonyls. Due to the weak association constants, trends should be treated with caution. Nevertheless, these results contrast a previous study where inorganic I₂ displayed stronger binding with thiocarbonyl than carbonyl counterparts by 2–3 orders of magnitude in various solvents (Robertson *et al.*, 2014). However, it is known that organic and inorganic XB donors have characteristic differences in binding affinities (Beale *et al.*, 2013; Beweries *et al.*, 2011; Robertson *et al.*, 2014; Smith *et al.*, 2014; Cabot & Hunter, 2009). The minimal decrease in

Figure 1

ChemDraw representation of XB and HB control receptors (1), (2) and (3) (above). The seven neutral Lewis bases that were investigated (below).

binding when comparing the hard oxygen and soft neutral sulfur acceptors may suggest that soft–soft complementarity is operating in solution.

The NMR data support multiple binding conformations that contribute to the associations observed in solution including both XB and C–H hydrogen bonding. For example, a ^{13}C NMR titration in which triphenylphosphine oxide was titrated into receptor (1) indicates that XB occurs in solution. Downfield shift of the C–I carbon was observed as a result of halogen bonding (see the supporting information). Additionally, downfield shift of Hb during the reported ^1H NMR titrations supports the C–H hydrogen bonding which also occurs in solution. In order to compare the chemical shift changes in the absence of halogen bonding, control molecule (3) was titrated with triphenylphosphine oxide, sulfide and selenide in CDCl_3 . Control (3) exhibited similar downfield shifting with the largest $\Delta\delta$ occurring for Ha/b, verifying the contribution of C–H hydrogen bonding in the system. However, the XB scaffold (1) displays slightly stronger binding compared with the HB control receptor (3), further implicating the contribution of XB in (1). The solution data for this system is complicated by multiple equilibria, thus we turned to X-ray crystallography for further clarity.

One likely binding mode is highlighted by a crystal structure that was obtained of receptor (2) halogen bonding to a *N,N*-dimethylformamide (DMF) molecule (Fig. 2). Yellow plates of (2)·DMF were grown from vapor diffusion of DCM into a nitromethane–DMF solution of receptor (2). The complex crystallized in space group *Pbcn* and displays one half of (2), one trifluoromethanesulfonate (OTf^-) counteranion and a half-occupied DMF molecule in the asymmetric unit. A

prominent feature of this crystal structure is bidentate halogen bonding to the carbonyl oxygen. Interestingly, the bidentate binding occurs orthogonal to the plane of the carbonyl. Receptor (2) XBs to DMF despite the presence of the negative OTf^- counteranions. The DMF in the structure displays orientational disorder and is situated near a crystallographic twofold rotation axis that passes through the binding pocket. In this crystal structure, a bidentate XB interaction is observed with $\text{Cl}\cdots\text{O}$ distances of 2.97 (2) and 2.82 (2) Å, which correspond to R_{IO} values of 0.84 and 0.80.¹ To optimize bidentate binding of the DMF molecule, the pyridinium rings rotate 7.5° out of coplanarity. Thus, the C–I $\cdots$ O angles are $162.2(6)$ and $169.4(5)^\circ$, which also indicate strong XBs. Absent of other close contacts, this bidentate XB interaction alone holds the DMF molecule in place. This crystal structure suggests that this binding conformation plays a role in solution (Table 2).

Anion titrations were also performed to evaluate XB HSAB complementarity. Triiodide (I_3^-) and thiocyanate (SCN^-) are considered anionic ‘soft’ Lewis bases due to their charge diffuse nature and highly polarizable atoms. Titrations of receptor (1) with SCN^- and I_3^- produced downfield ^1H NMR shifts of pyridinium protons (Ha and Hb). Receptor (1) previously displayed an anion-induced upfield shift due to halogen bonding when the solvent system was 3:2 CDCl_3 –(CD_3) $_2\text{CO}$. To clarify this, receptor (1) was titrated with TBA^+SCN^- in 3:2 CDCl_3 –(CD_3) $_2\text{CO}$, where an upfield shift of Ha and Hb were also observed (see the supporting information), suggesting that receptor (1) interacts with SCN^- in a similar fashion. Sequential 1:1 and 1:2 host–guest binding models, supported by Job plot (see above discussion), revealed analogous association constants for both I_3^- ($K_{11} = 1.2 \times 10^5 \text{ M}^{-1}$)² and SCN^- ($K_{11} = 1.1 \times 10^5 \text{ M}^{-1}$). The second binding event (K_{12}) for both I_3^- ($K_{12} = 2.8 \times 10^2 \text{ M}^{-1}$) and SCN^- ($K_{12} = 1.6 \times 10^2 \text{ M}^{-1}$) is significantly weaker, perhaps suggesting that multidentate binding plays a role in the first binding event. The enhanced binding affinities of the anions compared with the neutral Lewis bases is expected given the greater electron density of anions. Although the receptor was designed for bidentate halogen bonding, the crystal structures described below suggest that monodentate halogen bonding with each anion is also important. This could partially explain the similar binding constants as less size exclusion is expected from monodentate binding of receptor (1) with these anions.

Crystal studies with anions were also performed to examine XB soft–soft complementarity. SCN^- was studied because it provides two Lewis basic sites of different chemical hardness (Cauliez *et al.*, 2010; Fujimoto & Satoh, 1994). Crystal structures were examined for sulfur–halogen contacts. Two SCN^- solvate crystals with receptor (2) were obtained. The first structure highlights preferential XB contacts to the soft sulfur

Figure 2
(a) Top view of (2)·DMF crystal structure showing a bidentate XB to the DMF carbonyl oxygen. (b) Side view displaying the perpendicular XB interaction (displacement ellipsoids drawn at the 50% probability level).

¹ $R_{\text{IS}} = d(\text{I}\cdots\text{S})/(r_{\text{I}} + r_{\text{S}})$, where r_{I} and r_{S} are the van der Waals radii of I and S. For the definition of this interaction ratio see Zordan *et al.* (2005). These ratios equate to 84 and 80% of the EvdW radii.

² Note, the association constant for I_3^- should be treated as an approximate value due to the iodide–iodine–triiodide equilibrium in solution (Jones & Kaplan, 1928; Awtrey & Connick, 1951).

Table 2

Experimental details.

Experiments were carried out at 100 K using a Bruker D8 VENTURE Duo diffractometer.

	(2)·DMF	(2) ²⁺ ·2SCN [−] ·MeOH	(2) ²⁺ ·2SCN [−] ·DCM	(2) ²⁺ ·2I ₃ [−]
Crystal data				
CCDC	1520140	1520141	1520142	1520143
Chemical formula	C ₂₂ H ₁₆ I ₂ N ₂ ·C ₃ H ₇ NO·2CF ₃ O ₃ S	C ₂₂ H ₁₆ I ₂ N ₂ ·2SCN·CH ₄ O	C ₂₂ H ₁₆ I ₂ N ₂ ·0.97CH ₂ Cl ₂ ·2SCN	C ₂₂ H ₁₆ I ₂ N ₂ ·2I ₃
<i>M</i> _r	933.40	710.37	760.71	1323.57
Crystal system, space group	Orthorhombic, <i>Pbcn</i>	Triclinic, <i>P</i> $\bar{1}$	Triclinic, <i>P</i> $\bar{1}$	Monoclinic, <i>P</i> ₂ /n
<i>a</i> , <i>b</i> , <i>c</i> (Å)	22.4519 (12), 18.1915 (9), 8.0879 (4)	9.1203 (11), 11.3562 (14), 13.9355 (18)	7.7270 (3), 10.9671 (4), 16.9780 (7)	7.3983 (4), 10.4370 (5), 41.8567 (18)
α , β , γ (°)	90, 90, 90	77.294 (4), 71.958 (4), 77.390 (4)	103.375 (2), 98.725 (2), 94.093 (2)	90, 93.424 (2), 90
<i>V</i> (Å ³)	3303.4 (3)	1321.1 (3)	1375.03 (9)	3226.2 (3)
<i>Z</i>	4	2	2	4
Radiation type	Mo <i>K</i> α	Mo <i>K</i> α	Mo <i>K</i> α	Cu <i>K</i> α
μ (mm ^{−1})	2.11	2.56	2.65	60.50
Crystal size (mm)	0.5 × 0.05 × 0.03	0.15 × 0.1 × 0.05	0.5 × 0.05 × 0.02	0.5 × 0.05 × 0.05
Data collection				
Absorption correction	Multi-scan	Multi-scan	Multi-scan	Multi-scan
<i>T</i> _{min} , <i>T</i> _{max}	0.193, 0.266	0.252, 0.332	0.266, 0.335	0.010, 0.097
No. of measured, independent and observed [<i>I</i> > 2 σ (<i>I</i>)] reflections	83 218, 3786, 3280	41 885, 5062, 4063	105 156, 6282, 5184	26 322, 4551, 3685
<i>R</i> _{int}	0.075	0.076	0.072	0.066
$\theta_{\max}$ (°)	27.5	25.9	27.5	59.0
(sin θ/λ) _{max} (Å ^{−1})	0.649	0.615	0.649	0.556
Refinement				
<i>R</i> [<i>F</i> ² > 2 σ (<i>F</i> ²)], <i>wR</i> (<i>F</i> ²), <i>S</i>	0.065, 0.121, 1.31	0.058, 0.157, 1.07	0.031, 0.064, 1.06	0.044, 0.109, 1.06
No. of reflections	3786	5062	6282	4551
No. of parameters	239	314	328	291
$\Delta\rho_{\max}$, $\Delta\rho_{\min}$ (e Å ^{−3})	0.92, −1.29	3.37, −2.02	1.01, −0.65	1.05, −0.64

atom. Yellow single crystals of (2)²⁺·2SCN[−]·MeOH were grown by vapor diffusion of diethyl ether into an acetonitrile–methanol solution of receptor (2) with TBA⁺SCN[−]. The complex (2)²⁺·2SCN[−]·MeOH (Fig. 3) crystallized in the space group *P* $\bar{1}$ with one receptor, two anions and a methanol molecule in the asymmetric unit. The structure contains two monodentate XBs to distinct sulfurs of two crystallographically unique SCN[−] anions. The C—I···S distances

Figure 3

Crystal structure of (2)²⁺·2SCN[−]·MeOH highlighting two monodentate XBs to the SCN[−] sulfur and a O—H HB to one of the SCN[−] N atoms (displacement ellipsoids drawn at the 50% probability level).

3.230 (2) and 3.246 (2) Å correspond to *R*_{IS} values of 0.83 and 0.82. The C—I···S angles of 176.97 (18) and 169.17 (17)° verify strong XB interactions. Further examination shows that the hard nitrogen of one SCN[−] anion accepts a HB from the methanol with an OH···N distance of 1.92 (7) Å. The methanol oxygen accepts three C—H HBs from two receptors [distances ranging from 2.448 (7) to 2.553 (6) Å]. This SCN[−] also accepts an additional weak C—H HB *via* CH···S [2.9707 (19) Å]. The second SCN[−] molecule participates in four CH···N HB interactions [2.293 (8) to 2.668 (8) Å] and one weak anion–arene contact between the nitrogen atom of

Figure 4

Crystal packing of (2)²⁺·2SCN[−]·MeOH displays an off-set head-to-tail dimer (displacement ellipsoids drawn at the 50% probability level).

Figure 5
Crystal structure of $(2)^{2+} \cdot 2\text{SCN}^- \cdot \text{DCM}$ (a) highlighting the two monodentate XBs to the sulfur and nitrogen in SCN^- (DCM molecules omitted for clarity). Highlighted C—H XBing (b) to the sulfur (black dashes) and the nitrogen (red dashes) of the SCN^- molecule not participating in XBing (displacement ellipsoids drawn at the 50% probability level).

SCN^- and an electron-deficient pyridinium ring (Berryman *et al.*, 2007, 2006, 2008; Gamez *et al.*, 2007; Hay & Bryantsev, 2008; Schottel *et al.*, 2008). An offset head-to-tail π -stacking dimer [Fig. 4, plane-to-plane centroid distance 3.330 (16) Å] is also observed. This structure is an example of Etter's best donor/acceptor rule where HB and XB complementarity is observed (Etter, 1990) – the HB pairs with the hard nitrogen and the XB pairs with the soft sulfur of the SCN^- anion.

The second SCN^- crystal structure with receptor (2) lacks a strong HB donor and thus displays XBing to both the hard and soft ends of the anion. Yellow plates suitable for X-ray diffraction were grown from vapor diffusion of dichloromethane (DCM) into a nitromethane solution of receptor (2) and TBA^+SCN^- . The complex $(2)^{2+} \cdot 2\text{SCN}^- \cdot \text{DCM}$ crystallized in space group $P\bar{1}$ with one host receptor, two SCN^- and one DCM molecule in the asymmetric unit. A single SCN^- forms two monodentate XBs with two receptors (Fig. 5). In the absence of a strong HB donor both the soft and hard Lewis basic sites are occupied by a XB with $\text{C—I} \cdots \text{S}$ and $\text{C—I} \cdots \text{N}$ distances of 3.2964 (11) and 2.912 (4) Å corresponding to R_{IS} and R_{IN} values of 0.84 and 0.79, respectively. These values along with the $\text{C—I} \cdots \text{S}$ and $\text{C—I} \cdots \text{N}$ angles of 170.82 (8) and 175.08 (10)° indicate strong XB interactions. Interestingly, the second SCN^- (Fig. 5, right) does not form XB interactions, rather four C—H HBs *via* $\text{C—H} \cdots \text{S}$ [distances ranging from 2.8753 (10) to 3.0597 (9) Å] and $\text{C—H} \cdots \text{N}$ [2.280 (4) Å] are observed. This SCN^- also displays one anion–arene contact between the SCN^- carbon and an electron-deficient pyridinium ring. As seen in the previous crystal structure, an off-set head-to-tail dimer is present [plane-to-plane centroid distance 3.082 (10) Å].

The two SCN^- structures presented above display interesting differences. The $(2)^{2+} \cdot 2\text{SCN}^- \cdot \text{MeOH}$ complex crystallized with a strong HB donor. This resulted in noncovalent contacts that align with HSAB theory and highlights a potential future concept for crystal engineering. The soft

iodine XB donors interact with the soft sulfur atoms, while the hard hydrogen of the methanol displayed a preference for the nitrogen atom of the SCN^- . In contrast, the $(2)^{2+} \cdot 2\text{SCN}^- \cdot \text{DCM}$ complex, lacking a strong HB donor, formed XBs with both the hard and soft basic sites. While the solid-state packing is complex, the preceding evidence provides the ground work to further examine XB HSAB complementarity.

Triiodide (I_3^-) was investigated as a soft anion that does not contain a hard acceptor. Yellow–orange plates of X-ray diffraction quality were grown from vapor diffusion of diethyl ether into an acetonitrile solution of receptor (2) and TBA^+I_3^- . The complex $(2)^{2+} \cdot 2\text{I}_3^-$

crystallized in space group $P2_1/n$ with one host and two I_3^- anions in the asymmetric unit. One I_3^- anion (Fig. 6, blue) has a terminal I atom that receives bifurcated XBs from two distinct donors, with $\text{C—I} \cdots \text{I}$ distances of 3.6331 (11) and 3.7228 (11) Å (R_{II} values of 0.88 and 0.91, respectively). The associated $\text{C—I} \cdots \text{I}$ angles are 164.6 (3) and 160.2 (3)° which coincide with moderate XB interactions. The second I_3^- anion (Fig. 6, orange) displays a Type I (Mukherjee *et al.*, 2014) halogen–halogen contact with the I_3^- (Fig. 6, blue) molecule with a distance and angle of 3.7133 (13) Å and 158.47 (4)°. Interestingly, only C—H hydrogen bonding is observed with this I_3^- (Fig. 6, orange). Three $\text{CH} \cdots \text{I}$ HBs [distances ranging from 2.9700 (9) to 3.2387 (9) Å] and one weak anion–arene contact with an electron-deficient pyridinium ring are also observed. The crystal packing displays sheets of alternating dimers held together by π – π interactions between the pyridinium and benzene rings and XB with I_3^- (Fig. 6, blue). These

Figure 6
Space-filling representation of $(2)^{2+} \cdot 2\text{I}_3^-$ highlighting two receptors and four monodentate XBs to two crystallographically equivalent I_3^- molecules (blue). The second I_3^- (orange) forms a Type I halogen–halogen contact with the blue I_3^- .

Figure 7
View down the crystallographic *a* axis of off-set head-to-tail dimer columns held together by triiodide molecules (displacement ellipsoids drawn at the 50% probability level).

dimers create columns down the crystallographic *a* axis that are held together by the I_3^- molecules (Fig. 7). While the SCN^- anion is a ditopic Lewis base with both a hard and soft acceptor, I_3^- is solely a soft anionic XB acceptor. The $(2)^{2+} \cdot 2\text{I}_3^-$ complex displays two types of XBs: one monodentate organic XB to the terminal iodines of one I_3^- molecule and a Type I halogen–halogen contact which holds the crystal lattice together. These crystal structures illustrate the XB complementarity to chemically soft Lewis bases.

3. Conclusion

Comparisons between the HB and the XB are warranted. Undoubtedly, the history of the HB has provided the groundwork for investigating the underlying characteristics of the XB. However, as the XB gains in popularity, the nuances that make it unique reveal themselves. This investigation offers early quantification of halogen bonding to varied soft neutral and anionic Lewis bases in solution. XB HSAB complementarity is supported by three monodentate and one bidentate XB structures in the solid state. Further examination of this XB feature is currently underway in our lab.

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References

- Arman, H. D., Gieseck, R. L., Hanks, T. W. & Pennington, W. T. (2010). *Chem. Commun.* **46**, 1854–1856.
- Auffinger, P., Hays, F. A., Westhof, E. & Ho, P. S. (2004). *Proc. Natl Acad. Sci. USA*, **101**, 16789–16794.
- Awtrey, A. D. & Connick, R. E. (1951). *J. Am. Chem. Soc.* **73**, 1842–1843.
- Beale, T. M., Chudzinski, M. G., Sarwar, M. G. & Taylor, M. S. (2013). *Chem. Soc. Rev.* **42**, 1667–1680.
- Berryman, O. B., Bryantsev, V. S., Stay, D. P., Johnson, D. W. & Hay, B. P. (2007). *J. Am. Chem. Soc.* **129**, 48–58.
- Berryman, O. B., Hof, F., Hynes, M. J. & Johnson, D. W. (2006). *Chem. Commun.* pp. 506–508.
- Berryman, O. B., Sather, A. C., Hay, B. P., Meisner, J. S. & Johnson, D. W. (2008). *J. Am. Chem. Soc.* **130**, 10895–10897.
- Beweries, T., Brammer, L., Jasim, N. A., McGrady, J. E., Perutz, R. N. & Whitwood, A. C. (2011). *J. Am. Chem. Soc.* **133**, 14338–14348.
- Breugst, M., Zipse, H., Guthrie, J. P. & Mayr, H. (2010). *Angew. Chem. Int. Ed.* **49**, 5165–5169.
- Cabot, R. & Hunter, C. A. (2009). *Chem. Commun.* pp. 2005–2007.
- Cametti, M., Raatikainen, K., Metrangolo, P., Pilati, T., Terraneo, G. & Resnati, G. (2012). *Org. Biomol. Chem.* **10**, 1329–1333.
- Carlsson, A. C. C., Veiga, A. X. & Erdélyi, M. (2015). *Top. Curr. Chem.* **359**, 49–76.
- Cauliez, P., Polo, V., Roisnel, T., Llusar, R. & Fourmigué, M. (2010). *CrystEngComm*, **12**, 558–566.
- Cavallo, G., Metrangolo, P., Milani, R., Pilati, T., Priimagi, A., Resnati, G. & Terraneo, G. (2016). *Chem. Rev.* **116**, 2478–2601.
- Chudzinski, M. G. & Taylor, M. S. (2012). *J. Org. Chem.* **77**, 3483–3491.
- Etter, M. C. (1990). *Acc. Chem. Res.* **23**, 120–126.
- Frassinetti, C., Ghelli, S., Gans, P., Sabatini, A., Moruzzi, M. S. & Vacca, A. (1995). *Anal. Biochem.* **231**, 374–382.
- Fujimoto, H. & Satoh, S. (1994). *J. Phys. Chem.* **98**, 1436–1441.
- Gamez, P., Mooibroek, T. J., Teat, S. J. & Reedijk, J. (2007). *Acc. Chem. Res.* **40**, 435–444.
- Hay, B. P. & Bryantsev, V. S. (2008). *Chem. Commun.* pp. 2417–2428.
- Ho, T.-L. (1977). *Hard and Soft Acids and Bases Principle in Organic Chemistry*. New York: Academic Press.
- Jones, G. & Kaplan, B. B. (1928). *J. Am. Chem. Soc.* **50**, 1845–1864.
- Laurence, C., Graton, J., Berthelot, M. & El Ghomari, M. J. (2011). *Chem. Eur. J.* **17**, 10431–10444.
- Le Gal, Y., Lorcy, D., Jeannin, O., Barrière, F., Dorcet, V., Lieffrig, J. & Fourmigué, M. (2016). *CrystEngComm*, **18**, 5474–5481.
- Massena, C. J., Riel, A. M. S., Neuhaus, G. F., Decato, D. A. & Berryman, O. B. (2015). *Chem. Commun.* **51**, 1417–1420.
- Massena, C. J., Wageling, N. B., Decato, D. A., Martin Rodriguez, E., Rose, A. M. & Berryman, O. B. (2016). *Angew. Chem. Int. Ed.* **55**, 12398–12402.
- Mayr, H., Breugst, M. & Ofial, A. R. (2011). *Angew. Chem. Int. Ed.* **50**, 6470–6505.
- Metrangolo, P., Neukirch, H., Pilati, T. & Resnati, G. (2005). *Acc. Chem. Res.* **38**, 386–395.
- Michielsen, B., Verlact, C., van der Veken, B. J. & Herrebout, W. A. (2012). *J. Mol. Struct.* **1023**, 90–95.
- Mukherjee, A., Tothadi, S. & Desiraju, G. R. (2014). *Acc. Chem. Res.* **47**, 2514–2524.
- Nagels, N., Geboes, Y., Pinter, B., De Proft, F. & Herrebout, W. A. (2014). *Chem. Eur. J.* **20**, 8433–8443.
- Ouvrard, C., Le Questel, J.-Y., Berthelot, M. & Laurence, C. (2003). *Acta Cryst. B* **59**, 512–526.
- Pearson, R. G. (1963). *J. Am. Chem. Soc.* **85**, 3533–3539.

- Pinter, B., Nagels, N., Herrebout, W. A. & De Proft, F. (2013). *Chem. Eur. J.* **19**, 519–530.
- Platts, J. A., Howard, S. T. & Bracke, B. R. F. (1996). *J. Am. Chem. Soc.* **118**, 2726–2733.
- Politzer, P. & Murray, J. S. (2013). *ChemPhysChem*, **14**, 278–294.
- Rissanen, K. (2008). *CrystEngComm*, **10**, 1107–1113.
- Robertson, C. C., Perutz, R. N., Brammer, L. & Hunter, C. A. (2014). *Chem. Sci.* **5**, 4179–4183.
- Sarwar, M. G., Dragisic, B., Salsberg, L. J., Gouliaras, C. & Taylor, M. S. (2010). *J. Am. Chem. Soc.* **132**, 1646–1653.
- Schottel, B. L., Chifotides, H. T. & Dunbar, K. R. (2008). *Chem. Soc. Rev.* **37**, 68–83.
- Sennikov, P. G. (1994). *J. Phys. Chem.* **98**, 4973–4981.
- Smith, D. A., Brammer, L., Hunter, C. A. & Perutz, R. N. (2014). *J. Am. Chem. Soc.* **136**, 1288–1291.
- Zordan, F., Brammer, L. & Sherwood, P. (2005). *J. Am. Chem. Soc.* **127**, 5979–5989.