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Organic Complexes Built by Halogenated Molecules: Unexpected *in Situ* C−N Bond Formation in Metal-Free Solvothermal Conditions

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Supporting Information

ABSTRACT: Reactions of two halogenated derivatives of bis(4-hydroxyphenyl)sulphone (BPS, **1**), tetrabromobisphenol-S (TBBPS, **2**), and tetrachlorobisphenol-S (TCBPS, **3**), with piperazine (PZ, **4**), were investigated by means of the combinational usage of solvothermal and mechanochemical methods. The resultant organic complexes, $[(C_6H_2OBr_2)_2SO_2]\cdot[(C_4H_{10}N_2)_2CH_2]$ (**5**), $[(C_6H_2OBr_2)_2SO_2]_2\cdot(C_4H_{12}N_2)_2\cdot3(CH_3OH)$ (**6**), $[(C_6H_2OCl_2)_2SO_2]\cdot[(C_4H_{10}N_2)_2CH_2]$ (**7**), and $[(C_6H_2OCl_2)_2SO_2]_2\cdot(C_4H_{12}N_2)_2\cdot3(CH_3OH)$ (**8**), were fully characterized by single crystal and powder X-ray diffractions. In the cases of complexes **5** and **7** that were prepared from solvothermal conditions, a rare metal-free *in situ* ligand formation has been observed, in which the new organic molecule 1,2-bispiperazinylmethane was presumably originated from the double C−N coupling of two piperazines on a carbon atom coming from methanol. In addition, the relevant concomitants **6** and **8** were also isolated from the solutions of **5** and **7**, respectively. Complexes **6** and **8** contain 1:1 starting molecules of **2**/**3** with **4** assembled into helical structures.

Crystalline materials of organic complexes are notable representatives in supramolecular chemistry because of both their structural complexity and physical property of interest, in which the role of hydrogen bonds (H-bonds), as predominant driven forces, has been well-established.[1,2] Most hydrogen bonds are primarily electrostatic in nature and flexible in strength, according to the different electron donors and acceptors. Of note, relatively simple covalent modifications in external conditions of organic molecules can change the balance of weak interactions and alter the secondary structures. In addition, halogen atoms have been known to form well-defined adducts with electron donor species through noncovalent halogen bonds (X-bonds). However, it is only recently that heuristic principles are presented to develop a rational crystal engineering of halogen bonded organic complexes, relying on the directional and predictive nature of these intermolecular cohesive interactions.[3] As a consequence, halogen bonding has soon been proven as an effective supramolecular interaction in self-assembly processes and awakens considerable research interest in many practical realms, including molecular recognition, drug−receptor interaction, supramolecular organic conductors, and liquid crystals.[4] Our current strategy focuses on investigating the effects of halogenation on traditional organic modules in construction of supramolecular organic complexes. In the current systems, halogen atoms were introduced onto the organic precursors that possess terminal hydroxyl groups; thus, the halogen atoms are able to play dual roles both as modification to adjust the primary hydrogen bonds formed by the H-bond donating hydroxyl groups and as potential donor sites to form secondary X-bonds that may direct the hierarchical assemblies.

The supramolecular chemistry of bis(4-hydroxyphenyl)sulphone (BPS, **1**) was investigated and showed efficient and robust ability to form organic complexes with a series of organoamines *via* charge-assisted $O_{hydroxyl}\cdots H\cdots N$ hydrogen bonds with or without proton transfer.[5] We target on the halogenated BPS as modeling molecules based on the following considerations: (i) the ability of the hydroxyl groups on halogenated BPS to form hydrogen bonds can be boosted due to the substitution of electron-withdrawing halogen atoms; (ii) H-bond strengths of the halogenated BPS molecules can be carefully tuned through relatively simple covalent modifications with different halogen atoms,[1d] which, we believe, may endow some superiority in directing the molecular assembly and recognition; (iii) the halogenated BPS molecules are able to generate secondary halogen bonds due to the introduction of X-bond donors, which may result in new and interesting supramolecular assemblies. We have successfully demonstrated that tetrabromobisphenolsulphone (TBBPS, **2**) crystallized with 1,3-bis(4-pyridyl) propane (BPP), among others, differently from the parent BPS and resulted in an organic cocrystal with an unprecedented braidlike molecular assembly.[6] As part of the extension into a more complex sysmtem, we report herein the reactions of two halogenated

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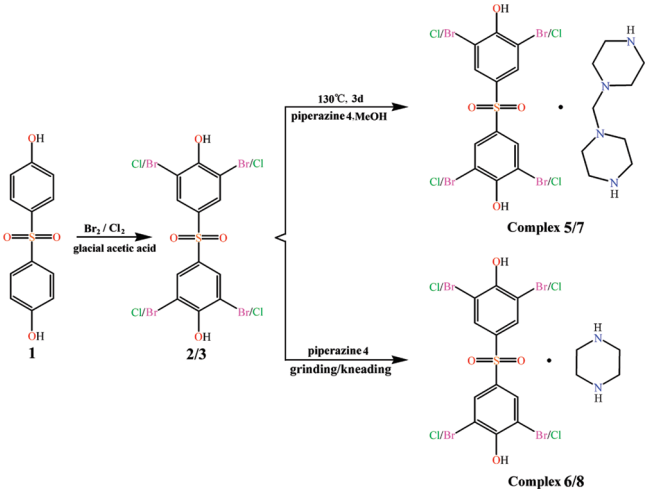
Scheme 1. Synthesis of TBBPS/TCBPS and complexes 5−8



molecules, tetrabromobisphenolsulphone (**2**) and tetrachlorobisphenolsulphone (TCBPS, **3**), with piperazine (PZ, **4**) by the combinational usage of solvothermal and mechanochemical methods.

The halogenated organic molecules, TBBPS and TCBPS, were prepared from the reactions of BPS with bromine or chlorine in glacial acetic acid at 85 °C (see Supporting Information in detail), respectively (Scheme 1). The solvothermal method was introduced because of the poor solubilities of TBBPS and TCBPS in methanol. Moreover, white precipitate appeared immediately when solutions of TBPPS/TCBPS and piperazine were mixed, which detered the further crystallization of single crystals. Reaction of 1:1 TBBPS and PZ in methanol at 135 °C yielded a small amount of colorless and irregular crystalline solids, which is insoluble in water and common organic solvents. Single crystal X-ray diffraction indicated an unexpected crystal phase, formulated as $[(C_6H_2OBr_2)_2SO_2]\cdot[(C_4H_{10}N_2)_2CH_2]$ (complex **5**), in which a new organic molecule formed *in situ*. The above solution was allowed to evaporate in ambient condition and resulted in light-yellow block crystals together with some unidentified yellow slurry. The structure of the block crystals was determined by single crystal X-ray diffraction and formulated as $[(C_6H_2OBr_2)_2SO_2]_2\cdot(C_4H_{12}N_2)_2\cdot 3(CH_3OH)$ (complex **6**). The bulk of complex **5** can be obtained from optimized reactions with 1:2 TBBPS and PZ in methanol. However, the pure bulk of complex **6** was perturbed by both the low yield and slurry impurities. Fortunately, mechanochemical reaction by manual grinding of 1:1 TBBPS and PZ in a agate mortar with several drops of methanol gave a bulky sample of complex **6** that was confirmed by XRPD (Figure S2 of the Supporting Information). Reactions using TCBPS to replace TBBPS gave complexes **7** and **8** accordingly.

Complexes **5** and **7** are isomorphous; therefore, only the structure of complex **5** is presented (Figure 1). Single-crystal X-ray crystallographic analysis shows that complex **5** crystallizes in monoclinic space group $P2_1/n$. It is evident that a new organic molecule, 1,2-bispiperazinylmethane (BPZM for short), was formed during the solvothermal reaction. The *in situ* generated BPZM molecules form a 1:1 complex with TBBPS (**5**). The molecular aggregation of complex **5** is dominated by $O_{hydroxyl}\cdots H-N$ hydrogen bonds between the hydroxyl O atoms of TBBPS and the piperazinyl nitrogen atoms of BPZM ($O_{hydroxyl}\cdots H-N$ 2.720−2.777 Å). The BPZM molecule adopts a

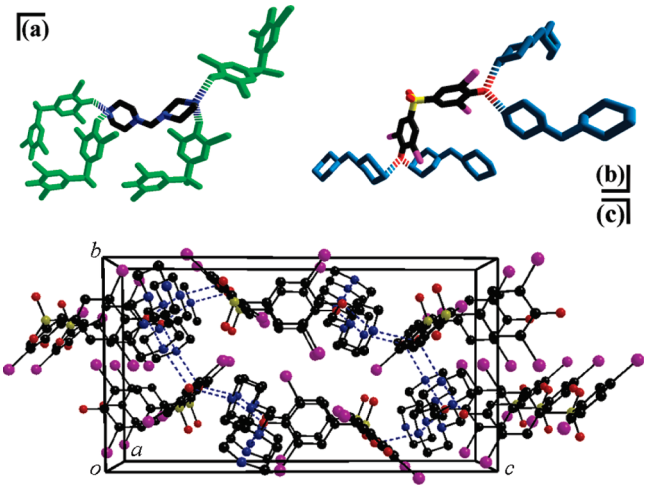


Figure 1. View of the hydrogen bonds between the BPZM and TBBPS (a and b); and the 3D supramolecular structure in complex **5** (c).

trans−*trans* configuration (defined by the central sp^3 carbon), and the terminal piperazinyl N···N distance is 7.554 Å, which is somewhat shorter than the actual donor−donor distance ($O_{hydroxyl}\cdots O_{hydroxyl}$) of 9.072 Å in TBBPS. Each BPZM connects to four TBBPS, and the TBBPS in turn interacts with four BPZM to form a three-dimensional (3D) supramolecular network. Topological analysis[7] considering H-bonds as primary intermolecular forces of complex **5** indicates that it possesses a four-connected uninodal **sra** ($SrAl_2$) net (point symbol $(4^2\cdot6^3\cdot8)$, vertex symbol $[4\cdot6\cdot4\cdot6\cdot6\cdot8_2]$) by choosing the two types of organic molecules as simple nodes.

A possible reaction mechanism concerning the formation of the new BPZM molecule is proposed and illustrated in Scheme S1 (Supporting Information). Reportedly, a similar reaction can be achieved in the presence of Al_2O_3.[8−10] Attempts at carrying out the reactions using the nonbrominated reagent **1** (BPS) afforded no outcome of expecting reactions. This result supports the hypothesis that the halogenated reagents **2** (TBBPS) and **3** (TCBPS) promote the C−N coupling under the metal-free solvothermal conditions.

Single-crystal X-ray crystallographic analysis reveals that complex **6** crystallizes in tetragonal space group $P4_12_12$ (flack parameter 0.02(2)). In the structure of **6**, TBBPS and PZ form a 1:1 complex with three MeOH solvent molecules *per* formula unit (Figure 2a and b). The assembly of complex **6** is directed by $O_{hydroxyl}\cdots H-N$ hydrogen bonds between the hydroxyl O atoms of TBBPS and the piperazinyl nitrogen atoms of PZ ($O_{hydroxyl}\cdots H-N$ 2.581−2.688 Å), which are considerably shorter than the O···H−N hydrogen bonds in complex **5** (2.720−2.777 Å). The TBBPS and PZ connect to each other in a way that the TBBPS molecules pack into double helices due to their "bent" nature and the PZ molecules locate in between the two helical chains (Figure 2c). The double helices pack along the crystallographic *c* axis into a 3D supramolecular structure involving secondary halogen bonds between Br atoms of TBBPS and O donors of methanol ($Br\cdots O_{methanol}$ = 3.276 Å) (Figure 2d). Complex **8** possesses an identical packing pattern as **6** but crystallized with an opposite absolute configuration (space group $P4_32_12$, flack parameter −0.02(9)).

Binary and ternary organic complexes formed by means of chiral crystallization from achiral molecular building blocks have been

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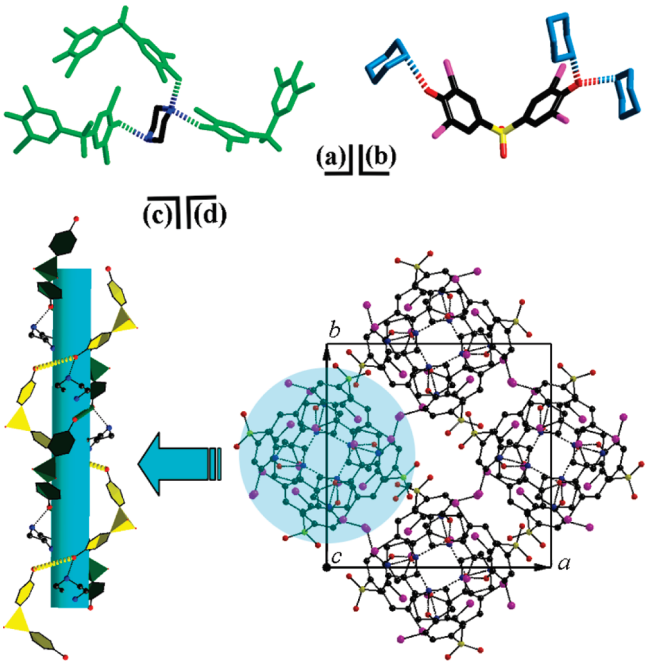

Figure 2. View of the hydrogen bonds between the PZ and TBBPS (a) and (b); the double helical subunit (c); and the 3D packing pattern of complex **7** (d).

rationalized in the system of benzoic acid with organic amines. A key factor has been the multiple roles that the carboxyl group and amino nitrogen atom play as electron donors and acceptors, giving birth to O···H···N supramolecular interactions as the main driven forces in the molecular packing.[11] Moreover, remnant functional groups capable of generating weaker intermolecular forces are also responsible for the chiral crystallization processes. Similarly, in the reaction system of halogenated bisphenol derivatives with piperazine, the $O_{hydroxyl}$···H−N interactions direct the molecular packing and the potential halogen bonding sites offer the opportunity for weaker molecular interactions, which, we believe, is the determinant of the chiral crystallizaiton. However, no legible circular dichroism (CD) has been observed for either a bulky sample (prepared by mechanochemical method) or single crystals. It is possible that the crystalline MeOH solvent molecules, which are extensively involved in secondary halogen bonds, are lost during the preparation of KCl discs by grinding and compressing, resulting in the disappearance of chirality.[12] Since complexes **6** and **8** display identical structures with opposite absolute configurations, it is also possible that the bulk samples are racemic and contain nearly equivalent crystals with opposite absolute configurations. One reliable but very time-consuming method would be to determine the absolute configuration of all single crystals in one batch.

Proton transfer from TBBPS/TCBPS to PZ is observed in all cases; thus, complexes **5**−**8** are organic salts. Moreover, the distances of $O_{hydroxyl}$···H−N hydrogen bonds are shorter than the *ordinary H-bond* (2.8/2.9 Å, minimum/average distances), and they are thus considered as *double charge-assisted H-bonds* comprised by strong $^{1/2-}$D···H^{+}···A$^{1/2-}$ interactions (D = H-bond donor; A = H-bond acceptor).[13] However, the reaction of parent BPS (**1**) with PZ (**4**) afforded a 2:1 salt (complex **9**) having 1D ring chain subunits, in which the doubly protonated PZ molecules connect the rings formed by face-to-face half deprotonated BPS moieties *via* two types of strong hydrogen bonds, $O_{hydroxyl}$···H−N (2.579 Å) and $O_{hydroxyl}$···H−$O_{hydroxyl}$ (2.560 Å), respectively (Figure S3a, Supporting Information).[5] The ring chains are further extended by week $O_{sulfuryl}$···H−N (2.918 Å and 2.985 Å) and $O_{sulfuryl}$···H−C (2.975 Å) hydrogen bonds into a 3D supramolecular structure (Figure S3b, Supporting Information). The structure of complex **9** is somewhat straightforward and significantly different from those of complexes **6** and **8** built by halogenated modules with PZ.

In summary, the present work serves to explore the effects of halogenations on the structures and physical properties of the new organic complexes. Furthermore, we introduce the solvothermal method in the synthesis of organic complexes in solving the problem related to the competition between heteromeric and homomeric crystallizations in conventional synthesis. It has been shown that the modification on traditional organic molecules would be a successful synthetic strategy to construct supramolecular organic complexes thanks to the hierarchy of intermolecular interactions. In the reaction system of halogenated BPS (TBBPS and TCBPS) with piperazine, the strength of primary O···H−N H-bonds has been rationally modified by the electron-withdrawing halogen atoms, and the inclusion of secondary Br···O X-bonds results in various changes in the crystal packing. Of note, the unexpected *in situ* ligand formation by C−N coupling in complex **5**/**7** is related to the halogenated modules, although a clear mechanism is awaiting disclosure.

CRYSTAL STRUCTURE DETERMINATION

Crystallographic data were collected on a *Rigaku Mercury CCD/AFC* diffractometer equipped with graphite-monochromated Mo Kα radiation with a radiation wavelength of 0.71073 Å by using the *ω*-scan technique. All absorption corrections were performed using the *CrystalClear* program.[14] Structures were solved by direct methods and refined on F^2 by full matrix least-squares using the *SHELXL-97* program package.[15] All the non-hydrogen atoms were refined anisotropically. The active H atoms on organic molecules were found on a Fourier-difference map, and other H atoms were generated geometrically. CCDC-775137 (**5**), 784281 (**6**), 784280 (**7**), and 784282 (**8**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Crystal/Refinement Details for 5. $C_{21}H_{26}Br_4N_4O_4S$, M = 750.16, monoclinic, $P2_1/n$, a = 10.2780(4), b = 12.0006(3), c = 21.9936(6), β = 95.190(3), V = 2701.62(2), Z = 4, R_1 [$I > 2\sigma(I)$] = 0.0490, wR_2 = 0.1386. **For 6**: $C_{17.5}H_{22}Br_4N_2O_{5.5}S$, M = 700.07, tetragonal, $P4_12_12$, a = 15.8417(6), b = 15.8417(6), c = 19.1079(1), V = 4795.3(4), Z = 8, R_1 [$I > 2\sigma(I)$] = 0.0626, wR_2 = 0.1882. **For 7**: $C_{21}H_{26}Cl_4N_4O_4S$, M = 572.32, monoclinic, $P2_1/n$, a = 10.3884(4), b = 11.4896(3), c = 21.6902(6), β = 94.662(3), V = 2580.35(1), Z = 4, R_1 [$I > 2\sigma(I)$] = 0.0520, wR_2 = 0.1808. **For 8**: $C_{17.5}H_{22}Cl_4N_2O_{5.5}S$, M = 522.23, tetragonal, $P4_32_12$, a = 15.543(3), b = 15.543(3), c = 19.210(5), V = 4641.1(2), Z = 8, R_1 [$I > 2\sigma(I)$] = 0.0555, wR_2 = 0.1705.

ASSOCIATED CONTENT

Supporting Information. Experimental details and general characterizations, ^{1}H NMR, XRPD, figures, and crystallographic data in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

(1) See references for example:(a) Remenar, J. F.; Morissette, S. L.; Peterson, M. L.; Moulton, B.; MacPhee, J. M.; Guzman, H. R.; Almarsson, Ö. *J. Am. Chem. Soc.* **2003**, *125*, 8456. (b) Childs, S. L.; Chyall, L. J.; Dunlap, J. T.; Smolenskaya, V. N.; Stahly, B. C.; Stahly, P. G. *J. Am. Chem. Soc.* **2004**, *126*, 13335. (c) Aakeröy, C. B.; Salmon, D. J. *CrystEngComm* **2005**, *7*, 439. (d) Aakeröy, C. B.; Desper, J.; Scott, B. M. T. *Chem. Commun.* **2006**, 1445. (e) Chiarella, R. A.; Davey, R. J.; Peterson, M. L. *Cryst. Growth Des.* **2007**, *7*, 1223. (f) Bhogala, B. R.; Nangia, A. *New J. Chem.* **2008**, *32*, 800. (g) Kirchner, M. T.; Bläser, D.; Boese, R. *Chem.—Eur. J.* **2010**, *16*, 2131. (h) Khan, M.; Enkelmann, V.; Brunklaus, G. *J. Am. Chem. Soc.* **2010**, *132*, 5254.

(2) See references for example:(a) Stanley, N.; Sethuraman, V.; Thomas Muthiah, P.; Luger, P.; Weber, M. *Cryst. Growth Des.* **2002**, *2*, 631. (b) Baskar Raj, S.; Stanley, N.; Thomas Muthiah, P.; Bocelli, G.; Ollá, R.; Cantoni, A. *Cryst. Growth Des.* **2003**, *3*, 567. (c) Almarsson, Ö.; Zaworotko, M. J. *Chem. Commun.* **2004**, 1889. (d) Vishweshwar, P.; McMahon, J. A.; Peterson, M. L.; Hickey, M. B.; Shattock, T. R.; Zaworotko, M. J. *Chem. Commun.* **2005**, 4601. (e) Vishweshwar, P.; McMahon, J. A.; Bis, J. A.; Zaworotko, M. J. *J. Pharm. Sci.* **2006**, *95*, 499. (f) Oliveira, M. A.; Peterson, M. L.; Klein, D. *Cryst. Growth Des.* **2008**, *8*, 4487. (g) Nichol, G. S.; Clegg, W. *Cryst. Growth Des.* **2009**, *8*, 1844. (h) Lee, T.; Wang, P. Y. *Cryst. Growth Des.* **2010**, *10*, 1419.

(3) Aakeröy, C. B.; Desper, J.; Helfrich, B. A.; Metrangolo, P.; Pilati, T.; Resnati, G.; Stevenazzib, A. *Chem. Commun.* **2007**, 4236.

(4) (a) Farina, A.; Meille, S. V.; Messina, M. T.; Metrangolo, P.; Resnati, G.; Vecchio, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 2433. (b) Nguyen, H. L.; Horton, P. N.; Hursthouse, M. B.; Legon, A. C.; Bruce, D. W. *J. Am. Chem. Soc.* **2004**, *126*, 16. (c) Caronna, T.; Liantonio, R.; Logothetis, T. A.; Metrangolo, P.; Pilati, T.; Resnati, G. *J. Am. Chem. Soc.* **2004**, *126*, 4500. (d) Mele, A.; Metrangolo, P.; Neukirch, H.; Pilati, T.; Resnati, G. *J. Am. Chem. Soc.* **2005**, *127*, 14972. (e) Neukirch, H.; Guido, E.; Liantonio, R.; Metrangolo, P.; Pilati, T.; Resnati, G. *Chem. Commun.* **2005**, 1534. (f) Metrangolo, P.; Präsang, C.; Resnati, G.; Liantonio, R.; Whitwood, A. C.; Bruce, D. W. *Chem. Commun.* **2006**, 3290. (g) Cariati, E.; Forni, A.; Biella, S.; Metrangolo, P.; Meyer, F.; Resnati, G.; Righetto, S.; Tordina, E.; Ugoa, R. *Chem. Commun.* **2007**, 2590.

(5) Ferguson, G.; Glidewell, C.; Gregson, R. M.; Lavender, E. S. *Acta Crystallogr., Sect. B: Struct. Sci.* **1999**, *55*, 573.

(6) Lü, J.; Han, L.-W.; Lin, J.-X.; Liu, T.-F.; Cao, R. *Cryst. Growth Des.* **2010**, *10*, 4217.

(7) Blatov, V. A. *IUCr Comput. Comm. Newslett.* **2006**, *7*, 4; see also http://www.topos.ssu.samara.ru.

(8) Hatano, B.; Nagahashi, K.; Kijima, T. *J. Org. Chem.* **2008**, *73*, 9188.

(9) References for *in situ* ligand formation. See for examples: (a) Feller, R. K.; Forster, P. M.; Wudl, F.; Cheetham, A. K. *Inorg. Chem.* **2007**, *46*, 8717. (b) Li, G.-B.; Liu, J.-M.; Yu, Z.-Q.; Wang, W.; Su, C.-Y. *Inorg. Chem.* **2009**, *48*, 8659.

(10) Reference for ligand formation in the presence of dihalomethane as solvents. See for example:Miyano, S.; Mori, A.; Hokari, H.; Ohta, K.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 1331.

(11) Tan, T.-F.; Han, J.; Pang, M.-L.; Song, H.-B.; Ma, Y.-X.; Meng, J.-B. *Cryst. Growth Des.* **2006**, *6*, 1186.

(12) Lennartson, A.; Håkansson, M. *CrystEngComm* **2009**, *11*, 1979.

(13) (a) Gilli, P.; Bertolasi, V.; Ferretti, V.; Gilli, G. *J. Am. Chem. Soc.* **2000**, *122*, 10405. (b) Gilli, P.; Bertolasi, V.; Pretto, L.; Ferretti, V.; Gilli, G. *J. Am. Chem. Soc.* **2004**, *126*, 3845. (c) Gilli, P.; Bertolasi, V.; Pretto, L.; Lycka, A.; Gilli, G. *J. Am. Chem. Soc.* **2002**, *124*, 13554. (d) Gilli, P.; Pretto, L.; Bertolasi, V.; Gilli, G. *Acc. Chem. Res.* **2009**, *42*, 33.

(14) Molecular Structure Corporation & Rigaku, 2000. *CrystalClear*, Version 1.36; MSC, 9009 New Trails Drive, The Woodlands, TX 77381-5209, USA, and Rigaku Corporation, 3-9-12 Akishima, Tokyo, Japan.

(15) Sheldrick, G. M. *SHELXS-97*, Program for Crystal Structure Solution and Refinement; University of Göttingen, 1997.