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Hydrogen Bond-Enhanced Halogen Bonding Organocatalyst with C(sp^3)−Br and Sulfoxide Moieties

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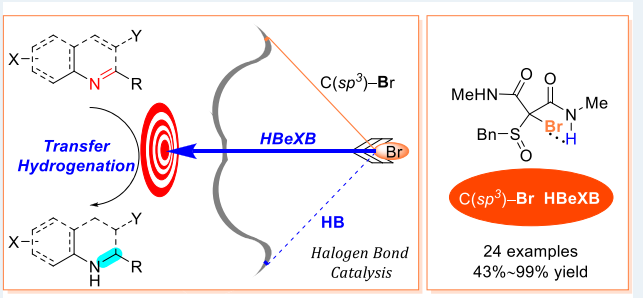
ABSTRACT: Neutral halogen bonding donors (XBDs) containing sp^3-hybridized carbon−bromine and sulfoxide moieties were designed and synthesized. They promoted quinolines and imines reduction easily with a relatively low catalyst loading (5 mol %). Their halogen bonding strengths were quantified using ^{31}P NMR spectroscopy and molecular electrostatic potential (MESP) analysis. Single-crystal X-ray analysis unambiguously confirmed the presence of intramolecular C(sp^3)−Br···H−N hydrogen bonding within the amide-derived XBD. Combined experimental and computational studies revealed that the amide-derived XBD acts as an efficient hydrogen bond-enhanced halogen bonding organocatalyst.



KEYWORDS: *C(sp^3)−Br halogen bond, sulfoxide, intramolecular hydrogen bond, cooperative organocatalysis, quinolines reduction*

Halogen bonding (XB), one of noncovalent interactions,[1] has gained increasing attention in the field of organocatalysis in recent decades.[2] Generally, for the halogen bonding catalyst based on carbon−halogen (C−X) bond donors (Figure 1a), the C(sp)−X type is supposed to be more

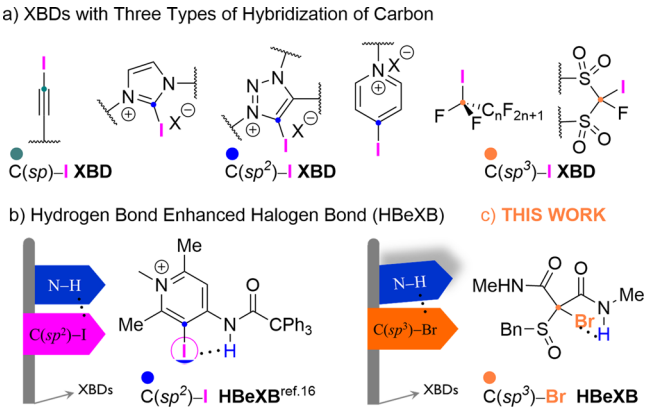


Figure 1. (a) Different types of XBDs. (b) Hydrogen bond-enhanced halogen bond (HBeXB). (c) This work.

powerful,[3] whereas the C(sp^2)−X one is more popular because of its structural diversity and easy preparation. The corresponding halogen bond donors (XBDs) can be neutral and even cationic, depending on the core halogenated scaffolds, which are constructed from readily available polyfluorinated phenyl,[4] triazole,[5] imidazolium,[6] pyridinium,[7] or triazolium[8] moieties. Since the first use of 2-iodoimidazolium triflate as the activating reagent for Ritter reaction,[6c] the cationic XBDs have been widely explored for organocatalysis because of their higher halogen bonding strength than that of the neutral analogue. Stimulated by the pioneering work from Huber and co-workers, a broad range of reactions catalyzed by XBD were sequentially disclosed, including Friedel−Crafts reaction,[9] Michael addition,[10] Diels−Alder cycloaddition,[11] and glycosylation.[12]

In sharp contrast, examples of XBDs with C(sp^3)−X motif are quite limited, which is in line with the trend that less s character of carbon will lead to a smaller σ-hole on the attached halogen.[13] In 2008, Bolm and co-workers successfully overcame this limitation by applying highly fluorinated iodoalkanes[14] as a XBD. More recently, Shibata's group designed new XBDs with a fluorobissulfonylmethyl iodide scaffold, which efficiently catalyzed the Mukaiyama aldol reaction and quinolines reduction.[15] It is noteworthy here that their design not only provided an attractive alternative for XBDs with C(sp^3)−X but also showed the feasibility of incorporating a chiral backbone into the XB catalyst. Moreover, it is important to point out that strengthening XBDs with C(sp^3)−X is theoretically possible by employing the novel strategy of hydrogen bond (HB)-enhanced XB, as

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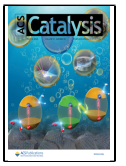

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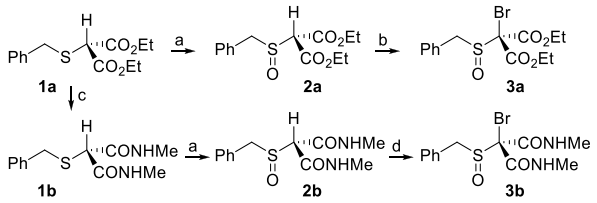
exemplified by XBDs with C(sp^2)−I, which are dramatically strengthened through an intramolecular cyclic five-membered HB to the electronegative belt of the iodine atom (Figure 1b).[16] Inspired and encouraged by the aforementioned advances in XB organocatalysts, we herein describe a novel type of HB-enhanced XB catalyst (Figure 1c) with a rarely reported C(sp^3)−Br moiety[17] and its successful activation of quinolines through N···Br halogen bonding.

In our initial design, XBD **3a** equipped with electron-withdrawing sulfinyl and malonyl groups was synthesized easily in 3 steps from inexpensive benzyl mercaptan and diethyl bromomalonate (Scheme 1).[18] Moreover, an attempt to

Scheme 1. Synthesis of XBDs with C(sp^3)−Br Moiety[a]

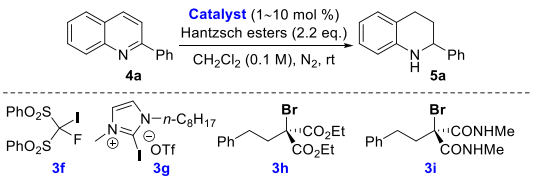


[a]Conditions: (a) 35 wt % H_2O_2, Na_2MoO_4, CF_3CH_2OH, rt; (b) NBS, TsOH·H_2O, CH_3CN, reflux, 2 h, 55% yield; (c) 27 wt % CH_3NH_2 in MeOH, 60 °C, 5 h, 54% yield; (d) Br_2, Et_3N, CH_2Cl_2, rt, 3 h, 74% yield.

prepare stronger XBD **3e** by electrophilic iodination of **2a** was successful. Unfortunately, the stability of **3e** is poor because of the rapid C(sp^3)−I bond cleavage at room temperature [Supporting Information (SI), Scheme S6]. Additionally, when malonyl groups of **1a** were replaced by more electron-withdrawing phenylsulfonyl groups, the corresponding sulfide **1c** was intact under various oxidizing conditions (SI, Scheme S4). Therefore, our approaches to a stronger XBD than **3a** for catalysis by introducing an iodine atom or more electron-withdrawing group failed. Since the amidation of esters in **1b** through ammonolysis is straightforward, XBD **3b** was accordingly prepared as a comparison for **3a**. It is worth mentioning that both **3a** and **3b** are stable under ambient conditions, and no Pummerer-type decomposition[19] was observed for their precursors **2a** and **2b**.

To examine the catalytic activities of our XBDs, transfer hydrogenation of 2-phenylquinoline (**4a**) with Hantzsch esters was selected as the model reaction (Table 1). In the absence of catalyst, the reaction was slow, and a 10% yield of target product tetrahydroquinoline **5a** was observed (entry 1). Pentafluoroiodobenzene (PFIB), a known XBD, provided **5a** with only 20% yield within 24 h (entry 2). In contrast, with 10 mol % of **3a**, **4a** was completely converted to **5a** within 9 h (entry 3). Encouraged by this preliminary result, XBD derivatives of **3a** with electron-withdrawing substituents on the phenyl ring were investigated (**3d**, **3d′**, SI, Table S1), though such variation showed no significant effect on the reaction rate. It is generally accepted that an ester group is more electron-withdrawing than an amide, and accordingly, **3a** is supposed to be a stronger XBD than **3b**. Surprisingly, a significant improvement of rate was observed for the reaction with **3b** (10 mol %), which provided **5a** in up to 89% yield within 3 h, whereas only 36% yield was achieved with **3a** (SI, Figure S1). The reaction catalyzed by **3b** could complete within 5 h (entry 4). When the loading of **3b** (5 mol %) was reduced, the reaction time was prolonged to 6.5 h (entry 5). A

Table 1. Catalytic Transfer Hydrogenation of 4a[a]



entry	catalyst	loading (mol %)	time (h)	yield[b] (%)
1	none		24	10
2	PFIB	10	24	20
3	**3a**	10	9	99 (99)[c]
4	**3b**	10	5	99
5	**3b**	5	6.5	99
6	**3b**	1	16	75
7	**3f**	5	6.5	99
8	**3g**	5	6.5	83
9	**2a**	10	24	39
10	**2b**	10	24	12
11	**3h**	10	24	10
12	**3i**	10	24	32

[a]Unless otherwise indicated, all reactions were carried out with **4a** (0.05 mmol, 1.0 equiv) and Hantzsch esters (0.11 mmol, 2.2 equiv) at room temperature under N_2 atmosphere. [b]Determined by ^{1}H NMR analysis. [c]Isolated yield in parentheses. Hantzsch esters: diethyl 2,6-dimethyl-1,4-dihydro-pyridine-3,5-dicarboxylate.

moderate yield of 75% was still obtained with a low loading of **3b** (1 mol %) but in a longer time (entry 6). Moreover, two representative XBDs **3f** and **3g** containing C(sp^3)−I and C(sp^2)−I moieties, respectively, were utilized for this reaction (entries 7 and 8). These results indicate that **3b** is comparable to them in catalytic potency.

Moreover, controlled experiments were conducted by utilizing the analogues of **3a** and **3b** (Table 1, entries 9−12). It was found that their precursors **2a** and **2b** with an acidic C(sp^3)−H act as Brønsted acid catalysts[20] in this reaction, albeit with relatively lower efficiency than **3a** and **3b** (entries 9−10). In addition, replacement of the sulfinyl group by methylene (**3h** and **3i**) weakened the XB strength dramatically (entries 11−12), which indicates the crucial role of a strong electron-withdrawing sulfoxide moiety in our design. The acidity of C(sp^3)−H in **2a** is generally considered to be higher than that of **2b** because of the slightly more electron-withdrawing effect of the ester in **2a**. Unlike the trend discussed above, **3b** with amide groups showed higher activity than **3a** with esters, which led to a faster reaction. This outcome was initially interpreted by assuming that the extra amide N−H hydrogen bond donors in **3b** assist catalysis through the activation of substrate **4a**. Indeed, substrate activation by XB and HBs in a synergistic fashion has been reported in the works of Arai et al. and Kanger et al.[21] However, the fact of a low catalytic efficiency of **2b** with only amide N−H bonds (entry 10) ruled out the major contribution of HBs to substrate activation. The actual activation mode by **3b** still remains to be elucidated.

With **3b** in hand, the scope of transfer hydrogenation was then explored under the optimized conditions (Scheme 2). First, the R^1 group on 2-subsituted quinolines was investigated. All target products were obtained in excellent yields (**5b**−**5j**, ∼95% to 99%). Among them, product **5j** is a key intermediate in the synthesis of (±)-galipinine, which is a natural product with a variety of biological activities.[22] 3-Methylquinoline and

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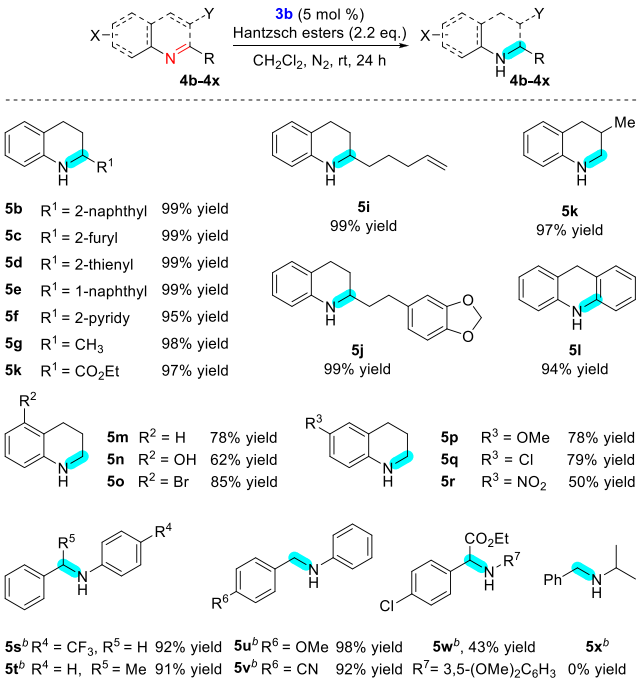
Scheme 2. Scope of Transfer Hydrogenation with 3b[a]

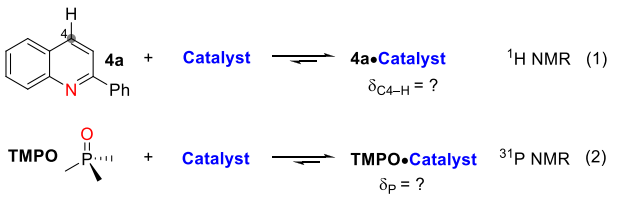


[a]Reactions at the 0.25 mmol scale for 24 h with isolated yield reported. [b]Reaction at the 0.1 mmol scale.

fused-ring acridines also gave excellent yields (**5k**−**5l**). We then investigated the functional group tolerance on the benzene ring of quinolines, and slightly lower yields were obtained (**5m**−**5r**). The reduction of quinoline **4m** without any substitutes still afforded **5m** with a good yield (78%). Quinolines substituted by hydroxyl and bromine at the 5-position gave 62% and 85% yield, respectively. Quinolines bearing a chlorine or methoxy group at the 6-position gave high yields (**5p**−**5q**, ∼78% to 85%). A satisfactory yield (**5r**, 50%) could be obtained even with a strong electron-withdrawing nitro substituent. The scope of imine was subsequently investigated. Diarylimines with different substitution patterns gave corresponding amines **5s**−**5v** in excellent yields, while no reaction occurred for the *N*-isopropyl imine **4x**.[23] In addition, the *α*-aryl amino ester **5w** was achieved in a moderated yield (43%).[24]

To gain more details of the underlying process, NMR spectroscopy, which is a powerful tool to investigate noncovalent interactions, was first employed (Table 2, eq 1 and 2).[25] However, $^{1}H(C_4-H)$ chemical shift changes in quinoline **4a** were found to be insignificant upon the addition of one equivalent of each of the catalysts (Table 2, column 3; SI, Figure S2). Despite the low sensitivity, the ^{1}H NMR analysis somewhat showed the XB between **3b** and substrate **4a** is observable [$\Delta\delta(^{1}H)$ = 0.08 ppm]. Furthermore, the association constants of **3a** and **3b** with **4a** were determined as 0.40 ± 0.006 and 0.44 ± 0.004 M^{-1}, respectively, by ^{1}H NMR titration experiments (SI, pages S36−S38). Conversely, the $^{31}P(R_3P{=}O)$ chemical shift changes have been used to measure the relative Lewis acidity[26] and recently quantify the halogen bonding ability.[27] Additionally, weak halogen bonding might be distinguished from hydrogen bonding by comparing the $\Delta\delta(^{31}P)$ values of trialkyl phosphine oxide,[28] which is a reliable probe to predict various noncovalent interactions in

Table 2. ^{1}H and ^{31}P NMR Studies



entry	catalyst	$\Delta\delta(^{1}H)$ (ppm)[a]	$\Delta\delta(^{31}P)$ (ppm)[b]
1	**3a**	0.03	1.01
2	**2a**	0.03	0.49
3	**3b**	0.08	12.12
4	**2b**	0.06	1.10

[a]Changes in chemical shift of **4a** and **TMPO** upon binding to catalyst: ^{1}H NMR analysis performed with 0.01 mmol of **4a** and 0.01 mmol of **catalyst** in 0.6 mL of $CDCl_3$ (eq 1). $\Delta\delta(^{1}H) = \delta_{C4-H}$ (**4a·Catalyst**) − δ_{C4-H} (free **4a**). [b]^{31}P NMR analysis performed with 0.005 mmol of **TMPO** and 0.025 mmol of **catalyst** (5 equiv) in 0.2 mL of CD_2Cl_2 and 0.4 mL of CH_2Cl_2 (eq 2). $\Delta\delta(^{31}P)$ = δ(**TMPO·Catalyst**) − δ(free **TMPO**).

solution. For the ^{31}P NMR analysis (Table 2, column 4; SI, Figure S3), we chose trimethyl phosphine oxide (**TMPO**) as the binding partner by adding excess catalyst molecules (5.0 equiv). Similar to the ^{1}H NMR analysis, **3b** showed the strongest binding interaction with **TMPO** on the basis of the much larger downfield ^{31}P NMR shift [$\Delta\delta(^{31}P)$ = 12.12 ppm; Figure 2a]. Moreover, intermolecular hydrogen bonding

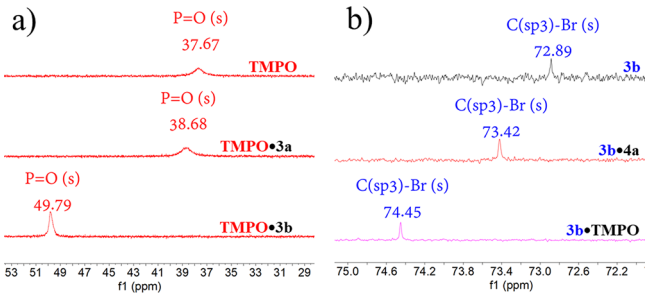


Figure 2. (a) ^{31}P NMR spectra of **TMPO**, **TMPO·3a**, and **TMPO·3b** in CD_2Cl_2. (b) ^{13}C NMR spectra of **3b**, **3b·4a**, and **3b·TMPO** in **$CDCl_3$**.

between **3b** and **TMPO** can be excluded on the basis of the ^{1}H NMR titration data (SI, Figure S13). Later, ^{13}C NMR studies of **3b** were performed, and downfield changes in the chemical shift of $^{13}C(sp^3)-Br$ upon the addition of **4a** (5.0 equiv) or **TMPO** (5.0 equiv) were detected (Figure 2b). The XB formations between **3b** and Lewis bases, such as quinoline **4a** and **TMPO**, were therefore confirmed.

To further probe the reaction mechanism, controlled experiments with radical scavengers, Lewis bases, and catalyst **3j** were performed (Scheme 3). In the presence of free radical 2,2,6,6-tetramethylpiperidinyl-1-oxy (**TEMPO**) which also acts as a XB acceptor,[29] a moderate yield of 48% was obtained. Meanwhile, the radical scavenger butylated hydroxytoluene (**BHT**) had negligible effect on the catalytic activity (83% yield). Accordingly, a radical pathway was excluded. With 3,5-lutidine, which is a stronger Lewis base than substrate **4a**, the reaction was significantly suppressed (6% yield), thereby supporting the role of **3b** on the catalytic cycle. In contrast, sterically hindered 2,6-di-*t*-butylpyridine was difficult to

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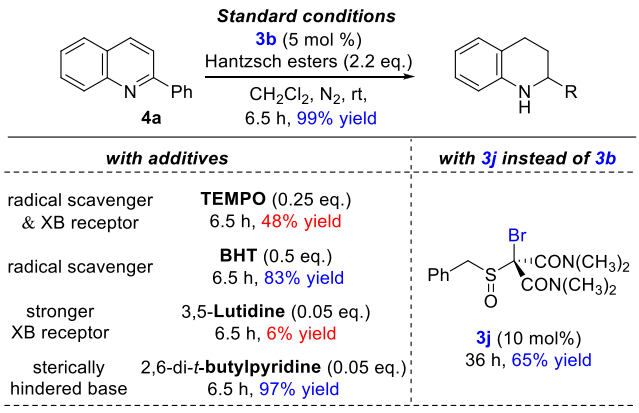
Scheme 3. Controlled Experiments



halogen bond to **3b** and had no influence on the catalytic activity of **3b** (97% yield). Additionally, the catalyst **3j** with amides N−Me and C(sp^3)−Br still promoted the reaction in a moderated yield (65%), thereby indicating the essential role of the C(sp^3)−Br site and the assisting role of N−H sites in **3b**. However, the cooperative mode of action of XB and HB sites in **3b** needs to be addressed.

Inspired by the aforementioned concept of a hydrogen-bond-enhanced halogen bond (HBeXB) for XBDs with C(sp^2)−I,[16a] we envisioned an intramolecular HBeXB may occur in XBD **3b**. With inspection of the ^{1}H NMR spectra of **2b** and **3b**, an apparent downfield shift of one of the amide protons on **3b** was observed (Figure 3a) in comparison with

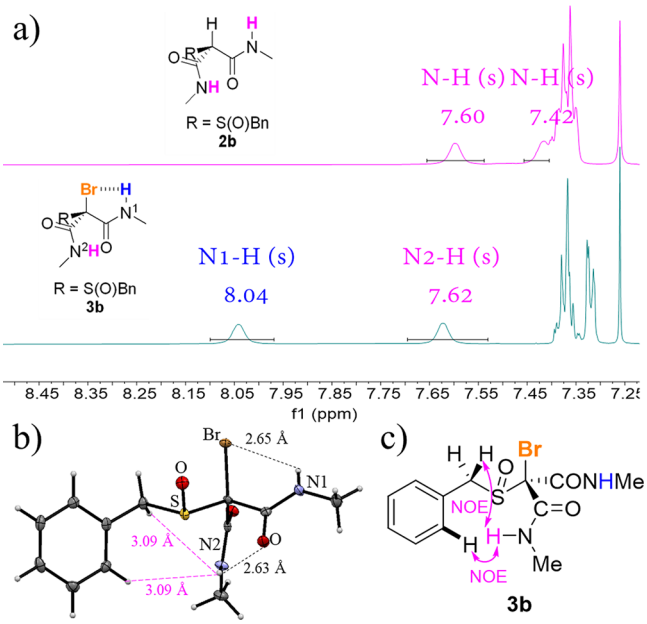


Figure 3. (a) ^{1}H NMR spectra of **2b** and **3b** in $CDCl_3$. (b) X-ray crystallographic structure of **3b** (CCDC 2213198, ellipsoids at 50% probability). (c) Key ^{1}H−^{1}H NOE correlations of **3b**.

2b, which suggested the occurrence of a HBeXB in **3b** in solution state. To our delight, it was further confirmed by X-ray analysis of **3b** (Figure 3b). The crystallographic analysis clearly revealed intramolecular C(sp^3)−Br···H−N(1) and extra C═O···H−N(2) hydrogen bonds with distances of 2.65 and 2.63 Å, respectively. The dihedral angle between the two planes of Br−C(sp^3)−C(O) and C(sp^3)−C(O)−N1 is 30.4°. It is worth mentioning that multiple intermolecular non-covalent interactions were also observed in the packing structures of **3b** (SI, Figure S27). In particular, an intermolecular bifurcated hydrogen bonding[16a] of N(1)−H to O═S in another molecule of **3b** was formed with distances of 2.14 Å. However, such an intermolecular HB was insignificant in solution because only negligible changes in chemical shifts of both N−Hs in **3b** were observed by either varying its concentration[30] or titrating it with HB acceptor **TMPO**[31] (SI, Figures S10 and S13). These results also indicated that the conformation of **3b** in solution state should be similar to the X-ray crystal structure of **3b** with two intramolecular HBs. Subsequently, NOESY analysis of **3b** confirmed that the conformer in solution is consistent with its crystal structure since only NOE signals between amide proton N(2)−H and the benzyl methylene proton C(sp^3)−H, as well as the *ortho*-proton of the phenyl ring C(sp^2)−H, were detected (3.09 and 3.09 Å, Figure 3c; see SI, Figures S11 and S12). Accordingly, two amide protons on **3b** could be readily distinguished, and their chemical shifts were assigned as 8.04 ppm [N(1)−H] and 7.62 ppm [N(2)−H], respectively. Overall, X-ray data and NMR studies indicated the formation of a new type of preorganized XBD through intramolecular HB.

Furthermore, the molecular electrostatic potential (MESP) in **3a** and **3b** was investigated by DFT calculations with the bromine atom pointing upward in Figure 4. The MESP maps

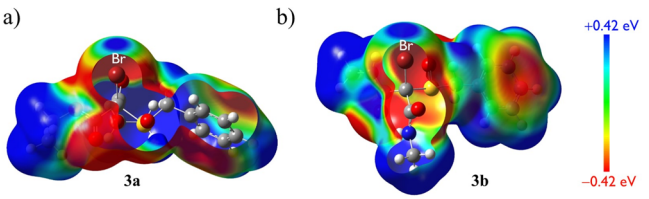


Figure 4. MESP maps for **3a** (a) and **3b** (b). All calculations were performed at B3LYP/def2-TZVPP using Gaussian 16.

and $V_{s,max}$ value of 13.78 kcal/mol at the bromine side confirmed the positive influence of two intramolecular HBs in **3b** on the σ-hole of **3b**. The data obtained by ^{1}H NMR monitoring also showed that **3b** makes the reaction process more efficient than **3a** (SI,Figures S24−S26). Taken together, our experimental, NMR, and computational studies demonstrate that a five-membered intramolecular HB ring with a nonplanar conformation was formed and consequently led to an extraordinary enhancement of XB strength in **3b**.

In conclusion, we present a new type of C(sp^3)−Br halogen bond donor. This neutral XBD bearing one sulfoxide and two amide moieties was fully characterized by NMR and X-ray analysis. A synergistic effect caused by hydrogen bonding directly to the XBD intramolecularly has been revealed both experimentally and computationally. For the first time, we elucidated the occurrence of HB-enhanced halogen bonding in a XBD base on C(sp^3)−Br. Moreover, the multifunctional sulfinyl group not only acts as an appropriate electron-deficient scaffold for XBDs but also provides an option for an asymmetric halogen bonding catalyst[2g,6a,32] with chirality at sulfur.[33] In our view, the strategy of a HBeXB might be extended to the hydrogen bond-enhanced tetrel bond (HBeTtB)[34] and chalcogen bond-enhanced halogen bond

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(CBeXB)[1f,35] in further studies. Efforts are ongoing to explore chiral halogen bonding catalysis[36] and design highly potent organocatalysts using nonclassical noncovalent cooperativity.[16c,37]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acscatal.3c01131.

General information, catalysts and substrates syntheses, optimization details, general experimental procedures, compound characterization and computational details (PDF)

Crystallographic data for catalyst **3b** (CIF)

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Molina, P.; Zapata, F.; Caballero, A. Anion Recognition Strategies Based on Combined Noncovalent Interactions. *Chem. Rev.* **2017**, *117*, 9907−9972. (b) Benz, S.; Poblador-Bahamonde, A. I.; Low-Ders, N.; Matile, S. Catalysis with Pnictogen, Chalcogen, and Halogen Bonds. *Angew. Chem., Int. Ed.* **2018**, *57*, 5408−5412. (c) Yuan, X.; Wang, Y. A Selenide Catalyst for the Activation of Alkenes through Se···π Bonding. *Angew. Chem., Int. Ed.* **2022**, *61*, e2f02203671. (d) Zhang, J.; Wei, J.; Ding, W. Y.; Li, S.; Xiang, S. H.; Tan, B. Asymmetric Pnictogen-Bonding Catalysis: Transfer Hydrogenation by a Chiral Antimony(V) Cation/Anion Pair. *J. Am. Chem. Soc.* **2021**, *143*, 6382−6387. (e) Zhang, Q.; Chan, Y. Y.; Zhang, M.; Yeung, Y. Y.; Ke, Z. Hypervalent Chalcogenonium···π Bonding Catalysis. *Angew. Chem., Int. Ed.* **2022**, *61*, e202208009. (f) Liu, J.; Zhou, M.; Deng, R.; Zheng, P.; Chi, Y. R. Chalcogen Bond-Guided Conformational Isomerization Enables Catalytic Dynamic Kinetic Resolution of Sulfoxides. *Nat. Commun.* **2022**, *13*, 4793. (g) Breugst, M.; Koenig, J. J. σ-Hole Interactions in Catalysis. *Eur. J. Org. Chem.* **2020**, *2020*, 5473−5487. (h) Gianneschi, N. C.; Bertin, P. A.; Nguyen, S. T.; Mirkin, C. A.; Zakharov, L. N.; Rheingold, A. L. A Supramolecular Approach to an Allosteric Catalyst. *J. Am. Chem. Soc.* **2003**, *125*, 10508−10509.

(2) (a) Bolm, C.; Bruckmann, A.; Pena, M. Organocatalysis through Halogen-Bond Activation. *Synlett* **2008**, *2008*, 900−902. (b) He, W.; Ge, Y. C.; Tan, C. H. Halogen-Bonding-Induced Hydrogen Transfer to C−N Bond with Hantzsch Ester. *Org. Lett.* **2014**, *16*, 3244−3247. (c) Robidas, R.; Reinhard, D. L.; Legault, C. Y.; Huber, S. M. Iodine(III)-Based Halogen Bond Donors: Properties and Applications. *Chem. Rec.* **2021**, *21*, 1912−1927. (d) Sutar, R. L.; Huber, S. M. Catalysis of Organic Reactions through Halogen Bonding. *ACS Catal.* **2019**, *9*, 9622−9639. (e) Kuwano, S.; Suzuki, T.; Yamanaka, M.; Tsutsumi, R.; Arai, T. Catalysis Based on C−I···π Halogen Bonds: Electrophilic Activation of 2-Alkenylindoles by Cationic Halogen-Bond Donors for [4 + 2] Cycloadditions. *Angew. Chem., Int. Ed.* **2019**, *58*, 10220−10224. (f) Kaasik, M.; Kanger, T. Supramolecular Halogen Bonds in Asymmetric Catalysis. *Front. Chem.* **2020**, *8*, 599064. (g) Kaasik, M.; Martonova, J.; Erkman, K.; Metsala, A.; Jarving, I.; Kanger, T. Enantioselective Michael Addition to Vinyl Phosphonates via Hydrogen Bond-Enhanced Halogen Bond Catalysis. *Chem. Sci.* **2021**, *12*, 7561−7568. (h) Puttreddy, R.; Jurcek, O.; Bhowmik, S.; Makela, T.; Rissanen, K. Very Strong $^{-}$N−X^{+}···$^{-}$O−N^{+} Halogen Bonds. *Chem. Commun.* **2016**, *52*, 2338−2341. (i) Guha, S.; Sekar, G. Metal-Free Halogen(I) Catalysts for the Oxidation of Aryl(heteroaryl) methanes to Ketones or Esters: Selectivity Control by Halogen Bonding. *Chem.—Eur. J.* **2018**, *24*, 14171−14182. (j) Zhang, Y.; Han, J.; Liu, Z.-J. Diaryliodonium Salts as Efficient Lewis Acid Catalysts for Direct Three Component Mannich Reactions. *RSC Adv.* **2015**, *5*, 25485−25488. (k) Yoshida, Y.; Ishikawa, S.; Mino, T.; Sakamoto, M. Bromonium Salts: Diaryl-λ^3-bromanes as Halogen-Bonding Organocatalysts. *Chem. Commun.* **2021**, *57*, 2519−2522. (l) Heinen, F.; Engelage, E.; Dreger, A.; Weiss, R.; Huber, S. M. Iodine(III) Derivatives as Halogen Bonding Organocatalysts. *Angew. Chem., Int. Ed.* **2018**, *57*, 3830−3833. (m) Yan, R.; Chen, K.; Li, Z.; Qu, Y.; Gao, L.; Tong, H.; Li, Y.; Li, J.; Hu, Y.; Guo, K. Fixation of CO_2 into Cyclic Carbonates by

Halogen-Bonding Catalysis. *ChemSusChem* **2021**, *14*, 738−744. (n) Yoshida, Y.; Mino, T.; Sakamoto, M. Chiral Hypervalent Bromine(III) (Bromonium Salt): Hydrogen- and Halogen-Bonding Bifunctional Asymmetric Catalysis by Diaryl-λ^3-bromanes. *ACS Catal.* **2021**, *11*, 13028−13033. (o) Yoshida, Y.; Fujimura, T.; Mino, T.; Sakamoto, M. Chiral Binaphthyl-Based Iodonium Salt (Hypervalent Iodine(III)) as Hydrogen- and Halogen-Bonding Bifunctional Catalyst: Insight into Abnormal Counteranion Effect and Asymmetric Synthesis of *N,S*-Acetals. *Adv. Synth. Catal.* **2022**, *364*, 1091−1098.

(3) Matsuzawa, A.; Takeuchi, S.; Sugita, K. Iodoalkyne-Based Catalyst-Mediated Activation of Thioamides through Halogen Bonding. *Chem.—Asian J.* **2016**, *11*, 2863−2866.

(4) Kniep, F.; Jungbauer, S. H.; Zhang, Q.; Walter, S. M.; Schindler, S.; Schnapperelle, I.; Herdtweck, E.; Huber, S. M. Organocatalysis by Neutral Multidentate Halogen-Bond Donors. *Angew. Chem., Int. Ed.* **2013**, *52*, 7028−7032.

(5) (a) Robinson, S. W.; Mustoe, C. L.; White, N. G.; Brown, A.; Thompson, A. L.; Kennepohl, P.; Beer, P. D. Evidence for Halogen Bond Covalency in Acyclic and Interlocked Halogen-Bonding Receptor Anion Recognition. *J. Am. Chem. Soc.* **2015**, *137*, 499−507. (b) Dreger, A.; Engelage, E.; Mallick, B.; Beer, P. D.; Huber, S. M. The Role of Charge in 1,2,3-Triazol(ium)-Based Halogen Bonding Activators. *Chem. Commun.* **2018**, *54*, 4013−4016.

(6) (a) Sutar, R. L.; Engelage, E.; Stoll, R.; Huber, S. M. Bidentate Chiral Bis(imidazolium)-Based Halogen-Bond Donors: Synthesis and Applications in Enantioselective Recognition and Catalysis. *Angew. Chem., Int. Ed.* **2020**, *59*, 6806−6810. (b) Jungbauer, S. H.; Huber, S. M. Cationic Multidentate Halogen-Bond Donors in Halide Abstraction Organocatalysis: Catalyst Optimization by Preorganization. *J. Am. Chem. Soc.* **2015**, *137*, 12110−12120. (c) Walter, S. M.; Kniep, F.; Herdtweck, E.; Huber, S. M. Halogen-Bond-Induced Activation of a Carbon−Heteroatom Bond. *Angew. Chem., Int. Ed.* **2011**, *50*, 7187−7191. (d) Takeda, Y.; Hisakuni, D.; Lin, C. H.; Minakata, S. 2-Halogenoimidazolium Salt Catalyzed Aza-Diels−Alder Reaction through Halogen-Bond Formation. *Org. Lett.* **2015**, *17*, 318−321.

(7) (a) Chan, Y.-C.; Yeung, Y.-Y. Halogen Bond Catalyzed Bromocarbocyclization. *Angew. Chem., Int. Ed.* **2018**, *57*, 3483−3487. (b) Kniep, F.; Walter, S. M.; Herdtweck, E.; Huber, S. M. 4,4'-Azobis(halopyridinium) Derivatives: Strong Multidentate Halogen-Bond Donors with a Redox-Active Core. *Chem.—Eur. J.* **2012**, *18*, 1306−1310. (c) Zhang, H.; Toy, P. H. Halogen Bond-Catalyzed Friedel-Crafts Reactions of Furans Using a 2,2'-Bipyridine-Based Catalyst. *Adv. Synth. Catal* **2021**, *363*, 215−221.

(8) (a) Haraguchi, R.; Hoshino, S.; Sakai, M.; Tanazawa, S. G.; Morita, Y.; Komatsu, T.; Fukuzawa, S. I. Bulky Iodotriazolium Tetrafluoroborates as Highly Active Halogen-Bonding-Donor Catalysts. *Chem. Commun.* **2018**, *54*, 10320−10323. (b) Kniep, F.; Rout, L.; Walter, S. M.; Bensch, H. K.; Jungbauer, S. H.; Herdtweck, E.; Huber, S. M. 5-Iodo-1,2,3-Triazolium-Based Multidentate Halogen-Bond Donors as Activating Reagents. *Chem. Commun.* **2012**, *48*, 9299−9301. (c) Peterson, A.; Kaasik, M.; Metsala, A.; Jarving, I.; Adamson, J.; Kanger, T. Tunable Chiral Triazole-Based Halogen Bond Donors: Assessment of Donor Strength in Solution with Nitrogen-Containing Acceptors. *RSC Adv.* **2019**, *9*, 11718−11721. (d) Kaasik, M.; Kaabel, S.; Kriis, K.; Jarving, I.; Aav, R.; Rissanen, K.; Kanger, T. Synthesis and Characterisation of Chiral Triazole-Based Halogen-Bond Donors: Halogen Bonds in the Solid State and in Solution. *Chem.—Eur. J.* **2017**, *23*, 7337−7344. (e) Kaasik, M.; Kaabel, S.; Kriis, K.; Järving, I.; Kanger, T. Synthesis of Chiral Triazole-Based Halogen Bond Donors. *Synthesis* **2019**, *51*, 2128−2135.

(9) (a) Ge, Y. C.; Yang, H.; Heusler, A.; Chua, Z.; Wong, M. W.; Tan, C. H. Halogen-Bonding-Induced Conjugate Addition of Thiophenes to Enones and Enals. *Chem.—Asian J.* **2019**, *14*, 2656−2661. (b) Liu, X.; Ma, S.; Toy, P. H. Halogen Bond-Catalyzed Friedel-Crafts Reactions of Aldehydes and Ketones Using a Bidentate Halogen Bond Donor Catalyst: Synthesis of Symmetrical Bis(indolyl) methanes. *Org. Lett.* **2019**, *21*, 9212−9216.

(10) Gliese, J. P.; Jungbauer, S. H.; Huber, S. M. A Halogen-Bonding-Catalyzed Michael Addition Reaction. *Chem. Commun.* **2017**, *53*, 12052−12055.

(11) (a) Liu, X.; Toy, P. H. Halogen Bond-Catalyzed Povarov Reactions. *Adv. Synth. Catal.* **2020**, *362*, 3437−3441. (b) Heinen, F.; Reinhard, D. L.; Engelage, E.; Huber, S. M. A Bidentate Iodine(III)-Based Halogen-Bond Donor as a Powerful Organocatalyst. *Angew. Chem., Int. Ed.* **2021**, *60*, 5069−5073. (c) Jungbauer, S. H.; Walter, S. M.; Schindler, S.; Rout, L.; Kniep, F.; Huber, S. M. Activation of a Carbonyl Compound by Halogen Bonding. *Chem. Commun.* **2014**, *50*, 6281−6284.

(12) (a) Xu, C.; Rao, V. U. B.; Weigen, J.; Loh, C. C. J. A Robust and Tunable Halogen Bond Organocatalyzed 2-Deoxyglycosylation Involving Quantum Tunneling. *Nat. Commun.* **2020**, *11*, 4911. (b) Xu, C.; Loh, C. C. J. A Multistage Halogen Bond Catalyzed Strain-Release Glycosylation Unravels New Hedgehog Signaling Inhibitors. *J. Am. Chem. Soc.* **2019**, *141*, 5381−5391.

(13) (a) Decato, D. A.; John, E. A.; Berryman, O. B. Halogen Bonding: An Introduction. *Halogen Bonding in Solution* **2021**, 1−41. (b) Nunzi, F.; Cesario, D.; Tarantelli, F.; Belpassi, L. Halogen Bond Interaction: Role of Hybridization and Induction. *Chem. Phys. Lett.* **2021**, *771*, 138522.

(14) Bruckmann, A.; Pena, M. A.; Bolm, C. Organocatalysis through Halogen-Bond Activation. *Synlett* **2008**, *2008*, 900−902.

(15) (a) Matsuzaki, K.; Uno, H.; Tokunaga, E.; Shibata, N. Fluorobissulfonylmethyl Iodides: An Efficient Scaffold for Halogen Bonding Catalysts with an sp^3-Hybridized Carbon−Iodine Moiety. *ACS Catal.* **2018**, *8*, 6601−6605. (b) Uno, H.; Matsuzaki, K.; Shiro, M.; Shibata, N. Design and Synthesis of a Chiral Halogen-Bond Donor with a Sp^3-Hybridized Carbon-Iodine Moiety in a Chiral Fluorobissulfonyl Scaffold. *Molecules* **2020**, *25*, 4539.

(16) (a) Decato, D. A.; Riel, A. M. S.; May, J. H.; Bryantsev, V. S.; Berryman, O. B. Theoretical, Solid-State, and Solution Quantification of the Hydrogen Bond-Enhanced Halogen Bond. *Angew. Chem., Int. Ed.* **2021**, *60*, 3685−3692. (b) Riel, A. M. S.; Decato, D. A.; Sun, J.; Berryman, O. B. Halogen Bonding Organocatalysis Enhanced through Intramolecular Hydrogen Bonds. *Chem. Commun.* **2022**, *58*, 1378−1381. (c) Riel, A. M. S.; Rowe, R. K.; Ho, E. N.; Carlsson, A. C.; Rappé, A. K.; Berryman, O. B.; Ho, P. S. Hydrogen Bond Enhanced Halogen Bonds: A Synergistic Interaction in Chemistry and Biochemistry. *Acc. Chem. Res.* **2019**, *52*, 2870−2880. (d) Riel, A. M. S.; Decato, D. A.; Sun, J.; Massena, C. J.; Jessop, M. J.; Berryman, O. B. The Intramolecular Hydrogen Bonded-Halogen Bond: A New Strategy for Preorganization and Enhanced Binding. *Chem. Sci.* **2018**, *9*, 5828−5836. (e) Decato, D. A.; Sun, J.; Boller, M. R.; Berryman, O. B. Pushing the Limits of the Hydrogen Bond Enhanced Halogen Bond-the Case of the C−H Hydrogen Bond. *Chem. Sci.* **2022**, *13*, 11156−11162. (f) Zhu, Y.-Y.; Yi, H.-P.; Li, C.; Jiang, X.-K.; Li, Z.-T. The N−H···X (X = Cl, Br, and I) Hydrogen-Bonding Pattern in Aromatic Amides: A Crystallographic and ^{1}H NMR Study. *Cryst. Growth Des.* **2008**, *8*, 1294−1300.

(17) (a) Gao, X.; Chang, R.; Rao, J.; Hao, D.; Zhang, Z.; Zhou, C.-Y.; Guo, Z. Halogen-Bonding-Promoted C−H Malonylation of Indoles under Visible-Light Irradiation. *J. Org. Chem.* **2022**, *87*, 8198−8202. (b) Zhang, X.; Ren, J.; Tan, S. M.; Tan, D.; Lee, R.; Tan, C.-H. An Enantioconvergent Halogenophilic Nucleophilic Substitution (S_N2X) Reaction. *Science* **2019**, *363*, 400−404. (c) Kazi, I.; Guha, S.; Sekar, G. CBr_4 as a Halogen Bond Donor Catalyst for the Selective Activation of Benzaldehydes to Synthesize α,β-Unsaturated Ketones. *Org. Lett.* **2017**, *19*, 1244−1247.

(18) Zong, L.; Wang, C.; Moeljadi, A. M.; Ye, X.; Ganguly, R.; Li, Y.; Hirao, H.; Tan, C. H. Bisguanidinium Dinuclear Oxodiperoxomolybdosulfate Ion Pair-Catalyzed Enantioselective Sulfoxidation. *Nat. Commun.* **2016**, *7*, 13455.

(19) Feldman, K. S. Modern Pummerer-Type Reactions. *Tetrahedron* **2006**, *62*, 5003−5034.

(20) (a) Rueping, M.; Koenigs, R. M. Brønsted Acid Differentiated Metal Catalysis by Kinetic Discrimination. *Chem. Commun.* **2011**, *47*, 304−306. (b) Rueping, M.; Antonchick, A. P.; Theissmann, T. A

https://doi.org/10.1021/acscatal.3c01131
ACS Catal. 2023, 13, 7103−7109

Highly Enantioselective Brønsted Acid Catalyzed Cascade Reaction: Organocatalytic Transfer Hydrogenation of Quinolines and Their Application in the Synthesis of Alkaloids. *Angew. Chem., Int. Ed.* **2006**, *45*, 3683−3686. (c) Rueping, M.; Theissmann, T.; Antonchick, A. P. Metal-Free Brønsted Acid Catalyzed Transfer Hydrogenation - New Organocatalytic Reduction of Quinolines. *Synlett* **2006**, *2006*, 1071−1074. (d) Simón, L.; Goodman, J. M. Theoretical Study of the Mechanism of Hantzsch Ester Hydrogenation of Imines Catalyzed by Chiral BINOL-Phosphoric Acids. *J. Am. Chem. Soc.* **2008**, *130*, 8741−8747. (e) Pastor, J.; Rezabal, E.; Voituriez, A.; Betzer, J.-F.; Marinetti, A.; Frison, G. Revised Theoretical Model on Enantiocontrol in Phosphoric Acid Catalyzed *H*-Transfer Hydrogenation of Quinoline. *J. Org. Chem.* **2018**, *83*, 2779−2787.

(21) (a) Kriis, K.; Martõnov, H.; Miller, A.; Erkman, K.; Järving, I.; Kaasik, M.; Kanger, T. Multifunctional Catalysts in the Asymmetric Mannich Reaction of Malononitrile with N-Phosphinoylimines: Coactivation by Halogen Bonding versus Hydrogen Bonding. *J. Org. Chem.* **2022**, *87*, 7422−7435. (b) Kuwano, S.; Suzuki, T.; Hosaka, Y.; Arai, T. A Chiral Organic Base Catalyst with Halogen-Bonding-Donor Functionality: Asymmetric Mannich Reactions of Malononitrile with *N*-Boc Aldimines and Ketimines. *Chem. Commun.* **2018**, *54*, 3847−3850.

(22) (a) Houghton, P. J.; Woldemariam, T. Z.; Watanabe, Y.; Yates, M. Activity Against Mycobacterium tuberculosis of Alkaloid Constituents of Angostura Bark, Galipea officinalis. *Planta Med.* **1999**, *65*, 250−254. (b) Jacquemond-Collet, I.; Benoit-Vical, F.; Valentin, M.; Stanislas, A.; Mallié, E.; Fourasté, I. Antiplasmodial and Cytotoxic Activity of Galipinine and other Tetrahydroquinolines from Galipea officinalis. *Planta Med.* **2002**, *68*, 68−69.

(23) Wakchaure, V. N.; Kaib, P. S. J.; Leutzsch, M.; List, B. Disulfonimide-Catalyzed Asymmetric Reduction of N-Alkyl Imines. *Angew. Chem., Int. Ed.* **2015**, *54*, 11852−11856.

(24) Kaptein, S. J. F.; Goethals, O.; Kiemel, D.; Marchand, A.; Kesteleyn, B.; Bonfanti, J.-F.; Bardiot, D.; Stoops, B.; Jonckers, T. H. M.; Dallmeier, K.; et al. A Pan-Serotype Dengue Virus Inhibitor Targeting the NS3−NS4B Interaction. *Nature* **2021**, *598*, 504−509.

(25) von der Heiden, D.; Vanderkooy, A.; Erdélyi, M. Halogen Bonding in Solution: NMR Spectroscopic Approaches. *Coord. Chem. Rev.* **2020**, *407*, 213147.

(26) (a) Mayer, U.; Gutmann, V.; Gerger, W. The Acceptor Number - A Quantitative Empirical Parameter for the Electrophilic Properties of Solvents. *Monatsh. Chem.* **1975**, *106*, 1235−1257. (b) Beckett, M. A.; Strickland, G. C.; Holland, J. R.; Sukumar Varma, K. A Convenient N.M.R. Method for the Measurement of Lewis Acidity at Boron Centres: Correlation of Reaction Rates of Lewis Acid Initiated Epoxide Polymerizations with Lewis Acidity. *Polymer* **1996**, *37*, 4629−4631.

(27) (a) Nödling, A. R.; Jakab, G.; Schreiner, P. R.; Hilt, G. ^{31}P NMR Spectroscopically Quantified Hydrogen-Bonding Strength of Thioureas and Their Catalytic Activity in Diels-Alder Reactions. *Eur. J. Org. Chem.* **2014**, *2014*, 6394−6398. (b) Zhao, X. R.; Wang, H.; Jin, W. J. The Competition of C−X···O═P Halogen Bond and π-hole···O═P Bond between Halopentafluorobenzenes C_6F_5X (X═F, Cl, Br, I) and Triethylphosphine Oxide. *J. Mol. Model.* **2013**, *19*, 5007−5014. (c) Zhao, X. R.; Shen, Q. J.; Jin, W. J. Acceptor Number of Halogenated Solvents and Its Potential as a Criterion for the Ability of Halogen Bonding as a Specific Solvent Effect using the ^{31}P NMR Chemical Shift of Triethylphosphine Oxide as a Probe. *Chem. Phys. Lett.* **2013**, *566*, 60−66. (d) Estager, J.; Oliferenko, A. A.; Seddon, K. R.; Swadźba-Kwaśny, M. Chlorometallate(iii) Ionic Liquids as Lewis Acidic Catalysts − a Quantitative Study of Acceptor Properties. *Dalton Trans.* **2010**, *39*, 11375−11382. (e) Chang, Y. P.; Tang, T.; Jagannathan, J. R.; Hirbawi, N.; Sun, S.; Brown, J.; Franz, A. K. NMR Quantification of Halogen-Bonding Ability To Evaluate Catalyst Activity. *Org. Lett.* **2020**, *22*, 6647−6652. (f) Diemoz, K. M.; Franz, A. K. NMR Quantification of Hydrogen-Bond-Activating Effects for Organocatalysts including Boronic Acids. *J. Org. Chem.* **2019**, *84*, 1126−1138. (g) Erdmann, P.; Greb, L. What Distinguishes the Strength and the Effect of a Lewis Acid: Analysis of the Gutmann-Beckett Method. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202114550.

(28) Chang, Y.-P.; Tang, T.; Jagannathan, J. R.; Hirbawi, N.; Sun, S.; Brown, J.; Franz, A. K. NMR Quantification of Halogen-Bonding Ability To Evaluate Catalyst Activity. *Org. Lett.* **2020**, *22*, 6647−6652.

(29) Mugnaini, V.; Punta, C.; Liantonio, R.; Metrangolo, P.; Recupero, F.; Resnati, G.; Pedulli, G. F.; Lucarini, M. Noncovalent Paramagnetic Complexes: Detection of Halogen Bonding in Solution by ESR Spectroscopy. *Tetrahedron Lett.* **2006**, *47*, 3265−3269.

(30) Froimowicz, P.; Zhang, K.; Ishida, H. Intramolecular Hydrogen Bonding in Benzoxazines: When Structural Design Becomes Functional. *Chem.—Eur. J.* **2016**, *22*, 2691−2707.

(31) Yan, X.; Zou, K.; Cao, J.; Li, X.; Zhao, Z.; Li, Z.; Wu, A.; Liang, W.; Mo, Y.; Jiang, Y. Single-Handed Supramolecular Double Helix of Homochiral Bis(N-amidothiourea) Supported by Double Crossed C-I···S Halogen Bonds. *Nat. Commun.* **2019**, *10*, 3610.

(32) (a) Zong, L.; Ban, X.; Kee, C. W.; Tan, C. H. Catalytic Enantioselective Alkylation of Sulfenate Anions to Chiral Heterocyclic Sulfoxides using Halogenated Pentanidium Salts. *Angew. Chem., Int. Ed.* **2014**, *53*, 11849−11853. (b) Kuwano, S.; Suzuki, T.; Hosaka, Y.; Arai, T. A Chiral Organic Base Catalyst with Halogen-Bonding-Donor Functionality: Asymmetric Mannich Reactions of Malononitrile with *N*-Boc Aldimines and Ketimines. *Chem. Commun.* **2018**, *54*, 3847−3850. (c) Squitieri, R. A.; Fitzpatrick, K. P.; Jaworski, A. A.; Scheidt, K. A. Synthesis and Evaluation of Azolium-Based Halogen-Bond Donors. *Chem.—Eur. J.* **2019**, *25*, 10069−10073. (d) Ostler, F.; Piekarski, D. G.; Danelzik, T.; Taylor, M. S.; García Mancheño, O. Neutral Chiral Tetrakis-Iodo-Triazole Halogen-Bond Donor for Chiral Recognition and Enantioselective Catalysis. *Chem.—Eur. J.* **2021**, *27*, 2315−2320.

(33) (a) Trost, B. M.; Rao, M. Development of Chiral Sulfoxide Ligands for Asymmetric Catalysis. *Angew. Chem., Int. Ed.* **2015**, *54*, 5026−5043. (b) Otocka, S.; Kwiatkowska, M.; Madalinska, L.; Kielbasinski, P. Chiral Organosulfur Ligands/Catalysts with a Stereogenic Sulfur Atom: Applications in Asymmetric Synthesis. *Chem. Rev.* **2017**, *117*, 4147−4181. (c) Wojaczyńska, E.; Wojaczyński, J. Modern Stereoselective Synthesis of Chiral Sulfinyl Compounds. *Chem. Rev.* **2020**, *120*, 4578−4611. (d) Su, X.; Zhou, W.; Li, Y.; Zhang, J. Design, Synthesis, and Application of a Chiral Sulfinamide Phosphine Catalyst for the Enantioselective Intramolecular Rauhut−Currier Reaction. *Angew. Chem., Int. Ed.* **2015**, *54*, 6874−6877. (e) Jia, T.; Wang, M.; Liao, J. Chiral Sulfoxide Ligands in Asymmetric Catalysis. In *Sulfur Chemistry*; Jiang, X., Ed.; Springer International Publishing, 2019; pp 399−427.

(34) Trujillo, C.; Alkorta, I.; Elguero, J.; Sánchez-Sanz, G. Cooperative Effects in Weak Interactions: Enhancement of Tetrel Bonds by Intramolecular Hydrogen Bonds. *Molecules* **2019**, *24*, 308.

(35) Wang, W.; Zhu, H.; Feng, L.; Yu, Q.; Hao, J.; Zhu, R.; Wang, Y. Dual Chalcogen-Chalcogen Bonding Catalysis. *J. Am. Chem. Soc.* **2020**, *142*, 3117−3124.

(36) Currently, **3a** with 80% *ee* and **3b** with 30% *ee* were obtained through asymmetric oxidation. With them, no enantioselectivity was observed in the transfer hydrogenation of substrate **4a**. Approaches to enantiopure catalysts and further design are in progress.

(37) (a) Alkorta, I.; Elguero, J.; Frontera, A. Not Only Hydrogen Bonds: Other Noncovalent Interactions. *Crystals* **2020**, *10*, 180. (b) Czarny, R. S.; Ho, A. N.; Shing Ho, P. A Biological Take on Halogen Bonding and Other Non-Classical Non-Covalent Interactions. *Chem. Rec.* **2021**, *21*, 1240−1251. (c) Jin, M. Y.; Zhen, Q.; Xiao, D.; Tao, G.; Xing, X.; Yu, P.; Xu, C. Engineered Non-Covalent π Interactions as Key Elements for Chiral Recognition. *Nat. Commun.* **2022**, *13*, 3276. (d) Tu, D.; Yan, H.; Poater, J.; Solà, M. The nido-Cage···π Bond: A Non-covalent Interaction between Boron Clusters and Aromatic Rings and Its Applications. *Angew. Chem., Int. Ed.* **2020**, *59*, 9018−9025. (e) Loh, C. C. J. Exploiting Non-Covalent Interactions in Selective Carbohydrate Synthesis. *Nat. Rev. Chem.* **2021**, *5*, 792−815.

https://doi.org/10.1021/acscatal.3c01131
ACS Catal. 2023, 13, 7103−7109