1. INTRODUCTION

Noncovalent interactions often facilitate chemical reactions through activating functional groups or stabilizing intermediates in many organic reactions. Many experimental and theoretical studies have been devoted to exploring the role of noncovalent interactions in organocatalysis, where small molecules are designed as catalysts or activators.1–5 Organocatalysis based on noncovalent interactions becomes a useful catalytic strategy because it is cheap, stable, environmentally friendly compared to metal-based catalysis.

Halogen bond, denoted as R−X···Y (R = substituent group, X = halogen atom, Y = nucleophilic group), is a kind of intermolecular interaction formed between an electrophilic region associated with a halogen atom in a molecular entity and a nucleophilic region in another one. Among various noncovalent interactions, XB has high directionality and broad tunability.6–8 The high directionality is a consequence of the σ-hole on the halogen atom X. The broad tunability arises from the fact that the binding strength would be greatly altered by surrounding environments, substituent groups, and so on.6,7,9–13 Considering these features, XB is useful in organocatalysis. The first XB-based organocatalysis was reported by Bolm et al. in 2008. They employed haloperfluoroalkanes as catalysts for the reduction of 2-phenylquinoline with Hantzsch ester.14 Since then, many works have been concentrated on the employments of XB in various chemical reactions.15–48

According to the literature,43–48 the formation of carboxation via the X abstraction process is a decisive step for the Ritter-type solvolysis reactions. Huber et al. reported that the XB donors can be successfully applied in the Br abstraction process, leading to the acceleration for the Ritter-type solvolysis of benzhydryl bromide (Scheme 1).15 In detail, they found that the background solvolysis is negligible after a reaction time of four days. The addition of cationic iodoimidazolium compounds leads to large product yields (from ~50 to ~80%). However, the addition of the cationic bis(imidazolium) compounds is unable to accelerate the reaction obviously.

The experimental findings highlight the importance of I atoms in the activators. Huber et al. stated in their review that “the poor performance of the noniodinated compounds seems surprising, since they may act as reasonably strong hydrogen bond donors”.49 Test calculations also indicate that the total binding reference is not the reason for the activation difference because the interaction energies in the XB donor–substrate and the HB donor–substrate are similar. We should pay attention to other noncovalent interactions in the reaction. Considering the functional groups (aromatic rings, C−H groups, and so on), we noticed that in the activator–substrate dimer, besides HB or XB, there exist lone pair···π, π···π stacking, C−H···π, and so on. From C13H11Br to C13H11···Br, these interactions will vary due to the charge redistribution. To understand the origin of the activation, these interaction variations should be clearly clarified.
The present work attempts to explore the role of noncovalent interactions in the Br abstraction of the Ritter reaction. Six activators, including cationic meta- and para-bidentate iodine donors (denoted as $\text{mdI}$ and $\text{pdI}$ in this paper; here, $\text{m}$ denotes meta; $\text{p}$ denotes para, $\text{d}$ denotes double; and $\text{I}$ denotes iodine atom, the same as below), cationic meta- and para-bidentate hydrogen donors (denoted as $\text{mdH}$ and $\text{pdH}$, here $\text{H}$ denotes hydrogen atom, the same as below), and cationic meta- and para−mono-dentate iodine donors (denoted as $\text{mHI}$ and $\text{pHI}$), are chosen in our paper (Figure 1). To confirm the existence of noncovalent interactions, the quantum theory of atoms in molecules (QTAIM) was used.50 The solvent effects, which are very important for the Ritter-type solvolysis reaction, are considered by conductorlike polarizable continuum model (CPCM).51,52 The energy decomposition analysis (EDA) method is a quantitative analysis tool for intermolecular interactions. The generalized Kohn−Sham energy decomposition analysis (GKS-EDA) method presented by our group,53,54 which is able to take the solvent effects into account for intermolecular interactions, was used to explore the origin of the noncovalent interactions in the Ritter-type solvolysis reaction.

2. METHODOLOGY AND COMPUTATIONAL DETAILS

With the CPCM calculations for the reaction system, the total solvation free energy of the substrate−activator adduct (the reactant state for the Br abstraction process) is expressed as

$$
\Delta G_{r}^{\text{TOT}} = \Delta G_{r}^{\text{TOT}} - \Delta G_{r}^{\text{BG}}
$$

Here, the superscript $\text{AB}$ denotes the substrate; $\text{A}$ and $\text{B}$ are the fragments of the substrate, while $\text{C}$ is the activator. $\Delta G_{r}^{\text{TOT}}$ is the total dimer interaction energy between $\text{AB}$ and $\text{C}$.

The total solvation free energy of the product is written as

$$
\Delta G_{p}^{\text{TOT}} = \Delta G_{p}^{\text{TOT}} - \Delta G_{p}^{\text{BG}}
$$

Thus, the reaction free energy in solution, $\Delta G_{rp}$, can be expressed as

$$
\Delta G_{rp} = \Delta G_{r}^{\text{TOT}} - \Delta G_{p}^{\text{TOT}}
$$

where $\Delta G_{BG}$ is the geometrical relaxation of $\text{AB}−\text{C}$ ($\Delta G_{r}^{\text{TOT}} - \Delta G_{p}^{\text{TOT}}$) denotes the variation of the total interaction free energy.
from reaction state to product state. Similarly, the reaction barrier can be expressed as the geometrical relaxation and the variation of the interaction free energy.

Combined with implicit solvation model, GKS-EDA decomposes the total interaction energy into the following terms

$$
\Delta G_{\text{TOT}} = \Delta G_{\text{ele}} + \Delta G_{\text{exrep}} + \Delta G_{\text{pol}} + \Delta G_{\text{corr}} + \Delta G_{\text{disp}} + \Delta G_{\text{desol}}
$$

In eq 4, \( \Delta G_{\text{ele}} \) is the electrostatic interaction term, which is quasiclassical Coulombic interaction between monomers. This term is computed using frozen electron density distribution of monomers in the supermolecular geometry. \( \Delta G_{\text{exrep}} \) is the exchange-repulsion term, arising from the normalization and antisymmetrization of the wave function. \( \Delta G_{\text{pol}} \) is the polarization term, denoting the orbital relaxation energy caused by the variation of the Kohn–Sham orbitals in a SCF process. \( \Delta G_{\text{corr}} \) is the correlation term defined by the generalized Kohn–Sham theory. This term depends on the density functional theory (DFT) functionals and orbitals simultaneously. \( \Delta G_{\text{disp}} \) is the dispersion term when a dispersion-corrected DFT functional is applied. \( \Delta G_{\text{desol}} \) is the desolvation term, which is the free energy penalty by solvent environments. To consider the cavity superposition error for the implicit solvation model, the cavities of monomers and complex are constructed based on the interaction distance of monomers. Thus, \( \Delta G_{\text{desol}} \) is not equal to the difference of solvation free energy between the complex and the sum of monomers.

The geometrical optimizations, the change from electrostatic potentials (ChelpG)\(^{55-57} \) and intrinsic reaction coordinate (IRC) calculations were conducted by Gaussian 16 package.\(^{58} \) All minima were characterized by vibrational frequency analysis, and the transition states were confirmed to have one single imaginary frequency corresponding to the cleavage of the expected bonds. GKS-EDA calculations were performed with a modified version of GAMESS package.\(^{59} \) AIM analysis was carried out by Multiwfn program.\(^{50,60} \) All DFT calculations were executed with the M06-2X functional. The aug-cc-pVDZ-pp basis set was used for Br and I, while cc-pVDZ was used for the rest atoms. For the CPCM calculations, the dielectric constant was set as 37.5 to model the solvent of acetonitrile, and the UFF radii model scaled by a factor of 1.1 was employed.\(^ {59} \)

3. RESULTS AND DISCUSSIONS

3.1. Activation of the Br Abstraction. The six dimeric benzyhydryl bromide–activator adducts, which are denoted as A–X (X = mdI, pdI, mdH, pdH, mHI, and pHI, here A denotes adduct), are displayed in Figure 2. Among them, A-mdI/A-pdI and A-mHI/A-pHI are the XB adducts, A-mdH is the HB adduct, while A-pdH is the adduct formed between Br and the central benzene ring. Figure 2 collects the important geometrical parameters, ChelpG charges, and total dimer interaction free energies in A–X. The C–Br bond length ranges from 2.000 to 2.044 Å, slightly larger than that in benzyhydryl bromide. The ChelpG charges of Br and C_{13}H_{11} indicate that the polarity of the C–Br bond is somewhat changed to a certain degree when C_{13}H_{11}Br interacts with the activators. For example, the charge on Br is 0.020 in A-mdI, while that in benzhydryl bromide is −0.218. As for the total dimer interaction free energies, it is shown that those of bidentate adducts (A-mdI, A-pdI, and A-mdH) are strong, while the rest are weak. Among them, A-mdI is the largest, while A-pHI is the smallest.

![Figure 2](https://dx.doi.org/10.1021/acsomega.0c03000)
The transit states for all of the XB complexes, denoted as $T-X$ ($X = \text{mdI}, \text{pdI}, \text{mHI}, \text{and pHI}$, here $T$ denotes transit state), are obtained. The IRC calculations confirm that these transit states undergo the reaction paths of the $C-Br$ breaking. The $T-X$ geometries shown in Figure S1 of the Supporting Information indicate the elongation of the $C-Br$ bond. However, no transit states for the $C-Br$ bond breaking are found for the complexes of bidentate hydrogen donors. It is shown that the large total dimer interaction energies do not always lead to successful activation. With the IRC calculations, the product complexes are obtained, which are denoted as $P-X$ ($X = \text{mdI}, \text{pdI}, \text{mHI}, \text{and pHI}$, here $P$ denotes product) and shown in Figure 3. In the product complexes, the benzhydryl groups are quasiplanar, the $I-Br$ distances are shortened, and the $C-Br$ bonds are lengthened compared to that of the adducts. Their geometries are much close to those of $T-X$ shown in Figure S1. Furthermore, the $I-Br$ distances in $P-X$ are almost the same as those in the activator···Br$^-$ complexes shown in Figure S2. All of the numerical results verify that these $P-X$ complexes belong to the ion-pair complexes, in which $C_{13}H_{11}Br$ has been activated as $C_{13}H_{11}^+···Br^-$. As can be seen from Figure 3, the total dimer interaction energies in the ion-pair complexes, from $-14.25$ to $-30.81$ kcal/mol, are greatly larger than those of the corresponding adducts.

The potential energy profiles of the $C-Br$ bond activation (the energy unit is in kcal/mol, the data in brackets are corrected by zero point energy corrections): (a) $A-\text{mdI} \rightarrow P-\text{mdI}$; (b) $A-\text{pdI} \rightarrow P-\text{pdI}$; (c) $A-\text{mHI} \rightarrow P-\text{mHI}$; and (d) $A-\text{pHI} \rightarrow P-\text{pHI}$.

The transit states are very close to the ion-pair complexes. The small $\Delta G_{rp}$ means the small barrier $\Delta G^\neq$. In the
Figure 5. GKS-EDA results for the total dimer interactions in the IRC pathways of (a) A-mdI → P-mdI and (b) A-mHI → P-mHI.

Figure 6. BCPs in the adducts: (a) A-mdI; (b) A-pdI; (c) A-mHI; (d) A-pHI; (e) A-mdH; and (f) A-pdH. The BCPs are indicated with red dots, with the corresponding bond path shown in gray.
profiles of mHI and phi, because of their smaller ΔG^TOT, the barriers are larger than those of mdl and pdl, in agreement with the experimental finding that the yields of mHI and phi (~50%) are smaller than those of mdl and pdl (~80%). The more stable the ion-pair complex is, the lower the barrier of the Br abstraction process has. The variation of the total free interaction energy in the process can be decomposed into the contributions of each interaction terms. Figure 5 demonstrates the curves of the GKS-EDA results for the total dimer interactions in the IRC pathways of mdl and mHI. It is found that the electrostatic, polarization, and correlation terms favor the total dimer interaction, while the rest terms do not. From A−X to P−X, the correlation term is not sensitive to the variation of the C−Br bond length. Electrostatic becomes more and more important, reaching to the most negative value when the substrate becomes C_{13}H_{11}⋯Br−.

### 3.2. Noncovalent Interactions in the XB Complexes.

Dividing the variation of the total dimer free interaction energy into the contributions of the noncovalent interactions can be helpful for us to understand the activation. The BCPs from the AIM analysis in Figure 6 illustrate various noncovalent interactions in the XB adducts. Besides the bidentate XBs, there are the lone pair⋯π interactions between the iodoimidazolium and the benzhydryl group, and the C−H⋯π interactions between C−H and aromatic rings. Table 1 collects the AIM results in A−X, including electron density ρ, Laplacian electron density ∇^2ρ, and the IV/G value in each BCP. The values of ρ, ∇^2ρ, and IV/G follow the order: XB > lone pair⋯π > C−H⋯π. It is noticed that in A−mdl and A−pdl, there are three BCPs for the lone pair⋯π interactions. The isosurface plots in Figure 7a−c demonstrate the molecular orbitals describing the I−Br XB and the lone pair⋯π interactions in A−X.

The BCPs in Figure 8 display all of the noncovalent interactions in the four ion-pair complexes. Besides the monodentate and bidentate I−Br−XB, there are the lone pair⋯π interactions and C−H⋯π interactions (π denotes the aromatic ring with the partial positive charge in the benzhydryl cation). From the AIM results shown in Table 2, the values of ρ, ∇^2ρ, IV/G for the lone pair⋯π and C−H⋯π interactions in the ion-pair complexes are similar to those in the XB adducts, while the IV/G values of the I−Br−XB are larger than the I−Br ones, suggesting the larger covalency of I−Br−XB. The orbitals are displayed in Figure 7d−f.

Given the variation in the charge distributions in C_{13}H_{11}−Br, it is impossible to compute these noncovalent interactions exactly in the activation process. Fortunately, we just need to know the difference in the noncovalent interaction energies between A−X and P−X. For P−X, the three noncovalent interactions can be easily computed because the C−Br bond is broken. In detail, the I−Br−XB can be computed as the activator−Br−interaction; lone pair⋯π can be modeled as the interaction between the iodoimidazolium cation (C_{2}H_{4}N_{2}I_{2}^+) and the C_{13}H_{11}−, while C−H⋯π interaction can be obtained from the interaction energy difference between (C_{2}H_{4}N_{2}I_{2}^+)⋯C_{13}H_{11}− and activator−C_{13}H_{11}−. The activator−Br− and (C_{2}H_{4}N_{2}I_{2}^+)⋯C_{13}H_{11}− are constructed from the geometries of the ion-pair complexes. Therefore, the total dimer interactions in P−X can be divided into the three contributions. For A−X, considering the partial polarity of the C−Br bond, the estimation of the noncovalent interactions requires the rational design of model molecules. To model the I−Br XB bond, Br is capped with a CH_{3} group, while the C_{13}H_{11} group is capped with the H atom

| Table 1. AIM Analysis Results and Total Interaction Energies of the Noncovalent Interactions in the Adducts (lone pair⋯π is abbreviated as lp⋯π) |
|---------------------------------------------------------------|
| types | ρ | ∇^2ρ | IV/G | ΔG^TOT/(kcal/mol) |
| C−H⋯π(a) | 0.0064 | 0.0183 | 0.8024 | ΔG^TOT(C−H⋯π) = −2.98 |
| C−H⋯π(b) | 0.0021 | 0.0074 | 0.6167 |
| C−H⋯π(c) | 0.0034 | 0.0104 | 0.7537 |
| XB(d) | 0.0097 | 0.0260 | 0.8236 | ΔG^TOT(XB) = −7.23 |
| XB(e) | 0.0120 | 0.0326 | 0.8474 |
| lp⋯π(f) | 0.0071 | 0.0180 | 0.8257 | ΔG^TOT(lp⋯π) = −6.23 |
| lp⋯π(g) | 0.0066 | 0.0160 | 0.8013 |
| lp⋯π(h) | 0.0078 | 0.0223 | 0.8000 |
| (a) | 0.0116 | 0.0324 | 0.8300 | ΔG^TOT(XB) = −8.36 |
| (b) | 0.0108 | 0.0297 | 0.8327 |
| (c) | 0.0037 | 0.0152 | 0.6221 | ΔG^TOT(C−H⋯π) = −1.48 |
| (d) | 0.0065 | 0.0177 | 0.8084 |
| (e) | 0.0076 | 0.0196 | 0.8086 |
| (f) | 0.0072 | 0.0186 | 0.8050 |
| (g) | 0.0040 | 0.0129 | 0.6998 |
| (h) | 0.0059 | 0.0146 | 0.8456 | ΔG^TOT(lp⋯π) = −5.43 |
| (i) | 0.0083 | 0.0225 | 0.8125 |
| (j) | 0.0105 | 0.0280 | 0.8312 | ΔG^TOT(XB) = −1.89 |
| (k) | 0.0052 | 0.0184 | 0.6973 |
| (l) | 0.0038 | 0.0145 | 0.5935 |
| C−H⋯π(a) | 0.0038 | 0.0145 | 0.5935 |
| C−H⋯π(b) | 0.0061 | 0.0157 | 0.8385 | ΔG^TOT(C−H⋯π) = −1.76 |
| lp⋯π(d) | 0.0076 | 0.0200 | 0.8155 |
| XB(e) | 0.0096 | 0.0251 | 0.8237 | ΔG^TOT(XB) = −2.90 |
| C−H⋯π(a) | 0.0059 | 0.0175 | 0.8161 |
| C−H⋯π(b) | 0.0043 | 0.0136 | 0.7240 |
| C−H⋯π(c) | 0.0107 | 0.0371 | 0.7944 |
| lp⋯π(d) | 0.0062 | 0.0159 | 0.8890 | ΔG^TOT(XB) = −6.49 |
| lp⋯π(e) | 0.0100 | 0.0260 | 0.9115 |
| lp⋯π(f) | 0.0090 | 0.0234 | 0.9044 |
| lp⋯π(g) | 0.0052 | 0.0181 | 0.6921 | ΔG^TOT(lp⋯π) = −7.76 |
| lp⋯π(h) | 0.0061 | 0.0167 | 0.8844 |
| (a) | 0.0071 | 0.0194 | 0.8810 |
| (b) | 0.0064 | 0.0172 | 0.8699 |
| (c) | 0.0055 | 0.0187 | 0.6741 | ΔG^TOT(C−H⋯π) = −5.85 |
| (d) | 0.0064 | 0.0172 | 0.8340 |

(is if C_{13}H_{11} is capped with a CH_{3} group, additional C−H⋯I interactions would be introduced). Thus, the activator−CH_{3}−Br interaction is used to model the bidentate XB. The lone pair⋯π and C−H⋯π interactions can be computed using the (C_{2}H_{4}N_{2}I_{2}^+)⋯C_{13}H_{12} complex. All of the model
molecules, constructed from the adducts’ geometries, are displayed in Figures S3–S6. As shown in Tables S1–S4, the summations of the GKS-EDA results for the noncovalent interactions are very close to those of the total dimer interactions, showing the accuracy of the model approximation.

Figure 7. Isosurface plots of the molecular orbitals for XB and lone pair···π: (a) XB in A-mdI; (b) lone pair···π in A-mdI; (c) lone pair···π in A-mdI; (d) XB in P-mdI; (e) lone pair···π in P-mdI; and (f) lone pair···π in P-mdI (isovalue = 0.020).

Figure 8. Geometries and BCPs of the ion-pair complexes: (a) P-mdI; (b) P-pdI; (c) P-mHI; and (d) P-pHI.
Table 2. AIM Analysis Results and Total Interaction Energies of the Noncovalent Interactions in the Ion-Pair Complexes

| types | ρ | V^r | W/G | ΔG^TOT/(kcal/mol) |
|-------|---|-----|-----|-------------------|
| P-mdI | C−H⋯π(a) | 0.0058 | 0.0180 | 0.7587 | ΔG^TOT(C−H⋯π) = −0.50 |
|       | C−H⋯π(b) | 0.0021 | 0.0067 | 0.6782 |
|       | C−H⋯π(c) | 0.0063 | 0.0183 | 0.8053 |
|       | XB(d) | 0.0192 | 0.0490 | 0.9231 | ΔG^TOT(XB) = −24.80 |
|       | XB(e) | 0.0186 | 0.0474 | 0.9199 |
|       | lp−π(a) | 0.0064 | 0.0163 | 0.8179 | ΔG^TOT(lp−π) = −1.80 |
|       | lp−π(g) | 0.0061 | 0.0153 | 0.8072 |
|       | lp−π(h) | 0.0058 | 0.0167 | 0.7607 |
| P-pdI | XB(a) | 0.0187 | 0.0481 | 0.9163 | ΔG^TOT(XB) = −29.23 |
|       | XB(b) | 0.0179 | 0.0462 | 0.9114 |
|       | C−H⋯π(c) | 0.0049 | 0.0197 | 0.6853 | ΔG^TOT(C−H⋯π) = −0.31 |
|       | C−H⋯π(d) | 0.0035 | 0.0106 | 0.7286 |
|       | lp−π(a) | 0.0062 | 0.0154 | 0.8184 | ΔG^TOT(lp−π) = −1.14 |
|       | lp−π(f) | 0.0066 | 0.0172 | 0.8039 |
|       | lp−π(g) | 0.0039 | 0.0113 | 0.7222 |
|       | lp−π(h) | 0.0085 | 0.0240 | 0.8014 |
| P-mHI | XB(c) | 0.0223 | 0.0547 | 0.9589 | ΔG^TOT(XB) = −15.35 |
|       | C−H⋯π(d) | 0.0035 | 0.0145 | 0.6001 | ΔG^TOT(C−H⋯π) = −0.74 |
|       | lp−π(a) | 0.0032 | 0.0079 | 0.7899 |
| P-pHI | C−H⋯π(a) | 0.0037 | 0.0111 | 0.7380 | ΔG^TOT(C−H⋯π) = −0.60 |
|       | C−H⋯π(b) | 0.0021 | 0.0088 | 0.5528 |
|       | lp−π(c) | 0.0085 | 0.0238 | 0.8031 | ΔG^TOT(lp−π) = −0.08 |
|       | XB(d) | 0.0230 | 0.0559 | 0.9664 | ΔG^TOT(XB) = −14.13 |

These noncovalent interaction energies are shown in the final columns of Tables 1 and 2. In general, it is apparent that the C−H⋯π interaction energies, ranging from −0.89 to −2.98 kcal/mol in the adducts and from −0.31 to −0.74 kcal/mol in the ion-pair complexes, decrease with the C−Br bond breaking. Due to the small interaction energy, C−H⋯π is not important for the activation process. Attention is paid to XB and lone pair⋯π/π’ interactions. In the XB adducts, both these interactions are important. XB and lone pair⋯π cover 44 and 45% of the total dimer interaction on average. In the ion-pair complexes, XB dominates the total dimer interactions, while lone pair⋯π’ is very small.

The GKS-EDA results of XB are shown in Table 3. In general, the XB’s in P−X are larger than those in A−X. The electrostatic terms dominate the XB interaction, while the polarization terms play a secondary role. In P−X, the I⋯Br− XB’s belong to the charge-assisted XB. The large attractive electrostatic and polarization terms are greatly counteracted by the large repulsive desolvation terms, leading to the moderate total dimer interactions. The I⋯Br− XB interaction energies are close to the corresponding activator⋯Br− interactions shown in Table S5. For example, the interaction energy of I⋯Br− XB in P-mdI is −24.80 kcal/mol, compared to that of Br−⋯mdI of −25.31 kcal/mol.

Table 3. GKS-EDA Results of the XB (kcal/mol)

| types         | ΔG^ele | ΔG^padi | ΔG^pol | ΔG^paul | ΔG^corr | ΔG^TOT |
|---------------|--------|---------|--------|---------|---------|--------|
| I⋯Br− XB      | −10.86 | 13.50   | −7.47  | 4.59    | −6.98   | −7.23  |
| A−pHI         | −11.86 | 14.02   | −7.58  | 4.18    | −7.11   | −8.36  |
| A−mHI         | −4.56  | 4.46    | −2.51  | 3.38    | −2.66   | −1.89  |
| A−pHI         | −5.31  | 5.53    | −3.52  | 3.70    | −3.30   | −2.90  |
| P-mdI         | −138.32| 38.09   | −43.81 | 131.15  | −11.91  | −24.80 |
| P-pdI         | −139.49| 37.89   | −42.00 | 126.56  | −12.19  | −29.23 |
| P-mHI         | −125.56| 24.98   | −31.37 | 123.79  | −7.19   | −15.35 |
| P-pHI         | −115.04| 25.95   | −32.96 | 115.15  | −7.22   | −14.13 |

As can be seen from Table 4, the physical origins of the lone pair⋯π/π’ are different from XB’s. In agreement with the conclusions of several theoretical and experimental studies,63−65 for the lone pair⋯π, the correlation terms are largest, showing the importance of dynamic correlation. In A−mHI, the lone pair⋯π is quite strong because the iodimidazolium group almost parallels to the benzene ring in benzhydryl with the short distance (about 3.45 Å). As figured out by the BCP of (d) in Figure 6c, the lone pair⋯π in A−mHI contains the π⋯π stacking, which can be verified from its large correlation term (−8.94 kcal/mol). In the lone pair⋯π’ interactions, the polarization and correlation terms are similar to those of the lone pair⋯π. The largest stabilizing term for lone pair⋯π’ is not correlation but desolvation, showing the role of solvent effects in the cation−cation system. As illustrated by Figure 9, the lone pair⋯π’ between the iodimidazolium cation and the benzene group contains the like-charge repulsion (π’⋯π’) and the lone pair⋯π stabilization. The like-charge repulsion can be well interpreted from the large repulsive electrostatic interaction shown in Table 4. Compared to P-mdI and P-pdI, because of the single I atom, the lone pair⋯π stabilizations in P-mHI and P-pHI are weak, leading to almost zero interaction energies, +0.19 kcal/mol in P-
Table 5. GKS-EDA Results for the Noncovalent Interactions in the HB Complexes (kcal/mol)

|       | ΔG^pol | ΔG^p fav | ΔG^int | ΔG^non | ΔG^TOT |
|-------|--------|----------|--------|--------|--------|
| A-mdH | bidentate HB | −10.19 | 7.99  | −4.48 | 4.47  | −4.29 | −6.49 |
|       | π···π   | −8.52  | 7.17  | −7.41 | 7.74  | −6.73 | −7.76 |
| A-pdH | lone pair···π | −5.67 | 5.70  | −1.31 | 3.69  | −5.15 | −2.75 |
|       | π···π   | −6.69  | 8.62  | −6.75 | 5.49  | −6.51 | −5.85 |

mHI and −0.08 kcal/mol in P-pHI. The like-charge repulsion energy can be approximated as the interaction free energy difference between the lone pair···π and the lone pair···π by the same XB donor, ranging from +4.43 to +5.63 kcal/mol.

3.3. Why Do the Hydrogen Bond Donors not Activate the Br Abstraction? Different behaviors of the noncovalent interactions lead to the different activation results. Moreover, (∆G^TOT − ∆G^pol) can be expressed as the sum of the contributions from XB, lone pair···π, and C−H···π. Among them, the contribution of XB, ranging from −9.98 to −20.87 kcal/mol, is the most important. It is the reason why the bidentate bromine activator, where two I atoms are replaced by two Br atoms, is still capable of activating the reaction. The weaker halogen bond results in the smaller stabilization energy and a higher barrier. It is confirmed by the IRC calculation shown in Figure S7. As can be seen, the barrier of the bidentate bromine activator, 11.8 kcal/mol, is higher than that of the bidentate iodine one. It is well in agreement with the smaller yield in the experiment.

To answer the question why mdH/pdH is unable to activate the process, the various noncovalent interactions in A-mdH and A-pdH are analyzed. According to the BCPs in Figure 6e,f, in A-mdH, there are the bidentate C−H···Br HB, C−H···π, and π···π stacking; however, in A-pdH, besides C−H···π and π···π stacking, there is no C−H···Br HB but lone pair···π interaction between the Br atom and the benzene ring. Using the model molecules shown in Figures S8 and S9, the GKS-EDA results for the noncovalent interactions are shown in Table 5. It is found that the π···π stacking interaction energy, −7.76 kcal/mol in A-mdH and −5.85 kcal/mol in A-pdH, is the most important for the total dimer interactions. Different from typical π···π stacking that is dominated by the correlation term, in the π···π stacking interactions, electrostatic and polarization terms are larger than the correlation term.

It can be easily observed that if A-mdH/A-pdH could be activated, the π···π stacking would not exist, while the π···π repulsion would arise; furthermore, the interactions between Br− and mdH/pdH belong to the C−H···Br− HBs (Figure S2). As such, the total dimer interaction energies can be estimated by the summation of the interaction energies of the C−H···Br− HB and the π···π repulsion, +4.43 to +5.63 kcal/mol discussed above. Considering that the HB interaction energies in Table S5 are −21.45 kcal/mol for Br−···mdH and −13.33 kcal/mol for Br−···pdH, the summations (HB plus π···π repulsion) are close to the total dimer interaction energies in A-mdH/A-pdH. It means that there is no extra stabilization of the ion-pair complex compared to A-mdH/A-pdH. It leads to the large ΔG^pol answering the fact that mdH and pdH are incapable of activating the Br abstraction process. Thus, the failure of mdH/pdH can be attributed to the fact that the C−H···Br− HBs are unable to compensate the π···π repulsion when benzhydryl becomes positively charged. In contrast, for the XB activator, the lone pair···π interaction resists the π···π repulsion, thus the interaction between the iodoimidazolium cation and the benzene group is still attractive. Thereafter, the I−···Br− XB can be fully devoted to the stabilizations of the ion-pair complexes.

4. CONCLUSIONS

In this work, the activation of the Br abstraction process in the Ritter-type solvolysis of benzhydryl bromide by a series of cationic XB and HB activators were investigated theoretically. Our study is in good agreement with the experimental results, which show that the cationic XB donors have the capability to promote the process, while the HB ones do not. To understand the activation, the origins of noncovalent interactions XB, HB, lone pair···π, and C−H···π in a series of the activator···substrate complexes, are explored. We can conclude the following:

1. The variation of the dimer interaction free energy is the most important for the activation. The XB activators have large stabilization energies with the substrate in the ion-pair complexes, leading to the decrease of ΔG^pol while the HB activators could not.

2. The different stabilization energies can be contributed by the variation of the noncovalent interactions. For the XB activators, XBs are greatly enhanced from adducts to the ion-pair complex. The lone pair···π interaction, which overcomes the π···π repulsion, ensures that the I−···Br− XB mainly responds for the stability of the ion-pair complex.

3. For the HB activators, the HB interaction is incapable of compensating the energy loss from the π···π attraction to the π···π repulsion, resulting in the almost unchanged total dimer interaction. Thus, the HB activators are unable to provide the additional stabilization for the ion-pair complex.

Furthermore, this work dissects a collection of various intermolecular interactions in a single bond activation, in which the role of lone pair···π interaction has been exhaustively highlighted. Lone pair···π is dominated by the correlation term in adduct but the desolvation term in the ion-pair complex. It shows the importance of solvated environments in the tunability of lone pair···π. Such analysis will permit thoughtful and quantitative evaluation of rational catalyst or activator design in organocatalysis, a matter of continuing interest.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.0c03000. Important geometric parameters of the transit states; interacting geometries of Br with all the activators; the C-Br bond activation by the bidentate bromine activator; model molecules for the noncovalent interactions; and GKS-EDA results for noncovalent interactions and total dimer interactions in adducts (PDF)
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