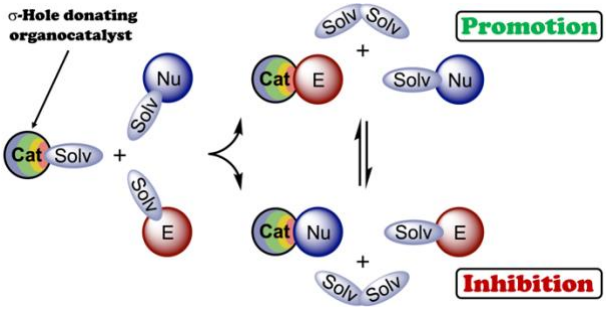
Solvent-modulated Binding Selectivity of Reaction Substrates to Onium-based σ-Hole Donors

Alexandra A. Sysoeva,[1] Alexander S. Novikov,[1] Mikhail V. Il'in,[1] Dmitrii S. Bolotin[1] *

[1] Institute of Chemistry, Saint Petersburg State University, Universitetskaya Nab. 7/9, Saint Petersburg, 199034, Russian Federation

* Corresponding author E-mail: d.s.bolotin@spbu.ru

The combination of experimental data and results of DFT calculations indicates that the catalytic activity of chalconium and halonium salts serving as σ-hole donating organocatalysts cannot be clearly estimated via analysis of the electrostatic potential on the catalysts' σ-holes and values of the catalyst···TS intermolecular interactions, such as polarization effects, charge transfer, or covalency of bonding. Moreover, the real catalytic effect might not correlate well with the values of Gibbs free energy of activation of the reactions, because solvation effects and other competitive binding processes play at least an equal or even more important role in the catalysis. It was shown in the present work that the solvation can either lead to the increase of equilibrium concentration of reactive catalyst···electrophile associates, thus accelerating the reaction, or brings favorable generation of catalyst···nucleophile species resulting in the suppression of the catalytic activity of the organocatalyst.



Introduction

Today, σ-hole donating species binding to reaction substrates via chalcogen (ChB) or halogen (XB) bonds—interactions between electron-deficient chalcogen or halogen atom and a Lewis base, respectively[1, 2]—play an important role in noncovalent organocatalysis,[3, 4] as they provide a more directional orientation and a higher electrophilic activation of ligated species compared to traditional hydrogen bond (HB)[5, 6] donating organocatalysts.[7, 8] ChB and XB donors also exhibit very low sensitivity to oxygen and water, thus having advantages over many metal-containing Lewis acids.[9, 10] Considering this, a wide dissemination of ChB and XB donors into the fields yet utilizing traditional HB donating organocatalysts,[10-13] as well as metal-based Lewis acids, can provide the evolution of sustainable catalysis in the direction of application of efficient and environmentally benign catalytic species.

The σ-hole donating organocatalysts exhibit similar general trends in catalytic activity, which implies its increase from lighter to heavier σ-hole carriers[14], thereby the compounds featuring electron-deficient tellurium and iodine elements have been shown to exhibit the highest catalytic activity among ChB[2, 15-17] and XB[18-20] bond donors. Moreover, the cationic organocatalytic species have a significantly higher activity compared to the uncharged compounds.[8, 17, 21-28] Recently, it has been shown that cationic chalcogen(IV)- or halogen(III)-derived σ-hole donors (chalconium and halonium salts; **Figure 1**) are remarkably more active than their chalcogen(II)- and halogen(I)-containing analogues. Thus, iodonium salts featuring two σ-holes at the iodine atom exhibit a higher catalytic activity than cationic iodine(I)-based catalysts[29] and effectively catalyze a wide range of organic reactions.[30-44] Similarly, telluronium salts featuring three σ-holes at the tellurium atom represent a higher catalytic activity than that of tellurium(II) derivatives and lighter chalcogen(IV)-derived species.[17, 45, 46]

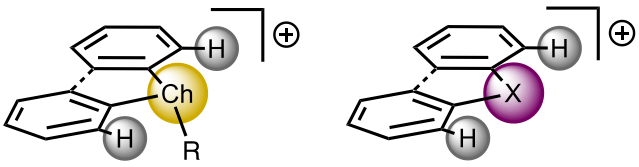
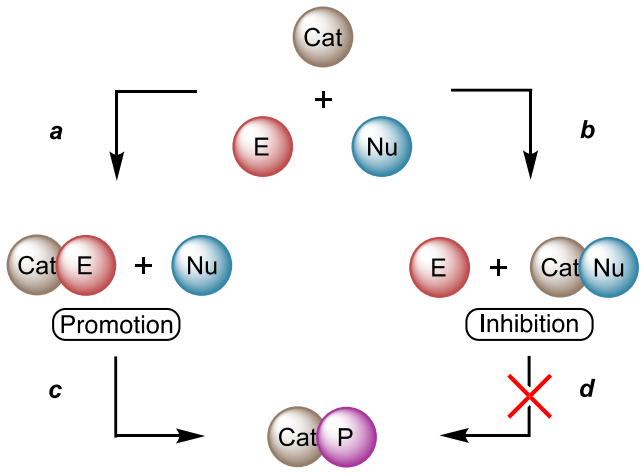


Figure 1. Chalconium and halonium species as highly catalytically active ChB- and XB-donating organocatalysts.

Although onium salts have been shown to catalyze a wide range of reactions, there is not a unanimous point of view on the nature of the electrophilic activation of reaction substrates by these species. In our previous work it was concluded that the dominant factor of the decrease of the Gibbs free energy of activation is polarization of a transition state provided by the organocatalysts, whereas a charge transfer, as well as covalency of the catalyst···substrate interaction, has a negligible effect.[42] Another work[47] represents an opposite view on this question and suggests that the substrate-to-catalyst charge transfer plays the dominant role.

Whatever the factors providing the electrophilic activation of a substrate are, it is only possible when this substrate is ligated to the organocatalytic species. During the reaction progress, the catalyst can reversibly bind not only to the target electrophile (**Scheme 1**, ***a***), but also to the nucleophilic agents and/or intermediates and the reaction product (**Scheme 1**, ***b***).[41, 43] These competitive processes should be considered since all of them are able to decrease the catalytic activity of the σ-hole donor. In the extreme case, if the catalyst predominantly binds to the nucleophile, the catalytic effect can be completely suppressed, and the reaction rate can even be reduced due to the decrease of equilibrium concentration of unbound nucleophilic species.



Scheme 1. Competitive routes of the catalyst···substrate binding.

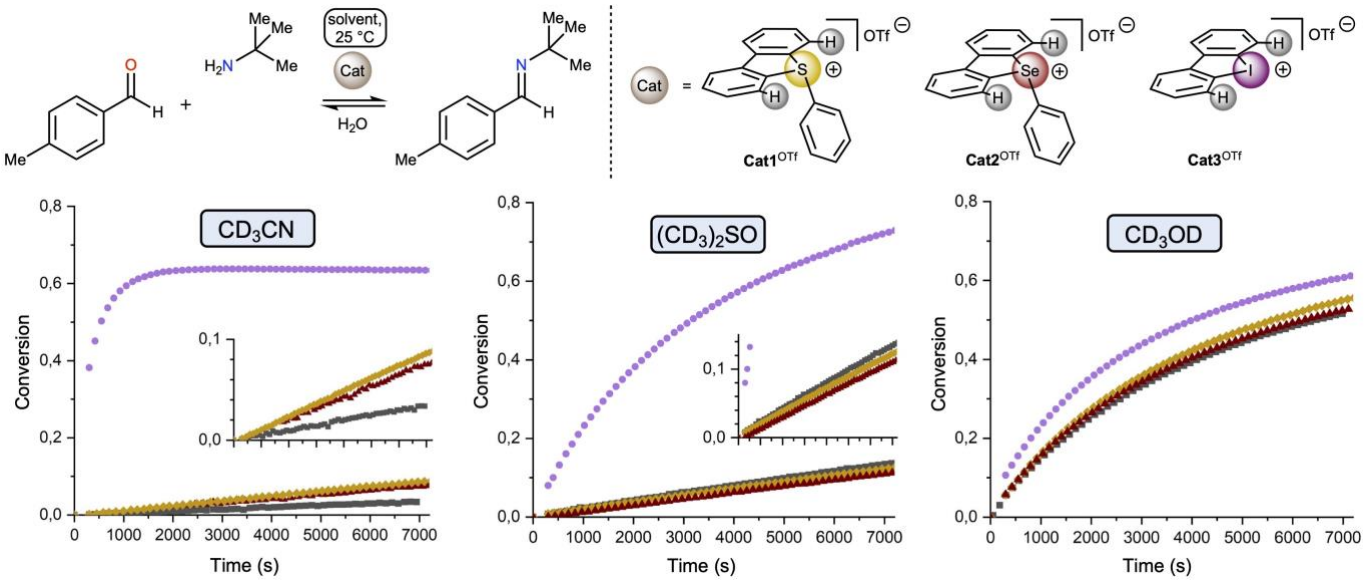
In this work, we have decided to shift the focus of the discussion from the nature of electrophilic activation to the less obvious but, possibly, more important binding factor. Recently we have suggested a reliable model for the consideration of the binding process during DFT calculations[48], and here we apply this model to the estimation of the solvent effects for the systems involving onium salt catalysis to shed light on how the nature of the solvent affects the equilibrium concentration of reactive catalyst···electrophile associates. Based upon the experimental and theoretical study on the catalytic activity of a series of onium salts in different solvents, the discussion of the factors affecting their catalytic activity related to the binding processes is represented.

Results and Discussion

Selection of onium salts and their catalytic activity in a model reaction. Onium cations are potentially reactive toward nucleophilic agents, owing to their tendency to form uncharged chalcogen(II)- and halogen(I)-containing species.[44, 49-53] Considering that the noncovalent organocatalysts must retain their chemical structure during the reaction progress, fully arylated onium salts have been chosen in this study, as they are less reactive toward nucleophilic agents than their alkyl, vinyl, alkynyl, and other counterparts. Taking into account that halonium salts containing condensed aryl rings are more acidic[51] and exhibit higher catalytic activity[41, 43] than their acyclic analogues, and considering that iodonium salts exhibit higher catalytic activity and stability toward nucleophilic species than their bromonium and chloronium congeners,[54] dibenziodolium triflate **Cat3**^{OTf} has been chosen as a representative example of XB donor. Among ChB donors, the dibenzothiophene and dibenzoselenophene derivatives (**Cat1**^{OTf} and **Cat2**^{OTf}, respectively), featuring two condensed phenyl rings, were selected as structural analogues of **Cat3**^{OTf} (**Scheme 2**). The telluronium salts are not considered in this study due to their low stability against the elimination of elemental tellurium.[55]

As a model reaction, Schiff base formation has been chosen. Reaction of *tert*-butyl amine with 4-methyl benzaldehyde in CD_3CN, $(CD_3)_2SO$, or CD_3OD at 25 °C leads to a reversible formation of the Schiff base 4-TolC(H)=N^{t}Bu (**Scheme 2**). ^{1}H NMR monitoring indicated that this reaction proceeds slowly in the aprotic solvents when non-catalyzed. The availability of 10 mol % of **Cat1**^{OTf} or **Cat2**^{OTf} provides no observable catalytic effect in $(CD_3)_2SO$, whereas a remarkable rise of the reaction rate has been detected in CD_3CN. In CD_3OD, the non-catalyzed reaction proceeded significantly faster than the one performed in the aprotic media; no catalytic effect was observed for **Cat2**^{OTf}, but **Cat1**^{OTf} exhibited a low but perceptible acceleration of the reaction. **Cat3**^{OTf} provided a significant acceleration of the model reaction in all the solvents, but the highest acceleration was detected in CD_3CN.

All these qualitative observations clearly indicate that the catalytic effect of the σ-hole donating catalysts significantly depends on the reaction media, and the solvent plays an important role in the process of catalysis, since it can totally suppress the activity of some of the organocatalytic species or, vice versa, allow the catalyst to show an outstanding activity.



Scheme 2. Structures of the selected catalysts **Cat1**^{OTf}–**Cat3**^{OTf}, model reaction and ^{1}H NMR monitoring of its progress in the presence of the catalysts (10 mol %) and their absence. Yellow — **Cat1**^{OTf}, red — **Cat2**^{OTf}, purple — **Cat3**^{OTf}.

Quantitative analysis of the kinetic data. To obtain quantitative benchmarks for further comparison with DFT calculations, the forward and reverse reaction rate constants were calculated based on the ^{1}H NMR monitoring data. The equilibrium constant K for the model reaction can be written as the following equation (**eq. 1**):

$$K = \frac{k_1}{k_{-1}} = \frac{x_{eq}(x_{eq}+d_0)}{(a_0-x_{eq})^2} \qquad \text{eq. 1}$$

where k_1 is the rate constant of the forward reaction (M^{-1} s^{-1}), k_{-1} is the rate constant of the reverse reaction (M^{-1} s^{-1}), x_{eq} is the equilibrium concentration of the imine (M), a_0 is the starting concentration of the aldehyde (M), d_0 is the starting concentration of water (M). The concentration-vs-time dependence can be linearized (**Figure 2**) by the following equation in coordinates $\ln\frac{x^*_{eq}(x-x_{eq})}{x_{eq}(x-x^*_{eq})}$ vs t:

$$\ln\frac{x^*_{eq}(x-x_{eq})}{x_{eq}(x-x^*_{eq})} = (k_1 - k_{-1})(x_{eq} - x^*_{eq})t,$$

$$\text{where } x^*_{eq} = \frac{2Ka_0+d_0}{K-1} - x_{eq} \qquad \text{eq. 2}$$

$$\begin{cases} k_1 = \dfrac{SK}{(x_{eq}-x^*_{eq})(K-1)} \\ k_{-1} = \dfrac{S}{(x_{eq}-x^*_{eq})(K-1)} \end{cases},$$

where $S = (k_1 - k_{-1})(x_{eq} - x^*_{eq})$ is the slope of the line. eqs. 3–4

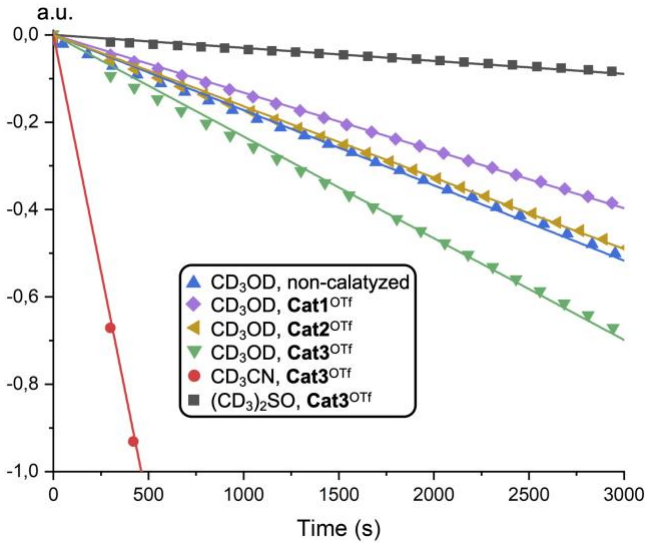


Figure 2. Linearized plot of the kinetic data for the calculation of the forward and reverse reaction rate constants.

Table 1. The calculated from the experimental kinetic data forward and reverse reaction rate constants in CD_3CN, $(CD_3)_2SO$, or CD_3OD for **Cat1**^{OTf}–**Cat3**^{OTf}.

Entry	Solvent	Catalyst	K	$k_1\times10^3$ (M^{-1} s^{-1})	$k_{-1}\times10^5$ (M^{-1} s^{-1})
1	CD_3OD	–	26	1.1	4.3
2	CD_3OD	**Cat1**^{OTf}	51	1.2	2.3
3	CD_3OD	**Cat2**^{OTf}	32	1.1	3.6
4	CD_3OD	**Cat3**^{OTf}	34	1.7	5.1
5	CD_3CN	**Cat3**^{OTf}	10	13	130
6	$(CD_3)_2SO$	**Cat3**^{OTf}	1800	2.2	0.12

Solution of the obtained equations by the least squares method has led to the values of k_1 and k_{-1} (**Table 1**). Due to a very low conversion, no precise calculation of the constants was possible for the non-catalyzed and catalyzed by the **Cat1**^{OTf} and **Cat2**^{OTf} reaction in CD_3CN or $(CD_3)_2SO$. A rough estimation of the reaction rates in these solvents gave $k_1^{MeCN}\sim10^{-5}$ M^{-1} s^{-1}, $k_{-1}^{MeCN}\sim10^{-6}$ M^{-1} s^{-1}, $k_1^{DMSO}\sim10^{-4}$ M^{-1} s^{-1}, $k_{-1}^{DMSO}\sim10^{-7}$ M^{-1} s^{-1}.

The k_1 and k_{-1} values clearly indicate that **Cat1**^{OTf}–**Cat3**^{OTf} have a significant effect on the rate of both forward and reverse reactions. In CD_3OD, **Cat3**^{OTf} serves as a typical Lewis acid and expectedly increases the k_1 and k_{-1} values (entries 1 and 4), whereas the effect of **Cat1**^{OTf} and **Cat2**^{OTf} turns out to be less predictable since they have next to no effect on the forward reaction rate but *inhibit* the reverse reaction (entries 1–3). This observation can be explained in terms of the dominant binding of **Cat1**^{OTf} and **Cat2**^{OTf} with H_2O molecules served as a nucleophile in the reverse reaction (imine + H_2O → aldehyde + amine). The selective ligation of H_2O might also explain their negligible catalytic effect on the forward reaction, because of the occupation of the coordination vacancies of the S and Se centers in **Cat1**^{OTf} and **Cat2**^{OTf}, respectively, which prevent the binding of the catalysts with the electrophile.

Density functional theory calculations for determination of the relative binding energies. For computational analysis of the **Cat**$^+$···substrate association process, we have used the model suggested by us previously,[48] because it gave the results similar to the experimentally obtained binding energies. This model presupposes the involvement of two solvent molecules taken in the explicit form in the computations: one ligated to the catalyst σ-hole and the other bound to the nucleophilic part of a reaction substrate (**Figure 3**). The Gibbs free energy of binding were calculated for a series of the most abundant solvents, which are typically utilized in organic syntheses (i.e. THF, Me_2SO, MeCN, DMF, Pyridine, $CHCl_3$, H_2O, and MeOH; **Table 2**).

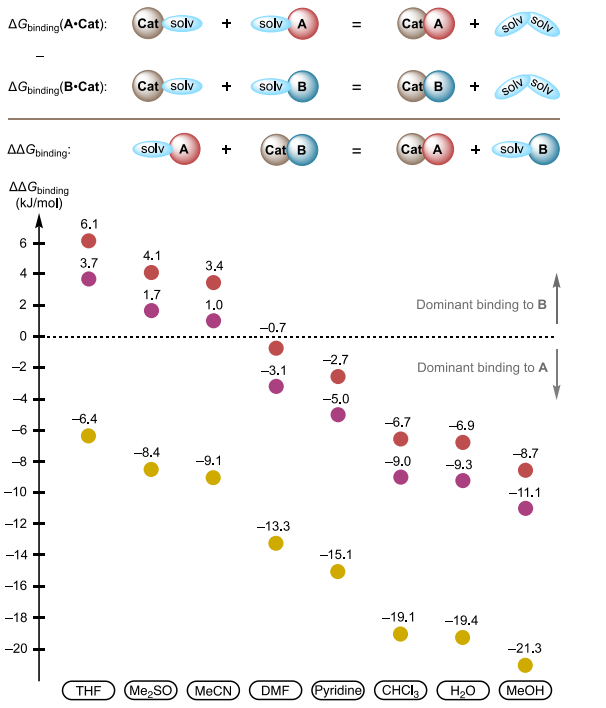
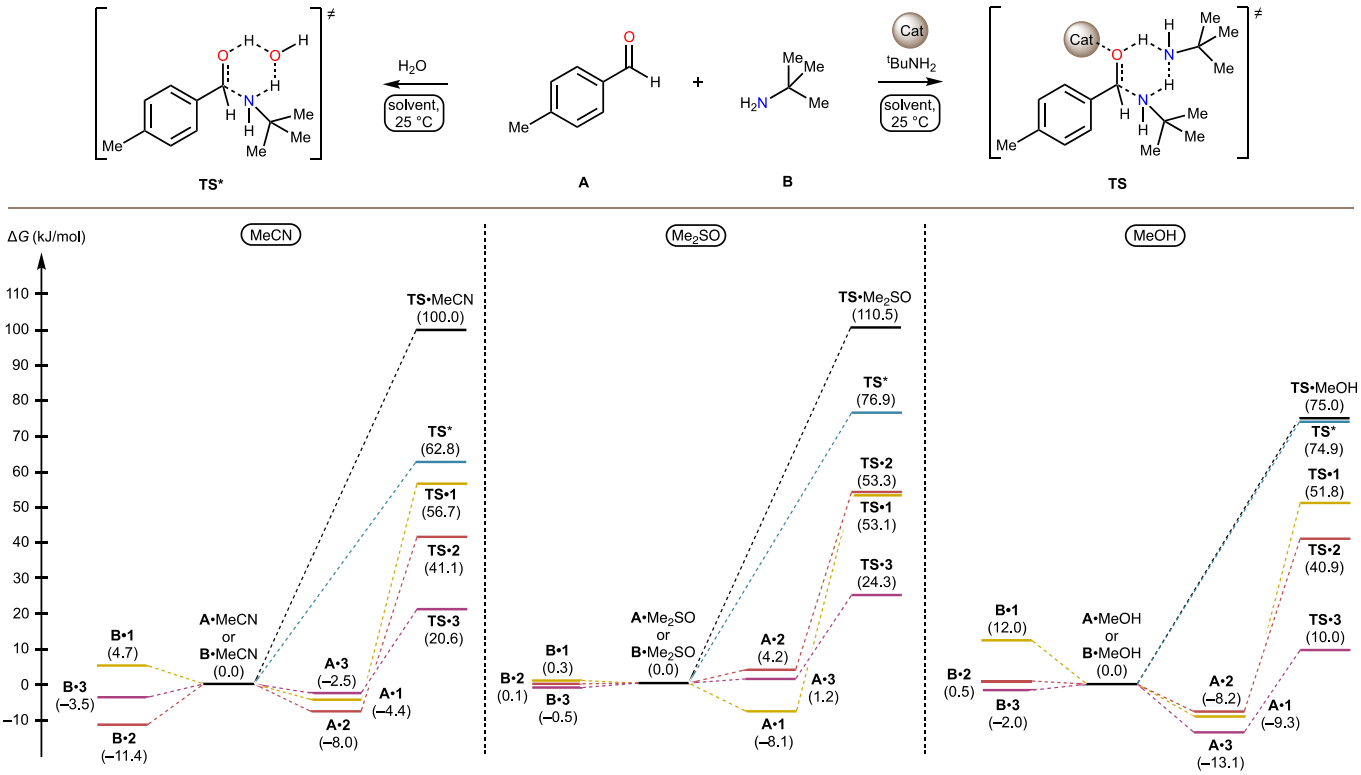


Figure 3. Schematic representation of the binding process and difference in the calculated energies of binding with **Cat1**$^+$–**Cat3**$^+$ between the aldehyde (**A**) and amine (**B**). Yellow — **Cat1**$^+$, red — **Cat2**$^+$, purple — **Cat3**$^+$.

Table 2. The calculated Gibbs free energy of binding for **Cat1**$^+$–**Cat3**$^+$ with the aldehyde (**A**) or amine (**B**) in a series of solvents.

Solvent	1		2		3	
	$\Delta G_{binding}$ (**A•Cat**)	$\Delta G_{binding}$ (**B•Cat**)	$\Delta G_{binding}$ (**A•Cat**)	$\Delta G_{binding}$ (**B•Cat**)	$\Delta G_{binding}$ (**A•Cat**)	$\Delta G_{binding}$ (**B•Cat**)
THF	1.2	7.6	4.2	–1.9	2.1	–1.6
Me_2SO	–8.1	0.3	4.2	0.1	1.2	–0.5
MeCN	–4.4	4.7	–8.0	–11.4	–2.5	–3.5
DMF	1.7	15.0	3.1	3.8	5.0	8.1
Pyridine	4.4	19.5	11.3	14.0	9.3	14.3
$CHCl_3$	–15.8	3.3	–27.8	–21.1	–34.7	–25.7
H_2O	–9.9	9.5	–11.8	–4.9	–12.1	–2.8
MeOH	–9.3	12.0	–8.2	0.5	–13.1	–2.0



Scheme 3. The calculated energy profiles for the aldehyde–amine coupling reaction.

The data indicate that **Cat1**$^+$ predominantly binds with the aldehyde in each solvent taken into consideration, but the relative ratio between equilibrium concentrations of **Cat1**$^+$···**A** and **Cat1**$^+$···**B** species—depending on the $\Delta G_{binding}$(**A•Cat**)–$\Delta G_{binding}$(**B•Cat**) value (**Figure 3**)—has significant differences. For the **Cat2**$^+$ and **Cat3**$^+$ species, the **Cat**$^+$···**B** is the dominant form in THF, Me_2SO, and MeCN, whereas the **Cat**$^+$···**A** associates prevail in the other chosen solvents. On the one hand, this observation indicates that a rational choice of the solvent for the catalyzed reaction can lead to a significant increase of equilibrium concentration of the activated form of an electrophile, making the most of the catalyst in the reaction. On the other hand, a poor choice of the solvent can lead to the total inhibition of the catalytic effect due to the complexation of a nucleophilic species to the catalyst.

Density functional theory calculations for determination of the Gibbs free energy of activation of the model reaction. DFT calculations of the Gibbs free energy of activation of the first step of the modelled reaction were carried out to better understand the impact of the association process on the reaction rate. In the model applied for the calculations, the 6-membered transition states were chosen. One of them involved two molecules of the amine (**TS**),[56, 57] whereas another one involved one molecule of the amine and H_2O molecule (**TS***)[58], since all the solvents utilized for the ^{1}H NMR monitoring contained traces of water, and H_2O is also eliminated in the progress of the reaction (**Scheme 3**).

In all chosen solvents (MeCN, Me_2SO, and MeOH), the iodolium cation **Cat3**$^+$ carrying significantly more positive electrostatic potential on its σ-holes[14, 43, 57] than the sulfonium and selenonium cations (**Cat1**$^+$ and **Cat2**$^+$, respectively) expectedly exhibited the highest reduction of the Gibbs free energy of activation. Nevertheless, all the catalytic species, as indicated by the results of DFT calculations, should provide a significant catalytic effect, which experimentally was not detected for **Cat1**^{OTf} and **Cat2**^{OTf} in Me_2SO, whereas in MeCN and MeOH, the effect was significantly lower than estimated from the calculations. This may indicate that their catalytic activity was reduced by the complexation with the reaction

substrates different from the electrophilic aldehyde. For MeOH, **Cat1**^{OTf} experimentally provided a higher catalytic effect than **Cat2**^{OTf}, whereas the calculated $\Delta G^{\neq}$ for **Cat1**$^{+}$ is higher than the one for **Cat2**$^{+}$-catalyzed process (61.1 kJ mol^{-1} vs 49.1 kJ mol^{-1}, respectively). Such difference between the experiment and theoretical consideration may be explained by the different equilibrium concentration of the activated form of the aldehyde (**A•Cat**). Indeed, for the **Cat1**^{OTf} species, the obtained computational data indicate almost selective association of **Cat1**$^{+}$ with the aldehyde **A** (–9.3 kJ mol^{-1} for **A•1** vs 12.0 kJ mol^{-1} for **B•1**), whereas **Cat2**$^{+}$ binds the reaction substrates significantly less selectively (–8.2 kJ mol^{-1} for **A•2** vs 0.5 kJ mol^{-1} for **B•2**).

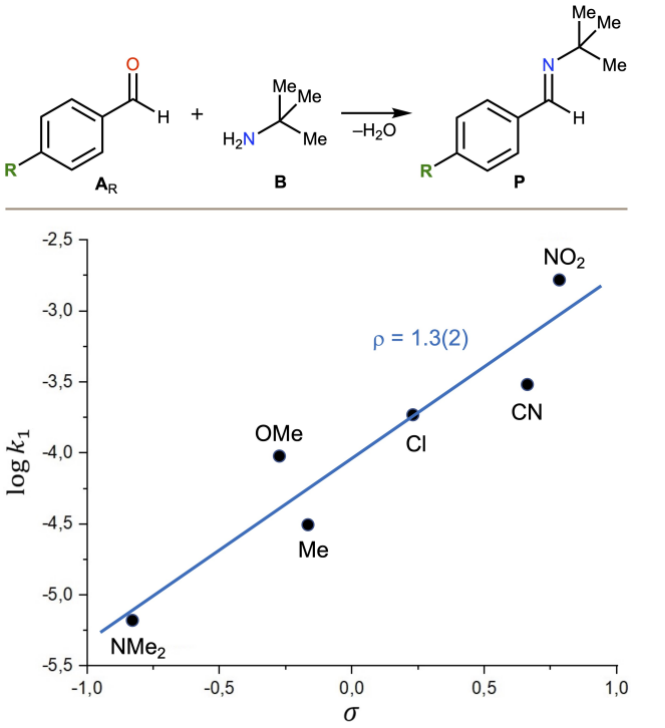
Correlation analysis for the determination of the nature of catalysis by Cat3^{OTf}**.** A correlation analysis has been performed for the non-catalyzed and **Cat3**^{OTf}-catalyzed model reaction in MeCN to determine the nature of the dibenziodolium catalytic effect (**Schemes 4** and **5**; **Table 3**). Reaction of the amine **B** with a series of *para*-substituted aldehydes $\mathbf{A}_R$ (R = NMe_2, OMe, Me, Cl, CN, and NO_2) in the absence of the catalyst showed the best correlation with the σ constants (ρ = 1.3(2); R^2 = 0.8938). Although the correlation coefficient is far from 1, it has a satisfactory value considering the complex nature of the transition state (**TS** or **TS***; **Scheme 3**), the energy of which also depends on the nucleophilicity of the carbonyl O atom. The value of the reaction parameter expectedly indicates that this reaction moderately depends on the electronic effects of R and is accelerated by the acceptor substituents (**Scheme 4**).

The plot for the reaction carried out in the presence of **Cat3**^{OTf} showed a significantly different correlation. Thus, for the donor substituents R, the best correlation was observed for the σ^{+} constants (ρ = 0.49(4); R^2 = 0.9877), whereas no influence of the substituent electronic effects was detected for the acceptor Rs (**Scheme 5**). These observations may indicate a significant impact of the association processes on the reaction kinetics.

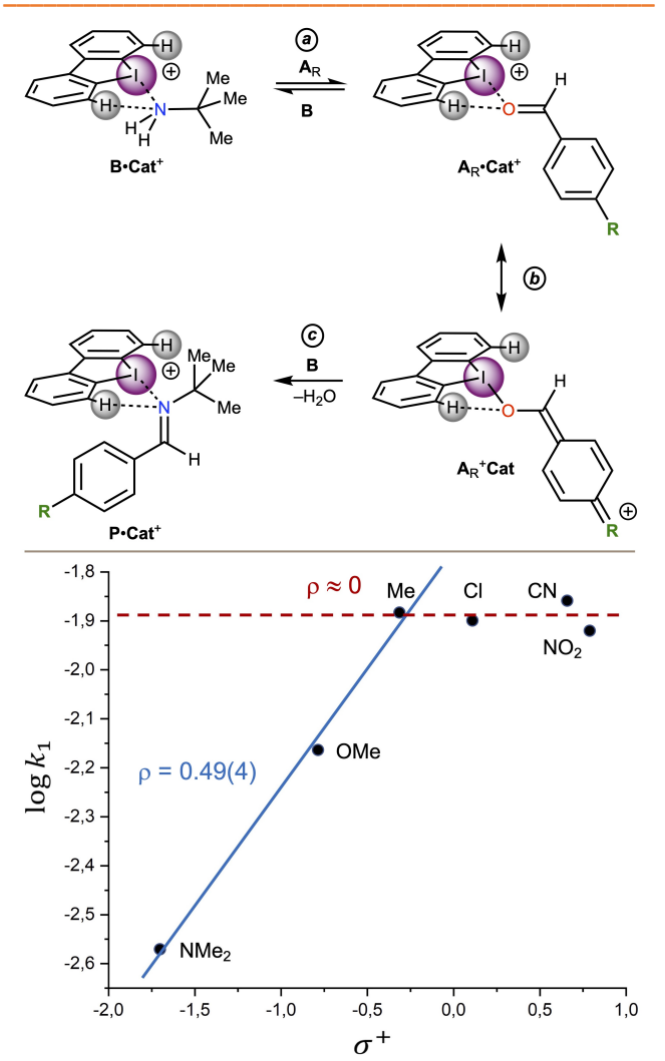
The aldehydes $\mathbf{A}_R$ featuring donor substituents effectively compete with the amine **B** to coordinate with the catalyst' σ-hole since donor R increases the nucleophilicity of the carbonyl O atom (**Scheme 5**, ***a***). A high equilibrium concentration of $\mathbf{A}_R$**•Cat**$^{+}$ with low electrophilicity of the ligand proves the amine nucleophilic attack to be the reaction rate-limiting step (**Scheme 5**, ***c***). The good correlation with σ^{+} constants can be explained in terms of notable contribution of the resonance structure $\mathbf{A}_R^{+}$**Cat** exhibiting the substrate-to-catalyst charge transfer (**Scheme 5**, ***b***).

The aldehydes $\mathbf{A}_R$ featuring acceptor substituents R cannot effectively compete with the amine **B** for the binding with the catalytic species **Cat3**$^{+}$, because the nucleophilicity of the carbonyl O atom is reduced. Considering this, dissociation of the **B•Cat**$^{+}$ associate—which does not depend on the nature of R in the aldehyde structure—might be the rate-limiting step. The following nucleophilic attack of the amine on the ligated aldehyde is not the rate-limiting step since acceptor Rs increases the electrophilicity of the carbonyl C atom.

All these observations on experimental kinetic data indicate that both factors, namely the electrophilic activation of the substrate by the catalyst and the catalyst-involving association processes, have a great impact on the reaction kinetics, and the ability of the catalyst to electrophilically activate the reaction substrates taken separately cannot adequately predict a real catalytic activity of the XB or ChB donating species.



Scheme 4. Correlation of forward rate constants with the substituent σ constants for the non-catalyzed reaction performed in MeCN.



Scheme 5. Correlation of forward rate constants with the substituent σ^{+} constants for the **Cat3**^{OTf}-catalyzed reaction performed in MeCN.

Table 3. Equilibrium and rate constants for the series of aldehydes.

R	K	**Cat3**^{OTf}-catalyzed		Noncatalyzed		σ	σ^+
		k_1	k_{-1}	k_1	k_{-1}		
NO_2	18.44	1.20(2)×10^{-2}	6.52(8)×10^{-4}	1.6(1)×10^{-3}	8.7(6)×10^{-5}	0.78	0.79
CN	44.91	1.38(1)×10^{-2}	3.08(3)×10^{-4}	3.12(2)×10^{-4}	6.95(3)×10^{-6}	0.66	0.66
Cl	17.20	1.25(4)×10^{-2}	7.3(2)×10^{-4}	1.894(5)×10^{-4}	1.611(4)×10^{-5}	0.23	0.11
Me	9.91	1.306(8)×10^{-2}	1.317(8)×10^{-3}	3.10(4)×10^{-5}	3.13(4)×10^{-6}	−0.17	−0.31
OMe	7.47	6.85(5)×10^{-3}	9.173(6)×10^{-4}	6.6(1)×10^{-6}	1.66(3)×10^{-6}	−0.27	−0.78
NMe_2	3.97	2.68(2)×10^{-3}	6.75(4)×10^{-4}	9.60(1)×10^{-6}	1.285(2)×10^{-6}	−0.83	−1.70

The σ and σ$^+$ constants are taken from ref.[59]

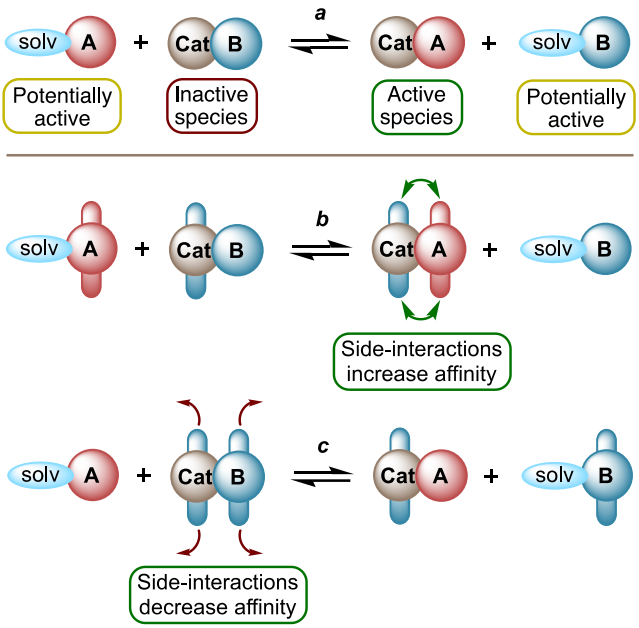
Conclusions

In this work, it was shown experimentally that the catalytic activity of σ-hole donating organocatalysts cannot be clearly predicted either from the analysis of catalyst···TS intermolecular interactions or from the value of reduction of the Gibbs free energy of activation of the reaction. Solvation effects and other competitive binding processes play at least an equal or even more important role in the catalysis.

During the reaction progress, the catalyst reversibly associates with a target electrophilic species thus accelerating the reaction due to the electrophilic activation, as well as binds the nucleophile giving inactive Cat···Nu species. Such an equilibrium at a great extent is caused by the solvation effects, and a rational choice of the solvent is required for the catalyst to fully display its catalytic ability (**Scheme 6, *a***). One of the ways to solve this problem is utilization of the solvents exhibiting high affinity to the nucleophile, which will compete with the catalyst in the binding with the nucleophile. In the simplest case, this approach should shift the equilibrium to the reactive Cat···electrophile species but reduce the activity of the "unbound" nucleophile. Such an effect can be observed in this work by analysis of the experimental and computational data for **Cat3**^{OTf}-catalyzed forward reaction rate constant in MeCN (k_{-1} = 13×10^{-3} M^{-1} s^{-1}; $\Delta\Delta G_{binding}$ = 1 kJ mol^{-1}) and MeOH (k_{-1} = 1.7×10^{-3} M^{-1} s^{-1}; $\Delta\Delta G_{binding}$ = −11.1 kJ mol^{-1}), where the forward reaction is slower in MeOH although the estimated equilibrium concentration of the Cat···electrophile associates is higher in this solvent.

Rational structural design of the catalysts providing their higher affinity to the electrophilic species (**Scheme 6, *b***) or discriminating binding to the nucleophile (**Scheme 6, *c***) seems to be a more complex yet effective approach. Incorporation in the catalyst structure of the side-groups providing additional van der Waals interactions as well as hydrogen-, pnictogen-, chalcogen-, or halogen bonds with the electrophile or steric/electrostatic repulsion from the nucleophile is the way to reach this goal.

We hope that this study, on the one hand, sheds light on the importance of complex association processes taking place in the progress of reactions catalyzed by the ChB or XB donors, which can drastically affect the catalytic activity of the organocatalysts and, on the other hand, sets the direction for further consideration of the side-interactions between the catalysts and reaction substrates, which can modulate their binding selectivity. The computational model utilized in this work and the obtained results might also be useful in the field of noncovalent ion and molecular recognition, which recently has been extensively realized utilizing ChB and XB donors.[2,16,25,60-63]



Scheme 6. Equilibrium between active and inactive catalyst···substrate associates.

Experimental Section

Materials and instrumentation. All solvents, *tert*-butylamine and 4-methylbenzaldehyde were obtained from commercial sources and used as received. The catalysts **Cat1**^{OTf}**–Cat3**^{OTf} were synthesized according to published procedures with some modifications.[41,64,65] All syntheses were conducted in air. Chromatographic separation was carried out using Macherey-Nagel silica gel 60 M (0.063–0.2 mm). Melting points were measured on a Stuart SMP30 apparatus in capillaries and are not corrected. Electrospray ionization mass-spectra were obtained on a Bruker maXis spectrometer equipped with an electrospray ionization (ESI) source. The instrument was operated in positive ion mode using an *m*/*z* range 50–1200. The nebulizer gas flow was 1.0 bar and the drying gas flow 4.0 L min^{-1}. For HRESI$^+$, the studied compounds were dissolved in MeOH. ^{1}H- and ^{13}C{^{1}H} NMR spectra were measured on a Bruker Avance 400 and Bruker Avance 500 spectrometers in $CDCl_3$, $(CD_3)_2SO$, CD_3OD at 298 K; the residual solvent signal was used as the internal standard.

^{1}H NMR monitoring of the modelled reaction. A solution of *tert*-butylamine (10.5 µL, 0.1 mmol) in CD_3CN, $(CD_3)_2SO$ or CD_3OD (300 µL) was added to a mixture of *para*-substituted benzaldehyde (0.1 mmol) and the catalyst **Cat1**^{OTf}**–Cat3**^{OTf} (0.01 mmol) or without

catalyst dissolved in the corresponding solvent (300 µL) and placed in an NMR tube. The closed NMR tube was shaken 3 times, immediately placed in an NMR spectrometer, and the ^{1}H NMR spectra were recorded every 2 min (four scans; repetition time = 4 s) for 2 h at 298 K. The reaction progress was monitored by measuring the time-dependent integral intensity of the proton signals in aldehyde and imine groups (see **Supporting Information**).

Computational details. The full geometry optimization of all model structures was carried out at the DFT level of theory using the M06-2X functional[66] with the help of the Gaussian-09 program package.[67] The M06-2X functional was specifically developed and parameterized for a correct description of noncovalent interactions and thermochemistry (especially in the case of main group chemical elements)[66] and was also validated for these purposes in several benchmark studies.[68-70] We have chosen this functional according to our previous experience and its successful performance in a number of halogen and chalcogen bonds studies in various similar supramolecular systems and organocatalysis processes.[43,48,71] The quasi-relativistic MWB46 pseudopotentials,[72] which described 46 core electrons, and the appropriate contracted basis sets were used for I atoms, while the standard 6-31G* basis sets were used for all other atoms. No symmetry restrictions were applied during the geometry optimizations. The Hessian matrices were calculated analytically for all optimized model structures to prove the location of the correct minimum or saddle point on the potential energy surface (no imaginary frequencies or only one imaginary frequency, respectively). The Cartesian atomic coordinates for all model structures are presented in xyz-file (**Supplementary Materials**).

Conflicts of interest

There are no conflicts to declare.

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Electronic supplementary information: Synthesis of the sulfonium salt **Cat1**^{OTf}; Synthesis of the sulfonium salt **Cat2**^{OTf}; Synthesis of the sulfonium salt **Cat3**^{OTf}; Spectra of **Cat1**^{OTf}–**Cat3**^{OTf}; Representative ^{1}H NMR monitoring spectra; Derivation of equations for calculating the reaction rate constants; **Table S1**. Calculated total electronic energies (E, in Hartree), enthalpies (H, in Hartree), Gibbs free energies (G, in Hartree), and entropies (S, cal/mol•K) for optimized equilibrium model structures.

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