Mechanistic Investigation of DBU-Based Ionic Liquids for Aza-Michael Reaction: 
Mass Spectrometry and DFT Studies of Catalyst Role

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1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU)-based ionic liquids (ILs) has exhibited a high 
catalytic activity in the aza-Michael reactions compared to conventional catalysts and with 
imidazole-based ILs. In the present work DBU-based ILs showed high catalytic potential for 
aza-Michael addition of aromatic amines to 2-cyclohexen-1-one under solvent-free condition. 
Electrospray ionization-mass spectrometry (ESI-MS) and density functional theory studies 
have been carried out to provide an effective activation mode of DBU-based ILs in aza-Michael 
addition. Our results show that both the presence of the acid hydrogen in the IL and the ability 
of the anion to carry out a hydrogen bond with the −NH2 group of the arylamine are fundamental 
for the reaction catalysis. The catalytic model proposed can be used for the rational development 
of new ILs with excellent catalytic properties.

Keywords: conjugate addition, aromatic amines, reaction mechanism, theoretical calculations, 
ESI-MS studies

Introduction

The aza-Michael additions can be used for C−N bond formation by the reaction of α,β-unsaturated 
carbonyl compounds with amines. The products β-aminocarbonylic are important intermediates for the 
synthesis of β-aminoalcohol, β-amino acid derivatives, and β-aminocarbamates, that are bioactive compounds.1-4

It was usually catalyzed by strong base or a Lewis acid, ultrasound, heterogeneous solid acid, ionic amino 
acids, etc.5-11 However, there are still many deficiencies of these catalysts mentioned above, such as the requirement 
of long reaction time, harsh reaction conditions, many side reactions and mainly most of the reported methods12-15 
are successful only with aliphatic amines and lead to low conversions for aromatic amines.

Toward this directive, the organocatalytic ionic liquids (ILs) has shown to be efficient in promoting the aza-Michael 
addition.16-22 Notably, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)-based ILs has exhibited a high catalytic activity 
in the aza-Michael reactions compared to conventional catalysts and with imidazole-based ILs.1,23-27 However, the 
effective role of catalysis by DBU-based ILs has not been completely investigated and to know the catalytic model is 
very important for designing and developing ionic liquids with excellent catalytic properties.

In this work, we evaluated the catalytic efficiency of DBU-based ILs (Scheme 1) by mass spectrometry (MS) 
and density functional theory (DFT) studies to provide a catalytic model in aza-Michael additions. For a better 
mechanistic understanding of aza-Michael IL-catalyzed reaction, a few questions need to be addressed: (i) the real 
role of the protic cation in the title reaction, DBU-based ILs with aprotic cation can also activate the substrate?; 
(ii) what is the effective function of the anion in the reaction? Accordingly, our results will provide important 
basis into the DBU-based IL activation mode and can be used to rational design of new organocatalysts.

Experimental

1H and 13C nuclear magnetic resonance (NMR) were recorded on a Bruker Avance III HD spectrometer operating 
at 500 MHz for 1H and 125 MHz for 13C in D2O and CDCl3. Chemical shifts (δ) were reported in parts per million (ppm), 
relative to the internal standard of 2,2-dimethyl-
2-silapentane-5-sulfonate (DSS). Mass spectrometry data were obtained on Impact II, Bruker Daltonics Corporation, Germany, using electrospray ionization source (ESI) positive mode.

[HDBU][Ac], [HDBU][TFA] and [HDBU][OTs], TFA: trifluoroacetate, were obtained according to procedures previously described in the literature. ILs and Michael adducts were characterized by NMR analysis.

**General procedure for preparation of ionic liquid [HDBU][HSO₄] and [HDBU][Br]**

DBU (1.5 mL, 10 mmol) and acetonitrile (3 mL) were charged into a 25 mL round-bottom flask. Then, the mixture was taken at 0 °C and H₂SO₄ (0.6 mL, 10 mmol) or 48% HBr (1.1 mL, 20 mmol) was added dropwise keeping the temperature at 0-5 °C. After addition, the mixture was stirred for 2 h at room temperature. The solution was washed repeatedly with ether (3 × 5 mL) to remove non-ionic residues and the oil residues was dried in vacuum at 60 °C for 12 h to afford desired ionic liquids as light yellow viscous liquids.

**[HDBU][HSO₄]**

¹H NMR (500 MHz, D₂O) δ 3.52-3.50 (m, 2H, H₉), 3.48-3.45 (m, 2H, H₁₁), 3.28-3.25 (m, 2H, H₂), 2.58-2.56 (m, 2H, H₆), 1.98-1.93 (m, 2H, H₁₀), 1.71-1.62 (m, 6H, H₃, H₄, H₅); ¹³C NMR (125 MHz, D₂O) δ 165.9, 54.1, 48.2, 37.9, 32.7, 28.4, 25.8, 23.3, 18.7.

**[HDBU][Br]**

¹H NMR (500 MHz, D₂O) δ 3.58-3.56 (m, 2H, H₉), 3.54-3.52 (m, 2H, H₁₁), 3.34-3.31 (m, 2H, H₂), 2.64-2.52 (m, 2H, H₆), 2.04-1.99 (m, 2H, H₁₀), 1.76-1.66 (m, 6H, H₃, H₄, H₅); ¹³C NMR (125 MHz, D₂O) δ 165.9, 54.2, 48.2, 38.0, 32.7, 28.4, 25.9, 23.3, 18.9.

**General procedure for preparation of [HDBU][BF₄]**

[HDBU][Br] (1.4 g, 6 mmol) and acetonitrile (5 mL) were charged into a 25 mL round-bottom flask. Then, NaBF₄ (0.7 g, 6 mmol) was added and the mixture was stirred for 24 h at 80 °C. The solution was filtered to remove NaBr and the solid was washed repeatedly with dichloromethane. The solvent was removed under reduced pressure and oil residues was dried in vacuum at 60 °C for 12 h to afford a light yellow viscous liquid.

¹H NMR (500 MHz, D₂O) δ 3.58-3.56 (m, 2H, H₉), 3.55-3.52 (m, 2H, H₁₁), 3.34-3.32 (m, 2H, H₂), 2.64-2.62 (m, 2H, H₆), 2.05-2.00 (m, 2H, H₁₀), 1.77-1.68 (m, 6H, H₃, H₄, H₅); ¹³C NMR (125 MHz, D₂O) δ 165.9, 54.1, 48.2, 38.0, 32.8, 28.5, 23.3, 18.9.

**General procedure for preparation of [BDBU][Br]**

DBU (1.5 mL, 10 mmol) and cyclohexane (5 mL) were charged into a 25 mL round-bottom flask. Then, bromobutane (1.2 mL, 17 mmol) was added for 1 h at room temperature and stirred for another 5 h at 60 °C. [BDBU][Br]
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To a mixture of the aromatic amine (1 mmol) and cycloexen-2-one (1 mmol) in 25 mL flask equipped with a magnetic stirrer, ionic liquid was added (0.3 equiv.). The reaction mixture was stirred at room temperature for the desired time. Upon completion of the reaction, the mixture was diluted with water (H₂O, 3 mL) and extracted with ethyl acetate (3 × 5 mL). The combined organic phase was concentrated through vacuum evaporation and the resulting crude product was analyzed by ¹H NMR. The ionic liquid after extraction was dried in vacuo at 60 °C for 5 h. The recovered ionic liquid was then reused in subsequent reactions.

3-Phenyldiamino-cyclohexan-1-one (3a)

¹H NMR (500 MHz, CDCl₃) δ 7.19-7.15 (m, 2H), 6.74-6.72 (m, 1H), 6.61-6.59 (m, 2H), 3.81-3.76 (m, 1H), 3.59 (d, 1H, J 6.5 Hertz), 2.84 (d, 1H), J 14.4, 6.0 Hertz), 2.40-2.36 (m, 2H), 2.29-2.25 (m, 1H), 2.06-2.02 (m, 1H), 1.78-1.74 (m, 1H), 1.72-1.70 (m, 2H).

3-(4-Nitro)phenyldiamino-cyclohexan-1-one (3b)

¹H NMR (500 MHz, CDCl₃) δ 8.08 (d, 2H), J 9.2 Hertz), 6.55 (d, 2H), J 9.2 Hz), 4.71 (d, 1H), J 3.93-3.89 (m, 1H), 2.87-2.82 (m, 1H), 2.43-2.36 (m, 3H), 2.24-2.20 (m, 1H), 2.12-2.08 (m, 1H), 1.84-1.77 (m, 2H).

3-(2-Nitro)phenyldiamino-cyclohexan-1-one (3c)

¹H NMR (500 MHz, CDCl₃) δ 8.17-8.15 (d, 1H), J 8.6, 1.6 Hz), 7.46-7.42 (m, 1H), 6.85-6.83 (d, 1H), J 8.6 Hz), 6.69-6.67 (m, 1H), 3.99-3.64 (m, 1H), 2.89-2.84 (m, 1H), 2.48-2.39 (m, 3H), 2.32-2.17 (m, 1H), 2.16-2.11 (m, 1H), 1.87-1.77 (m, 2H).

3-(3-Nitro)phenyldiamino-cyclohexan-1-one (3d)

¹H NMR (500 MHz, CDCl₃) δ 8.05 (m, 1H), J 8.1, 2.2, 0.9 Hz), 7.40 (t, 1H), J 2.2 Hz), 7.29-7.28 (m, 1H), 6.88-6.86 (m, 1H), J 8.1, 2.2, 0.9 Hz), 3.72-3.87 (m, 1H), 2.88-2.83 (m, 1H), 2.41-2.35 (m, 3H), 2.25-2.20 (m, 1H), 2.12-2.06 (m, 1H), 1.86-1.76 (m, 2H).

3-(2-Fluoro)phenyldiamino-cyclohexan-1-one (3e)

¹H NMR (500 MHz, CDCl₃) δ 8.03-6.99 (m, 1H), 6.95-6.93 (m, 1H), 6.81-6.78 (m, 1H), 6.76-6.67 (m, 1H), 3.91-3.87 (m, 1H), 2.88-2.84 (m, 1H), 2.39-2.33 (m, 3H), 2.26-2.22 (m, 1H), 2.09-2.06 (m, 1H), 1.76-1.70 (m, 2H).

3-(4-Fluoro)phenyldiamino-cyclohexan-1-one (3f)

¹H NMR (500 MHz, CDCl₃) δ 6.88 (d, 2H), J 8.9 Hz), 6.54 (d, 2H), J 8.9, 4.4 Hz), 3.73-3.68 (m, 1H), 3.54 (d, 1H), 2.83-2.78 (m, 1H), 2.37-2.25 (m, 3H), 2.19-2.14 (m, 1H), 2.07-2.02 (m, 1H), 1.76-1.66 (m, 2H).
3-(2-Methoxy)phenylamino-cyclohexan-1-one (3g)

1H NMR (500 MHz, CDCl3) δ 6.88 (ddd, 1H, J 7.7, 7.7, 1.5 Hz), 6.80 (dd, 1H, J 8.0, 1.5 Hz), 6.70 (ddd, 1H, J 7.7, 7.7, 1.5 Hz), 6.62 (dd, 1H, J 8.0, 1.5 Hz), 3.85 (s, 3H), 3.79-3.75 (m, 1H), 2.87-2.83 (m, 1H), 2.38-2.30 (m, 3H), 2.24-2.19 (m, 1H), 2.10-2.04 (m, 1H), 1.77-1.70 (m, 2H).

3-(4-Methoxy)phenylamino-cyclohexan-1-one (3h)

1H NMR (500 MHz, CDCl3) δ 6.78 (d, 2H, J 8.9 Hz), 6.58 (d, 2H, J 8.9 Hz), 3.74 (s, 3H), 3.71-3.66 (m, 1H), 2.80 (m, 1H), 2.39-2.33 (m, 3H), 2.18-2.16 (m, 1H), 2.03-2.02 (m, 1H), 1.76-1.70 (m, 2H).

3-(4-Chloro)phenylamino-cyclohexan-1-one (3i)

1H NMR (500 MHz, CDCl3) δ 7.13 (d, 2H, J 8.9 Hz), 6.52 (d, 2H, J 8.9 Hz), 3.75 (m, 1H), 2.84-2.80 (m, 1H), 2.38-2.31 (m, 3H), 2.20-2.17 (m, 1H), 2.05-2.02 (m, 1H), 1.79-1.70 (m, 2H).

3-(4-Bromo)phenylamino-cyclohexan-1-one (3j)

1H NMR (500 MHz, CDCl3) δ 7.25 (d, 2H, J 9.0 Hz), 6.47 (d, 2H, J 8.5 Hz), 3.76-3.69 (m, 1H), 2.82-2.78 (m, 1H), 2.37-2.29 (m, 3H), 2.18-2.14 (m, 1H), 2.05-2.03 (m, 1H), 1.77-1.70 (m, 2H).

3-(4-Methyl)phenylamino-cyclohexan-1-one (3k)

1H NMR (500 MHz, CDCl3) δ 7.00 (d, 2H, J 8.5 Hz), 6.54 (d, 2H, J 8.5 Hz), 3.75 (m, 1H), 2.82 (m, 1H), 2.37-2.31 (m, 3H), 2.25 (s, 3H), 2.20-2.17 (m, 1H), 2.05-2.02 (m, 1H), 1.76-1.69 (m, 2H).

3-Imidazole-cyclohexan-1-one (3l)

1H NMR (500 MHz, CDCl3) δ 7.49 (s, 1H), 7.00 (t, 1H, J 1.18 Hz), 6.93 (t, 1H, J 1.39 Hz), 4.74 (m, 1H), 2.78 (m, 1H), 2.44-2.33 (m, 3H), 2.29-2.26 (m, 1H), 2.05-2.01 (m, 1H), 1.74-1.64 (m, 2H).

3-(1-Naphthylamino)-cyclohexan-1-one (3m)

1H NMR (500 MHz, CDCl3) δ 7.85-7.80 (m, 2H), 7.49-7.46 (m, 2H), 7.37-7.30 (m, 2H), 6.80 (dd, 1H, J 6.9, 1.5 Hz), 4.21 (s, 1H), 4.01 (m, H), 2.98 (m, 1H), 2.38-2.33 (m, 3H), 2.14-2.09 (m, 1H), 2.05-2.03 (m, 1H), 1.88-1.83 (m, 2H).

General procedure for ion-fishing of supramolecular adduct using ESI(+)-MS

A mixture of aniline (0.24 mL, 2.6 mmol) and cycloexen-2-one (0.25 mL, 1.0 equiv, 2.6 mmol) was stirred magnetically at room temperature in the presence of ionic liquid (0.3 equiv). After 15 min, an aliquot portion (10 μL) of the reaction mixture was taken out by micro pipette and dissolved in acetonitrile (1 mL) and when necessary, formic acid (1%). From the resultant solution an aliquot amount (50 μL) was subjected to ESI(+)-MS. Sampling was performed every 15 min for 120 min of reaction.

The ion-fishing study was performed on a high-resolution mass spectrometer (Impact II, Bruker Daltonics Corporation, Germany), equipped with an electrospray ionization source. The capillary voltage was operated in positive ionization mode, set at 4000 V and with an end plate potential of −500 V. The dry gas parameters were set to 10 μL min⁻¹ at 180 °C with a nebulization gas pressure of 0.4 bar. Data were collected from m/z 50-500 with an acquisition rate of 5 spectra per s, and the ions of interest were selected to MS/MS fragmentation.

Computational methods

Theoretical calculations were performed with the Gaussian 09 program package, revision B.01. The PyMOL program was used to visualize structures and surfaces. The structures of supramolecular complexes were optimized using the density functional method M06-2X coupled with the 6-31++G(d,p) basis set function. Frequency calculations were performed to characterize the structure as a minimum or as a transition state (TS) and to obtain the zero-point energy (ZPE) and thermal correction to Gibbs free energy. Corrections due to basis set superposition error (BSSE) were also calculated at the same level of theory for the complexes. In order to confirm that the transitional state connects the desired reaction, intrinsic reaction coordinate (IRC) calculations were performed at the same level of theory of the optimizations.

Results and Discussion

Synthesis and catalytic potential evaluation of the DBU-based ILs

The route to synthesize the DBU-based ILs and their structures are presented in Scheme 1. The synthetic procedures and the characterization are discussed in details in the Experimental section. [HDBU][Ac], [HDBU][TFA] and [HDBU][OTs] were obtained in a single step with the addition of the carboxylic acid directly to the DBU base, according to procedures previously described in the literature. The ILs [HDBU][HSO4], [HDBU][BF4], [BDBU][HSO4] and [BDBU][BF4] were obtained according to the methodology used to obtain imidazole-based ILs. [HDBU][HSO4] was obtained in a single step from the
reaction of DBU with H$_2$SO$_4$ in acetonitrile. However, the [BDBU][HSO$_4$] and [BDBU][BF$_4$] were obtained in two steps, from DBU reaction with butyl bromide leading to the formation of [BDBU][Br], followed by anion exchange in the presence of NaBF$_4$, respectively. [HDBU][BF$_4$] was also obtained in two steps, from DBU reaction with hydrobromic acid leading to the formation of [HDBU][Br], followed by anion exchange in the presence of NaBF$_4$. All ILs were obtained in satisfactory yields (90-96%) and were characterized by NMR analysis (see, Supplementary Information (SI) section).

Firstly, the catalytic potential of the ILs was evaluated for the aza-Michael addition of aniline to 2-cyclohexene-1-one (Table 1). For comparison, some imidazolium ILs were also used in the model reaction. A summary of the results obtained is provided in Table 1.

Table 1. Aza-Michael addition of aromatic amines to 2-cyclohexene-1-one catalyzed by ILs.

| IL           | entry | Conversion$^a$ / % | X: H | entry | Conversion$^a$ / % | X: NO$_2$ |
|--------------|-------|--------------------|------|-------|--------------------|----------|
| [HDBU][Ac]   | 1     | 85 (58)$^a$        |      | 12    | 32                 |          |
| [HDBU][TFA]  | 2     | 87                 |      | 13    | 84                 |          |
| [HDBU][OTs]  | 3     | 42                 |      | 14    | 89                 |          |
| [HDBU][BF$_4$]| 4     | 83                 |      | 15    | 75                 |          |
| [HDBU][HSO$_4$]| 5    | 82 (80)$^a$        |      | 16    | 91 (89)$^a$        |          |
| [BDBU][HSO$_4$]| 6   | 80$^a$             |      | 17    | 17$^b$             |          |
| [BDBU][BF$_4$]| 7     | 39                 |      | 18    | 18                 |          |
| [Hmin][HSO$_4$]| 8   | 35                 |      | 19    | 86                 |          |
| [Bmin][HSO$_4$]| 9   | 79                 |      | 20    | 90                 |          |
| [Bmin][OH]   | 10    | 68$^a$             |      | 21    | 21                 |          |

$^a$Reaction conditions: aromatic amines (1 mmol), cyclohexene (1 mmol), IL 0.3 mol%; $^b$determined by $^1$H NMR; $^c$reaction for 3 h; $^d$reaction at 60 °C; $^e$no reaction; $^f$reference 17, reaction for 9 h. IL: ionic liquid; DBU: 1,8-diazabicyclo[5.4.0]undec-7-ene; TFA: trifluoroacetate.

Ionic liquids [HDBU][Ac], [HDBU][TFA], [HDBU][BF$_4$] and [HDBU][HSO$_4$] were found to be very effective and afforded the desired aza-Michael adduct in high conversion rates at room temperature and solvent free conditions (Table 1, entries 1, 2, 4 and 5, respectively). Since [BDBU][HSO$_4$] is a very viscous ILs the reaction was performed at 60 °C (Table 1, entry 6).

The low catalytic efficiency of [BDBU][BF$_4$] suggests that the protic cation plays a relevant role in the catalysis of the reaction (Table 1, entry 7). However, the high catalytic efficiency of [HDBU][HSO$_4$] led us to believe that the protic anion also could be responsible for catalysis (Table 1, entry 6).

The efficiency of the ILs on the addition of p-nitroaniline, a poor nucleophile, to 2-cyclohexen-1-one has also been assessed. [HDBU][TFA], [HDBU][OTs], [HDBU][BF$_4$] and [HDBU][HSO$_4$] showed to be very effective at room temperature and solvent free conditions (Table 1, entries 13-16). It is important to note that the reaction with [HDBU][HSO$_4$] occurred in a shorter time (3 h) than for the other evaluated ILs (5 h) without significant decrease in yield. Among imidazolium ILs used, only [Bmin][HSO$_4$] promoted the reaction with an efficiency comparable to [HDBU][HSO$_4$].

With the efficient catalytic system in hand, we examine the utility and generality of a wide range of aromatic amines for the [HDBU][HSO$_4$]-aza-Michael reactions using cyclohexene-2-one as substrate. All results summarized in Table 2 showed good to excellent conversion rates (entries 1-11), including aromatic amines with high electron-withdrawing group at benzene ring (entries, 1-3). Four novel adducts (3c, 3d, 3g and 3m) were obtained (Table 2, entries, 1, 2, 5 and 11) showing the great versatility of the ionic liquid [HDBU][HSO$_4$]. In addition, [HDBU][HSO$_4$] presented a lower reaction time when compared to other DBU derivatives reported in the literature, showing to be an excellent catalyst for the

Table 2. Aza-Michael addition of aromatic amines to 2-cyclohexene-1-one catalyzed by [HDBU][HSO$_4$]$^a$

| entry | Amine | Product | Conversion$^a$ / % |
|-------|-------|---------|--------------------|
| 1     | \(\alpha\)-NO$_2$C$_6$H$_4$NH$_2$ | 3c      | 87                 |
| 2     | \(m\)-NO$_2$C$_6$H$_4$NH$_2$ | 3d      | 87                 |
| 3     | \(\alpha\)-F-C$_6$H$_4$NH$_2$ | 3e      | 93                 |
| 4     | \(p\)-F-C$_6$H$_4$NH$_2$ | 3f      | 91                 |
| 5     | \(\alpha\)-OCH$_3$C$_6$H$_4$NH$_2$ | 3g      | 83                 |
| 6     | \(p\)-OCH$_3$C$_6$H$_4$NH$_2$ | 3h      | 71                 |
| 7     | \(p\)-Cl-C$_6$H$_4$NH$_2$ | 3i      | 85                 |
| 8     | \(p\)-Br-C$_6$H$_4$NH$_2$ | 3j      | 85                 |
| 9     | \(p\)-CH$_3$C$_6$H$_4$NH$_2$ | 3k      | 78                 |
| 10    | imidazole | 3l      | 74                 |
| 11    | 1-naphthylamine | 3m      | 65                 |

$^a$Reaction conditions: aromatic amines (1 mmol), Michael acceptors (1 mmol), 0.3 mol% [HDBU][HSO$_4$], 3 h, rt; $^a$determined by \(^1\)H NMR.
aza-Michael reaction of aromatic amines, which present low reactivity with other ILs. As per the literature survey, till date, there have been no reports on the use of [HDBU] [HSO₄] as catalyst for carrying out aza-Michael addition between various deactivated arylamines with Michael acceptor.

**Supramolecular assembly by ESI-MS study**

Electrospray ionization mass spectrometry (ESI-MS) study was performed to investigate effective catalyst role in the aza-Michael addition for the reaction between 2-cyclohexen-1-one (1a) and aniline (2a) using different DBU-based ionic liquids. The catalytic role of DBU-based IL with the substrates is envisaged through the formation of the non-covalent complex (NCC) by electrophile nucleophile dual activation (Scheme 2) similar to related in literature for [Bmin][MeSO₄].

The total ion chromatogram (TIC) from the [HDBU] [HSO₄] catalyzed reaction (Figures S19 and S20, SI section) revealed the presence of ions at m/z 439.2708 (m₁), 364.2243 (m₂), 361.2246 (m₃), 343.2142 (m₄), 286.1781 (m₅), 268.1677 (m₆), 190.1216 (m₇), 172.1111 (m₈), 153.1385 (m₉) and 94.0648 (m₁₀), which are corresponding to [NCC], [imine + 2 × 1a + H⁺], [imine + 3a + H⁺], [2 × imine + H⁺], [1a + 3a + H⁺], [imine + 1a + H⁺], [3a + H⁺], [imine + H⁺], [DBU + H⁺] and [2a + H⁺], respectively.

The support for determination of non-covalent complex was obtained from the mass (MS/MS) studies of 439.2684 (m₁) ion observed in the TIC. ESI(+)-MS/MS revealed the presence of ions at m/z 346.2118, 268.1660, 250.1556 and 172.1098 that are assigned in Figure 1.

The TICs for the reactions between 2-cyclohexen-1-one and aniline with ILs [HDBU][Ac], [HDBU][TFA], [HDBU][OTs] and [HDBU][BF₄] also show the ions of the supramolecular complexes, suggesting that these ILs catalyze the aza-Michael addition in the same way that [HDBU][HSO₄].

On the other hand, the TIC from the reaction between 2-cyclohexen-1-one and aniline with [BDBU][HSO₄] (Figures S30, S31 and S32, SI section), revealed only the presence of ions at m/z 268.1693 (d₁), 209.2012 (d₂), 190.1224 (d₃), 172.1118 (d₄), 153.1384 (d₅) and 94.0650 (d₆) corresponding to [imine + 1a + H⁺], [BDBU]⁺, [3a + H⁺], [imine + H⁺], [DBU + H⁺], [2a + H⁺], [BDBU][HSO₄] was not detected (m/z 495.2767).

These results are in accordance with the catalytic model proposed (Scheme 2), pointing out that the protic cation plays a relevant role in the catalysis of the reaction. In this model, there are the formation of a non-covalent complex (Scheme 2) in which the acidic hydrogen of cation DBU forms a hydrogen bond with the carbonyl oxygen of Michael acceptor (1a) (electrophilic activation), while the oxygen atom of one of the S=O group in HSO₄⁻ forms a hydrogen bond with the N−H hydrogen of aromatic amine and drives the β-carbon attack (nucleophilic activation). Nucleophilic attack followed by transfer of proton from the NH₂ group of 2a through the hydrogen bridge in the hydrogen bonded cluster to the carbonyl oxygen of 1a forms the enol of the aza-Michael adduct 3a and brings the IL back to the catalytic cycle. In the case of [BDBU][HSO₄], we suppose that the reaction occurs by another path, where the acidic hydrogen of the anion may be activating the carbonyl of 2a.

The decrease in the conversion of 3a using [BDBU][BF₄] (Table 1, entry 8) that has an aprotic cation (moiety that

![Scheme 2](image-url)
supports electrophilic activation) and also do not have acidic hydrogen in the anion corroborate the catalyst role proposed (Scheme 2).

ESI-MS analysis was also performed for the reaction between 2-cyclohexen-1-one (1a) and cyclohexylamine (2b) with [HDBU][HSO₄] to evaluate if aza-Michael addition of aliphatic amines occurs by the same mechanism proposed for the aromatic amines. For this reaction, an equivalent mass pattern for the non-covalent complex (m/z 445.2610) between the reactants and IL was not detected in the TIC (Figure S33, SI section). Aliphatic amines are not good donor of N−H hydrogen to form the hydrogen bond with the IL anion, which is determinant for the formation of the non-covalent complex. This result confirms that the nucleophilic activation by the IL anion had crucial role in aza-Michael addition of aromatic amines.

Theoretical investigation of mechanism reaction

The purpose of including the theoretical study here was to corroborate the catalytic role proposed from experimental analysis. For the reaction with [HDBU][HSO₄] were optimized: a transition state for each reaction step (TS1 and TS2); an initial complex involving reagents and the IL; a complex involving the intermediate and the IL; and a complex involving the Michael products and the IL. The results obtained from the mass spectrometry experiments were used for the rational construction of the complex involving the reagents and also for the TS1 transition state.

The optimized structures and the energy diagram for the aza-Michael addition are shown in Figure 2. The dotted lines indicate for transitional states a normal vibration coordinate. The transition state for the first step of the reaction (TS1), involving the addition of aniline to β-carbon of 2-cyclohexen-1-one was characterized by IRC calculations. In TS1 is observed the approximation of the nitrogen of 2a to the β carbon of 1a, one of the hydrogen of the amino group of 2a toward HSO₄⁻ anion and two interactions toward carbonyl oxygen of 1a, one of the acidic hydrogen of the cation and other of the anion hydrogen. This shows that both the cation and the counter ion play a key role in the catalysis of the reaction. These results are in agreement with the data obtained experimentally. When the IL is no protic, it is not possible to form the non-covalent complex and then this catalytic efficiency decreases, as verified for [BDBU][BF₄] (Table 1, entry 8). In TS2, it is observed the transfer of a hydrogen from sulfuric acid to the α carbon of the enol and the removal of the hydrogen from the carbonyl protonated by the DBU, restoring the ionic liquid, according catalytic cycle proposed (Scheme 1).

Calculated Gibbs energy shows that the products are more stable than reagents and intermediate (enol). The activation Gibbs energy calculated for TS1 is 20.2 kcal mol⁻¹, and for TS2 is 6.8 kcal mol⁻¹. Thus, the ionic liquid acts directly on the determining step of the reaction rate.

The results obtained for the [HDBU][Ac] and [HDBU][TFA] are similar and data are compiled in Table S1,
The detailed mechanism of aza-Michael adducts formation from 2-cycloexen-1-one with aromatic amines promoted by DBU-based ILs has been examined using ESI-MS experiments and DFT calculations. The cations and anions of ionic liquids are found to synergistically promote the addition reaction by nucleophilic activation and proton transfer and simultaneously stabilizing transition states by hydrogen bonding interaction. The non-covalent complex formed between reagents and ILs have been identified and characterized by ESI-MS. The mechanistic model proposed can be used as basis of rational design and selection of organocatalysts.

Supplementary Information

Supplementary information is available free of charge at http://jbcs.sbq.org.br as PDF file.

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Author Contributions

Gisele F. Gauze was responsible for the conceptualization, formal analysis, funding acquisition, project administration,
supervision, writing original draft, review and editing; Augusto A. Cândido for the investigation, methodology, validation, data curation and writing original draft; Thiago C. Rozada for the investigation, methodology, data curation, visualization and software of theoretical calculations; Andrew M. F. Rozada for investigation, methodology, formal analysis and writing original draft; João R. B. Souza for the investigation, methodology, data curation, visualization and ESI-MS experiments; Fernanda A. Rosa for the conceptualization, supervision, writing review and editing; Ermani A. Basso for the project administration, supervision, writing review and editing.

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