

# Mechanistic Insight into Self-Propagation of Organo-Mediated Beckmann Rearrangement: A Combined Experimental and Computational Study

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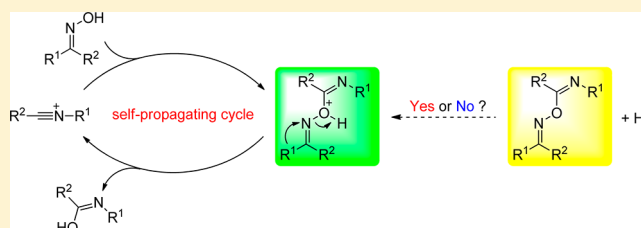
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## Supporting Information

**ABSTRACT:** Organo-mediated Beckmann rearrangement in the liquid phase, which has the advantage of high efficiency and straightforward experimental procedures, plays an important role in the synthesis of amides from oximes. However, the catalytic mechanisms of these organic-based promoters are still not well understood. In this work, we report a combined experimental and computational study on the mechanism of Beckmann rearrangement mediated by organic-based promoters, using TsCl as an example. A novel self-propagating cycle is proposed, and key intermediates of this self-propagating cycle are confirmed by both experiments and DFT calculations. In addition, the reason why cyclohexanone oxime is not a good substrate of the organo-mediated Beckmann rearrangement is discussed, and a strategy for improving the yield is proposed.



## INTRODUCTION

Beckmann rearrangement (BKR), as a classic rearrangement of oximes, offers a useful method to construct amides and lactams.<sup>1</sup> However, traditional BKR usually requires harsh conditions and generates a large amount of byproduct.<sup>2</sup> Recently, many catalytic systems, such as vapor phase,<sup>3</sup> supercritical water,<sup>4</sup> ionic liquids,<sup>5</sup> and small molecule involved liquid-phase systems,<sup>6</sup> have been developed. Organo-mediated BKR in liquid phase are attracting more attention because of their high efficiency and straightforward experimental procedures. Cyanuric chloride (CNC),<sup>7</sup> reported by Ishihara and co-workers, is the first highly efficient organic-based promoter for BKR. Other promoters, such as bis(2-oxo-3-oxazolidinyl)-phosphinic chloride (BOP-Cl),<sup>8</sup> 1,3,5-triazo-2,4,6-triphosphorine-2,2,4,4,6,6-chloride (TAPC),<sup>9</sup> *p*-toluenesulfonyl chloride (TsCl),<sup>10</sup> 1-chloro-2,3-diphenylcyclo-propenium ion,<sup>11</sup> bromodimethylsulfonium bromide–zinc chloride (BDMS–ZnCl<sub>2</sub>),<sup>12</sup> propylphosphonic anhydride (T3P),<sup>13</sup> and triphenylphosphine/iodine (Ph<sub>3</sub>P/I<sub>2</sub>),<sup>14</sup> were also reported.

In the CNC system, a Meisenheimer complex intermediate, which links the substrate ketoxime and the product amide, has been proposed.<sup>7</sup> Most of the proposed mechanisms for organo-mediated BKR resemble that of CNC.<sup>8,10,11</sup> Recently, Lambert suggested that those organo-mediated BKR might instead use a reagent initiated and subsequently self-propagating mechanism via a dimer-like intermediate,<sup>15</sup> which is similar to a mechanism proposed by Chapman in 1935.<sup>16</sup> Unfortunately, the dimer-like key intermediate has never been experimentally

observed in the BKR. In addition, whereas organic-based promoters carry out the BKR of aromatic oximes efficiently, upon using cyclohexanone oxime as substrate (important for producing 6-nylon), the yield is not satisfied in the presence of the normal load of promoters.<sup>8–13</sup> For example, using the CNC promoter, a 5 mol % CNC load gives 97% yield of acetanilide for acetophenone oxime, while a 10 mol % CNC load gives only 30% yield of caprolactam.<sup>7</sup> As none of the previously proposed mechanisms discuss the poor performance of organic-based promoters for the BKR of cyclohexanone oxime, a more detailed study on the mechanism of cyclohexanone oxime is required. We herein report a combined experimental and computational study on the mechanism of BKR mediated by organic-based promoters, using TsCl as an example. The reason why cyclohexanone oxime is not a good substrate for the organo-mediated BKR is also discussed.

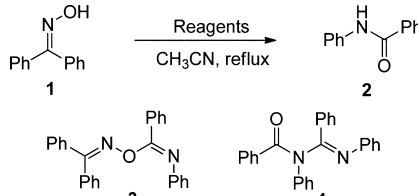
## RESULTS AND DISCUSSION

**Self-Propagation Mechanism in TsCl-Mediated Beckmann Rearrangements.** Based on Ishihara's mechanism, we proposed a similar mechanism for the BKR using TsCl.<sup>10</sup> However, our <sup>18</sup>O isotopic tracing experiment disapproves Ishihara's mechanism, and we then proposed a new mechanism similar to Lambert and Chapman's self-propagation mechanism.<sup>9b</sup> In order to prove this self-propagation mechanism, a

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dimer-like compound **3**<sup>16</sup> was synthesized and was used to catalyze the rearrangement of benzophenone oxime.<sup>17</sup> Interestingly, **3** does not catalyze BKR (Table 1, entry 1), suggesting

**Table 1.** BKR of Benzophenone Oxime **1** with Different Reagents<sup>a</sup>

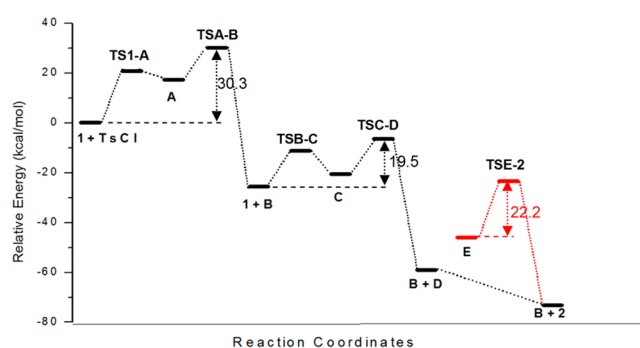


entry	reagents (mol %)	conversion of <b>1</b> (%)	yield of <b>4</b> (%)
1	<b>3</b> (10)	0	
2	HCl (10)	46	
3	<b>3</b> (10) + HCl (10)	92	12 <sup>b</sup>
4 <sup>c</sup>	TsCl (2)	100	

<sup>a</sup>The rearrangement of benzophenone oxime (**1** mmol) was carried out in anhydrous CH<sub>3</sub>CN (3 mL) at 90 °C for 2 h. <sup>b</sup>Data based on **3**. <sup>c</sup>The rearrangement of benzophenone oxime (**1** mmol) was carried out in anhydrous CH<sub>3</sub>CN (2 mL) at 90 °C for 1 h.

that **3** is not the catalyst for the self-propagating cycle. To better understand the self-propagating mechanism, DFT calculations were then systematically performed on the TsCl-mediated BKR.

The BKR of the benzophenone oxime **1** initiated by TsCl is described in Scheme 1, and the energies of the key intermediates are shown in Figure 1. In cycle I, **1** first reacts with TsCl forming **A**, followed by phenyl group migration of **A**, forming the nitrilium cation **B** and TsOH. Another molecule of **1** then attacks **B** to give a dimer-like cation intermediate **C**, which then retrieves **B** and releases **D** (the enol form of the product **2**). It should be noted that protonation of the oxygen of **C** reduces the barrier for the BKR of **C** because the positively charged oxygen atom would confer a strong attraction for electrons on the adjacent nitrogen (Scheme 1). As intermediate **C** might be a key intermediate of the self-propagating cycle I,

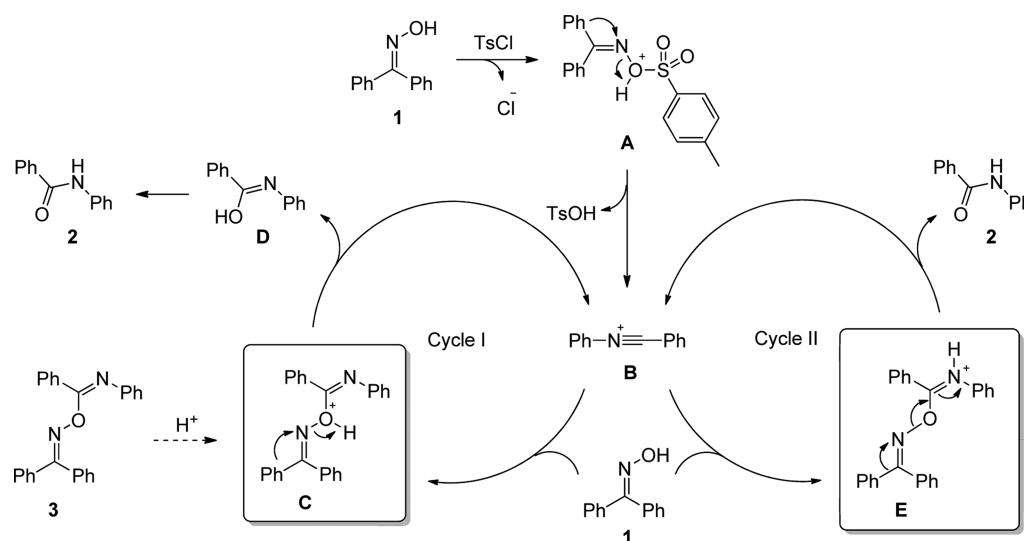


**Figure 1.** Relative free energy profile of the BKR of **1** mediated by TsCl; Gibbs free energies are at the M06-2X/6-31+G (d, p) level.

we use the cocatalyst **3** + HCl (10 mol %: 10 mol %, mimicking **C**) to catalyze the BKR of **1**. As expected, **3** + HCl can catalyze the BKR of **1**, and the efficiency thereof is much higher than using HCl or **3** individually (Table 1, entries 1–3). However, the catalytic efficiency of **3** + HCl is much lower than that of TsCl (Table 1, entries 3 and 4), and **4** was detected as a byproduct (Table 1, entry 4, crystal structure of **4**, see the Supporting Information). These results suggest that intermediate **C** cannot be completely replaced by **3** + HCl, and the reason might be 2-fold. First, the H<sup>+</sup> from HCl is not only added to the oxygen atom of **3**, but also added to the nitrogen atoms of **3** as well as other position such as the nitrogen and oxygen atoms of the substrate, the product, and even to the solvent molecules. Second, **3** easily reacts with HCl to give **4** under nitrogen (Experimental Section). Cycle II, which was proposed by Chapman<sup>16</sup> and Lambert,<sup>15</sup> was shown to be kinetically less favored than cycle I (rearrangement barriers for **C** and **E** are 14.3 and 22.2 kcal/mol, respectively; Scheme 1 and Figure 1). Therefore, based in Scheme 1, Figure 1 and Table 1, we suggest that **B** and **C** (from cycle I) are the two most likely intermediates for the organo-mediated BKR.

According to our calculations, the rate-limiting step of cycle I is the initialization step, with a barrier height 30.3 kcal/mol (Figure 1). Once **B** is generated, the catalytic cycle can be easily completed. The catalytic role of **B** has been confirmed by

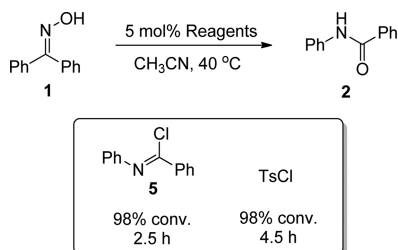
**Scheme 1.** Proposed Mechanisms for the TsCl-Mediated BKR of Benzophenone Oxime **1**<sup>a</sup>



<sup>a</sup>Cycle I is proposed by us; cycle II was proposed by Chapman and Lambert.<sup>15,16</sup>

Lambert using benzophenone oxime.<sup>15</sup> In our experiment, we found that both the *N*-phenylbenzimidoyl chloride (**5**;<sup>18</sup> 5 mol % load) and TsCl (5 mol % load) promote the BKR of **1** at 40 °C with excellent yields, and **5** seems to be more efficient than TsCl (2.5 h reaction time for **5** versus 4.5 h for TsCl; Scheme 2), suggesting that the initialization step for **5** is faster than that

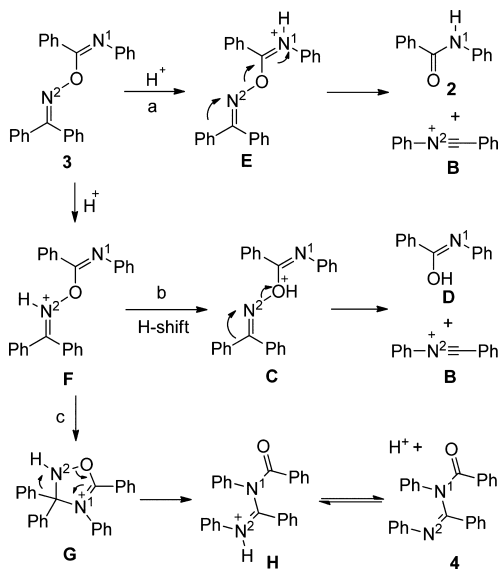
**Scheme 2. Comparison of the Reaction Rates of Imidoyl Chloride (**5**) and TsCl**



for TsCl. This is consistent with our computational results that the initialization step is rate-limiting for the BKR mediated by TsCl.

We then performed more calculations to better understand why **3** + HCl is less efficient than TsCl and how byproduct **4** is formed. Possible pathways are summarized in Scheme 3. H<sup>+</sup>

**Scheme 3. Possible Pathways for the **3** + HCl System**



may be added to three positions in **3**: N<sup>1</sup>, N<sup>2</sup>, and O, with the proton affinities being 267.4, 251.1, and 225.1 kcal/mol, respectively. Therefore, for compound **3**, protonation of N<sup>1</sup> or N<sup>2</sup> is more favored than that of O. Three possible pathways were then considered (Scheme 3): pathway a, N<sup>1</sup>-protonation forming **E**, followed by phenyl group migration giving **2** and **B** (similar to Lambert's mechanism;<sup>15</sup> entering catalytic cycle II); pathway b, N<sup>2</sup>-protonation and 1,2-H shift yielding the O-protonated intermediate **C**, followed by phenyl migration forming **D** and **B** (entering catalytic cycle I); pathway c, N<sup>2</sup>-protonation forming **F**, which undergoes intramolecular rearrangement via **G** and **H**, followed by deprotonation to give byproduct **4**.

For pathways a, b, and c, the rate-limiting barriers are 22.2, 23.0, and 26.9 kcal/mol, respectively (Figure 2), suggesting that

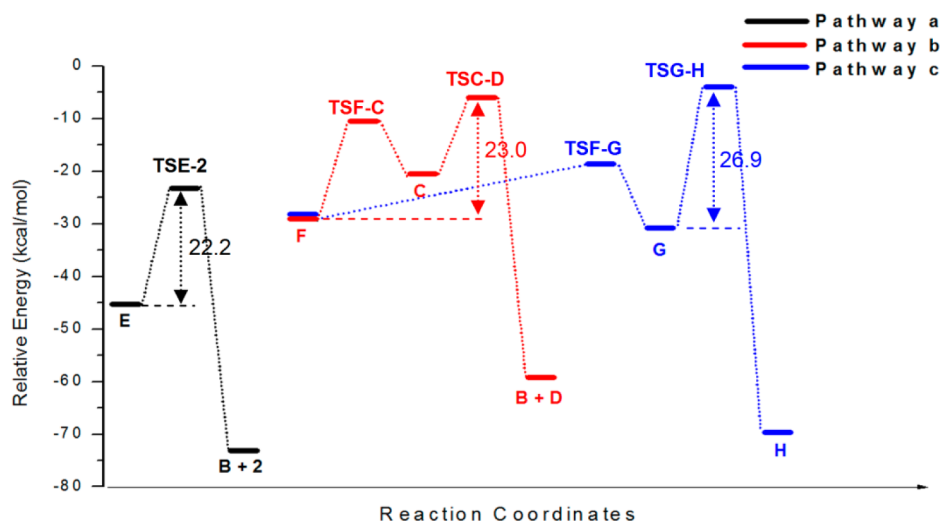
pathways a and b are kinetically more favored than pathway c. Hence, we suggest that the formation of **4** is not the main reason why **3** + HCl is less efficient than TsCl. We thus propose that in the **3** + HCl system, the H<sup>+</sup> from HCl may add to the nitrogen of substrate **1** (proton affinity 258.0 kcal/mol) as well as to other positions, making the effective concentration of **C** much lower than the load of **3**. In the TsCl system, on the other hand, a considerable amount of **B** is generated already at the initialization step. As mentioned above, the formation of **B** and **C** in situ is important for the organo-mediated BKR and cannot be replaced by **3** + HCl or classical BKR catalyzed by H<sup>+</sup>, where **B** is quenched by the H<sub>2</sub>O generated in the dehydration step before entering cycle I.

**Mechanism for the Beckmann Rearrangement of Cyclohexanone Oxime.** The BKR of cyclohexanone oxime **6** is of industrial significance. However, **6** is not a good substrate of the organo-mediated BKR. According to our calculations, the rate-limiting barrier for the BKR of **6** (25.6 kcal/mol; Scheme 4a and Figure 3) is lower than that of **1** (30.3 kcal/mol; Scheme 1 cycle I and Figure 1). However, the organo-mediated BKR of **6** generally has very low yield.<sup>8–13</sup> A likely reason is that the intermediate cation **J**, whose role is similar to **B**, is too reactive to continuously catalyze the reaction. **J** may be easily attacked by **6** or other nucleophiles, such as the product **7** (Scheme 4). The yield of byproduct **8**, which can be formed via **J** + **7** (Scheme 4b), is up to 30% in the TsCl-mediated BKR of **6**.<sup>9a,19</sup> The conversion **M** → **8** + H<sup>+</sup> is reversible (Scheme 4b), and **8** may be converted back to **J** + **7** via **M** when the concentration of **8** and H<sup>+</sup> increases.

Increasing the promoter load, which results in higher initial concentration of **J**, is currently the most common method for improving the yield of **7** in the BKR of **6**.<sup>10,15</sup> Although the percentage conversion of **6** generally increases with a larger promoter load, the selectivity between **7** and **8** is not significantly improved,<sup>19</sup> because the higher concentration of **J** may also lead to a larger amount of **8**. Computational results show that the C–N single bond between the two rings of **M** is weak (the estimated bond energy is 29.3 kcal/mol), suggesting that the sp<sup>2</sup> carbon atom in this C–N bond could be attacked by nucleophiles such as H<sub>2</sub>O and **6**. Further calculations show that the barrier height for the conversion **M** + H<sub>2</sub>O → **7** + **L** is 22.9 kcal/mol. As expected, under acidic conditions, **8** can react with H<sub>2</sub>O to give **7** (Scheme 5), and similar results were also reported elsewhere.<sup>9a</sup> In addition, the barrier height for the conversion **M** + **6** → **7** + **K** (Scheme 6) is 26.0 kcal/mol. Hence, we expect that adding both the organic-based promoter and acid may improve the yield of **7**, since H<sup>+</sup> could inhibit the formation of **8** from **M**, and the conversion **M** + **6** → **7** + **K** will drive **M** back to the catalytic cycle as shown in Scheme 4. Our hypothesis has been confirmed by Ishii et al.,<sup>20</sup> who used 0.5 mol % of CNC + 1.2 mL of TFA to promote the BKR of **6** to obtain 99% conversion of **6** and 99% yield of **7** (using 10 mol % of CNC or 2 mL of TFA individually cannot achieve this yield).

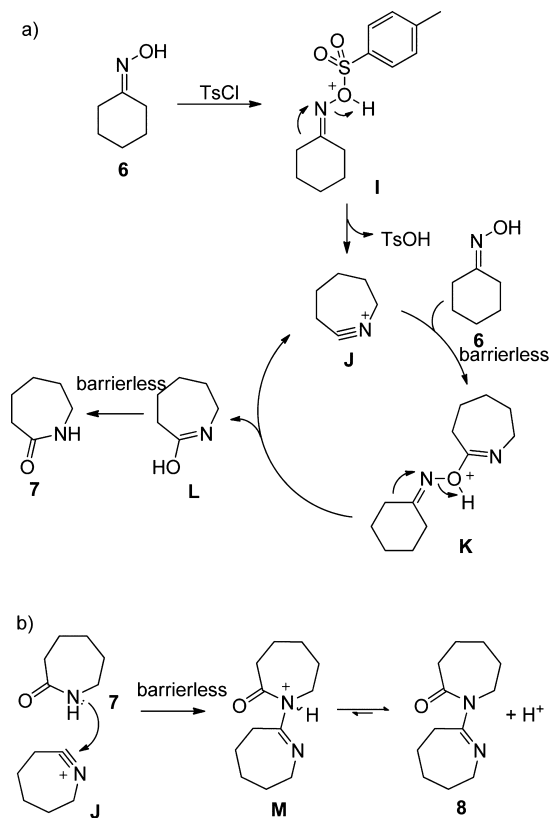
## CONCLUSION

The self-propagation mechanism of the BKR mediated by organic-based promoters has been studied using both experiments and DFT calculations. The nitrilium cation intermediate **B** and the dimer-like intermediate **C** are the two most likely intermediates of the self-propagating cycle. Intermediate **E**, which was proposed by Lambert et al.,<sup>15,16</sup> is shown to be kinetically less favored than **C**. We also found that intermediate **C** cannot be simply replaced by **3** + H<sup>+</sup>, suggesting that in situ

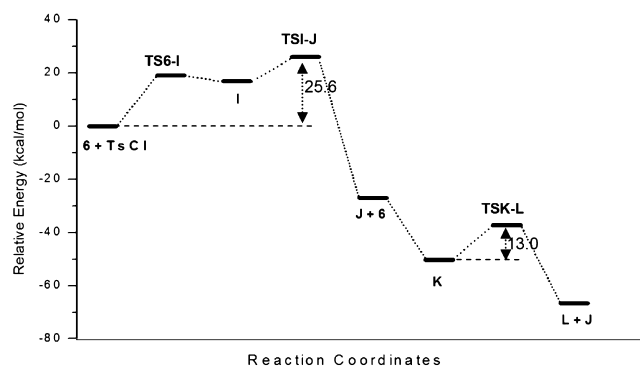


**Figure 2.** Comparison of relative free energies for the different pathways of the 3 + HCl system; Gibbs free energies are at the M06-2X/6-31+G (d, p) level.

#### Scheme 4. Proposed Pathways for the TsCl-Mediated BKR of Cyclohexanone Oxime (6)

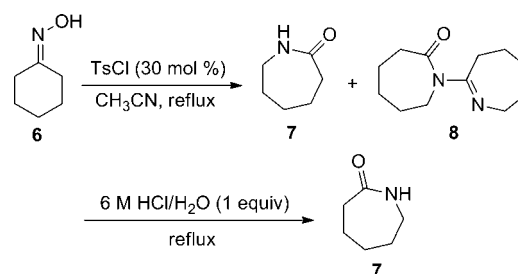


generated C is essential for the organo-mediated BKR in terms of high efficiency. In the BKR of cyclohexanone oxime 6, we found that the nitrilium cation intermediate J, whose role is similar to B, is too reactive to continuously catalyze the conversion 6 → 7. The formation of a dimer-like byproduct 8 was found to occur very easily *via* direct nucleophilic attack of 7 to the active species J, which we propose to account for the poor performance of organo-mediated BKR of cyclohexanone oxime. Furthermore, we propose that adding both the organic-

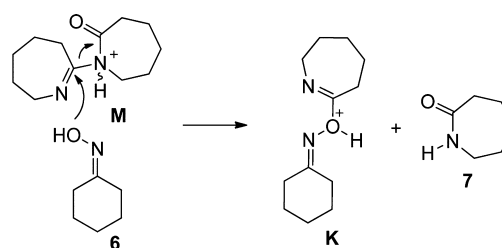


**Figure 3.** Relative free energy profile of the BKR of 6 mediated by TsCl; Gibbs free energies are at the M06-2X/6-31+G (d, p) level.

#### Scheme 5. Conversion of 8 to 7 in the Presence of H<sup>+</sup> and H<sub>2</sub>O



#### Scheme 6. Possible Pathway of M Attacked by 6 in the Presence of H<sup>+</sup>



based promoter and proper acid might improve the conversion of **6** and the selectivity of **7** by pushing **8** back to **K**.

## EXPERIMENTAL SECTION

**General Information.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a 400 MHz spectrometer. The progress of all reactions was monitored by TLC on precoated silica gel plates. Column chromatography was performed using silica gel (100–200 mesh) with ethyl acetate and petroleum ether as eluent, unless otherwise indicated. Solvents and reagents were obtained from commercial sources. Solvents were anhydrous unless otherwise noted.

**General Procedure for Beckmann Rearrangement of 1 (Table 1 and Scheme 2).** To a solution of benzophenone oxime **1** in anhydrous  $\text{CH}_3\text{CN}$  were added the corresponding reagents [**3**/HCl/(**3** + HCl)/TsCl/**5**] under a nitrogen atmosphere, and the reaction mixture was heated at the corresponding temperature (90 or 40 °C, depending on the reagents). After completion, the solution was concentrated on rotary vacuum evaporator and purified by column chromatography on silica gel (5% EtOAc/petroleum ether) to give the product *N*-phenylbenzamide (**2**). Mp: 164–165 °C (lit.<sup>21</sup> mp 164–165 °C).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.03 (s, 1H), 7.87 (d,  $J=7.3$  Hz, 2 H), 7.66 (d,  $J=7.9$  Hz, 2 H), 7.54 (t,  $J=7.3$  Hz, 1 H), 7.46 (t,  $J=7.4$  Hz, 2 H), 7.37 (t,  $J=7.9$  Hz, 2 H), 7.16 (t,  $J=7.4$  Hz, 1 H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  165.9, 138.0, 135.0, 131.8, 129.1, 128.8, 127.1, 124.6, 120.3.

**Preparation of 3.**<sup>17</sup> To a stirred solution of ketoxime **1** (2 mmol) in anhydrous THF (8 mL) at –40 °C was added LDA (1.1 equiv, 2 M) dropwise under a nitrogen atmosphere, and the mixture was stirred at –40 °C for 30 min. Then a solution of (*Z*)-*N*-((1*H*-benzo[*d*]-[1,2,3]triazol-1-yl)(phenyl)methylene)aniline<sup>22</sup> (1.0 equiv) in dry THF (5 mL) was added slowly, and the reaction mixture was heated to reflux and stirred for another 3 h. After completion, the solvent was removed on a rotary vacuum evaporator, and the residue was extracted with *n*-hexane at –40 °C and recrystallized with ethanol to give **3** as a light yellow solid in 27.0% yield (203 mg). The structure of compound **3** was identified by X-ray crystallography.

**Transformation of 3 to 4.** To a stirred solution of ketoxime **3** (37.6 mg, 0.1 mmol) in anhydrous  $\text{CH}_3\text{CN}$  (0.3 mL) was added HCl/ $\text{CH}_3\text{CN}$  (0.2 mL, 0.1 M) under a nitrogen atmosphere, and the mixture was stirred at 60 °C for 20 min. After completion, the reaction mixture was purified by column chromatography on silica gel (5% EtOAc/petroleum ether) to give **4** as a white solid in 92.1% yield (33.7 mg). The structure of compound **4** was identified by X-ray crystallography.

**Beckmann Rearrangement of 6 by TsCl and the Reaction of 8 Mediated by HCl/H<sub>2</sub>O.** A solution of cyclohexanone oxime **6** (226.3 mg, 2 mmol) and TsCl (114.4 mg, 0.6 mmol) in  $\text{CH}_3\text{CN}$  (2 mL) was stirred at reflux temperature under a nitrogen atmosphere for 3 h. After being cooled to room temperature, 0.1 mL of the reaction mixture was determined by GC–MS. HCl/H<sub>2</sub>O (0.33 mL, 6 M) was added to the remaining mixture, which was refluxed for an additional 50 min. After completion, the reaction was cooled to room temperature and then determined by GC–MS. MS ( $\text{ES}^+$ )  $m/z$ : [ $\text{M} + \text{H}$ ]<sup>+</sup> calcd for  $\text{C}_{12}\text{H}_{20}\text{N}_2\text{O}$  (**8**) 208.2, found 208.2.

**Computational Details.** The density functional theory (DFT) method M062X<sup>23</sup> was used to study the Gibbs free energy profiles of different pathways. To take the solvent effect into account, all geometry optimizations were performed with inclusion of an implicit solvent ( $\text{CH}_3\text{CN}$ ) through the integral equation formalism of the polarized continuum model (IEFPCM).<sup>24</sup> Geometries were optimized at the M062X/6-31+G (d, p) level, followed by frequency calculations at the same level of theory to ensure that these were stationary structures on their respective energy surfaces and to extract Gibbs free energy corrections at 298 K. Intrinsic reaction coordinate (IRC) calculations were performed on all the transition states to ensure that they connected the correct reactants and products in each step. For several systems, explicit solvent molecules ( $\text{CH}_3\text{CN}$ ) were included, so that reactions involving proton elimination and proton transfer

mediated by the solvent could be evaluated. The Gaussian 09 software<sup>25</sup> was used for all the theoretical calculations.

## ASSOCIATED CONTENT

### Supporting Information

Copies of  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound **2**, crystal data for compounds **3** (CCDC 917941) and **4** (CCDC 917942), GC–MS data for the reactions of **6**, computational details, figures for optimized geometries in Schemes 1, 3, 4, and **6**, and Cartesian coordinates for optimized geometries. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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### Notes

The authors declare no competing financial interest.

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## REFERENCES

- (1) Blatt, A. H. *Chem. Rev.* **1933**, *12*, 215–260.
- (2) (a) Kopple, K. D.; Katz, J. J. *J. Org. Chem.* **1959**, *24*, 1975–1977. (b) Sato, H.; Yoshioka, H.; Izumi, Y. *J. Mol. Catal. A: Chem.* **1999**, *149*, 25–32.
- (3) For selected examples of BKR in the vapor phase, see: (a) Kim, S.; Kim, M.; Seo, G.; Uh, Y. *Res. Chem. Intermed.* **2012**, *38*, 1181–1190. (b) Nagashima, S.; Kamiguchi, S.; Ohguchi, S.; Chihara, T. *Catal. Today* **2011**, *164*, 135–138. (c) Ngamcharussrivichai, C.; Wu, P.; Tatsumi, T. *Appl. Catal., A* **2005**, *288*, 158–168. (d) Li, W.-C.; Lu, A.-H.; Palkovits, R.; Schmidt, W.; Spliethoff, B.; Schüth, F. *J. Am. Chem. Soc.* **2005**, *127*, 12595–12600.
- (4) For selected examples of BKR in supercritical water, see: (a) Takahashi, H.; Tanabe, K.; Aketa, M.; Kishi, R.; Furukawa, S.-i.; Nakano, M. *J. Chem. Phys.* **2007**, *126*, 084508. (b) Boero, M.; Ikeshoji, T.; Liew, C. C.; Terakura, K.; Parrinello, M. *J. Am. Chem. Soc.* **2004**, *126*, 6280–6286. (c) Ikushima, Y.; Hatakeda, K.; Sato, O.; Yokoyama, T.; Arai, M. *J. Am. Chem. Soc.* **2000**, *122*, 1908–1918. (d) Ikushima, Y.; Hatakeda, K.; Sato, O.; Yokoyama, T.; Arai, M. *Angew. Chem., Int. Ed.* **1999**, *38*, 2910–2914. (e) Sato, O.; Ikushima, Y.; Yokoyama, T. *J. Org. Chem.* **1998**, *63*, 9100–9102.
- (5) For selected examples of BKR in ionic liquids, see: (a) Blasco, T.; Corma, A.; Iborra, S.; Lezcano-González, I.; Montón, R. *J. Catal.* **2010**, *275*, 78–83. (b) Verevkin, S. P.; Emel'yanenko, V. N.; Toktonov, A. V.; Goodrich, P.; Hardacre, C. *Ind. Eng. Chem. Res.* **2009**, *48*, 9809–9816. (c) Qiao, K.; Deng, Y.; Yokoyama, C.; Sato, H.; Yamashina, M. *Chem. Lett.* **2004**, *33*, 1350–1351. (d) Gui, J.; Deng, Y.; Hu, Z.; Sun, Z. *Tetrahedron Lett.* **2004**, *45*, 2681–2683.
- (6) For selected examples of BKR in liquid phase with small molecule, see: (a) Liu, L.-F.; Liu, H.; Pi, H.-J.; Yang, S.; Yao, M.; Du, W.; Deng, W.-P. *Synth. Commun.* **2011**, *41*, 553–560. (b) An, N.; Pi, H.-J.; Liu, L.-F.; Du, W.; Deng, W.-P. *Chin. J. Chem.* **2011**, *29*, 947–950. (c) Tandon, V. K.; Awasthi, A. K.; Maurya, H. K.; Mishra, P. J. *Heterocycl. Chem.* **2012**, *49*, 424–427. (d) Ramalingan, C.; Park, Y.-T. *J. Org. Chem.* **2007**, *72*, 4536–4538. (e) Chandrasekhar, S.; Gopalaiiah, K. *Tetrahedron Lett.* **2003**, *44*, 755–756. (f) De Luca, L.; Giacomelli, G.; Porcheddu, A. *J. Org. Chem.* **2002**, *67*, 6272–6274.

- (7) Furuya, Y.; Ishihara, K.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, *127*, 11240–11241.
- (8) Zhu, M.; Cha, C.; Deng, W.-P.; Shi, X.-X. *Tetrahedron Lett.* **2006**, *47*, 4861–4863.
- (9) (a) Hashimoto, M.; Obora, Y.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **2008**, *73*, 2894–2897. (b) Dong, J. D. Restudies on Sulfonyl Chloride Catalyzed Beckmann Rearrangement Reaction and Its Application. Master's Thesis, East China University of Science and Technology, 2009, pp 21–31.
- (10) Pi, H.-J.; Dong, J.-D.; An, N.; Du, W.; Deng, W.-P. *Tetrahedron* **2009**, *65*, 7790–7793.
- (11) Srivastava, V. P.; Patel, R.; Garima; Yadav, L. D. S. *Chem. Commun.* **2010**, *46*, 5808–5810.
- (12) Yadav, L. D. S.; Patel, R.; Srivastava, V. P. *Synthesis* **2010**, *11*, 1771–1776.
- (13) Augustine, J. K.; Kumar, R.; Bombrun, A.; Mandal, A. B. *Tetrahedron Lett.* **2011**, *52*, 1074–1077.
- (14) Xu, F.; Wang, N.-G.; Tian, Y.-P.; Chen, Y.-M.; Liu, W.-C. *Synth. Commun.* **2012**, *42*, 3532–3539.
- (15) Vanos, C. M.; Lambert, T. H. *Chem. Sci.* **2010**, *1*, 705–708.
- (16) Chapman, A. W. *J. Chem. Soc.* **1935**, 1223–1229.
- (17) Pi, H. J. Studies on Synthetic Methodology of Novel Scaffolds with Potential Biological Activities and Its Applications. Ph.D. Thesis, East China University of Science and Technology, 2010, pp 62–63.
- (18) Riggs, R. L.; Morton, C. J. H.; Slawin, A. M. Z.; Smith, D. M.; Westwood, N. J.; Austen, W. S. D.; Stuart, K. E. *Tetrahedron* **2005**, *61*, 11230–11243.
- (19) From our experiments, such as GC–MS; see the Supporting Information.
- (20) Hashimoto, M.; Obora, Y.; Ishii, Y. *Org. Process Res. Dev.* **2009**, *13*, 411–414.
- (21) Sardarian, A. R.; Shahsavari-Fard, Z.; Shahsavari, H. R.; Ebrahimi, Z. *Tetrahedron Lett.* **2007**, *48*, 2639–2643.
- (22) Pi, H. J.; Liu, L. F.; Jiang, S. S.; Du, W.; Deng, W. P. *Tetrahedron* **2010**, *66*, 6097–6100.
- (23) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215–241.
- (24) Tomasi, J.; Mennucci, B.; Cancès, E. *J. Mol. Struct.* **1999**, *211*, 474–515.
- (25) Gaussian 09, Revision A.1: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gompert, R.; S.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Ö. Farkas, Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford, CT, 2009.