Solid Acid-Catalyzed Dehydration of Pinacol Derivatives in Ionic Liquid: Simple and Efficient Access to Branched 1,3-Dienes

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ABSTRACT: The selective dehydration of pinacol derivatives to branched 1,3-dienes is extremely challenging because of the predominance of pinacol rearrangement. Herein, we successfully achieve this goal by employing a recyclable solid acid/ionic liquid catalyst system. The dehydration of alkyl- and cycloalkyl-derived diols in an Amberlyst-15/[Emim]Cl system afforded the corresponding 1,3-dienes in good yields, while a Nafion/[Emim]Cl system was demonstrated to be a better catalyst system for the dehydration of aryl-substituted substrates. Our protocol features straightforward and simple access to branched 1,3-dienes, high chemoselectivity, a recyclable catalyst system, a facile separation of dienes just by decantation, and a broad substrate scope.

KEYWORDS: branched 1,3-dienes, pinacol dehydration, ionic liquid, solid acid, Amberlyst-15, Nafion, [Emim]Cl

INTRODUCTION

1,3-Dienes are key structural motifs in a variety of natural products and bioactive molecules.1 Moreover, because of their high reactivity in many reactions (such as Diels−Alder cycloaddition, polymerization, etc.), 1,3-dienes have found wide applications in organic synthesis2 and polymer science.3 Thus, to date, tremendous methods have been developed for their synthesis. The conventional approaches include transition metal-catalyzed cross-couplings,4 olefination of unsaturated carbonyl compounds (Horner−Wadsworth−Emmons reaction, for instance),5 and enyne metathesis (Scheme 1).6 However, these methods often suffer from high-cost transition metal catalysts, toxic reagents and solvents, harsh reaction conditions, and a multistep process. Besides, most of them focus on the synthesis of linear dienes, while the selective formation of branched dienes is cumbersome. Consequently, the exploration of new synthetic routes to branched 1,3-dienes, which fulfill the criteria of green chemistry, is in great demand.

The dehydration of diols is arguably the simplest and most straightforward access to 1,3-dienes. The past decade has witnessed substantial achievements in the gas-phase dehydration of linear diols (such as 1,3-, 2,3-, and 1,4-butanediol) toward 1,3-butadiene.7 In contrast, the dehydration of branched vic-diols to highly substituted dienes still lags behind because of the predominance of pinacol rearrangement. Pinacol derivatives, as an intriguing class of vic-diols, can be easily synthesized through a low-valent metal-mediated reductive coupling8 or electrolytic reduction9 of carbonyl compounds, that is, the so-called pinacol coupling. Very recently, Rueping et al. reported a sustainable visible light-induced pinacol coupling of ketones or aldehydes to diols.10 With these well-established synthetic methods in hand, we herein develop a recyclable solid acid/ionic liquid system for the selective dehydration of pinacol derivatives to various branched 1,3-dienes (Scheme 1). This approach features straightforward and simple access to...
branched 1,3-dienes, high chemoselectivity, a recyclable catalyst system, a facile separation of dienes just by decantation, and a broad substrate scope.

**RESULTS AND DISCUSSION**

At the outset, we chose the dehydration of pinacol as the model reaction. It is well-known that this process typically involves two competitive pathways: (1) 1,2-elimination of H₂O to form 2,3-dimethylbutadiene (i.e., 2a in Scheme 2) and (2) pinacol rearrangement to form pinacolone (i.e., 3a in Scheme 2). In the past decades, a broad range of acid catalysts, including Brønsted acids,11 Lewis acids,12 solid acids,13 and supercritical water,14 have been used in the dehydration of pinacol. However, almost all of the reactions exclusively proceeded via a rearrangement pathway to produce 3a. The selective dehydration of pinacol to 2a was rarely reported.15 To increase diene selectivity, we investigated the influence of solvents on H₂SO₄-catalyzed pinacol dehydration. The results are illustrated in Table 1.

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>solvent</th>
<th>carbon yield of 2a (%)</th>
<th>2a:3a²</th>
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<tr>
<td>1</td>
<td>H₂SO₄</td>
<td>–</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>H₂SO₄</td>
<td>toluene</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>H₂SO₄</td>
<td>H₂O</td>
<td>trace</td>
<td>&lt;1:20</td>
</tr>
<tr>
<td>4</td>
<td>H₂SO₄</td>
<td>DMSO</td>
<td>58</td>
<td>3:1</td>
</tr>
<tr>
<td>5</td>
<td>H₂SO₄</td>
<td>NMP</td>
<td>71</td>
<td>7:1</td>
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<tr>
<td>6</td>
<td>H₂SO₄</td>
<td>[Emim]Cl</td>
<td>85</td>
<td>16:1</td>
</tr>
<tr>
<td>7</td>
<td>H₂SO₄</td>
<td>Bu₄NCl</td>
<td>28</td>
<td>23:1</td>
</tr>
<tr>
<td>8</td>
<td>H₂SO₄</td>
<td>[EtPy]Cl</td>
<td>28</td>
<td>24:1</td>
</tr>
<tr>
<td>9</td>
<td>H₂SO₄</td>
<td>[Emim]NTf₂</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>10</td>
<td>H₂SO₄</td>
<td>[Emim]BF₃</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>11</td>
<td>H₂SO₄</td>
<td>[Pmim]Cl</td>
<td>77</td>
<td>11:1</td>
</tr>
<tr>
<td>12</td>
<td>H₂SO₄</td>
<td>[Bmim]Cl</td>
<td>63</td>
<td>9:1</td>
</tr>
<tr>
<td>13</td>
<td>–</td>
<td>[Emim]HSO₄</td>
<td>no reaction</td>
<td>–</td>
</tr>
<tr>
<td>14</td>
<td>–</td>
<td>[(HSO₄)₃C₆H₄Cl]</td>
<td>32</td>
<td>1:1</td>
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<tr>
<td>15</td>
<td>–</td>
<td>[(HSO₄)₃C₆H₄Cl]</td>
<td>32</td>
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</tr>
<tr>
<td>16</td>
<td>H₂SO₄</td>
<td>polyethylene glycol 4000</td>
<td>5</td>
<td>1:8</td>
</tr>
</tbody>
</table>

²Reaction conditions: 1a (1.0 g), solvent (4.0 g), catalyst (100 mg), 120 °C for 12 h. ³Detected by GC using tridecane as the internal standard. ⁴Pinacolone 3a was obtained as the single product.

In some of the literature, it is suggested that polyethylene glycol (PEG) has physical properties similar to those of ILs, thus sometimes serving as an alternative reaction medium.18 However, PEG was proven to be ineffective in this reaction (Table 1, entry 16).

Subsequently, we investigated the catalytic performances of various Bronsted acids. As delineated in Figure 1, the weak acid HOAc and medium acid H₃PO₄ cannot facilitate the dehydration process, while strong acids CF₃SO₃H, H₂SO₄, and CF₃COOH exhibited good activities. The sequence for the carbon yields of 2a is CF₃SO₃H ≈ H₂SO₄ > CF₃COOH > H₃PO₄ (HOAc), which is consistent with their acid strengths. According to ref 19, the pKa values of HOAc, H₃PO₄, CF₃COOH, H₂SO₄, and CF₃SO₃H are 4.76, 2.16, −0.23, −3.0, and −14, respectively. This phenomenon indicates that acid strength is very important for dehydration. Besides, some Lewis acids were also found to be active for the process. The carbon yields of 2a over the investigated catalysts decreased in the following order: ZrCl₄ > TiCl₄ > AlCl₃ > FeCl₃. This is

![Scheme 2. Pinacol Dehydration to 2,3-Dimethylbutadiene and Pinacolone](image-url)
consistent with the acid strength sequence of these catalysts that has been classified by Kobayashi et al. On the basis of these results, we can see that both strong Bronsted and Lewis acids efficiently catalyzed the dehydration of pinacol to 2a in [Emim]Cl.

To avoid the corrosion and environmental issues associated with the utilization of homogeneous acids, we also explored the catalytic performances of an array of solid acids. As shown in Figure 2, several commonly used H-type zeolites were active for the process. H-MOR (Si/Al = 24), H-BEA (Si/Al = 25), and H-ZSM-5 (Si/Al = 25) could promote the dehydration but only with low carbon yields. H-USY (Si/Al = 3) showed a slight improvement in the diene yield. In the cases of Amberlyst-15 and Nafion resins, which have a strong acidic -SO₃H group, the dehydration proceeded smoothly to afford 2a in 85% and 86% carbon yields, respectively. These results are comparable with the ones obtained over strong homogeneous catalysts. Considering the lower cost and high activity of Amberlyst-15 resin, we believe it is a promising catalyst for the production of 2a on a large scale.

Figure 1. Carbon yields of 2a and 3a over different acid catalysts. Reaction conditions: 1a (1.0 g), [Emim]Cl (4.0 g), catalyst (100 mg), 120 °C for 12 h.

Figure 2. Carbon yields of 2a and 3a over various solid acid catalysts. Reaction conditions: 1a (1.0 g), catalyst (100 mg), [Emim]Cl (4.0 g), 120 °C for 12 h.

The influence of the catalyst loading on the pinacol dehydration was also investigated. As shown in Figure 4, the carbon yield of 2a reached its maximum (85%) when 100 mg of Amberlyst-15 resin was used and then stabilized with a further increase in catalyst loading. Thus, the optimal catalyst loading for the reaction is 10 wt % pinacol.

Another advantage of the Amberlyst-15/[Emim]Cl system is the easy separation of the product. As we can see from Figure 5, pinacol merges into [Emim]Cl at the beginning of the reaction.

Figure 3. Carbon yields of 2a and 3a over Amberlyst-15 resin as a function of [Emim]Cl mass. Reaction conditions: 1a (1.0 g), Amberlyst-15 (100 mg), 120 °C for 12 h.

Figure 4. Carbon yields of 2a and 3a over Amberlyst-15 resin as a function of catalyst loading. Reaction conditions: 1a (1.0 g), [Emim] Cl (4.0 g), 120 °C for 12 h.

Figure 5. Photographs of the mixture during the reaction: (a) a solid mixture at room temperature, (b) a homogeneous liquid with Amberlyst-15 at 120 °C, and (c) a biphasic system obtained upon completion of the reaction.
With the increase in reaction time, the mixture switches from monophasic to biphasic, because product diene 2a is nonpolar and immiscible with [Emim]Cl. Notably, when the final mixture is subjected to a low temperature, the lower layer ([Emim]Cl, Amberlyst-15, and the byproduct water) became solid or highly viscous while the upper layer (diene 2a, GC purity of >93%) was still liquid, thus allowing a facile separation of 2a just by decantation.

To fulfill the need of real application, we also checked the reusability of the Amberlyst-15/[Emim]Cl system for the dehydration of pinacol (Figure 6). With the increase in recycling time, the carbon yield of 2a slightly decreased while that of unexpected product 3a increased. These results were possibly due to the negative effect of the byproduct water generated during the dehydration. To verify this hypothesis, we studied the effect of water on the catalytic performance of the Amberlyst-15/[Emim]Cl system. To do this, we added a different amount of water to the system before reaction. As depicted in Figure 7, an evident decline in the carbon yield of 2a and an increase in the carbon yield of 3a were observed simultaneously with an increasing amount of external water. These phenomena suggest that pinacol rearrangement is prone to occur in the presence of water, which is in accordance with the result observed using water as a solvent (Table 1, entry 3).

As a solution to this problem, we dried the lower layer at 120 °C for 4 h after each usage to remove the byproduct water. As we expected, the reusability of the Amberlyst-15/[Emim]Cl catalyst system was significantly improved by such a treatment (Figure 8). No evident change in the activity or selectivity was observed during the four repeated uses.

To gain more insights into the influence of Cl\(^-\), some control experiments were performed (Scheme 3). The pinacol dehydration in the Amberlyst-15/DMSO system produced 2a in low yield (16%) and selectivity (2.2:1 2a:3a) (Figure S2). However, after the addition of 20 mmol of LiCl to the mixture, the yield of 2a significantly increased and the molar ratio of 2a and 3a increased to 12.2:1 (Figure S3). On the basis of these results, we think that Cl\(^-\) possibly plays a predominant role in the selective pinacol dehydration in [Emim]Cl. On one hand, Cl\(^-\) interacts with the hydroxyl proton of pinacol through hydrogen bonding. On the other hand, Cl\(^-\) could efficiently stabilize the carbocation intermediate, thereby enhancing diene selectivity.

Furthermore, we also conducted the NMR experiments to further investigate the interactions between ILs and pinacol. The NMR data of neat IL, pinacol, and the mixture of IL and pinacol are listed in Table 2. Compared with the chemical shift of the Cl atom of neat pinacol (75.18 ppm), that in the mixture of [Emim]Cl and pinacol moves upfield (74.82 ppm, \(\Delta \delta = 0.36\) ppm). Simultaneously, the mixture led to an increase in the \(^1\)H and \(^13\)C shift at position 2 of the imidazole ring (Table 2, entry 5). In contrast, the NMR data of the mixture of [Emim]BF\(_4\) and pinacol showed no difference with neat two components (Table 2, entry 6). These results reveal that [Emim]Cl strongly interacts with pinacol, whereas [Emim]BF\(_4\) does not. In comparison with the weakly coordinating anion BF\(_4^-\), the small anion Cl\(^-\) is a good hydrogen bond acceptor, which

![Figure 6. Carbon yields of 2a and 3a over the Amberlyst-15/[Emim]Cl catalyst system as a function of recycle time (without removal of the byproduct water). Reaction conditions: 1a (1.0 g), Amberlyst-15 (100 mg), [Emim]Cl (4.0 g), 120 °C for 12 h.](#)

![Figure 7. Carbon yields of 2a and 3a over the Amberlyst-15/[Emim]Cl catalyst system as a function of the amount of external water added before reaction. Reaction conditions: 1a (1.0 g), Amberlyst-15 (100 mg), [Emim]Cl (4.0 g), 120 °C for 12 h.](#)

![Figure 8. Carbon yields of 2a and 3a over the Amberlyst-15/[Emim]Cl catalyst system as a function of recycle time (removal of the byproduct water). Reaction conditions: 1a (1.0 g), Amberlyst-15 (100 mg), [Emim]Cl (4.0 g), 120 °C for 12 h. The lower layer was dried at 120 °C for 4 h after each use.](#)

![Scheme 3. Effect of Cl\(^-\) on the Pinacol Dehydration](#)
possibly interacts with the hydroxyl proton of pinacol (Cim=Cl—OH).
In addition, when pinacol is subjected to [Bmim]Cl, an upfield shift of C1 was also observed (74.96 ppm, Δδ = 0.22 ppm). However, the upfield shift value of pinacol in [Bmim]Cl (0.22 ppm) was smaller than that in [Emim]Cl (0.36 ppm), which indicates that the sterically hindered butyl group possibly hampers the interaction between IL and pinacol, thus leading to a decreased diene selectivity in [Bmim]Cl. It has been reported that the acidic H2 proton of IL and pinacol, thus leading to a decreased diene selectivity in [Emim]Cl (0.36 ppm), which indicates that the sterically hindered butyl group possibly hampers the interaction between IL and pinacol, thus leading to a decreased diene selectivity in [Bmim]Cl. It has been reported that the acidic H2 proton of the imidazole ring probably also interacts with the oxygen atom of the hydroxyl group through hydrogen bonding (Cim=Cl—OH), which cannot be excluded from the process.

Table 2. NMR Data of Neat IL, Pinacol, and the Mixture of IL and Pinacol

<table>
<thead>
<tr>
<th>entry</th>
<th>imidazole ring</th>
<th>C1 atom of pinacol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>δ_H (ppm)</td>
<td>δ_C (ppm)</td>
</tr>
<tr>
<td>1</td>
<td>[Emim]Cl</td>
<td>10.08</td>
</tr>
<tr>
<td>2</td>
<td>[Emim]BF_4</td>
<td>8.52</td>
</tr>
<tr>
<td>3</td>
<td>[Bmim]Cl</td>
<td>10.23</td>
</tr>
<tr>
<td>4</td>
<td>pinacol</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>[Emim]Cl/pinacol (4:1)</td>
<td>10.22</td>
</tr>
<tr>
<td>6</td>
<td>[Emim]BF_4/pinacol (4:1)</td>
<td>8.52</td>
</tr>
<tr>
<td>7</td>
<td>[Bmim]Cl/pinacol (4:1)</td>
<td>10.39</td>
</tr>
</tbody>
</table>

To illustrate the generality of the Amberlyst-15/[Emim]Cl system, we further explored the dehydration of a series of diols that were easily synthesized by the pinacol coupling of the carbonyl compounds. As summarized in Table 3, when unsymmetrical 2-butano-derived diol 1b was subjected to the standard conditions (condition A), the elimination of H_2O, to our surprise, occurred at the adjacent CH_2 position rather than at the CH_3 position, leading to the formation of (E,E)-diene 2b as the main product. Pinacol analogues 1c and 1d could also be readily converted into 1,3-dienes with high efficiencies. Remarkably, cyclic vic-diols 1e and 1f underwent the process smoothly, providing the corresponding dienes in 86 and 94% yields, respectively. We were disappointed that the dehydration of phenyl-substituted diol 1g in the Amberlyst-15/[Emim]Cl catalyst system produced 2g in only 18% yield and most of the substrate remained unchanged. Given that the maximal operating temperature of Amberlyst-15 is 120 °C, we then chose Nafion resin with high thermal stability as the catalyst to achieve better results. As expected, the yield of 2g increased to 75% when the dehydration was conducted at 160 °C (condition B). Thus, in the cases of aryl-substituted diols, the Nafion/[Emim]Cl system was the optimal catalyst system. Diols 1h and 1i bearing 4-Me and 4-Cl were tolerated in the reaction. The electronic properties of the substituents on the phenyl ring exerted a strong influence on the results. For example, the dehydration of 1j, possessing an electron-donating OMe group, afforded 2j in 74% yield, whereas electron-withdrawing OMe group, afforded 2j in 74% yield, whereas electron-withdrawing substrate 1k cannot undergo the reaction under the investigated conditions. It is noted that a mixture of 2l and 2l' was obtained using propiophenone-derived pinacol 1l as a substrate. The scope of the reaction can be further extended to 2-naphthyl-substituted pinacol 1m, albeit with a slightly decreased yield. However, the dehydration of linear diol 1n, generated from 1-octanal, did not occur in either catalyst system, which was presumably ascribed to the relatively low stability of the secondary carbocation intermediate.

Additionally, this approach also has a potential application in the total synthesis of some intriguing molecules. Vannusals A and B make up a class of marine natural products that were isolated from the interstitial ciliate *Euplotes vannus*. Because of their complex and unusual structures, their synthesis has attracted the interest of synthetic chemists. As described by Nicolaou and co-workers, diene 2e is the important building block for the total synthesis of vannusals A and B (Scheme 4). In their work, 2e was prepared by the dehydration of diol 1e in the presence of POCl_3 and pyridine. From an economical and environmental point of view, our protocol provides a recyclable alternative for the production of 2e, which can further undergo the same processes to elaborate vannusals A and B. We believe that our approach will replace the conventional POCl_3/pyridine method in the future.

CONCLUSION

In summary, a recyclable solid acid/ionic liquid system has been developed for the catalytic dehydration of pinacol derivatives to branched 1,3-dienes. The reaction of alky-
cycloalkyl-derived diols in the Amberlyst-15/[Emim][Cl] system afforded the corresponding 1,3-dienes in good yields, while the Nafion/[Emim][Cl] was system demonstrated to be the optimal catalyst system for the dehydrogenation of aryl-substituted substrates. The presence of [Emim][Cl] significantly improved diene selectivity. Furthermore, the high polarity of ionic liquid also allows a facile separation of dienes just by decantation. Our protocol features straightforward and simple access to branched 1,3-dienes, high chemoselectivity, a recyclable catalyst system, a facile workup process, and a broad substrate scope. Because of the ubiquitous role of 1,3-dienes in cycloadditions and polymerizations, this work will have potential applications in organic synthesis and polymer science.

ASSOCIATED CONTENT

Supporting Information
The Supporting Information is available free of charge at the ACS Publications website at DOI: 10.1021/acscatal.7b00066. Experimental details, characterization data of the reactants and products, and copies of GC chromatograms and NMR spectra (PDF).

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Notes
The authors declare no competing financial interest.

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REFERENCES

(15) There is only one report of the pinacol dehydration to diene 2a, in which a corrosive liquid acid, careful control of the temperature, and an additional distillation process were required: Kyriakides, L. P. J. Org. Chem. 1976, 41, 1537–1538.


■ NOTE ADDED AFTER ASAP PUBLICATION

The version of this paper that was published ASAP on March 14, 2017, contained an incorrect version of the Supporting Information. The correct version was posted March 15, 2017.