Brønsted Acid Catalysed Aerobic Reduction of Olefins by Diimide Generated In Situ from Hydrazine

Yukihiro Arakawa a  
Takahiro Kohda a  
Keiji Minagawa b  
Yasushi Imada a,*  

a Department of Applied Chemistry, Tokushima University, Minamijosanjima, Tokushima 770-8506, Japan  
b Institute of Liberal Arts and Sciences, Tokushima University, Minamijosanjima, Tokushima 770-8502, Japan  
imada@tokushima-u.ac.jp

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Abstract  
Aerobic reduction of olefins with hydrazine was proven to be efficiently catalysed by readily available Brønsted acids, such as p-toluene sulfonic acid monohydrate, providing hydrogenated products in very good yields and chemoselectivity under mild conditions.

Key words: Brønsted acid, diimide, reduction, olefins, hydrazine

Generation of diimide from hydrazine and its use as a hydrogen transfer agent in situ, first discovered in 1905 and studied in depth in the 1960s, have been recently revisited by chemists to develop advanced olefin reduction technologies that utilise no transition metals or hydrogen to produce hydrogenated products in a chemoselective and stereospecific manner with nontoxic by-products (Scheme 1). The groups of Dong3 and Balci4 independently reported that the aerobic reduction of olefins with hydrazine proceeded smoothly under an atmosphere of O2 in ethanol without any additives or catalysts, although large excesses of hydrazine (4–8 equivalents) along with prolonged reaction times (mostly ≥24 h) and/or high reaction temperatures were required to be efficient due to the rapid disproportionation of diimide into hydrazine and N2. Prabhu et al. reported the catalytic activity of guanidine nitrate, which allowed the amounts of hydrazine to be lowered to two equivalents at ambient temperature but this process still required long reaction times (12–24 h) even in the presence of 10 mol% of the catalyst.5 Leow et al. demonstrated that UVA light irradiation could accelerate the reduction performed at ambient temperature in acetonitrile under air by inducing the trans to cis isomerization of diimide, in which reaction times of 18–24 h (even under 1 atm of O2) were often required with 2–3 equivalents of hydrazine.6 Guin et al. reported that the addition of a stoichiometric amount of arylboronate ester could accelerate reduction such that the reaction was complete within 1.5–8 h at 32 °C in acetonitrile with four equivalents of hydrazine; although stoichiometric amounts of phenol and boric acid were formed.7 We introduced synthetic flavins as efficient catalysts for the generation of diimide from hydrazine, which provided a convenient and safe process for the aerobic reduction of olefins, requiring as little as one equivalent of hydrazine.8 However, despite their versatility, expanded by ourselves and others,9 the N5-alkylated flavin derivatives with highest activities are not commercially available and so this methodology has not been generally adopted in the laboratory or in industry. Kappe et al. utilised a gas–liquid continuous-flow system for diimide olefin reduction, which dramatically shortened reaction times to 10–30 min at 100 °C under 20 bar with 4–5 equivalents of hydrazine.10 Although such flow technologies are a useful and safe way of using highly labile diimide,10,11 they require special instrumentation that is still not common in research laboratories. As a result, the development of an efficient and readily available methodology for the aerobic reduction of olefins with hydrazine remains desirable.

Scheme 1  Aerobic reduction of olefins with hydrazine

In the course of our research on the aerobic reduction of olefins with hydrazine, we examined an article published by Koch in 1968, in which the catalytic effect of acetic acid
(AcOH) for the aerobic reduction of methyl oleate with hydrazine in aprotic solvents such as acetonitrile and the kinetics of the process were presented.\textsuperscript{12} Although the role of AcOH was not fully rationalised in the original report, it was commented later by Pasto and Taylor in a review\textsuperscript{2a} that AcOH could catalyse slow equilibration of unreactive trans-diimide and reactive cis-diimide. Nevertheless, we were quite surprised that no other Brønsted acids have so far been explored as catalysts for the aerobic reduction of olefins with hydrazine.

Within this manuscript, the catalytic activities of a variety of Brønsted acids for the aerobic reduction of olefins with hydrazine are disclosed. We demonstrate that \textit{p}-toluenesulfonic acid monohydrate (TsOH·H₂O), one of the most common, inexpensive, and readily available organic acids, is particularly useful as a catalyst in terms of both reaction efficiency and availability, which allows a range of olefins to be reduced with high chemoselectivity under mild conditions.

Initially, several commercially available organic acids having different acidities, AcOH \(\text{pK}_a = 23.51\) (CH₃CN),\textsuperscript{13a} 4.76 (H₂O),\textsuperscript{13b} diphenylphosphate [DPP, \(\text{pK}_a = 1.9\) (H₂O)],\textsuperscript{13c} methanesulfonic acid [MsOH, \(\text{pK}_a = 10.0\) (CH₃CN)],\textsuperscript{13d} toluenesulfonic acid monohydrate [TsOH·H₂O, \(\text{pK}_a = 8.6\) (CH₃CN)],\textsuperscript{13a} and bis[1,1,2,2,3,3,4,4,4-nonafluoro-1-butanesulfonyl]imide [(C₄F₉SO₂)₂NH, \(\text{pK}_a = 0.0\) (CH₃CN)],\textsuperscript{13e} were explored for the aerobic reduction of 4-phenyl-1-butene (1a) to butylbenzene (2a). The reactions were carried out with 0.25 mmol of 1a and 2 equivalents of hydrazine monohydrate (NH₂NH₂·H₂O) under 1 atm of O₂ at 35 °C in the presence of 5 mol% of each acid in acetonitrile and the reaction was closely monitored by GC analysis for 60 minutes (Scheme 2). A control experiment showed that the reaction in the absence of any acids could proceed only very slowly to give 2a in 5% yield after 60 minutes. The catalytic behaviour of AcOH, reported by Koch,\textsuperscript{12} was reproduced, resulting in 2a being obtained in 17% yield after the same reaction time. We anticipated that much stronger acids should promote the reaction more by rendering the equilibration of trans- and cis-diimide faster. As expected, DPP showed considerably higher catalytic activity compared with AcOH, giving a yield of 50% in 1 hour. Remarkably, nearly quantitative yields were observed when TsOH·H₂O or (C₄F₉SO₂)₂NH (even stronger acids than DPP) was used under the same conditions; while MsOH was unexpectedly sluggish. In this case, the reaction mixture became heterogeneous, with formation of a white precipitate that could be a hydrazonium salt of MsOH, rendering the catalyst ineffective. To evaluate the catalytic activity of each Brønsted acid more precisely, the ratios \(\frac{k_{\text{obs}}}{k_0}\) of the initial rate of the reaction with acid \(k_{\text{obs}}\) and that without acid \(k_0\) were determined to be 20 for AcOH, 70 for DPP, 185 for TsOH·H₂O, 4 for MsOH, and 215 for (C₄F₉SO₂)₂NH. Although the highest value of \(\frac{k_{\text{obs}}}{k_0}\) was obtained with (C₄F₉SO₂)₂NH, it was not as high as expected from the difference in \(\text{pK}_a\) values of (C₄F₉SO₂)₂NH and TsOH·H₂O (see above). In addition, TsOH·H₂O is much less expensive than (C₄F₉SO₂)₂NH and it is readily available. Thus, we decided to optimise the reaction conditions for the present aerobic reduction catalysed by TsOH·H₂O.

A significant decrease in reactivity was observed when 1.1 equivalents of NH₂NH₂·H₂O were employed (Table S1, entries 1–3). Reducing the amount of TsOH·H₂O to 2 mol% led to lower efficiency, while increasing it to 10 mol% did not improve the reactivity appreciably (Table S1, entries 4–6). When the reaction was carried out under air, a white precipitate – presumably a hydrazonium salt of TsOH – was observed to form gradually, which could explain why a prolonged reaction time even with 3.5 equivalents of NH₂NH₂·H₂O was required to give 2a in a reasonable yield under such conditions (Table S1, entry 7). It should be noted that no reaction occurred under a nitrogen atmosphere (Table S1, entry 8). Further optimization of the reaction parameters showed acetonitrile to be the best solvent and 35 °C to be the most suitable reaction temperature for efficient catalysis (Table S1, entries 9–17).
With the optimal reaction conditions in hand, we demonstrated the utility of the TsOH-catalysed aerobic olefin reduction with hydrazine by applying the procedure to a range of substrates (Table 1). The reactions were performed on a 1 mmol substrate scale and evaluated by GC analysis and/or isolated yields of hydrogenated products after full conversion of the substrates. Monosubstituted olefins 1a–k as well as disubstituted olefins 1l–o could be efficiently reduced with excellent functional group tolerance. For instance, benzyl, epoxy, nitro, and azide groups, which are typically labile under metal-catalysed hydrogenation conditions, were unaffected by the reaction conditions (entries 5–8 and 14). There was also no adverse effect in the reduction of an olefin containing a sulfide functional group (entry 9), which often inhibits the catalytic activity of transition-metal complexes. The reduction of linalool (1j), bearing two carbon–carbon double bonds, afforded the monohydrogenated product 2j and the fully hydrogenated product in a ratio of 95:5, indicating the compatibility of the trisubstituted olefin as well as acid-labile tertiary alcohol group to the reaction conditions (entry 10). In addition, the present method can complement the aerobic hydrazine reduction catalysed by neutral flavins, because phenolic olefins such as o-allylphenol (1k, entry 11) are less reactive under flavin-related catalysis due to their acidic property reducing the reactivity of the basic hydrazine. Reduction of sterically more demanding α,β- as well as α,α-disubstituted olefins was also feasible without using extra hydrazine, although higher temperatures and prolonged reaction times were required for acyclic substrates 1m, 1n, and 1o (entries 13–15).

As initially envisaged, it is plausible that Brønsted acids accelerate the interconversion between trans- and cis-diacimide and thereby facilitate the aerobic olefin reduction system. Although it could be expected that they would irreversibly form hydrazonium salts (+NH₂NH₂) and be deactivated, such an undesirable situation is apparently negligible as far as they are used under an atmosphere of O₂ in acetonitrile, except in the case of MsOH. For the representative catalysis with TsOH·H₂O, hydrazine can undergo reversible protonation to form +NH₂NH₂ as well as irreversible oxida-

<table>
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* Reactions were performed using 1 mmol of olefin, 2 mmol of hydrazine monohydrate in 4 mL of acetonitrile in the presence of 5 mol% TsOH·H₂O under 1 atm of O₂ at 35 °C and monitored by GC analysis.
† Time for full conversion.
‡ Isolated yield, unless otherwise noted.
§ Conversion determined by GC analysis.
‖ Determined by ¹H NMR measurement.
| Conducted at 70 °C.
In conclusion, we have introduced a new protocol for the aerobic reduction of olefins with hydrazine by using readily available Brønsted acids as catalysts. In particular, the use of 5 mol% TsOH·H2O and two equivalents of hydrazine monohydrate allowed a range of olefins to be reduced with excellent chemoselectivities under mild aerobic conditions. The present method is straightforward and should find wide application in organic synthesis. An asymmetric version of the protocol with chiral Brønsted acids is being explored in our laboratory.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588790.

References and Notes

(14) A mixture of a solution of the olefin (1.0 mmol) in acetonitrile (2 mL) and a 0.05 M stock solution of TsOH·H2O in acetonitrile (1 mL, 5 mol%) was stirred under an atmosphere of oxygen at 35 °C (for 1a–1) or 70 °C (for 1m–o) for 5 min. To the resulting mixture was added a solution of NH2NH2·H2O (60 mg, 1.2 mmol) in acetonitrile (1 mL) and the mixture was further stirred at the corresponding temperature and monitored by GC analysis. After complete consumption of the olefin, the reaction was quenched with saturated aqueous NaHCO3 (3 mL), and Et2O (15 mL) and H2O (7 mL) were added. The aqueous layer was removed and the residual organic layer was washed with H2O (2 × 10 mL) and brine (10 mL), dried over Na2SO4, filtered, and concentrated under reduced pressure to give the corresponding hydrogenated product 2a–o. Data for butylbenzene (2a) [CAS No. 104-51-8]: yield: 127 mg (92%). 1H NMR (400 MHz, CDCl3, 25 °C): δ = 0.92 (t, J = 7.3 Hz, 3 H, CH3), 1.30–1.42 (m, 2 H, CH2), 1.55–1.65 (m, 2 H, CH2), 2.61 (t, J = 7.8 Hz, 2 H, ArCH2), 7.12–7.31 (m, 5 H, ArH). 13C NMR (100 MHz, CDCl3, 25 °C): δ = 13.9, 22.4, 33.7, 35.7, 125.5, 128.2, 128.4, 142.9. MS (EI): m/z (%): 134 (26) [M+], 105 (8) [C6H5CH2CH2], 91 (100) [C6H5CH2], 77 (6) [C2H5], 65 (16) [C6H5], 51 (11) [C6H5], 39 (18) [C6H3].