Catalyst-Free Hydrogenation of Alkenes and Alkynes with Hydrazine in the Presence of Oxygen

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Abstract: A series of alkenes and alkynes was subjected to reduction with hydrazine hydrate in ethanol in the presence of oxygen. An efficient method was developed for the reduction of C–C double bonds and C–C triple bonds with diimide, generated in situ from hydrazine hydrate by oxidation with oxygen. The reduction process proceeded for 24–48 hours with high chemoselectivity and excellent yields. This reduction procedure offers synthetic advantages over metal-catalyzed hydrogenation as well as other systems.

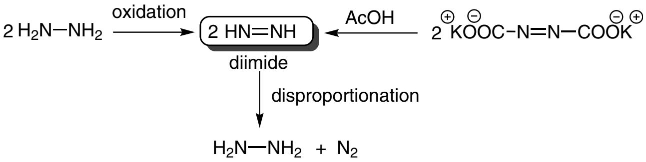
Key words: reduction, oxidation, hydrazine, hydrogenation, diimide

Hydrogenation of alkenes is an important reaction for the synthesis of organic molecules. Alkenes react with hydrogen in the presence of a metal catalyst to give the corresponding alkanes in a process that has been known since the 19th century,[1] however, there are many other methods of effecting reduction.[2] The transfer of hydrogen to double bonds can be accomplished under either heterogeneous[3] or homogeneous[4] conditions but, generally, hydrogen is used with noble-metal catalysts, either finely divided or supported on carriers. Commonly Pd, Pt, and Rh are used as catalysts under very mild conditions with reaction temperatures rarely exceeding 100 °C. The catalyst can be easily removed from the reaction medium by simple filtration. Homogeneous catalysts have exhibited high activity and selectivity with special applications, and most homogeneous catalytic reactions, among them enantioselective reactions, apply tertiary phosphines as the most conventional ligands.[5] Catalytic hydrogenation requires special care in the handling of hydrogen (a highly flammable and explosive gas) and, in some cases, rather expensive catalysts and high pressures are needed for the reaction to proceed.

Hydrazine is an alternate and safe reactant for hydrogenation, and the decomposition of hydrazine can result in the formation of a range of products. Decomposition over metals such as Pd and Pt tends to yield mostly nitrogen and hydrogen, which can lead to hydrogenolysis of C–O bonds[6] and reduction of nitrobenzene derivatives to hydroxylamines in good yields.[7] A highly active and selective nano-catalyst, Rh/HAP (rhodium supported on hydroxy-apatite),[8] as well as a Ni-Zr alloy[9] have also been used efficiently for hydrogen generation from aqueous hydrazine, for the reduction of nitroarenes.

A range of C–C double bonds can be hydrogenated with neutral flavin catalysts in the presence of 1–2 equivalents of hydrazine under atmospheric O_2.[10] This is attributed to diimide generation by the aerobic oxidation of hydrazine with flavin derivatives rather than by direct reduction with hydrazine. This finding led to the development of a mild and convenient method for the aerobic reduction of olefins.[11] More recently, Kleinke and Jamison reported H_2-free hydrogenation of C–C double bonds via diimide generated from the new reagent combination of N,O-bistrifluoroacetyl-hydroxylamine and hydroxylamine.[12]

Diimide is a short-lived intermediate that can be generated by various methods. Besides the oxidation of hydrazine with various reagents, diimide can be easily produced by reaction of potassium azodicarboxylate and acetic acid in methanol (Scheme 1).[13] Benzenesulfonylhydrazide[14] as well as *o*-nitrobenzenesulfonyl-hydrazide with triethylamine[15] have also recently been used as diimide sources.



Scheme 1 Generation of diimide

Diimide reduces alkenes and alkynes, resulting in the *syn*-addition of hydrogen. This observation has led to the conclusion that the mechanism involves concerted hydrogen transfer from *cis*-diimide to the substrate.[17] Diimide reduction has advantages over classical reduction with hydrogen molecules. Studies show that diimide attacks *trans* double bonds[16] and strained double bonds[18] more rapidly than *cis* double bonds and unstrained double bonds. Furthermore, diimide can reduce C–C double bonds in the presence of weak oxygen–oxygen bonds[19] as well as a disulfide linkage (Scheme 2).

In 1914, Falciola and Mannino reported that hydrazine reduces oleic acid to stearic acid.[20] Later, in 1960, Cross[21] communicated that gibberellic acid was smoothly converted into tetrahydrogibberellic acid in hydrazine–ethanol. Corey et al.[22] generated diimide by either oxida-

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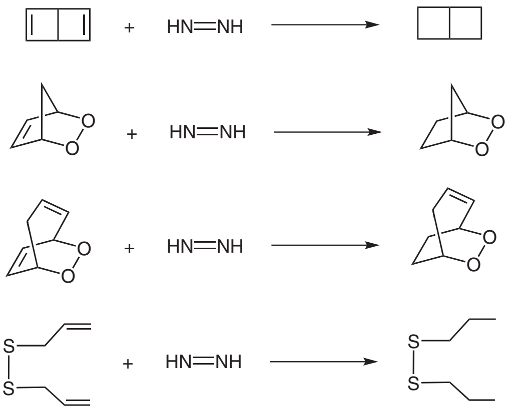
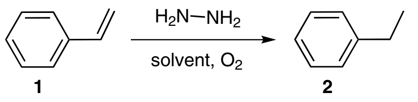


Scheme 2 Reduction of double bonds by diimide

tion of hydrazine with air in the presence of copper ions (trace) or with a hydrogen peroxide–copper ion (trace) system and applied this to the reduction of various alkenes. More recently, Chen et al.[23] described a reduction protocol for C–C double bonds in which an eight-fold excess of hydrazine hydrate was used at the reflux temperature of various solvents. In the present communication, we report that hydrazine hydrate reduces a range of alkenes and alkynes smoothly at 35 °C in the presence of oxygen without any catalyst or metal.

In the initial study, styrene (**1**) was used as the starting material to examine the effect of solvent as well as the effect of oxygen. The reaction was first carried out with four equivalents of hydrazine hydrate in ethanol under a nitrogen atmosphere at 35 °C. After 24 hours only 10% of the starting material had been reduced to ethylbenzene (**2**) and 90% of **1** was recovered (Scheme 3, Table 1, entry 1). We assume that the oxygen dissolved in ethanol was responsible for partial oxidation of hydrazine to diimide, which then reduced the double bond. When the reaction was exposed to air, ethylbenzene was formed in 71% yield after 24 hours (Table 1, entry 2). However, when the reaction was carried out under oxygen, the transformation proceeded smoothly, giving the desired product **2** in 99% yield (entry 3).



Scheme 3 Reduction of styrene

We then examined a range of solvents under an oxygen atmosphere to improve the efficiency of the reaction (Table 1). The solvent was found to play an important role in the system and the choice of solvent had a marked effect on the yield. Reduction in tetrahydrofuran or dimethyl formamide was not complete after 24 hours (Table 1, entries 5 and 6). The reaction in ethanol (Table 1, entry 3) was complete within 24 hours, but in methanol the yield was slightly lower than that in ethanol (Table 1, entry 4).

We further investigated the reduction potential of three types of hydrazines; hydrazine monohydrate in ethanol, hydrazine·HCl, and anhydrous hydrazine in THF. All reduction reactions were carried out in ethanol at 35 °C in the presence of oxygen. Treatment of styrene with four equivalents of hydrazine monohydrochloride in ethanol for 24 hours resulted in a lower yield of **2** (9%, entry 7). When the reaction was carried out with anhydrous hydrazine in THF (entry 8), GC-MS analysis of the reaction mixture indicated the presence of **2** (69%) and **1** (31%). A comparison of the reductions with three different hydrazines showed a dramatic difference in reactivity. Therefore, we decided to continue the investigation with hydrazine monohydrate in ethanol.

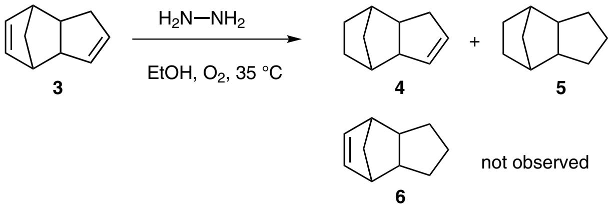
Under the optimized reaction conditions, we examined the hydrogenation of 3a,4,7,7a-tetrahydro-1*H*-4,7-methanoindene (**3**; dicyclopentadiene) as a model system to test the effect of strain on the hydrogenation reaction (Scheme 4). Hydrocarbon **3** contains two different double bonds incorporated into the bicyclic unit, with one being more strained than the other. Treatment of **3** with four equiva-

Table 1 Optimization of Conditions for Reduction of Styrene (**1**) with Hydrazine

Entry	Reactant (4 equiv)	Solvent	Temp (°C)	Time (h)	Atmosphere	Yield (%)[a]	
						2	**1**
1	$H_2N–NH_2·H_2O$	EtOH	35	24	N_2	10	90
2	$H_2N–NH_2·H_2O$	EtOH	35	24	air	71	28
3	$H_2N–NH_2·H_2O$	EtOH	35	24	O_2	99	–
4	$H_2N–NH_2·H_2O$	MeOH	35	24	O_2	88	12
5	$H_2N–NH_2·H_2O$	THF	35	48	O_2	75	25
6	$H_2N–NH_2·H_2O$	DMF	35	24	O_2	60	40
7	$H_2N–NH_2·HCl$	EtOH	35	24	O_2	9	91
8	$H_2N–NH_2$ in THF	EtOH	35	24	O_2	69	31

[a] Conversion and yields were determined by GC/MS analysis.

lents of hydrazine monohydrate in ethanol for 24 hours resulted in the formation of partly reduced hydrocarbon **4** in 94% yield (Table 2, entry 1).



Scheme 4 Reduction of hydrocarbon **3**

The starting material was consumed and fully reduced product **5** was formed in only 1% yield. The reactivity differences of the two double bonds in **3** can be attributed to the difference in bond angle strain, with the more strained olefin reacting more rapidly.[24] When the reaction time was increased to 48 hours, the amount of **5** increased to 15% (Table 2, entry 2). By screening for the influence of time on product yield, we found that the amount of fully reduced product **5** could be increased to 87% (Table 2, entries 3–8). To complete the reduction, the addition of further hydrazine hydrate was necessary. Product **6** was not formed.

Once the reaction conditions for this reduction had been established, we examined the scope of the reaction by submitting a range of alkenes and alkynes to reduction with hydrazine at 35 °C in ethanol; the results are summarized in Table 3.

Table 2 Reduction of **3** with Hydrazine[a]

Entry	Reactant	Time (h)	Yield **4**/**5** (%)
1	$H_2NNH_2{\cdot}H_2O$	24	94:1
2	$H_2NNH_2{\cdot}H_2O$	48	85:15
3	$H_2NNH_2{\cdot}H_2O$	65	62:38
4	$H_2NNH_2{\cdot}H_2O$	72	52:48
5	$H_2NNH_2{\cdot}H_2O$	92	32:68
6	$H_2NNH_2{\cdot}H_2O$	118	14:86
7	$H_2NNH_2{\cdot}H_2O$	137	13:87
8	$H_2NNH_2{\cdot}H_2O$	144	13:87

[a] All reactions were carried out under an oxygen atmosphere in EtOH at 35 °C.

Table 3 Reduction of Alkenes and Alkynes

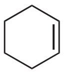
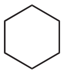
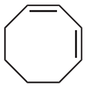
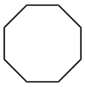
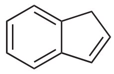
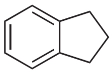
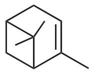
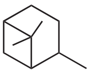
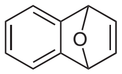
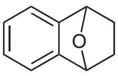
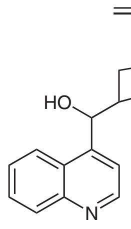
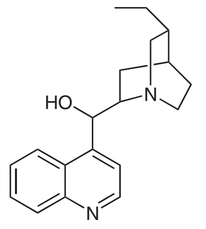
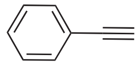
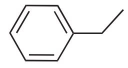
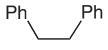
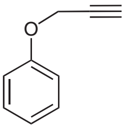
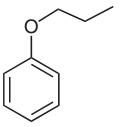
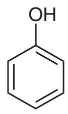
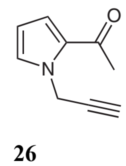
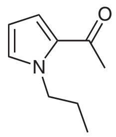
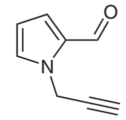
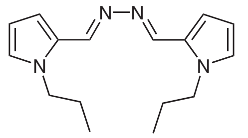
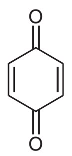
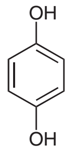
Entry	Alkene or Alkyne	Product	Time (h)	Yield (%)[a]
1	 **7**	 **8**	18	95
2	 **9**	 **10**	52	94
3	 **11**	 **12**	24	>98
4	 **13**	 **14**	47	76[b,25]
5	 **15**	 **16**	24	>99[26]

Table 3 Reduction of Alkenes and Alkynes (continued)

Entry	Alkene or Alkyne	Product	Time (h)	Yield (%)[a]
6	 **17**	 **18**	25	>99[27]
7	 **19**	 **2**	36	90
8	$\mathrm{Ph}{-}{\equiv}{-}\mathrm{Ph}$ **20**	 **21**  **22**	144	12/86[b,c,28]
9	 **23**	 **24**  **25**	48	95/5
10	 **26**	 **27**	38	>99
11	 **28**	 **29**	39	98
12	 **30**	 **31**	36	89[b]

[a] Conversion and yield were determined by GC/MS analysis.

[b] Consumption of **13**, **20** and **30** was 77, 70, and 80%, respectively.

[c] Yield based on consumed starting material.

First we submitted a range of alkenes (**7**, **9**, **11**, **13**, **15**, and **17**) to reduction with diimide. In all cases, after 18–52 hours, the starting materials were consumed and the corresponding reduced products (**8**, **10**, **12**, **14**, **16**, and **18**) were formed in excellent yields (Table 3, entries 1, 2, 4, 5, and 6). In the case of **13**, the reduction was sluggish compared to the other systems, however, the yield based on the consumed product was also excellent. The decreased reactivity was attributed to the steric hindrance around the double bond in **13**. The reduction of acetylene derivatives also proceeded smoothly in the presence of oxygen, giving the corresponding products in high yields.

Reduction of phenylacetylene (**19**; Table 3, entry 7) was completed in 36 hours in 90% of yield. However, diphenylacetylene (**20**) was much less reactive than phenylacetylene, and its reaction with hydrazine was not complete after 144 hours (Table 3, entry 8), with only 70% of the starting material consumed. 1,2-*cis*-Diphenylethene (**21**) and 1,2-diphenylethane (**22**) were formed in a ratio of 12:86. The *cis*-configuration of diphenylethene was determined with the help of ^{13}C NMR satellite peaks;[29] the vicinal coupling in the ethylene unit was found to be 12.2 Hz. In styrene, *cis*-coupling has a value of ^3J = 10.9 Hz, whereas *trans*-coupling ^3J = 17.6 Hz.[30] This finding supports further the proposed *cis*-reduction and formation of diimide as the reducing agent. Prop-2-yn-1-yloxy-benzene (**23**) showed similar reactivity to that of phenylacetylene, giving propoxybenzene (**24**) in 95% yield (Table 3, entry 9); in this case, phenol was also formed as a by-product (5%) arising from reduction of the C–O bond. 1-[(1-(Prop-2-yn-1-yl)-1*H*-pyrrol-2-yl)]ethanone (**26**) was also smoothly reduced to *N*-propyl derivative (**27**; Table 3, entry 10). However, the corresponding aldehyde **28** reacted first with hydrazine to give the diazine derivative (Table 3, entry 11), followed by reduction of the propargyl groups to give the final product **29**. Finally, *p*-benzoquinone (**30**) underwent smooth reduction to form hydroquinone (**31**) in 89% yield.

In conclusion, the scope of hydrazine reduction in the presence of oxygen has been studied in detail.[31] We assume that the diimide formed initially is responsible for reduction of the C–C double bonds. This method provides a simple and selective reduction protocol of double bonds as well as alkynes and offers advantages over metal-catalyzed hydrogenation and other reducing systems.

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(31) **Procedure for hydrogenation:** A round-bottom flask was charged with alkene or alkyne (1 mmol) and EtOH (1 mL) [except for cinchonine (3 mL) because of its lower solubility]. To this mixture was added hydrazine monohydrate (4 mmol), then the reaction was placed under an atmosphere of oxygen (balloon). The resulting mixture was stirred at 35 °C for the appropriate time. After consumption of the starting material, the solvent was removed under vacuum and the residue was extracted with EtOAc. The organic phase was dried over $MgSO_4$ (for isolated products). Volatile products were not isolated and they were analyzed directly by using GC-MS.

1,2,3,4-Tetrahydro-1,4-epoxynaphthalene (16):[26] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.16–7.13 (m, AA′ of AA′BB′, 2 H), 7.09–7.06 (m, BB′ of AA′BB′, 2 H), 5.32 (dd, *J* = 3.0, 1.8 Hz, 2 H), 2.01–1.95 (m, AA′ of AA′BB′, 2 H), 1.32–1.27 (m, BB′ of AA′BB′, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.6, 126.5, 118.7, 78.9, 26.6.

(1*E*,2*E*)-1,2-Bis[(1-propyl-1*H*-Pyrrol-2-yl)methylene]hydrazine (29): Obtained as a pale-orange viscous liquid that was recrystallized from MeOH to give a yellow powder (mp 59–60.5 °C). Isolated yield: 89%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40 (br, 2 H), 6.75 (app. t, *J* = 2.1 Hz, 2 H), 6.56 (br s, 2 H), 6.11 (dd, *J* = 3.7, 2.6 Hz, 1 H), 4.24 (t, *J* = 7.2 Hz, 4 H), 1.75 (hext, *J* = 7.2 Hz, 4 H), 0.85 (t, *J* = 7.2 Hz, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.4, 126.5, 125.9, 116.1, 107.4, 49.2, 23.3, 9.7; IR: 2957, 2921, 2856, 1619, 1522, 1460, 1416, 1402, 1368, 1295, 1213, 1065. HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{23}N_4$: 271.1923; found: 271.1905.

1-(1-Propyl-1*H*-pyrrol-2-yl)ethanone (27):[32] Isolated yield: 91%; dark-brown viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.96 (dd, *J* = 4.0, 1.6 Hz, 1 H), 6.85 (app t, *J* = 2.5 Hz, 1 H), 6.12 (dd, *J* = 4.0, 2.5 Hz, 1 H), 4.27 (t, *J* = 7.2 Hz, 2 H), 2.43 (s, 3 H), 1.75 (hext, *J* = 7.2 Hz, 2 H), 0.89 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.2, 130.2, 130.1, 120.2, 107.8, 51.4, 27.3, 24.6, 11.0.

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