A simple and straightforward approach toward selective C=C bond reduction by hydrazine

Hao Chen, Jianmin Wang, Xuechuan Hong, Hai-Bing Zhou, and Chune Dong

Abstract: A simple and straightforward method for reducing the C=C double bond with hydrazine is described. A number of representative C=C bonds in various steric and electronic environments were examined. Substituted alkenes can be selectively reduced in EtOH in the presence of hydrazine to give the corresponding products in up to 100% yields.

Key words: hydrazine, reduction, C=C double bond.

Résumé : On décrit une méthode simple et directe de réduire une double liaison C=C à l'aide d'hydrazine. On a appliqué la méthode à un certain nombre de doubles liaisons typiques, dans des environnements stériques et électroniques variés. Il est possible de réduire sélectivement des alcènes substitués dans l'éthanol, en présence d'hydrazine, pour conduire aux produits correspondants avec des rendements allant jusqu'à 100 %.

Mots-clés : hydrazine, réduction, double liaison C=C.

[Traduit par la Rédaction]

Introduction

The reduction of functionalized alkenes is one of the most fundamental reactions in organic chemistry.[1] In recent decades, various transition-metal catalysts such as Rh, Pt, and Pd were generally applied for the selective reduction of alkenes to the corresponding alkanes.[2,3] Despite the important progress in this field, these reported processes not only had harsh conditions and limited selectivity, but also produced significant amounts of inorganic and organic wastes that are of environmental concern. Thus, the development of more efficient, environmentally friendly, and economical nonmetal reagents for selective reduction of functionalized alkenes is of interest to the organic synthesis and medicinal chemistry communities as well.

In contrast, diimide reduction appears to offer an attractive solution, since NH=NH acts as a mild reducing agent for a variety of unsaturated bonds.[4,5] This reduction process has the potential to be environmentally benign, since nitrogen gas is the sole waste product. Imada et al.[6] reported the first green method for aerobic hydrogenation; the olefins can be reduced by treatment with hydrazine in the presence of FLEt·ClO_4 under an O_2 atmosphere to give the product in excellent yields, with environmentally benign water and molecular nitrogen as the only waste products. *o*-Nitrobenzenesulfonylhydrazide (NBSH) is known to be another convenient precursor of diimide, since the *o*-nitrobenzene sulfinate is a good leaving group under mild conditions. In 2009, Marsh and Carbery[7] demonstrated NBSH forming the simple and efficient diimide alkene's reductions protocol. Meanwhile, it was also recognized that when the level of substitution of alkenes increases, the reaction becomes less efficient and low conversion is observed. Obviously, these methods provide improved results over traditional methods. However, the limitation of scope and the presence of organo or metal catalysts all preclude the straightforward approach to selective C=C double bond reduction.[8] Therefore, the development of more efficient, commercial available, and simple reducing agents is highly desirable.

To the best of our knowledge, there has not been a report on the facile reduction of the C=C double bond by hydrazine under mild conditions. Herein, we wish to report an unexpected reduction reaction of functionalized alkenes with commercially available hydrazine under simple thermal conditions that leads to a general and efficient method for selective C=C double bond reduction of substituted alkenes.

Results and discussion

Our studies were initiated by the reaction of 2-allylphenol **1a** with commercial hydrazine hydrate **2**. The reaction was carried out in air. To our delight, when 8 equiv of **2** was used, **1a** was fully converted to 2-propylphenol **3a** (Table 1, entry 7). As reasonably expected, no product was observed when the reaction was run under an argon atmosphere (Table 1, entry 10), which clearly indicates that diimide reduction occurred. After a brief survey of the reaction conditions, it was found that solvents and the amount of hydrazine were critical for the reaction efficiency (Table 1). 2-Allylphenol was treated with 2 equiv of hydrazine in EtOH at 80 °C, leading to trace amounts of the desired product after 14 h (Table 1, entry 9). Further study indicated that a 34% yield

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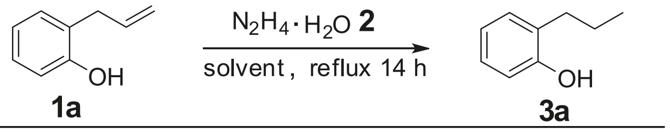
Table 1. Reduction of 2-allylphenol under various conditions.



Entry	**2** (equiv)	Solvent	Conversion (%)[a]
1	8	MeOH	22
2	8	H_2O	35
3	8	CH_3CN	59
4	8	THF	9
5	8	DCM	2
6	8	Toluene	17
7	8	EtOH	100
8	4	EtOH	34
9	2	EtOH	1
10[b]	8	EtOH	No reaction

Note: Reaction conditions: 2-allylphenol (**1a**, 2 mmol), appropriate amount of hydrazine hydrate (**2**), solvent, reflux 14 h.

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture.

[b] The reaction was run under an argon atmosphere.

of product was obtained when 4 equiv of **2** was employed (Table 1, entry 8). Additionally, among the tested solvents, ethanol was identified as the solvent of choice. Acetonitrile gave an inferior result, but dichloromethane, THF, and toluene were observed to be ineffective (Table 1, entries 1–6).

Having identified the optimal reaction conditions, we next explored the scope and limitations of this reduction reaction with hydrazine using various alkenes derivatives (**1b**–**1r**). The results are summarized in Table 2. Clearly, our reduction system proved rather effective for the selective reduction of a wide variety of substituted alkenes, providing the corresponding product in excellent yields. In addition to 2-allylphenol **1a**, terminal alkenes **1b** and **1c** also reacted smoothly with hydrazine giving the corresponding products in excellent yields (Table 2, entries 2 and 3). Additionally, a polarized alkene, such as **1d**, was efficiently reduced by hydrazine in 5.5 h, forming product **3d** in excellent yield (Table 2, entry 4). Aromatic alkenes with the phenyl ring substituted with an electron-donating or an electron-withdrawing group also performed well in this reduction (Table 2, entries 5–13). For example, *p*-methoxyl methyl cinnamate (**1i**) and *p*-trifluoromethyl cinnamic acid (**1l**) underwent smooth reduction (Table 2, entries 9 and 12). It can be clearly seen that when the level of th ealkene substitution increases, the reduction becomes less efficient. Tetra-substituted alkene **1r** remained inert under the same reaction conditions (Table 2, entry 18). Interestingly, in the case of styrene, a 16% yield of enthylbenzene was obtained (Table 2, entry 17), which indicates that, for mono-substituted alkenes, conjugation might play an important role in hydrazine-promoted reduction.

Clearly, this reduction system offers synthetic advantages with respect to metal-catalyzed hydrogenation and other reducing systems as well.

Conclusions

In conclusion, a simple, efficient, and highly selective C=C double bond reduction protocol has been developed. The hydrazine-mediated reducing system has been successfully applied to various substituted alkene reductions to form the desired products in excellent yields. We believe this reduction method, from a synthetic point of view, is a valuable alternative not only for the laboratory but also for industry.

Experimental section

General information

All reagents and solvents were obtained from commercial sources and were used without further purification. The hydrazine hydrate used in this study was 80% solution. Column chromatography was performed with silica gel (300–400 mesh). NMR spectroscopy was performed on a Bruker (400 MHz) spectrometer using TMS as the internal standard. Products were characterized by comparison of their ^{1}H NMR spectroscopic data with those reported in the literatures.

General procedure for reduction reactions with hydrazine hydrate

To 1 mmol of substrate **1** dissolved in 1.0 mL of solvent was added 8 mmol of hydrazine **2** and the mixture was heated to reflux for 5.5–24 h in air. After the reaction finished, the solvent was removed and the residue was extracted three times with ethyl acetate (3 × 5 mL) and dried over $MgSO_4$. The product was characterized by NMR.

Acknowledgments

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References

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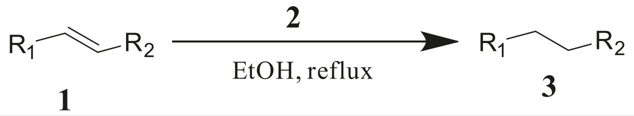
Table 2. Scope of the reduction reactions promoted by hydrazine.



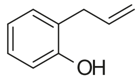
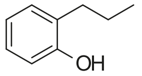
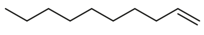
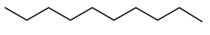
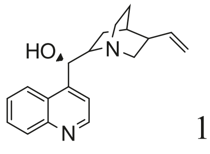
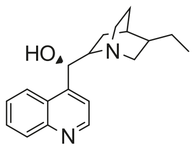
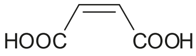
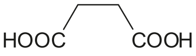
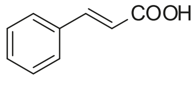
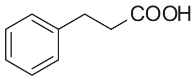
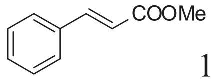
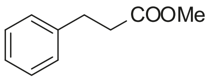
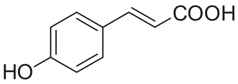
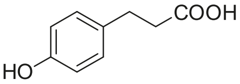
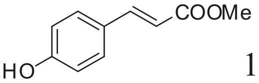
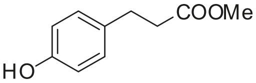
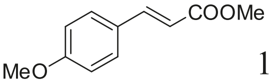
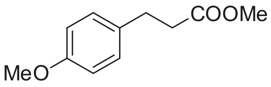
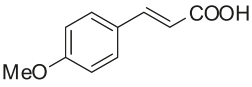
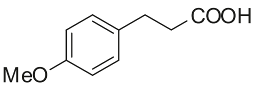
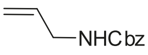
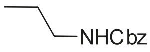
Entry	Substrate		Product		Yield (%)
1		1a		3a	100
2[a]		1b		3b	100
3[a]		1c		3c	100
4[b]		1d		3d	94
5[b]		1e		3e	96
6[b]		1f		3f	98
7[b]		1g		3g	96
8[b]		1h		3h	95
9[b]		1i		3i	98
10[b]		1j		3j	92
11[a]		1k		3k	100

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Table 2. *(concluded).*

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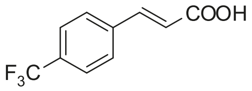
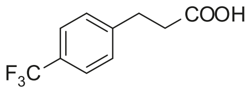
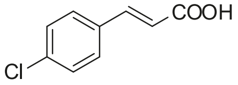
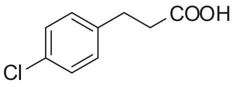
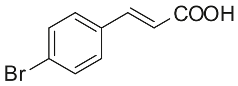
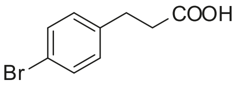
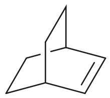
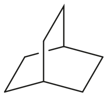
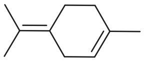
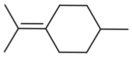
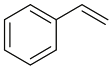
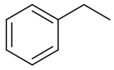
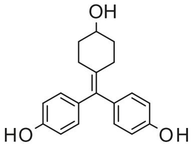
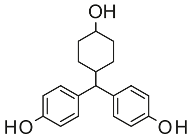
12^b	 1l	 3l	>99
13^b	 1m	 3m	>99
14^b	 1n	 3n	91
15^a	 1o	 3o	42
16^a	 1p	 3p	42
17^a	 1q	 3q	16
18	 1r	 3r	—^{c}

Note: Reaction conditions: **1** (5 mmol), hydrazine hydrate (**2**, 8 equiv), reflux in EtOH (5 mL), 14 h.

[a] Reaction time was 24 h.

[b] Reaction time was 5.5 h and the same result was observed in H_2O.

[c] No reaction.

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