A New and One-Pot Synthesis of *α,β*-Unsaturated Ketones by Dehydrogenation of Various Ketones with *N-tert*-Butyl Phenylsulfinimidoyl Chloride

Teruaki Mukaiyama,* Jun-ichi Matsuo, and Hideo Kitagawa
Department of Applied Chemistry, Faculty of Science, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162-8601

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α,β-Unsaturated ketones were synthesized by one-pot procedure from various ketones in good to excellent yields on treatment of their lithium enolates with *N-tert*-butyl phenylsulfinimidoyl chloride (**1**) under mild conditions.

Transformation of saturated carbonyl compounds to *α,β*-unsaturated ones by dehydrogenation[1] is important since *α,β*-unsaturated carbonyl compounds are versatile intermediates in synthetic organic chemistry, especially in the synthesis to introduce a desired substituent at their *β*-positions. For this transformation, some methods are known to be useful although the procedures are consisted of more than two steps. For example, carbonyl compounds are converted to *α*-halo compounds first and then they are dehydrohalogenated with appropriate bases at rather high temperatures in traditional halogenation–dehydrohalogenation method.[2] Methods such as sulfenylation–sulfoxide elimination[3] and selenylation–selenoxide elimination[4] are also frequently being employed because of their versatility. In those procedures, *α*-sulfur or selen compounds are usually prepared from metal enolates and then they are oxidized to cause elimination at suitable temperatures. Additionally, *α,β*-unsaturated ketones or esters are synthesized by using catalytic amounts of palladium(II) acetate from silyl enol ethers or silyl ketene acetals which are prepared in advance from their parent carbonyl compounds.[5] On the other hand, there are several methods reported for direct dehydrogenation of carbonyl compounds,[6] although their reaction conditions are severe and the kind of carbonyl compounds is limited. Therefore, a mild and direct dehydrogenation reaction of carbonyl compounds is strongly desired especially for the case of complex molecules having labile functional groups. Of many efforts to realize the transformation under mild conditions, the elimination of selenoxides is most advantageous because it takes place at lower temperatures. On the other hand, selenium based reagents have some disadvantageous properties such as toxicity, unpleasant odors, etc. In this communication, we would like to report a new and one-pot dehydrogenation reaction of various ketones forming the corresponding *α,β*-unsaturated carbonyl compounds by using *N-tert*-butyl phenylsulfinimidoyl chloride (**1**)[7] under very mild reaction conditions.

It was recently reported from our laboratory that a new and efficient oxidation reaction of primary and secondary alcohols by using **1** and DBU was performed to form the corresponding carbonyl compounds.[7] Then, it was considered that saturated carbonyl compounds would be directly dehydrogenated to the corresponding *α,β*-unsaturated ones by treating their enolates with **1**.

In the first place, dehydrogenation of cyclohexanone (**2**) forming cyclohexenone (**3**) was examined under the reaction conditions as listed in Table 1. In order to examine the effect of the metals, lithium, sodium, and potassium enolates were tried. Their in situ formed enolates were treated with a small excess of **1** at –78 °C in THF. When the lithium enolate was generated from **2** by the use of LDA, **3** was obtained in 93% yield while other metal enolates such as sodium or potassium enolates gave poor results. The above dehydrogenation reaction proceeded efficiently also via the lithium enolate formed from the corresponding trimethylsilyl enol ether by a reaction with methyllithium[8] (Scheme 1). This result suggested that diisopropylamine formed after deprotonation with LDA did not work as a base in a subsequent elimination step. Then, an intramolecular proton abstraction by a sulfinimidoyl group is proposed which is to be discussed later.

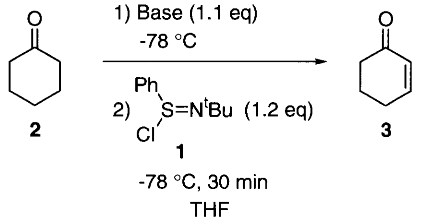
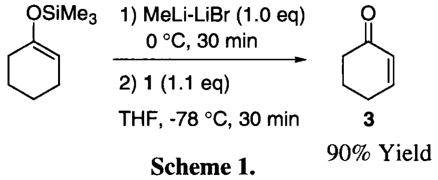


Table 1. Effect of bases in one-pot *α,β*-unsaturated ketone formation by using **1**

Entry	Base[a]	Yield/%[b]
1	LDA	93
2	NHMDS	31
3	KHMDS	32

[a]LDA; lithium diisopropylamide. NHMDS; sodium bis(trimethylsilyl)amide. KHMDS; potassium bis(trimethylsilyl)amide. [b]Determined by GC analyses using an internal standard.

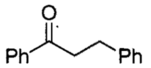
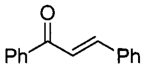
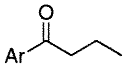
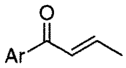
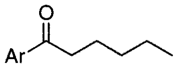
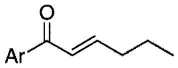
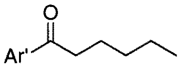
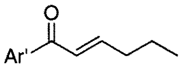
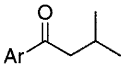
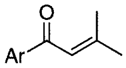
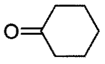
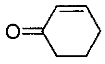
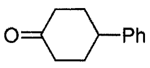
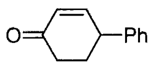
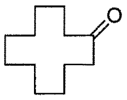
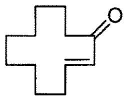
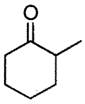
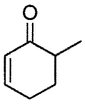


Scheme 1.

The direct one-pot dehydrogenation of various ketones was performed by using LDA and **1** (Table 2). The dehydrogenation of both acyclic and cyclic ketones proceeded efficiently at –78 °C except for the reaction of 1-(*p*-bromophenyl)-1-hexanone (entry 4), which is probably due to the incomplete introduction of the sulfinimidoyl group. Concerning stereoselective formation of (*E*)- or (*Z*)-*α,β*-unsaturated ketones, only (*E*)-isomers were detected in this procedure. In some cases, addition of 15-

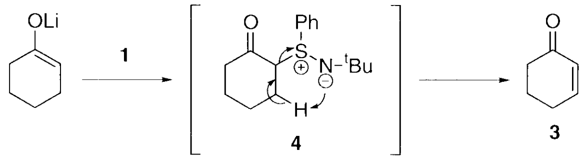
crown-5 slightly improved the yields of enones but normally, the reaction worked well without adding it. Other additives such as HMPA or TMEDA did not improve yields of enones. Interestingly, the less substituted position was selectively dehydrogenated and 6-methyl-2-cyclohexen-1-one was obtained exclusively when 2-methylcyclohexanone was dehydrogenated by this procedure (entry 9).

Table 2. One-pot dehydrogenation of various ketones to the corresponding α,β-unsaturated ketones by using **1**[a]

Entry	Substrate[b]	Product[b]	Yield/%[c]
1[d]			95
2			77
3			93
4			67
5			77[e]
6			93[f]
7[d]			84
8			84[f]
9			92[f]

[a]Reaction conditions; i) LDA (1.1 eq), -78 °C, ii) **1** (1.2 eq), -78 °C, 30 min. [b]Ar; p-MeOC$_6$H$_4$. Ar'; p-BrC$_6$H$_4$. [c]Isolated yields unless otherwise mentioned. [d]15-Crown-5 (1.1 eq) was added. [e]Determined by ^{1}H NMR using an internal standard. [f]Determined by GC analyses using an internal standard.

Typical experimental procedure is as follows (Table 1, entry 1). Under an argon atmosphere, to a mixture of diisopropylamine (151 mg, 1.49 mmol) in THF (1.5 mL) was added n-BuLi (1.68 N in hexanes, 0.79 mL) at –78 °C and the resulting mixture was stirred for 10 min. Then, a solution of **2** (119 mg, 1.21 mmol) in THF (1.5 mL) was added and the mixture was stirred for 10 min at –78 °C. Finally, a solution of **1** (345 mg, 1.46 mmol) in THF (1.0 mL) was added at –78 °C and the resulting pale yellow solution was stirred for 30 min at the same temperature. The reaction was quenched by adding 1% hydrochloric acid (5 mL) and the mixture was extracted with dichloromethane (20 mL × 3). The yield of **3** was determined by GC analysis using an internal standard (93%).



Scheme 2.

The present reaction proceeds much easier to afford the dehydrogenated products at –78 °C than the respective reactions of using sulfoxides which generally require elevated temperatures around 60 to 120 °C and selenoxides which cause elimination at temperatures between 0 and 25 °C. It was then assumed that a lithium enolate would react with **1** to give a similar C-sulfinimidoylated intermediate (**4**) as in the cases of sulfoxides and selenoxides.[9] Thus formed **4** is immediately converted to α,β-unsaturated ketones even at –78 °C by the intramolecular elimination via a five-membered transition state (see Scheme 2).[10]

References and Notes

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