O-mesityl(sulfonyl)hydroxylamine: A Novel Reagent for Reduction of Electron Deficient α,β-Unsaturated Carbonyl Derivatives

Gondi Sudershan Reddy,[1*]

[1] Departments of Chemistry, National Taiwan Normal University, Taipei, Taiwan, 116 (ROC).

Correspondence email: gondisr@gmail.com

Abstract: Hydrogenation of electron deficient **α,β**-unsaturated carbonyl derivatives using *O*-mesityl(sulfonyl)hydroxylamine in the presence of catalytic amount of ytterbium triflate to obtain good to excellent is described.

Key words: *O*-mesityl(sulfonyl)hydroxylamine (MSA), α,β-unsaturated carbonyl, Hydrogenation, $Yb(OTf)_3$, selectivity.

Introduction: Selective hydrogenation of olefin bond of conjugated carbonyl compounds in the presence of other function groups is an important task in organic synthesis. As hydrogen[1,2] from gas cylinder is potentially explosive and requires to be used with caution in a special apparatus, search for alternative methods to conventional hydrogenation procedures such as heterogeneous and homogeneous catalytic transfer hydrogenation is still going on. Surprisingly, there are only a few methods available in the literature for effecting the reduction of the olefin in α,β-unsaturated carbonyl/nitro molecules. The most common used reagents for the reduction of conjugated carbonyl compounds are palladium assisted hydrogen transfer by ammonium formate,[3] formic acid,[4] Diphenyl sulfide,[5] polystyrene,[6] or potassium formate,[7] Palladium acetate,[8] metal catalyzed reduction by sodium hydrogen telluride,[9] copper nanoparticles,[10] samarium iodide,[11] lithium aluminum hydride with $SbCl_3$,[12] sodium boroacetate,[13] sodium borohydride reduced hydroxy ester,[14] nickel chloride,[15,16] iridium,[17] ruthenium,[18] silane hydride[19] and Yeast in organic solvent system.[20]

Recently, *O*-mesityl(sulfonyl)hydroxylamine is used for aziridination of simple olefins.[21] It is a versatile class of reagents and has been used for the various functional group transformation, migration of O-Phenylhydroxylamine,[22] N-Unsubstituted Arylsulfilimines,[23] Hydroxy-amine,[24] Hydrazine,[25] and Beckman Rearrangement.[26] Surprisingly, no significant effort has yet been made to utilize this potential reagent for the regio and stereoselective hydrogenation of double bonds of α,β-unsaturated compounds. In the course of research programme directed towards the synthesis of novel reagent for hydrogenation of olefins. We found a new and convenient entry to a hydrogenation method. Herein we disclose that *O*-mesityl(sulfonyl)hydroxylamine (**MSA, 11a**), is a very efficient reagent in the selective hydrogenation of olefin conjugated to carbonyl group without effecting other functional groups in the molecule. Thus, treatment of camphor pyrazolidinone derived acrylate **1a** with *O*-mesityl(sulfonyl)hydroxylamine in CH_2Cl_2 provided **2a** in 70% material yield (Table 1 entry 7). The structure was initially assigned by ^1H, ^{13}C-NMR and HRMS analyses and further confirmed by single crystal X-ray analysis.

Scheme-1

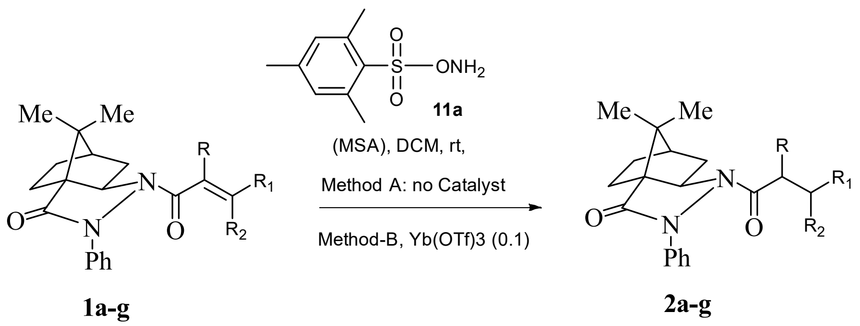


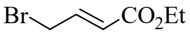
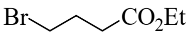
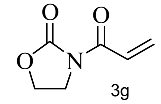
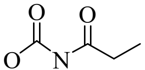
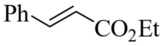
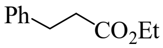
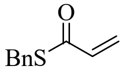
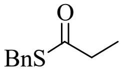
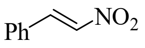
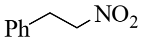
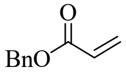
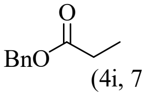
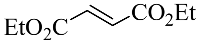
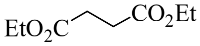
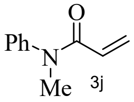
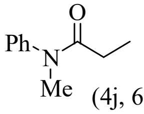
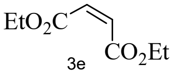
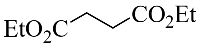
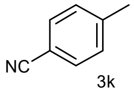
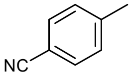
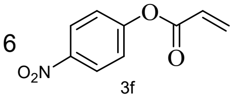
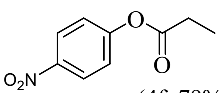
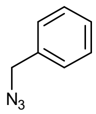
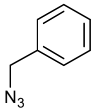
Table-1

entry	Substrate	R	R1	R2	solvent	Time (h)	Method-A Yield (%)	Method-B Yield (%)
1	**1a**	H	H	H	CH_2Cl_2	24	60	91
2	**1a**	H	H	H	toluene	36	57	
3	**1a**	H	H	H	CH_3CN	72	41	
4	**1a**	H	H	H	$CHCl_3$	48	56	
5	**1b**	H	CH_3	H	CH_2Cl_2	24	54	90
6	**1c**	H	C_3H_7	H	CH_2Cl_2	24	56	88
7	**1d**	H	Ph	H	CH_2Cl_2	24	58	76
8	**1e**	H	COOEt	H	CH_2Cl_2	18	78	93
9	**1f**	CH_3	H	CH_3	CH_2Cl_2	24	9	15
10	**1g**	Br	H	H	CH_2Cl_2	48	5	12
11	**1h**	CH_3	CH_3	H	CH_2Cl_2	72	0	0
12	**1i**	H	CH_3	CH_3	CH_2Cl_2	72	0	0

To test the generality of the procedure, various substates were subjected to the reaction conditions (see table 1) and it is concluded that the ease of reduction is sensitive to steric and electronic factor. For example, when cinnamoyl ester (entry 8, Method-A) high yield is obtained, due to two electron withdrawing group on either side. Whereas low chemical yield (<10%) was obtained with α-methyl (entry 9, Method-A) or α-bromo (entry 10, Method-A) substituent while no desired products were isolated when α,β-dimethyl (entry 11, Method-A) or β,β–dimethyl (entry 12, Method-A) substrates were used. Even more interestingly the chemical yields were significantly improved in the presence of catalytic amount of Lewis acid (entries 1 and 5-8, Method-B). In case of α,β-dimethyl (entry 11, Method-B) or β,β–dimethyl (entry 12, Method-B), even increase the catalyst load to 0.5% and prolong reaction time also did not gave the products. The used of triethylamine or DBU is ineffective on the rate of reaction.

To further explore the utility of *O*-mesityl(sulfonyl)hydroxylamine as a new and convenient entry to hydrogenation methods, a variety of α,β-unsaturated carbonyl derivatives were studied, and the results are summarized in Table 2. The carbon carbon double bond in several structurally varied amides underwent hydrogenation to give the corresponding saturated analogues in moderate to excellent yields by this procedure. The substituents on the olefins apparently have influence on the course of hydrogenation. Other reducible groups such as ethyl ester or amide, halogen, nitro groups were fully compatible with the reaction conditions and remained unaltered. The mechanistic explanation of this reaction remained unclear and it is believed that self coupling of reagent occurs to form the diimide[27,28] compounds with liberation of hydrogen gas, which is consumed by olefins during reaction.

Table 2 Selective hydrogenation of various α,β-unsaturated carbonyl derivatives using *O*-mesityl(sulfonyl)hydroxylamine in the presence of Yb(OTf)$_3$.[a]

entry	substrate	product	entry	substrate	product
1	 3a	 (4a, 80%)	7	 3g	 (4g, 90%)
2	 3b	 (4b, 91%)	8	 3h	 (4h, 62%)
3	 3c	 (4c, 42%)^{X}	9	 3i	 (4i, 70%)
4	 3d	 (4d, 90%)	10	 3j	 (4j, 60%)
5	 3e	 (4d, 90%)	11	 3k	
6	 3f	 (4f, 79%)	12	 3l	

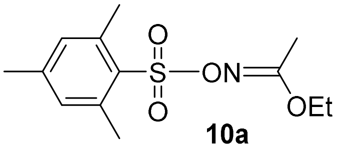
[a] The conjugated carbonyl compound (1.0 mmol) was stirred with *O*-mesityl(sulfonyl)hydroxylamine (10 mmol) and ytterbium triflate (0.1 mmol) in CH$_2$Cl$_2$ (10 mL) at ambient temperature. [b] Isolated yield. ^{X} = yield based on NMR integration.

In separate experiments, the compounds with nitrile group and azide were treated under same reaction conditions, we recovered starting materials only, it further enhances the selective reduction of unsaturated carbonyl compounds over nitrile and azides.

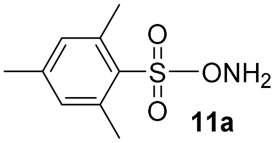
The experimental procedure is very simple and straight forward. The conjugated carbonyl compound (0.25-0.5 mmol) was stirred with *O*-mesityl(sulfonyl)hydroxylamine (1-2 mmol) and ytterbium triflate (0.025-0.05 mmol) in dichloromethane (5-10 mL) was stirred for a certain period of time as required to complete the reaction. (usually 24h). After completion of reaction, dilute with water, extract with dichloromethane. Wash the organic layer with water, brine, dried over $MgSO_4$ and concentrated under reduced pressure to get the crude product, which on column chromatography purification gives pure product.in 60-93% yield.

Stability study of Sulfonyl hydroxylamine derivatives

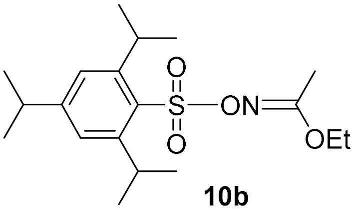
Four sulfonyl amines that is *O*-(2,4,6-trimethylbenzenesulfonyl) hydroxylamine (**11a**), *O*-(2,4,6-triisopropylbenzenesulfonoyl) hydroxylamine (**11b**), *O*-(4-methylbenzenesulfonoyl) hydroxyl amine (**11c**), *O*-(4-nitrobenzenesulfonoyl) hydroxylamine (**11d**) were prepared according to the known procedure, and found that *O*-(2,4,6-trimethylbenzenesulfonyl) hydroxylamine (**11b**) is very effective in hydrogenation reaction. The stability of sulfonyl amine is **11b**>**11a**>**11c**>**11d**. but reactivity order is **11a**>**11b**>**11c**>**11d**. Present of nitro group on benzene is reduced the stability and reactivity. Whereas the triisopropyl group (**11b**) is very stable, but reactivity is low when compare with trimethyl group (**2**), because of bulky isopropyl group at ortho position on aromatic ring.



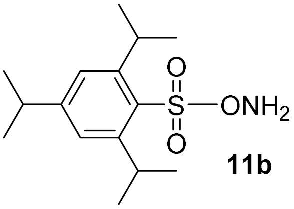
10a



11a



10b



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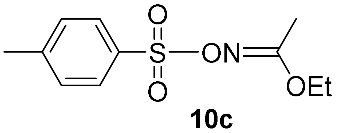

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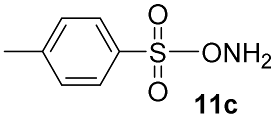

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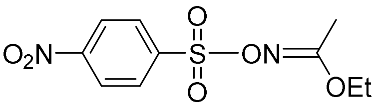
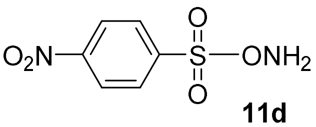


10d



11d

In summary, the mild condition, high yields of products, operational simplicity, easy availability of reagent and no external use of explosive hydrogen gas makes this methodology a more useful and practical alternative to the existing methods for reduction of α,β- unsaturated carbonyl compounds. This extends the synthetic application to *O*-mesityl(sulfonyl)hydroxylamine. We believe that this method will find useful applications in the field of organic synthesis.

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■ **Competing interests:** There is no Competing Interests pending.

Data and materials availability: Crystallographic model data is available through the CCDC under identifier 1999014 [(6R,7aR)-8,8-dimethyl-2-phenyl-1-(3-phenylpropanoyl)hexahydro-3a,6-methanoindazol-3(2H)-one, **2d]**. 1990770 [(6R,7aR)-1-(2-bromopropanoyl)-8,8-dimethyl-2-phenylhexahydro-3a,6-methanoindazol-3(2H)-one, **2g**],

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