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A New Approach to 2,3-Dihydro-1*H*-1,5-Benzodiazepines from the Reaction of *o*-Nitrophenylazide with α,β-Unsaturated Ketones Promoted by Samarium Diiodide

Xiao Yuan CHEN[3], Wei Hui ZHONG[1], Yong Min ZHANG*[,1,2]

[1]Department of Chemistry, Zhejiang University at Xixi Campus, Hangzhou 310028
[2]Laboratory of Organometallic Chemistry, Chinese Academy of Sciences, Shanghai 200032
[3]Department of Chemistry, Hunan Jishou University, Jishou 416000

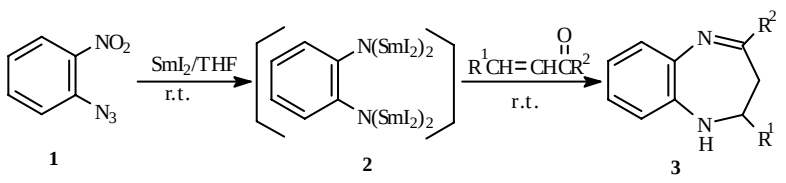
Abstract: *o*-Nitrophenylazide was reduced by SmI_2 in anhydrous THF at room temperature to produce active intermediate **2** (samarium amide), "living" double-anion *in situ* which reacted smoothly with α,β-unsaturated ketones to afford 2,3-dihydro-1*H*-1,5-benzodiazepines in good yields under mild and neutral conditions.

Keyword: Samarium diiodide, reduction, nitro group, azide, 2,3-dihydro-1*H*-1,5-benzodiazepine.

Applications of samarium diiodide as a mild, neutral, selective and versatile single-electron transfer reducing and coupling reagent in organic synthesis have grown significantly in the last decade[1]. It is well known that both nitro compounds[2a] and azide compounds[2b] can be easily reduced by SmI_2 to the corresponding amines. Little attention has been given to the intermediates derived from nitro or azide groups by treatment of SmI_2, which may lead to reactions difficult to accomplish by other existing methodologies[3].

2,3-Dihydro-1*H*-1,5-benzodiazepine derivatives have attracted interest due to their biological properties such as anticonvulsant activity[4]. The methods for preparing these compounds using *o*-phenylenediamines as starting materials involved harsh conditions such as using acid or base catalysts, moderate thermal conditions and long reaction time[5]. Here we described a new approach to 2,3-dihydro-1*H*-1,5-benzodiazepines *via* simultaneous reduction of nitro group and azide group of *o*-nitrophenylazide **1** by SmI_2 followed by reaction with α,β-unsaturated ketones (**Scheme 1**).

Scheme 1



1 **2** **3**

The results are summarized in **Table 1**. When *o*-nitrophenylazide **1** was treated with SmI_2 at room temperature, the simultaneous reduction of nitro group and azide

group resulted in the formation of trivalent samarium species. According to the literatures[3], we considered the trivalent samarium species was the intermediate **2** (samarium amide) which was "living" double-anion *in situ* and might react smoothly with α,β-unsaturated ketones to afford 2,3-dihydro-1*H*-1,5-benzodiazepines **3**. The results proved our consideration. According to **Table 1**, It was found that chalcones (**entries 3a-g**) are more reactive towards the new anion species **2** than any other α,β-unsaturated ketones (**entries 3h-i**).

Table 1 Preparation of 2,3-dihydro-1H-1,5-benzodiazepines promoted by SmI_2[a]

Entry	R^1	R^2	T(h)	Yield(%)[b]
3a	Ph	Ph	3	87
3b	p-MeC_6H_4	Ph	3	85
3c	p-$MeOC_6H_4$	Ph	3	78
3d	p-ClC_6H_4	Ph	2	83
3e	p-BrC_6H_4	Ph	2	78
3f	3,4-$(OCH_2O)_2C_6H_3$	Ph	4	76
3g	m-$NO_2C_6H_4$	Ph	2	87
3h	Ph	Me	5	58
3i	Ph	C_6H_5CH=CH	4	65

[a]1mmol of *o*-nitrophenylazide, 1mmol of α,β-unsaturated ketones and 8mmol of SmI_2 were used. [b]Isolated yields based on *o*-nitrophenylazide. All products were characterized by IR, ^1H NMR, MS spectra and elemental analysis.

In summary, a new approach to 2,3-dihydro-1*H*-1,5-benzodiazepines has been provided using available starting materials under mild and neutral conditions.

General procedure: a solution of *o*-nitrophenylazide **1** (1 mmol) in anhydrous THF (2 mL) were added dropwise to a solution of SmI_2 (8 mmol) in THF (30 mL) at room temperature under a dry nitrogen atmosphere. The mixture was stirred for 5 minutes and became yellow gradually. Then α,β-unsaturated ketones (1.1 mmol) in THF (2 mL) were added. After stirring at room temperature for a given time (**Table 1**, the reaction was monitored by TLC), the reaction was quenched with dilute hydrochloric acid (0.1mol/L, 1 ml). The crude product was isolated and purified by preparative TLC on silica gel using ethyl acetate and cyclohexane (1: 6) as an eluent.

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