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A Novel Synthesis of 3,4-Dihydro-(2H)-1,2,4-Benzothiadiaizine-1,1-Dioxides Promoted by Samarium Diiodide

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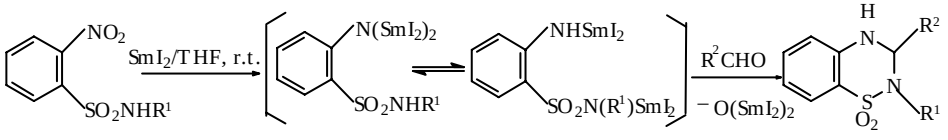
Abstract: 3,4-Dihydro-(2H)-1,2,4-benzothiadizine-1,1-dioixdes were prepared in good yields *via* reductive cyclization of o-nitrobenzenesulfonamides with aldehydes promoted by SmI_2 under mild and neutral condition.

Keywords: Samarium diiodide, 2H-1,2,4-benzothiadizine-1,1-dioxide, reductive cyclization.

Applications of samarium diiodide as a mild, neutral, selective and versatile single-electron transfer reducing and coupling reagent in organic synthesis have significantly grown in the last decade[1]. Previous work on some deoxygenation and some reductive cleavage of S-S, Se-Se, Te-Te bonds with SmI_2 was reported[2]. It is well known that nitro compounds can be reduced easily by SmI_2. However, they are just reduced to the corresponding amines[3], little attention has been concerned on the intermediate derived from a nitro group by SmI_2 treatment, which may be induce some reactions difficult to accomplish by other existing methodologies[4]. Herein, we wish to report the preparation of 3,4-dihydro-(2H)-1,2,4-benzothiadizine-1,1-dioixides in one pot *via* reductive cyclization of *o*-nitrobenzenesulfonamides with aldehydes promoted by SmI_2 under mild and neutral condition.

Scheme 1



1 **2** **3**

The results are summarized in **Table 1**. When *o*-nitrobenzenesulfonamides **1** were treated with SmI_2 at room temperature, the reduction of nitro group resulted in the formation of the trivalent samarium species. According to the relative literature[4], we considered these species may be samarium amides **2**, which are "living" anions and reacted smoothly with aldehydes to afford 3-substituted 3,4-dihydro-(2H)-1,2,4-benzothiadizine-1,1-dioxides **3** in moderate to high yields.

2H-1.2.4-benzothiadizine-1,1-dioxide derivatives have attracted strong interest due to their biological properties such as their diuretic activity[5a], antihypertensive activity[5b]. Several methods had been introduced to prepare this kind of compounds[5]. Here we

provided a novel route to synthesize 3,4-dihydro-(2H)-1,2,4-benzothiadizine-1,1-dioxides, the advantage of which are readily available starting materials, straightforward and simple synthetic procedures, mild reaction conditions and moderate to high yield.

Table 1 Reaction of *o*-nitrobenzenesulfonamides with aldehydes promoted by SmI_2[a]

Entry	R^1	R^2	Reaction condition		Yield(%)[b]
			T / ℃	t / h	
3a	H	n-Pr	r.t.	2	90
3b	H	n-Bu	r.t.	2	85
3c	H	n-C_6H_{13}	r.t,	3	83
3d	H	$C_6H_5CH_2$	r.t.	3	76
3e	H	C_6H_5	r.t	3	80
3f	H	p-$MeOC_6H_4$	r.t	3	81
3g	H	m-BrC_6H_4	r.t	3	83
3h	H	p-$NO_2C_6H_4$	r.t	3	72
3i	Me	n-Pr	40	3	65
3j	Me	C_6H_5	40	3	60

[a] 1 equiv. nitro compounds, 1.2 equiv.aldehydes and 6 equiv. SmI_2 were used; [b] isolated yields based on nitro compounds; all the products were characterized by ^1H NMR and IR spectra.

General procedure: A solution of *o*-nitrobezenesulfomamides **1** (1 mmol) in anhydrous THF (2 ml) was added dropwise to a solution of SmI_2 (6 mmol) in THF (20 ml) at room temperature under dry nitrogen atmosphere. The mixture was stirred for 0.5 hrs and became yellow gradually. Then aldehydes (1.2 mmol) in THF (2 ml) were added. After stirred for a given time (**Table 1**), the reaction was quenched with dilute hydrochloric acid (0.1mol/L, 3 ml). The crude product was isolated with usual ways and purified by preparative TLC on silica using with ethyl acetate and cyclohexane (1: 2) as eluent.

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