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Aminolysis of Aziridines Catalyzed by Samarium Iodides

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Abstract Samarium diiodide is an efficient catalyst for the aminolysis of either activated or non activated aziridines with aromatic amines. A variety of *N*-diprotected *β*-diamines has been prepared including new products. The comparison of the *N*-protecting groups of aziridines in reactions catalyzed by samarium diiodide or by samarium iodobinaphtholate indicates that *N*-Boc protection leads to the best results.

Keywords Samarium diiodide · Aminolysis · Aziridine · Ring opening reaction · Catalysis

1 Introduction

The ring opening of aziridines by amines gives a straightforward and atom economic access towards 1,2-diamines which are important key scaffolds for biologically active molecules [1–5] and widely used in enantioselective catalysis as chiral ligands or organocatalysts [6, 7]. The reactivity of aziridines towards ring opening reactions is lower than that of epoxides and depends on the presence or not of an electron withdrawing group on the nitrogen atom. Ring opening reactions of aziridines including reactions with nitrogen nucleophiles have been recently reviewed by Hu [8]. Regio- and enantioselective aminolyses of aziridines have been developed with achiral and chiral Lewis acid catalysts. Aminolysis of *N*-tosyl aziridines were reported using rare earth triflates, indium bromide, rare earth or indium chlorides and $TaCl_5$ on silicagel [9–12]. $LiClO_4$ has also been employed as a catalyst for the ring opening of *N*-tosylaziridines by aromatic amines [13] but in stoichiometric amount for the opening of *N*-benzyl and *N*-alkyl aziridines with aliphatic amines [14]. Aminolyses of aziridines *N*-substituted by aromatic or benzyl groups with aromatic amines were performed in the presence of catalytic amounts of $Sn(OTf)_2$ and $Cu(OTf)_2$ [15]. Tris(pentafluorophenyl)borane catalyzes the opening of *N*-benzyl and *N*-alkyl aziridines with benzyl amine as the sole nucleophile [16]. A few catalysts such as $BiCl_3$ [17] and $LiNTf_2$ [18] proved to be active for the ring opening of both activated and non activated aziridines. The comparison of scandium triflate-catalyzed reactions of various *N*-substituted cyclic aziridines with aniline showed a higher reaction rate for *N*-phenyl than for *N*-tosyl or *N*-benzoyl aziridines. Aminolyses of *N*-phenyl aziridines with various aromatic amines could be realized in mild conditions (as low as 1 mol% scandium triflate) [19]. Other procedures have been described for the transformation of aziridines in 1,2-diamines such as the use of *β*-cyclodextrin [20] and phosphines as catalysts [21, 22] or by performing reactions in the presence of silica gel [23] or montmorillonite K-10 under microwave irradiation [24, 25].

Although very efficient catalysts have been developed for the asymmetric ring opening of aziridines by trimethylsilyl azide [26], the first enantioselective catalysts for the aminolyses of aziridines have been reported in the last years. Niobium coordinated to a substituted binol ligand afforded asymmetric inductions depending on the nitrogen substituent of the aziridine, (up to 84% ee with an aziridine

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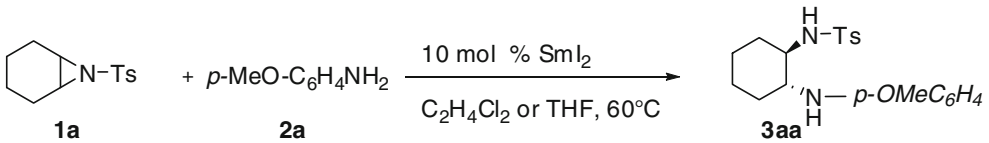
substituted by an *o*-anisyl group) [27, 28]. A tridentate binol ligand associated to titanium [29] for the aminolysis of *N*–*o*-anisyl aziridines and to zirconium [30] for *N*-benzhydryl aziridines afforded high enantioselection. A titanium/binol catalyst was highly enantioselective for the opening of *N*-phenyl and *N*-*p*-anisyl aziridines by aromatic amines [31]. Thus the nitrogen protecting group of aziridine has a dramatic effect on the activity and enantioselectivity of Lewis acid catalysts.

We have previously investigated the use of samarium diiodide and samarium iodobinaphtholate as catalyst and enantioselective catalyst for the formation of carbon–nitrogen bonds [32]. Samarium diiodide revealed efficient for the ring opening of epoxides by amines [33, 34], while high enantiomeric excesses were recorded for the aminolysis of cyclic epoxides containing or not another heteroatom by aromatic amines [35–37]. We now present our results on the use of samarium diiodide as a catalyst for the transformation of aziridines in vicinal diamines.

2 Results

As a first step towards the preparation of enantioenriched *β*-diamines by asymmetric lanthanide iodides we envisaged the study of the ring opening of *meso* aziridines with aromatic amines catalyzed by samarium diiodide. For test reactions we chose aziridines leading to cyclohexyl diamines and focused on aminolyses involving *o* and *p*-anisidine for a facile deprotection of the nitrogen of reaction products. The activity of samarium diiodide was first investigated on the reaction involving *N*-tosyl cyclohexyl aziridine **1a** and *p*-anisidine as aromatic amine. Aminolyses of epoxides have been performed in THF or in chlorinated solvents, CH_2Cl_2 or $C_2H_4Cl_2$ and the opening reactions of cyclic epoxides containing nitrogen atoms were realized at 60 °C. Since aziridines are expected to require harsher conditions than epoxides for ring opening reactions we tested first the catalytic reactions in DCE (Scheme 1). We were pleased to find that using 10 mol% samarium diiodide in DCE, the conversion of **1a** was nearly achieved after one night and *β*-diamine **3aa** was isolated in good yield (Table 1, entry 1). We further tried to optimize reactions conditions. Using a higher amine/aziridine ratio did not allow to decrease the reaction time or the reaction temperature (entry 2). When a lower catalytic ratio (5%) was used total conversion could be obtained but in an increased reaction time (38 h) (entries 3–5). Similarly when reaction was performed in THF with 10 mol % samarium diiodide the *β*-diamine **3aa** could be isolated in high yield but a longer reaction time than in DCE was required (compare entries 1 and 7). Using 5 mol% samarium diiodide in THF at 60 °C led after one night to a smaller conversion than in DCE (compare entries 3 and 8). Thus, the ring opening of *N*-tosyl aziridine **1a** by *p*-anisidine catalyzed by samarium diiodide can be realized at 60 °C either in DCE or in THF albeit the reaction is slower in the latter solvent. In these reactions samarium diiodide acts as a precatalyst which generates a trivalent Lewis acid catalyst as previously observed for the formation of various carbon–nitrogen bonds with this catalytic system [32–34]. A mechanism similar to that proposed by Jacobsen for the ring opening of epoxides by $TMSN_3$ can be proposed for these aminolyses of aziridines [38]. As a result, the difference of reactivity of samarium diiodide in DCE and THF could be explained since Lewis acidity of lanthanides decreases in coordinating solvent.



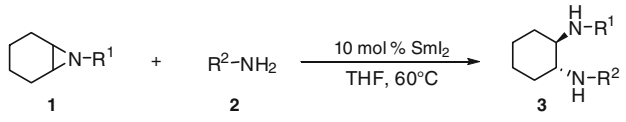
Scheme 1 Ring opening of aziridine **1a** by *p*-anisidine **2a** catalyzed by SmI_2

Table 1 Ring opening of aziridine **1a** by *p*-anisidine **2a** catalyzed by SmI_2

Entry	Solvent	Mol% SmI_2	*t* (h)	Conversion (yield)[a]
1	DCE	10	17	95 (73)
2	DCE[b]	10	18	100 (71)
3	DCE	5	16	76
4	DCE	5	22	93
5	DCE	5	38	100
6	THF	10	15	83
7	THF	10	40	98 (70)
8	THF	5	16	40

[a] Conversion % (isolated yield %), reaction performed with ratio **2a/1a**: 1.2

[b] Reaction performed with 10% SmI_2 and ratio **2a/1a**: 2



R^1 = Ts, Bn, Ph, Boc

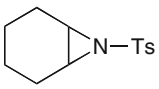
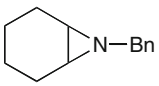
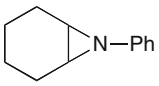
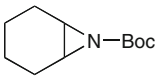
R^2 = *p*-MeO-C_6H_4, *o*-MeO-C_6H_4, CH_2Ph

Scheme 2 Ring opening of aziridines **1** by amines **2** catalyzed by SmI_2

The influence of the nature of the nitrogen substituent of aziridine and of the amine on the ring opening reactions catalyzed by samarium diiodide was next examined (Scheme 2; Table 2). Although reactions are more rapid in DCE we chose to use THF as solvent for an easier procedure. Since samarium diiodide is prepared in THF it avoids the evaporation of the solvent and the manipulation of $SmI_2(THF)_2$ which is far more sensitive to oxygen and moisture than the commercially available THF solutions of samarium diiodide. The ring opening of *N*-tosyl aziridine **1a** by *o*-anisidine **2b** could be realized in similar conditions than the reaction involving *p*-anisidine **2a** (Table 2, entries 1 and 4). Benzyl amine **2c** was further employed for the aminolysis of **1a** and afforded *β*-diamine **3ac** in a smaller reaction time than reactions with *o*- and *p*-anisidine (entry 5). The reactivity of cyclohexyl aziridine **1b** substituted by benzyl for the ring opening by *p*- and *o*-anisidine was next investigated. The total conversion in *β*-diamine was observed in both cases but after a longer time for *o*-anisidine which afforded product **3bb** in good yield (entries 6–8). *N*-Phenyl substituted aziridine **1c** was transformed by *o*- and *p*-anisidine after 17 h in *β*-diamines **3ca** and **3cb** which were isolated in good yields (entries 9 and 10). For *N*-Boc aziridine **1d** the reaction was slower with *o*-anisidine than with *p*-anisidine as observed for *N*-benzyl aziridine **1b** (entries 11-13). Performing the aminolysis of *N*-tosyl aziridine **1a** by *p*-anisidine under microwaves irradiation either at 60 °C or at 80 °C allowed to decrease strongly the reaction time and to isolate diamine **3aa** in high yield (entries 2 and 3).

While the ring opening of aziridines **1a** with *p*-anisidine [9–12] and **1c** with *o*-and *p*-anisidine [19] have been tested with other catalytic systems, aminolysis of *N*-benzyl aziridine **1b** and *N*-Boc aziridine **1d** were not previously described. The results gathered in Table 2 show that samarium diiodide is an efficient catalytic system for aziridines protected by tosyl and *t*-butoxycarbonyl group but also by phenyl or benzyl groups. However, considering the stability of the products and the reaction rates phenyl and *t*-butoxycarbonyl seem the best protecting groups for the transformation of aziridines into *β*-diamines.

Table 2 Ring opening of aziridines **1** by amines **2** catalyzed by SmI_2

Entry	Aziridine	Amine R^2NH_2	Product	*t* (h)	Conversion (%)	Yield %[a]
1	 **1a**	**2a** *p*-MeO–C_6H_4–NH_2	**3aa**	40	98	70
2		**2a** *p*-MeO–C_6H_4–NH_2	**3aa**	2[b]	65	40
3		**2a** *p*-MeO–C_6H_4–NH_2	**3aa**	2[c]	90	81[d]
4		**2b** *o*-MeO–C_6H_4–NH_2	**3ab**	40	90	[e]
5		**2c** C_6H_5–NH_2	**3ac**	17	100	68
6	 **1b**	**2a** *p*-MeO–C_6H_4–NH_2	**3ba**	17	100	[e]
7		**2b** *o*-MeO–C_6H_4–NH_2	**3bb**	17	85	
8		**2b** *o*-MeO–C_6H_4–NH_2	**3bb**	26	100	74
9	 **1c**	**2a** *p*-MeO–C_6H_4–NH_2	**3ca**	17	100	70
10		**2b** *o*-MeO–C_6H_4–NH_2	**3cb**	17	100	65
11	 **1d**	**2a** *p*-MeO–C_6H_4–NH_2	**3da**	16	100	74
12		**2b** *o*-MeO–C_6H_4–NH_2	**3db**	17	90	
13		**2b** *o*-MeO–C_6H_4–NH_2	**3db**	26	100	59

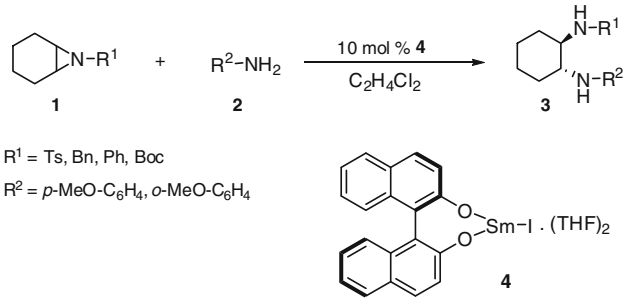
[a] Isolated yield, reactions performed with 10% SmI_2 and ratio **3/2**: 1.2

[b] Reaction performed with 10% SmI_2 and ratio **3/2**: 1.2 under microwaves at 60 °C, 60 watt

[c] Reaction performed with 10% SmI_2 and ratio **3/2**: 1.2 under microwaves at 80 °C, 60 watt

[d] Reaction realized in the same conditions without catalyst did not yield to diamine **3aa**

[e] The product decomposed on silica and could not be purified



Scheme 3 Aminolysis of aziridines with aromatic amines catalyzed by samarium iodobinaphtolate

Table 3 Aminolysis of aziridines with aromatic amines catalyzed by samarium iodobinaphtolate

Entry	Aziridine	Amine	T (°C)	t (h)	Conv. (%)	ee (%)[a]
1	**1a**	**2a** *p*-MeO–C_6H_4–NH_2	40	44	100	7
2	**1b**	**2b** *o*-MeO–C_6H_4–NH_2	60	46	41	5
3	**1b**	**2a** *p*-MeO–C_6H_4–NH_2	60	46	62	5
4	**1c**	**2b** *o*-MeO–C_6H_4–NH_2	60	21	100	0
5	**1c**	**2b** *p*-MeO–C_6H_4–NH_2	60	21	100	0
6	**1d**	**2b** *o*-MeO–C_6H_4–NH_2	40	41	17	12
7	**1d**	**2b** *p*-MeO–C_6H_4–NH_2	60	48	100	27

[a] Enantiomeric excess measured by HPLC

Since samarium iodobinaphtholate afforded interesting results for the enantioselective aminolysis of epoxides [35–37] we have now tested this complex for the aminolysis of aziridines (Scheme 3). We found it catalyzes the ring opening of aziridines **1** with *o*- and *p*-anisidine affording the corresponding 1,2 diamines with total conversion but low enantioselectivities (Table 3). Encouraging results are obtained with *N*-Boc aziridine **1d** (entries 6, 7). The enantioselective desymmetrization of various aziridines with aromatic amines catalyzed by lanthanide iodobinaphthoxides is currently under study.

3 Conclusion

Samarium diiodide catalyzes the ring opening of aziridines by aromatic amines in mild conditions to form β-diamines in good yields. The reactions can be performed in THF and within short times under microwaves conditions. We have synthesized several new di-protected 1,2 diamines. Comparing samarium diiodide and samarium iodobinaphtholate catalyzed ring opening of aziridines with different protecting groups showed that *t*-butoxycarbonyl gives the best results with both catalysts and is the protection that should be considered for the aminolysis of aziridines. Studies on the desymmetrization of aziridines by other asymmetric catalytic systems are ongoing.

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