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Ytterbium Triflate Catalyzed Ring Opening of Aziridines with Amines

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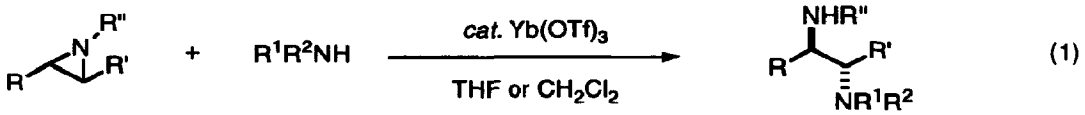
Abstract : Ring opening of aziridines with amines takes place readily in the presence of catalytic amount of ytterbium triflate, giving the corresponding 1, 2-diamines in good to high yields.

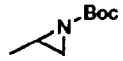
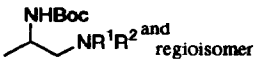
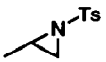
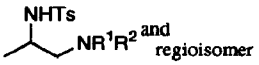
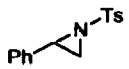
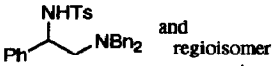
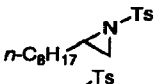
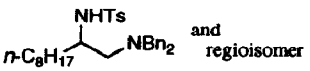
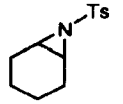
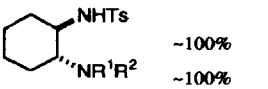
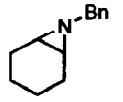
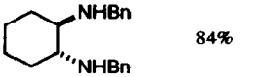
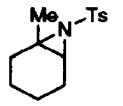
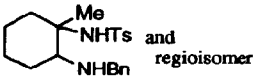
Vicinal diamines are a synthetically, biologically, and medicinally important class of compounds.[1] One of the most straightforward synthetic procedures for the formation of 1, 2-diamines is the ring opening of aziridines with amines.[2] However, this classical method has been disregarded primarily due to limitations of the reaction conditions: low nucleophilicity of amines requires elevated temperatures, and the unavailability of the aziridine starting materials. In recent years, several excellent methods for the synthesis of aziridines have been developed[3] and thus aziridines are now as readily available as epoxides. Accordingly, it was thought that the development of a new synthetic method for the formation of 1, 2-diamines *via* the ring opening of aziridines with amines would be timely and useful to significant number of synthetic chemists.[4]



(1)

We report that the ring opening reaction is catalyzed by ytterbium triflate (eq. 1) and is, to the best of our knowledge, the first example of such a reaction.[5] The results are summarized in Table 1. Ring opening proceeded smoothly in the presence of catalytic amounts of $Yb(OTf)_3$; [either 10 mol% (entries 2-9) or 20 mol% (entries 10-20) $Yb(OTf)_3$], however, no reaction took place in the absence of $Yb(OTf)_3$ (entry 1). The use of N-protected aziridines, such as Boc, Ts, and benzyl aziridines, was essential for the reaction to proceed smoothly, since N-unprotected aziridines may themselves act as nucleophiles leading to the formation of oligomers or polymers. Protection with the *p*-toluenesulfonyl group was utilized most frequently, but Boc (entries 2-4) and benzyl (entry 18) protection were also effective. The ring opening reaction proceeded even at room temperature (condition A; entries 8, 9, and 12. condition C; entries 3-7, and 13), but the reaction was accelerated by refluxing the reaction mixture (C and D). In general, the rate of reaction in THF was slower than that in CH_2Cl_2 presumably because the Lewis acidity of the catalyst in THF is decreased by coordination of the Lewis basic solvent. Although the

Table 1. $Yb(OTf)_3$ Catalyzed Ring Opening of Aziridines with Amines.

Entry	Aziridine[a]	Amine(R^1R^2NH)	Catalyst	Condition[b]	Reaction time	Product and Yield[c]	
1		Bn_2NH	None	B	24h	No Reaction	
						 and regioisomer	
2		Bn_2NH	10mol%$Yb(OTf)_3$	B	12h	75 : 25	~100%
3		Bn_2NH	10mol%$Yb(OTf)_3$	C	10h	62 : 38	91%
4		$BnNH_2$	10mol%$Yb(OTf)_3$	C	10h	65 : 35	82%
						 and regioisomer	
5		Bn_2NH	10mol%$Yb(OTf)_3$	C	2h	77 : 23	84%
6		$BnNH_2$	10mol%$Yb(OTf)_3$	C	10h	>99 : <1	75%
7		Et_2NH	10mol%$Yb(OTf)_3$	C	8h	>99 : <1	95%
						 and regioisomer	
8		Bn_2NH	10mol%$Yb(OTf)_3$	A	40h	67 : 33	77%[d]
						 and regioisomer	
9		Bn_2NH	10mol%$Yb(OTf)_3$	A	72h	>99 : <1	98%
							
10		$BnNH_2$	20mol%$Yb(OTf)_3$	B	24h		~100%
11		$BnNH_2$	20mol%$Yb(OTf)_3$	D	24h		~100%
12		$BnNH_2$	20mol%$Yb(OTf)_3$	A	72h		~100%
13		$BnNH_2$	20mol%$Yb(OTf)_3$	C	72h		98%
14		Et_2NH	20mol%$Yb(OTf)_3$	D	24h		82%
15		$PhNH_2$	20mol%$Yb(OTf)_3$	D	24h		98%
16			20mol%$Yb(OTf)_3$	D	24h		~100%
17		Bn_2NH	20mol%$Yb(OTf)_3$	D	48h	No Reaction	
							
18		$BnNH_2$	20mol%$Yb(OTf)_3$	D	48h		84%
						 and regioisomer	
19		$BnNH_2$	20mol%$Yb(OTf)_3$	D	48h	68 : 32	42%[d]
20		$BnNH_2$	20mol%$Yb(OTf)_3$	D	48h	63 : 47	49%[d]

[a]Bn = $PhCH_2$, Boc = t-BuOCO, Ts = p-$CH_3C_6H_4SO_2$. [b]Condition A; THF/RT, B; THF/reflux, C; CH_2Cl_2/RT, D ; CH_2Cl_2/reflux. [c]Isolated yield. [d]Unidentified polymers were obtained as by-products.

$Yb(OTf)_3$ catalyzed ring opening was quite effective for mono- and di-substituted aziridines, the reaction of tri-substituted aziridine was sluggish and unidentified polymers were present as by-products (entries 8, 19, and 20). Other catalysts such as 10 mol% $La(OTf)_3$, $Sm(OTf)_3$, $Y(OTf)_3$, and $Pr(OTf)_3$ were also effective for the ring opening of N-tosylcyclohexeneimine with benzylamine ; the 1, 2-diamine was obtained in greater than 95% yield [THF, room temperature, 72 h (cf. entry 12)]. As expected, the amines attacked the less hindered site of aziridine ring regioselectively, and the trans-1, 2-diamines were obtained stereoselectively.

The reaction of N-tosylcyclohexeneimine with benzylamine is representative. To a solution of $Yb(OTf)_3$ (57 mg, 0.10 mmol) in THF or CH_2Cl_2 (1.0 ml) , were added N-tosylcyclohexeneimine (126 mg, 0.10 mol) and benzylamine (0.11 ml, 1.0 mmol) and the mixture was stirred at room temperature or reflux and the reaction was monitored by TLC. After comsuption of the starting material, distilled water was added. The organic layer was extracted with three portions of CH_2Cl_2, washed with brine and dried over anhydrous Na_2SO_4. Filtration and removal of solvent under reduced pressure gave the crude product which was purified by silicagel column chromatography using hexane-AcOEt (3:1) as an eluent to give trans-N-benzyl-N'-tosyl-1, 2-cyclohexanediamine (179 mg) in essentially quantitative yield.

Very recently, it has been found that lanthanoid triflates catalyze the aminolysis of 1, 2-epoxides,[6a, b] oxetanes,[6b] β-lactones[6b] in an extraordinarily efficient manner. Reaction of N-tosylaziridines with cyanotrimethylsilane in the presence of lanthanoid tricyanide gave N-tosyl β-amino nitriles by selective attack of cyanide at the less substituted carbon of the ring.[7] Ring opening of epoxides and an aziridine with acetone cyanohydrin is promoted by a catalytic amount of lanthanoid alkoxide to furnish β-hydroxy nitriles and β-amino nitriles, respectively.[8] It is possible that the catalytic mechanism of the present ring opening of aziridines is similar to that of the catalytic ring cleavage of epoxides or aziridines reported previously.

Two probable mechanisms for the present ring opening reaction are concievable. $Yb(OTf)_3$ may act as a Lewis acid, which coordinates the nitrogen atom of the aziridines and facilitates the ring opening. Another possibility is that $Yb(OTf)_3$ may react with an amine (R_2NH) to produce $Yb(NR_2)Ln$ as an intermediate species which subsequently reacts rapidly with aziridines. We are now pursuing a mechanistic study of this type of reaction in order to clarify which mechanism is responsible for the present unprecedented catalytic reaction. Regardless of the precise mechanism, the $Yb(OTf)_3$ catalyzed ring opening of aziridines with amines will become a useful procedure for the synthesis of 1, 2-diamines because of its effciency and simplicity.

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