An efficient method for the ring opening of epoxides with aromatic amines by Sb(III) chloride under microwave irradiation

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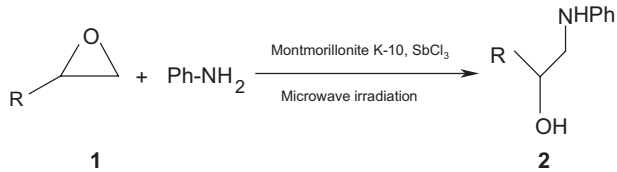
$SbCl_3$ supported on montmorillonite K-10 is an efficient catalyst for the ring opening of epoxides with aromatic amines under solvent-free conditions and microwave irradiation to give the corresponding β-amino alcohols in high yields with high regioselectivity

Keywords: epoxides, $SbCl_3$, aromatic amines, β-amino alcohols

β-Amino alcohols are a very important class of organic compounds and have considerable application in medicinal chemistry.[1,2] The classical synthesis of β-amino alcohols consists of heating an epoxide with an excess of amine.[2,3] These reactions are usually carried out in a solvent, requiring many hours of reflux, which is environmentally unfriendly. Recently, the use of catalysts to carry out these reactions under mild conditions has been developed.[4-11] However, there are still some limitations with these methods including the failure of deactivated aromatic amines and some sterically hindered aromatic amines to open the epoxides, the need for an excess of reagent, reactions at reflux temperatures and sluggish reactions. Therefore, it is desirable to develop improved catalysts for the activation of epoxides, which render them to be more susceptible to nucleophilic attack under mild conditions. Stringent environmental protection laws in recent years prompted an increasing emphasis on the use and design of eco-friendly reagents, solid state procedures, and solvent-free reactions.[12] Application of microwaves is currently under extensive examination,[13] and dry procedures have recently attracted much attention.[14] We report herein a simple fast and efficient procedure for the nucleophilic opening of epoxides with aromatic amines catalysed by Sb(III) chloride, supported on montmorillonite K-10 under microwave irradiation. The corresponding β-amino alcohols are obtained in high yields with high regioselectivity. In the absence of Sb(III) chloride, the epoxide ring opening reaction of *n*-hexyl oxirane (**1d**) with aniline under similar reaction conditions does not occur even after 20 minutes microwave irradiation, indicating that the $SbCl_3$ effectively promotes the opening of the epoxides. An alternative reaction of *n*-hexyl oxirane (**1d**) with aniline under similar reaction conditions without microwave irradiation led to the formation of only 36% of **3a** after 6 hours mixing in the presence of Sb(III) chloride impregnated on montmorillonite K-10, at room temperature. Note that when unsymmetrical epoxides were allowed to react in the presence of Sb (III) chloride, the ring opening takes place



1 **2**

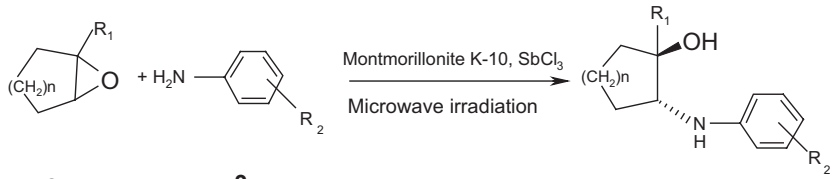
Scheme 1

in a completely regioselective fashion. The attack at the less substituted oxirane carbon affording the desired compound as the only product. However, when styrene oxide (**1j**) was allowed to react with aniline under the mentioned conditions, two regioisomers (**2j**, **3j**) were formed in the ratio 20:80. The major product (**3j**) was obtained by attack of aniline at the benzylic carbon of the epoxide.

Furthermore, cycloalkyl epoxides such as cyclopentene and cyclohexene oxide reacted with aromatic amines in excellent yields in which a *trans* stereospecificity was observed (Scheme 2 and Table 2). In the case of cyclohexene oxide, the *trans* stereochemistry of β-amino alcohols was determined from the coupling constant of the ring methine protons at δ 3.33 (ddd, J = 10.2, 10.1 and 5.5 Hz, 1H, N–CH) and at δ 3.54 (ddd, 10.1, 8.6 and 4.2 Hz, 1H, O–CH) in ^{1}H NMR of **4k**.

After using $SbCl_3$ supported on montmorillonite K-10 for the ring opening of *n*-hexyl oxirane (**1d**) with aniline under microwave irradiation the catalyst can be recovered after reaction with hydrochloric acid, and then it was used for the ring opening of *n*-hexyl oxirane (**1d**) with aniline. The second use of $SbCl_3$ for the ring opening of *n*-hexyl oxirane (**1d**) with aniline to **2d** showed about 5% decrease in the reactivity. However, the third use showed no further decrease in reaction yields (*cf.* Table 3).

This simple procedure gives short reaction times, and generally gives high yields under microwave irradiation after several uses of $SbCl_3$ supported on montmorillonite K-10.



2 **3** **4 (a-m)**

Scheme 2

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Table 1 Sb(III) chloride-catalysed ring opening of terminal epoxides with aniline produced via Scheme I

Entry	Epoxide **1**	R	Time/min	Product **2**[a] [Ref.]	Yield/%[b]
1	**1a**	C_2H_5	4	**2a** [15, 16]	88
2	**1b**	*n*-C_3H_7	4	**2b** [15, 16]	88
3	**1c**	*n*-C_5H_{11}	6	**2c** 15, 16]	84
4	**1d**	*n*-C_6H_{13}	8	**2d** [9]	78
5	**1e**	$PhOCH_2$	5	**2e** [10]	93
6	**1f**	*o*-$CH_3C_6H_4OCH_2$	7	**2f** [10]	83
7	**1g**	*m*-CH_3 $C_6H_4OCH_2$	7	**2g** [10]	82
8	**1h**	*p*-CH_3 $C_6H_4OCH_2$	6	**2h** [10]	84
9	**1i**	*p*-Cl $C_6H_4OCH_2$	7	**2i** [8]	78
10	**1j**	Ph	10	**2j + 3j**[c] [15, 16]	71 (20:80)

[a]All compounds were characterised by IR, ^{1}H NMR and compared with authentic samples.[8-11,15,16]
[b]Isolated yields.
[c]**3j** = $PhCH(NHPh)CH_2OH$.

Table 2 Sb(III) chloride-catalysed ring opening of cycloalkyl epoxides with aromatic amines produced via Scheme 2

Entry	Epoxide **2**	R_2(aniline **3**)	Time/min	Product [a]**4**	Yield/%[b]
1	Cyclopentene oxide	H	4	**4a**	91
2	Cyclopentene oxide	*p*-OCH_3	4	**4b**	92
3	Cyclopentene oxide	*p*-CH_3	4	**4c**	91
4	Cyclopentene oxide	*p*-Br	6	**4d**	89
5	Cyclopentene oxide	*p*-NO_2	10	**4e**	62
6	Cyclohexene oxide	H	5	**4f**	93
7	Cyclohexene oxide	*p*-OCH_3	4	**4g**	93
8	Cyclohexene oxide	*p*-CH_3	4	**4h**	93
9	Cyclohexene oxide	*p*-Br	6	**4i**	90
10	Cyclohexene oxide	*p*-NO_2	10	**4j**	59
11	Cyclohexene oxide	*o*-Ac	10	**4k**	89
12	2-Methyl cyclohexene oxide	H	5	**4l**	89
13	2-Methyl cyclohexene oxide	*p*-NO_2	10	**4m**	58

[a]All compounds were characterised by IR, ^{1}H NMR and compared with authentic samples.[9,11,15,16]
[b]Isolated yields.

Table 3 Reusability of Sb(III) chloride for ring opening of *n*-hexyl oxirane (**1d**) with aniline

Experiment[a]	Product	Yield/%
1st	**2d**	78
2nd	**2d**	73
3rd	**2d**	71

[a]The reactions were carried out under similar conditions as those in Table 1.

Experimental

General

All chemicals were purchased from Merck, Aldrich and Riedel Haen AG and were used without further purification. IR and ^{1}H NMR spectra were recorded on a FT–IR Unicam Mattson 1000 instrument using KBr disks or as neat samples and a Bruker AC (80-MHz) instrument with $CDCl_3$ as solvent and TMS as internal references. A Sears Kenmore microwave oven equipped with a turntable at full power (900 Watts) was used.

Ring opening of epoxides with aniline, general procedure

A mixture of epoxide (**1**, 10 mmol) and aniline (0.93 g, 10 mmol), was added to montmorillonite K-10 (2.0 g) that was mixed with $SbCl_3$ (0.225 g, 1 mmol). The mixture was irradiated at high power (900 W) in a microwave oven for length of time indicated (*c.f.* Tables 1 and 2). The course of the reaction was monitored by TLC, during which time complete disappearance of the starting material was observed. The mixture was cooled to room temperature, CH_2Cl_2 (15 ml) was added and heterogeneous catalyst filtered off. Use of Et_2O gave ~10% fall in yield (tried for **2a**, **2b** and **2f**). The solvent was removed at reduced pressure and the respective product (**2**) was purified by column chromatography over a short silica gel pad. The pure products were obtained in yields indicated in Table 1. The structures of all pure products were confirmed by IR, ^{1}H NMR and compared with data obtained from authentic amino alcohols.[8-11,15,16]

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