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Lewis base-catalyzed addition of triethylaluminum to epoxides

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Abstract

Lewis bases like phosphines, arsines, and antimonies catalyze the nucleophilic addition of triethylaluminum to epoxides very efficiently. They are proposed to coordinate to triethylaluminum with formation of monomeric and more reactive triethylaluminum Lewis base adducts.

Keywords: Lewis bases; epoxides; triethylaluminum; catalysis.

Recently, substantial research efforts have been devoted to desymmetrization reactions of *meso* epoxides giving rise to functionalized, optically active alcohols as valuable fine chemicals for organic synthesis.[1] In particular, several highly efficient methods for the catalytic, enantioselective opening of *meso* epoxides by hetero nucleophiles have emerged most of which have a chiral Lewis acid in common which activates the epoxide towards the nucleophile and differentiates the enantiotopic carbon atoms of the epoxide. As a noteworthy exception Denmark et al. achieved a Lewis base-catalyzed addition of $SiCl_4$ to epoxides to deliver enantiomerically enriched chlorohydrins by way of reagent rather than substrate activation.[2] In contrast, the catalyzed addition of carbon nucleophiles towards epoxides has received less attention presumably reflecting the difficulty to prepare an organometallic reagent which is sufficiently reactive towards the epoxide and compatible with the metal catalyst at the same time.[3] We speculated that this problem could be overcome by employing an organometallic reagent which is activated by a Lewis base in close analogy to the amine-catalyzed addition of dialkylzinc reagents to aldehydes.[4]

In this letter we wish to report our results on Lewis base-catalyzed ring opening reactions of epoxides by triethylaluminum. Cyclohexene oxide (**1**) as well as *cis*-2-butene oxide (**2**) were readily opened by triethylaluminum in high yields at ambient temperature with only 5 mol% of the Lewis base employed (Scheme 1 and Table 1).[5] Phosphines as well as arsines and antimonies were identified as suitable catalysts. Whereas the uncatalyzed addition of triethylaluminum to cyclohexene oxide did not proceed at all at rt,[6] *trans*-2-ethyl cyclohexanol (**3**) was obtained in 99% yield after 24 h at rt with 5 mol% of either triphenylphosphine or tris(dimethylamino)phosphine. Likewise, the addition of triethylaluminum to *cis*-2-butene oxide (**2**) catalyzed by 5 mol% of triphenylphosphine gave *trans*-3-methyl-2-pentanol (**4**) in 82% yield again with no background reaction being observed.

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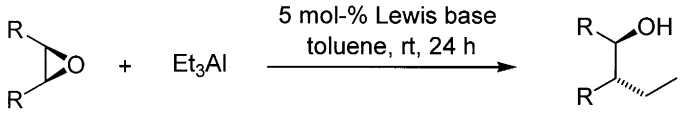


1: R = -$(CH_2)_4$-
2: R = CH_3

3: R = -$(CH_2)_4$-
4: R = CH_3

Scheme 1.

Table 1
Lewis base-catalyzed addition of triethylaluminum to epoxides (Scheme 1)

Epoxide	R	Lewis Base (5 mol-%)	Yield (%)[2]
1	-$(CH_2)_4$-	none	0
1	-$(CH_2)_4$-	$P(NMe_2)_3$	99
1	-$(CH_2)_4$-	PBu_3	89
1	-$(CH_2)_4$-	PPh_3	99
1	-$(CH_2)_4$-	$AsPh_3$	95
1	-$(CH_2)_4$-	$SbPh_3$	89
2	CH_3	none	0
2	CH_3	$P(NMe_2)_3$	70
2	CH_3	PPh_3	82
2	CH_3	$AsPh_3$	72
2	CH_3	$SbPh_3$	31

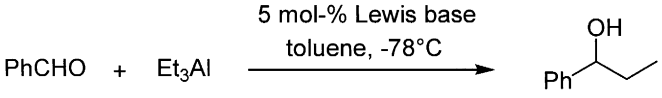
1) Reaction conditions: 1 eq Et_3Al, toluene, rt, 24 h; 2) determined by GC against an internal standard.

Just one equivalent of the aluminum reagent was sufficient for a complete reaction although the addition was accelerated when two equivalents were used. Tributylphosphine, triphenylarsine, and triphenylantimony could also be used as catalysts giving comparable results in the case of cyclohexene oxide (**1**) and inferior results with *cis*-2-butene oxide (**2**). Amines (NEt_3, TMEDA) turned out to be totally ineffective as catalysts. The choice of the solvent was crucial to the success of the reaction. Only non-coordinating solvents like toluene and hexane were suitable whereas in particular etheral solvents significantly slowed down the reaction due to coordination to the Lewis acidic aluminum reagent thereby attenuating its reactivity. The catalyzed reaction could not be extended to terminal epoxides because they were sufficiently reactive to take part in an uncatalyzed process even at low temperatures.

In order to shed light on the catalytic activity of the Lewis base ^{27}Al and ^{31}P NMR spectra were recorded with solutions of triethylaluminum and tris(dimethylamino)phosphine each alone and after mixing both compounds.[7] In the ^{27}Al NMR spectrum a significant downfield shift from δ=155 ppm to δ=165 ppm (relative to external $AlCl_3$) was observed when going from triethylaluminum to a 1:1 mixture of triethylaluminum and tris(dimethylamino)phosphine. In the ^{31}P NMR spectrum a corresponding upfield shift from δ=123 ppm to δ=97 ppm was noted (relative to external H_3PO_4). These results clearly support a coordination of the phosphine to the aluminum reagent which may result in the breakage of the triethylaluminum dimer and formation of a monomeric triethylaluminum–phosphine adduct which apparently releases the ethyl group more easily and is thus more reactive than the triethylaluminum dimer. A quite similar coordination of phosphines to silicon was recently noted in the phosphine-catalyzed addition of trimethylsilyl cyanide[8] and silyl ketene acetals[9] to aldehydes.

The phosphine-catalyzed rate acceleration was also observed in the reaction of triethylaluminum with other electrophiles. The typically fast reaction of triethylaluminum with benzaldehyde[10] in toluene at

0°C could be slowed down significantly at −78°C so that only 15% of 1-phenyl-1-propanol (**5**) were obtained after 3 h. In the presence of 5 mol% of tris(dimethylamino)phosphine, however, a 94% yield of the addition product **5** was obtained after 3 h at −78°C (Scheme 2 and Table 2). Tributylphosphine and triethyl phosphite gave equally good results. Here, amines also displayed catalytic activity although the rate acceleration was not as pronounced as in the case of the phosphines.



5

Scheme 2.

Table 2
Lewis base-catalyzed addition of triethylaluminum to benzaldehyde (Scheme 2)

Lewis Base (5 mol-%)	Yield (%)^2
none	15
P(NMe$_2$)$_3$	94
PBu$_3$	89
P(OEt)$_3$	87
TMEDA^3	81
NEt$_3$^{3}	84

1) Reaction conditions: 1 eq Et$_3$Al, toluene, -78°C, 3 h; 2) determined by GC against an internal standard; 3) reaction time: 24 h, -78°C.

In conclusion, we have demonstrated that a range of P-, As-, and Sb-containing Lewis bases very efficiently catalyze the addition of triethylaluminum to epoxides and aldehydes through coordination to the aluminum reagent and presumably formation of monomeric Lewis base-aluminum adducts. This protocol clearly holds potential for asymmetric catalysis when chiral, enantiomerically pure Lewis bases are employed in the indicated reactions.

Acknowledgements

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5. Typical experimental procedure: to a solution of 0.10 ml (1.00 mmol) cyclohexene oxide (**1**) in 2 ml dry toluene was added 9 µl (0.05 mmol) tris(dimethylamino)phosphine and subsequently 1.00 ml (1.00 mmol) 1 M Et_3Al-solution in hexane. The mixture was stirred for 24 h at rt, quenched with 2 ml 1 M HCl and extracted with ether. The combined organic extracts were dried over $MgSO_4$ and evaporated in vacuo. The yields given in Table 1 were determined by GC against *n*-decane as internal standard. For preparative purposes the crude product was purified by chromatography over silica gel (ether:pentane 1:1) to yield 116 mg (91%) of *trans*-2-ethyl-1-cyclohexanol (**3**). The structure of the products **3**–**5** was determined by NMR, IR, UV, MS in comparison to the published data, for compound **3** see: (a) Bryan Jones, J.; Takemura, T. *Can. J. Chem*. **1982**, *60*, 2950; for compound **4** see: (b) Berrada, S.; Desert, S.; Metzner, P. *Tetrahedron* **1988**, *44*, 3575; for compound **5** see: (c) Guijarro, D.; Guillena, G.; Mancheno, B.; Yus, M. *Tetrahedron* **1994**, *50*, 3427.
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