Tetrahedron Letters, Vol.31, No.4, pp 575-576, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

AN UNUSUAL CHEMOSELECTIVITY IN COBALT(II) CHLORIDE CATALYSED CLEAVAGE OF OXIRANES WITH ANILINES: A HIGHLY REGIOSELECTIVE SYNTHESIS OF β-AMINO ALCOHOLS

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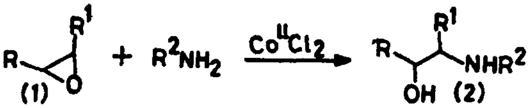
Summary. Cobalt(II) chloride catalyses the regioselective cleavage of oxiranes with anilines and p-methoxyaniline to the corresponding β-amino alcohols in excellent yields. Benzylic and aliphatic amines do not react under these conditions.

β-Amino alcohols are pharmaceutically important organic compounds and lately their synthesis has attracted the attention of organic chemist. The most straightforward route to β-amino alcohols involves the regioselective ring opening of oxiranes[1] with excess amines at elevated temperature. However, recently metal amides have been employed[2] for such a transformation although a prior conversion of amines to metal amides certainly poses some restriction in terms of the utility of this reaction on a large scale. In an attempt to perform this reaction without the mandatory conversion of amines to metal amides, we explored the possibility of metal catalysed opening of oxiranes with amines. To our surprise we found that Cobalt(II) chloride smoothly catalyses the opening of oxiranes with anilines but it fails to do so with benzylic and aliphatic amines. A preliminary account of these findings are given below:

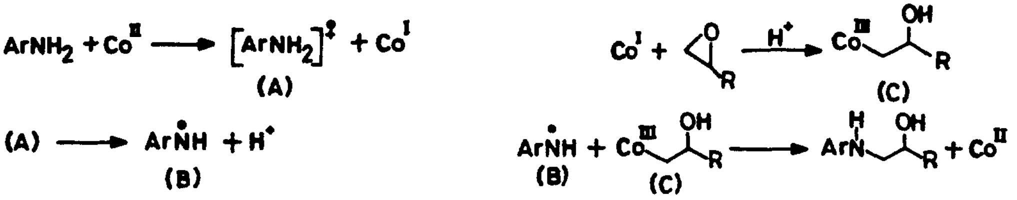
Oxiranes (10 mmol), aniline or p-methoxyaniline (10 mmol) is added to a stirred solution of anhydrous Cobalt(II) chloride ($\sim$ 30 mg) in dry acetonitrile and the resulting mixture is stirred under nitrogen at ambient temperature for 4-8 hours. Acetonitrile is removed under vacuum and the residue taken into ether and the ether layer is washed with saturated solution of sodium bicarbonate and water. Drying ($MgSO_4$) and evaporation gave a semi-solid which on purification by column chromatography (SiO_2) yielded the β-aminoalcohols. The results are compiled in table. This reaction is highly regioselective as only one regioisomer is obtained in all the reactions. p-Methoxyaniline reacts faster than aniline and no cleavage of oxiranes is observed with benzylamine, n-propylamine, isobutylamine and p-nitroaniline even after 24 hours (table, entry 1 and 2). This unusual chemoselectivity of oxiranes with aniline (a less reactive amine compared to aliphatic amines) can not be explained by usual ionic process, however this can be accounted for if we invoke a electron transfer process. Thus one electron transfer from aniline to Cobalt(II) complex will lead to the formation of anilinium radical cation (A)[3] and Cobalt(I) species (Scheme). The radical cation (A) will loose a proton to give anilinium radical (B). Cobalt(I) species formed during this process will open the oxirane in presence of a proton to yield a Cobalt(III) oxirane complex (C), which can undergo a homolytic (SH_2) type of displacement by radical (B) to give the observed product (2) and Cobalt(II) complex. The support for this proposed mechanism can be obtained from the observation that this reaction is highly stereoselective and this stereoselectivity can only be explained if the oxirane is attacked by the "supernucleophilic" Cobalt(I) in an SN^2 manner. The opening of oxiranes with Cobalt(I) species is very well precedented[4] in literature. Also, the chemoselective nature of this reaction suggests the possibility of a electron transfer as a anilinium radical cation will be more stable than the radical cation derived from a aliphatic or benzylic amine. Irrespective of the mechanism, the Cobalt(II) chloride catalysed opening of oxiranes with anilines offers a very efficient route to β-aminoalcohols.

Table: Cobalt(II) chloride catalysed cleavage of oxiranes with anilines



Entry	R	R^1	Product, R^2 (Yield %)[1,2,3]
1.	C_2H_5	H	C_6H_5(69)2a; p-oMe-C_6H_4(67)2b; -$CH_2C_6H_5$(0)2c; p-NO_2-C_6H_4(0)2d; $C_3H_7^n$(0)2e; C_4H_9(trace)2f;
2.	C_6H_5	H	C_6H_5(72)2g; p-oMe-C_6H_4(83)2h; C_6H_5-CH_2(0)2i; $C_3H_7^n$(0) 2j;
3.	CH_2-Cl	H	C_6H_5(78)2k; p-oMeC_6H_4(70); 2l;
4.	C_6H_5-O-CH_2	H	C_6H_5(60)2m; p-oMeC_6H_4(65)2n;
5.	-$(CH_2)_4$-		C_6H_5(73)2o; p-oMeC_6H_4(64)2p

1) Yield of the isolated products; 2) All the compounds were properly characterised by IR and ^1H NMR spectra and the ^1H NMR of crude did not indicate the presence of other regioisomer in all the reactions; 3) All the products (barring compounds 2m and 2n) were semi-solid at ambient temperature.



Scheme

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(Received in UK 29 November 1989)