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Calcium Trifluoroacetate as an Efficient Catalyst for Ring-opening of Epoxides by Amines under Solvent-free Conditions

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Abstract

$Ca(CF_3CO_2)_2$ efficiently catalyzed the selective ring-opening of epoxides by amines leading to the synthesis of β-aminoalcohols. The reaction works well with various aromatic and aliphatic amines under solvent-free conditions. Corresponding β-aminoalcohols were obtained in excellent yields with high regioselectivity. The catalyst was easily prepared by reaction of CaH_2 in trifluoroacetic acid.

Keywords: Calcium trifluoroacetate; Epoxides ring-opening; Amines; Solvent-free; β-Aminoalcohol.

1. Introduction

β-Aminoalcohols are of considerable interest as intermediates in the synthesis of a large range of natural and synthetic pharmacological products,[1] including their use as chiral auxiliaries for asymmetric synthesis.[2] Aminolysis of epoxides is a widely studied process investigated in the preparation of these compounds.[3] Commonly, β-aminoalcohols were obtained under drastic conditions such as high temperatures[4–7] which were inappropriate for certain functional groups; though the aminolysis of epoxides at low temperatures was reported in the literature with LiOTf,[8] $CoCl_2$,[9] $Ln(OTf)_3$ (Ln = Yb, Nd, Gd),[10,11] $SmCl_3$,[12] $Cu(OTf)_2$,[13] $Sn(OTf)_2$[13] and $Ca(OTf)_2$.[14] However, some of these protocols require excess of amines, stoichiometric amount of catalysts, high temperatures, inert conditions, halogenated solvents, moisture sensitive/hazardous/costly catalysts. Recently, Yadav and co-workers[15] described the catalytic activity of $Sm(OTf)_3$ in the selective ring-opening of epoxides with several aromatic and aliphatic amines under solvent-free conditions. However, most of the catalysts so far were effective only in the aminolysis of epoxides with aromatic amines.[9–13] Moreover, unsatisfactory yields due to the undesirable side reactions of rearrangement of the epoxide make necessary the development of efficient and environmentally friendly methods based on low-cost catalysts, mild and solvent-free conditions.

Recently, we have demonstrated the catalytic efficiency of calcium trifluoroacetate $Ca(CF_3CO_2)_2$ for the synthesis of β-enaminoesters by enamination of β-dicarbonyl compounds.[16] Here, we report a mild, practical, and efficient method for the ring opening of epoxide with amines using the same $Ca(CF_3CO_2)_2$ catalyst. Undoubtedly, calcium trifluoroacetate as a highly chemo-selective catalyst[16] has some interesting features in terms of synthesis, cost and environmental impact.

2. Experimental

2. 1. General Details

All the reagents and solvents used in the experiments were purchased from commercial sources and used as received without further purification (Aldrich, Acros).

The reaction mixtures were analyzed on a Trace GC Thermo Finnigan chromatograph equipped with an FID detector. GC parameters for capillary columns BP (25 m × 0.25 mm, SGE): injector 250 °C; detector 250 °C; oven 70 °C for 5 min then 3 °C min^{-1} until 250 °C for 30 min; column pressure 20 kPa, column flow 6.3 mL min^{-1}; linear velocity 53.1 cm s^{-1}; total flow 138 mL min^{-1}. IR spectra were obtained in KBr with a Perkin–Elmer Spectrum 100, equipped with a Specac Golden Gate Diamond ATR as a solid sample support. The ^1H and ^{13}C NMR spectra were recorded at 25 °C on Bruker Avance DPX 300 (300 MHz) spectrometer in $CDCl_3$ using TMS as the internal standard.

2. 2. Experimental Procedure

Aminolysis of cyclohexene oxide **1** by aniline: in a screw-capped vial equipped with a magnetic stirrer, Ca $(CF_3CO_2)_2$ (30 mg, 5 mol%) (freshly prepared using our previously published method)[16] was added to aniline (0.190 g, 2.04 mmol) and cyclohexene oxide (0.196 g, 2.0 mmol). The resulting mixture was left under vigorous stirring at 40 °C for 31 h and was extracted with AcOEt (2 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford the desired product. All the spectroscopic data of the products were compared with those reported in the literature.

2. 3. Spectral Data of Isolated Products

2-(Phenylamino)cyclohexanol (3a)

EIMS (*m/z*) 192; IR: ν 3614, 3388, 2937, 2860, 1619, 1513, 1254, 754 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.84–0.97 (m, 1H), 1.15–1.33 (m, 3H), 1.59–1.68 (m, 2H), 1.93–2.04 (m, 2H), 2.92 (dt, *J* = 9.3, 4.2 Hz, 1H), 3.13 (dt, *J* = 9.9, 4.5 Hz, 1H), 3.26 (m, 2H), 6.5–6.59 (m, 3H), 7.01 (dd, *J* = 6.06, 3.2 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 23.3, 23.8, 30.4, 32.3, 58.8, 72.9, 113.1, 116.9, 127.7, 146.7.

2-(4-Fluorophenylamino)cyclohexanol (3b)

EIMS (*m/z*) 210; IR: 3586 , 3383, 2927, 2856, 1522, 1270, 1224, 743 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.9–1.0 (m, 1H), 1.2–1.3 (m, 3H), 1.6–1.7 (m, 2H), 1.9–2.1 (m, 2H), 2.95 (dt, *J* = 9.6, 3.9 Hz, 1H), 3.3–3.4 (m, 3H), 6.55 (d, *J* = 8.5 Hz, 2H), 6.9 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 24.2, 24.9, 31.3, 33.3, 61.5, 74.2, 115.9, 116.2, 143.2, 156.6 (C–F, d, *J* = 236.2 Hz).

2-(2-Fluorophenylamino)cyclohexanol (3c)

EIMS (*m/z*) 210; IR: ν 3621, 3407, 2933, 2858, 1606, 1511, 1258, 1206, 881 cm^{-1}; ^1H NMR ($CDCl_3$) : δ 0.9–1.0 (m, 1H), 1.2–1.3 (m, 3H), 1.6–1.7 (m, 2H), 1.9–2.00 (m, 2H), 2.95 (dt, *J* = 9.4, 4.05 Hz, 1H), 3.25–3.35 (m, 3H), 6.45–6.55 (m, 1H), 6.75–6.85 (m, 1H), 6.9–7.05 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 24.4, 25.1, 31.8, 33.4, 59.8, 74.1, 113.7 , 114.8, 117.3, 124.6, 136.4, 152.25 (C–F, d, *J* = 236.2 Hz).

2-(4-Bromophenylamino)cyclohexanol (3d)

EIMS (*m/z*) 271; IR: ν 3617,3379, 2933, 2859, 1590, 1257,621 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.00–1.10 (m, 1H), 1.2–1.3 (m, 3H), 1.7–1.8 (m, 2H), 2.00–2.1 (m, 2H), 3.00–3.10 (m, 2H), 3.3–3.4 (m, 1H), 6.5–6.6 (m, 2H), 7.10–7.20 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 24.2, 24.9, 31.5, 33.2, 60.3, 74.5, 110.1, 116.2, 131.6, 146.8.

2-(Naphthalen-1-ylamino)cyclohexanol (3e)

EIMS (*m/z*) 242; IR: ν 3598, 3362, 2945, 2832, 1604, 1521, 789 cm^{-1}; ^1H NMR ($CDCl_3$) : δ 1.1–1.2 (m, 1H), 1.33–1.53 (m, 3H), 1.75–1.84 (m, 2H), 2.15–2.4 (m, 2H), 2.86 (s, 1H), 3.13 (dt, *J* = 10.8, 3.9 Hz, 1H), 3.51 (dt, *J* = 9.6, 4.2 Hz, 1H), 4.00 (s, 1H), 6.8 (d, *J* = 7.2, 1H), 7.33 (dd, *J* = 14.35, 7.3 Hz, 2H), 7.48 (m, 1H), 3.47–3.55 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 24.5, 25.1, 31.4, 33.6, 60.1, 74.6, 106.6, 118.5, 120.1, 124.5, 124.9, 125.8, 126.5, 128.9, 134.7, 142.9.

2-(Ethylphenylamino)cyclohexanol (3f)

EIMS (*m/z*) 220; IR: ν 3388, 2934, 2863, 1618, 1512, 1245, 693 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.06–1.1 (t, *J* = 7.2 Hz, 3H), 1.14–1.28 (m, 4H), 1.66–1.68 (m, 2H), 2.00–2.1 (m, 1H), 2.86 (s, 1H), 2.75 (s, 1H), 3.11–3.21 (m, 3H), 3.47 (dt, *J* = 9.9, 4.2, Hz, 1H), 6.7 (t, *J* = 7.5 Hz, 1H), 6.8 (d, *J* = 8.4 Hz, 2H), 7.1 (t, *J* = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 14.5, 24.4, 25.7, 26.7, 33.5, 38.7, 67.9, 70.2, 117.4, 119.3, 129.1, 149.1.

2-(Benzylamino)cyclohexanol (3g)

EIMS (*m/z*) 206; IR: ν 3398, 2926, 2860, 1616, 1519, 1256, 714 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.05–1.1 (m, 4H), 1.6–1.8 (m, 2H), 1.96–2.12 (m, 2H), 3.14 (dt, *J* = 9.6, 3.9 Hz, 1H), 3.36 (dt, *J* = 9.6, 4.8 Hz, 1H), 3.79 (s, 2H), 7.12–7.35 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 23.3, 24.7, 28.4, 33.5, 47.7, 61.8, 70.4, 125.9, 127.3, 127.8, 140.8.

2-(Methylamino)cyclohexanol (3h)

EIMS (*m/z*) 130; IR: ν 3362, 2945, 2832, 1604, 1521, 1254, 1204, 752 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.2–1.3 (m, 4H), 1.7–1.74 (m, 3H), 2.02–2.1 (m, 2H), 2.2–2.33 (m, 2H) , 2.53 (s, 1H), 3.52 (dt, *J* = 9.6 ,4.5 Hz, 1H), 5.11 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 24.2, 25.7, 28.2, 31.3, 34.1, 65.2, 71.4.

2-(Isopropylamino)cyclohexanol (3i)

EIMS (*m/z*) 158; IR: ν 3379, 2945, 2831, 1624, 1561,1227, 789 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.06 (d, *J* = 6.6 Hz, 3H), 1.12 (d, *J* = 6.6 Hz, 3H), 1.2–1.26 (m, 4H), 1.66

(m, 2H), 1.95 (m, 2H), 2.43 (dt, *J* = 10.8, 3.6 Hz, 1H), 3.08 (septet, *J* = 6.6 Hz, 2H), 3.21 (dt, *J* = 9.6, 4.8 Hz, 1H), 5.17 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 19.8, 21.7, 23.1, 23.8, 28.3, 32.6, 44.9, 59.4, 71.2.

2-(Diethylamino)cyclohexanol (3j)
EIMS (*m/z*) 172; IR: ν 2951, 1721, 1561,1227, 1209, 1017 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.98 (t, *J* = 7.2 Hz, 3H), 1.07–1.19 (m, 4H), 1.63–1.70 (m, 2H), 2.12–2.35 (m, 2H), 2.51–2.68 (m, 2H), 3.2 (m, 1H), 3.76 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 18.4, 21.8, 23.3, 24.7, 32.2, 42.2, 65.1, 67.9.

2-(Pyrrolidin-1-yl)cyclohexanol (3k)
EIMS (*m/z*) 170; IR: ν 3387, 2951, 2872, 1607, 1507, 1217, 723 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.1–1.3 (m, 3H), 1.67–1.71 (m, 4H), 1.8–1.98 (m, 2H), 2.34–2.53 (m, 3H), 3.24 (dt, *J* = 9.6, 4.2 Hz, 1H), 4.3 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 21.3, 25.1, 26.1, 28.1, 35.3, 47.1, 64.9, 71.5.

2-(Dimethylamino)cyclohexanol (3l)
EIMS (*m/z*) 144; IR: ν 2943, 1632, 1521, 1286, 1243, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.1–1.4 (m, 4H), 1.6–1.9 (m, 3H), 2.7 (s, 3H), 3.0–3.1 (m, 1H), 3.2–3.3 (m, 1H), 3.6–3.7 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 22.8, 23.9, 24.3, 32.9, 34.4, 68.5, 70.3.

1-(Phenylamino)hexan-2-ol (5a)
EIMS (*m/z*) 194; IR: ν 3327, 2971, 2842, 1617, 1537, 1239 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.86 (t, *J* = 7.1 Hz, 3H), 1.13–1.44 (m, 6H), 2.87–2.94 (m, 3H), 3.15–3.20 (m, 1H), 3.7–3.74 (m, 1H), 6.47–6.55 (m, 2H), 6.6–6.64 (m, 1H), 7.04–7.20 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 14.1, 22.7, 27.8, 34.8, 50.4, 70.3, 113.4, 118.1, 129.2, 148.1.

1-(Benzylamino)hexan-2-ol (5b)
EIMS (*m/z*) 208; IR: ν 3385, 2957, 2834, 1623, 1534, 1308 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.85 (t, *J* = 6.3 Hz, 3H), 1.26–1.34 (m, 6H), 2.37–2.63 (m, 2H), 3.6–3.7 (m, 1H), 3.72–3.77 (m, 1H), 4.6 (s, 2H), 7.24–7.36 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 14.5, 22.8, 27.8, 34.7, 49.1, 60.5, 69.3, 127.6, 128.3, 129.1, 138.4.

3. Results and Discussion

We have found that calcium trifluoroacetate efficiently catalyzed aminolysis of epoxides with aromatic and simple aliphatic amines. Calcium trifluoroacetate was easily prepared by reaction of trifluoroacetic acid with calcium dihydride at room temperature.[16] Aminolysis of epoxides with amines is carried out using 5 mol% of the catalyst under solvent-free conditions. Products were purified by chromatography on silica gel. In almost all of the cases the resulting crude β-aminoalcohols showed a single spot on the TLC chromatogram and could be used without further purification.

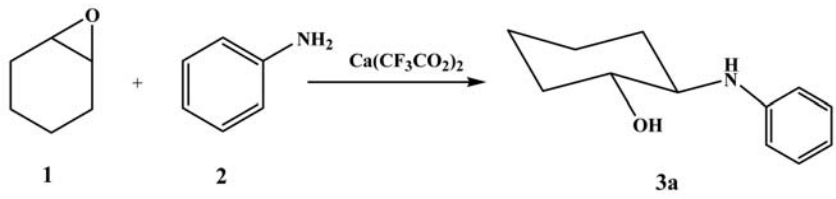
In a first set of experiments, we have investigated aminolysis of cyclohexene oxide (**1**) with aniline (**2**) in terms of catalytic activity of $Ca(CF_3COO)_2$. The reactions were monitored by GC and the results are provided in Table 1. In this part, we have studied the effect of the nature of solvent and the ratio substrate/catalyst.

In a typical experiment, 2 mmol of cyclohexene oxide and 2.04 mmol of aniline were stirred in the presence of a catalytic amount of $Ca(CF_3COO)_2$ (5 mol%) under solvent-free conditions at 40 °C for 31 h, to obtain the corresponding aminoalcohol **3** in 98% yield (Table 1, entry 1). The reaction was repeated in water and in THF leading to the corresponding aminoalcohol with good yields (Table 1, entries 2 and 3). However, only moderate catalytic activity was observed in acetonitrile and in [1,4]-dioxane where the yields of the product 2-*N*-phenylaminocyclohexanol do not exceed 53% (Table 1, entries 4 and 5).

In order to confirm the role of the catalyst, a blank reaction was carried out under identical reaction conditions with aniline and cyclohexene oxide (Table 1, entry 6). The reaction occurs with low yield (18%). Using trifluoroacetic acid as the catalyst, the reaction gave the corresponding product in only 25% yield (Table 1, entry 7). This investigation clearly shows the role of $Ca(CF_3COO)_2$ in the activation of the epoxide group toward the desired aminoalcohol in a short reaction time.

According to our previous studies,[16,17] the *trans* diastereomer was obtained in high yield demonstrating the stereoselective efficiency of $Ca(CF_3CO_2)_2$ for the desired transformation.

Pertinently, aminolysis of cyclohexene oxide was found to be effective under solvent-free conditions. In most cases, the reactions are carried out with aromatic amines only. To extend the methodology of the synthesis of various β-aminoalcohols, we have studied the reactivity of our catalyst toward aliphatic and aromatic amines. The results are summarized in Table 2.



Scheme 1: Aminolysis of cyclohexene oxide

Table 1: Effect of solvent and substrate/catalyst ratio (S/C) in the aminolysis of cyclohexene oxide by aniline.

Entry	Solvents	S/C	Conversion (%)[a]	Yield[b,c] (%)
1	Solvent-free	20	99	98
2	H_2O	20	80	75
3	THF	20	72	66
4	CH_3CN	20	55	53
5	[1,4]-Dioxane	20	47	37
6[d]	Solvent-free	None	20	18
7[e]	Solvent-free	20	30	25
8	Solvent-free	25	98	95
9	Solvent-free	40	78	71
10	Solvent-free	50	53	49

Conditions: solvent (0.1 M), temperature 40 °C. Reaction time 31 h , 2.0 mmol of **1** and 2.04 mmol of aniline

[a] The conversion was determined by gas chromatography. [b] Isolated yield. [c] The structure of the product was established by NMR and MS. [d] Reaction without catalyst. [e] Reaction with trifluoroacetic acid as the catalyst.

The reaction of **1** with 4-fluoroaniline, benzylamine, isopropylamine, methylamine and pyrrolidine (Table 2, entries 1, 6, 8, 12 and 13) provides excellent yields (90–100%). These results reveal that the present method is useful for aromatic as well as for aliphatic amines. Similar precursors such as $CoCl_2$, $Cu(OTf)_2$, zirconium sulfophenyl phosphonate, $TaCl_5$, $[Rh(CO)_2Cl]_2$, $CeCl_3$–NaI, VCl_3, and $BiCl_3$ are not applicable as they do not efficiently catalyze the reaction of epoxides with aliphatic amines.[6–13] These results could be explained by the formation of complex metal salts with aliphatic amines having strong Lewis acid properties thus leading to the catalyst poisoning. Here, we demonstrate that $Ca(CF_3CO_2)_2$ effectively catalyzes the epoxide ring-opening reaction by aliphatic amines (Table 2, entries 6–12). The comparison of the results, obtained with pyrrolidine and benzylamine using our methodology established that the present method is equal to or even better than the procedures reported so far.[18b,19]

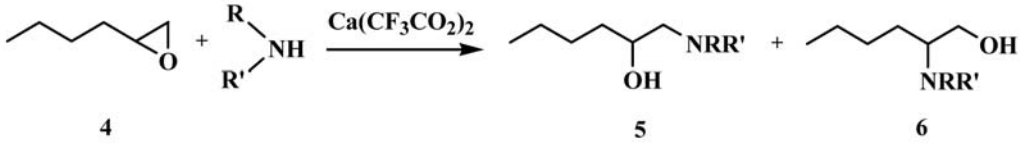
The observed yields in Table 2 can be rationalized taking into account the electronic and steric factors. It appears clearly that electron-withdrawing effects decrease the nucleophilicity of the amine functional group in contrast to the electron-donating groups. In addition, the position of fluorine as the electron withdrawing atom in aromatic ring, significantly affects the nucleophilicity of the amine. Thus, 4-fluoroaniline is highly nucleophilic, far more than 2-fluoroaniline; this is well confirmed by the low yield obtained with 2-fluoroaniline (Table 2, entries 1–2).

Table 2: Aminolyse of cyclohexene oxide by various amines

Entry	Amine	Time (h)	Conversion (%)	Yield (%)[b,d]
1	4-Fluoroaniline	24	86 (100)	82 (100)
2	2-Fluoroaniline	24	38 (42)	34 (39)
3	4-Bromoaniline	24	20 (41)	16 (21)
4	Naphtylamine	24	45 (61)	39 (56)
5	Ethylphenylamine	24	31 (40)	18 (26)
6	Benzylamine	24	100	93
7	Isopropylamine	31	73	69
8[c]	Isopropylamine	31	100	95
9	Dimethylamine	31	82	75
10[c]	Dimethylamine	31	87	79
11	Diethylamine	31	51	34
12	Methylamine	31	100	90
13	Pyrrolidine	31	100	100

Conditions: 2.0 mmol of **1** and 2.04 mmol of amine, S/C = 20, temperature 40 °C. The values in brackets represent conversions and yields after prolonged time (31 h).

[a] The conversion was determined by gas chromatography. [b] Isolated yield. [c] Temperature 60 °C. [d] The structure of the product was established by NMR and MS.



Scheme 1: Aminolysis of cyclohexene oxide

Moreover, the steric effect which is more significant in 2-fluoroaniline, disadvantages the reactivity of the amine function. For the bromoanilines, as the bromine is less electronegative than fluorine, the 4-fluoroaniline is more nucleophilic than 4-bromoaniline. Furthermore, the steric hindrance of the bromine is significant in comparison to the fluorine. Therefore, using 2-bromoaniline, the reaction occurs with low activity. Only trace of the desired product is detected. The same result was observed with 4-chloro-2-methyl-phenylamine. With aliphatic amines, the yields obtained can be explained by the steric effect. According to the electronic effects, in spite of the fact that $MeNH_2$ possesses the lowest basicity compared to dimethylamine, isopropylamine and diethylamine, it gives the best yield (the methyl group presents the smallest sterical hindrance).

In a third set of experiments, we have investigated the regioselectivity of the epoxide ring-opening reaction. 1,2-Hexene oxide **4** was chosen as a representative unsymmetrical epoxide (Table 3). The regioselectivity

Table 3: Aminolysis of 1,2-hexene oxide by amines

Entry	Amine	Yield (%)[a]	
		5	**6**
1	Aniline	91	9
2	4-Fluoroaniline	92	8
3	Benzylamine	97	3
4	Methylamine	100	0
5	Pyrrolidine	100	0

Conditions: 1,2-hexene oxide / $Ca(CF_3CO_2)_2$ = 20, temperature 40 °C, time (31 h). The conversion was 100%, determined by gas chromatography.
[a] Isolated yield.

was determined by GC analysis. The formation of the aminoalcohol by nucleophilic attack at the terminal carbon of **4** was determined by the appearance of a hydroxy carbon signal at δ 70 ppm in the ^{13}C NMR spectra.

A pertinent regioselectivities of 91:9 in favor of nucleophilic attack of the aniline at the terminal carbon was observed with 100% conversion (Table 3, entry 1). In the same manner, several aromatic amines such as 4-fluoroaniline (Table 3, entry 2) provide 100% conversion with 92:8 selectivity. Therefore, to compare the regioselectivity of the present study with the reported one,[20,21] **4** was treated with benzylamine, methylamine and pyrrolidine. The reactions lead to 97:3, 100:0, 100:0 selectivities, respectively, in favor of the formation of the aminoalcohol from the nucleophilic attack at the less hindered terminal carbon of the epoxide ring.

With unsymmetrical epoxides, the observed preference for the nucleophilic attack at the terminal position of **4** can be rationalized taking into consideration the electronic and steric factors. Coordination of the epoxide oxygen with the Lewis acidic site of the catalyst induces a carbocationic character at the epoxide ring. Selective nucleophilic attack at the terminal carbon of the epoxide ring takes place due to the steric factors. The exclusive formation of the aminoalcohol from the nucleophilic attack at the terminal carbon in **4** by a methylamine and pyrrolidine (Table 3, entries 4 and 5) compared to a 97:3, 92:8, 91:9 regioselectivities observed with benzylamine, 4-fluoroaniline and aniline, respectively (Table 3, entries 1–3) highlights the role of the steric factors.

4. Conclusion

In conclusion, the present study describes an improved and efficient sustainable and environmentally friendly process for the synthesis of β-aminoalcohols by the aminolysis of 1,2-epoxides using $Ca(CF_3CO_2)_2$ as catalyst. Both aromatic and aliphatic amines can be used. The advantages include high yields and regioselectivities under mild and benign conditions.

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Povzetek

$Ca(CF_3CO_2)_2$ učinkovito katalizira selektivno odpiranje epoksidnih obročov z amini pri čemer nastanejo β-aminoalkoholi. Reakcija je učinkovita z različnimi aromatskimi in alifatskimi amini pod pogoji brez uporabe topil. Ustrezni β-aminoalkoholi nastanejo z zelo dobrimi izkoristki in z visoko regioselektivnostjo. Priprava katalizatorja iz CaH_2 in trifluoroocetne kisline je enostavna.