isomer ((*E*)-18-F): mp > 200 °C dec: ^{1}H NMR δ 1.0–2.6 (m), 3.1 (bs); ^{19}F NMR (CF_3COOH, 282 MHz) δ −60.06. Single crystals were obtained by slow evaporation of a solution in ethyl acetate–hexane (1:4). A ^{13}C NMR spectrum could not be obtained for either epimer because of poor solubility.

X-ray Diffraction Studies. For the parent compound 18-H, a colorless crystal of dimensions 0.33 × 0.25 × 0.23 mm was mounted on a R3m/μ update of a Nicolet $P2_1$ diffractometer. Unit cell dimensions were obtained from a least-squares refinement of 25 reflections. Crystal data: $C_{23}H_{24}N_4$, M_r = 356.48, monoclinic; $P2_1/c$; a = 14.710 (3), b = 10.597 (2), and c = 13.151 (2) Å, β = 114.63 (1)°; V = 1863.4 (6) Å^3; Z = 4, D_x = 1.270 g cm^{-3}; μ = 0.72 cm^{-1}; $F(000)$ = 760. Intensity data were collected by the ω-scan technique ($3 \le 2\theta \le 55°$) with a variable scan rate (4 to 29.3° min^{-1}) using graphite-monochromated radiation (Mo Kα, λ = 0.71073 Å). A total of 5733 reflections were collected of which 4290 were independent (R_{int} = 0.008), yielding 3137 with intensities greater than $3\sigma(I)$. Lorentz and polarization corrections and a ω-scan based absorption correction were applied. The structure was solved by direct methods and refined by a block-cascade least-squares technique. The structure was refined to R = 0.0561 and R_ω = 0.0794 with 341 parameters and 3137 reflections giving S = 1.597, $(\lambda/\sigma)_{max}$ = 0.022 and the largest peaks in a final difference map of −0.28 and 0.26 e Å^{-3}. The function $\sum w(|F_o| - |F_c|)^2$ was minimized with $w = [\sigma^2(F_o) + 0.00017F_o]^{-1}$. All programs supplied by Nicolet Instrument Corp. for Desktop 30 Microeclipse and Nova 4/C configuration with atomic scattering factors and anomalous dispersion corrections from *International Tables for X-ray Crystallography*.

Similarly, for (*E*)-18-F ($C_{23}H_{23}N_4F$), M_r = 374.50, monoclinic; $P2_1/c$; a = 9.529 (2), b = 16.523 (4), and c = 12.516 (2) Å, β = 105.81 (1)°; V = 1896.0 Å^3; z = 4, D_x = 1.310 g cm^{-3}; μ = 0.81 cm^{-1}; $F(000)$ = 792; 2522 reflections R = 0.0520.

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Supplementary Material Available: X-ray data for 18-H and 18-F, ^{13}C NMR spectra of (*Z*)-3-Ph, 10-F, (*E*)- and (*Z*)-11-F, 13-H, (*E*)- and (*Z*)-13-F, 17, and 18-H, and ^{1}H NMR spectra of (*E*)- and (*Z*)-11-F and 14-H (at 600 MHz) (25 pages). Ordering information is given on any current masthead page.

Notes

Regioalternating Selectivity in the Metal Salt Catalyzed Aminolysis of Styrene Oxide

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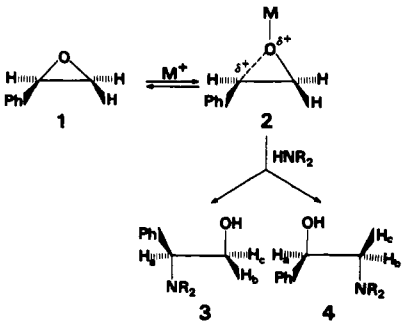
β-Amino alcohols are an important class of organic compounds[1] of considerable use in medicinal chemistry.[2] The most practical and widely used route to the synthesis of these compounds is the direct aminolysis of 1,2-epoxides;[1] however, these reactions, which are usually carried out with a large excess of ammonia or amines in protic solvents at elevated temperatures, often fail when poorly nucleophilic amines or highly substituted epoxides are concerned.[1] Recently, we discovered[3] a new, mild, and efficient method for the aminolysis of 1,2-epoxides in nonprotic solvents through the catalytic assistance of metal ion salts (Li^+, Na^+, Mg^{2+}, Ca^{2+}, Zn^{2+}). Besides the nature of the amine and epoxide, the reaction rate also depends on the type of the metal ion of the catalyst salt.[3] For example, in the alkaline metal ion series, the reactivity slows down dramatically on passing from lithium- to potassium-based salts.[3] The efficiency of this simple catalysis is confirmed by the fact that under appropriate conditions it is possible to obtain, in fair yield, the reaction of cyclohexene oxide with the poorly nucleophilic, sterically hindered diisopropylamine,[3] a reaction not previously accomplished. The stereoselectivity observed in these reactions[3] is complete inversion of configuration. Unsymmetrical epoxides[3] undergo regioselective addition of the nucleophile to the less substituted carbon. The exception is styrene oxide (1) in which an almost equimolar mixture of the two regioisomeric phenyl-substituted β-amino alcohols 3 and 4, (Scheme I) was obtained (see reaction with diethylamine in the presence of lithium perchlorate, entry 11, Table I). In view of the particular interest in phenylethanolamines in medicinal chemistry,[2] we wanted to study the regiochemical behavior of these new metal salt catalysts in the aminolysis of 1 in order to verify whether the regioselectivity could be appreciably modified depending on the amine and/or the catalyst in such a way as to direct the regiochemistry of these reactions selectively.

Scheme I



Results and Discussion

Table I reports the regioselectivity of the ring-opening reactions of 1 with several amines using $LiClO_4$ as the catalyst, (entries 1–12) together with the results obtained in the aminolysis reaction of 1 with a representative amine (diethylamine), using different metal salts as catalysts (entries 13–16). For the sake of comparison, the result of the opening reaction of 1 with diethylamine, carried out in the classic way without any metal catalyst in a protic solvent (EtOH)[1] is also reported (entry 17). The yields of

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0022-3263/91/1956-5939$02.50/0

Table I. Regioselectivity of the Aminolysis of Styrene Oxide (1) in the Presence of Metal Salts

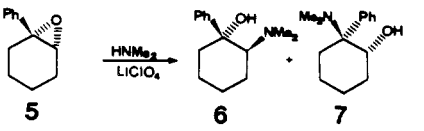
entry	amine[a]	salt (solvent)[b]	reaction time[c] (h)	yield[d] (%)	3[e]	4[e]
1	*p*-nitroaniline	$LiClO_4$ (A)	20 (65 °C)	66	95	5
2	aniline	$LiClO_4$ (A)	3.5	95	92	8
3	*N*-methylaniline	$LiClO_4$ (A)	4	94	90	10
4	*p*-methoxyaniline	$LiClO_4$ (A)	2.5	94	87	13
5	$BnNH_2$	$LiClO_4$ (A)	1.5	98	58	42
6	piperidine	$LiClO_4$ (A)	0.5	98	58	42
7	$BuNH_2$	$LiClO_4$ (A)	1	96	53	47
8	*t*-$BuNH_2$	$LiClO_4$ (A)	1	94	47	53
9	$(i\text{-}Pr)_2NH$	$LiClO_4$ (A)	24	93	<1	>99
10	$(Cy)_2NH$	$LiClO_4$ (A)	72	88	<1	>99
11	Et_2NH	$LiClO_4$ (A)	0.5	96	43	57
12	Et_2NH	$LiClO_4$[f] (A)	2.5	92	53	47
13	Et_2NH	$Zn(Tf)_2$ (A)	0.5	92	55	45
14	Et_2NH	$Mg(ClO_4)_2$ (A)	0.5	94	30	70
15	Et_2NH	$CaCl_2$ (A)	4	93	20	80
16	Et_2NH	$NaClO_4$ (A)	6	92	12	88
17	Et_2NH	(B)	96 (80 °C)	90	5	95
18	Et_2NH	$LiClO_4$ (B)	2.5	92	20	80
19	Et_2NH	$LiClO_4$ (C)	2.5	90	52	48
20	Et_2NH	$LiClO_4$ (D)	2.5	94	43	57

[a] Cy = cyclohexyl. [b] Entry 17 was carried out without any metal salt being added: Tf = triflate; A, CH_3CN; B, EtOH; C, Et_2O; D, acetone. [c] With the only exception of entries 1 and 17 all the reactions were carried out at 25 °C (see General Procedure). [d] Yields based on GC analysis (with the only exception of entries 1, 2, 4, 5, and 10), ^1H NMR examination, and weight of the crude isolated reaction product. [e] The amine used determines the nature of the NR_2 group in the general structures of regioisomeric amino alcohols 3 and 4; for their identification, see Experimental Section. [f] A double amount of salt was employed.

all the reactions in Table I are quite satisfactory, the reaction times are limited, and the operating conditions are not drastic, even when poorly nucleophilic or sterically hindered amines are used (entries 1–4, 9, and 10). It must be pointed out that the reaction of 1 with the sterically hindered dicyclohexylamine carried out in ethanol at the refluxing temperature for 3 days in the absence of any metal catalysts led to the recovery of almost 50% of unreacted epoxide (see Experimental Section). The results indicate that it is possible to obtain a reversal of the regiochemistry of the opening process on passing from the reaction with *p*-nitroaniline (entry 1) to the one with diisopropyl- and dicyclohexylamine (entries 9 and 10, respectively), even with the same catalyst ($LiClO_4$). On the basis of the regiochemistry observed in each case, the amines can be divided, roughly speaking, into three main classes: (i) aromatic amines of low nucleophilicity that give almost exclusively the amino alcohol 3 derived from the attack on the benzylic oxirane carbon of 1, (entries 1–4), (ii) benzylamine and other aliphatic unhindered amines that afford almost equimolar amounts of the two regioisomers 3 and 4 (entries 5–8, and 11), and (iii) sterically hindered amines (e.g., dicyclohexyl- and diisopropylamine) that afford, in a completely regioselective way, amino alcohol 4 formed by the attack on the less substituted nonbenzylic oxirane carbon of 1 (entries 9 and 10). The metal ion of the salt is also able to modulate the regiochemistry of the reactions markedly, as shown by the results of the reaction of 1 with diethylamine in the presence of different metal salts (entries 11–16). Weaker Lewis acid cations like Na^+ promote more S_N2-type nucleophilic attack on the less substituted carbon (entry 16). Better Lewis acids,[3] e.g., Zn^{2+}, Li^+, and Mg^{2+} (entries 11–14), are more effective in directing the attack of the amine to the benzylic carbon.

The metal-assisted aminolysis of epoxides proceeds through an A_1-type mechanism.[4] The attack of the amine on the metal-coordinated epoxide 2[3] (in this intermediate the positive charge appears to be better localized on the benzylic carbon than on the primary one, as shown in Scheme I) will lead to 3 and/or 4. Due to the presence of the phenyl, the transition state leading to 3 should possess more "carbocationic character" than that leading to 4. The use of less nucleophilic anilines (entries 1–4) slows down the attack of the nucleophile and therefore favors the breaking of the C–O bond in the transition state. As a consequence, the attack of the amine will take place preferentially through the more carbocationic transition state leading to 3, which can better allow the rupture of the C–O bond. In an analogous way, the use of stronger Lewis acids can favor the breaking of the C–O bond, thus leading to more carbocationic transition states. This will again make the more carbocationic transition state leading to 3 relatively more favorable. On the other hand, the use of bulky α-branched secondary amines (entries 9 and 10) increases the energy content of the more crowded transition state leading to 3, thus favoring the attack of the amine at the less substituted carbon. It may be pointed out that in these aminolysis reactions, the degree of carbocationic character, in the transition states, should be limited. This consideration derives from the chemical behavior of cycloaliphatic 2-aryloxiranes, such as 1-phenylcyclohexene oxide (5). Compound 5 is a substrate that typically shows a very large tendency toward the syn opening process; that is, it reacts through highly carbocationic structures when A_1-type reactions are concerned.[5] However, when 5 reacts with dimethylamine in the presence of $LiClO_4$ in the same reaction conditions as used for 1, an almost 1:1 ratio of the two regioisomers 6 and 7 is obtained, both with complete anti stereoselectivity (see Scheme II and Experimental Section).

Scheme II



The results (entries 11 and 18–20) indicate that acetonitrile, Et_2O, or acetone can be utilized with only small

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variations in the regiochemical results. On the contrary, the use of a protic solvent (EtOH) in the presence of $LiClO_4$ (entry 18) drastically shifts the regiochemical outcome of the opening reaction of 1 toward the anti Markovnikov adduct, amino alcohol 4. One might expect the high solvating power of the protic solvent (EtOH) to make the lithium cation less available for coordination with the oxirane oxygen, giving less carbocationic character as a consequence. However, a comparison of entry 17 with entry 18 shows the catalytic effect of the Li^+ is still operative even in protic solvents.

Finally, doubling the amount of $LiClO_4$ catalyst increases the yield of amino alcohol 3 slightly (compare entry 12 with entry 11) so that it is similar to that obtained with the more efficient, but more expensive, Zn^{2+} catalyst (entry 13).

Conclusions

The results show that the regioselectivity of the metal salt catalyzed reaction of 1 with amines can be altered by the amine and the metal ion, thus obtaining a regioalternating selectivity.[6]

Experimental Section

For general experimental procedures see ref 6b. GC analyses were performed with a 30 m × 0.53 mm (i.d.) × 1 μm (film thickness) DB-17 fused silica column, at a column temperature 200 ° and a nitrogen flow of 2 mL/min. Preparative and semipreparative TLC was performed with a 6:4 mixture of petroleum ether and ether and few drops of 30% aqueous NH_3 as the eluant.

Identification of compounds 3 and 4 (Table I) was based, where possible, on a comparison with authentic samples prepared in accordance with literature procedures (entries 2,[7] 3,[8] 5,[8b,9] 6,[8b,10,11] 7,[8b,12] 8,[13] 9,[11] and 11–20[8b,9a,14]) or by an alternative synthetic route (aminolysis of 1 in EtOH at 90 °C, entries 1 and 4, Table I). When previously reported (entries 2 and 5–7),[7a,9c,10,12] the ^1H NMR parameters of amino alcohols 3 and 4 were perfectly consistent with literature data. In all caes, the regiochemistry of the amino alcohols 3 and 4 was firmly established by means of ^1H NMR spectra of these compounds, on the basis of the signal of the benzylic proton that resonates consistently at lower field in the type 4 than in the type 3 regioisomer,[15] the only exception being entry 3. When not previously reported (entries 3, 5–9, and 11), the relevant ^1H NMR parameters of the corresponding known amino alcohols (free bases), obtained in the reaction of 1 according to General Procedure, are given. Amino alcohols 6 and 7 were prepared as previously described.[16]

General Procedure of the Aminolysis of 1 in the Presence of Metal Salts. A solution of 1 (0.60 g, 5 mmol) in the indicated solvent (2 mL) and the anhydrous metal salt (10 mmol) was stirred until complete solution of the salt. The resulting solution was stirred at rt as the required amount of the amine (10 mmol) was added (see Table I). The reaction mixture was stirred for the time and temperature indicated in Table I. Evaporation of the washed (water) and dried ether extracts yielded a mixture of amino alcohols 3 and 4, which was analyzed by means of ^1H NMR (entries 1–20) and GC (entries 3, 6–9, and 11–20). Recrystallization of the crude reaction product (entries 1 and 10) or preparative TLC (entries 2–9 and 11) afforded pure amino alcohols 3 and/or 4.

Entry 1, Table I. The crude solid reaction product was recrystallized from a 2:1 hexane/$CHCl_3$ mixture to give pure 3 (NR_2 = p-$O_2NC_6H_4NH$) as a solid: mp 100–101 °C; ^1H NMR δ 7.95 and 6.46 (2d, 2 H each, AA'XX' system, J = 9.2 Hz, ArH), 7.38–7.27 (m, 5 H, ArH), 4.57 (dd, 1 H, $J_{a,b}$ = 4.1 Hz, $J_{a,c}$ = 6.2 Hz, H_a), 4.00 (dd, 1 H, $J_{b,c}$ = 11.4 Hz, $J_{a,b}$ = 4.1 Hz, H_b), 3.81 (dd, 1 H, $J_{b,c}$ = 11.4 Hz, $J_{a,c}$ = 6.2 Hz, H_c). Anal. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.10; H, 5.46; N, 10.84. Found: C, 65.35; H, 5.24; N, 10.46.

4 (NR_2 = p-$O_2NC_6H_4NH$). A solution of 1 (5 mmol) in anhydrous EtOH (3 mL) was treated with p-nitroaniline (4.5 mmol), and the resulting reaction mixture was kept under stirring at 90 °C for 72 h. Cooling, dilution with water, extraction with ether, and evaporation of the dried ether extracts afforded a semisolid residue consisting of a 26:9:65 mixture of the corresponding amino alcohols 3 and 4 (ratio 74:26) and unreacted epoxide 1. An analytical sample of this mixture (0.50 g) was subjected to preparative TLC. Extraction of the two most intense bands afforded 3 (R_f = 0.48, 0.050 g) and 4 (NR_2 = p-$O_2NC_6H_4NH$, R_f = 0.55, 0.025 g), as a solid: mp 102–103 °C; ^1H NMR δ 8.08 and 6.56 (2d, 2 H each, AA'XX', J = 9.6 Hz, ArH), 7.43–7.36 (m, 5 H, ArH), 5.01–4.94 (m, 1 H, H_a), 3.50–3.38 (m, 2 H, H_b and H_c). Anal. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.10; H, 5.46; N, 10.84. Found: C, 65.15; H, 5.60; N, 11.02.

Entry 3, Table I. The crude reaction product was subjected to preparative TLC. Extraction of the two most intense bands afforded 3 and 4 (NR_2 = NHMePh).

3 (NR_2 = NMePh):[8a] liquid; ^1H NMR δ 7.39–6.81 (m, 10 H, ArH), 5.12 (unresolved t, J = 6.2 Hz, H_a), 4.13 (unresolved d, 2 H, J = 6.2 Hz, H_b and H_c), 2.74 (s, 3 H, CH_3).

4 (NR_2 = NMePh):[8b] liquid; ^1H NMR δ 7.46–7.22 (m, 7 H, ArH), 6.89–6.74 (m, 3 H, ArH), 5.00 (dd, 1 H, $J_{a,b}$ = 4.9 Hz, $J_{a,c}$ = 8.1 Hz, H_a), 3.52 (dd, 1 H, $J_{a,c}$ = 8.1 Hz, $J_{b,c}$ = 14.8 Hz, H_c), 3.39 (dd, 1 H, $J_{a,b}$ = 4.9 Hz, $J_{b,c}$ = 14.8 Hz, H_b), 2.94 (s, 3 H, CH_3).

Entry 4, Table I. The crude oily reaction product was subjected to preparative TLC. Extraction of the most intense band afforded pure 3 (NR_2 = p-$CH_3OC_6H_4NH$) as a liquid:[17] ^1H NMR δ 7.34–7.17 (m, 5 H, ArH), 6.64 and 6.46 (2d, 2 H each, AA'BB', J = 8.9 Hz, ArH), 4.30 (dd, 1 H, $J_{a,b}$ = 4.1 Hz, $J_{a,c}$ = 7.8 Hz, H_a), 3.62 (s, 3 H, OCH_3), 3.81–3.42 (m, 2 H, H_b and H_c). Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.75. Found: C, 74.20; H, 7.35; N, 5.80. Oxalate: mp 149–150 °C. Anal. Calcd for $C_{17}H_{19}NO_6$: C, 61.25; H, 5.74; N, 4.19. Found: C, 61.40; H, 5.55; N, 4.43.

4 (NR_2 = p-$CH_3OC_6H_4NH$). Reaction of 1 (5 mmol) in anhydrous EtOH (3 mL) with p-anisidine (4.5 mmol) at 90 °C as described above for the corresponding reaction with p-nitroaniline afforded an oily residue consisting of a 68:32 mixture of the corresponding amino alcohols 3 and 4. A sample (0.50 g) of this crude product was subjected to preparative TLC. Extraction of the fastest moving band afforded pure 4 (NR_2 = p-$CH_3OC_6H_4NH$) as a liquid: ^1H NMR δ 7.45–6.52 (m, 9 H, ArH), 4.87 (dd, 1 H, $J_{a,b}$ = 3.2 Hz, $J_{a,c}$ = 9.2 Hz, H_a), 3.73 (s, 3 H, OCH_3), 3.49 (dd, 1 H, $J_{b,c}$ = 14.0 Hz, $J_{a,b}$ = 3.2 Hz, H_b), 3.30 (dd, 1 H, $J_{b,c}$ = 14.0 Hz, $J_{a,c}$ = 9.2 Hz, H_c). Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.75. Found: C, 74.35; H, 7.15; N, 7.45. Oxalate: mp 136–138 °C. Anal. Calcd for $C_{17}H_{19}NO_6$: C, 61.25; H, 5.74; N, 4.19. Found: C, 61.01; H, 7.36; N, 3.95.

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(17) Several attempts to repeat the reaction of 1 with p-anisidine in acetonitrile in the presence of $CoCl_2$ as a catalyst for 24 h at room temperature in accordance with the methodology previously described by other authors[18] afforded an 80:20 mixture of the amino alcohols 3 and 4 (NR_2 = p-$CH_3OC_6H_4NH$) still containing 50% of the starting epoxide 1, contrary to expectations.[18] The authors[18] reported that compound 4 was the only reaction product. On the basis of our data, it appears to us that the regiochemistry assigned by them to the compound (4) they obtained should be reversed to 3 (NR_2 = p-$CH_3OC_6H_4NH$).

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Entry 5, Table I. The crude solid reaction product was subjected to preparative TLC. Extraction of the two most intense bands afforded **4** (NR_2 = NHBn),[8b,9] as a solid, mp 99–101 °C (lit.[9c] mp 100–102 °C) and **3** (NR_2 = NHBn),[9a] as a solid, mp 73–75 °C: ^{1}H NMR δ 7.42–7.22 (m, 10 H, ArH), 3.82 (dd, 1 H, $J_{a,b}$ = 4.3 Hz, $J_{a,c}$ = 8.7 Hz, H_a), 3.77 (d, 1 H, J = 13.0 Hz, PhCH_AH$_B$N), 3.71 (dd, 1 H, $J_{a,b}$ = 4.3 Hz, $J_{b,c}$ = 10.6 Hz, H_b), 3.59 (dd, 1 H, J = 13.0 Hz, PhCH$_A$$H_B$N), 3.55 (dd, 1 H, $J_{a,c}$ = 8.7 Hz, $J_{b,c}$ = 10.6 Hz, H_c). Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.53; N, 6.15. Found: C, 79.35; H, 7.84; N, 6.25.

Entry 6, Table I. The crude reaction product was subjected to preparative TLC. Extraction of the two most intense bands afforded **4** (NR_2 = piperidine),[8b,10,11] as a solid, mp 69–71 °C (lit.[11] mp 71–72.5 °C), and **3** (NR_2 = piperidine), as a liquid: ^{1}H NMR δ 7.36–7.14 (m, 5 H, ArH), 3.98 (m, 1 H, H_a), 3.64 (m, 2 H, H_b and H_c), 2.62–2.24 (m, 4 H, CH_2NCH_2), 1.65–1.30 (m, 8 H, aliphatic H). Anal. Calcd for $C_{13}H_{19}NO$: C, 76.05; H, 9.32; N, 6.82. Found: C, 76.15; H, 9.41; N, 6.91.

Entry 7, Table I. The crude semisolid reaction product was subjected to preparative TLC; extraction of the fastest moving band afforded pure **3** (NR_2 = NHBu) as a liquid: ^{1}H NMR δ 7.38–7.26 (m, 5 H, ArH), 3.80–3.49 (unresolved, 3 H, H_a, H_b, and H_c), 2.57–2.44 (m, 2 H, NHCH_2), 1.50–1.25 (m, 4 H, $(CH_2)_2$), 0.87 (t, 3 H, J = 7.1 Hz, CH_3). Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.90; N, 7.24. Found: C, 74.37; H, 9.75; N, 7.31. Oxalate: mp 140–141 °C. Anal. Calcd for $C_{14}H_{21}NO_5$: C, 59.77; H, 7.52; N, 4.94. Found: C, 59.85; H, 7.63; N, 4.80.

The slower moving band contained **4** (NR_2 = NHBu).[8b,12]

Entry 8, Table I. The crude reaction product was subjected to preparative TLC. Extraction of the two most intense bands afforded **3** and **4** (NR_2 = NH-*t*-Bu).

3 (NR_2 = NH-*t*-Bu),[13] as a solid: mp 60–61 °C (lit.[13] mp 61–62 °C); ^{1}H NMR δ 7.39–7.21 (m, 5 H, ArH), 3.85 (dd, 1 H, $J_{a,b}$ = 4.9 Hz, $J_{a,c}$ = 9.6 Hz, H_a), 3.53 (dd, 1 H, $J_{b,c}$ = 10.4 Hz, $J_{a,b}$ = 4.9 Hz, H_b), 3.28 (dd, 1 H, $J_{b,c}$ = 10.4 Hz, $J_{a,c}$ = 9.6 Hz, H_c), 1.01 (s, 9 H, *t*-Bu).

4 (NR_2 = NH-*t*-Bu),[13] as a solid: mp 85–87 °C (lit.[13] mp 86–87 °C); ^{1}H NMR δ 7.36–7.22 (m, 5 H, ArH), 4.66 (dd, 1 H, $J_{a,b}$ = 3.6 Hz, $J_{a,c}$ = 9.0 Hz, H_a), 2.81 (dd, 1 H, $J_{b,c}$ = 11.7 Hz, $J_{a,b}$ = 3.6 Hz, H_b), 2.63 (dd, 1 H, $J_{b,c}$ = 11.7 Hz, $J_{a,c}$ = 9.0 Hz, H_c), 1.07 (s, 9 H, *t*-Bu).

Entry 9, Table I. **4** (NR_2 = N(*i*-Pr)$_2$),[11] as a liquid; ^{1}H NMR δ 7.40–7.23 (m, 5 H, ArH), 4.54 (dd, 1 H, $J_{a,b}$ = 3.9 Hz, $J_{a,c}$ = 10.5 Hz, H_a), 3.09 (septet, 2 H, J = 6.6 Hz, 2C*H*Me$_2$), 2.71 (dd, 1 H, $J_{b,c}$ = 13.4 Hz, $J_{a,b}$ = 3.9 Hz, H_b), 2.32 (dd, 1 H, $J_{b,c}$ = 13.4 Hz, $J_{a,c}$ = 10.5 Hz, H_c), 1.10 and 0.99 (2d, 6 H each, J = 6.6 Hz, 4 Me). Hydrochloride: mp 130–131 °C. Anal. Calcd for $C_{14}H_{24}ClNO$: C, 65.22; H, 9.38; N, 5.43. Found: C 65.10; H, 9.45; N, 5.65.

Entry 10, Table I. The crude solid reaction product was recrystallized from hexane/ether to give pure **4** (NR_2 = N(Cy)$_2$) as a solid: mp 59–60 °C; ^{1}H NMR δ 7.36–7.20 (m, 5 H, ArH), 4.52 (dd, 1 H, $J_{a,b}$ = 3.8 Hz, $J_{a,c}$ = 10.5 Hz, H_a), 2.87 (dd, 1 H, $J_{b,c}$ = 13.3 Hz, $J_{a,b}$ = 3.8 Hz, H_b), 2.36 (dd, 1 H, $J_{b,c}$ = 13.2 Hz, $J_{a,c}$ = 10.5 Hz, H_c). Anal. Calcd for $C_{20}H_{31}NO$: C, 55.77; H, 10.36; N, 4.64. Found: C, 55.85; H, 10.21; N, 4.55.

Reaction of 1 with Dicyclohexylamine in EtOH. A solution of epoxide **1** (0.60 g, 5.0 mmol) in EtOH (3 mL) was treated with dicyclohexylamine (2.0 mL, 10.0 mmol), and the reaction mixture was stirred and heated at 80 °C for 3 days. Evaporation of the solvent afforded a crude liquid residue consisting of an 1:1 mixture of the opening product **4** (NR_2 = N(Cy)$_2$) and of the starting unreacted epoxide **1** (^{1}H NMR).

Entry 11, Table I. The crude reaction product was subjected to preparative TLC. Extraction of the two most intense bands afforded **3** and **4** (NR_2 = NEt$_2$).

3 (NR_2 = NEt$_2$),[9a] as a liquid; ^{1}H NMR δ 7.36–7.17 (m, 5 H, ArH), 4.00–3.85 (m, 2 H, H_b and H_c), 3.69–3.60 (m, 1 H, H_a), 2.81–2.63 (m, 2 H, CH_2N), 2.33–2.16 (m, 2 H, CH_2N), 1.08 (unresolved t, 6 H, J = 7.1 Hz, 2 CH_3). Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.90; N, 7.24. Found: C, 74.43; H, 9.70; N, 7.42.

4 (NR_2 = NEt$_2$),[8b,9a,14] as a liquid: ^{1}H NMR δ 7.40–7.17 (m, 5 H, ArH), 4.63 (dd, 1 H, $J_{a,b}$ = 3.7 Hz, $J_{a,c}$ = 10.5 Hz, H_a), 2.78–2.20 (m, 6 H, 3 CH_2N), 1.06 (unresolved t, 6 H, J = 7.2 Hz, 2 CH_3).

Reaction of Epoxide 5 with Dimethylamine in the Presence of $LiClO_4$. A solution of epoxide **5** (0.177 g, 1 mmol) and anhydrous $LiClO_4$ (0.214 g, 2 mmol) in anhydrous acetonitrile (0.2 mL) was cooled at 0 °C then treated with dimethylamine (0.13 mL, 1.96 mmol). The reaction mixture was stirred at rt for 40 h and then diluted with water and extracted with ether. Evaporation of the washed (water) ether extracts afforded a crude product (0.23 g) consisting of a 46:54 mixture of **6** and **7** (^{1}H NMR and GC).[16]

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Registry No. **1**, 96-09-3; **3** (NR_2 = *p*-$NO_2C_6H_4NH$), 135285-97-1; **3** (NR_2 = PhNH), 135285-98-2; **3** (NR_2 = PhMeN), 135285-99-3; **3** (NR_2 = *p*-MeOC_6H34NH), 135286-00-9; **3** (NR_2 = BnNH), 135357-90-3; **3** (NR_2 = 1-piperidinyl), 135286-01-0; **3** (NR_2 = BuNH), 135286-02-1; **3** (NR_2 = *t*-BuNH), 135286-03-2; **3** (NR_2 = Et$_2$N), 135357-91-4; **4** (NR_2 = *p*-$NO_2C_6H_4NH$), 135286-04-3; **4** (NR_2 = PhNH), 99342-73-1; **4** (NR_2 = PhMeN), 135286-05-4; **4** (NR_2 = *p*-MeOC_6H_4NH), 135286-06-5; **4** (NR_2 = BnNH), 107171-75-5; **4** (NR_2 = 1-piperidinyl), 40116-77-6; **4** (NR_2 = BuNH), 135357-92-5; **4** (NR_2 = *t*-BuNH), 14467-51-7; **4** (NR_2 = (i-Pr)$_2$N), 135286-07-6; **4** (NR_2 = Cy$_2$N), 135286-08-7; **4** (NR_2 = Et$_2$N), 135357-93-6; $PhNH_2$, 62-53-3; PhNHMe, 100-61-8; *p*-MeO$C_6H_4NH_2$, 104-94-9; $BnNH_2$, 100-46-9; $BuNH_2$, 109-73-9; *t*-$BuNH_2$, 75-64-9; (*i*-Pr)$_2$NH, 108-18-9; Cy$_2$NH, 101-83-7; Et$_2$NH, 109-89-7; *p*-$NO_2C_6H_4NH_2$, 100-01-6; $LiClO_4$, 7791-03-9; Zn(Tf)$_2$, 54010-75-2; Mg$(ClO_4)_2$, 10034-81-8; $CaCl_2$, 10043-52-4; $NClO_4$, 7647-14-5.

Activation Energy for a 1,2-Hydrogen Shift in (Phenoxymethyl)chlorocarbene

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The application of laser flash photolysis (LFP) to the area of carbene chemistry has been extremely popular in recent years.[1] While there are numerous absolute rate constants and Arrhenius parameters for intermolecular carbene reactions, less is known about intramolecular 1,2-hydrogen shifts for carbene reactions. Only recently, the 1,2-hydrogen shifts of benzylchlorocarbene,[2,3] methylchlorocarbene,[4,5] and alkylchlorocarbenes[6] have been determined.

As well, theoretical predictions[7] of activation energies for 1,2-hydrogen shifts in singlet carbenes have been advanced, but there are only few experimental values available for comparison. We now report the Arrhenius parameters for a 1,2-H shift in (phenoxymethyl)chlorocarbene (PMCC).

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