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Aqueous ammonia: a versatile reagent for symmetrical di(*F*-alkylated) aminodiols synthesis

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Abstract

The action of aqueous ammonia on *F*-alkyloxiranes gave, in mild conditions, exclusively di(*F*-alkylated) aminodiols. © 2000 Published by Elsevier Science Ltd.

Keywords: fluorinated oxirane; aqueous ammonia; aminodiol.

The opening reaction of oxiranes with primary and secondary amines[1–3] or ammonia.[4] constitutes an important method of preparation of aminoalcohols. These are frequently used as precursors in organic synthesis. To avoid subsequent alkylation of the aminoalcohol, a high excess of amine is generally required.

In the case of *F*-alkylated oxiranes, the action of primary and secondary amines leads also to the corresponding *F*-alkylated aminoalcohols.[5,6] The action of ammonia on these fluorinated oxiranes has not been reported to our knowledge, nevertheless the corresponding aminoalcohols were obtained via the sodium azide method.[7–10]

In the present study, aqueous ammonia was used to open *F*-alkylated oxiranes. When treated with concentrated aqueous ammonia (28%),[11] epoxide **1** furnished, according to Scheme 1, only the aminodiol **2** in satisfactory yield (Table 1). These aminodiols were obtained as a *meso* and *threo* mixture. Their solubility in organic solvents is poor because of the presence of two fluophilic *F*-alkyl groups and two hydrophilic hydroxy groups within the molecule. The best NMR signals separation of the diastereoisomers has been realized in CD_3COCD_3, CD_3OD or D_5-pyridine taken as solvents.

As the reactions allowing the preparation of these aminodiols (i) do not generate new assymetric carbon centers, (ii) do not involve the inversion of the starting ones, and (iii) take place on the primary carbon atom of the starting *F*-alkyloxirane by the action of NH_3 followed by the action of -NH_2 of the aminoalcohol intermediate, on the primary carbon atom of an another starting *F*-

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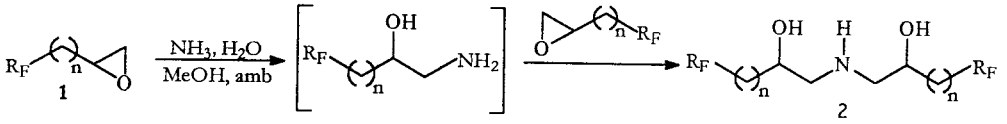
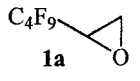
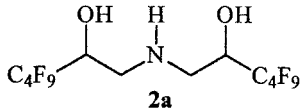
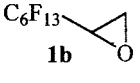
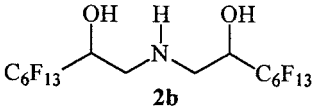
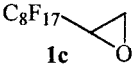
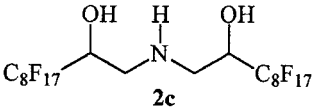
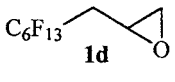
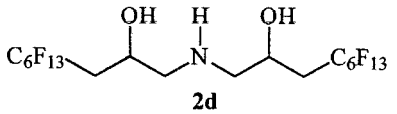
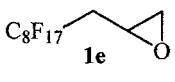
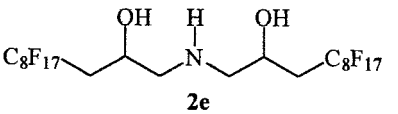


n=0; R_F=C_4F_9, C_6F_{13}, C_8F_{17}
n=1; R_F=C_6F_{13}, C_8F_{17}

Scheme 1.

Table 1
Aminodiols prepared

Epoxide	Aminodiol	Time (d)	mp (°C)	Yield (%)
 **1a**	 **2a**	1	93	57
 **1b**	 **2b**	1	117	60
 **1c**	 **2c**	2	151	70
 **1d**	 **2d**	3	68	60
 **1e**	 **2e**	3	109	65

alkyloxirane (Scheme 1), there is no stereoselectivity and the four possibilities of combinations (RR, SS, RS and SR) are equal so that these aminodiols should be obtained as an equimolar mixture of the *meso* and the *threo* isomers.

This conclusion was confirmed by ^{1}H NMR analysis of the assymetric carbon protons which gave two partially overlapped quintuplets (n = 1) or heptuplets (n = 0, $^3J_{FH} \approx 2^3J_{HH}$) with the same intensity. The separation between these quintuplets or heptuplets depends on the nature of the solvent.

The formation of aminodiol is noteworthy for the following reasons: (i) the aminoalcohol was not isolated; once formed, it reacts on the *F*-alkyloxirane present in the medium, to furnish the corresponding aminodiol. Thus the nucleophilicity of the nitrogen atom in the aminoalcohol seems to be unaffected by the electronic withdrawing effects of the perfluoroalkyl group; (ii) alkylation of the aminodiol was not observed; it is prevented probably by steric hindrance; (iii) the epoxide ring was regioselectively opened since the second possible regioisomer was not

detected. This regioselectivity induced by the perfluoroalkyl group remains very high despite the presence of the separating methylene group between the perfluoroalkyl group and the epoxide ring (epoxide **1e**–**d**). The aminodiols obtained were characterised by spectroscopic and HRMS methods.[12] These new compounds may prove useful for some synthetic purposes such as the synthesis of fluorinated crown ethers.[13]

Acknowledgements

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11. Experimental: preparation of di(*F*-alkylated) azadiols: General procedure. Epoxide **1** (10 mmol) was added to 28% aqueous ammonia in methanol (20 mL). The mixture was stirred at room temperature until completion of reaction (TLC: kieselgel 60 $F_{254,}$ chloroform/ethyl acetate 80/20). Solvent and excess of NH_3 and H_2O were removed under vacuum. The crude product was taken up in ether, washed with water and dried on Na_2SO_4. After filtration, the solvent was removed and the residue was purified by recrystallization from chloroform.
12. Spectral data: The fluorine atoms of $CF_2\alpha$ group in compounds **2a**–**c** give distinguishable signals in NMR and are assigned as an AB system in the following. Compound **2a**: ^{1}H NMR (300 MHz, CD_3 OD): $\delta = 2.91$ (m, 4H, $2CH_2-N$), 4.30 (m, 2H, 2CH−O). ^{19}F NMR (282 MHz, $CFCl_3$): $\delta = -82.24$ (6F, $2CF_3$), –121.48 (2F, $2CF_A\alpha$), –123.26 (4F, $2CF_2\beta$), –125.45 (2F, $2CF_B\alpha$), –127.10 (4F, $2CF_2\omega$) ppm. HRMS (EI): M^+ Calculated = 541.0344. Found = 541.0342. Compound **2b**: ^{1}H NMR (300 MHz, CD_3 OD): $\delta = 2.99$ (m, 4H, $2CH_2-N$), 4.33 (m, 2H, 2CH−O), ^{19}F NMR (282 MHz, $CFCl_3$): $\delta = -79.46$ (6F, $2CF_3$), –118.60 (2F, $2CF_A\alpha$) –119.96 (8F, $2CF_2\sigma$, $2CF_2\delta$), –120.75 (4F, $2CF_2\beta$), –123.22 (2F, $2CF_B\alpha$), –124.45 (4F, $2CF_2\omega$) ppm. HMRS (EI): M^+ Calculated = 741.0216. Found = 741.0218. Compound **2c**: ^{1}H NMR (300 MHz, CD_3 OD): $\delta = 3.38$ (m, 4H, $2CH_2-N$), 4.85 (m, 2H, 2CH−O). ^{19}F NMR (282 MHz, $CFCl_3$): $\delta = -79.35$ (6F, $2CF_3$), –118.51 (2F, $2CF_A\alpha$), –119.63 (16F, $2CF_2\sigma$, $2CF_2\delta$, $2CF_2\varepsilon$, $2CF_2\xi$), –120.60 (4F, $2CF_2\beta$), –123.38 (2F, $2CF_B\alpha$), –124.16 (4F, $2CF_2\omega$) ppm. HRMS (EI): M^+ Calculated = 941.0088. Found = 941.0090. Compound **2d**: ^{1}H NMR (300 MHz, CD_3OD): $\delta = 2.33$ (m, 4H, $2CH_2-C_6F_{13}$), 2.73 (m, 4H, $2CH_2$-N), 4.16 (m, 2H, 2CH−O). ^{19}F NMR (282 MHz, $CFCl_3$): $\delta = -79.63$ (6F, $2CF_3$), –111.04 (4F, $2CF_2\alpha$), –119.88 (4F, $2CF_2\beta$), –121.37 (8F, $2CF_2\sigma$, $2CF_2\delta$), –124.41 (4F, $2CF_2\omega$) ppm. HRMS (EI): M^+ Calculated = 769.0529. Found = 769.0527. Compound **2e**: ^{1}H NMR (300 MHz, CD_3OD): $\delta = 2.40$ (m, 4H, $2CH_2$-C_8F_{17}), 2.71 (m, 4H, $2CH_2-N$), 4.07 (m, 2H, 2CH−O). ^{19}F NMR (282 MHz, $CFCl_3$): $\delta = -79.53$ (6F, $2CF_3$), –111.26 (4F, $2CF_2\alpha$), –119.66 (4F, $2CF_2\beta$), –119.99 (8F, $2CF_2\sigma$, $2CF_2\delta$), –121.27 (8F, $2CF_2\varepsilon$, $2CF_2\xi$), –124.43 (4F, $2CF_2\omega$) ppm. HRMS (EI): M^+ Calculated = 969.0657. Found = 969.0654.
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