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S. Szönyi [a], A. Ayari [a], M. Nasreddine [a] & A. Cambon [a]

[a] Laboratoire de Chimie Organique du Fluor, Université de Nice-Sophia Antipolis, Parc Valrose, 06034, Nice cedex, France

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SYNTHESIS OF NEW F-ALKYL β-AMINO ALCOHOLS

S.Szönyi*, A.Ayari, M.Nasreddine and A.Cambon

Laboratoire de Chimie Organique du Fluor
Université de Nice-Sophia Antipolis, Parc Valrose
06034 Nice cedex - France

Abstract : F-alkyl oxiranes **1** and p-methylbenzene-sulfonate ester intermediates **3** derived from 2-F-alkyl ethane - 1,2-diols **2** are converted into F-alkyl β-amino alcohols **5** respectively by a two-step process.

The insertion of an amino group into organic molecules via azides derivatives is an important process to produce nucleotides, aminosugars, α-amino acids or β-aminoalcohols[1,2].

There is a great deal of classical and recent methods to obtain vicinal alkylated azidohydrins[3-4] and to achieve their reduction into β-amino alcohols[5-7]. But a survey of literature revealed very few examples of F-alkyl azides[8-12] and we did'nt find examples of α-hydroxyl azides with long F-alkylated chain.

* To whom correspondence should be addressed.

In this paper, we describe the preparation of F-alkyl β-amino alcohols from F-alkyl oxiranes $R_F-CH(O)CH_2$ 1[13] and 2-F-alkyl ethane 1,2-diols $R_F-CH(OH)-CH_2OH$ 2[14] with R_F = C_4F_9, C_6F_{13}, C_8F_{17}. The transformation of the epoxides 1 into the corresponding azidohydrins 4 with the NaN_3 /H_2O/dioxan reagent was attempted but the yields don't exceed 30-45% ; but we found that the NaN_3 /NH_4Cl/H_2O reagent in MeOH is a convenient reagent system to give the 2-F-alkyl 2-hydroxy azides 4 in good yields (TABLE) and good regioselectivity according to the pathway A.

$$R_F-CH(O)CH_2 \xrightarrow[H_2O/MeOH]{NaN_3/NH_4Cl} R_F-CH(OH)-CH_2-N_3$$

1

4a (R_F = C_4F_9)
4b (R_F = C_6F_{13})
4c (R_F = C_8F_{17})

Pathway A

We obtained also the azidohydrins 4 according to the pathway B. At first, the diols 2 were transformed into the corresponding monotosylates 3 with p-toluenesulfonyl chloride and in the presence of pyridine [15]. Then the tosyl group is substituted by the azide group with sodium azide dissolved in water and in

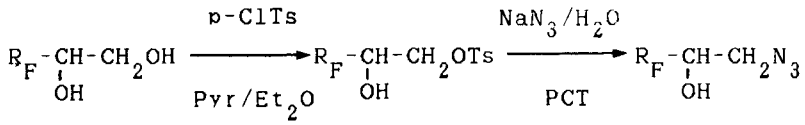
TABLE

Compounds	Yields (%)	b.p.or m.p.(°C)
3a	83	$150/5.10^{-3}$ mm Hg
3b	82	68
3c	84	75
4a	-/56[2]	-
4b	75[1]/51[2]	50/55 mm Hg
4c	82[1]/52[2]	60
5a	-	-
5b	68	66
5c	72	95

1) Pathway A

2) Pathway B

presence of a phase transfer reagent such as aliquat 336* [16]



2 3a($R_F = C_4F_9$) 3b($R_F = C_6F_{13}$) 3c($R_F = C_8F_{17}$) 4

Pathway B

*Aliquat 336 = Methyl Tricapryl Ammonium Chloride (PCT)

Pathway B is longer than pathway A as the reaction proceeds through one more derivative, the monotosylate 3. In addition, pathway B gives the azidohydrins 4 with diminished yields in comparison with those obtained with the pathway A. After isolation of azidohydrins 4 we could reduce them easily into the corresponding β-aminoalcohols 5 by means of tin chloride in methanol. The reaction is effected at room temperature during 20 hours and the yields are satisfactory (TABLE).

$$R_F\text{-}\underset{\underset{OH}{|}}{CH}\text{-}CH_2N_3 \xrightarrow{SnCl_2/MeOH} R_F\text{-}\underset{\underset{OH}{|}}{CH}\text{-}CH_2NH_2$$

4

5a ($R_F = C_4F_9$)

5b ($R_F = C_6F_{13}$)

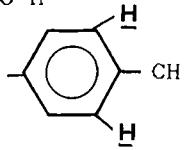
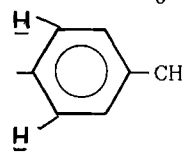
5c ($R_F = C_8F_{17}$)

EXPERIMENTAL PART

^1H NMR spectra were recorded in $CDCl_3$ on a Brücker W-80 spectrometer operating at 80 Mz using $(CH_3)_4$ Si (TMS) as internal standard. ^{19}F NMR spectra were recorded in $CDCl_3$ on a Brücker W-90 spectrometer operating at 84,67 Mz using $CFCl_3$ as internal standard. Infrared spectra were performed on a Brücker IFS 45 spectrometer and mass spectra were run on a Nermag R 10-10 C Mass spectrometer coupled with a gas chromatograph. Microanalyses were determined by the CNRS laboratories in Lyon (France).

Typical procedure for 2-F-hexyl-2-hydroxyethyl tosylate 3b :

To a solution of 10 mmoles of p-toluenesulfonyl chloride in anhydrous diethyl ether cooled in an ice bath (0°C), are added in small portions with constant stirring 5 mmoles of diol **2** and 10 mmoles of pyridine in anhydrous diethyl ether. The mixture, which is stirred for 2 hours at 0°C then for 3 days at 40°C, is hydrolysed by a solution of 2N hydrochloric acid. The aqueous layer is washed with water, aqueous 5% sodium bicarbonate , then dried over sodium sulphate and the ether removed. The residue is purified by column chromatography on silica gel eluting with hexane /ethyl acetate 3:1 to afford the monotosylate 3b.

$C_{15}F_{13}H_{11}O_4S$(534). Elem.Anal. : Calc(%) C 33,72, F 46,22 , H 2,07 , S 6,00 , Found (%) C 33,80 , F 46,53 , H 2,00 , S 5,68 ; MS : M^+534, Ts^+ 155, $(M-R_F)^+$ 215, $(CH_2{=}O{-}Ts)^+$185 , CF_3^+ 69 , $C_2F_5^+$ 119 , $C_3F_5^+$ 131, $C_3F_7^+$ 169 ; I.R. (cm^{-1}) : υ_{C-F}=1350-1100 , υ_{SO_2}=1370, $\upsilon_{C=C}$(Ts) 1590 , υ_{O-H}=3500 ; ^{1}H NMR ($CDCl_3$) δ (ppm) : $C\underline{H}_3$= 2,4 (s,3H) ,  CH_3 = 7,5(d,2H) ,  CH_3 =7,9(d,2H) , R_F-$C\underline{H}(OH)C\underline{H}_2$ = 4,5(m,3) , (O$\underline{H}$) = 2,9 (s,1H) ; ^{19}F NMR ($CDCl_3$)δ(ppm) : CF_3 -81,1 , $CF_{2\omega}$-126,5 $CF_{2\gamma}$+$CF_{2\omega}$ -122,9 , $CF_{2\alpha}$-119,6 and -126,2 (J=290 Hz).

Typical procedure for 2-F-hexyl-2-hydroxyethyl azide **4b** :

Pathway A : A mixture of 10 mmoles of monotosylate **3b**, 20 mmoles of sodium azide in 3,8 ml of water and 0,5 mmole of Aliquat 336 is heated for 20 hours at 100 °C , then is decanted under heat . The lower organic layer is dissolved in diethylether. The ethereal layer is dried over sodium sulphate, filtered and the ether is removed to afford the azide derivative **4b** which is purified by distillation under reduced pressure.

Pathway B : to a solution of 40 mmoles of sodium azide and 8,4 mmoles of ammonium chloride in 4 ml of water, are added 4 mmoles of epoxide 1 dissolved in 32 ml of methanol. The mixture is stirred for 7 hours at reflux, then methanol is removed under atmospheric pressure. Then 20 ml of water and diethyl ether are added to the residue. The ethereal layer is dried over sodium sulphate, filtered and the ether is removed to afford the azide derivative **4b** as a yellow oil which is distilled under reduced pressure.

$C_8 F_{13} H_4 N_3 O$ (405). Elem.Anal. : Calc.(%) C 23,66 , F 60,81 , H 1,24 , N 10,35 , Found (%) C 23,64, F 60,84 , H 1,23, N 10,32 ; MS : M^+505 , $CF_2{=}CF{-}CH{=}\overset{+}{O}H$ 111 , $CH_2 N_3^+$ 56 , $C_6F_{13}{-}CH{=}\overset{+}{O}H$ 349 , N_3^+ 42 , CF_3^+ 69, $C_2F_5^+$

131 ; I.R.(cm^{-1}) : υ_{C-F} 1350-1100 , υ_{C-N_3} 2114 , υ_{C-OH} 3425 ; ^1H NMR ($CDCl_3$) δ (ppm) : C-H 4,3(m,1H) , CH_2 3,7 (d,2H) , OH 3,2(s,1H).

Typical procedure for 2-F-alkyl-2-hydroxyethyl amine **5b**

To a solution of 4,5 mmoles of tin chloride in 4 ml of methanol are added 3,25 mmoles of azidohydrins **4** in 2 ml of methanol. The mixture is stirred for 20 hours at room temperature. The methanol is removed. To the residue are added 10 ml of caustic soda 2N and diethyl ether.

The ethereal layer is dried over sodium sulphate, filtered and evaporated to give the amine derivative **5b** which is purified by recrystallization from petroleum ether.

$C_8F_{13}H_6NO$ (379) Elem.Anal. Calc.(%) C 25,33 , F 65,17 , H 1,58 , N 3,69 . Found(%) C 25,30 , F 65,20 , H 1,59 , N 3,67 ; MS : M^+479 , NH -CH -CH=$\dot{O}$H 60 , CF_3^+ 69, $C_2F_5^+$ 131. I.R.(cm^{-1}) υ_{C-F} 1350-1100, υ_{NH_2} and υ_{OH} 3400-3300 ; ^1H NMR ($CDCl_3$) δ (ppm) C-H 4,5(m,1H) , CH_2 3,6(d,2H) , OH 2,8(s,1H) , NH_2 1,3(s,2H).

REFERENCES

1 "Chemistry of the Azido Groups", Pataï S. ed., Interscience, New-York, 1971.

2 Scriven E.F.V. and Turnbull K.,Chem.Rev.,1988,88,297.

3 Saito S.,Bunya N.,Inaba M.,Mori Wake T. and Torii S. Tetrahedron Lett.,1985,26,5309.

4 Onaka M.,Sugita K. and Izumi Y.,J.Org.Chem.,1989,54, 1116.

5 Maiti S.N.,Singh M.P. and Micetich R.G., Tetrahedron Lett.,1986,27,1423.

6 Soai K.,Yokoyama S.and Ookawa A.,Synthesis,1987,48.

7 Maiti S.N.,Spevak P. and Reddy A.V.N., Synthetic Commun., 1989,18,1201.

8 Knunyants I.L.,Bykhovskaya E.G.,Proc.Acad.Sci.USSR Chem.Sect.(Engl.Transl.),1960,131,411.

9 Banks R.E. and Mc Glinchey M.J.,J.Chem.Soc.,1971,3971.

10 Krespan C.G.,J.Org.Chem.,1986,51,332.

11 Rondestvedt C.S.Jr.,Thayer G.L.Jr.,J.Org.Chem. 1977, 42,2680.

12 Szönyi F. and Cambon A., J.Fluorine Chem.,1989,42,59.

13 Chaabouni M.M.,Szönyi S.,Baklouti A. and Cambon A., J.Fluorine Chem.,1990,46,307.

14 Ayari A.,Szönyi S.,Rouvier E. and Cambon A.,J.Fluorine Chem.,1990,50,67.

15 Malik A.A.,Preston S.B.,Archibald T.G.,Cohen M.P.and Baum K.,Synthesis,1989,450.

16 Scanounik B.,Tisler M.,Polanc S. and Gracner M., Synthesis,1978,65.

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