Tetrahedron Letters, Vol. 34, No. 32, pp. 5093-5094, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

Synthesis of Oxetanes with Perfluorinated-alkyl Substituents

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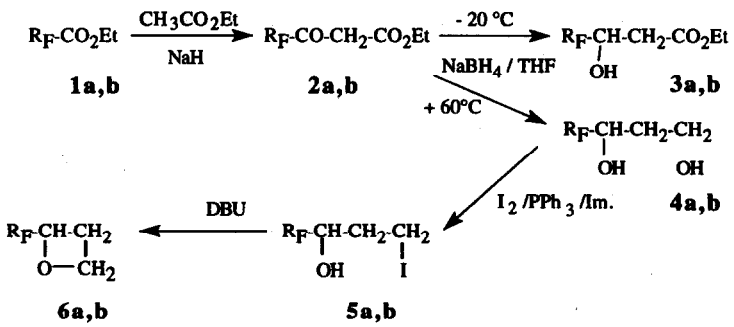
Abstract : Perfluoroalkylated oxetanes have been obtained exclusively, in 36% yield, by reduction of perfluoroalkylated β-ketoester, followed by iodination and dehydroiodination.

F-alkyl alcohols are a useful class of precursors for the synthesis of amphiphilic molecules needed as components of highly fluorinated dispersed systems such as fluorocarbon emulsions or very stable vesicles[1]. During our search for convenient routes for the synthesis of such molecules we obtained a family of hitterto unknown fluorinated oxetanes.

This paper describes the controlled reduction of *F*-alkyl β-ketoesters to diols or β-hydroxyesters and the conversion of diols into *F*-alkyl oxetanes (scheme 1). Several oxetanes in which the cycle itself was totally or partially fluorinated have already been synthesized[2]. So far no hydrogenated oxetanes bearing a *F*-alkyl chain in position 2 have not been reported.



Scheme 1 (a = C_5F_{11}, b = C_7F_{15})

Ethyl 3-*F*-alkyl 3-oxo propanoates **2** are easily prepared in high yield (90%) by condensation of ethyl acetate on *F*-esters **1**[3]. The second step is the reduction of the β-ketoesters **2**. This reduction has been attempted with Ni/H_2, Ni/H_2/tartaric acid/NaBr[4], $Zn(BH_4)_2$[5], $NaBH_4$[6]. Only the last reagent gave good results. We tried

to induce stereoselectivity with $NaBH_4$/tartaric acid[6] as reducing agent but the enantioselectivity was too low (45/55)[7] to be of interest; so $NaBH_4$ was used alone. At room temperature a mixture of diol **4**[8] and β-hydroxyester **3** is obtained by reduction of **2** with only 3eq. of $NaBH_4$ *in THF*. In these conditions, the reaction can be controlled thermally and oriented to yield only one of the two products. At 60°C, only diol **4** is obtained; at -20°C the β-hydroxyester **3** is formed exclusively.

The selective iodination of the primary alcohol achieved with PPh3/I2/Imidazol in dichloromethane, gave **5**. The monoiodinated compound was obtained in good yield (90%)[9] and confirmed by MS analysis. Finally, **5** was converted into the new *F*-alkyl oxetane **6**[10] by treatment with DBU (66% yield)[11]. Various bases have been tested : KOH, K_2CO_3, Pyridine, $N(Et)_3$; best results (kinetics, yields) were obtained with DBU.

Acknowledgements : We wish to thank ATOCHEM for the gift of the starting *F*-alkylated products.

REFERENCES

1. a) Riess J.G. *Vox Sang.* **1991**, *61*, 225-239. b) Riess, J.G. *Biomat., Art. Cells, Immob. Biotech.* **1992**, *20*, 183-204.
2. a) Améduri B. and Boutevin B. *Adv. Polymer Sc.* **1992**, *102*, 133-169. b) Boutevin B. and Robin J.J. *Adv. Polymer Sc.* **1992**, *102*, 105-131. c) Améduri B.; Boutevin B. and Karam L. *J. Fluor. Chem.* **1993**, to be published. d) Yohnosuke O.; Takashi T. and Shoji T. EP 0 148 482, **1984**.
3. a) Bayer V.; Pastor R. and Cambon A. *J. Fluor. Chem.* **1982**, *20*, 187-202. b) Tai A.; Kikukawa T.; Sugimura T.; Inoue Y.; Osawa T. and Fujii S. *J. Chem. Soc. Chem. Commun.* **1991**, 795-796.
4. a) Brunner H.; Muschiol M.; Wischert T. and Wiehl J. *Tetrahedron Asym.* **1990**, *1*, 159-162. b) Gensler W.J.; Johnson F.A. and Sloan A.D.B. *J. Am. Chem. Soc.* **1960**, *82*, 6074-6081.
5. Sarkar D.C.; Das A.R. and Ranu B.C. *J. Org. Chem.* **1990**, 5799-5801.
6. Yatagai M. and Oonuki T. EP 0 320 096, **1989**.
7. Fellous R.; Lizzani-Cuvelier L. and Loiseau A.M. *J. High Res. Chromatogr.* **1990**, *13*, 785-789.
8. ^1H RMN (δppm, CD_3OD, TMS) : 1.71-2.04 (m, 2H, CH_2); 3.77/3.79/3.80/3.82 (AB syst., 2H, CH_2-O); 4.28-4.94 (massif, 1H, CH). ^{13}C RMN (δppm, CD_3OD) : 32.83 (CH_2); 58.08 (CH_2-O); 67.43 (dd, $^2J_{C-F}$=26.7Hz, CH). ^{19}F RMN **4a** (50% yield) (δppm, CD_3OD, $CFCl_3$) : -80.8 (CF_3); -118.8/-120.3/-125.6/-127.1 (AB syst., $CF_2\alpha$); -120.6/-122.2/-122.5/-124.1 (AB syst., CF_2b); 121.1 ($CF_2\gamma$); -125.9 ($CF_2\omega$). **4b** (59% yield): -81.0 (CF_3); -119.0/-120.5/-125.8/-127.3 (AB syst., $CF_2\alpha$); -121.1/-121.6/-122.5 (4 CF_2); -126.1 ($CF_2\omega$).
9. a) Garegg P.J.; Regberg T.; Stawinski J. and Strömberg R. *J. Chem. Soc. Perkin Trans II* **1987**, 271-274. b) Lange G.L. and Gottardo C. *Synth. Comm.* **1990**, *20*, 1473-1479.
10. ^1H NMR (δppm, $CDCl_3$, TMS) : 2.83-2.98 (m, 2H, CH_2); 4.75 (t, $^3J_{H-H}$=76Hz, 2H, CH_2-O); 5.07-5.26 (tt, 1H, CH) ^{13}C NMR (δppm, CD_3OD) : 21.24 (CH_2); 70.85 (CH_2-O); 76.90 (t, $^2J_{C-F}$=32Hz, CH). ^{19}F NMR.**6** (67% yield) (δppm, CD_3OD, $CFCl_3$) : -81.3 (CF_3); -129.5 ($CF_2\omega$); -123.7-122.4 (2 CF_2); -126.8 ($CF_2\alpha$). **6b** (65 % yield). -81.4 (CF_3); -129.9 ($CF_2\omega$); -123.9/-123.3/-122.7 (4 CF_2); -126.8 ($CF_2\alpha$).
11. Antonioletti A.; Bonadies F. and Scettri A. *Tetrahedron Lett.* **1988**, *29*, 4987-4990.

(Received in France 13 May 1993; accepted 16 June 1993)