Pergamon

*Tetrahedron Letters*, Vol. 35, No. 27, pp. 4851-4852, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)00893-0

# An Improved Procedure for the Synthesis of Fluoromethylketones: Flash Vacuum Pyrolytic Elimination

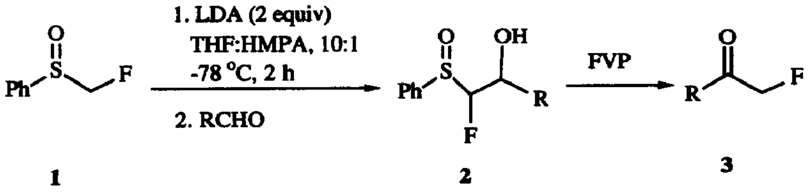
**Vichai Reutrakul*, Thongchai Kruahong and Manat Pohmakotr**

Department of Chemistry, Faculty of Science, Mahidol University, Rama 6 Road, Bangkok 10400, Thailand.

*Abstract: Fluoromethylketones **3** are synthesized in good yields by a flash vacuum pyrolytic elimination of **2**. Studies on the improved synthesis of **2** leads to the evidence on the existence of α,α-dilithio fluoromethyl phenyl sulfoxide.*

The introduction of fluorine atom into organic molecules causes profound changes of their chemical and consequently their biological activities. Fluorinated compounds have found applications in biology, medicine[1] and electronics[2] as biological probe, therapeutic agents and new ferroelectric liquid crystals, respectively.

The main ongoing research interest in fluorine chemistry is still the search for new and/or improved methods for the synthesis of fluorine containing molecules.[3] We communicated earlier[4] on the synthesis of fluoromethylketones by pyrrolytic elimination in sealed tube at 180-182 °C (reactions carried out in refluxing toluene and xylene gave no desired fluoromethylketones) in low yields due to the difficulty in separating the products from sulfenic acid and the instability of the fluoromethylketones under reaction conditions. As part of our continuing exploratory work on the utilization of α-fluoromethyl phenyl sulfoxide **1** as a fluorinated one-carbon reagent in organic synthesis, we have utilized a flash vacuum pyrolytic technique (FVP)[5] for the elimination of the sulfenic acid from α-fluoro-β-hydroxy phenylsulfinyl adducts **2** to give the corresponding fluoromethylketones[6] **3** in synthetically useful yields (Scheme 1).



**2**: R= $C_8H_{17}$ (82%), $C_{11}H_{23}$ (74%), $C_{13}H_{27}$ (49%), Ph (83%), $PhCH_2$ (91%)

**3**: R= $C_8H_{17}$ (48%), $C_{11}H_{23}$(48%), $C_{13}H_{27}$ (43%), Ph (57%), $PhCH_2$ (45%)

**Scheme 1**

The following reaction conditions are representative. Compound **2** was subjected to flash vacuum pyrolysis (FVP) using a glass column (78 cm) packed with glass helices and the product was trapped in a flask immersing in dry ice-acetone mixture. The best conditions were; reaction flask temperature, 216 °C and column temperature, 508 °C at 0.1 mmHg. The pure fluoromethylketone **3**[7] was obtained by PLC purification of the pyrolysate using either hexane or 5% ethyl acetate-hexane as an eluent. The yields are as indicated in Scheme **1**.

The α-fluoro-β-hydroxy phenyl sulfoxides **2** were prepared in high yields by the reaction of aldehydes with α-fluoromethyl phenyl sulfoxide **1** using *2 equivalents of LDA* in THF at -78 °C. Presumably, the reactive species is the α,α-dilithio fluoromethyl phenyl sulfoxide.[8] When one equivalent of LDA was employed, the adducts were obtained in much lower yields.

**References and Notes**

1. a) Filler, R. and Kobayashi, Y. (Ed.) *Biomedicinal Aspects of Fluorine Chemistry*, Elsevier, Amsterdam, **1982**. b) Welch, J. T. *Tetrahedron* **1987**, *43*, 3123. c) Resnati, G. *ibid*, **1993**, *49*, 9385.
2. a) Walba, D.M.; Razavi, H. A.; Clark, N. A. and Parmar, D. S. *J. Am. Chem. Soc.* **1988**, *110*, 8686. b) Kitazume, T.; Ohnogi, T. and Itoh, K. *ibid*, **1990**, *112*, 6608.
3. a) Schlosser, M. *Tetrahedron* **1978**, *34*, 3. b) Purrington, S. T.; Kagan, B. S. and Patrick, T. B. *Chem. Rev.* **1986**, *86*, 997. c) Rozen, S. *Acc. Chem. Res.* **1988**, *21*, 307. d) Bravo, P. and Rastani, G. *Tetrahedron Asymm.* **1990**, *1*, 661. e) Yoneda, N. *Tetrahedron* **1991**, *47*, 5329. f) Wilkinson, J. A. *Chem. Rev.* **1992**, *92*, 505. g) Robins, M. J. and Wnuk, S. F. *J. Org. Chem.* **1993**, *58*, 3800 and references cited.
4. Reutrakul, V. and Rukachaisirikul, V. *Tetrahedron Lett.* **1983**, *24*, 725 and references cited.
5. For other applications of FVP technique see: a) Chantarasiri, N.; Dinprasert, P.; Thebtharanonth, C.; Thebtaranonth, Y. and Yenjai, C. *J. Chem. Soc. Chem. Commun.* **1990**, 286. b) Pohmakotr, M. and Popuang, S. *Tetrahedron Lett.* **1991**, *32*, 275.
6. For leading references on the synthesis of α-fluoro carbonyl compounds see: a) Rozen, S. and Filler, R. *Tetrahedron* **1985**, *41*, 1111. b) Differding, E. and Lang, R. W. *Tetrahedron Lett.* **1988**, *29*, 6087. c) Davis, F. A. and Hau, W. *ibid*, **1992**, *23*, 1153. d) Lal, G. S. *J. Org. Chem.* **1993**, *58*, 2791. e) Satoh, T.; Shishikura, J. I. and Yamakawa, K. *Chem. Pharm. Bull.* **1990**, *38*, 1798. f) Patrick, T. B.; Hasseini, S. and Bains, S. *Tetrahedron Lett.* **1990**, *31*, 179. g) Satoh, T.; Itoh, N.; Onda, K. I.; Kitoh, Y.; Yamakawa, K. *Bull. Chem. Soc. Jpn* **1992**, *65*, 2800.
7. All compounds were characterized by spectral data and elemental analysis or HRMS molecular weight determination.
8. Extensive deuteration was carried out to probe the existence of the α,α-dilithio fluoromethyl phenyl sulfoxide. However, only 60% dideuterated product was obtained. For examples of incomplete deuteration with LDA see: a) Laube, V. T.; Dunitz, J. D.; Seebach, D. *Helv. Chim. Acta* **1985**, *68*, 1373. b) Achquar, A. E.; Roumestant, M. L. and Viallefont, P. *Tetrahedron Lett.* **1988**, *29*, 2441.

(*Received in UK* 7 *April* 1994; *accepted* 6 *May* 1994)