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Synthesis of $\gamma\gamma\gamma$-trifluorocarbonyl compounds

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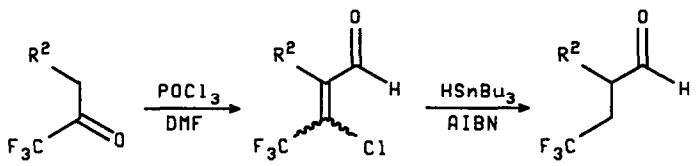
Key words : β-chloro β-trifluoromethylacroleines and enones ; tributyltin hydride.

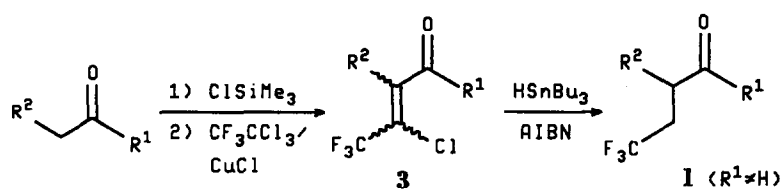
Abstract : $\gamma\gamma\gamma$-Trifluorocarbonyl compounds are easily obtained in a good yield by introduction of the 1,1,1-trifluoroethyl moiety (CF_3-CH_2-) on the α-methylene group of a ketone.

The introduction of a trifluoromethylgroup is a major subject in organic chemistry due to the biological potentiality of these compounds[1]. Synthesis of some trifluoromethyl compounds is now well documentated[2,3,4]. But compounds **1** with two methylene (or methine) groups built in between a trifluoromethyl and a carbonyl group are not easy to prepare. Wakselman[5] and Ogoshi[6] obtained some derivatives from 1,1,1-trifluoro-2-penten-4-one. Nevertheless in these compounds the trifluoromethyl group increases the lipophilicity without disturbing the biological and chemical reactivity. Recently, Umemoto[7] has described a synthesis of such compounds from 1,1-perfluoroalkylphenyliodonium triflate (hypervalent iodide) and silylethers.

We report here a practical and general method to prepare compounds such **1** from β-chloro β-trifluoromethylacroleins **2** or enones **3**. **2** and **3** are easely obtained from a Vilsmeier's reaction[8] or from vinylsilylether and 1,1,1-trichloro-2,2,2-trifluoroethane[9].

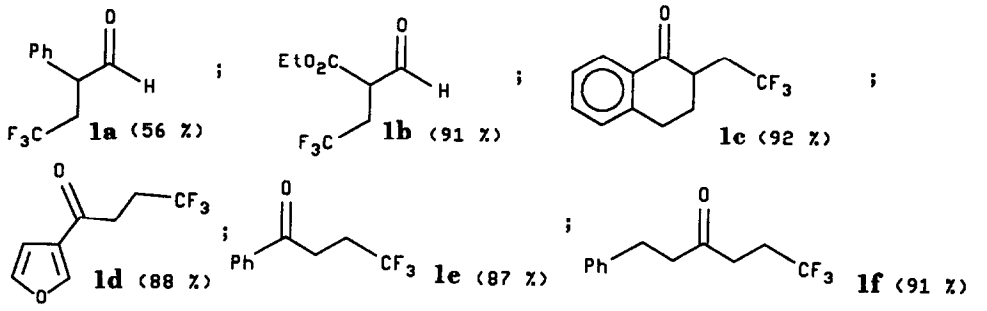


2 **1**



3 **1** ($R^1 \neq H$)

Reduction of **2** or **3** by tributyltin hydride[10] produces the β-trifluoromethylaldehydes **1** or ketones **1**. This strategy avoids the use of the hypervalent iodide which is not commercialy available and not easy to prepare. Yields are good to excellent. Some typical compounds **1** are described (% yield isolated from **2** or **3**)[11] :



So in using this methodology, it is easy to introduce the CF_3-CH_2 moiety in α position of a ketone (for example : α-tetralone →**1c** ; acetophenone →**1e**).

References and Notes

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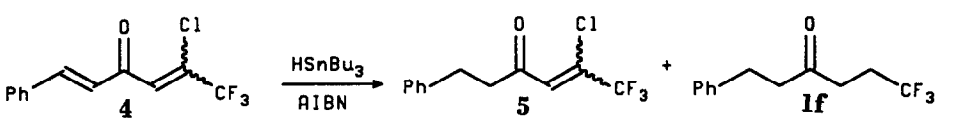
11 Typical procedure : to a solution of **2** or **3** (1 mmol) in dry C_6H_6 (5 ml), catalytic amount of AIBN and 4 mmol of Bu_3SnH are added. The mixture was stirred under N_2 (benzene reflux 1 h). The solvent removed in vacuum. Column chromatography on silica gel of the residue allows the purification of the products reported. **1ab**[6]. **1c** m.p.=58-59°C ; IR : 1685 $\nu_{C=O}$; ^1H NMR ($CDCl_3$) : 1.87-2.22 (m, 2H), 2.40-2.52 (m, 1H), 2.71-2.86 (m, 1H), 2.90-3.52 (m,3H), 7.22-7.33 (m, 2H), 7.43-7.51 (m, 1H), 7.99-8.03 (m, 1H) ; ^{19}F NMR ($CDCl_3$) : -64.33 (J_{HF}=12 Hz) ; MS m/z : 228, 118 (100 %). **1d** IR : 1680 $\nu_{C=O}$; ^1H NMR ($CDCl_3$) : 2.43-2.67 (m, 2H), 3.09-3.17 (m, 2H), 6.57 (d,d, J=1.7 and J=3.6 Hz, 1H), 7.50 (d, J=3.6 Hz, 1H), 7.61 (m, 1H) ; ^{19}F NMR ($CDCl_3$) : -67.33 (t, J_{HF}=11 Hz) ; MS m/z : 192, 95 (100 %). **1e**[7]. **1f** is obtained from **4**[7] :



The typical procedure applied to **4** produces a mixture of **5** (78 %) and **1f** (8 %). The same reduction applied to **5** gives **1f** (91 %). **5** IR (film) : 1710 $\nu_{C=O}$, 1625 $\nu_{C=C}$; ^1H NMR ($CDCl_3$) : 2.93 (4H), 6.85 (1H), 7.23 (5H) ; ^{19}F NMR ($CDCl_3$) : -71.0 (s). **1f** IR (film) : 1720 $\nu_{C=O}$, 1155 $_{CF3}$; ^1H NMR ($CDCl_3$) : 2.24-2.48 (m, 2H), 2.55-2.69 (m, 2H), 2.70-2.77 (m, 2H), 2.86-2.93 (m, 2H), 7.14-7.31 (m, 5H). ^{19}F NMR ($CDCl_3$) : -67.33 (t, J_{HF}=11.5 Hz). MS m/z : 230, 105 (100 %).

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