

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

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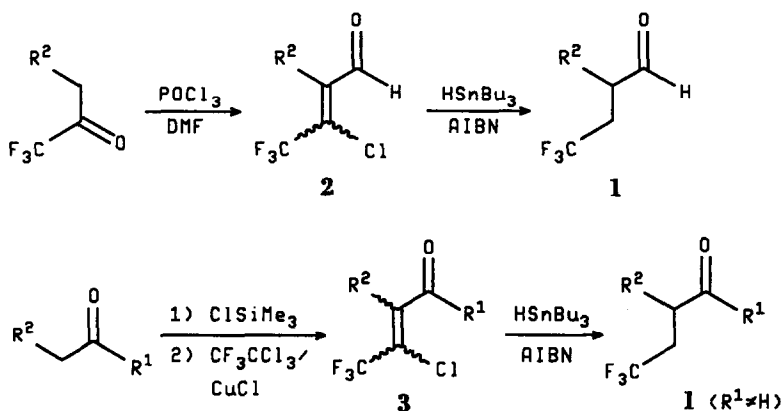
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Key words : β -chloro β -trifluoromethylacroleins and enones ; tributyltin hydride.

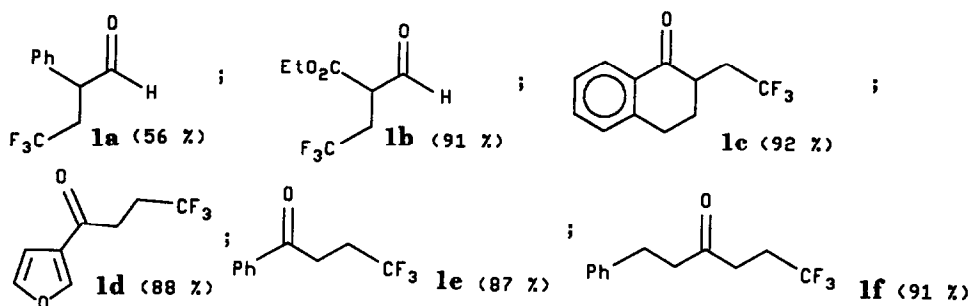
Abstract : $\gamma\gamma\gamma$ -Trifluorocarbonyl compounds are easily obtained in a good yield by introduction of the 1,1,1-trifluoroethyl moiety ($\text{CF}_3\text{-CH}_2\text{-}$) on the α -methylene group of a ketone.

The introduction of a trifluoromethyl group is a major subject in organic chemistry due to the biological potentiality of these compounds¹. Synthesis of some trifluoromethyl compounds is now well documented^{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. Wakselman⁵ and Ogoshi⁶ 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, Umemoto⁷ 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 easily obtained from a Vilsmeier's reaction⁸ or from vinylsilylether and 1,1,1-trichloro-2,2,2-trifluoroethane⁹.



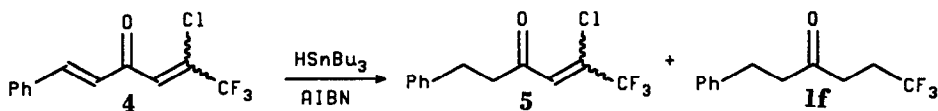
Reduction of **2** or **3** by tributyltin hydride¹⁰ produces the β -trifluoromethylaldehydes **1** or ketones **1**. This strategy avoids the use of the hypervalent iodide which is not commercially available and not easy to prepare. Yields are good to excellent. Some typical compounds **1** are described (% yield isolated from **2** or **3**)¹¹:



So in using this methodology, it is easy to introduce the $\text{CF}_3\text{-CH}_2$ moiety in α position of a ketone (for example : α -tetralone $\rightarrow$ **1c** ; acetophenone $\rightarrow$ **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 $\nu_{\text{C=O}}$; ^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 ($J_{\text{HF}}=12$ Hz) ; MS m/z : 228, 118 (100 %). **1d** IR : 1680 $\nu_{\text{C=O}}$; ^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, $J_{\text{HF}}=11$ 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 $\nu_{\text{C=O}}$, 1625 $\nu_{\text{C=C}}$; ^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 $\nu_{\text{C=O}}$, 1155 ν_{CF_3} ; ^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, $J_{\text{HF}}=11.5$ Hz). MS m/z : 230, 105 (100 %).

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