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Synthesis of Pentafluorinated β-Hydroxy Ketones


Pentafluorinated β-Hydroxy Ketone Synthesis via Lithium-Mediated Aldol Reaction

Significance: A fast and mild synthesis of pentafluorinated β-hydroxy ketones has been disclosed. The reaction proceeds via a lithium-promoted aldol reaction of readily available difluoroenolate precursors with trifluoromethyl ketones furnishing the corresponding pentafluorinated β-hydroxy ketones in good to excellent yield.

Comment: The described reaction is very versatile since it proceeds under ambient temperature and tolerates a broad range of functional groups. Furthermore, the authors show that the reduction of the pentafluorinated β-hydroxy ketones furnishes quantitatively the corresponding 1,3-diols favoring the syn-isomer.

Selected examples:

R¹ = Ph, 4-ClC₆H₄, Naph, (CH₂)₂Ph
R² = Ar, 2-thienyl, Bn

THF, 25 °C
LHMDS (2 equiv)
Li⁺ (1 equiv)

63% yield

89% yield

92% yield

83% yield

94% yield

95% yield

93% yield

95% yield

93% yield

63% yield

84% yield

95% yield

93% yield

95% yield

92% yield

94% yield

93% yield