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Introduction

β-Trifluoromethyl enones are important synthetic precursors of molecules containing chiral centers with a trifluoromethyl substituent, a structural motif which is present in biologically active compounds, chiral reagents and in materials for optoelectronic devices.1 The presence of the strong electron-withdrawing β-trifluoromethyl group increases the electrophilicity of the double bond expediting the conjugate nucleophilic additions.

Preparation

β-Trifluoromethyl-α,β-unsaturated ketones can be prepared by different methods.2 Among them, one of the most general applications is the aldol reaction of trifluoroacetaldehyde ethyl hemiacetal with a ketone followed by dehydration.

Table 1 Use of β-Trifluoromethyl-α,β-unsaturated Ketones

| (A) Arylation | The enantioselective conjugate arylation of β-trifluoromethyl-α,β-unsaturated ketones was carried out by treatment with arylboronic acids 5 under catalysis with the Rh(I)-BINAP (L1) complex. The products 6 were obtained in high yields and enantioselectivities with a variety of arylboronic acids.3 |
| (B) Friedel–Crafts Alkylation | Pedro and co-workers reported the first example of enantioselective Friedel–Crafts alkylation of indoles 7 with β-trifluoromethyl-α,β-unsaturated ketones, using a chiral Zr(IV)-BINOL (L2) complex as catalyst. Functionalized indoles 8 bearing a stereogenic tertiary center attached to a trifluoromethyl group were afforded with good yields and high enantiomeric excesses.4a A similar reaction was described later by Feng and co-workers using a yttrium(III) complex.4b |
| (C) Epoxidation | The asymmetric epoxidation of α,β-unsaturated carbonyl compounds using a chiral Sc(III)-N,N′-dioxide (L3) complex was achieved by Feng and co-workers. The authors describe several examples with β-trifluoromethyl-α,β-unsaturated ketones giving the corresponding epoxides 10 in excellent yields and enantioselectivities under mild conditions.5 |

Scheme 1 Synthesis of β-Trifluoromethyl-α,β-unsaturated ketones
(D) Haloamination
The enantioselective haloamination of β-trifluoromethyl enones 4 was achieved upon treatment with TsNH₂ and the electrophilic halogen source 11 in the presence of a catalytic amount of a complex of Sc(OTf)₃ with the N,N'-dioxide ligand L₄. N, NBS and TsNCl₂ were used as halogen sources to provide the desired haloaminated products 12 in excellent yields, diastereo- and enantioselectivities.⁷

(E) Michael Addition: Synthesis of β-Trifluoromethyl-pyrrole Carboxylates
Shibata and co-workers carried out the conjugate addition of glycinate imine 13 to 4 under PTC conditions with a cinchona alkaloid derived catalyst L₅. Pyrrole carboxylates 14 were obtained with excellent yields, diastereo- and enantioselectivities after a deprotection–cyclization–dehydration sequence.⁷⁶ Enantioenriched β-trifluoromethyl pyrrolines were also obtained via organocatalytic conjugate addition of nitromethane to enones 4 followed by a nitro-reduction–cyclization–dehydration sequence.⁷⁷

(F) Alkynylation
The enantioselective conjugate addition of terminal alkynes 15 to β-trifluoromethyl-α,β-unsaturated ketones 4 catalyzed by a chiral Cu(I)–taniaphos (L₆) complex afforded ketones bearing a trifluoromethylated propargylic chiral center in β-position. The alkynylation products 16 were obtained with good yields and high enantiomeric excesses. Iodocyclisation of 16 furnished access to 4-trifluoromethyl-4H-pyran without any loss of optical purity.⁸

References