β-Trifluoromethyl-α,β-unsaturated Ketones

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Amparo Sanz-Marco was born in Valencia, Spain, in 1986. She obtained her B.Sc. and M.Sc. degrees in chemistry from the University of Valencia, where she is currently pursuing her Ph.D. under the supervision of Prof. José Ramón Pedro and Prof. Gonzalo Blay. She has carried out a pre-doctoral stay at Boston College, Massachusetts, USA, with Prof. James P. Morken. Her Ph.D. research is focused on asymmetric conjugate alkynylation.

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
**References**


