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 alkenylation.

**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. 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. 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

<table>
<thead>
<tr>
<th><strong>(A) Arylation</strong></th>
<th><strong>(B) Friedel–Crafts Alkylation</strong></th>
<th><strong>(C) Epoxidation</strong></th>
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<tr>
<td>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 aryloboronic acids.</td>
<td>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.</td>
<td>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.</td>
</tr>
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</table>

**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. NIS, NBS and TsNCl2 were used as halogen sources to provide the desired haloaminated products 12 in excellent yields, diastereo- and enantioselectivities.6

![Reaction scheme for haloamination](image)

(E) Michael Addition: Synthesis of β-Trifluoromethyl-pyrroline Carboxylates
Shibata and co-workers carried out the conjugate addition of glycinate imines 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.7a Enantioenriched β-trifluoromethyl pyrrolines were also obtained via organocatalytic conjugate addition of nitromethane to enones 4 followed by a nitroreduction–cyclization–dehydration sequence.7b

![Reaction scheme for Michael addition](image)

(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-pyridines without any loss of optical purity.8

![Reaction scheme for alkynylation](image)

References