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Radical allylation of trifluoromethylated xanthates: use of DEAD for removing the allyltributyltin excess

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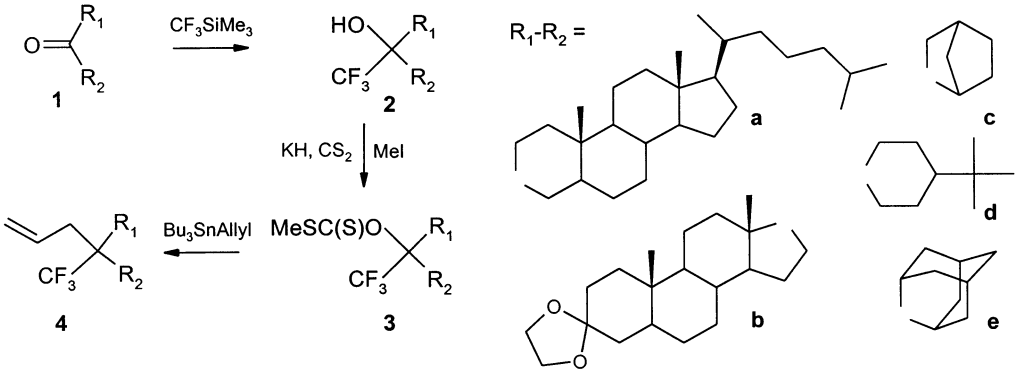
Abstract—Radical allylation of trifluoromethylated xanthates allows the preparation of quaternary carbon centers bearing the trifluoromethyl group. An excess of the allyltributyltin reagent must be used in order to achieve satisfactory yields of the adducts. The excess of reagent could be conveniently removed by the use of diethylazodicarboxylate (DEAD).

Although numerous methods are now known for the introduction of a trifluoromethyl group on organic substrates,[1] the elaboration of quaternary carbon centers bearing this group is not an easy task. Specific structures have been obtained by cycloaddition reactions or ionic condensations.[2] Radical reactions have been less used in this area.[12] Here, we want to describe our results concerning the intermolecular allylation of trifluoromethylated tertiary carbon radicals, leading to trifluoromethylated quaternary carbons **4** (Scheme 1).[13]

The starting trifluoromethylated alcohols **2** have been prepared by condensation of the Ruppert Reagent CF_3SiMe_3 with the corresponding carbonyl compound **1** in basic medium (1 M Bu_4NF/THF).[22] Formation of their xanthate derivatives **3** has been performed under classical conditions (KH/THF/CS_2, then alkylation by MeI).[23] The tertiary trifluoromethylated radicals have been formed from these xanthates **3** either by UV irradiation, or preferably by chemical initiation. Triethylborane (1 M in hexane) has been useful for the generation of the radical intermediate at low temperature. Their allylation by allyltributyltin occurred following a radical cycle.[24] Several secondary reactions have been observed: Chugaev elimination leading to trifluoromethylated olefins, reduction of the xanthate group and in some cases rearrangement of the starting *O*,*S*-dialkyldithiocarbonate to an *S*,*S*-dialkyldithiocarbonate. In order to minimize these by-products, particular conditions have been used: reaction at low (−20°C, entries **a** and **b**) or room temperature (other entries), with a great excess of allyltributyltin (2–10 equiv.) and without solvent. The results are gathered in Table 1.



Scheme 1.

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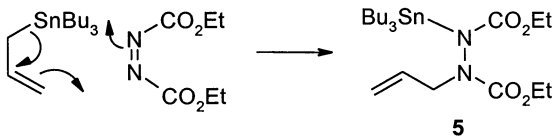
Table 1. Allyl-trifluoromethyl compounds produced via Scheme 1

Entry	**1→2**[a]	**2→3**[a]	**3→4**[a]
a	52 (CF_3 α/β: 96/4)	92	55 (CF_3 α/β: 27/73)
b	77 (CF_3 α 100%)	94	7 (CF_3 β 100%)
c	58 (CF_3 *endo*/*exo*: 2/98)	78	84 (CF_3 *endo*/*exo*: 96/4)
d	58 (CF_3 ax/eq: 77/23)	87	82 (CF_3 ax/eq: 22/78)
e	94	92	56

[a] Isolated yields (%).

The allylated products were isolated by chromatography on silica. Owing to the use of a great excess of allyltributyltin, several separations were necessary in the initial experiments to obtain pure products. Various methods were examined in order to remove the remaining tin reagent. The lithium perchlorate catalyzed insertion of the azo bond in diethylazodicarboxylate (DEAD) into one allyl–tin bond of tetraallyltin has been reported recently.[25] We have observed that allyltributyltin is similarly transformed by DEAD to the metalloene adduct **5** (Scheme 2).



5

Scheme 2.

This condensation is quantitative after a few hours without catalyst. The metalloene adduct **5** remains on the silica column when the allylation product **4** is eluted. Consequently, this procedure allows an easy removal of the allyltributyltin excess.

Typical procedure:

Triethylborane (6 mL, 6 mmol, 1 M in hexane) was added dropwise to a stirred solution of the xanthate **3d** (1.7 g, 5.4 mmol, 77/23 mixture of the axial and equatorial isomers) and allyltributyltin (11 mL, 37.8 mmol, 7 equiv.) at room temperature. The progress of the reaction was monitored by TLC (pentane) and the loss of the yellow color of the solution. After 1 h diethylazodicarboxylate (7 mL, 46 mmol) was added to the mixture and the formation of the metalloene adduct **5** was followed visually by the fading of the red color of the azo compound. After 2 h column chromatography of the reaction mixture (silica gel, pentane) afforded 1.1 g (4.43 mmol, 82%) of **4d** as a colorless oil (22/78 inseparable mixture of the axial and equatorial trifluoromethyl isomers).[26]

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2. Until now, the Diels–Alder reaction of a trifluoromethyl bearing dienophile with a non-fluorinated diene has been the most popular method for this purpose. However, this kind of reaction either proceeds in low yield (Ref. 3) unless the fluorinated dienophile is highly activated (Ref. 4) or needs very high pressure (Ref. 5). Among other methods, the alkylation of stabilized trifluoromethylated enolates either in a classical way (Ref. 6) or via the Torgov (Ref. 7) or the Michael reactions (Ref. 8) has met with some success. More recently, its counterpart, the pseudo-cationic trifluoromethylation of unfluorinated enolates was described (Ref. 9). Some functional compounds have been obtained from trifluoromethylated allylic alcohols by a Claisen rearrangement (Ref. 10). In the sugar series, a stereoselective S_N2' reaction of copper derivatives with mesylates of similar alcohols has been reported (Ref. 11).
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rich geminally disubstituted alkenes, appeared in the literature (Ref. 19); but, as expected from the steric requirements of the trifluoromethyl group, in both cases the yield was low. Intramolecular tandem cyclization mediated by a trifluoromethyl substituted double bond has also been used in the preparation of angularly trifluoromethylated indanes (Ref. 20). Two groups (Ref. 21) independently reported the synthesis of some trifluoromethylated five- and six-membered rings by the intramolecular addition of a secondary trifluoromethyl bearing carbon radical on a double bond.

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26. 1-Allyl-1-trifluoromethyl-4-*t*-butylcyclohexane **4d** had: calcd for $C_{14}H_{23}F_3$: C, 67.71; H, 9.34%; found: C, 67.59; H, 9.64%. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −69.6 (s, 22%, *cis* isomer, CF_3 ax); −77.03 (s, 78%, *trans* isomer, CF_3 eq.). ^1H NMR (300 MHz, $CDCl_3$) δ: 0.86 (s, *t*-Bu, *cis* isomer); 0.89 (s, *t*-Bu, *trans* isomer); 1.0 (1H, m, H-4, *cis* isomer); 1.15 (1H, m, H-4, *trans* isomer); 1.31 (m, 4H); 1.5–1.75 (m, 10H); 1.99 (2H, dm, H-2 eq., *trans* isomer); 2.19 (d, 2H, ^3J = 7.4 Hz, -CH_2-CH=, *trans* isomer); 2.36 (d, 2H, ^3J = 7.4 Hz, -CH_2-CH=, *cis* isomer); 5.1 (dd, CH_2=, $^3J_{H,H\text{-}trans}$ = 12.5 Hz, $^3J_{H,H\text{-}cis}$ = 10 Hz, both isomers); 5.82 (-CH=, ddt, $^3J_{H,H\text{-}trans}$ = 12.5 Hz, $^3J_{H,H\text{-}cis}$ = 10 Hz, $^3J_{H,CH_2}$ = 7.4 Hz, both isomers). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.13 (C3, s, *trans* isomer); 22.86 (C3, q, $^4J_{C\text{-}F}$ = 1.6 Hz, *cis* isomer); 27.3 [CH_3, s, *trans* isomer]; 27.45 [CH_3, s, *cis* isomer]; 28.12 (=CH-CH_2-C-CF_3, q, $^3J_{C\text{-}F}$ = 2.2 Hz, *trans* isomer); 30.54 (C2, q, $^3J_{C\text{-}F}$ = 1.1 Hz, *trans* isomer); 33.98 (C2, q, $^3J_{C\text{-}F}$ = 1.1 Hz, *cis* isomer); 32.35 (CMe_3, s, *trans* isomer *trans*); 32.36 (CMe_3, s, *cis* isomer); 41.7 (C1, q, $^2J_{C\text{-}F}$ = 81.6 Hz, *cis* isomer); 42.14 (=CH-CH_2, q, $^3J_{C\text{-}F}$ = 3.3 Hz, *cis* isomer); 42.6 (C1, q, $^2J_{C\text{-}F}$ = 83.6 Hz, *trans* isomer); 46.97 (C4, s, *cis* isomer); 47.03 (C4, s, *trans* isomer); 117.7 (=CH_2, *trans* isomer); 118.6 (=CH_2, *cis* isomer); 129.46 (CF_3, *trans* isomer, $^1J_{C\text{-}F}$ = 283.4 Hz); 129.85 (CF_3, *cis* isomer, $^1J_{C\text{-}F}$ = 285.8 Hz); 133.0 (-CH=, s, *trans* isomer); 133.6 (-CH=, s, *cis* isomer).