Zinc-promoted Barbier-type Reaction of 2-Bromo-3,3,3-trifluoropropene with Aldehydes

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A zinc-promoted Barbier-type reaction of 2-bromo-3,3,3-trifluoropropene with aldehydes to give CF_3-substituted allylic alcohols in good yields is reported.

Fluorinated organometallic reagents are useful synthetic intermediates for introducing a fluorinated unit into organic molecules.[1] Fluorinated organolithium and magnesium reagents, which usually possess normal reactivity towards carbonyl compounds similar to that of their non-fluorinated counterparts to give fluorinated alcohols, have limited synthetic applicability owing to their thermal instability.[2] On the other hand, fluorinated organozinc reagents are thermally stable. Among them, fluorinated vinylzinc reagents, which can be converted into copper(I) compounds and coupled with aryl and vinyl halides in the presence of palladium catalyst,[3] failed to react with carbonyl compounds. In our search for new methods for introducing the CF_3 unit into organic compounds, we found that a zinc-promoted Barbier-type reaction of 2-bromo-3,3,3-trifluoropropene **1** with aldehydes could give CF_3-substituted allylic alcohols in good yield.

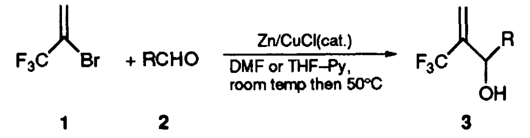
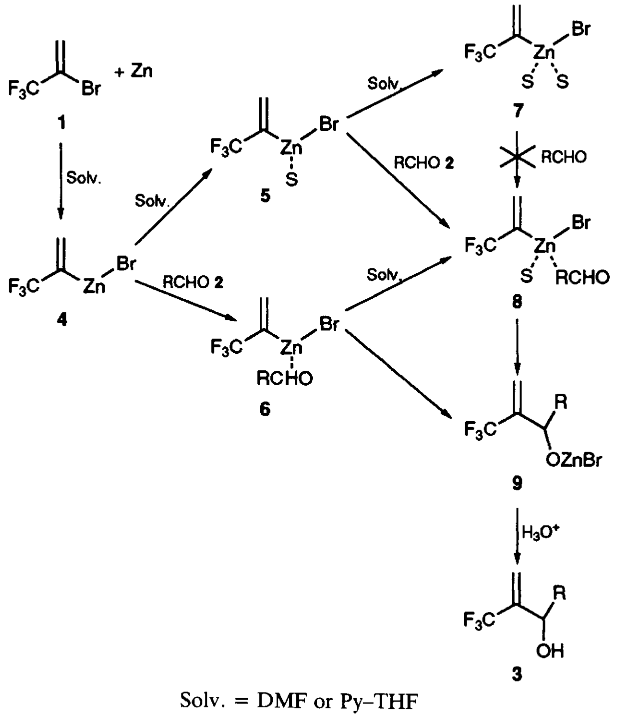


Table 1 Zinc-promoted Barbier-type reaction of 2-bromo-3,3,3-trifluoropropene with aldehydes[a]

Entry	R	Reaction time/h	Product[b]	Yield (%)[c]
1	Ph (**2a**)	12	**3a**	95
2	2-ClC_6H_4 (**2b**)	10	**3b**	91
3	3-ClC_6H_4 (**2c**)	8	**3c**	92
4	4-ClC_6H_4 (**2d**)	9	**3d**	95
5	4-FC_6H_4 (**2e**)	10	**3e**	90
6	4-$MeOC_6H_4$ (**2f**)	9	**3f**	80
7	4-MeC_6H_4 (**2g**)	9	**3g**	85
8	*n*-propyl (**2h**)	10	**3h**	70
9	isopropyl (**2i**)	10	**3i**	72

[a] Reactions were carried out in DMF for entries 1–4 and in pyridine–THF (1:2) for entries 5–9. [b] All new compounds were characterised by mass spectrometry, IR, ^1H NMR, ^{19}F NMR and microanalysis. [c] Isolated yields based on the aldehyde consumed.



Solv. = DMF or Py–THF

Scheme 1

In a typical procedure, zinc dust (6.4 g, 100 mmol), copper(I) chloride (100 mg, 1 mmol), benzaldehyde (5.3 g, 50 mmol) and 2-bromo-3,3,3-trifluoropropene (13 g, 75 mmol) were mixed together in either DMF (30 ml) or pyridine (Py; 10 ml)–THF (20 ml). The resultant mixture was stirred at 20 °C for 4 h and then 4–8 h at 50 °C under nitrogen. Usual work-up gave product **3** in 94% yield. With pyridine–THF the separation procedure could be simplified.

Note that the pre-prepared trifluoroisopropenylzinc bromide failed to react with aldehydes in the same solvent. The reluctance of the trifluoroisopropenyl metal reagents to react with carbonyl compounds was also supported by another finding that even the pre-prepared trifluoroisopropenylmagnesium bromide failed to react with aldehydes. Like other fluorinated vinylzinc compounds, the pre-prepared trifluoroisopropenylzinc bromide could undergo only the cross-coupling reaction with aryl and vinyl halides in the presence of palladium catalyst.[4]

Compared with the reported method using trifluoroisopropenyllithium,[5] such a Barbier-type reaction procedure possesses the following advantages: (*i*) the reaction can be performed at ambient temperature; (*ii*) the undesirable β-elimination of fluoride, as with the trifluoroisopropenyllithium, is avoided and high yields of the products are thus guaranteed.

Based on the known facts,[6] the unique reactivity of 2-bromo-3,3,3-trifluoropropene towards aldehydes in such Barbier-type reactions can be explained by Scheme 1. In the absence of aldehyde, the trifluoroisopropenylzinc formed *in situ* was solvated to **7** and became inactive.

In summary, 2-bromo-3,3,3-trifluoropropene reacts with aldehydes by a zinc-promoted Barbier-type reaction to give CF_3-substituted allylic alcohols in good yields in a convenient way. Based on the supposed reaction mechanism, we envisage that this method may have great potential for further application to other fluorinated vinyl halides for preparing fluorinated allylic alcohols. The study is in progress.

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