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α,α-Difluoroallyl Carbanion: Indium-mediation in Its Facile Coupling with Aldehydes

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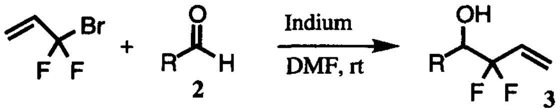
Abstract: Indium-mediated coupling of aldehydes with 3-bromo-3,3-difluoropropene gives 1-substituted-2,2-difluorobut-3-en-1-ols in high yields at room temperature. The coupling takes place at the *gem*-difluorocarbon selectively. Ketones are inert under the conditions examined. © 1997 Elsevier Science Ltd.

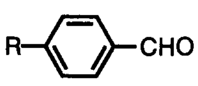
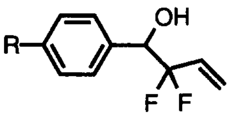
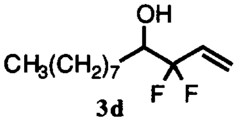
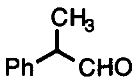
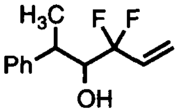
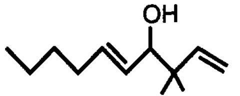
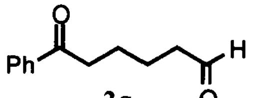
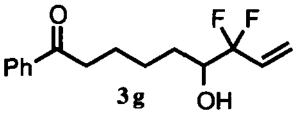
The introduction of a *gem*-difluoromethylene moiety into organic molecules has provided us with attractive results in scientific and industrial fields.[1] Although a number of procedures have been developed to introduce this functionality into organic compounds, the coupling of *gem*-difluoroallyl carbanion with carbonyl compounds is the most important since the resulting *gem*-difluorohomoallyl alcohols have an alkene moiety capable of conversion into other functionalities.[2-4]

We now report the reaction of 3-bromo-3,3-difluoropropene (**1**) with aldehydes (**2**) at room temperature in the presence of indium to afford *gem*-difluorohomoallyl alcohols (**3**) in high yields. The results are summarized in **Table 1**. In many cases, aldehydes (**2**) gave **3** almost quantitatively. Only the CF_2 terminus of **1** attacked the carbonyl of the aldehydes (α-attack). The present result is in accord with the theoretical treatment by Tonachini,[5] where the negative charge is shown to reside at the α-carbon in the *gem*-difluoroallyl anion (CF_2 site). As noted in entry 6, the reaction with the α, β-unsaturated aldehyde **2f** gave the 1,2-adduct **3f** exclusively. Interestingly, ketones did not react with **1** under these reaction conditions. In the case of a compound (**2g**) bearing both aldehyde and ketone functionalities, **1** reacted only with the aldehyde carbonyl to give **3g** chemoselectively (entry 7). These results are in contrast with those in the zinc-mediated difluoroallylation,[4] where little or no difference was observed between aldehydes and ketones, and also with conventional allylindium chemistry,[6] where allylic indium compounds have been found to react with a wide variety of ketones.

A typical experimental procedure is as follows: A suspension consisting of aldehydes (0.50 mmol), **1** (76 μl, 0.75 mmol),[7] powdered indium (86 mg, 0.75 mmol)[8] and DMF (5 ml) was stirred for 3h at room temperature. The reaction mixture was quenched with 10%HCl and extracted with 3 x 20 ml of ether. The combined organic extract was washed with brine, dried over sodium sulfate, filtered, and evaporated to afford the crude **3**. Chromatography on silica gel gave a pure sample.

Table 1.



Entry	Starting Material	Product	Yield
1	 **2a** (R=H)		**3a** (R=H) 99%
2	**2b** (R=OH)		**3b** (R=OH) 97%
3	**2c** (R=Br)		**3c** (R=Br) 95%
4	$CH_3(CH_2)_7CHO$ **2d**	 **3d**	93%
5	 $PhCH(CH_3)CHO$ **2e**	 **3e**	87%*
6	 **2f**	 **3f**	99%
7	 **2g**	 **3g**	77%

All the compounds were characterized on the basis of mass, IR, ^1H and ^{19}F NMR spectral data.

* A single isomer was obtained. The stereochemistry of **3e** has not yet been determined.

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7. 3-Bromo-3,3-difluoropropene (**1**) was obtained from Fluorochem Limited.
8. Powdered indium was obtained from Nacalai Tesque Co.

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