

## Indium-mediated Coupling of Aldehydes with Prop-2-ynyl Bromides in Aqueous Media

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Indium-mediated coupling of aldehydes **1** with prop-2-ynyl bromides **2** occurs regioselectively to give either homoprop-2-ynyl alcohols **3** or allenylic alcohols **4** depending on the  $\gamma$ -substituent of the prop-2-ynyl bromide.

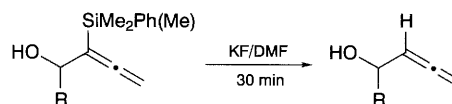
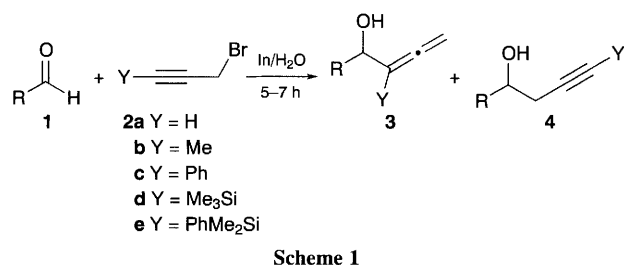
Metal-mediated reactions in aqueous media have recently found considerable applications in organic synthesis.<sup>1,2</sup> Such organometallic type reactions in aqueous media offer a number of advantages over conventional organometallic reactions in organic solvents including: (1) the need for inflammable anhydrous organic solvents is obviated; (2) protection of 'reactive' hydroxy or acidic functional groups is no longer required; (3) compounds insoluble in organic solvents (*e.g.* carbohydrates) can react directly; and (4) possible change in selectivity owing to the change from organic solvents to aqueous media. However, the type of reactions possible have been somewhat limited. The most useful is the coupling of allylic halides with carbonyl compounds in aqueous media to give the corresponding homoallylic alcohols.<sup>3</sup> Variations of the allylic theme have been the use of 1,3-dihalopropenes,<sup>4</sup> 2-chloromethyl-3-iodopropene,<sup>5</sup> or 2-bromomethylacrylates.<sup>6</sup> It would seem reasonable to extend the coupling reaction to prop-2-ynyl halides **2** according to Scheme 1. Indeed, the coupling between the parent prop-2-ynyl bromide (**2a**, Y = H) with aldehydes mediated by tin in aqueous media has been examined.<sup>7</sup> The reaction was found to give a mixture of regioisomers (**3** and **4**) in nearly equal proportions and was thus synthetically not too useful. The same reaction mediated by indium in aqueous media was examined briefly in another context without any definite conclusion regarding the re-

gioselectivity issue.<sup>8</sup> We report now that using indium as the metal, the coupling reaction was found to be regioselective, and conditions can be found that favour either **3** or **4** selectively. The results are summarized in Table 1.

With the parent prop-2-ynyl bromide (**2a**, Y = H), indium-mediated coupling with aliphatic or aryl aldehydes (entries 1 and 2) in water gave mainly the homoprop-2-ynyl alcohols **4** in good yields. In contrast, when the prop-2-ynyl bromide is  $\gamma$ -substituted (**2b**, Y = Me or **2c**, Y = Ph), the coupling products were predominantly or exclusively the allenylic alcohols **3**, again in good yields. Worthy of note is the reaction of formaldehyde with **2c** (entry 4). In this case, the formaldehyde was added as an aqueous solution and must have existed mainly in the hydrated form. For  $\alpha,\beta$ -unsaturated aldehydes (entries 5 and 6), the coupling occurred exclusively in a 1,2-fashion.

Typical coupling conditions were: a mixture of the aldehyde (1 mmol), prop-2-ynyl bromide (2 mmol) in water (2 ml) was rapidly stirred. To this mixture was slowly added indium powder (2 mmol). The reaction mixture was stirred at room temp. for 5–7 h. The mixture was then extracted with diethyl ether (2  $\times$  10 ml), filtered and the filtrate washed (water). The organic layer was separated, washed (brine) and dried (MgSO<sub>4</sub>). The solvent was evaporated and the product was purified by flash chromatography.

Based on the above observation, we have devised an approach to obtain selectively the unsubstituted allenylic alcohols **3** (Y = H). 1-Silyl-3-bromopropyne (**2d**, Y = Me<sub>3</sub>Si or **2e**, Y = Me<sub>2</sub>PhSi) was coupled with aldehydes (entries 10–13) to give the corresponding allenylic alcohols **3** (Y = Me<sub>3</sub>Si or Me<sub>2</sub>PhSi) which could be separated readily from the minor



**Table 1** Indium-mediated coupling of prop-2-ynyl systems with aldehydes in water

Entry	Aldehydes R=	Prop-2-ynyl bromides	Combined yields (%)	Allene : Acetylene	
				<b>3</b>	<b>4</b>
1	n-C <sub>8</sub> H <sub>17</sub>	BrCH <sub>2</sub> CCH	97	12	88
2	1-Naphthyl	BrCH <sub>2</sub> CCH	50	10	90
3	n-C <sub>8</sub> H <sub>17</sub>	BrCH <sub>2</sub> CCPh	89	95	5
4	H	BrCH <sub>2</sub> CCPh	94	99	1
5	BuCCMe	BrCH <sub>2</sub> CCPh	93	90	10
6		BrCH <sub>2</sub> CCPh	96	99	1
7		BrCH <sub>2</sub> CCPh	75	93	7
8	n-C <sub>8</sub> H <sub>17</sub>	BrCH <sub>2</sub> CCMe	99	100	0
9	1-Naphthyl	BrCH <sub>2</sub> CCMe	<98	100	0
10	Ph	BrCH <sub>2</sub> CCSiMe <sub>3</sub>	60	80	20
11	n-C <sub>8</sub> H <sub>17</sub>	BrCH <sub>2</sub> CCSiMe <sub>3</sub>	82	67	33
12	1-Naphthyl	BrCH <sub>2</sub> CCSiMe <sub>2</sub> Ph	70	80	20
13	Me <sub>2</sub> CH	BrCH <sub>2</sub> CCSiMe <sub>2</sub> Ph	60	80	20

isomeric prop-2-ynyl products **4** by flash chromatography. Protodesilylation of **3** (Y = Me<sub>3</sub>Si or Me<sub>2</sub>PhSi) with KF/DMF gave quantitatively the unsubstituted allenyl alcohols **3** (Y = H) without any contamination of the isomer **4**. The protodesilylation reaction by fluoride ion is patterned after a similar reaction on  $\beta$ -hydroxyvinylsilanes.<sup>9</sup> Even though the reaction has since been applied to numerous systems, this is the first example of a protodesilylation reaction on an allenylsilane system, as far as we are aware. In view of the increasing use of allenyl alcohols as building blocks in organic synthesis,<sup>10</sup> the present indium-mediated coupling reaction may find useful applications.

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