

## PREPARATION AND REACTIONS OF CYCLIC ALLYLIC HIGHER ORDER CYANOCUPRATES

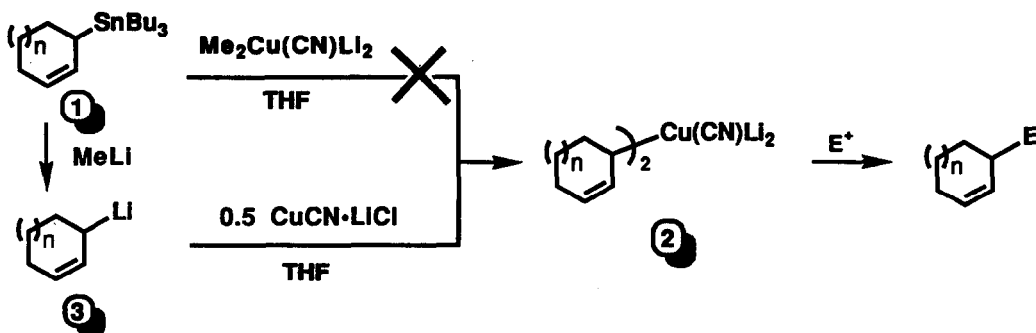
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**Abstract.** Treatment of cyclic allylic stannanes with MeLi followed by CuCN affords the corresponding allylic cuprates which deliver the cycloalkenyl moiety to a variety of organic substrates.

While composing a major review on the field of organocopper chemistry since Posner's classic contributions on this subject,<sup>1</sup> it was apparent that allylic cuprates *do not* figure prominently in most synthetic schemes. We reasoned that a lack of usage might well be attributed to a lack of understanding of these species.<sup>2</sup> Indeed, it can now be appreciated that while both lower order (L.O.) cuprates (allyl)<sub>2</sub>CuLi and their higher order (H.O.) analogs contain  $\sigma$ -bound ligands,<sup>3</sup> the former are thermally sensitive, while the latter are easily prepared and handled even at 0°C or above.<sup>4</sup> Moreover, it has recently been shown that H.O. diallylic cuprates are among the most reactive copper reagents known.<sup>4</sup> Reducing their reactivity by formation of neutral, non-*ate* organocopper complexes RCu (R = an allylic group), in the presence of TMS-Cl provides a potent combination capable of delivering an allylic ligand in a 1,4 sense to  $\alpha,\beta$ -unsaturated ketones.<sup>5</sup> It is not surprising, therefore, that not a single example of chemistry involving a *cyclic* allylic cuprate of any sort (L.O. or H.O.) has been described, to our knowledge. We now report that a cycloalkenyl residue can in fact be introduced at its allylic position into various educts using H.O. cuprate technology.



Originally, we had hoped that transmetalations of **1** with  $\text{Me}_2\text{Cu}(\text{CN})\text{Li}_2$ , as are smoothly effected with *acyclic* allylic stannanes,<sup>4</sup> would likewise afford reagents **2**. Presumably due to the nature of these secondary carbanionic species, the ligand exchange process does not go to completion. Residual  $\text{Me}_2\text{Cu}(\text{CN})\text{Li}_2$ , of course, is not tolerable in most circumstances, and hence we were forced to resort to lithiation with ethereal  $\text{MeLi}$ .<sup>6</sup> In THF at  $0^\circ\text{C}$ , one equivalent of  $\text{MeLi}$  is sufficient to convert **1** to **3**, to which is then added 0.5 equivalents of  $\text{CuCN}$  solubilized as its  $\text{LiCl}$  (1.0 equivalent) complex.<sup>7</sup> The resulting cuprate is then appropriately constituted to react with various organic substrates.

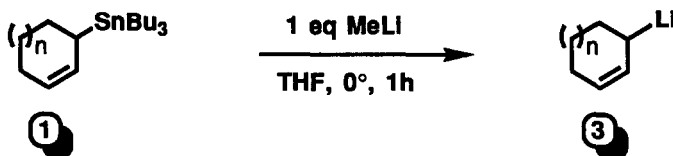
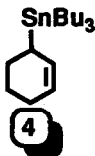
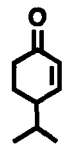
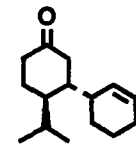

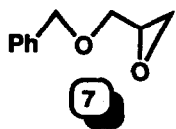
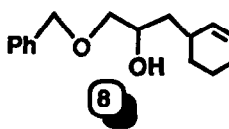

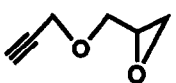
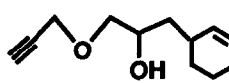

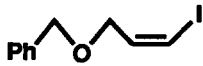
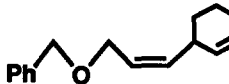
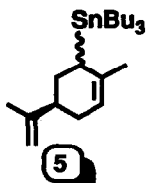
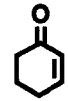
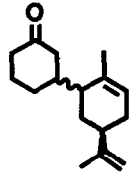
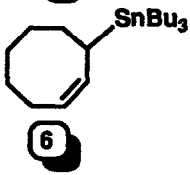
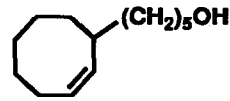

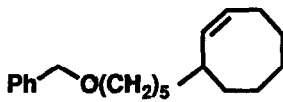

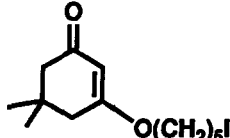
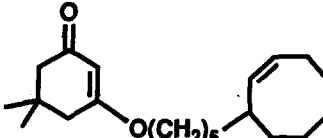


Table I highlights a number of examples of allylic stannanes which readily form cuprates **2**. Thus, both six- (**4**) and eight-membered (**6**) ring systems have been utilized, with one case (**5**) invoking an allylic cuprate derived from carveol. The stannanes are easily prepared, albeit in low yields (ca. 30-40%, unoptimized) *via* the corresponding Grignard reagents with subsequent trapping by  $n\text{-Bu}_3\text{SnCl}$ . Coupling reactions could be performed with unhindered enones, primary and vinylic halides, as well as epoxides. The presence of an acetylenic proton does not interfere with this chemistry. 1,4-Diene formation with a vinylic iodide occurs with retention of double bond geometry. Primary bromides were anticipated to give better results relative to iodides due to the likelihood of competing reduction with the more reactive halide.<sup>8</sup> Yields, nonetheless, tend to be uniformly good to excellent.

Reactivity-wise, cuprates **2** appear to be rather robust, all of the examples in Table I undergoing carbon-carbon bond formation at  $-78^\circ\text{C}$  in less than 5 minutes. Substrate addition to the normally orange, homogeneous THF solutions of **2** result in an obvious color change; usually there is darkening to a reddish solution which does not dissipate over time.

A typical experimental procedure for the preparation of **8** (see Table I) is as follows:  $\text{MeLi}$  ( $421\mu\text{L}$ ,  $0.54\text{mmol}$ ) was added dropwise to a solution of cyclohexenyl stannane ( $200\text{mg}$ ,  $0.54\text{mmol}$ ) in THF ( $0.72\text{mL}$ ,  $0.75\text{M}$ ) at  $-78^\circ\text{C}$ . The yellow mixture is warmed to  $0^\circ\text{C}$  for 40 minutes before recooling to  $-78^\circ\text{C}$ . A solution of  $\text{CuCN}$  ( $24\text{mg}$ ,  $0.27\text{mmol}$ ) and  $\text{LiCl}$  ( $11.5\text{mg}$ ,  $0.27\text{mmol}$ ) in THF ( $0.6\text{mL}$ ,  $0.4\text{M}$ ) at  $-78^\circ\text{C}$  is then added *via* cannula to the yellow mixture, followed by addition of epoxide **7** ( $37\text{mg}$ ,  $0.225\text{mmol}$ ). After 5 minutes the reaction solution is poured into a rapidly stirring solution of 10% aqueous  $\text{NH}_4\text{OH}/\text{aq. NH}_4\text{Cl}$  and allowed to stir for 30 minutes. The aqueous layer is then extracted with  $\text{Et}_2\text{O}$  and the combined organic layers dried over  $\text{Na}_2\text{SO}_4$ . Subsequent filtration and concentration *in vacuo* provided a residue which was passed through a silica gel column using 15%  $\text{EtOAc}/\text{hexanes}$  to give  $55\text{mg}$  (99%)

**Table I. Reactions of Cyclic Diallylic Cyanocuprates **2** with Electrophiles in THF at -78° over 5 minutes.**

Stannane	Substrate	Product(s) <sup>a</sup>	Yield(%) <sup>b</sup>
			83
			99
			91
			76
			72 <sup>c</sup>
	Br-(CH <sub>2</sub> ) <sub>5</sub> OMEM		90 <sup>d</sup>
	Ph-CH <sub>2</sub> O(CH <sub>2</sub> ) <sub>5</sub> I		76
			77

<sup>a</sup>Fully characterized by IR, NMR, MS, and HRMS data. <sup>b</sup>Isolated.

<sup>c</sup>A 73:27 mix of isomers. <sup>d</sup>The MEM group was lost on workup.

of a clear, colorless oil; TLC  $R_f$  0.35 (30/70 EtOAc/hexanes); IR (neat)  $\text{cm}^{-1}$  3420, 1455, 1100; NMR ( $\text{CDCl}_3$ )  $\delta$  7.33 (m, 5H), 5.69-5.52 (m, 2H), 4.56 (s, 2H), 3.90 (bm, 1H), 3.54-3.52 (dd,  $J = 10, 3$  Hz, 1H), 3.37-3.33 (dt,  $J = 9, 1$  Hz, 1H), 2.37-2.33 (m, 1H), 2.10-1.99 (m, 2H), 1.94-1.80 (m, 1H), 1.75-1.70 (m, 1H), 1.60-1.44 (m, 2H), 1.35-1.25 (m, 2H); EI Mass Spec:  $m/e$  (relative intensity) 155 ( $\text{M}^+ - \text{CH}_2\text{Ph}$ , 4), 91 (100); HRCIMS calcd for  $\text{C}_{16}\text{H}_{22}\text{O}_2$  ( $\text{M}^+ - \text{H}$ ) 245.1542; found 245.1538.

In summary, a new series of organocopper complexes is disclosed which allow for coupling of cyclic allylic ligands with several different types of functional groups normally receptive toward cuprate reagents.

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#### References and Notes

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