

Tetrahedron Letters 40 (1999) 2331-2334

TETRAHEDRON LETTERS

## **Regioselective Allylation and Alkylation of Electron-deficient Alkenes with** Organogallium and Organoindium Reagents

Shuki Araki,\* Tomoaki Horie, Motoshi Kato, Tsunehisa Hirashita, Hatsuo Yamamura, and Masao Kawai

Department of Applied Chemistry, Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya 466, Japan Received 16 November 1998; revised 11 January 1999; accepted 18 January 1999

Abstract: Triorganogallium and -indium reagents reacted with  $\alpha$ ,  $\beta$ -unsaturated nitrile and carbonyl compounds to give 1.4-addition products regioselectively. The reaction of allylgallium and allylindium sequihalides with  $\alpha$ ,  $\beta$ -unsaturated carbonyl compounds proceeded in a 1,2-addition mode, whereas a 1.4-addition took place with  $\alpha$ ,  $\beta$ -unsaturated nitriles. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Allylation; Gallium and compounds; Indium and compounds; Michael reactions

There has been increasing interest in the use of organoindium reagents in organic synthesis, because these reagents have recently been proved to be useful for several organic transformations.<sup>1</sup> On the other hand, organogallium reagents have received scarce attention.<sup>2</sup> In this paper, we describe that triallylgallium as well as triallylindium reagents allylate  $\alpha$ , $\beta$ -unsaturated nitrile and carbonyl compounds regioselectively to give 1,4-addition products. For comparison, the regioselectivity of the allylation of these electron-deficient alkenes with allylgallium(indium) sesquihalides is also disclosed.

Triallylgallium and tricinnamylgallium were prepared *in situ* by treating gallium trichloride with allylmagnesium bromide and cinnamyllithium, respectively. Triallylindium was similarly prepared from indium trichloride via transmetallation. The results of the allylation of  $\alpha$ ,  $\beta$ -unsaturated nitriles and carbonyl compounds with these allylating reagents are summarized in Table 1. Both reagents gave high yields of 1,4-addition products exclusively.<sup>3</sup> Cinnamylation occurred at the  $\gamma$ -position regioselectively (entries 3 and 9). The diastereoselectivity was only modest even with the geometrically pure substrate alkene (entries 7 and 13). Alkenes with only one electron-withdrawing group such as benzylideneacetone underwent the 1,2-addition with triallylgallium (84% yield).<sup>4</sup> It is worthwhile to compare this gallium- and indium-based conjugate allylation with the reaction of allylic Grignard reagents; allylmagnesium bromide reacted with benzylideneacetylacetone under similar conditions to give 1,2-addition products exclusively (66% yield of diallylation and 10% of monoallylation products).<sup>5</sup>

Trimethylgallium similarly methylated electron-deficient alkenes regioselectively (Table 2). It is interesting to compare the present results with the alkylation of nitroalkenes by trialkylgallium; the reaction

R <sup>1</sup>	E <sup>1</sup>	+ ( B <sup>2</sup>	~ LM	THF		
<u> </u>	E <sup>2</sup>	+ (	2		1	ΥΥ 8 <sup>2</sup> Ε <sup>2</sup>
Entry	Alke	ne		Allyli	metal	Yield/% <sup>a)</sup>
	R	E	$\mathbf{E}^2$	М	<b>R</b> <sup>2</sup>	
1	Et	CN	CN	Ga	Н	76
2	Ph	CN	CN	Ga	Н	78
3	Ph	CN	CN	Ga	Ph	76 (70:30)
4	Ph	COMe	COMe	Ga	Н	95
5	Ph	$CO_2Et$	$CO_2Et$	Ga	Н	89
6 <sup>b)</sup>	Ph	COMe	$CO_2Et$	Ga	Н	95 (61:39)
7°)	Ph	CN	$CO_2Et$	Ga	Н	74 (59:41)
8	Ph	CN	CN	In	Н	88
9	Ph	CN	CN	In	Ph	51 (76:24)
10	Ph	COMe	COMe	In	Н	81
11	Ph	$CO_2Et$	$CO_2Et$	In	Н	80
12 <sup>d</sup>	Ph	COMe	$CO_2Et$	In	Н	84 (61:39)
<u>13°</u>	Ph	CN	CO <sub>2</sub> Et	In	н	85 (53:47)

Table 1. Allylation of Electron-deficient Alkenes with Triallylgallium and Triallylindium

R<sup>1</sup>

"Figures in parentheses refer to diastereomeric ratio. "Alkene (E:Z=54:46) was used. <sup>(1)</sup> Geometrically pure *E*-alkene was used. <sup>(1)</sup> Alkene (*E*:Z=20:80) was used.

Table 2.	Methylation of Elec	ctron-deficient Alken	es with Trimethylgallium
	Ph_E <sup>1</sup> +	Me <sub>3</sub> Ga <u>Et<sub>2</sub>O</u>	Ph Me E <sup>1</sup>

E	Ē	É	
Entry	Alkene		Yield/% <sup>a)</sup>
•	E	$\mathbf{E}^2$	
1	CN	CN	27
2	COMe	COMe	71
3 <sup>h)</sup>	CN	$CO_2Et$	87 (58:42)
4 <sup>c1</sup>	COMe	$CO_2Et$	87 (60:40)

<sup>a)</sup> Figures in parentheses refer to diastereomeric ratio.

<sup>b</sup>Geometrically pure E-alkene was used <sup>c)</sup>Alkene

(E:Z=37:63) was used.

gives the products in which the nitro group is substituted with an alkyl group via a radical mechanism.<sup>2g</sup> Again, methylation of benzylideneacetylacetone with methyllithium proceeded in a 1,2-addition mode to give the corresponding hydroxy ketone in 51% yield. The methylation with trimethylindium gave a complex mixture of products.

In sharp contrast to the reaction with triallylgallium and -indium reagents, allylgallium and allylindium sesquiiodides reacted with  $\alpha$ , $\beta$ -unsaturated carbonyl compounds to give 1,2-addition products **A** exclusively (Table 3, entries 1-4). The yields with allylgallium sesquiiodide are much lower than those with allylindium sesquiiodides even with use of a large amount of the gallium reagent. Electron-deficient alkenes without ketone functionalities reacted with allylic indium sesquihalides to give moderate yields of conjugate addition products **B** (entries 5-8). These results are consistent with the recent report that the indium-mediated allylation of benzylidenmalononitrile in an aqueous medium gave 1,4-addition products.<sup>2k</sup> The yields as well as the diastereomeric ratios are roughly comparable in organic and aqueous media. Allylgallium sesquiiodide did not react with  $\alpha$ , $\beta$ -unsaturated nitriles.

Allylic indium reagents, in particular allylindium sesquihalides, have recently been proved to be versatile allylating reagents in both organic<sup>1</sup> and aqueous media.<sup>6</sup> The present work demonstrates that triorganogallium and -indium are another choice of reagents which show different selectivity from that of conventional Grignard and organolithium reagents as well as allylgallium(indium) sesquihalides. Although the reason why triorganogallium(indium) shows the high 1,4-selectivity is not completely understood, it may be explainable in terms of the softness of these reagents.<sup>7</sup> Further synthetic applications of triorganogallium(indium) reagents are now under investigation.

Table 3.	Allylation of	Electron-deficient	Alkenes with	Allylic M	letal Sesquihalides
----------	---------------	--------------------	--------------	-----------	---------------------

R1	={ E <sup>2</sup>	+	( R <sup>2</sup>	$\rightarrow_{3}^{M_{2}X_{3}}$	DMF	HQ ₽ <sup>1</sup> '`=(	Me R <sup>2</sup> E <sup>2</sup>	or	$ \begin{array}{c}                                     $
Entry		Alkene			Allylmetal			Yield/% "	
		$\mathbf{R}^{1}$	E	<b>E</b> <sup>2</sup>	$\mathbf{R}^2$	М	X	_A	<u>B</u>
	1	Ph	COMe	COMe	Н	Ga	I	30	-
	2 <sup>b)</sup>	Ph	COMe	$CO_2Et$	Н	Ga	I	17	-
	3	Ph	COMe	COMe	Н	In	Ι	33°)	-
	4 <sup>6)</sup>	Ph	COMe	CO <sub>2</sub> Et	Н	In	I	84	-
	5	Ph	CN	CN	Н	In	I	-	37
	6 <sup>d)</sup>	Ph	CN	CN	Ph	In	Br	-	76 (70:30)
	7	Н	CN	CN	Ph	In	Br	-	30
	8°)	Ph	CN	CO,Et	Н	In	I	-	40 (57:43)

<sup>a)</sup> Figures in parentheses refer to diastereomeric ratio. <sup>b)</sup> Alkene (*E*:Z=37:63) was used. <sup>c)</sup> Diallylated product (diol) was also obtained in 37% yield. <sup>d)</sup> At -30 °C for 4 h. <sup>e)</sup> Geometrically pure *E*-alkene was used.

## **Typical Experimental Procedures**

The following reactions represent the general procedures.

1. Table 1, entry 2: To a stirred solution of gallium trichloride (0.23 g, 1.3 mmol) in dry THF (3 ml) was added allylmagnesium bromide (1.0 M in ether, 3.9 ml, 3.9 mmol), and the mixture was stirred at room temperature for 2 h. Benzylidenemalononitrile (0.10 g, 0.65 mmol) in THF (5 ml) was added and the mixture was stirred overnight at room temperature. The reaction was quenched with diluted hydrochloric acid (1 N) and the product was extracted with ether. Purification by column chromatography (SiO<sub>2</sub>, hexane : ethyl acetate = 7 : 3) gave (1-phenyl-3-butenyl)malononitrile in 78% yield.

2. Table 3, entry 1: Allylgallium sesquiiodide was prepared by mixing allyl iodide (0.18 ml, 2.0 mmol) and a lump of a gallium metal (70 mg, 1.0 mmol) in DMF (5 ml). A solution of benzylideneacetylacetone (94 mg, 0.50 mmol) in DMF (5 ml) was added and the mixture was ultrasonicated for 1 h at room temperature. Aqueous workup and column chromatography (SiO<sub>2</sub>, dichloromethane) gave 3-benzylidene-4-hydroxy-4-methyl-6-hepten-2-one in 30% yield.

## REFERENCES

- 1. For a review of organoindium compounds: see, Cintas, P. Synlett 1995, 1087-1096.
- For selected examples of organogallium reagents in organic synthesis: see, (a) Araki, S.; Ito, K.; Butsugan, Y. Appl. Organomet. Chem. 1988, 2, 475-478; (b) Han, Y.; Huang, Y-Z. Tetrahedron Lett. 1994, 35, 9433-9434; (c) Han, Y.; Fang, L.; Tao, W-T.; Huang, Y-Z. Tetrahedron Lett. 1995, 36, 1287; (d) Yamaguchi, M.; Hayashi, A.; Hirama, M. Chem. Lett. 1995, 1093-1094; (e) Han, Y.; Huang, Y-Z. Tetrahedron Lett. 1995, 36, 7277-7280; (f) Zhang, X-L.; Han, Y.; Tao, W-T.; Huang, Y-Z. J. Chem. Soc., Perkin Trans. 1 1995, 189-191; (g) Han, Y.; Huang, Y-Z.; Zhou, C-M. Tetrahedron Lett. 1996, 37, 3347-3350; (h) Yamaguchi, M.; Kido, Y.; Hayashi, A.; Hirama, M. Angew. Chem., Int. Ed. Engl. 1997, 36, 1313-1315; (i) Yamaguchi, M.; Sotokawa, T.; Hirama, M. Chem. Commun. 1997, 743-744; (j) Boo, W.; Zhang, Y. Synth. Commun. 1997, 27, 615-620; (k) Wang, L.; Sun, X.; Zhang, Y. Synth. Commun. 1998, 28, 3263-3267.
- 3. All products gave satisfactory spectral and analytical data.
- For 1,2- as well as 1,4-addition reactions of organoindium reagents to enones: see, Araki, S.; Ito, H.; Katsumura, N.; Butsugan, Y. J. Organomet. Chem. 1989, 369, 291-296; Araki, S.; Shimizu, T.; Jin, S.-J.; Butsugan, Y. J. Chem. Soc., Chem. Commun. 1991, 824-825.
- For examples of 1,4-allylation of electron-deficient alkenes: see, Yamamoto, Y.; Nishii, S.; Maruyama, K. J. Chem. Soc., Chem. Commun. 1985, 386-388; Yamamoto, Y.; Nishii, S. J. Org. Chem. 1988, 53, 3597-3603.
- Li, C. J. Tetrahedron 1996, 52, 5643-5668; Li, C. J.; Chan, T. H. "Organic Reactions in Aqueous Media", Wiley-Interscience, NY, 1977.
- The following experimental results may support this hypothesis. Allylation of benzylideneacetylacetone with (allyl)<sub>2</sub>GaCl gave 80% yield of the 1,4-addition product, whereas harder (allyl)GaCl<sub>2</sub> gave much less 1,4-addition (< 50% yield) together with undefined products.</li>