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

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Abstract: Triorganogallium and -indium reagents reacted with α,β-unsaturated nitrile and carbonyl compounds to give 1,4-addition products regioselectively. The reaction of allylgallium and allylindium sesquihalides with α,β-unsaturated carbonyl compounds proceeded in a 1,2-addition mode, whereas a 1,4-addition took place with α,β-unsaturated nitriles.

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.[1] On the other hand, organogallium reagents have received scarce attention.[2] In this paper, we describe that triallylgallium as well as triallylindium reagents allylate α,β-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 α,β-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.[3] Cinnamylation occurred at the γ-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).[4] 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).[5]

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

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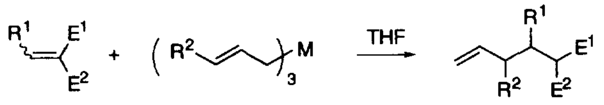
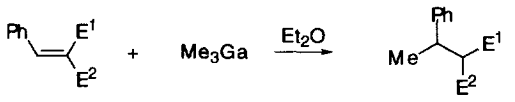
Table 1. Allylation of Electron-deficient Alkenes with Triallylgallium and Triallylindium



Entry	Alkene			Allylmetal		Yield/%[a]
	R^1	E^1	E^2	M	R^2	
1	Et	CN	CN	Ga	H	76
2	Ph	CN	CN	Ga	H	78
3	Ph	CN	CN	Ga	Ph	76 (70:30)
4	Ph	COMe	COMe	Ga	H	95
5	Ph	CO_2Et	CO_2Et	Ga	H	89
6[b]	Ph	COMe	CO_2Et	Ga	H	95 (61:39)
7[c]	Ph	CN	CO_2Et	Ga	H	74 (59:41)
8	Ph	CN	CN	In	H	88
9	Ph	CN	CN	In	Ph	51 (76:24)
10	Ph	COMe	COMe	In	H	81
11	Ph	CO_2Et	CO_2Et	In	H	80
12[d]	Ph	COMe	CO_2Et	In	H	84 (61:39)
13[c]	Ph	CN	CO_2Et	In	H	85 (53:47)

[a] Figures in parentheses refer to diastereomeric ratio. [b] Alkene (*E*:*Z*=54:46) was used. [c] Geometrically pure *E*-alkene was used. [d] Alkene (*E*:*Z*=20:80) was used.

Table 2. Methylation of Electron-deficient Alkenes with Trimethylgallium



Entry	Alkene		Yield/%[a]
	E^1	E^2	
1	CN	CN	27
2	COMe	COMe	71
3[b]	CN	CO_2Et	87 (58:42)
4[c]	COMe	CO_2Et	87 (60:40)

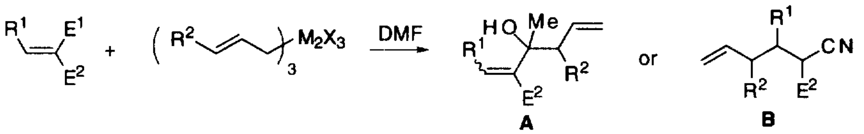
[a] Figures in parentheses refer to diastereomeric ratio. [b] Geometrically pure *E*-alkene was used. [c] Alkene (*E*:*Z*=37:63) was used.

gives the products in which the nitro group is substituted with an alkyl group via a radical mechanism.[2g] 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 α,β-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.[2k] The yields as well as the diastereomeric ratios are roughly comparable in organic and aqueous media. Allylgallium sesquiiodide did not react with α,β-unsaturated nitriles.

Allylic indium reagents, in particular allylindium sesquihalides, have recently been proved to be versatile allylating reagents in both organic[1] and aqueous media.[6] 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.[7] Further synthetic applications of triorganogallium(indium) reagents are now under investigation.

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



Entry	Alkene			Allylmetal			Yield/%[a]	
	R^1	E^1	E^2	R^2	M	X	**A**	**B**
1	Ph	COMe	COMe	H	Ga	I	30	-
2[b]	Ph	COMe	CO_2Et	H	Ga	I	17	-
3	Ph	COMe	COMe	H	In	I	33[c]	-
4[b]	Ph	COMe	CO_2Et	H	In	I	84	-
5	Ph	CN	CN	H	In	I	-	37
6[d]	Ph	CN	CN	Ph	In	Br	-	76 (70:30)
7	H	CN	CN	Ph	In	Br	-	30
8[e]	Ph	CN	CO_2Et	H	In	I	-	40 (57:43)

[a] Figures in parentheses refer to diastereomeric ratio. [b] Alkene (*E*:*Z*=37:63) was used. [c] Diallylated product (diol) was also obtained in 37% yield. [d] At -30 °C for 4 h. [e] 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_2, 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_2, dichloromethane) gave 3-benzylidene-4-hydroxy-4-methyl-6-hepten-2-one in 30% yield.

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7. The following experimental results may support this hypothesis. Allylation of benzylideneacetylacetone with $(allyl)_2GaCl$ gave 80% yield of the 1,4-addition product, whereas harder $(allyl)GaCl_2$ gave much less 1,4-addition (< 50% yield) together with undefined products.