

Allyl- and propargylchromium reagents generated by a chromium(III) ate-type reagent as a reductant and their reactions with electrophiles†

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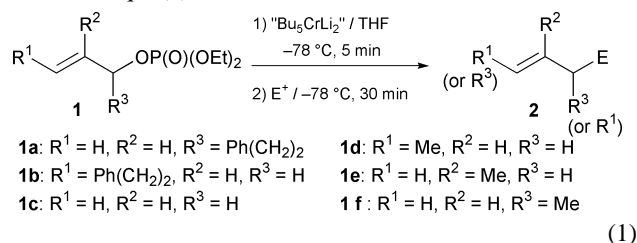
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A chromium ate-type reagent 'Bu₅CrLi₂' reacts with allylic and propargylic phosphates to generate the corresponding allyl- and propargylchromium (propargyl = prop-2-ynyl) reagents which further react with a variety of electrophiles such as aldehydes, ketones, imines, and isocyanates to afford the corresponding adducts in high yields.

Organochromium(III) reagents are well-known to be nucleophilic, and have been used for the selective transformation of organic molecules. These reagents are usually generated from organic halides or their equivalents by reduction with chromium(II) as a 'one-electron' reductant.¹ We found that a chromium ate-type reagent, 'Bu₅CrLi₂'[‡] easily prepared from chromium(III) chloride and butyllithium reacted with an equimolar amount of allylic phosphates to produce a nucleophilic allylation agent² where the butylchromium ate reagent served not as an alkylation agent, but formally as a 'two-electron' reductant [eqn. (1)].



At the outset, we had found that 'Bu₄CrLi' reacted with an allylic phosphate, which can be easily prepared from the corresponding allyl alcohol, to produce reduction products, after aqueous workup. Therefore, we examined the reactivity of some butylchromium(III) reagents to 5-phenylpent-1-en-3-yl diethyl phosphate (**1a**) in a simple reduction to yield a mixture of terminal and internal alkenes. As can be seen in Table 1, 'Bu₅CrLi₂' was the most reactive toward the allyl phosphate **1a**. With 'Bu₄CrLi' it took 3 h to consume the starting material, and in a reaction of 'Bu₃Cr', 31% of **1a** was recovered even after 24 h. § Next, we tested reactions of allyl bromide,³ phosphate,⁴ and acetate with 'Bu₅CrLi₂'. Allyl phosphate, diethyl 5-phenylpent-2-enyl phosphate (**1b**) was the best choice as precursor of the postulated allylchromium reagent, compared to 5-phenylpent-2-enyl bromide and acetate (Table 2). With an allylic bromide, butylation and dimerization competed with the desired reduction, and the acetate gave the starting allyl alcohol, suggesting a nucleophilic reaction of the 'Bu₅CrLi₂' reagent to the carbonyl of an acetoxy moiety.

By virtue of the reducing ability of the chromium ate-type reagent 'Bu₅CrLi₂', an allylchromium reagent was prepared from allyl phosphate **1c** under mild conditions, and the thus-generated reagent reacted with many types of electrophiles (Table 3). ¶ Throughout this conversion, an allylic moiety of phosphate **1c** changes from electrophilic to nucleophilic.⁵ Besides aliphatic (entries 1–3) and aromatic aldehydes (entry

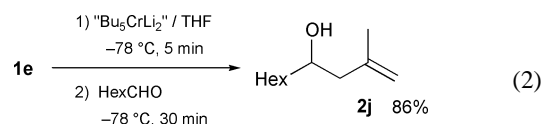
Table 1 Reaction with allyl phosphate **1a**^a

Entry	Chromium reagent	Conditions	Alkene (%) ^b
1	'Bu ₅ CrLi ₂ '	–78 °C, 5 min	96 (83:17)
2	'Bu ₄ CrLi'	–78 °C, 1 h	77 (82:18) ^c
3	'Bu ₄ CrLi'	–78 °C, 3 h	91 (83:17)
4	'Bu ₃ Cr'	–78 °C, 24 h	61 (80:20) ^d

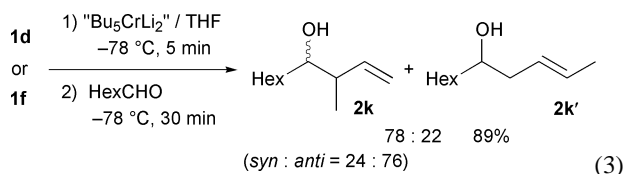
^a The reduction was conducted at –78 °C for 5 min using 1.2 equiv. of 'Bu₅CrLi₂'. Reactions were quenched with saturated NH₄Cl solution.

^b Isolated yield and isomeric ratio are shown in parentheses. ^c 20% of starting material **1a** was recovered. ^d 31% of starting material **1a** was recovered.

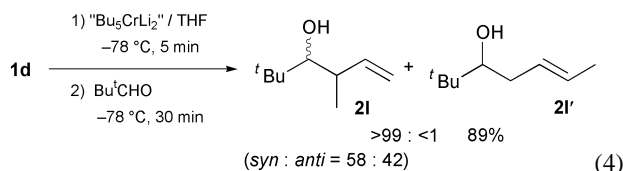
4), ketones also reacted with the present allylchromium reagent (entries 5 and 6). To cyclohex-2-enone, 1,2-addition took place to give the corresponding homoallyl alcohol **2g** (entry 7). Imine and isocyanate gave homoallylamine **2h** and but-3-enoyl amide **2i**, respectively, in high yields (entries 8 and 9). The generation and reactions of other substituted allylchromium reagents were also successful. A β-methylallyl-type reagent reacted efficiently with an aldehyde [eqn. (2)]. Unsymmetrical reagents were also



generated from **1d** and **1f** under the same conditions, –78 °C, 5 min, and these isomeric reagents both reacted with heptanal to give the same mixture of α- and γ-allylation products, suggesting that these reactions proceeded through a common intermediate [eqn. (3)]. Interestingly, the same reagent derived

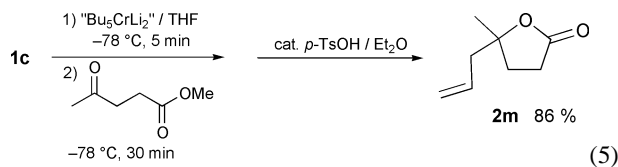


from **1d** afforded only γ-allylation product **2l**, when reacted with pivalaldehyde [eqn. (4)]. These results imply that the

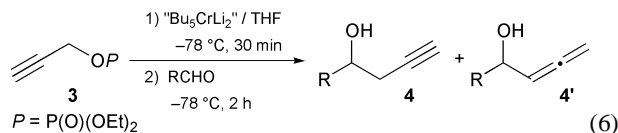


common intermediate would possibly be labile or not responsible for the regiochemical outcome, and the regioselectivity would be affected by the steric requirements of both a bulky allylchromium reagent and an aldehyde in the transition state for the allylation. The reagent was chemoselective for ketones in the presence of esters. The chemoselective allylation with the present allylchromium reagent is exemplified by eqn. (5).

† Electronic supplementary information (ESI) available: experimental details. See <http://www.rsc.org/suppdata/cc/b0/b009351n/>



The present protocol can be applied even to the generation of a propargylic reagent⁶ from the corresponding phosphate **3** [eqn. (6)]. With aromatic aldehydes, only homopropargyl



alcohols **4** were obtained, while with an aliphatic aldehyde, allenylmethyl alcohol **4'** was also co-produced as well as homopropargyl alcohol **4** (Table 4).

Table 2 Reactions of allylic bromide, phosphate and acetate with 'Bu₅CrLi₂'^a

Entry	Substrate	Conditions	Alkene (%) ^b
1		-78 °C, 5 min	73 (70 : 30) ^c
2		-78 °C, 5 min	96 (83 : 17)
3		-78 °C, 3 h	18 (69 : 31) ^d

^aThe reduction was conducted at -78 °C for 5 min using 1.2 equiv. of "Bu₅CrLi₂". Reactions were quenched with saturated NH₄Cl solution. ^bIsolated yield and isomeric ratio are shown in parentheses. ^c15% of butylated product and 4% of dimer were detected. ^d35% of allylic alcohol and 40% of the starting material were recovered.

Table 3 Reaction of allyl phosphate **1c** with electrophile^a

Entry	Electrophile	Product 2	Yield (%)
1			93
2			85
3			79
4			91
5			96
6			91
7			83
8			84
9	PhNCO		75

^aThe reduction was conducted at -78 °C for 5 min using 1.2 equiv. of "Bu₅CrLi₂". To the allylchromium reagent, 4 equiv. of an electrophile were added, and the mixture was stirred at -78 °C for 30 min. Reactions were quenched with saturated NH₄Cl solution. ^bIsolated yield.

Table 4 Reaction of propargylchromium reagent^a

Entry	R'CHO	Product ratio (%)		Yield (%) ^b (4 + 4')
		4	4'	
1	Ph	99 4a	<1	75
2		99 4b	<1	73
3	Hex	88 4c	12 4c'	70

^aThe reduction was conducted at -78 °C for 30 min using 1.2 equiv. of "Bu₅CrLi₂". An aldehyde (4 equiv.) was added at -78 °C and the mixture was stirred at the same temperature for 2 h. Reactions were quenched with saturated NH₄Cl solution. ^bIsolated yield.

In conclusion, a chromium ate-type reagent 'Bu₅CrLi₂' reduces allyl and propargyl phosphates to generate allyl- and propargylchromium reagents, respectively, where no alkylation takes place, while these thus-generated reagents act as nucleophilic reagents toward a variety of electrophiles. From a synthetic point of view, many types of allyl- and propargylchromium reagents can be generated by the present protocol, starting from allyl and propargyl alcohols. Further study on the generation and reaction of these reagents is now in progress.

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Notes and references

‡ Formulae 'Bu_nCrLi_{n-3}' are tentatively used, since the precise structures of the species are not clear at present.

§ These 'Bu_nCrLi_{n-3}' species are possibly in equilibrium through disproportionation.

¶ A solution of 'Bu₅CrLi₂' in THF was prepared from BuLi in hexane (1.62 mL, 2.6 mmol) and a suspension of chromium(III) chloride in THF (0.52 mmol in 5 mL) with stirring at -78 °C for 30 min. Allyl phosphate (0.43 mmol) was added at -78 °C, and the mixture was stirred for 5 min. To the flask, an electrophile (1.72 mmol) was added and the resulting mixture was further stirred for 30 min. After quenching with saturated NH₄Cl and conventional workup, the crude mixture was subjected to chromatography to give a pure product.

|| The stereoselectivity in the reactions of a crotyl-type reagent to aldehydes was not so high compared to that of the reported crotylchromium reagent generated by the reduction with a chromium(II) reagent. At the moment, reaction conditions for the selectivity were not optimized, and more likely, this lower selectivity may possibly be due to the crowded chromium-metal center to which remaining butyls would coordinate.

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