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CARBON-CARBON BOND FORMATION WITH BISMUTH SALT.
A CHEMOSELECTIVE GRIGNARD-TYPE ADDITION OF ALLYL UNIT TO ALDEHYDES

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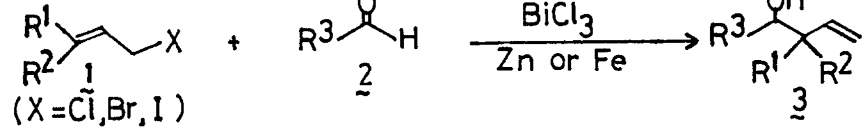
Abstract: In the presence of bismuth(III) chloride-metallic zinc or bismuth(III) chloride-metallic iron, allylic halides were found to react with aldehydes under mild conditions to give the corresponding homoallylic alcohols in high yields with high chemoselectivity.

Among group 5B elements, bismuth is expected to play some role for organic synthesis according to its enhanced metallic character. To our knowlege, however, organic synthesis using bismuth element has been scarcely studied.[1)] Only one example, *i*,*e*., metallic bismuth mediated allylation of aldehydes to homoallylic alcohols in DMF (Method A), was disclosed recently by us.[2,3)] Though effective for the Grignard-type allylation, this reaction is sometimes troublesome in THF.[4)] Herewith, we wish to communicate the first example that bismuth(III) chloride-metallic zinc (Method B) or bismuth(III) chloride-metallic iron (Method C) can be utilized in the title reaction in THF with high chemoselectivity.[5)] The overall scheme is shown below.

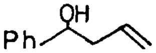
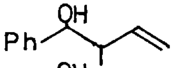
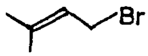
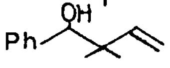
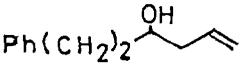
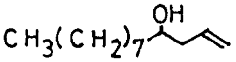
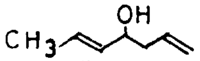
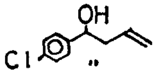
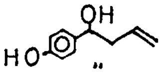
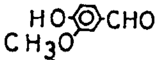
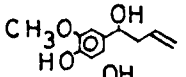
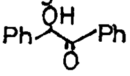
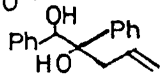
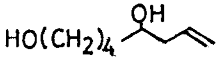
Scheme 1



The reaction was carried out as follows: 1) Method B, bismuth(III) chloride was treated with metallic zinc in THF at room temperature for 1h and then the resulting black suspension was reacted with a mixture of an allylic halide and an aldehyde for 2h; 2) Method C, a mixture of an allylic halide, an aldehyde, and bismuth(III) chloride was treated with metallic iron in THF at room temperature for 4-7h. Typical results are summarized in Table 1 including some results of Method A as reference.

Hardly any expected product was obtained by Method A-C from allyl chloride, while the product was obtained by Method A in the presence of sodium iodide or tetraethylammonium bromide as seen from the table (run 4). Both allyl bromide and allyl iodide themselves could be used as allylation reagents. The benzaldehyde/prenyl bromide reaction gave satisfactory yield, and the more substituted γ-carbon of an allyl group was attached regioselectively to the carbonyl carbon (run 6). The reaction of

Table 1 Bismuth Mediated Synthesis of Homoallylic Alcohols[a]

Run	Allyl halide	Aldehyde	Method	Product(%, yield)[b]
1		PhCHO	B	 (99)
2	"	"	C	" (92)
3		"	C	" (99)
4		"	A	" (80)[c]
5		"	C	 (93, 85:15)[d]
6		"	C	 (80)
7		$Ph(CH_2)_2CHO$	B	 (99)
8	"	"	C	" (91)
9	"	$CH_3(CH_2)_7CHO$	B	 (71)
10	"	"	C	" (98)[e]
11	"		B	 (99)[e]
12	"	"	C	" (90)[e]
13	"		B	 (91)
14	"	"	C	" (96)
15	"		A	 (76)
16	"	"	B	" (49)
17	"	"	C	" (81)
18	"		A	 (85)[e]
19	"		B	 (75)
20	"	$HO(CH_2)_4CHO$	A	 (80)[e]
21	"	"	B	" (45)
22	"	"	C	" (64)

a. Experiments were carried out in 2-3 mmol scale of the carbonyl components. The molar ratio of an allyl halide : bismuth(III) chloride : zinc (or iron) : an aldehyde = 1.2 : 1.2 : 1.8 (or 1.2) : 1.0

b. All the products gave satisfactory IR and ^1H NMR spectra and some products were also identified by comparison with an authentic samples. Isolated yields are given unless otherwise stated.

c. Sodium iodide was necessary to obtain the product. When tetraethylammonium bromide was used instead of sodium iodide, the product was obtained in 62% yield.

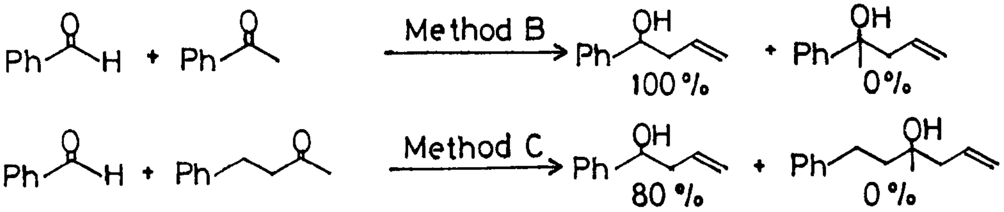
d. The ratio of erythro : threo. Determined by ^1H NMR (the absorption of the methine proton $\underline{H}$-C-OH): erythro, δ4.50 (d, J=5.7 Hz); threo, δ4.30 (d, J=7.0 Hz).[5c)]

e. The extract from the reaction mixture was pure by ^1H NMR without purification.

benzaldehyde with crotyl bromide by Method C gave predominant erythro selectivity regardless of geometry of crotyl unit (run 5).6) When an α,β-unsaturated aldehyde was used, 1,2-addition product was obtained selectively (run 11 and 12). Both aromatic and aliphatic aldehydes reacted smoothly to afford the corresponding homoallylic alcohols in good yields.

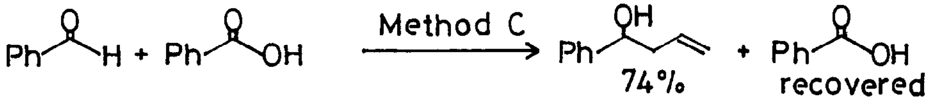
A striking feature of the reaction is the high chemoselectivity. When acetophenone was used, the desired product was not obtained in any significant amount by Method C,7) while it was obtained in 56% yield by Method B.8) Based on this reactivity difference between aldehydes and ketones, we could discriminate benzaldehyde from acetophenone or benzylacetone as shown in the next scheme.9)

Scheme 2



Noteworthy is the fact that the corresponding homoallylic alcohols were obtained from aldehydes containing a hydroxyl group using one equivalent of allylation reagent (run 15-22), which may signify that some allylbismuth reagent prepared *in situ* does not react with a hydroxyl group.10) Furthermore, one equivalent of allylation reagent reacted with benzaldehyde even if benzoic acid was present in the reaction mixture, and benzoic acid was recovered intact.

Scheme 3



Functionalized compounds other than aldehydes and ketones are unreactive toward the allylation reagent. Namely, nitriles and esters were recovered unchanged. Another characteristic of the present reaction is that alkyl and aryl halides are unreactive toward bismuth and, therefore further applications for selective carbon-carbon bond formation will be found.

Treatment of bismuth(III) chloride gave black powder immediately with metallic zinc, and did gradually with metallic iron. Although details of the intermediate species are not at hand, a brief note by Nesmeyanov that bismuth(III) chloride was reduced to metallic bismuth by metallic zinc is informative.11) We assume that some allylbismuth reagent is formed through the oxidative addition of an allylic halide to metallic bismuth formed *in situ*. The related works and the mechanistic studies are now in progress and will be reported elsewhere.

References and Notes

(1) Recently, Barton reported the functional group oxidation and the phenylation by pentavalent organobismuth reagents. D. H. R. Barton, J.-C. Blazejewski, B. Charpiot, J.-P. Finet, W. B. Motherwell, M. T. B. Papoula, and S. P. Stanforth, *J. Chem. Soc., Perkin Trans. I,* 2667 (1985), and references cited therein.

(2) M. Wada, and K-y. Akiba, *Tetrahedron Lett.,* **26**, 4211 (1985).

(3) Recently, allylation of carbonyl compounds using metallic Mn, Zn, Sn, or Ce was reported. (a) T. Hiyama, M. Sawahara, and M. Obayashi, *Chem. Lett.,* 1237 (1983); (b) P. Christian, and J. L. Luche, *J. Org. Chem.,* **50**, 910 (1985); (c) T. Mukaiyama, and T. Harada, *Chem. Lett.*, 1527 (1981); (d) J. Nokami, J. Otera, T. Sudo, and R. Okawara, *Organometallics.* **2**, 191 (1983); (e) K. Uneyama, H. Matsuda, and S. Torii, *Tetrahedron Lett.*, **25**, 6017 (1984); (f) T. Imamoto, T. Kusumoto, Y. Tawarayama, Y. Sugiura, T. Mita, Y. Hatanaka, and M. Yokoyama, *J. Org. Chem.,* **49**, 3904 (1984).

(4) The yields of **3** decreased when THF was used as a solvent, and we have also encountered that the yields were not reproducible in THF.

(5) Carbonyl addition of allyl unit with $MnCl_2$-$LiAlH_4$ or $CrCl_3$-$LiAlH_4$ has been reported. (a) T. Hiyama, M. Obayashi, and A. Nakamura, *Organometallics.* **1**, 1249 (1982); (b) Y. Okude, S. Hirano, T. Hiyama, and H. Nozaki, *J. Am. Chem. Soc.*, **99**, 3179 (1977); (c) T. Hiyama, K. Kimura, and H. Nozaki, *Tetrahedron Lett.*, **22**, 1037 (1981).

(6) Used crotyl bromide is a mixture of cis and trans isomer (30:70). The related studies and the mechanistic details of the stereoselectivity will be published elsewhere.

(7) The desired product was also little obtained by Method A.2) These are in sharp constrast to the findings that allylic metal reagents prepared *in situ* attack ketones, by Mn,3a) Zn,3b) Sn,3c-3e) Ce,3f) $MnCl_2$-$LiAlH_4$,5a) or $CrCl_3$-$LiAlH_4$.5b,5c)

(8) It is thought that $ZnCl_2$ generated *in situ* presumably promoted the addition of an allyl group to acetophenone.

(9) In the discrimination of benzaldehyde from acetophenone, when metallic zinc itself was used under otherwise the same conditions acetophenone adduct was obtained in 6% yield.

(10) In this connection, the benzaldehyde/allyl bromide (1 : 1 molar ratio) reaction by $BiCl_3$-Fe took place in even aqueous media (THF : H_2O = 10 : 1) to give the adduct in 44% yield for 17h at room temperature.

(11) A. N. Nesmeyanov, T. P. Tolstaya, and L. S. Isaeva, *Dokl. Akad. Nauk. S. S. S. R.*, **122**, 614 (1958). *Chem. Abstr.*, **53**, 4178 (1959).

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