Pergamon

Tetrahedron Letters 40 (1999) 3863–3866

TETRAHEDRON
LETTERS

Organometallic Reactions in Aqueous Media. Allylation of Aldehydes with Diallylmercury or Allylmercury Bromide

Tak Hang Chan and Yang Yang*

Department of Chemistry, McGill University,
Montreal, Quebec, Canada H3A 2K6

Received 9 February 1999; revised 10 March 1999; accepted 15 March 1999

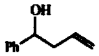
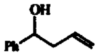
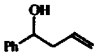
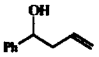
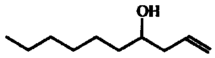
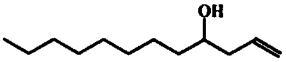
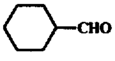
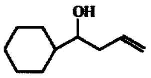
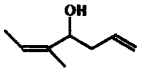
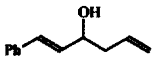
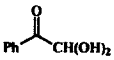
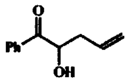
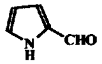
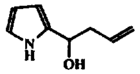
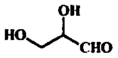
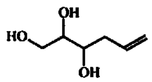
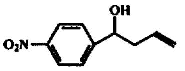
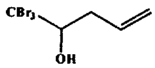
Abstract: By using diallylmercury or allylmercury bromide (activated by tetraalkylammonium bromide), a variety of aldehydes can be allylated smoothly in water to give the corresponding homoallylic alcohols.

Allylation of carbonyl compounds with allylmetals to give the corresponding homoallylic alcohols is considered to be one of the most important carbon-carbon bond formation methods in organic synthesis.[1] Although a number of allylmetallic reagents have been developed to realize efficient allylation reaction of C=X electrophilies, most of them are air and moisture sensitive. Therefore, the allylation reaction is usually performed under strictly anhydrous condition in organic solvent. In recent years, there has been considerable interest in performing organometallic reactions in aqueous media.[2] By using aqueous media, the inflammable and anhydrous organic solvent can be avoided. Moreover, compounds bearing reactive functional groups, such as hydroxy and carboxylic function, can be reacted directly without the protection-deprotection protocol in such reactions. Up to now, such aqueous organometallic-type reactions have been based on the Barbier-type conditions using various metals directly with allylic halides in aqueous media. Despite the success of performing Barbier-type allylation reactions in aqueous media, the use of metal directly in the reaction may lead to side reactions, such as reduction and/or pinacol coupling of the carbonyl compound, reduction and/or Wurtz coupling of the halide. We are therefore interested in the possibility of allylation of carbonyl compounds with allylmetals in aqueous media.

Organomercurials are among the oldest known and useful organometallics in chemistry.[3] However, despite extensive exploitation of organomercurials as versatile reagents in organic synthesis, allylmercury compounds have not been examined as allylmetallic reagents, presumably because of the perception that organomercurials are in general not sufficiently reactive towards carbonyl compounds. On the other hand, it is well known that C-Hg bond is stable to water.[4] Herein, we report that allylation of aldehydes can be performed smoothly with allylmercury reagents in aqueous media.[5] The results are summarized in Table 1. It is clear that diallylmercury ***(Warning: organomercury compounds are known to be toxic)***[6] reacts with various aldehydes to give the corresponding homoallylic alcohols in good yields (*entries 3-20*). The allylation reactions can be performed under mild conditions without any need to activate the carbonyl compounds

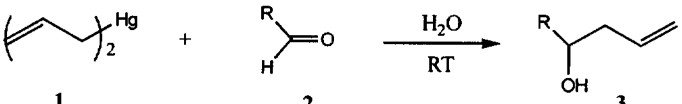
0040-4039/99/$ - see front matter © 1999 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(99)00644-9

Table 1 Allylation Reaction of Aldehydes[a] by Diallylmercury (1) and Allymerucry Bromide (4)

Entry	Aldehydes(2)	Allylation Reagents	Products(3)	Yields(%)[b]
1	PhCHO	4	-	0
2	PhCHO	4/NaBr		26
3	PhCHO	1/CH$_2$Cl$_2$		88
4	PhCHO[b]	1		80
5	PhCHO	4/THAB		88
6	n-C$_6$H$_{13}$CHO	1		99
7	n-C$_8$H$_{17}$CHO	1		99
8		4/THAB[c]		80
9		1		99
10		4/THAB[c]		77
11		1		61
12		1		94
13		4/THAB		55
14		1		99
15		4/THAB		72
16		1		75
17		1		85
18	p-NO$_2$-PhCHO	1		91
19		4/THAB		74
20	Br$_3$CCHO	1		99
21		4/THAB		64
22	PhCOCH$_3$	1	-	0
23	CH$_3$COCOOEt	1	-	0

(a) The reaction was performed in water except entry 3. (b) Isolated yields. (c) The reaction was performed at 40°C overnight.

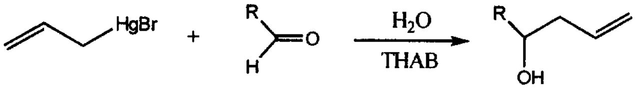
with Lewis acid. The reaction can also be performed in organic solvent (CH_2Cl_2) to give allylation product with similar yield (*entry 3*). When α,β-unsaturated aldehydes were used, no conjugation allylation and only 1,2-addition products were obtained (*entries 7,8*). It is worth pointing out that although diallylmercury can be used as an efficient allylation reagent in aqueous media, its toxicity together with its volatility render it undesirable as a reagent.[6] On the other hand, the results in Table 1 showed that only 0.6 equivalent of diallylmercury was required to give satisfactory yield in the reaction, therefore both allyl groups of diallylmercury must have participated in the reaction. We therefore explored the use of allylmercury bromide, which is much easier to handle and presumed safer.



1 2 3

Scheme 1

We found that allylmercury bromide did not allylate aldehydes under identical conditions (*entry 1*). This was attributed to the lower nucleophilicity of allylmercury bromide. Activation of either the electrophile or the nucleophile is required. We were gratified to find that with the addition of tetrahexylammonium bromide (THAB) to the reaction mixture, the nucleophilicity of allylmercury bromide was sufficiently enhanced and the allylation reaction with aldehydes proceeded smoothly in water.[7] (Scheme 2) Aliphatic aldehydes seemed to be less reactive than aromatic aldehydes and relatively higher temperature (40°C) of reaction was needed. Although sodium bromide also can promote the allylation reaction to some extent in place of THAB, the yield was less satisfactory (*entries 2*). Similar to diallylmercury, only 1,2-addition product was observed when α,β-unsaturated aldehyde was used (*entry 11*).



4 2 3

Scheme 2

Since the reaction can be performed in aqueous media, it is not surprising that functional groups bearing active hydrogen on the substrates are tolerated. Thus, using diallylmercury or allylmercury bromide in water, phenylglyoxal hydrate and glyceraldehyde can be allylated (*entries 14, 15, 17*). On the other hand, both mercury reagents show considerable chemoselectivity in not reacting with ketone or ester carbonyl functions The chemoselectivity can be demonstrated by comparison with the indium-mediated Barbier type reaction.[2] An equal mixture of benzaldehyde and ethyl pyruvate was allylated with limited amount of indium and allyl bromide in water to give mixture of corresponding allylation products in a ratio of about 4:1. The allylation of the same equal mixture of benzaldehyde and ethyl pyruvate with diallylmercury gave only addition product of benzaldehyde. This shows that diallylmercury is unreactive even towards an activated ketone such as the pyruvate carbonyl function (*entry 23*). Similar chemoselectivity is demonstrated in the allylation of phenylglyoxal hydrate. Diallylmercury reacted with phenylglyoxal hydrate to give allylation at the aldehydic carbonyl group only (*entry 14, 15*). Indium/allyl bromide in water, on the other hand, allylates both the aldehydic and the ketonic carbonyl groups.[8]

One advantage of using allylmetallic reagent instead of the Barbier-type reaction conditions with metal is the sensitivity of some functional group to reduction by the metal. For example, nitro group is usually not tolerated in the Barbier-type reaction due to the ease of reduction of the nitro group by metallic zinc, or tin, or indium.[9] In the present case, *p*-nitrobenzaldehyde reacted readily with diallylmercury or allylmercury bromide to give the allylation product with the nitro group intact (*entry 18, 19*). Similarly, α-bromocarbonyl compounds such as tribormoacetaldehyde was allylated uneventfully without the reduction of the α-bromo moiety as would be expected under metal mediated conditions[10] (*entry 20, 21*).

Acknowledgement: We thank NSERC for financial support of this research.

References:

[1] See the review: Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207 and references cited therein

[2] See the reviews: (a) Li, C. J.; Chan, T. H. "*Organic Reactions in Aqueous Media*" John Wiley & Sons Inc., New York, **1997** (b) Li, C. J. *Chem. Rev.* **1993**, *93*, 2023 (c) Lubineau. A.; Auge, J.; Queneau, Y. *Synthesis* **1994**, 741 (d) Li, C. J. *Tetrahedron* **1996**, *52*, 5643 (e) Chan, T. H; Li, C. J.; Lee, M. C.; Wei, Z. Y. *Can. J. Chem.* **1994**, *72*, 1181

[3] Larock, L. C. "Organomercury Compounds in Organic Synthesis" Springer-Verlag, Berlin, **1985**

[4] (a) Wardell, J. L.: in *Comprehensive Organometallic Chemistry*, *Vol. 2* Chapter 17, **1982**, Ed. Wilkinson, G.; Stone, F.G. A.; Abel, E. W., Pergamon, Oxford, U. K. (b) Davies, A. G. in *Comprehensive Organometallic Chemistry II, Vol. 3* Chapter 3, **1995**, Pergamon, Oxford U. K.

[5] Typical experimental procedures: (A) With diallymercury: A mixture of the aldehyde (1 mmol) and diallylmercury[11] (0.6 mmol) (**WARNING**: *Organomercury compounds are known to be toxic*) in 3~5ml water at room temperature was stirred overnight. The reaction was then quenched with 1N HCl (1 mL). The mixture was extracted with ethyl ether (3X10mL). The combined organic layer was washed with saturated aqueous sodium bicarbonate and dried. The organic solvent was evaporated and the product homoallylic alcohol was obtained usually pure according to ^{1}H NMR and can be further purified by flash chromatography over silica gel. (B) With allymercury bromide: The reaction was performed with identical procedure as above but by adding THAB (1mmol) together with allylmercury bromide (1mmol) instead of diallylmercury.

[6] For discussion of toxicity of mercury compounds and their handling, see: (a) Piotrowski, J. K. "*Exposure for Organic Compounds in Industrial Toxicology*" Government Printing Office, **1977**, Washington, D.C. (b)Prpic-Majic, D. *Rad Sigurmost*, **1998**, *2(1)*, 1-20 (c) Patty, F. A. "*Industrial Hygiene and Toxicology Vol. II Toxicology*" Ed. Fassett, D. W.; Irish, D. D. John Wiley & Sons Inc., New York, **1978**

[7] For other examples about promoting nucleophilic reaction with quaternary ammonium catalyst see: (a) Masuyama, Y.; Kishida, M.; Kurusu, Y. *J. Chem. Soc., Chem. Commun.* **1995**, 1405 (b) Masuyama, Y.; Nakata, J.; Kurusu, Y. *J. Chem. Soc., Perkin Trans. I* **1991**, 2598 (c) Masuyama, Y.; Kishida, M.; Kurusu. Y. *Tetrahedron. Lett.* **1996**, *37*,7103. (d) Masuyama, Y.; Ito. A.; Kurusu, Y. *Chem. Commun.* **1998**, 315 (e) Trost, B. M.; Organ, M. G.; O'Doherty, G. A. *J. Am. Chem. Soc.* **1995**, *117*, 9662 (f) Grushin, V.V.; Alper, H. *J. Org. Chem.* **1992**, *57*, 2188

[8] The ease of allylation of the ketone carbonyl in this case is presumably due to chelating effect of the allylindium intermediate with the hydroxy function . See Paquette, L.; Lobben, P. C. *J. Org. Chem.*, **1998**, *63*, 5604 and references cited therein.

[9] Chan, T. H.; Isaac, B. M. *Pure & Appl. Chem.* **1996**, *68*, 919

[10] For reactions of α-halocarbonyl compounds with metal in aqueous media, see: (a) Chan, T. H.; Li, C. J.; Wei, Z. Y. *J. Chem. Soc., Chem. Commun.* **1990**, 505 (b) Chan, T. H.; Li, C. J.; Wei, Z. Y. *Can. J. Chem.* **1994**, *72*, 1181 (c) Bieber, L. W.; Malvestiti, I.; Storch, E. C. *J. Org. Chem.* **1997**, *62*, 9061. For reduction of vicinal bromohydrins by metals in aqueous media, see: Chan, T. H.; Li, C. J. *Organometallics* **1990**, *9*, 2649

[11] (a) Borisov, A. E.; Savel'eva, I. S.; Serdyuk, S. R. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1965**, 896 (b) Ziegler, H. E.; Roberts, J. D. *J. Org. Chem.* **1969**, *34*, 2826