Pergamon

Tetrahedron Letters 43 (2002) 5097–5099

TETRAHEDRON
LETTERS

Gallium-mediated allylation of carbonyl compounds in water

Zhiyong Wang,[a,]* Shizhen Yuan[a] and Chao-Jun Li[b]

[a]*Department of Chemistry, University of Science and Technology of China, Hefei, Anhui 230026, China*
[b]*Department of Chemistry, University of Tulane, New Orleans, LA 70118, USA*

Received 26 February 2002; revised 15 May 2002; accepted 24 May 2002

Abstract—Ga-mediated allylation of aldehydes or ketones in distilled or tap water generated the corresponding homoallyl alcohols in high yields without the assistance of either acidic media or sonication. © 2002 Published by Elsevier Science Ltd.

The importance of organometallic reactions in organic synthesis is well recognized. Recently, there has been a considerable interest in developing organometallic reactions in water of which allylation of aldehydes and ketones to give homoallylic alcohols has received the most attention.[1] This reaction has been achieved by using metals such as Mn/Cu,[2] Sn,[3] Zn,[4] Bi,[5] In,[6] Mg,[7] or organometallic compounds such as diallylmercury, allylmercurybromide,[8] allyltributylstannanes[9] and tetra-allylgermane.[10] Nevertheless, it is necessary for most of these reactions to be carried out with acidic co-reagents such as ammonium chloride, hydrobromic acid, or co-solvents such as a mixture of THF and water. Herein, we wish to report a simple allylation of carbonyl compounds mediated by gallium in distilled or tap water without the help of acidic co-reagents (e.g. HBr, AcOH) or an organic co-solvent (e.g. THF, Et_2O).

Previously Li and Chan reported the use of indium to mediate Barbier–Grignard type reactions in water.[6] Subsequently, indium has been used widely in organic synthesis in aqueous media. After comparing the first ionization and reduction potentials of gallium with those of indium (Ga: FIP, 5.99 eV, E^0, $Ga^{3+}/Ga = -0.56$ V; In: FIP, 5.79 eV, E^0, $In^{3+}/In = -0.345$ V), we expected similar properties between the two metals. As in the case of indium, the reduction potential of gallium is not too negative, and thus it is not sensitive to water and does not form oxides readily in air.

Our initial study was carried out by reacting benzaldehyde with allyl bromide in the presence of gallium under various conditions. The results are summarized in Table 1.

It was found that at room temperature no significant formation of the desired product was observed even after prolonged stirring. When the reactions were performed under acidic conditions, the addition of 1N HCl or saturated NH_4Cl led to the generation of complicated mixtures. Subsequently, it was found that allylation of benzaldehyde proceeded smoothly at 45°C in either distilled water or tap water. Subsequently, a variety of aldehydes and ketones were examined using this allylation method (Scheme 1). The results are listed in Table 2.

Most of the reactions proceeded smoothly in good yield and side reactions such as reduction and coupling were not observed (entries 1–7). An acid sensitive acetal survived the reaction conditions (entry 3) whereas the acetal can be hydrolyzed in 0.1N HCl at 45°C. Aromatic aldehydes can be allylated in high yields (entries 1, 2, 3 and 6). The allylation of acetophenone also gave the corresponding product in 61% yield (entry 8). Aliphatic aldehydes or ketones were also allylated smoothly under the current conditions (entries 10 and 11). *p*-*N*,*N*-Dimethylamino-benzaldehyde also provided the corresponding product in 42% yield (entry 9).

The diastereoselectivity of the allylation catalyzed by gallium was studied. Allylation of 2,3-dihydroxy-propanal with allyl bromide gave the corresponding product with the diastereoselectivity depending on the solvent. When the reaction was carried out in water, the

---

* Corresponding author. Tel.: 86-551-3603544; fax: 86-551-3631760; e-mail: zwang3@ustc.edu.cn

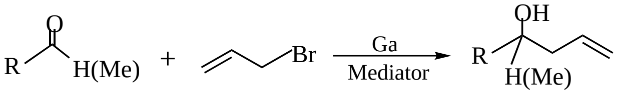
0040-4039/02/$ - see front matter © 2002 Published by Elsevier Science Ltd.
PII: S0040-4039(02)00995-4

Table 1. Allylation of benzaldehyde mediated by gallium under various conditions

Entry	Mediator	Reaction temperature (°C)	Reaction time (h)	Allylation yield (%)[a,b]
1	H_2O	rt	12	41
2	1N HCl	rt	4	59
3	0.1N HCl	rt	4	82
4	NH_4Cl (aq. satd)	rt	4	71
5	H_2O	45	6	76

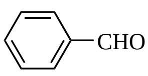
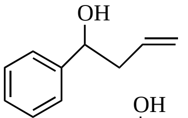
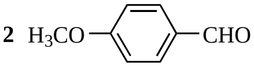
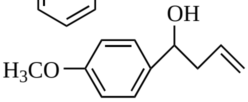
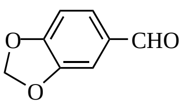
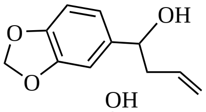
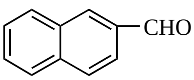
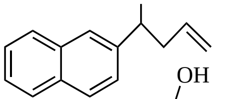
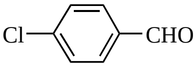
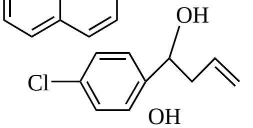
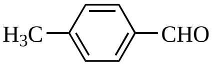
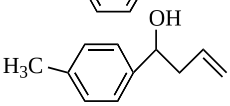
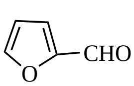
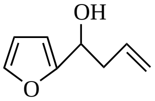
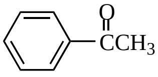
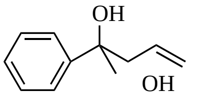
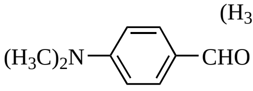
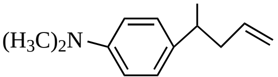
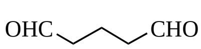
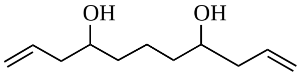
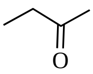
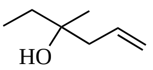
[a] The isolated yields are reported.

[b] The pure product was identified by IR, ^1H, ^{13}C NMR and HRMS.



Scheme 1.

Table 2. Allylation reactions mediated by Ga in water

Entry	Substrate	Product[a]	Yield (%)[b]
1			76
2			82
3			79
4			64
5			73
6			80
7			68
8			61
9			42
10			57
11			46

a. Products were identified by IR, ^1H NMR, ^{13}C NMR and HRMS. b. Isolated yields.

dominant product was the *syn*-isomer. In contrast, the *anti*-isomer was the dominant product when THF was employed as the reaction solvent, see Table 3. The *syn*-isomer may be regarded as the chelation-controlled product, due to the hydrogen bond between the two hydroxyl groups. The aqueous environment favors chelation of the α-hydroxyl. Moreover, it was found that steric hindrance around the carbonyl group had an influence on the diastereoselectivity of the allylation. For example, benzaldehyde reacted with ethyl 4-bromobutenoate in water (entry 3, Table 3) to give rise to the *anti*-isomer as the dominant product. It is likely that steric hindrance governed this diastereoselectivity because of the bulk of the phenyl group. Here the assignment of *syn* and *anti* stereochemistry were based on chemical shift values.[11]

In conclusion, gallium was found to be an effective metal for mediating allylation of carbonyl compounds in water at 45°C. The reaction conditions are mild in that no acidic additives are required. This method provides a useful alternative to the other presently used procedures.

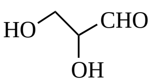
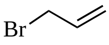
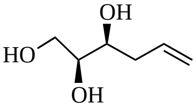
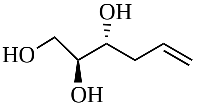
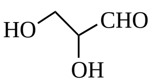
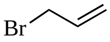
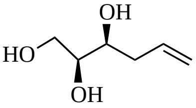
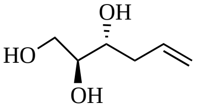
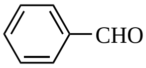
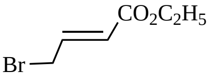
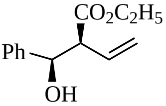
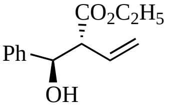
A typical experimental procedure is as follows:

Distilled water or tap water (5 ml), a gallium ingot (2 mmol), the carbonyl compound (1 mmol) and allyl bromide (1.7 mmol) were placed in a round-bottomed flask then the reaction mixture was stirred vigorously for 6 h at 45°C. Subsequently, the reaction mixture was extracted with ether and the organic phase washed with saturated brine, dried over anhydrous magnesium sulfate and concentrated in vacuo. The pure products were obtained by flash chromatography on silica gel eluting with petroleum ether/EtOAc (4:1), and identified by IR, ^1H, ^{13}C NMR and HRMS.

Acknowledgements

The authors are grateful to the National Nature Science Foundation of China (No. 50073021) and the Green Chemistry Fund, University of Science and Technology, China, for support.

Table 3. The diastereoselectivity of allylations catalyzed by Ga in different solvents

Entry	Aldehyde	Halide	Product (*syn* : *anti*)[a]		*Syn:Anti* Yield(%)[b]	Reaction conditions
1					8.3:1 86	Ga/H_2O 45 °C/16 h
2					1:4.2 74	Ga/THF 45 °C/16 h
3					1:2.2 67	Ga/H_2O 45 °C/16 h

a. The products were identified by IR, ^1H NMR, ^{13}C NMR and HRMS. b. Isolated yields.

References

1. *Green Chemistry*: *Frontiers in Benign Chemical Synthesis and Processing*; Anastas, P.; Williamson, T. C., Eds.; Oxford University Press: New York, 1988.
2. Li, C. J.; Meng, Y.; Yi, X. H. *J. Org. Chem.* **1997**, *62*, 8632.
3. (a) Nokami, J.; Otera, J.; Sudo, T. *Organometallics* **1983**, *2*, 191; (b) Nokami, J.; Otera, J.; Sudo, T.; Okawara, R. *Chem. Lett.* **1984**, 869.
4. (a) Petrier, C.; Luche, J. L. *J. Org. Chem.* **1985**, *50*, 910; (b) Einhorn, C.; Luche, J. L. *J. Organomet. Chem.* **1987**, *322*, 177; (c) Petrier, C.; Einhorn, J.; Luche, J. C. *Tetrahedron Lett.* **1985**, *26*, 1445.
5. Wada, M.; Ohki, H.; Akiba, K. Y. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1738.
6. (a) Li, C. J.; Chan, T. H. *Tetrahedron Lett.* **1991**, *32*, 7017; (b) Chan, T. H.; Li, C. J. *J. Chem. Soc., Chem. Commun.* **1992**, 747.
7. (a) Zhang, W. C.; Li, C. J. *J. Org. Chem.* **1999**, *64*, 3230; (b) Wada, M.; Fukuma, T.; Morioka, M.; Takahashi, T.; Miyoshi, N. *Tetrahedron Lett.* **1997**, *38*, 8045.
8. Chan, T. H.; Yang, Y. *Tetrahedron Lett.* **1999**, *40*, 3863.
9. Loh, T. P.; Xu, J. *Tetrahedron Lett.* **1999**, *40*, 2431.
10. Akiyama, T.; Iwai, J. *Tetrahedron Lett.* **1997**, *38*, 853.
11. (b) Annunziata, R.; Benaglia, M.; Cinqnini, M.; Raimondi, L. *Eur. J. Org. Chem.* **1999**, 3369; (c) Imai, T.; Nishida, S. *Synthesis* **1993**, 395.