Highly Efficient Allylation of Aldehydes Promoted by Maleic Acid in Aqueous Media

Gui-long Li, Gang Zhao*

Laboratory of Modern Synthetic Organic Chemistry, Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 FengLin Lu, Shanghai 200032, P. R. of China
Fax +86(21)64166128; E-mail: zhaog@mail.sioc.ac.cn

Received 29 July 2005

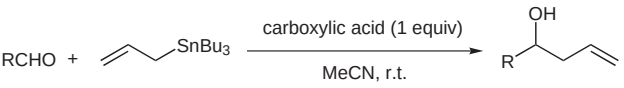
Abstract: A highly efficient promoter for allylation of aldehydes in aqueous media was developed. Under the promotion of maleic acid, the allylation of various aldehydes can be finished in a short period of reaction time to afford the corresponding homoallylic alcohols in high to quantitative yields.

Key words: aldehydes, allylation, aqueous media, allyltributyltin, maleic acid

The allylation of aldehydes, as a very important method for forming synthetically useful homoallylic alcohols, has subjected extensive investigation.[1] In recent years, there has been an upsurge of interest in using water as the solvent in terms of both economical and ecological aspects.[2] Yamamoto et al. described that using 5 mol% of tetraallyltin or $SnCl_4$ could catalyze the allylation of aldehydes and ketones with allyltributyltin in aqueous HCl solution and THF.[3] Since then, there have been several examples reported in this field.[4]

Recently, during our studies of allylation of carbonyl compounds, we found that carboxylic acids with appropriate acidity and solubility are general, practical and highly efficient promoters for the allylation of aldehydes with allyltributyltin in acetonitrile (Equation 1).[5] In this allylation, *p*-nitrobenzoic acid gave nearly quantitative yields, other stronger carboxylic acids were found much faster than *p*-nitro benzoic acid, but lower yields were obtained due to the decomposition of allyltributyltin during the allylation. Moreover, when maleic acid was used as a promoter, the allylation was finished within one hour in a yield of 81%. Herein, we report that maleic acid can be used as a highly efficient promoter for the allylation of aldehydes with allyltributyltin in aqueous media under mild reaction conditions.

We have reported originally that the allylation, which was mediated by *p*-nitrobenzoic acid (insoluble in water), was very sluggish in water[5] (entry 1, Table 1). So, in order to carry out this allylation in aqueous media, two crucial factors (the solubility and acidity of the carboxylic acids) are taken into consideration. In the first step, several water-soluble carboxylic acids were screened according to their pK_a values. The reaction of benzaldehyde (0.5 mmol) and



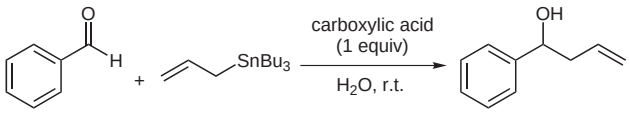
Equation 1

allyltributyltin (0.6 mmol) was promoted under various carboxylic acids (0.5 mmol) in water (1.0 mL) at room temperature. The results were summarized in Table 1. The weaker carboxylic acids ($pK_a \geq 2.85$) only gave trace amounts of allylation product of **3a** (entries 2–5). Comparatively, with the decrease of pK_a values, the stronger carboxylic acids ($pK_a \leq 2.83$) provided good to high yield of the desired product (entries 6–8). Among these carboxylic acids, maleic acid gave the best result with a yield of 95% within a short period of reaction time (1.25 h, entry 7). The further decrease of pK_a value of the carboxylic acid, for example, using trifluoroacetic acid as a promoter ($pK_a = 0.23$, entry 8), resulted in a lower allylation yield (89%) due to the fact that allyltributyltin was partially decomposed under such a strong acidic reaction condition. Reducing the amount of maleic acid to 0.5 equivalents only a yield of 66% (**3a**) was obtained (entry 9). It is noteworthy that compared with the fact that the tin reagent was totally decomposed in acetonitrile within one hour in the presence of maleic acid (monitrored by TLC); only little amount of allyltributyltin was decomposed in deuterium oxide within 23 hours under the promotion of maleic acid (monitored by ^1H NMR in deuterium oxide). And the reaction in aqueous phase is slower than that in MeCN.[5]

Next, a variety of aldehydes were examined. As shown in Table 2, apparently, the electronic nature of the substitutes of aromatic aldehydes has little effect on the high yields (entries 1–6). Salicylaldehyde is soluble in water, which may benefit the allylation (entry 6). As for the aliphatic aldehydes, the allylation promoted under maleic acid in aqueous medium also exhibited high efficiency. For example, the allylation of cyclohexanecarboxaldehyde afforded **3h** in a yield of 84% within 110 minutes (entry 7). Nonyl aldehyde needed a longer period of reaction time to complete the allylation (83%, entry 8) and this can be rationalized on the basis of its hydrophobic property. In the mixed solvent ($THF–H_2O = 2:8$, v/v), the allylation of water-insoluble *p*-nitrobenzaldehyde could proceed smoothly to produce the corresponding product in quantitative yield (entry 9). When a reaction using acetophenone as a substrate was performed, no reaction

SYNLETT 2005, No. 16, pp 2540–2542
Advanced online publication: 21.09.2005
DOI: 10.1055/s-2005-917088; Art ID: U26005ST

Table 1 Screening of Carbonic Acid Promoters for Allylation of Benzaldehyde in Aqueous Media[a]

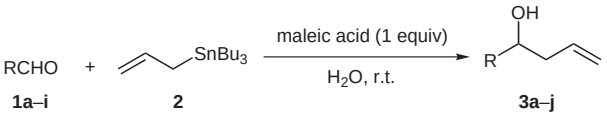


1a **2** **3a**

Entry	Carboxylic acid	pK_a[6]	Time (h)	Yield (%)[b]
1	*p*-Nitrobenzoic acid	3.42	23	Trace
2	Succinic acid	4.21	23	Trace
3	L-(+)-Tartaric acid	3.22	23	Trace
4	Citric acid	3.17	8	Trace
5	Chloroacetic acid	2.85	1.25	Trace
6	Malonic acid	2.83	8	53
7	Maleic acid	1.92	1.25	95
8	Trifluoroacetic acid	0.23	1.25	89
9	Maleic acid	1.92	5	66 [c]

[a] Ratio: **1a**:**2** = 1 equiv (0.5 mmol):1.2 equiv (0.6 mmol).
[b] Isolated yields.
[c] 0.5 Equiv (0.25 mmol) of maleic acid was used as promoter.

Table 2 The Scope of Aldehydes in the Allylation Promoted by Maleic Acid[a]



1a–i **2** **3a–j**

Entry	Aldehydes	Time (min)	Product[b]	Yield (%)[c]
1	C_6H_5CHO	75	**3a**	95
2	*m*-$MeOC_6H_4CHO$	80	**3b**	97
3	3,4,5-$F_3C_6H_2CHO$	70	**3c**	86
4	*p*-*n*-$BuOC_6H_4CHO$	120	**3d**	97
5	*p*-FC_6H_4CHO	75	**3e**	94
6	Salicylaldehyde	110	**3f**	Quant.
7	*c*-$C_6H_{11}CHO$	110	**3g**	84
8	*n*-$C_8H_{17}CHO$	6 h	**3h**	83
9	*p*-$NO_2C_6H_4CHO$	150	**3i**	Quant.[d]
10	*E*-PhCH=CHCHO	120	**3j**	Quant.

[a] Ratio: **1**:**2** = 1 equiv (0.5 mmol):1.2 equiv (0.6 mmol).
[b] All products were identified by ^{1}H NMR, IR, MS.
[c] Isolated yields.
[d] Solvent: THF–H_2O = 0.2:0.8 (mL).

occurred. In addition, the maleic acid was also efficient for allylation of α,β-unsaturated aldehyde (quantitative yield, entry 10). Finally, the reaction of the crotylation of benzaldehyde using maleic acid as a promoter in water was carried out. The yield was got in 69%; however, the regioselectivity was poor (α-adduct:γ-adduct = 1.77:1.98).

In summary, we have developed a highly efficient promoter for the allylation of aldehydes in aqueous media. Under the promotion of maleic acid, the allylation of various aldehydes was very fast and afforded high to quantitative yields of desired products in a short period of reaction time under mild conditions.

All the ^{1}H NMR and ^{13}C NMR spectra were recorded with TMS as an internal standard on a Bruker AM-300 or Varian EM-360 (300 and 75 MHz, respectively). IR spectra were recorded on a Nicolet AV360 spectrometer. EI Mass spectra were determined on an HP-5989A spectrometer. Elemental analysis for carbon and hydrogen were performed on a Rapid CHN-O analyzer.

Allyltributyltin was prepared by the reaction of allyl Grignard with *n*-Bu_3SnCl. All carboxylic acids, aldehydes and solvents are commercially available and were used without further purification.

Typical Procedure for the Allylation of Aldehydes

To a solution of maleic acid (57 mg, 0.5 mmol) in H_2O (1.0 mL) were added successively 4-*n*-butoxybenzaldehyde (89 mg, 0.5 mmol) and allyltributyltin (198 mg, 0.6 mmol) at r.t. After its completion (120 min, monitored by TLC), the reaction was quenched with aq NaOH (2 M, 2 mL). Then extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to furnish the crude product, which was purified by silica gel chromatography [typical eluent: petroleum ether–EtOAc = 15:1(v/v)] to afford 1-(4-*n*-butoxyphenyl)-3-buten-1-ol (**3d**).

1-(4-*n*-butoxyphenyl)-3-buten-1-ol (3d)

Yield 107 mg, 97%; R_f = 0.81(petroleum ether–EtOAc = 7:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, 2 H, *J* = 8.3 Hz), 6.86 (d, 2 H, *J* = 8.5 Hz), 5.84–5.75 (m, 1 H), 5.18–5.11 (m, 2 H), 4.66 (t, 1 H, *J* = 6.4 Hz), 3.93 (t, 2 H, *J* = 6.3 Hz), 2.47 (t, 2 H, *J* = 6.2, 6.8 Hz), 1.97 (s, 1 H), 1.81–1.72 (m, 2 H), 1.53–1.45 (m, 2 H), 0.95 (t, 3 H, *J* = 7.8, 6.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.7, 135.9, 134.6, 127.0, 118.0, 114.4, 73.0, 67.8, 43.6, 31.3, 19.2, 13.7. IR (KBr, film): ν = 3415, 3075, 2959, 2873, 1640, 1612, 1512, 1240 cm^{-1}. MS (EI, 70 eV): *m*/*z* = 220 [M^+], 179, 123, 95, 77, 41. Anal. Calcd for $C_{14}H_{20}O_2$ (220.31): C, 76.33; H, 9.15. Found: C, 75.94; H, 9.31.

Acknowledgment

Financial support by the Major State of Basic Research Development Program (No.G2000048007), the National Natural Science Foundation of China, QT Program and Shanghai Natural Science Council are gratefully acknowledged.

References

(1) For recent reviews see: (a) Davies, A. G. *Organotin Chemistry*; Wiley-VCH: Weinheim, **2004**. (b) *Main Group Metals in Organic Synthesis*, Vol. 2; Yamamoto, H.; Oshima, K., Eds.; Wiley-VCH: Weinheim, **2004**. (c) Junzo, O. *Modern Carbonyl Chemistry*; Wiley-VCH: Weinheim, **2000**. (d) Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163. (e) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31. (f) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207. (g) Nishigaichi, Y.; Takuwa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395.

(2) (a) Cornils, B.; Wolfgang, A. In *Aqueous-Phase Organometallic Catalysis: Concepts and Applications*, 2nd ed.; Wiley-VCH: Weinheim, **2004**. (b) Kobayashi, S.; Manabe, K.; Nagayama, S. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, **2000**. (c) Li, C.-J. *Chem. Rev.* **1993**, *93*, 2023.

(3) Yanagisawa, A.; Morodome, M.; Nakashima, H.; Yamamoto, H. *Synlett* **1997**, 1309.

(4) Lewis acids and Brønsted acids see: (a) Kobayashi, S.; Aoyama, N.; Manabe, K. *Synlett* **2002**, 483. (b) Shibata, I.; Yoshimura, N.; Yabu, M.; Baba, A. *Eur. J. Org. Chem.* **2001**, 3207. (c) Loh, T.-P.; Xu, J.; Hu, Q.-Y.; Vittal, J. J. *Tetrahedron: Asymmetry* **2000**, *11*, 1565. (d) Loh, T.-P.; Zhou, J.-R. *Tetrahedron Lett.* **2000**, *41*, 5261. (e) Loh, T.-P.; Xu, J. *Tetrahedron Lett.* **1999**, *40*, 2431.

(5) Li, G.-L.; Zhao, G. *J. Org. Chem.* **2005**, *70*, 4272.

(6) The values are cited from: (a) David, R. L. *CRC Handbook of Chemistry and Physics*, 78th ed.; Boca Raton, CRC Press: New York, **1997**. (b) Hand, C. W.; Blewitt, H. L. *Acid-Base Chemistry*; Macmillan Publishing Co.: New York, **1986**.