Allylation reactions of aromatic aldehydes and ketones with lithium in THF under ultrasonic irradiation

Yan-Jiang Bian[a]*, Jian-You Zhang[a], Ji-Tai Li[b]

[a]Department Of Chemistry, Langfang Normal College, Hebei, Langfang 065000, P. R. China

[b]College of Chemistry and Environmental Science, Hebei University, Baoding 071002, P.R China

The allylation reactions of aromatic aldehydes and ketones were carried out in 69–90% yield using Li–THF system under ultrasound irradiation at r.t. for 40 min. The reactions of the same system with stirring gave homoallyl alcohols in 49–67% yield at r.t. for 4 h.

Keywords: ultrasound irradiation, allylation, lithium

Carbon–carbon bond formation is the essence of organic synthesis. A powerful method for constructing carbon–carbon bond is the allylation reaction between an allyl halide and carbonyl compounds.[1] Metals such as tin,[2-6] indium,[7] samarium,[8] gallium,[9] yetterbium,[10] manganese,[11] magnesium,[12] zinc,[13-18] have been found to be effective for such transformations. However, there were always difficulties due to long reaction times or reduction reactions.

Ultrasound has increasingly been used in organic synthesis. Many metal-mediated organic reactions have been accelerated under ultrasound.[19-23] A search of the literature revealed that no report has appeared on the results of the allylation reactions using lithium to date. Herein, we report the results of the allylation reactions of aromatic aldehydes and ketones by Li with stirring or under ultrasound irradiation respectively.

In order to optimise the conditions we screened the reaction of benzaldehyde with allyl bromide in a variety of Li–THF reaction systems (Table 1). From the results in Table 1, the optimum reaction conditions are benzaldehyde: allyl bromide: Li = 1:3:8, time: 40 min. In order to demonstrate the positive effect of ultrasound irradiation on the reaction, the same reaction in entry (**a–i**) (Table 2) also has been studied under stirring.

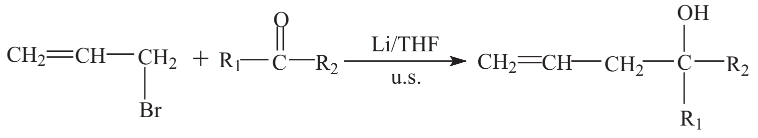
As shown in Table 2, the allylation reaction was carried out under ultrasonic irradiation giving higher yield. For example, benzaldehyde (**1a**), furfural (**1c**) and piperonal (**1e**) reacted with allyl bromide in Li–THF system giving nearly quantitative yields of the corresponding homoallylic alcohols (**2a**, **2c**, **2e**) under ultrasonic irradiation for 40 min. In the case of stirring for 4 h, the yields of the corresponding homoallylic

Table 1 Optimisation of the allylation reaction of C_6H_5CHO mediated by Li in THF under ultrasonic irradiation with various conditions

Entry	Reaction system	THF/ml	Time/min	Isolated yield/%
1	Benzaldehyde:allyl bromide:Li = 1:1:1	4	40	41
2	Benzaldehyde:allyl bromide:Li = 1:2:1	4	40	53
3	Benzaldehyde:allyl bromide:Li = 1:3:1	4	40	62
4	Benzaldehyde:allyl bromide:Li = 1:4:1	4	40	62.4
5	Benzaldehyde:allyl bromide:Li = 1:3:2	4	40	75
6	Benzaldehyde:allyl bromide:Li = 1:3:4	4	40	79
7	Benzaldehyde:allyl bromide:Li = 1:3:6	4	40	88
8	Benzaldehyde:allyl bromide:Li = 1:3:8	4	40	90
9	Benzaldehyde:allyl bromide:Li = 1:3:9	4	40	90.2
10	Benzaldehyde:allyl bromide:Li = 1:3:8	4	50	90.3

Isolated yield based on the substrate; THF: 4 ml; ultrasound irradiation: 40KHz: temperature: r. t.

Table 2 The allylation reactions of aromatic aldehydes and ketones mediated by Li in THF under ultrasound irradiation or stirring



1 (a-h) **2 (a-h)**

Entry	Substrate	Isolated yield/%		R_f^*
		Stirring (4 h)	Ultrasound (40 min)	
1a	C_6H_5CHO	66	90	0.61
1b	$4\text{-}ClC_6H_4CHO$	66	83	0.59
1c	Furfural	54	90	0.52
1d	Cinnamaldehyde	49	75	0.68
1e	$3,4\text{-}(OCH_2O)C_6H_3CHO$	67	89	0.53
1f	$4\text{-}CH_3OC_6H_4CHO$	59	81	0.50
1g	$C_6H_5COC_6H_5$	56	70	0.81
1h	$C_6H_5COCH_3$	57	69	0.68

Isolated yield based on the substrate; Ultrasound irradiation time for 40 min and stirring for 4 h.
[a]Eluant: petroleum ether: diethyl ether (V:V) = 1:1

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* Correspondent. E-mail: bianyanjiang@126.com

alcohols were only 66, 54 and 67% respectively. The data indicates that the reaction time is reduced and the yields are improved under ultrasound irradiation condition. In order to examine the effects of the carbonyl group of ketone, we choose benzophenone (**1g**) and acetophenone (**1h**) as substrates. It was found that the corresponding products were obtained respectively in 70 and 69% yield under ultrasound irradiation. We infer that the steric hindrance around the carbonyl group may inhibit the allylation reactions.

Based on these results, we have demonstrated that ultrasound irradiation can markedly speed up the allylation reaction of aromatic aldehydes and ketones with Li–THF system. The main advantage of the present procedure is the higher yield and the shorter reaction time. This new approach has considerable practical value due to its efficiency and simplicity.

Experimental

Liquid substrates were distilled before use. IR spectra were recorded on a Bio-Rad FTS-40 spectrometer (KBr). MS spectra were determined on an AEI MS-50 SD90 spectrometer (EI, 70 eV). ^{1}H NMR spectra were measured on VXR-300S spectrometer (300 MHz) by using $CDCl_3$ as solvent and TMS as internal standard. Sonication was performed in a Shanghai SK8200LH ultrasonic cleaner (with a frequency of 40k Hz and a nominal power 500W; Shanghai Kudos Ultrasonic Instrument Co., Ltd). The reaction flask was located at the maximum energy area in the cleaner, where the surface of reactants is slightly lower than the level of the water. The reaction temperature was controlled by addition or removal of water from ultrasonic bath.

A 50 ml Pyrex flask was charged with the desired aldehyde or ketone (1 mmol), allyl bromide (3 mmol), lithium (8 mmol) and THF(4 ml). The mixture was irradiated in the water bath of an ultrasonic cleaner in air at 25–30°C for 40 min (or stirring 4 h). After the completion of the reaction, the resulting suspension was filtered to remove the Li. The filtrate was extracted with ethyl acetate (3 × 10 ml). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over anhydrous magnesium sulfate for 12 h. Ethyl acetate was evaporated under reduced pressure to give the crude product, which was separated by column chromatography on silica (200–300 mesh), eluted with a mixture of petroleum ether and diethyl ether. All the products were identified by their IR, MS, ^{1}H NMR, spectral data.

2a:[24] Oil; ^{1}H NMR: δ_H2.40 (t, J = 6.6 Hz, 2H), 2.90–2.98 (br, 1H), 4.58 (t, J = 6.6 Hz, 1H), 5.02–5.05 (m, 1H), 5.04–5.06 (m, 1H), 5.64–5.70 (m, 1H), 7.25–7.68 (m, 5H). MS *m/z* (%): 148 (M$^+$). IR (KBr) ν 3405, 1191, 990 cm^{-1}.

2b:[24] Oil; ^{1}H NMR: δ_H2.41 (t, J = 6.6 Hz, 2H), 3.03–3.10 (br, 1H), 4.57 (t, J = 6.6 Hz, 1H), 5.05–5.08 (m, 1H), 5.10 (m, 1H), 5.68–5.72 (m, 1H), 7.18 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H). MS *m/z* (%): 182 (M$^+$). IR (KBr) ν 3406, 1195, 985 cm^{-1}.

2c:[24] Oil; ^{1}H NMR: δ_H 1.90–2.15 (br, 1H), 2.63 (q, J = 7.1 Hz, 2H), 4.72 (t, J = 7.1 Hz, 1H), 5.15–5.18 (m, 1H), 5.15–5.20 (m, 1H), 5.76–5.82 (m, 1H), 6.28–6.36 (m, J = 3.3 Hz, 1H), 7.26–7.40 (m, J = 3.3 Hz, 1H). MS *m/z* (%): 138 (M$^+$). IR (KBr) ν 3401, 1192, 992 cm^{-1}.

2d:[24] Oil; ^{1}H NMR: δ_H 2.02 (1H, s), 2.40–2.50 (2H, m), 4.32–4.44 (1H, t), 5.14–5.26 (2H, m), 5.78–5.88 (1H, m), 6.60–6.72 (1H, m), 7.18–7.40 (5H, m). MS *m/z* (%): 174 (M$^+$). IR (KBr) ν 3400, 1642, 988 cm^{-1}.

2e:[24] Oil; ^{1}H NMR: δ_H 2.40 (t, J = 6.4 Hz, 2H), 2.49–2.60 (br, 1H), 4.56 (t, J = 6.4 Hz, 1H), 5.08 (m, 1H), 5.10 (m, 1H), 5.68–5.76 (m, 1H), 5.90 (s, 2H), 6.68–6.74 (m, 2H), 6.80 (s, 1H). MS *m/z* (%): 192 (M$^+$). IR (KBr) ν 3420, 1192, 990 cm^{-1}.

2f:[24] Oil; ^{1}H NMR: δ_H 2.43 (q, J = 6.6 Hz, 2H), 2.79–2.86 (br, 1H), 3.76 (s, 3H), 4.61 (t, J = 6.6, 1H), 5.04–5.09 (m, 1H), 5.08–5.12 (m, 1H), 5.72–5.82 (m, 1H), 6.82 (d, J = 8.8, 2H), 7.21 (d, J = 8.8, 2H). MS *m/z* (%): 178 (M$^+$). IR (KBr) ν 3410, 1191, 991.

2g:[24] Oil; ^{1}H NMR: δ_H 2.48–2.72 (s, 1H), 3.12–3.40 (d, 2H), 5.12–5.58 (d, 2H), 5.68–6.02 (m, 1H), 6.96–7.80 (m, 10H). MS *m/z* (%): 224 (M$^+$). IR (KBr) ν 3505, 1196, 994.

2h:[24] Oil; ^{1}H NMR: δ_H 1.23–1.42 (s, 3H), 1.48–1.73 (s, 1H), 2.26–2.60 (d, 2H), 4.62–5.08 (d, 2H), 5.16–5.69 (m, 1H), 6.86–7.39 (m, 5H). MS *m/z* (%): 162 (M$^+$). IR (KBr) ν 3430, 1192, 990.

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