



Solvent- and catalyst-free *gem*-bisallylation of carboxylic acid derivatives with allylzinc bromide

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ABSTRACT

A rapid and efficient procedure for the solvent-free synthesis of *gem*-bisallylation products has been achieved by allylzinc bromide with carboxylic acid derivatives in the absence of any catalysts at room temperature.

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The addition reaction of organometallics and carbonyl compounds provides a fundamental methodology in synthetic organic chemistry.¹ Monoallylation and *gem*-bisallylation typically give homoallylic alcohol and bisallyl alkyl carbinol, which have potential for use in the synthesis of variety of compounds including hydroxyl lactone and spirolactone.² Various carbonyl compounds are widely used as convenient starting materials for such transformations. Usually, homoallylic alcohols were obtained utilizing these methods, but little attention has been paid to the geminal bisallylation of carbonyl compounds.³ The bisallylation reaction has been just developed in recent 10 years, and different methods have been just developed based on the use of a variety of metals such as In,⁴ Sm,⁵ Zn,⁶ and Al.⁷

Organozinc reagents have been known for more than 150 years.⁸ However, their applications in organic synthesis were limited to very specific reactions due to their moderate reactivity. These reagents were soon replaced by the more reactive organomagnesium and organolithium reagents which found broad applications in organic synthesis. However, it became clear that this high reactivity has some drawbacks, such as low chemoselectivity and only allowing R groups bearing relatively few functionalities. It was noticed that organozinc reagents could be easily prepared and have higher functional group compatibility in comparison with organolithium and Grignard reagents. Furthermore, the low reactivity of organozinc reagents could be increased by adding transition metal catalyst.^{9–11} Today, organozinc compounds are one of the most useful organometallic reagents. The applications of organozinc compounds range from asymmetric synthesis, preparation of biologically relevant molecules, and new materials in combinatorial chemistry.

The elimination of volatile organic solvents in organic syntheses is the most important goal in 'green' chemistry. Recently, solvent-free reactions have received increasing attentions because of the advantages: short reaction time, high yield, low costs, reduced pollution, and simplicity in process and handling.¹² As environmentally friendly 'green' synthesis has become more important, chemists have been searching for solvent-free reactions under mild conditions.¹³

Research work on organozinc halides has been performed in our laboratory over the past few years.¹⁴ With our increasing interests in efficient, economic, and environmentally friendly reactions, we have explored the reaction of organozinc reagents under solvent-free conditions. In this Letter, we wish to report a convenient, environmentally friendly, and efficient *gem*-bisallylation of acid chloride, acid anhydride, and ester using allylzinc bromide under solvent-free conditions.

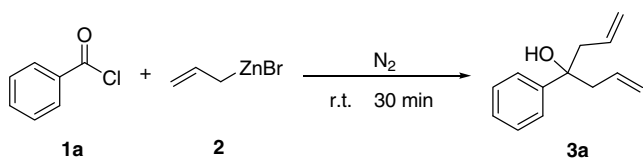
The *gem*-bisallylation reaction of benzoyl chloride (**1a**) and allylzinc bromide (**2**) was selected as model reaction for optimizing reaction conditions. The results are summarized in Table 1. It was found that the best result for formation of 4-phenylhepta-1,6-dien-4-ol (**3a**) could be obtained when the relative molar ratio of **2**:**1a** was increased to 4:1 (Table 1, entry 3). Although **3a** could be obtained in the presence of THF as solvent, the reaction proceeded more smoothly and efficiently under solvent-free conditions. It is evident that the molar ratio of 4 (**2**):**1a**) is essential for obtaining a maximum yield under solvent-free conditions.

With these encouraging results listed in Table 1, we investigated the *gem*-bisallylation reactions further with a number of carboxylic acid derivatives including acid chlorides, carboxylic esters, and acid anhydrides under the conditions established above. The results are summarized in Table 2.

From the results shown in Table 2, it can be seen that most of the reactions proceeded smoothly at room temperature in good to excellent yields. In general, bisallylation of aromatic acid

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Table 1
Optimized conditions via *gem*-bisallylation reaction of **1a** and **2**^a

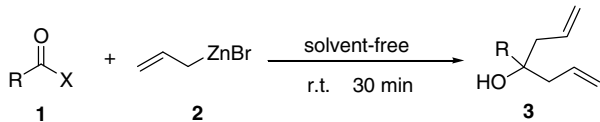


Entry	Solvent	Molar ratio of 2/1a	Yield of 3a ^b (%)
1	None	2	68
2	None	3	87
3	None	4	96
4	THF	4	91
5	CH ₂ Cl ₂	4	96
6	C ₆ H ₆	4	95
7	Et ₂ O	4	92
8	DMF	4	0

^a Reaction conditions: at room temperature under nitrogen for 30 min.

^b Isolated yield.

Table 2
gem-Bisallylation reaction of derivatives of carboxylic acids with allylzinc bromide^a



R= aryl, alkyl
X= Cl, Br, OR', OCOR'

Entry	R	X	Product ^b	Yield ^c (%)
1	C ₆ H ₅	Cl		96
2	<i>p</i> -Cl-C ₆ H ₅	Cl		83 (91) ^d
3	<i>o</i> -Cl-C ₆ H ₅	Cl		88
4	<i>p</i> -CH ₃ O-C ₆ H ₄	Cl		77
5	<i>m</i> -CH ₃ -C ₆ H ₄	Cl		92
6	C ₆ H ₅ -CH=CH	Cl		82
7	2-Furyl	Cl		92

Table 2 (continued)

Entry	R	X	Product ^b	Yield ^c (%)
8	CH ₃	Cl		70
9	C ₂ H ₅	Cl		74
10	BrCH ₂	Br		81
11	Ph	OCH ₃		88
12	<i>m</i> -CH ₃ -C ₆ H ₄	OC ₂ H ₅		92
13	Ph	OCH ₂ Ph		68
14	BrCH ₂	OCH ₃		92
15	BrCH ₂	OC ₂ H ₅		89
16	CH ₂ CH	OCH ₃		68
17	CH ₂ CH	OC ₂ H ₅		66
18	Ph	OCOPh		90
19				70

^a Reaction conditions: carboxylic acid derivatives (2.0 mmol), allylzinc bromide (8.0 mmol), solvent-free, at room temperature under nitrogen for 30 min.

^b All products were characterized by IR, ¹H NMR, ¹³C NMR, and MS.

^c Isolated yield.

^d The reaction temperature was reduced with a ice-water bath (about at 0–5 °C).

chlorides (Table 2, entries 1–7) gave the corresponding products in good to excellent yields under solvent-free conditions. Aliphatic acid chlorides were also bisallylated smoothly under the same conditions in good yields (Table 2, entries 8–10). It was concluded that electron-withdrawing or donating groups on the aromatic ring of aromatic acid chlorides did not seem to affect the reaction significantly in the yield of products. But the position of the substituent on the phenyl ring affects the product yields. For example, 2-chlorobenzoylate (Table 2, entry 3) and 4-chlorobenzoylate (Table 2, entry 2) afforded allylated products in the yield of 88 and 75%, respectively. And the yields of the *gem*-bisallylation reaction of acid chlorides, carboxylic esters, and acid anhydrides decrease in sequence. For example, benzoyl chloride, benzoic anhydride, and methyl benzoate reacted with allylzinc bromide to give the same *gem*-bisallylated products of **3a** in 96%, 90%, and 88% yields, respectively (Table 2, entries 1, 11, 18). Furthermore, allylzinc bromide would react with cyclic anhydrides such as isobenzofuran-1,3-dione to generate the corresponding *gem*-bisallylated esters, and the product yield is 70% (Table 2, entry 19).

In conclusion, we have developed a novel and simple procedure for the *gem*-bisallylation of carboxylic acid derivatives using allylzinc bromide under solvent-free and catalyst-free conditions at room temperature.¹⁵ The reaction here has the following advantages: milder conditions, shorter reaction times, environmentally benign, and high yield.

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- General experimental procedure for gem-bisallylation of carboxylic acid derivatives*: Organozinc halides RZnX (8.0 mmol) were prepared according to Knochel's procedure.¹⁰ The solvent (THF) of the RZnX was removed in vacuo, then carboxylic acid derivatives (2.0 mmol) were added slowly, and the resulting mixture stirred for 30 min. After complete conversion as indicated by TLC, the reaction mixture was quenched with aqueous saturated NH₄Cl (10 mL) and extracted with Et₂O (3 × 10 mL). The combined organic extracts were dried over anhydrous MgSO₄ and concentrated. The resulting product was purified by column chromatograph on silica gel (petroleum/ethyl acetate 40:1) to afford the pure product. Typical spectra data are as follows: 4-Phenylhepta-1,6-dien-4-ol (**3a**) IR (ν/cm⁻¹): 3356, 3074, 2924, 1639, 1441, 1340, 1053, 1035, 998, 918; ¹H NMR (400 MHz, CDCl₃, TMS): δ = 7.42–7.22 (m, 5H), 5.66–5.56 (m, 2H), 5.13–5.07 (m, 4H), 2.72–2.49 (m, 4H), 2.09 (s, 1H), ¹³C NMR (100 MHz, CDCl₃): δ = 133.4, 128.1, 128.1, 126.6, 125.2, 119.2, 75.0, 46.8; EI-MS (m/z, %): 147 (M⁺–41, 10.13), 105 (100.00), 77 (53.99), 51 (18.75), 41 (28.91), 39 (28.07). 3,3-Diallylisobenzofuran-1(3H)-one (**3I**) IR (ν/cm⁻¹): 3508, 3079, 2911, 1726, 1642, 1466, 1286, 1080, 997, 923; ¹H NMR (400 MHz, CDCl₃, TMS): δ = 7.87–7.27 (m, 4H), 5.60–5.50 (m, 2H), 5.06 (t, J = 8.0 Hz, 4H), 2.79–2.64 (m, 4H); ¹³C NMR (100 MHz, CDCl₃): δ = 169.8, 151.5, 133.8, 130.6, 129.0, 126.8, 125.6, 121.5, 120.3, 88.2, 42.6; EI-MS (m/z, %): 215 (M⁺+1, 0.48), 214 (M⁺, 6.2), 173 (100.00), 131 (1.58), 117 (80.76), 76 (38.03), 39 (53.32).