Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters 48 (2007) 6348–6351
Tetrahedron Letters

An efficient of Grignard-type procedure for the preparation of *gem*-diallylated compound

Kao-Hsien Shen, Chun-Wei Kuo and Ching-Fa Yao*

Department of Chemistry, National Taiwan Normal University 88, Sec. 4, Tingchow Road, Taipei 116, Taiwan, ROC

Received 17 January 2007; revised 2 July 2007; accepted 3 July 2007
Available online 10 July 2007

Abstract—An efficient and a new procedure for the conversion of various carboxylic acid derivatives into the corresponding *gem*-diallylated compound under mild reaction condition has been developed. The triallylaluminum mediated Grignard-type addition of carboxylic acid derivative was utilized as a key operation to affect the transformation. The procedure is operationally simple, giving good to excellent product yields for a broad range of substrates. The chemoselectivity and regioselectivity of triallylaluminum were also demonstrated.

The allylation of carbonyl derivative is of great interest in carbon–carbon bond formation, due to the versatility of homoallylic alcohol as synthetic intermediate.[1] Monoallylation and *gem*-diallylation typically give homoallylic alcohol and diallyl alkyl carbinol, which have potential for the use in the synthesis of variety of compounds, including hydroxyl lactone and spirolactone.[2] Different types of metal including In, Sm, Mg, Zn, and Si have been used for this purpose.[3] Reports of the *gem*-diallylation of the derivative of carboxylic acid using organoaluminum reagent are relatively rare. It has been reported that aldehyde, ketone, and imine can be efficiently allylated in the presence of catalytic amount of a metal salt, such as $PbBr_2$ and $TiCl_4$, wherein aluminum acts as an electron pool and the metal salt functions as an electron transfer catalyst.[4] However, *gem*-diallylation reaction of the derivative of carboxylic acid, especially acyl azide, has not been investigated in great detail.[5] It is noteworthy that, in a study of the reaction of organometallic compound with iminoether, organoaluminum compound was reported to react, but only a few organoaluminum compound was examined and only the ester derivative were tested as a reactant.[6] As a result, based on the available data it is difficult to evaluate the utility of the reaction with respect to reaction of other carboxylic acid derivatives. Thus, it would be desirable to develop an efficient method for the *gem*-diallylation of a wide variety of substrates with allylaluminum compound in a Grignard-type addition, since aluminum is an inexpensive and convenient alternative to conventionally used metal, such as samarium and silicon. In this Letter, we wish to report on a convenient and an efficient procedure for the *gem*-diallylation of acid chloride, acid anhydride, acid azide, and ester using triallylaluminum **1** in excellent to good yields.

Allylaluminum reagents are typically prepared by coupling a commercially available organoaluminum chloride such as Me_2AlCl with an appropriate Grignard or lithium regent.[7] However, we used a different method for the preparation of triallylaluminum **1**, following a procedure reported in the literature.[8,9] Triallylaluminum was prepared by reacting allyl bromide and pure elemental Al in refluxing ether, followed by the concentration of the reaction mixture (Scheme 1). We previously reported that triallylaluminum reacts with aldehydes, ketones, aldimines and ketimines in excellent yields.[10] Herein, we report on the efficient *gem*-diallylation of a variety of carboxylic acid derivatives with triallylaluminum **1** in ether solution, to yield various 4-hydroxypenta-1,6-dienes **3** (Scheme 2).

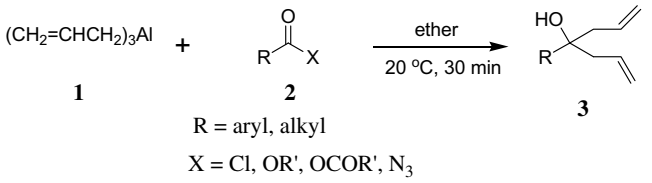
In a preliminary experiment, benzoyl chloride was reacted with triallylaluminum (0.9 mmol) in anhydrous

$$3\,CH_2{=}CHCH_2Br + 2\,Al \xrightarrow[\text{reflux}]{\text{ether}} \underset{\mathbf{1}}{(CH_2{=}CHCH_2)_3Al} + AlBr_3$$

Scheme 1.

* Corresponding author. Tel./fax: +886 2 2930 9092; e-mail: cheyaocf@scc.ntnu.edu.tw

0040-4039/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2007.07.008



Scheme 2.

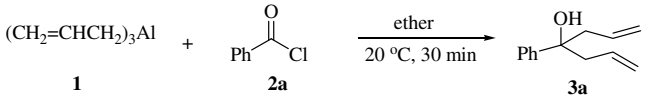
ether at 20 °C, to give the corresponding *gem*-diallylation product in 60% yield after 30 min. In order to increase the product yield, we gradually increased the amount of triallylaluminum and the results are shown in Table 1. From Table 1, it is evident that 1.2 mmol of triallylaluminum is essential for obtaining a maximum yield.

With this encouraging result in hand, we then investigated other derivatives of carboxylic acids including acid chlorides, carboxylic esters, acid anhydrides, and acyl azides under the optimized conditions and the results are summarized in Table 2. The corresponding *gem*-diallylated products are produced in good to excellent yields, starting from a relatively wide variety of derivatives. Both aromatic and aliphatic substrates are converted smoothly to the corresponding *gem*-diallylated products in good to excellent yields.

Both aromatic and aliphatic substrates were converted to the corresponding diallyl alkyl carbinols in excellent yields. The results clearly show that a substituent on the phenyl ring, whether electron-donating or electron-withdrawing, had almost no influence on the reactions. Further, the position of the substituent on the phenyl ring does not affect the product yields. For example, 4-methylbenzoylate **2j** (entry 10) and 4-chlorobenzoylate **2l** (entry 12) afforded allylated products in excellent yields. Similarly, the use of the corresponding 2-substituted benzoyl chloride **2c** (entry 3) and 2-substituted benzoylate **2k** and **2m** (entries 11 and 13) also resulted in excellent yields. Sterically hindered acid anhydrides such as methyl pivalate **2r** (entry 18) and isobutyric anhydride **2w** (entry 23) also afforded good yields of products.

It is noteworthy that this is the first example of the *gem*-diallylation of 1-adamantanecarbonyl chloride and azide with an organometallic reagent. The higher yield

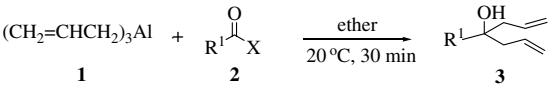
Table 1. Effect of the loading of triallylaluminum in a reaction with benzoyl chloride[a]

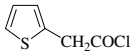
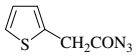


Entry	1	3a[b] (%)
1	0.9	60
2	1.0	72
3	1.2	97

[a] All reactions were carried out with benzoyl chloride (1.0 mmol), ether (3 mL) and triallylaluminum at 20 °C under nitrogen for 30 min.
[b] Isolated yield for pure products.

Table 2. Reaction of derivates of carboxylic acids with triallylaluminum **1** to generate *gem*-bisallylated alcohols **3**[a]



Entry	2	R^1	X	3	Yields[b] (%)
1	**2a**	Ph	Cl	**3a**	97
2	**2b**	4-ClC_6H_4	Cl	**3b**	98
3	**2c**	2-ClC_6H_4	Cl	**3c**	97
4	**2d**	Benzyl	Cl	**3d**	98
5	**2e**	Et	Cl	**3e**	98
6	**2f**	1-Adamantyl	Cl	**3f**	94
7	**2g**	2-Thienyl	Cl	**3g**	92
8	**2h**			**3h**	98
9	**2i**	Ph	OCH_3	**3a**	98
10	**2j**	4-MeC_6H_4	OCH_3	**3i**	98
11	**2k**	2-MeC_6H_4	OCH_3	**3j**	96
12	**2l**	4-ClC_6H_4	OCH_3	**3b**	98
13	**2m**	2-ClC_6H_4	OCH_3	**3c**	97
14	**2n**	Benzyl	OCH_3	**3d**	98
15	**2o**	2-Thienyl	OCH_3	**3g**	98
16	**2p**	Pr	OCH_3	**3k**	91
17	**2q**	CH_3	OCH_3	**3l**	98
18	**2r**	*t*-Bu	OCH_3	**3m**	96
19	**2s**	Ph	OC_6H_5	**3a**	98
20	**2t**	CH_3	$OCOCH_3$	**3l**	98
21	**2u**	Ph	OCOPh	**3a**	98
22	**2v**	Pr	OCOPr	**3k**	98
23	**2w**	*i*-Pr	$OCOPr^i$	**3n**	81
24	**2x**	Ph	N_3	**3a**	88
25	**2y**	4-ClC_6H_4	N_3	**3b**	98
26	**2z**	Benzyl	N_3	**3d**	88
27	**2aa**	1-Adamantyl	N_3	**3f**	92
28	**2ab**			**3h**	84

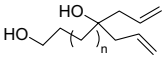
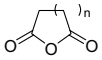
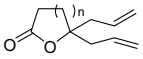
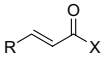
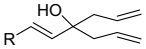
[a] All reactions were carried out with substrate (1.0 mmol) and triallylaluminum (1.2 mmol) in ether (3 mL) at 20 °C under nitrogen for 30 min.
[b] Isolated yields for pure products.

obtained with 1-adamantanecarbonyl chloride **2f** (entry 6) and 1-adamantanecarbonyl azide **2aa** (entry 27) demonstrates the versatile nature of triallylaluminum as an efficient *gem*-allylating agent for a wide range of substrates and these types of sterically rigid structures are helpful in studying face selectivity.[12]

As above, triallylaluminum has been employed with carboxylic esters to give the corresponding *gem*-diallyl alkyl carbinols. Moreover, this reagent would react with lactones such as γ-butylactone **4** and δ-valerlactone **5** to give the corresponding *gem*-diallyl alkyl carbinols **6** and **7** in 81% and 84% yields, respectively (Table 3, entries 1 and 2). Furthermore, this reagent would react with cyclic anhydrides such as succinic anhydride **8** and glutaric anhydrides **9** to generate the corresponding *gem*-diallylated esters in good yields, and the product yields are 94% and 71%, respectively (Table 3, entries 3 and 4).

The regioselectivity of triallylaluminum was confirmed by extending the scope of this reagent to cinnamoyl

Table 3. Reaction of derivates of carboxylic acids with triallylaluminum **1** to generate *gem*-diallyl alkyl carbinols

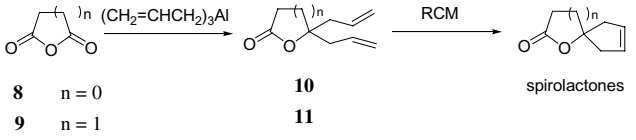
Entry[a]	Substrate		Product		Yields[b] (%)
1		**4** $n = 0$		**6**	81
2		**5** $n = 1$		**7**	84
3		**8** $n = 0$		**10**	94
4		**9** $n = 1$		**11**	71
5		**12** R = Ph, X = Cl		**16**	98
6		**13** R = Ph, X = N_3		**16**	96
7		**14** R = Ph, X = OCH_3		**16**	92
8		**15** R = CH_3, X = OCH_3		**17**	81

[a] All reactions were carried out with substrate (1.0 mmol) and triallylaluminum (1.2 mmol) in THF (3 mL) at 20 °C under nitrogen for 30 min.
[b] Isolated yields for pure products.

derivatives such as cinnamoyl chloride **12**, cinnamoyl azide **13**, and methyl cinnamate **14** to generate the corresponding *gem*-diallyl alkyl carbinols in excellent yields (98%, 96% and 92%). The triallylaluminum reagent is also shown chemoselective when methyl crotonate **15** was used as a substrate, only the 1,2-addition product was obtained selectively, and no 1,4-addition product was detected (Table 3, entries 8).

Compared to other organometallic allylation reagents, the preparation of triallylaluminum is relatively easy and the operation procedures are quite simple and convenient. For example, the preparation of allylsamarium reagents from samarium metal and allyl bromide is more expensive and reactions of allylsamarium are limited to acid azides, acid chlorides do not react with allylsamarium, **3f** and allyltrimethylsilane requires a longer time (16 h) and lower temperature (−60 °C).[12b] Similarly, the preparation of allylzinc is also troublesome, requiring a longer reaction time and the use of allyltin reagents is environmentally harmful due to its toxic nature. Spirolactones are important structural units, and spirobicyclic cores display an important role in the development of new bioactive substances.[2] 5,5-Diallyldihydro-furan-2-one **10** and 6,6-diallyl-tetrahydro-pyran-2-one **11** can be easily converted into spirolactones, which have been reported.[11] The preparation of spirolactones uses a sequence involving allylation of cyclic anhydrides followed by ring closing metathesis (RCM) (Scheme 3).

In conclusion, we report on the development of a simple and general procedure for the *gem*-diallylation of derivatives of carboxylic acids using triallylaluminum.[13] The advantages of the reaction are as follows: (1) the reaction is applicable to a wide variety of carboxyl derivatives, (2) the preparation of triallylaluminum is relatively straightforward, (3) the reaction time is short, (4) the reaction proceeds at room temperature, (5) the product yields are high and (6) the reaction proceeds, even when sterically hindered starting products are employed. To the best of our knowledge, this is the first report of the use of triallylaluminum as a reagent for the *gem*-diallylation of acid chlorides, acid anhydrides, and acyl azides. Because of the advantages listed above, the preparation of *gem*-diallylated alcohols using triallylaluminum makes this method an attractive alternative to existing processes.



Scheme 3.

Acknowledgements

Financial support provided by the National Science Council of the Republic of China and National Taiwan Normal University (96TOP001) is gratefully acknowledged. We also thank Professor Dr. Milton. S. Feather, for his helpful discussions during the preparation of this manuscript.

References and notes

1. For a review, see: (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207; (b) Hoffman, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555; (c) Marshall, J. A. *CHEMTRACTS* **1992**, *5*, 75; (d) Jia, Y.; Zhang, M.; Tao, F.; Zhou, J. *Synth. Commun.* **2002**, *32*, 2829; (e) Sormunen, G. J.; Lewis, D. E. *Synth. Commun.* **2004**, *34*, 3473.
2. (a) Bardshiri, E.; Simpson, T. J.; Scott, A. I.; Shishido, K. J. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1765; (b) Geisler, J.; Cleve, A.; Harre, M. *Tetrahedron* **2000**, *56*, 6489; (c) Graul, A. I. *Drug News Perspect.* **2001**, *14*, 12; (d) Rabasseda, X.; Silverstre, J.; Castaner, J. *Drugs Future* **1999**, *24*, 488.
3. For example: (a) Durant, A.; Delplancke, J. L.; Libert, V.; Reisse, J. *Eur. J. Org. Chem.* **1999**, 2845; (b) Machrouhi, F.; Parlea, E.; Namy, J.-L. *Eur. J. Org. Chem.* **1998**, 2431; (c) Bubnov, Y. N.; Misharin, M. A.; Ingnatenko, A. V. *Tetrahedron Lett.* **1997**, *38*, 6259; (d) Snowden, R. L.; Muller, B. L.; Schulte-Elte, K. H. *Tetrahedron Lett.* **1982**, *23*, 335; (e) Tanaka, H.; Nakahata, S.; Watanabe, H.; Zhao, J.; Kuroboshi, M.; Toril, S. *Inorg. Chim. Acta* **1999**, *296*, 204; (f) Li, J.; Liu, Y.; Zhang, Y. *J. Chem. Res. (S)* **2003**, 438; (g) Jia, Y.; Zhang, M.; Tao, F.; Zhou, J. *Synth. Commun.* **2002**, *32*, 2829; (h) Sormunen, G. J.; Lewis, D. E. *Synth. Commun.* **2004**, *34*, 3473; (i) Li, Z.; Zhang, Y. *Tetrahedron* **2002**, *58*, 5301; (j) Ishino, Y.; Mihara, M.; Kageyama, M. *Tetrahedron Lett.* **2002**, *43*, 6601; (k) Pellissier, H.; Wilmouth, S.; Santelli, M. *Bull. Soc. Chim Fr.* **1995**, *132*, 637; (l) Yadav, J. S.; Chand, P. K.; Anjaneyulu, S. *Tetrahedron Lett.* **2002**, *43*, 3783.

4. (a) Uneyama, K.; Kamaki, N.; Moriya, A.; Torii, S. *J. Org. Chem.* **1985**, *50*, 5396; (b) Tanaka, H.; Yamashita, S.; Hamatani, T.; Ikemoto, Y.; Torii, S. *Synth. Commun.* **1987**, *17*, 789; (c) Tanaka, H.; Nakahata, S.; Watanabe, H.; Zhao, J.; Kuroboshi, M.; Toril, S. *Inorg. Chim. Acta* **1999**, *296*, 204.
5. Kataoka, Y.; Makihira, I.; Akiyama, H.; Tani, K. *Tetrahedraon* **1997**, *53*, 9525.
6. Bellassoued, M.; Gaudemar, M. *Bull. Soc. Chim. Belg.* **1986**, *95*, 65.
7. (a) Paley, R. S.; Snow, S. R. *Tetrahedron Lett.* **1990**, *31*, 5853; (b) Rainier, J. D.; Cox, J. M. *Org. Lett.* **2000**, *2*, 2707; (c) Allwein, S. P.; Cox, J. M.; Howard, B. E.; Johnson, H. W. B.; Rainier, J. D. *Tetrahedron* **2002**, *58*, 1997.
8. Triallylaluminum **1** was prepared according to the procedures described in Ref. 10.
9. The concentration of triallylaluminum **1** was determined by the following methods: (a) Gilman, H.; Haubein, A. H. *J. Am. Chem. Soc.* **1944**, *66*, 1515; (b) Bergbreiter, D. E.; Pendergrass, E. *J. Org. Chem.* **1981**, *46*, 219; (c) Bowen, M. E.; Aavula, B. R.; Mash, E. A. *J. Org. Chem.* **2002**, *67*, 9087.
10. Shen, K.-H.; Yao, C.-F. *J. Org. Chem.* **2006**, *71*, 3980.
11. (a) Sabitha, G.; Reddy, C. S.; Babu, R. S.; Yadav, J. S. *Synlett* **2001**, 1787; (b) Michaut, M.; Santelli, M.; Parrain, J.-L. *J. Organomet. Chem.* **2000**, *606*, 93; (c) Michaut, M.; Santeli, M.; Parrain, J.-L. *Tetrahedron Lett.* **2003**, *44*, 2157.
12. (a) Carey, F. A.; Sundberg, R. J. Part A: Structure and Mechanisms. *Advanced Organic Chemistry*, 4th ed.; Kluwer Academic/Plenum: New York, 2000; pp 171–176; (b) Kaselj, M.; Chung, W.-S.; le Noble, W. J. *Chem. Rev.* **1999**, *99*, 1387; (c) Gung, B. W. *Chem. Rev.* **1999**, *99*, 1377.
13. *General procedures for diallylation of derivatives of carboxylic acid*: A typical experimental procedure is described for the *gem*-diallylation of benzoyl chloride **2a** with triallylaluminum **1**. To a stirred solution of benzoyl chloride **2a** (1.0 mmol) in ether (3 mL), the triallylaluminum reagent **1** (1.2 mmol, 0.6 M × 2 mL) was added rapidly at 20 °C under nitrogen. After 30 min., the mixture was quenched by adding ice cold dilute $HCl_{(aq)}$ at 0 °C. The reaction mixture was extracted with Et_2O (3 × 25 mL) and the combined ether layers were dried over anhydrous $MgSO_4$. The mixture was filtered and then the solvent was evaporated under reduced pressure to give a quantitative yield of **3a**. The crude product was passed through a small plug of silica to give pure **3a** as colorless oil in 98% yield. All spectral data are consistent with those reported in the literature. A similar procedure was followed for the *gem*-diallylation of carboxylic esters, anhydrides, and acyl azides. 4-Adamantan-1-yl-hepta-1,6-dien-4-ol (**3f**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.60–1.69 (m, 12H), 1.73 (br s 1H), 1.95–1.99 (m, 3H), 2.29 (dd, 2H, $J = 14.2$, 6.4 Hz), 2.37 (dd, 2H, $J = 14.2$, 6.4 Hz), 5.05–5.09 (m, 4H), 5.86–5.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.6, 36.3, 37.0, 39.0, 40.0, 75.9, 117.7, 135.5; GC/MS: *m*/*z* 246 (M+); HRMS Calcd for $C_{17}H_{26}O$ [M+], 246.1984; found, 246.1981.