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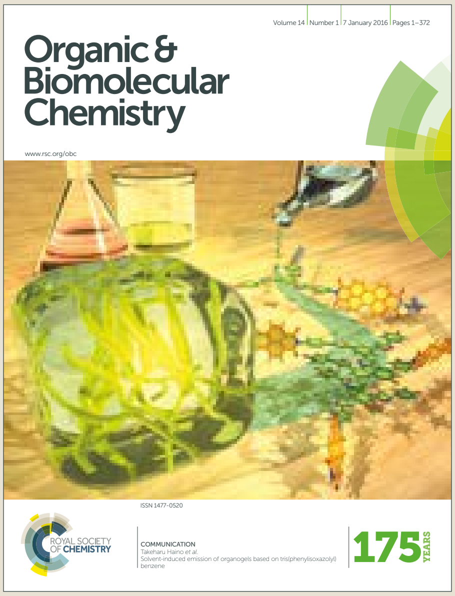

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ARTICLE

Synthesis of 2-Aryloxy Butenoates by Copper-Catalysed Allylic C–H Carboxylation of Allyl Aryl Ethers with Carbon Dioxide

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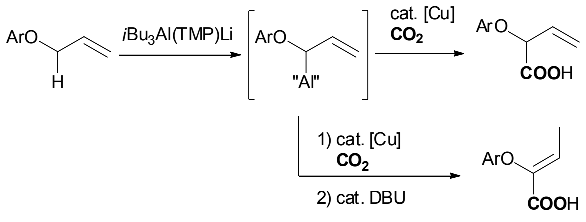
The efficient synthesis of 2-aryloxy-3-butenoic acid esters by the allylic C–H bond carboxylation of allyl aryl ethers with CO_2 has been achieved through the deprotonative alumination with an aluminium ate compound ($i$$Bu_3$Al(TMP)Li) followed by the NHC-copper-catalysed carboxylation of the resulting aryloxy allylaluminum species. Functional groups such as halogens (F, Cl, Br, I), CF_3, amino, methylthio, silyloxy and hetero aromatic groups survived the reaction conditions. The regio- and stereoselective transformation (isomerization) of the 2-aryloxy-3-butenoate products to the (*Z*)-2-aryloxy-2-butenate isomers has also been achieved in the presence of a catalytic amount of DBU. These transformations thus constitute an efficient protocol for the divergent synthesis of both 2-aryloxy-3- and 2-butenonates from a single allyl aryl ether substrate using CO_2 as a C1 building block.

Introduction

The development of efficient and selective methods for the synthesis of 2-aryloxy butenoic acid derivatives is of much interest and importance, because these compounds could serve as useful building blocks for the synthesis of α-aryloxy carboxylic acid derivatives, which are important structural motifs in medicinal and bioorganic chemistry.[1] Among possible approaches for the synthesis of 2-aryloxy butenoic acids,[2] the deprotonative allylic C–H carboxylation of allyl aryl ethers with carbon dioxide (CO_2) could, in principle, be the most efficient and straightforward route. However, such transformation has not been reported previously.[3] A general problem in this approach is the intrinsic instability of an aryloxy allyl metal species generated by the deprotonation of an allyl aryl ether for the carboxylation with CO_2. It was previously shown that the deprotonation of an allylic C–H bond of allyl phenyl ethers by strong bases such as alkyllithium, lithium amide, and *t*BuOK could easily cause undesired side reactions, such as Wittig rearrangement,[4] isomerization[5] and deallylation.[6] Uchiyama and co-workers reported the use of an aluminum ate compound such as $i$$Bu_3$Al(TMP)Li (TMP = 2,2,6,6-tetramethylpiperidide) as a base for the selective allylic C–H deprotonation of allyl aryl ethers without causing apparent side reactions.[7] However, the reactivity of the resulting aryloxy allylaluminum species towards CO_2 remained unexplored.

Recently, the use of CO_2 for carboxylation reactions has received intensive attention.[3,8-10] In this context, we have reported the carboxylation of various substrates,[10] including aryl[10f] and alkenyl[10e] aluminum species, with CO_2 catalysed by NHC-copper complexes. These studies encouraged us to examine the allylic C–H carboxylation of aryl allyl ethers with CO_2. Herein, we report the efficient synthesis of 2-aryloxy butenoates through the copper-catalysed carboxylation of aryloxy allylaluminum species generated by the deprotonative C–H alumination of allyl aryl ethers with $i$$Bu_3$Al(TMP)Li using CO_2 as a C1 building block. Both 2-aryloxy-3-butenoates and (*Z*)-2-aryloxy-2-butenates have been easily obtained in a regio- and stereoselective fashion from the same allyl aryl ether substrates under appropriate reaction conditions (see Scheme 1).



Scheme 1 Regio- and stereodivergent synthesis of α-aryloxy butenoic acids through formal allylic C–H carboxylation of allyl aryl ethers with CO_2

Results and Discussion

Synthesis of methyl 2-aryloxy-3-butenoates

At first, the carboxylation of the allylaluminum species **2a** generated in situ by the deprotonative alumination of allyl

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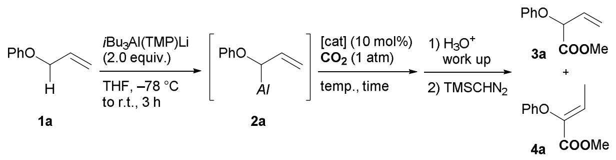
phenyl ether **1a** with *i*Bu_3Al(TMP)Li in THF was examined under various conditions. The allylaluminum **2a** alone was relatively unreactive towards CO_2 (1 atm) in THF at room temperature, giving the expected carboxylation product methyl 2-phenyloxy-3-butenoate **3a** only in 10% yield in 2 h after hydrolytic workup and treatment of the resulting crude material with $TMSCHN_2$ (Table 1, entry 1). By the initial catalyst screening, we found that (IMes)CuO*t*Bu (IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene) showed high catalytic activity for the carboxylation of **2a**. In the presence of (IMes)CuO*t*Bu (10 mol%), the reaction of **2a** with CO_2 smoothly completed at room temperature in 2 h to afford an inseparable mixture of **3a** and methyl 2-phenyloxy-2-butenoate **4a** (ratio of 85:5) in 90% yield (Table 1, entry 2). The ratio of **4a** increased as the extension of the reaction period without decrease of the total yield of **3a** and **4a** (Table 1, entries 2-4). These results suggested that 2-butenoate **4a** was formed through an isomerization of the initial product in basic condition, which originally lead to 3-butenoate **3a**. Also the reaction temperature had a significant effect on the selectivity. The reaction at higher temperature (50 ℃ for 48 h) gave 4a as a major product in 70% yield along with a small amount of 3a (9%) (Table 1, entry 5). In contrast, 3-butenoate **3a** was selectively obtained in 91% yield as a sole product when the carboxylation of **2a** was carried out at 0 °C for 2 h (Table 1, entry 6). The catalyst prepared in situ from (IMes)CuCl (10 mol%) and *t*BuOK (10 mol%) showed almost same catalytic activity with (IMes)CuO*t*Bu (Table 1, entry 7). The copper catalysts bearing IPr (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) and SIPr (SIPr = 1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene) were slightly less effective (Table 1, entries 8 and 9). In the absence of these NHC ligands, the yield of **3a** was much lower (Table 1, entry 10).

Table 1 Optimization of reaction conditions for the synthesis of methyl 3-butenoate[a]



entry	[cat]	temp. (°C)	time (h)	yield, %[b]	
				3a	4a
1	-	r.t.	2	10	-
2	(IMes)CuO*t*Bu [c,d]	r.t.	2	85	5
3	(IMes)CuO*t*Bu [c,d]	r.t.	12	66	20
4	(IMes)CuO*t*Bu [c,d]	r.t.	24	45	44
5	(IMes)CuO*t*Bu [c,d]	50	48	9	70
6	(IMes)CuO*t*Bu	0	2	91	-
7	(IMes)CuCl/*t*BuOK [e]	0	2	90	-
8	(IPr)CuCl/*t*BuOK [e]	0	2	70	-
9	(SIPr)CuCl/*t*BuOK [e]	0	2	69	-
10	CuCl/*t*BuOK [e]	0	2	35	-

[a] The reactions were carried out using *i*Bu_3Al(TMP)Li (2.0 equiv.), substrate (0.5 mmol), catalyst (10 mol%), and CO_2 (1 atm) in THF unless otherwise noted. [b] Isolated yield. [c] The product was obtained as an inseparable mixture of **3a** and **4a**. [d] The yields were calculated by ^{1}H NMR. [e] The ratio of Cu salt to *t*BuOK was 1:1.

With this optimized condition (Table 1, entry 6) in hand, we examined the carboxylation of various aryl allyl ethers to synthesize 2-aryloxy-3-butenoates. The results are summarized in Table 2. Similar to the carboxylation of **1a**, substituted-phenyl allyl ethers bearing a slightly electron-donating alkyl group, such as 4-*t*Bu- and 4-Bn- groups, on their phenyl moiety were good substrate to provide the corresponding methyl 2-aryloxy-3-butenoates **3b** and **3c** in 88% and 85% yields, respectively. Also an allyl ether bearing 2,3-dihydro-1H-indenyl group as the aryl moiety also gave the desired product **3d** in high yield. In the same way, methyl 2-(2-naphtoxy)-3-butenoate **3e** (80%) could be prepared from the corresponding naphthyl allyl ether. Substituted-phenyl allyl ethers bearing an electron-rich substituent, such as *m*-NMe_2-, *p*-SMe-, *p*-TBDMSO-, and *p*-MeO groups, on their phenyl group were also suitable substrate giving the corresponding methyl 2-aryloxy-3-butenoate **3f**, **3g**, **3h**, and **3i** in high yields, selectively. Although these substituents might act as a directing group on potential *ortho*-metallation on the phenyl ring,[11] there was no evidence of such unwanted reaction under the present reaction conditions. Also electron-withdrawing property of *p*-CF_3 group on the phenyl ring did not cause any negative effect, both on reactivity and regioselectivity; the reaction of allyl *p*-trifluoromethylphenyl ether provided methyl 2-aryloxy-3-butenoate **3j** in 89% yield. It is also noteworthy that the carboxylation of *p*-fluoro-,[12] *p*-chloro-, *p/o*-bromo-, and *p*-iodo-substituted-phenyl allyl ethers selectively occurred at allylic C–H bond under the present catalyst conditions, affording the desired carboxylation products (**3k**, **3l**, **3m**, **3n,** and **3o**) in high yields, while the C–X (X = F, Cl, Br, I) bonds remained unchanged. Hetero-aromatic units were also acceptable substituents on the aryl moiety; for instance, **3p** was obtained in 75% yield from the corresponding aryl allyl ether bearing a 2*H*-1,2,3-benzotriazol-2-yl group. The carboxylation of aryl allyl ethers bearing a disubstituted allyl group such as **1q** and **1r** could also proceed under the present conditions, though the yields were slightly lower (**3q**, 70% and **3r**, 65%) than that of the parent mono-substituted aryl ether (**3m**). The aryl allyl ether bearing a γ-alkyl group gave a mixture of α- and γ-carboxylation products. Moreover, the present method could be applicable to the propargylic C–H carboxylation of a phenyl propargyl ether; 2-phenyloxy-3-nonynoate **3s** was obtained in in 79% yield from the corresponding substituted-propargyl ether. Moreover, this method could be applied to the carboxylation of carbamic acid allyl esters. The allyic C–H carboxylation of allyl diisopropylcarbamate smoothly proceeded to give the corresponding methyl 3-butenoate derivative **3t** in 91% yield. Remarkably, α-methylallyl diisopropylcarbamate smoothly underwent the allylic C–H carboxylation at the more sterically

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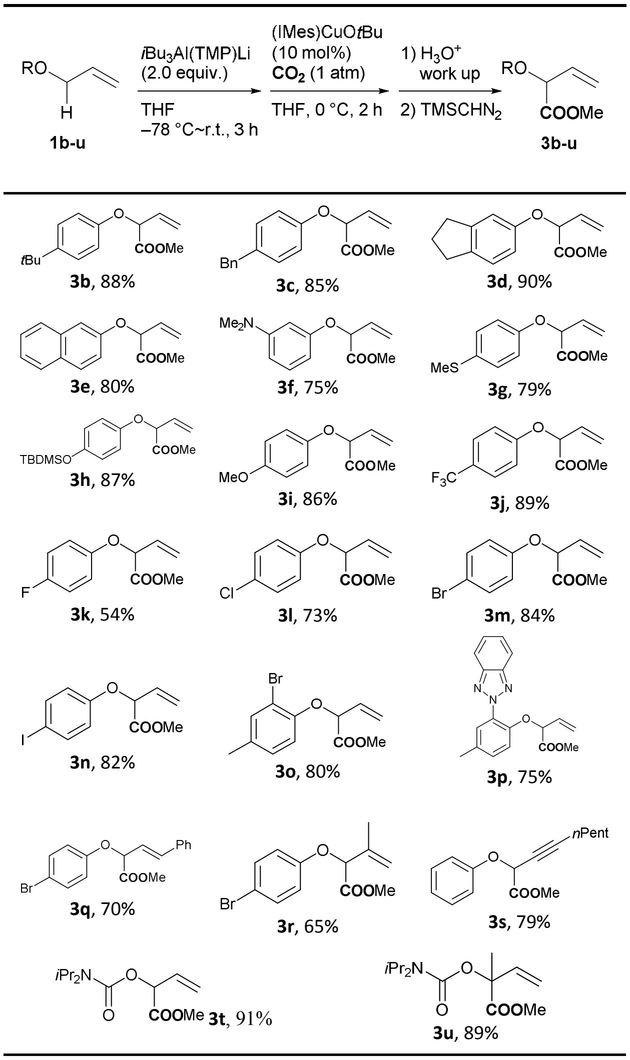
hindered position selectively to give carboxylic acid ester **3u** bearing a quaternary carbon center in 89% yield. Alkyl allyl ethers were not suitable for the present protocol; the reaction of *tert*-buyl allyl ether or benzyl allyl ether produced a mixture of uncharacterizable products.

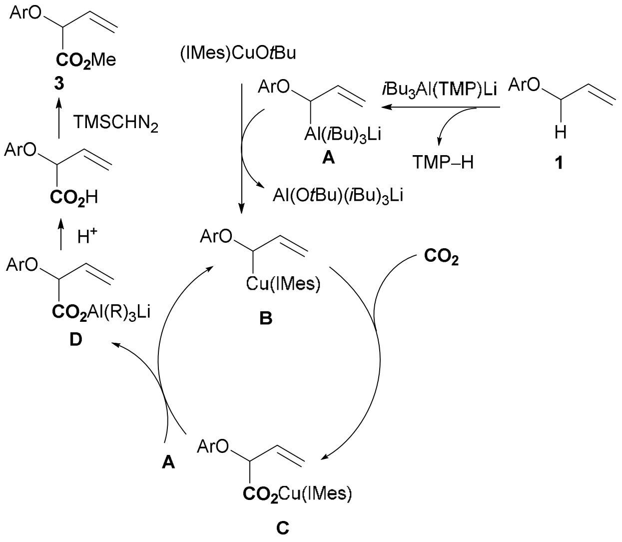
Table 2 Substrate scope on the synthesis of methyl 3-butenoate[a]



3b, 88%
3c, 85%
3d, 90%
3e, 80%
3f, 75%
3g, 79%
3h, 87%
3i, 86%
3j, 89%
3k, 54%
3l, 73%
3m, 84%
3n, 82%
3o, 80%
3p, 75%
3q, 70%
3r, 65%
3s, 79%
3t, 91%
3u, 89%

[a] The reactions were carried out using iBu$_3$Al(TMP)Li (2.0 equiv.), substrate (0.5 mmol), catalyst (10 mol%), and CO$_2$ (1 atm) in THF unless otherwise noted. [b] Isolated yield.

A possible reaction mechanism for the present deprotonative allylic C–H carboxylation is shown in Scheme 2. Deprotonation of an allylic compound by the aluminum ate base iBu$_3$Al(TMP)Li would generate allylaluminum species **A**. Then, transmetalation between **A** and (IMes)CuOtBu would proceed to give the allylcopper species **B** along with the release of Al(OtBu)(iBu)$_3$Li. Carboxylation would take place on allylcopper species **B** by insertion of CO$_2$ into copper-carbon bond in **B** to afford copper carboxylate species **C**.[13] Transmetalation reaction between **C** and another molecule of allylaluminum species **A** would give the aluminum carboxylate **D** regenerating allylcopper species **B**. The hydrolysis of **D** would afford a free 3-butenoic acid which was isolated as methyl 3-butenoate **3** after treatment with TMSCHN$_2$.



Scheme 2 A possible reaction pathway for the allylic C–H bond carboxylation.

Regio- and stereoselective synthesis of methyl 2-aryloxy-(*Z*)-2-butenoates

In addition to 2-aryloxy-3-butenoic acids, 2-aryloxy-2-butenoic acid derivatives have been recognized as an attractive building block in organic synthesis,[2h,2i,14] therefore, we next examined the selective synthesis of methyl 2-aryloxy-2-butenoates by modifying the present method for the formal allylic C–H carboxylation. As previously mentioned, in the carboxylation of **1a**, the amount of methyl 2-phenoxy-2-butenoate **4a** increased accompanied by the extended reaction period and elevated reaction temperature (Table 1, entries 1-6). From these results, we speculated that isomerization from the initial product such as **D** in Scheme 2 to the secondary product leading to **4a** might take place, possibly through a base-promoted deprotonation/protonation mechanism because excess amounts of basic components such as iBu$_3$Al(TMP)Li exist in the present reaction system and the initial product **D** has an acidic proton placed at α-position to the carbonyl group.

Upon this hypothesis, we initially attempted the isomerization reaction of the isolated methyl 2-phenoxy-3-butenoate **3a** by using a stoichiometric amount of KOtBu and DBU as the base. Interestingly, the results were quite different depending on the base used. When **3a** was treated with KOtBu (1.0 equiv.) in THF at room temperature for 24 h, phenol was obtained as a major product in 80% via deallylation reaction,[6] and the yield of the desired isomerization product **4a** was only 12%. In contrast, 2-butenoic acid ester **4a** was quantitatively obtained when **3a** was treated with DBU (1.0 equiv.) at room temperature for 24 h. In addition, a catalytic amount of DBU

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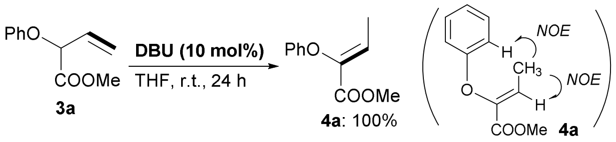
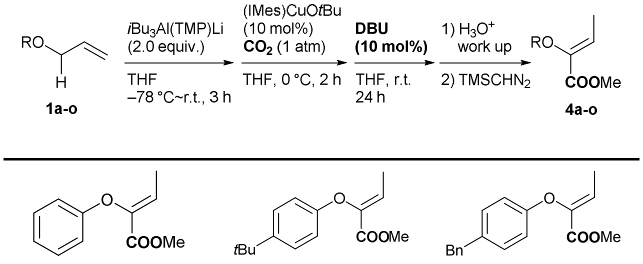
(10 mol%) was effective to complete the isomerization to give **4a** in a quantitative yield (Scheme 3). ^{1}H NMR NOE experiments on **4a** confirmed that the double bond has a (*Z*)-configuration. Moreover, we could achieve the one-pot synthesis of **4a** without isolation of **3a** (Table 3); by simply treating the reaction mixture after the carboxylation of **1a** by a catalytic amount of DBU (10 mol%) at room temperature for 24 h, **4a** was obtained in 91% yield in a completely regio- and stereoselective manner.



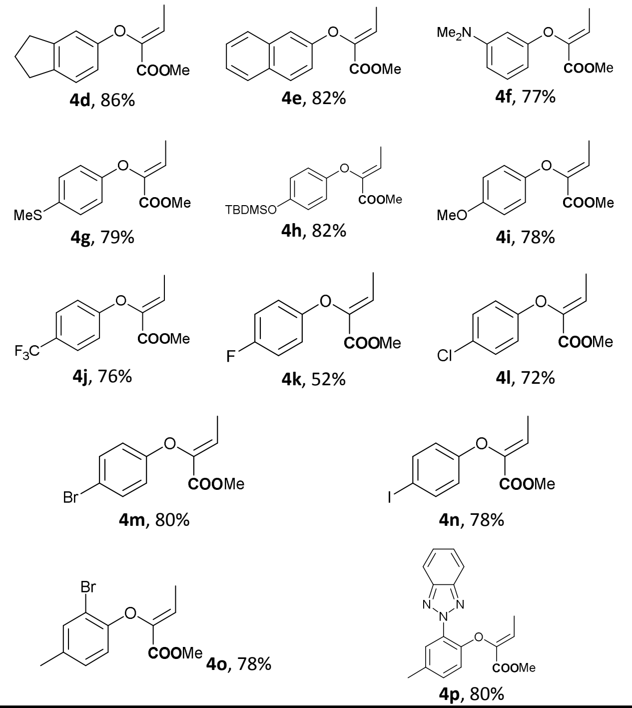
Scheme 3 Isomerization of **3a** to **4a** by using catalytic amount of DBU.

This newly developed protocol for the synthesis of **4a** was applicable to various substrates (Table 3). The present method worked efficiently with the substrates bearing alkyl substituents (4-*t*Bu, 4-Bn and dihydroindenyl) on the aryl moieties to give the corresponding 2-aryloxy-(*Z*)-2-butenoic acid ester **4b**, **4c** and **4d** in 87%, 83% and 86% yields, respectively. Naphtyl allyl ether was also suitable substrate for this method involving the DBU-catalysed isomerization and **4e** was selectively obtained in 82% yield. The electron donating substituents (4-SMe, 3-NMe$_2$ and 4-OMe, 4-OSiMe$_2$*t*Bu) on the aryl moiety of the substrates did not disturb the DBU-catalysed isomerization and 2-aryl-(*Z*)-2-butenoates **4f-i** were obtained in high yields in a regio- and stereoselective manner. Moreover, the aryl allyl ethers bearing a trifluoromethyl group, halogen substituent, or benzotriazolyl group on the aryl moiety could selectively give the desired 2-aryl-(*Z*)-2-butenoates **4j-p** in moderate to high yields under the similar conditions. In all cases demonstrated in Table 3, the yields of 2-aryl-2-butenoates **4** were almost comparable with those of the 2-aryl-3-butenoates **3** obtained in the reactions above-mentioned in Table 2. However, the present DBU catalyzed isomerization was unsuccessful on aryl ally ethers **1q**, **1r** and allyl carbamate **1t**. In the reaction of **1q**, the isomerization did not proceed due to the thermodynamic stability of conjugated styrene moiety even in the presence of an excess amount of DBU. The reactions of **1q** and **1r** under the same conditions gave complicated product mixtures.

Table 3 Substrate scope on the synthesis of methyl 2-butenoate[a]



4a, 91% **4b**, 87% **4c**, 83%



4d, 86% **4e**, 82% **4f**, 77%

4g, 79% **4h**, 82% **4i**, 78%

4j, 76% **4k**, 52% **4l**, 72%

4m, 80% **4n**, 78%

4o, 78% **4p**, 80%

[a] The reactions were carried out using *i*Bu$_3$Al(TMP)Li (2.0 equiv.), substrate (0.5 mmol), catalyst (10 mol%), DBU (10 mol%), and CO$_2$ (1 atm) in THF unless otherwise noted. [b] Isolated yield.

The DBU-catalysed isomerization process could be explained as illustrated in Scheme 4. In our reaction, aluminum carboxylate **D** was formed as the initial product after carboxylation process. The isomerization would start with deprotonation of an acidic proton attached to the α-carbon of the carbonyl group of **D** by DBU. On this occasion, the stereo-electronic effect would require the subtracted proton to be perpendicular to the π-face of the allyl group shown as **E** and **E'**. Among these two conformers, **E** would be more favourable due to the lower allylic 1,3-strain,[15] thus the deprotonation would take place preferentially from **E** to afford [DBU-H]$^+$ and an allyl anion **F** bearing an *anti*-configuration. Then, protonation of **F** would proceed at the sterically less hindered terminal sp^2 carbon by [DBU-H]$^+$ to give aluminum carboxylate **G** bearing a (*Z*)-configuration regenerating DBU.

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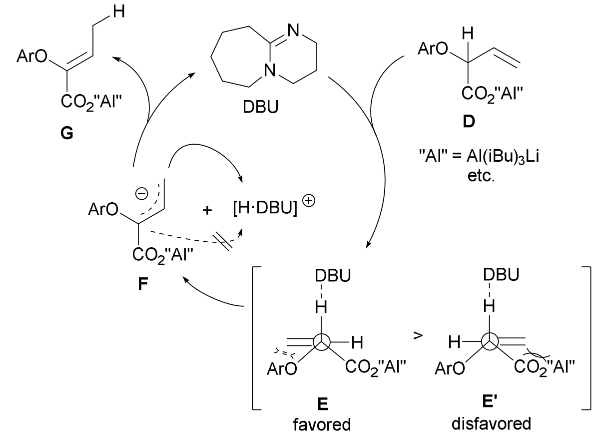
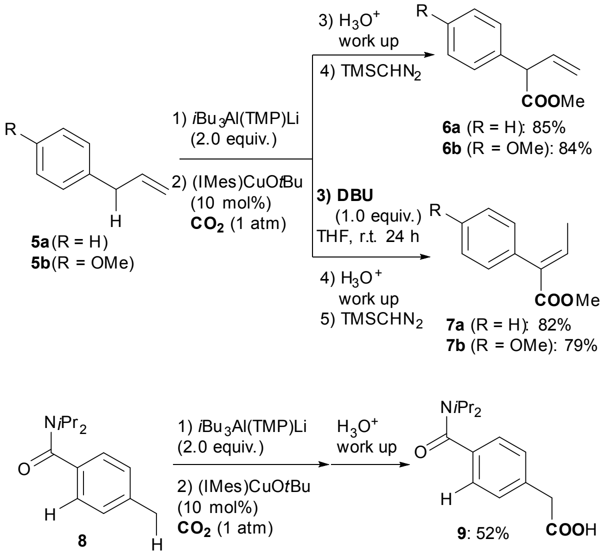


Scheme 4 A possible reaction pathway for the isomerization by DBU

Allylic C–H carboxylation of allylbenzenes with CO_2

Finally, carboxylations of less acidic substrates such as allylbenzenes by the present methods were examined. As shown in Scheme 5, the deprotonative alumination of benzylic C–H bonds of allylbenzenes **5a** and **5b** smoothly proceeded by *i*$Bu_3Al(TMP)Li$ and the subsequent Cu-catalysed carboxylation of the resulting benzylaluminum took place under the similar conditions to give corresponding methyl 2-aryl-3-butenoate **6a** (85%) and **6b** (84%), respectively. When the reaction mixtures of the carboxylation reactions were treated with DBU (1.0 equiv) at room temperature, isomerization of the generated aluminum 2-aryl-3-butenoate took place smoothly to afford methyl (*E*)-2-aryl-2-butenoates **7a** and **7b** in high yields. Moreover, the present protocol could also applicable to the formal benzylic carboxyation of *p*-methylbenzamide **8** to provide **9** selectively in 52% yield despite the presence of potentially reactive aromatic *ortho*-C–H bonds.



Scheme 5. Carboxylation of several allylic and benzylic compounds.

Conclusion

In summary, we have achieved efficient and regioselective synthesis of 2-aryloxy-3-butenoic acid esters by formal C–H carboxylation of allyl aryl ethers. The reaction consists of the deprotonative allylic C–H bond alumination of the allyl aryl ethers by an aluminum ate base (*i*$Bu_3Al(TMP)Li$) and the subsequent carboxylation of the resulting allylaluminum species with CO_2 catalysed by an NHC-copper complex. The carboxylation proceeds in highly regioselective manner in high yield and the present protocol features relatively broad substrate scope, certain functional group tolerance, simple one-pot reaction operation. Moreover, regioselective synthesis of (*Z*)-2-aryloxy-2-butenoic acid esters has also been realized by DBU-catalysed one-pot double bond isomerization of the initially formed 2-aryloxy-3-butenoates. Thus, the divergent synthesis of 2-aryoxy-3- and 2-butenoates from the single staring materials using CO_2 as the C_1 building block has been achieved. These methods could be applied also to benzylic carboxylation of allylbenzenes or a toluene derivative, which demonstrated the potential of the present sequential deprotonative alumination-carboxylation strategy.

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Notes and references

1 (a) F. Gualtieri, C. Bottalico, A. Calandrella, S. Dei, M. P. Giovannoni, S. Mealli, M. N. Romanelli, S. Scapecchi, E. Teodori, N. Galeotti, C. Ghelardini, A. Giotti and A. Bartolini, *J. Med. Chem.*, 1994, **37**, 1712; (b) S. K. Gorla, M. Kavitha, M. Zhang, J. E. W. Chin, X. Liu, B. Striepen, M. Grzyska, Y. Kim, A. Joachimiak, L. Hedstrom and G. D. Cuny, *J. Med. Chem.*, 2013, **56**, 4028; (c) K. Mandapati, S. K. Gorla, A. L. House, E. S. McKenney, M. Zhang, S. N. Rao, D. R. Gollapalli, B. J. Mann, J. B. Goldberg, G. D. Cuny, I. J. Glomski and L. Hedstrom, *ACS Med. Chem. Lett.*, 2014, **5**, 846; (d) R. S. Ferreira, M. A. Dessoy, I. Pauli, M. L. Souza, R. Krogh, A. I. L. Sales, G. Oliva, L. C. Dias and A. D. Andricopulo, *J. Med. Chem.*, 2014, **57**, 2380; (e) Y. Xu, C. J. Rito, G. J. Etgen, R. J. Ardecky, J. S. Bean, W. R. Bensch, J. R. Bosley, C. L. Broderick, D. A. Brooks, S. J. Dominianni, P. J. Hahn, S. Liu, D. E. Mais, C. M. Rafizadeh, K. M. Ogilvie, B. A. Oldham, M. Peters, D. K. Rungta, A. J. Shuker, G. A. Stephenson, A. E. Tripp, S. B. Wilson, L. L. Winneroski, R. Zink, R. F. Kauffman and J. R. McCarthy, *J. Med. Chem.*, 2004, **47**, 2422.

2 For the synthesis of 2-aryloxy-3-butenoates, see: (a) Y. Nishimoto, H. Ueda, M. Yasuda, and A. Baba, *Angew. Chem., Int. Ed.*, 2012, **51**, 8073; (b) Y. Nishimoto, Y. Kita, H. Ueda, H. Imaoka, K. Chiba, M. Yasuda and A. Baba. *Chem. Eur. J.*, 2016, **22**, 11837; (c) Y. Landis and D. Planchenault, *Synlett*, 1995, 1191. For the synthesis of 2-aryloxy-2-butenoates, see: (d) T. Padmanathan and M. U. S. Sultanbawa, *J. Chem. Soc.*, 1963, 4210. (e) K. Tanaka, T. Nakai and N. Ishikawa, *Chem. Lett.*, 1977, 1379; (f) V. Rosnati, A. Saba and A. Salibeni,

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DOI: 10.1039/C7OB00341B

Tetrahedron. Lett., 1981, **22**, 167; (g) P. Seneci, I. Leger, M. Souchet and G. Nadler, *Tetrahedron*, 1991, **53**, 17097; (h) P. E. Maligres, S. W. Krska, and G. R. Humphrey, *Org. Lett.*, 2004, **6**, 3147; (i) S. Li, S. Zhu, J. Xie, S. Song, C. Zhang, and Q. Zhou, *J. Am. Chem. Soc.*, 2010, **132**, 1172.

3 For examples of carboxylation reactions via allyl metal species without α-aryloxy group, see: (a) M. Shi and K. M. Nicholas, *J. Am. Chem. Soc.*, 1997, **119**, 5057; (b) R. Johansson and O. F. Wendt, *Dalton Trans.*, 2007, 488; (c) D.P.Hruszkewycz, J. Wu, N. Hazari and C. D. Incarvito, *J. Am. Chem. Soc.*, 2011, **133**, 3280; (d) J .Wu, N. Hazari, *Chem. Commun.*, 2011, **47**, 1069; (e) H. A. Duong, P. B. Huleatt, Q. Tan, and E. L. Shuying, *Org. Lett.*, 2013, **15**, 4034; (f) B. Miao and S. Ma, *Chem. Commun.,* 2014, **50**, 3285; (g) T. Moragas, J. Cornella and R. Martin, *J. Am. Chem. Soc.,* 2014, **136**, 17702; (i) T. Mita, Y. Higuchi and Y. Sato, *Chem. Eur. J.,* 2015, **21**, 16391.

4 (a) D. R. Dimmel and S. B. Gharpure, *J. Am. Chem. Soc.*, 1971, **93**, 3991; (b) W. F. Bailey, M. D. England, M. J. Mealy, C. Thongsornkleeb and L. Teng, *Org. Lett.*, 2000, **2**, 489; (c) J. Barluenga, F. J. Fañanás, R. Sanz, C. Marcos and M. Trabada, *Org. Lett.*, 2002, **4**, 1587; (d) S. Strunk and M. Schlosser, *Eur. J. Org. Chem.*, 2006, 4393.

5 (a) D. A. Evans, G. C. Andrews and B. Buckwalter, *J. Am. Chem. Soc.*, 1974, **96**, 5560; (b) W. C. Still and T. L. Macdonald, *J. Am. Chem. Soc.*, 1974, **96**, 5561; (c) C. Su and P. G. Williard, *Org. Lett.*, 2010, **12**, 5378.

6 (a) C. D. Broaddus, *J. Org. Chem.*, 1965, **30**, 4131; (b) W. F. Bailey, M. D. England, M. J. Mealy, C. Thongsornkleeb and L. Teng, *Org. Lett.*, 2000, **2**, 489.

7 H. Naka, M. Uchiyama, Y. Matsumoto, A. E. Wheatley, M. McPartin, J. V. Morey and Y. Kondo, *J. Am. Chem. Soc.*, 2007, **129**, 1921.

8 Recent reviews: (a) T. Sakakura, J.-C. Choi and H. Yasuda, *Chem. Rev.,* 2007, **107**, 2365; (b) R. Martin, A. W. Kleij, *ChemSusChem* 2011, **4**, 1259; (c) Y. Tsuji and T. Fujihara, *Chem. Commun*., 2012, **48**, 9956; (d) L. Zhang, Z. Hou, *Chem. Sci.*, 2013, **4**, 3395 (e) Q. Liu, L. Wu, R. Jackstell and M. Beller, *Nat. Commun*., 2015, **6**, 5933. (f) L. Zhang and Z. Hou, *Current Opin. Green Sus. Chem*, **2017**, *3*, 17.

9 Selected recent examples: (a) T. Moragas, M. Gaydou, and R. Martin, *Angew. Chem., Int. Ed.* 2016, **55**, 5053; (b) K. Nogi, T. Fujihara, J. Terao and Y. Tsuji, *J. Am. Chem. Soc.*, 2016, **138**, 5547; (c) S. S. Bhojgude, T. Roy, R. G. Gonnade, and A. T. Biju, *Org. Lett.*, 2016, **18**, 5424; (d) Z. Zhang, L. Liao, S. Yan, L. Wang, Y. He, J. Ye, J. Li, Y. Zhi and D. Yu, *Angew. Chem. Int. Ed.*, 2016, **55**, 7068; (e) T. W. Butcher, E. J. McClain, T. G. Hamilton, T. M. Perrone, K. M. Kroner, G. C. Donohoe, N. G. Akhmedov, J. L. Petersen and B. V. Popp, *Org. Lett.*, 2016, **18**, 6428; (f) M. Juhl, S. L. R. Laursen, Y. Huang, D. U. Nielsen, K. Daasbjerg and T. Skrystrup, *ACS Catl.* 2017, **7**, 1392; (g) T. Suga, T. Saitou, J. Takaya, and N. Iwasawa, *Chem. Sci.* 2017, **8**, 1454.

10 (a) T. Ohishi, M. Nishiura and Z. Hou, *Angew. Chem. Int. Ed.*, 2008, **47**, 5792; (b) L. Zhang, J. Cheng, T. Ohishi and Z. Hou, *Angew. Chem., Int. Ed.*, 2010, **49**, 8670; (c) T. Ohishi, L. Zhang, M. Nishiura and Z. Hou, *Angew. Chem., Int. Ed.*, 2011, **50**, 8114; (d) L. Zhang, J. Cheng, B. Carry and Z. Hou, *J. Am. Chem. Soc.*, 2012, **134**, 14314; (e) M. Takimoto and Z. Hou, *Chem. Eur. J.*, 2013, **19**, 11439; (f) A. Ueno, M. Takimoto, W. N. O. Wylie, M. Nishiura, T. Ikariya and Z. Hou, *Chem. Asian J.*, 2015, **10**, 1010; (g) M. Takimoto, S. S. Gholap and Z. Hou, *Chem. Eur. J.*, 2015, **21**, 15218; (h) S. S. Gholap, M. Takimoto, and Z. Hou, *Chem. Eur. J.,* 2016, **22**, 8547; (i) B. Carry, L. Zhang, M. Nishiura and Z. Hou, *Angew. Chem., Int. Ed.*, 2016, **55**, 6257.

11 (a) W. Bauer, P. A. A. Klusener, S. Harder, J. A. Kanters, A. J. M. Duisenberg, L. Brandsma and P. V. R. Schleyer, *Organometallics*, 1988, **7**, 552; (b) T.Ishikawa, A. Ogawa and T. Hirao, *J. Am. Chem. Soc.*, 1998, **120**, 5124; (c) Y. Kim, M. Kim and F. P. Gabbaï, *Org. Lett.*, 2010, **12**, 600; (d) Y. Kim, H. Zhao and F. P. Gabbaï, *Angew. Chem., Int. Ed.*, 2009, **48**, 4957; (e) D. W. Slocum, T. K. Reinscheld, C. B. White, M. D. Timmons, P. A. Shelton, M. G. Slocum, R. D. Sandlin, E. G. Holland, D. Kusmic, J. A. Jennings, K. C. Tekin, Q. Nguyen, S. J. Bush, J. M. Keller and P. E. Whitley, *Organometallics*, 2013, **32**, 1674.

12 In case of fluoro substituted starting material **1k**, deallylation occurred prior to deprotonation and carboxylation.

13 There might be another pathway for the carboxylation process. The resulting allyl copper species **B** would be in equilibrium with a more sterically accessible σ-allyl copper species, in which the copper atom is placed at the terminal carbon (copper species **B'**). Then, carboxylation at the γ-carbon in this copper species **B'** by the S_E' mechanism would take place to give the carboxylate **C**. For related examples, see: M. Kanai, R. Wada, T. Shibuguchi and M. Shibasaki, *Pure Appl. Chem.*, 2008, **80**, 1055. See also ref 3e.

14 For recent examples, see: (a) X. Cheng, J. Xie, S. Li and L. Zhou, *Adv. Synth. Catal.*, 2006, **348**, 1271; (b) P. E. Maligres, G. R. Humphrey, J. Marcoux, M. C. Hillier, D. Zhao, S. Krska and E. J. J. Grabowski, *Org. Process Res. Dev.*, 2009, **13**, 525; (c) A. Monos-Turvey, E. M. M. Bulloch, P. J. Rutledge, E. N. Baker, J. S. Lott and R. J. Payne, *ChemMedChem*, 2010, **5**, 1067.

15 For the example of similar 1,3-allylic strain, see (a) K. N. Houk, S. R. Moses, Y. Wu, N. G. Rondan, V. Jäger, R. Schohe and F. R. Fronczek, *J. Am. Chem. Soc.*, 1984, **106**, 3880; (b) E. Vedejs and C. K. McClure, *J. Am. Chem. Soc.*, 1986, **108**, 1094; (c) K. N. Houk, H. Duh, Y. Wu and S. R. Moses, *J. Am. Chem. Soc.*, 1986, **108**, 2754; (d) M. T. Reetz, F. Kayser and K. Harms, *Tetrahedron Lett.*, 1992, **33**, 3453.