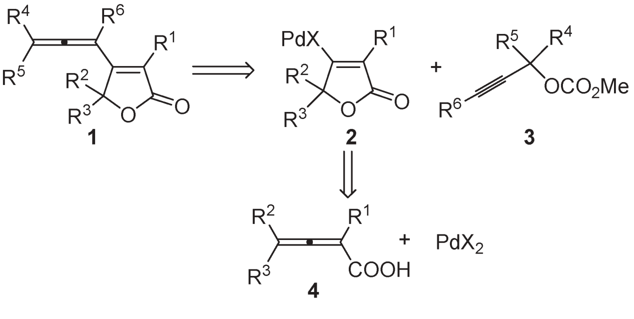
From allene to allene: a palladium-catalyzed approach to β-allenyl butenolides and their application to the synthesis of polysubstituted benzene derivatives†

Shengming Ma,*[ab] Zhenhua Gu[a] and Youqian Deng[b]

Received (in Cambridge, UK) 21st September 2005, Accepted 26th October 2005
First published as an Advance Article on the web 14th November 2005
DOI: 10.1039/b513371h

An allene to allene protocol for the synthesis of β-allenyl butenolides in moderate to high yields from 2,3-allenoic acids and propargylic carbonates catalyzed by $Pd(OAc)_2$–TFP has been developed; the products were applied successfully to the Diels–Alder reaction with electron-deficient alkynes to afford polysubstituted benzene derivatives with an excellent regioselectivity.

Allenes are a class of compounds of current interest with unique reactivity.[1–3] Recently, our group and others have established two- or three-component monoallene cyclization approaches to carbo- or heterocycles.[2f,4] Hashmi *et al.* reported the Au(III)- and Pd(II)-catalyzed homodimerization reaction of 1,2-allenyl ketones forming corresponding 2- or 3-alkenyl furans.[5] We also noticed the bisallene approaches of two 2,3-allenoic acids and the heterodimerization reaction of 2,3-allenoic acids with 1,2-allenyl ketones to afford bisbutenolides and 4-(furan-3′-yl)-butenolides, respectively.[6] Although these functionalized allenes afforded cyclic products efficiently, no allene structure was present in the products. In this communication we wish to report a Pd-catalyzed two-component reaction of 2,3-allenoic acid with propargylic carbonates, in which 2,3-allenoic acids cyclized to form the butenolide's skeleton while a new allenyl moiety was formed from the propargylic carbonates (Scheme 1). Due to the high reactivity of the allene-ene functionality,[7] the products have been successfully applied to the Diels–Alder reaction to afford polysubstituted benzene derivatives.

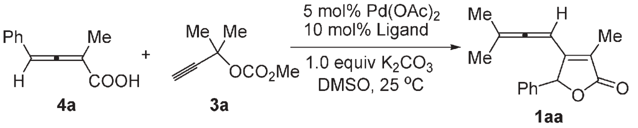


Scheme 1 The proposed synthetic route.

On the basis of the previous work, we reasoned that the β-allenyl butenolides **1** may be generally constructed from the reaction of propargylic carbonates **3**[8] with intermediate **2**, which may be generated easily *via* cyclic oxypalladation of the 2,3-allenoic acid **4** with Pd(II) species (Scheme 1).[2f] The challenge here is the formation of the allene moiety *via* β-heteroatom elimination[9] and avoiding further reactions of the *in situ* formed allene moiety.

Our first approach was based on the reaction of 2,3-allenoic acid **4a** and **3a**. A survey of some of bidentate phosphine ligands indicates that (*R*)-BINAP can only afford a trace amount of product **1aa** (Entry 1, Table 1). However, it is quite fortunate to see that dppb [1,4-bis(diphenylphosphino)butane] and dppp [1,3-bis(diphenylphosphino)propane] indeed afforded **1aa** in 10% and 14% yields, respectively (Entries 2, and 3, Table 1). Furthermore, using dppe [1,2-bis(diphenylphosphino)ethane] as the ligand the reaction can afford a moderate yield of **1aa** (Entry 4, Table 1). Further screening indicates that using tri-(2-furyl)phosphine (TFP) as the ligand can afford **1aa** in 59% yield (Entry 7, Table 1).[10] In terms of solvent effect, DMSO is better than other solvents, such as NMP, DMF, DME *etc.* (see supporting information for the results in different solvents†). The reduction of K_2CO_3 to 5 mol% led to a lower yield of **1aa** (Entry 8, Table 1). Thus, we have established the proposed protocol for the cross-coupling

Table 1 The ligand effect on the $Pd(OAc)_2$-catalyzed cross-coupling reaction of **4a** with **3a**[a]



Entry	Ligand	Time/h	Yield of **1aa** (%)[b]
1	(*R*)-BINAP[c]	19.5	Trace
2	Dppb[c]	17.5	10
3	Dppp[c]	21	14
4	Dppe[c]	17	51
5	PCy_3	19.5	14
6	P(*o*-tolyl)$_3$	21	17
7	TFP	14	59
8[d]	TFP	23	50

[a] Under an argon atmosphere, the mixture of 0.25 mmol of **4a**, 0.50 mmol of **3a**, 5 mol% $Pd(OAc)_2$, and 10 mol% ligand in 3 mL DMSO was stirred at 25 °C. [b] Isolated yield. [c] 5 mol% ligand was used. [d] 5 mol% of K_2CO_3 was used.

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[a] *State Key Laboratory of Organometallic Chemistry Shanghai Institute of Organic Chemistry Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, P. R. China. E-mail: masm@mail.sioc.ac.cn; Fax: +86 21-6416-7510*
[b] *Laboratory of Molecular Synthesis and Recognition, Department of Chemistry, Zhejiang University, Hangzhou, Zhejiang 310027, P. R. China*

† Electronic supplementary information (ESI) available: Experimental procedures and characterization data of all new compounds. See DOI: 10.1039/b513371h

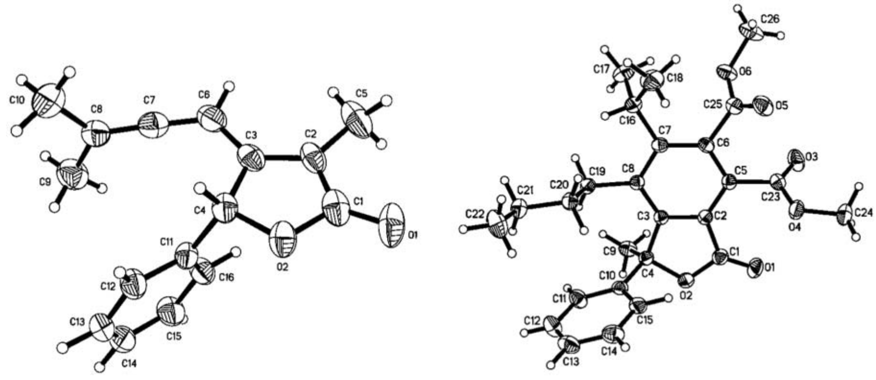


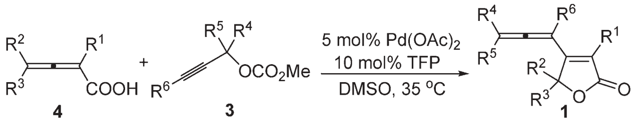
Fig. 1 ORTEP structures of **1aa** and **6fda**.

cyclization of 2,3-allenoic acids **4** with **3** affording β-allenyl butenolides **1** (Entry 7, Table 1). The X-ray diffraction study of **1aa** clearly proved the presence of the allenyl group in the β-position of the butenolide skeletons, which has not been further transformed under the current reaction conditions (Fig. 1).‡

The optimized reaction conditions proved to be generally applicable, allowing for an efficient coupling of 2,3-allenoic acids **4** with **3**. Some typical results are listed in Table 2. Various differently substituted 2,3-allenoic acids with R^1 being alkyl (Entries 1–9, Table 2) or hydrogen (Entries 10–12, Table 2), R^2 = aryl (Entries 1–8, and 10–12, Table 2) or alkyl (Entry 9, Table 2), and R^3 being hydrogen (Entries 1–9, Table 2) or alkyl (Entries 10–12, Table 2) can smoothly afford the products **1** in moderate to high yields.

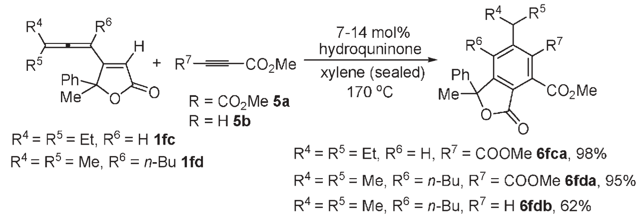
Synthesis of differently polysubstituted benzenes is a synthetic challenge.[11] The Diels–Alder reaction of **1** with the electron-deficient alkynes **5a** or **5b** afforded polysubstituted benzo-γ-lactones **6** highly regioselectively in the presence of 7–14 mol% of hydroquninone in xylene (Scheme 2).[12] The structure of these benzo-γ-lactones was further established by the X-ray studies of **6fda** (Fig. 1).§

Table 2 The Pd-catalyzed cross-coupling reaction of **4** with **3**^{a}



Entry	Substrate **4** R^1	R^2	R^3	Substrate **3** R^4	R^5	R^6	Time/h	Yield of **1** (%)^b
1	Me	Ph	H (**4a**)	–(CH$_2$)$_5$–		H (**3b**)	5	68 (**1ab**)
2	Me	Ph	H (**4a**)	Et	Et	H (**3c**)	10	60 (**1ac**)
3	Pr	Ph	H (**4b**)	Me	Me	H (**3a**)	11	54 (**1ba**)
4^c	Pr	Ph	H (**4b**)	Et	Et	H (**3c**)	9	64 (**1bc**)
5	Me	1′-Nap	H (**4c**)	Me	Me	H (**3a**)	10	63 (**1ca**)
6^c	Me	1′-Nap	H (**4c**)	–(CH$_2$)$_5$–		H (**3b**)	10	52 (**1cb**)
7^c	Me	1′-Nap	H (**4c**)	Et	Et	H (**3c**)	10	68 (**1cc**)
8	Pr	1′-Nap	H (**4d**)	Et	Et	H (**3c**)	10	71 (**1dc**)
9	Me	Me	H (**4e**)	Me	Me	H (**3a**)	6	54 (**1ea**)
10	H	Ph	Me (**4f**)	Et	Et	H (**3c**)	12	82 (**1fc**)
11	H	Ph	Me (**4f**)	Me	Me	Bu (**3d**)	16	93 (**1fd**)
12	H	Ph	Et (**4g**)	Me	Me	Ph (**3e**)	17	91 (**1ge**)

^{a} Under an argon atmosphere, the mixture of 0.25 mmol of **4**, 0.50 mmol of **3**, 5 mol% Pd(OAc)$_2$, and 10 mol% TFP in 1 mL of DMSO was stirred at 35 °C for the time indicated in the table. ^{b} Isolated yield. ^{c} The reaction was carried out at 40 °C.



$R^4 = R^5$ = Et, R^6 = H **1fc**

$R^4 = R^5$ = Me, R^6 = *n*-Bu **1fd**

$R^4 = R^5$ = Et, R^6 = H, R^7 = COOMe **6fca**, 98%

$R^4 = R^5$ = Me, R^6 = *n*-Bu, R^7 = COOMe **6fda**, 95%

$R^4 = R^5$ = Me, R^6 = *n*-Bu, R^7 = H **6fdb**, 62%

Scheme 2 The Diels–Alder reaction of **1** with alkynes **5**.

In conclusion, we have established a protocol for palladium-catalyzed coupling reaction of 2,3-allenoic acids with propargylic carbonates forming β-allenyl butenolides, in which the newly formed allene moiety does not undergo further transformation. These compounds may be applied to the highly selective synthesis of polysubstituted benzene derivatives.

Notes and references

‡ Crystal data for **1aa**: $C_{16}H_{16}O_2$, *MW* = 240.29, Orthorhombic, space group *Pbca*, Final *R* indices [$I > 2\sigma(I)$], *R*1 = 0.0409, w*R*2 = 0.0625, *R* indices (all data) *R*1 = 0.1877, w*R*2 = 0.0882, *a* = 11.592(2) Å, *b* = 14.568(3) Å, *c* = 16.342(3) Å, α = 90°, β = 90°, γ = 90°, *V* = 2759.7(8) Å^3, *T* = 293(2) K, *Z* = 8, reflections collected/unique: 15724/3266 (R_{int} = 0.1496), number of observations [$>2\sigma(I)$] 917, parameters: 227. CCDC 270605. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b513371h

§ Crystal data for **6fda**: $C_{26}H_{30}O_6$, *MW* = 438.50, Monoclinic, space group *P*2(1)/*n*, Final *R* indices [$I > 2\sigma(I)$], *R*1 = 0.0511, w*R*2 = 0.0965, *R* indices (all data) *R*1 = 0.0992, w*R*2 = 0.1120, *a* = 10.0344(17) Å, *b* = 13.210(2) Å, *c* = 18.172(3) Å, α = 90°, β = 99.356(4)°, γ = 90°, *V* = 2376.7(7) Å^3, *T* = 293(2) K, *Z* = 4, reflections collected/unique: 14147/5404 (R_{int} = 0.0670), number of observations [$>2\sigma(I)$] 2955, parameters: 328. CCDC 273892. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b513371h

1 (*a*) *The Chemistry of the Allenes*, ed. S. R. Landor, Academic, London, 1982, vol. 1; (*b*) *Modern Allene Chemistry*, ed. N. Krause and A. S. K. Hashmi, Wiley-VCH, Weinheim, 2004, vol. 1–2; (*c*) J. Tsuji, in *Topics in Organometallic Chemistry* Springer-Verlag, Berlin Heidelberg, 2005.

2 (*a*) R. Zimmer, C. U. Dinesh, E. Nandanan and F. A. Khan, *Chem. Rev.*, 2000, **100**, 3067; (*b*) R. W. Bates and V. Satcharoen, *Chem. Soc. Rev.*, 2002, **31**, 12; (*c*) S. Ma, *Acc. Chem. Res.*, 2003, **36**, 701; (*d*) A. Hoffmann-Röder and N. Krause, *Angew. Chem., Int. Ed.*, 2004, **43**, 1196; (*e*) H.-U. Reissig, W. Schade, M. O. Amombo, R. Pulz and A. Hausherr, *Pure Appl. Chem.*, 2002, **74**, 175; (*f*) S. Ma, *Chem. Rev.*, 2005, **105**, 2829.

3 For some of the most recent typical reactions of allenes, see: (*a*) B. M. Trost, C. Jakel and B. Plietker, *J. Am. Chem. Soc.*, 2003, **125**, 4438; (*b*) J. Franzen and J.-E. Bäckvall, *J. Am. Chem. Soc.*, 2003, **125**, 6056; (*c*) J. Huang and R. P. Hsung, *J. Am. Chem. Soc.*, 2005, **127**, 50; (*d*) K.-J. Chang, D. K. Rayabarapu, F.-Y. Yang and C.-H. Cheng, *J. Am. Chem. Soc.*, 2005, **127**, 126; (*e*) S.-S. Ng and T. F. Jamison, *J. Am. Chem. Soc.*, 2005, **127**, 7320.

4 (*a*) R. D. Walkup and G. Park, *J. Am. Chem. Soc.*, 1990, **112**, 1597; (*b*) F. P. J. T. Rutjes, K. C. M. F. Tjen, L. B. Wolf, W. F. J. Karstens, H. E. Schoemaker and H. Hiemstra, *Org. Lett.*, 1999, **1**, 717; (*c*) H. Ohno, M. Anzei, A. Toda, S. Ohshi, N. Fujii, T. Tanaka, Y. Takanato and T. Ibuka, *J. Org. Chem.*, 2001, **66**, 4904; (*d*) Y.-H. Ha and S.-K. Kang, *Org. Lett.*, 2000, **4**, 1143; (*e*) S.-K. Kang, Y.-H. Ha, B.-S. Ko, Y. Lim and J. Jung, *Angew. Chem., Int. Ed.*, 2002, **41**, 343; (*f*) H. Hamaguchi, S. Kosaka, H. Ohno and T. Tanaka, *Angew. Chem., Int. Ed.*, 2005, **44**, 1513.

5 (*a*) A. S. K. Hashmi, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1581; (*b*) A. S. K. Hashmi, T. L. Ruppert, T. Knöfel and J. W. Bats, *J. Org. Chem.*, 1997, **62**, 7295; (*c*) A. S. K. Hashmi, L. Schwarz, J. –H. Choi and T. M. Frost, *Angew. Chem., Int. Ed.*, 2000, **39**, 2285.

6 (*a*) S. Ma, Z. Yu and Z. Gu, *Chem.–Eur. J.*, 2005, **11**, 2351; (*b*) S. Ma and Z. Yu, *Angew. Chem., Int. Ed.*, 2002, **41**, 1775.

7 (*a*) M. Murakami, K. Itami and Y. Ito, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2691; (*b*) M. S. Sigman and B. E. Eaton, *J. Am. Chem. Soc.*, 1996, **118**, 11783; (*c*) M. Murakami, K. Itami and Y. Ito, *J. Am. Chem. Soc.*, 1997, **119**, 7163; (*d*) M. V. Chevliakov and J. Montgomery, *J. Am. Chem. Soc.*, 1999, **121**, 11139; (*e*) K. M. Brummond, H. Chen, B. Mitasev and A. D. Casarez, *Org. Lett.*, 2004, **6**, 2161; (*f*) T. Makino and K. Itoh, *J. Org. Chem.*, 2004, **69**, 395.

8 (*a*) J. Tsuji and T. Mandai, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2589; (*b*) J. Tsuji and Y. Mandai, in *Metal-Catalyzed Cross-Coupling Reaction*, ed. F. Diedrich and P. J. Stang, Wiley-VCH, New York, 1998, p. 455.

9 The formation of allenes from β-H or β-heteroatom elimination of transition-metals is not easy, for β-H elimination to afford allenes, see: (*a*) S. Pivsa-Art, T. Satoh, M. Miura and M. Nomura, *Chem. Lett.*, 1997, 823; (*b*) C. Fu and S. Ma, *Org. Lett.*, 2005, **7**, 1605. For β-heteroatom elimination to afford allenes, see: (*c*) S. Ogoshi, S. Nishiguchi, K. Tsutsumi and H. Kurosawa, *J. Org. Chem.*, 1995, **60**, 4650.

10 D. Bouyssi, J. Gore, G. Balme, D. Louis and J. Wallach, *Tetrahedron Lett.*, 1993, **34**, 3129.

11 (*a*) N. E. Schore, *Chem. Rev.*, 1988, **88**, 1081; (*b*) M. Murakami, M. Ubukata, K. Itami and Y. Ito, *Angew. Chem., Int. Ed.*, 1998, **37**, 2248; (*c*) T. Takahashi, M. Ishikawa and S. Huo, *J. Am. Chem. Soc.*, 2002, **124**, 388; (*d*) T. Takhashi, Y. Li, P. Stepnicka, M. Kitamura, Y. Liu, K. Nakajima and M. Kotora, *J. Am. Chem. Soc.*, 2002, **124**, 576; (*e*) Z. Xi, K. Sato, Y. Gao, J. Lu and T. Takahashi, *J. Am. Chem. Soc.*, 2003, **125**, 9568.

12 (*a*) T. Tokoroyama, Y. Fukuyama, T. Kubota and K. Yokotani, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1557; (*b*) P. Wu, M. Chu and F. W. Fowler, *J. Org. Chem.*, 1988, **53**, 963.