JOC*Article*

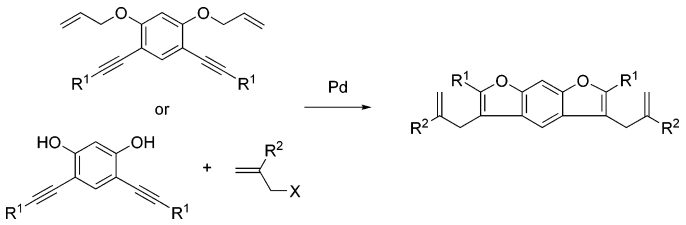
Palladium-Catalyzed Double Annulations To Construct Multisubstituted Benzodifurans

Zhiqiang Liang,[†,‡] Shengming Ma,*[,†] Jihong Yu,[‡] and Ruren Xu[‡]

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, People's Republic of China, and State Key Laboratory of Inorganic Synthesis and Preparative Chemistry, Jilin University, Changchun 130012, People's Republic of China

masm@mail.sioc.ac.cn

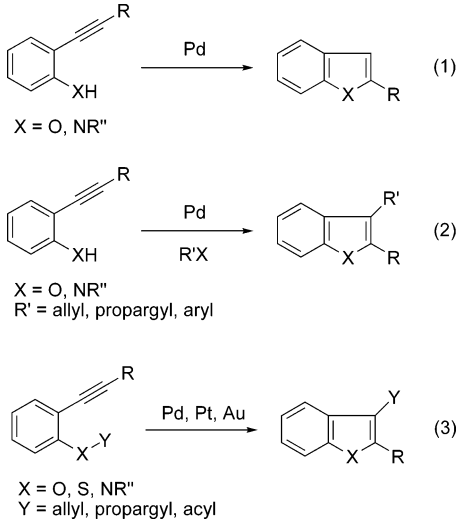
Received July 25, 2007



Efficient synthetic routes to construct multisubstituted benzo[1,2-*b*:5,4-*b*′]difurans and benzo[1,2-*b*:4,5-*b*′]difurans from bis(allyloxy)bis(alkynyl)benzenes or bis(alkynyl)dihydroxybenzenes and allylic halides utilizing palladium-catalyzed double annulations is reported. By further applying a double ring-closing metathesis reaction, pentacyclic compounds were also prepared.

Introduction

During the past decade, transition metal, especially palladium-catalyzed, annulation of *o*-alkynylarylamines, alcohols, and their derivatives to construct benzoheterocycles has been extensively studied (eq 1).[1,2] The 2,3-disubstituted indoles and benzofurans shown in eq 2 could be synthesized from the Pd-catalyzed cyclization of *o*-alkynylanilines, phenols, and their derivatives with organic halides (eq 2).[1] Furthermore, Pd-, Pt-, and Au-catalyzed annulation of 1-alkynylphenyl ethers, thioethers, or esters accompanied by migration of the allyl, propargyl, or aryl group (Y) affording benzoheterocycles was also reported (eq 3).[2]



Benzofurans are an important class of oxygen-containing heterocyclic compounds, which show potential biological activity, and numerous synthetic methods for benzofurans have been reported.[2a,b,3,4] On the other hand, benzodifurans have also received increasing attention because of their biological and pharmacological properties.[5] But, reports on their synthesis are still quite limited.[5,6]

Recently, we focused our attention on the construction of two or more rings with one synthetic operation. For example, recently we reported bicyclic carbopalladation,[7,8] double or triple

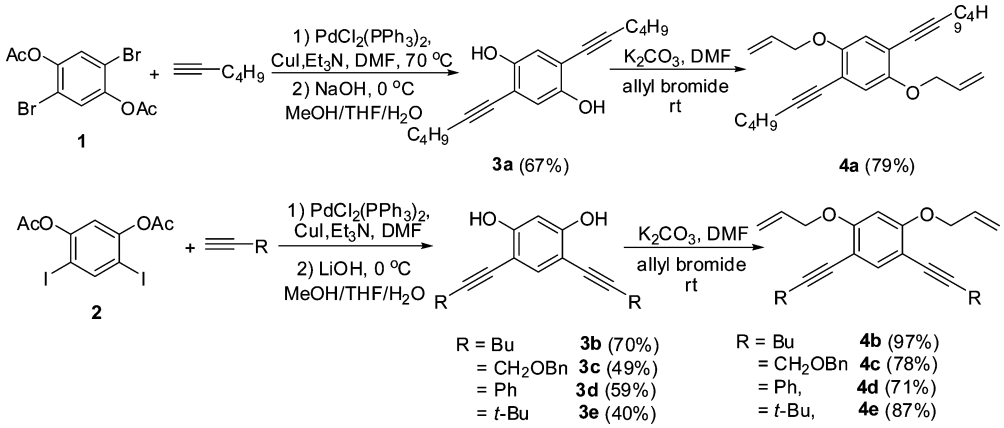
* Corresponding author. Fax: (+86)21-64167510.
† Chinese Academy of Sciences.
‡ Jilin University.

(1) For reviews, see: (a) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (b) Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2258. (c) Cacchi, F.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873. (d) Battistuzzi, G.; Cacchi, S.; Fabrizi, G. *Eur. J. Org. Chem.* **2002**, 2671. (e) Cacchi, S.; Fabrizi, G.; Goggiomani, A. *Heterocycles* **2002**, *56*, 613. (f) Balme, G.; Bouyssi, D.; Lomberget, T.; Monteiro, N. *Synthesis* **2003**, 2115.

(2) (a) Nakamura, I.; Mizushima, Y.; Yamamoto, Y. *J. Am. Chem. Soc.* **2005**, *127*, 15022. (b) Fürstner, A.; Davies, P. W. *J. Am. Chem. Soc.* **2005**, *127*, 15024. (c) Nakamura, I.; Sato, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 4473. (d) Fürstner, A.; Heilmann, E. K.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46* 4760.

10.1021/jo7016263 CCC: $37.00
Published on Web 10/24/2007

SCHEME 1



Suzuki coupling reactions,[9] and triple cyclic Heck reactions affording fused bicyclic or tetracyclic compounds, respectively; we also used a double ring-closing metathesis (RCM) reaction[10,11] to construct bicyclic quinolizidine alkaloids[12] and tricyclic benzodipyrans and their analogues.[13] Here, we report an efficient and versatile method of the synthesis of multisubstituted benzodifurans from bis(alkynyl)dihydroxybenzenes and bis(allyloxy)bis(alkynyl)benzenes.

Results and Discussion

Synthesis of Starting Materials. Dibromide **1** and diiodide **2**[13] were selected as the starting materials for synthesis of the substrates. Their Sonogashira coupling[14] with terminal alkynes followed by hydrolysis gave products **3a**−**e**, which were treated with allyl bromide in the presence of K_2CO_3 in DMF to give **4a**−**e** in acceptable yields (Scheme 1).

Similarly, compound **5** was synthesized from the Sonagashira coupling reaction of diiodide **2** with trimethylsilyl ethyne.[15] Double allylation of **5** afforded compound **6**, which was desilylated in the presence of KF in methanol to give **7**. Compounds **9a**−**c** were then prepared from **7** by its reaction with the corresponding allylic halides in the presence of K_2CO_3 and a catalytic amount of CuI in DMF, respectively.[4b] Unsymmetric compound **10** with different allylic groups at the terminal positions of the carbon−carbon triple bonds was obtained from the allylation of compound **8**, which was prepared from the monoallylic alkylation of compound **7** (Scheme 2).

Pd-Catalyzed Double Cyclization of 2,4-Bis(allyloxy)-1,5-bis(alkynyl)benzenes. For the synthesis of 2-substituted-3-allylbenzofurans, Balme et al. reported a $Pd(PPh_3)_4$-catalyzed allylative heteroannulation of *o*-alkynyl-allyloxybenzenes in a mixed solvent (THF/CH_3CN 4:1).[4c] When $Pd_2(dba)_3$·$CHCl_3$ and PPh_3 were used as the catalyst, the reaction of **4a** in CH_3CN under reflux afforded double cyclization product **11a** and monocyclization product **12a** in 23 and 69% yields, respectively (entry 1, Table 1). As shown in Table 1, the reaction of **4a** at 100 °C in toluene gave **11a** in 44% yield along with the monocyclic product **12** (39%, entry 2, Table 1). However, when the reaction was conducted in DMF at 100 °C, the desired

(3) (a) Cagniant, P.; Cagniant, D. *Adv. Heterocycl. Chem.* **1975**, *18*, 343. (b) Donnelly, D. M. X.; Meegan, M. J. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. 4, pp 657−712. (c) Sundberg, R. J.; Van Nguyen, P. In *Progress in Heterocyclic Chemistry*; Suschitzky, H., Scriven, E. F. V., Eds.; Pergamon Press: Oxford, 1993; Vol. 5, p 129. (d) Ono, M.; Kawashima, H.; Nonaka, A.; Kawai, T.; Haratake, M.; Mori, H.; Kung, M. P.; Kung, H. F.; Saji, H.; Nakayama, M. *J. Med. Chem.* **2006**, *49*, 2725.

(4) (a) Arcadi, A.; Cacchi, S.; Del Rosario, M.; Fabrizi, G.; Marinelli, F. *J. Org. Chem.* **1996**, *61*, 9280 and references therein. (b) Monteiro, N.; Balme, G. *Synlett* **1998**, 746. (c) Monteiro, N.; Arnold, A.; Balme, G. *Synlett* **1998**, 1111. (d) Cacchi, S.; Fabrizi, G.; Moro, L. *Synlett* **1998**, 741. (e) Liao, Y.; Smith, J.; Fathi, R.; Yang, Z. *Org. Lett.* **2005**, *7*, 2707. (f) Liang, Y.; Tang, S.; Zhang, X. D.; Mao, L. Q.; Xie, Y. X.; Li, J. H. *Org. Lett.* **2006**, *8*, 3017. (g) Nakamura, M.; Ilies, L.; Otsubo, S.; Nakamura, E. *Org. Lett.* **2006**, *8*, 2803. (h) Youn, S. W.; Eom, J. I. *Org. Lett.* **2005**, *7*, 3355 and references therein. (i) Katritzky, A. R.; Ji, Y.; Fang, Y.; Prakash, I. *J. Org. Chem.* **2001**, *66*, 5613.

(5) (a) Rene, L.; Buisson, J. P.; Royer, R.; Averbeck, D. *Eur. J. Med. Chem. Chim. Ther.* **1977**, *12*, 31. (b) Royer, R.; Bisagni, E.; Hudry, C.; Cheutin, A.; Desvoye, M. L. *Bull. Soc. Chim. Fr.* **1963**, 1003. (c) Chambers, J. J.; Kurrasch-Orbaugh, D. M.; Parker, M. A.; Nichols, D. E. *J. Med. Chem.* **2001**, *44*, 1003. (d) Chawla, H. P. S.; Grover, P. K.; Anand, N.; Kamboj, V. P.; Kar, A. B. *J. Med. Chem.* **1970**, *13*, 54.

(6) (a) Park, K. K.; Lim, H.; Kim, S.-H.; Bae, D. H. *J. Chem. Soc., Perkin Trans. 1* **2002**, 310. (b) Park, K. K.; Kim, S.-H.; Park, J. W. *J. Photochem. Photobiol., A* **2004**, *163*, 241. (c) Abdul-Azizl, M.; Auping, J. V.; Meador, M. A. *J. Org. Chem.* **1995**, *60*, 1303. (d) Terent'ev, A. P.; Grinev, A. N.; Bon-Khvar, P. *Zh. Obshch. Khim.* **1954**, *24*, 2050. (e) Worden, L. R.; Burgstahler, A. W.; Kaufman, K. D.; Weis, J. A.; Schaaf, T. K. *J. Heterocycl. Chem.* **1969**, *6*, 191.

(7) (a) Ma, S.; Xu, B. *J. Org. Chem.* **1998**, *63*, 9156. (b) Ma, S.; Xu, B.; Ni, B. *J. Org. Chem.* **2000**, *65*, 8532.

(8) Ma, S.; Ni, B.; Lin, S.; Liang, Z. *J. Organomet. Chem.* **2005**, *690*, 5389.

(9) Ma, S.; Ni, B. *J. Org. Chem.* **2002**, *67*, 8280.

(10) Schmidt, B.; Hermanns, J. *Curr. Org. Chem.* **2006**, *10*, 1363 and references cited therein.

(11) (a) Grubbs, R. H. *Handbook of Metathesis*; Wiley-VCH: Weinheim, Germany, 2003; Vols. 1−3. For recent reviews, see: (b) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012. (c) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18. (d) Schrock, R. R. In *Carbene Chemistry*; Bertrand, G., Ed.; Marcel Dekker: New York, 2002; pp 205−230. (e) Grubbs, R. H.; Trnka, T. M.; Sanford, M. S. In *Current Methods in Inorganic Chemistry*; Kurokawa, H., Yamamoto, A., Eds.; Elsevier: Amsterdam, 2003; Vol. 3, pp 187−231. (f) Arjona, O.; Csáky, A. G.; Plumet, J. *Eur. J. Org. Chem.* **2003**, 611. (g) Connon, S. J.; Blechert, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 1900. (h) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592. (i) Hoveyda, A. H.; Gillingham, D. G.; Van Veldhuizen, J. J.; Kataoka, O.; Garber, S. B.; Kingsbury, J. S.; Harrity, J. P. A. *Org. Biomol. Chem.* **2004**, *2*, 8. (j) Deiters, A.; Martin, S. F. *Chem. Rev.* **2004**, *104*, 2199. (k) McReynolds, M. D.; Dougherty, J. M.; Hanson, P. R. *Chem. Rev.* **2004**, *104*, 2239. (l) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4490. (m) Schrock, R. R. *Angew. Chem., Int. Ed.* **2006**, *45*, 3748. (n) Chauvin, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 3741. (o) Grubbs, R. H. *Angew. Chem., Int. Ed.* **2006**, *45*, 3760.

(12) (a) Ma, S.; Ni, B. *Org. Lett.* **2002**, *4*, 639. (b) Ma, S.; Ni, B. *Chem. Eur. J.* **2004**, *10*, 3286. (c) Ma, S.; Ni, B.; Liang, Z. *J. Org. Chem.* **2004**, *69*, 6305.

(13) Liang, Z.; Ma, S.; Yu, J.; Xu, R. *Tetrahedron* **2007**, *63*, 977.

(14) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467.

(15) Rosillo, M.; Domínguez, G.; Casarrubios, L.; Amador, U.; Pérez-Castells, J. *J. Org. Chem.* **2004**, *69*, 2084.

SCHEME 2

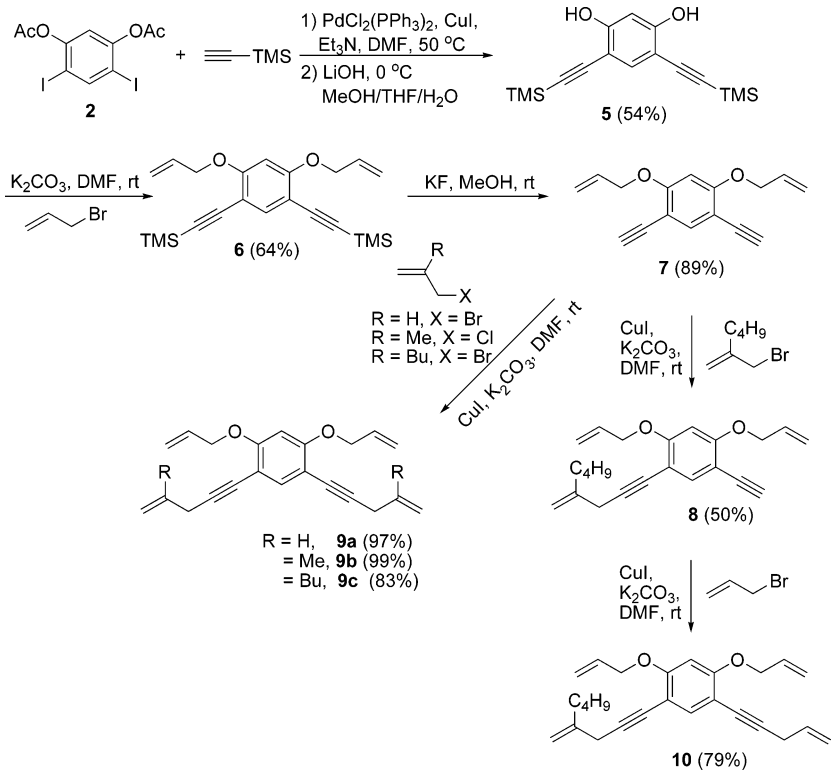
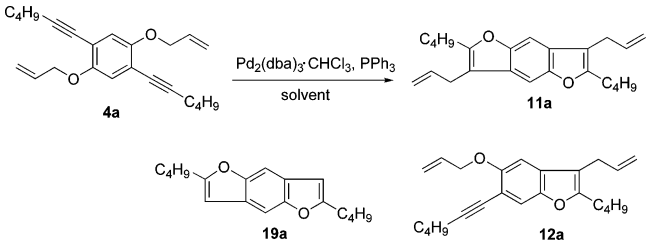


TABLE 1. Double Cyclizative Allyl Group Migration of 4a under Different Reaction Conditions



entry	solvent	*T* (°C)	time (h)	yield of **11a** (%) (**11a**/**19a**)[a]	yield of **12a** (%)
1	CH_3CN	reflux	12.5	23 (>20:1)	69
2	Toluene	100	13	44 (20:1)	39
3	DMF	100	13	24 (17:1)	
4	DMF	80	18.5	71 (>20:1)	
5	DMF[b]	80	18.5	64 (10:1)	
6	DMF	60	9	93 (16:1)	

[a] Ratio of **11a**/**19a** determined by NMR (300 MHz) analysis. [b] 5 mol % of $Pd(OAc)_2$ was used as the catalyst.

product **11a** was formed exclusively in 24% yield (entry 3, Table 1). Further study indicated that the reaction temperature is very important for this reaction. The best results were obtained by running the reaction in DMF at 60 °C affording **11a** in 93% yield (entry 6, Table 1). When $Pd(OAc)_2$ was used instead of $Pd_2(dba)_3{\cdot}CHCl_3$, the yield was much lower (entry 5, Table 1). Under these conditions, a trace amount of **19a** was formed from **4a**.

Under this optimized reaction condition, the corresponding products (i.e., 2,3,5,6-tetrasubstituted benzodifurans **11b**−**i**) were synthesized in acceptable yields. Some typical results are listed in Table 2. Various differently substituted 1,5-bis(allyloxy)-2,4-bis(alkynyl)benzenes that bear *n*-butyl (entry 1, Table 2), benzyloxymethyl (entry 2, Table 2), phenyl (entry 3, Table 2), and an allylic group (entries 5−8, Table 2) at each terminal position of the carbon−carbon triple bond were successfully converted into tetrasubstituted benzodifurans **11b**−**i** in moderate to good yields.

The products **11f**−**i** containing two 1,7-diene moieties may undergo double RCM reactions[10] to construct two new six-membered cycles. First, the tetraene substrate **11h** was converted to the fused pentacyclic compound **13** under the catalysis of the second generation of the Grubbs catalyst **15**[16] in CH_2Cl_2 under reflux. This product was then oxidized with DDQ in toluene at 80 °C to give 3,9-bisbutyl-dibenzo[*a*,*a*′]benzo[1,2-*b*:5,4-*b*′]difuran **14c** (Scheme 3). Furthermore, the one-pot sequential double RCM of tetraenes **11f**−**i**/oxidation reaction was studied:[17] after the double RCM reactions of **11f**−**i** under the same conditions, CH_2Cl_2 was removed under vacuum, which was followed by the addition of a solution of DDQ in toluene to afford the tetracyclic products **14a**−**d** in moderate yields after stirring for 4−8 h at 80 °C (Scheme 3).

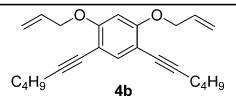
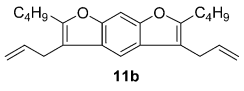
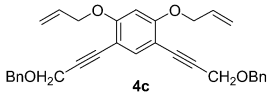
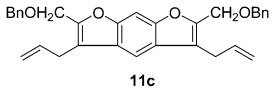
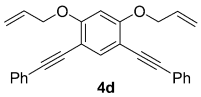
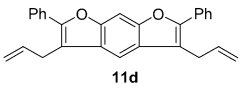
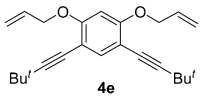
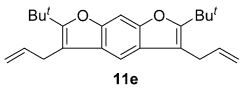
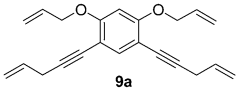
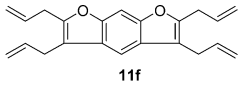
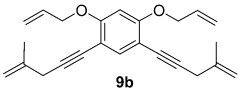
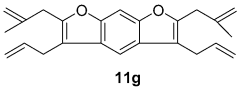
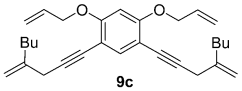
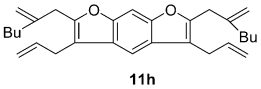
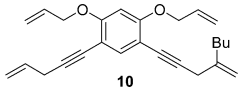
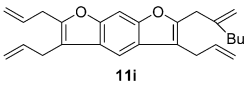
In addition, the substrate **16** was cycloisomerized with the catalysis of $Pd(OAc)_2$ in the presence of Cs_2CO_3 in DMA to form **17** in 93% yield, which was then converted to the tricyclic product **18** under the catalysis of $Pd_2(dba)_3{\cdot}CHCl_3$ and PPh_3 in DMF in 85% yield (Scheme 4).

Pd-Catalyzed Two-Component Cyclization of Dihydroxydialkynylbenzenes and Allylic Halides. In the synthesis of these benzodifurans depicted previously, the substituents attached to the oxygen atoms in the substrates were limited to the simplest allyl group. We thought that Pd-catalyzed double

(16) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett*. **1999**, *1*, 953.

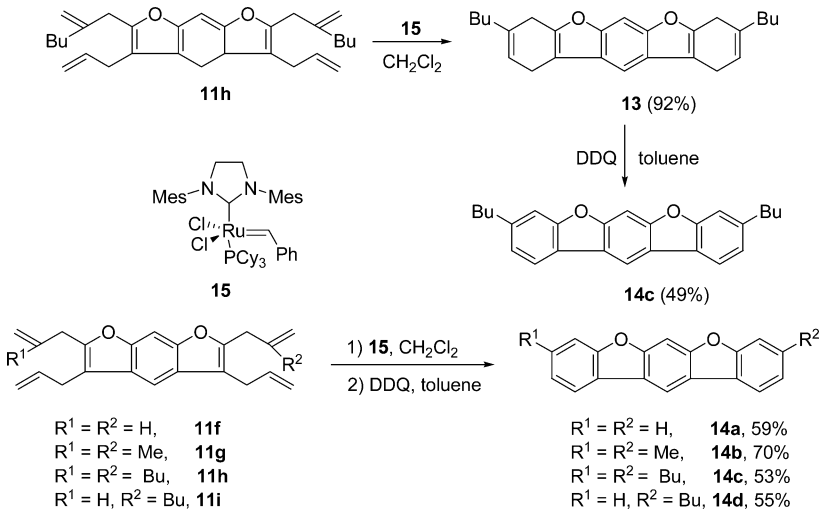
(17) (a) Kotha, S.; Mandal, K. *Tetrahedron Lett.* **2004**, *45*, 2585. (b) Kotha, S.; Shah, V. R.; Mandal, K. *Adv. Synth. Catal*. **2007**, *349*, 1159. (c) Ma, S.; Yu, F.; Zhao, J. *Synlett* **2007**, 583.

TABLE 2. Double Cyclizative Allyl Group Migration to Form Tetrasubstituted Benzodifurans

Entry	Substrates **4**	Products **11**	Isolated Yield of **11** (%)[a]
1	 **4b**	 **11b**	71 (15:1)
2	 **4c**	 **11c**	59 (>20:1)
3	 **4d**	 **11d**	81 (10:1)
4	 **4e**	 **11e**	trace[b,c]
5	 **9a**	 **11f**	88 (>20:1)
6	 **9b**	 **11g**	88 (>20:1)[c]
7	 **9c**	 **11h**	66 (>20:1)[c]
8	 **10**	 **11i**	51 (>20:1)[c]

[a] Ratio of **11/19** determined by NMR (300 MHz) analysis of the crude reaction mixture. [b] 80% monocyclic compound was formed with 16% substrate **4e** being recovered. [c] $Pd(PPh_3)_4$ was used as catalyst.

SCHEME 3



annulations of bis(alkylnyl)dihydroxybenzenes with allylic halides could generate corresponding tetrasubstituted benzofurans. The cyclization of 2,5-bis(hex-1′-ynyl)-1,4-dihydroxybenzene **3a** in the presence of allyl bromide was used to optimize the reaction conditions, and some representative results are listed in Table 3. It should be noted that this reaction may be rather complicated because of the possible formation of other products, such as **4a**, **18**, and **19a**. In fact, the reaction in the presence of

SCHEME 4

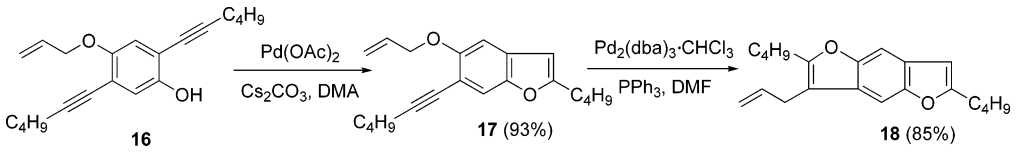
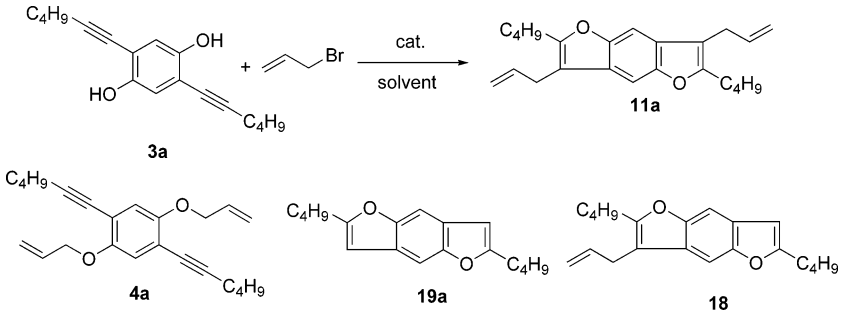


TABLE 3. Double Annulations of 3a with Allyl Bromide under Different Reaction Conditions



entry	catalyst (5 mol %)	allyl bromide (equiv)	solvent	*T* (°C)	**11a**/**18**/**19a**[a]
1	$PdCl_2$	8	CH_3CN	reflux	*b*
2	$PdCl_2$	10	CH_3CN	reflux	*c*
3	$PdCl_2$	10	DMF	80	1.8:3:1
4	$PdCl_2$	20	DMF	80	3.5:4:1
5	$PdCl_2(CH_3CN)_2$	20	DMF	80	7:6:1
6	$PdCl_2(PhCN)_2$	20	DMF	80	5:5:1
7	$PdCl_2(PPh_3)_2$	20	DMF	80	2:3:1
8	$PdCl_2$	20	DMA	80	80% (9:1)[d]
9	$PdCl_2$	10	DMA	80	66% (6.6:1)[d]
10	$PdCl_2$	20	DMA	40	74% (>20:1)[d]

[a] Determined by NMR (300 MHz) analysis. [b] 6 equiv of K_2CO_3 was used, and 26% **4a** was isolated. [c] **19a** was formed. [d] Ratio of **11a**/**18**. Formation of **19a** was very limited, if at all.

K_2CO_3 and $PdCl_2$ in CH_3CN under reflux gave **4a** in 26% yield (entry 1, Table 3). When the reaction was conducted in the absence of the inorganic base, only a trace amount of the cycloisomerization product **19a** was formed (entry 2, Table 3). After changing the solvent to DMF, the reaction was very complicated, affording an unseparable mixture of **4a**, **18**, and **19a** by using $PdCl_2$ or $PdCl_2(PPh_3)_2$ as the catalyst (entries 3−7, Table 3). However, when the reaction was conducted in DMA, the yield was improved to 80% with the **11a**/**18**/**19a** ratio being 9:1:0 (entry 8, Table 3). The fewer the equivalents of allyl bromide used, the lower the yield and selectivity (entries 8 and 9, Table 3). Best results were obtained when the reaction was conducted in the presence of 5 mol % $PdCl_2$ and 20 equiv of allyl bromide in DMA at 40 °C, leading to a 74% yield of **11a** with the ratio of **11a**/**18**/**19a** being >20:1:0.

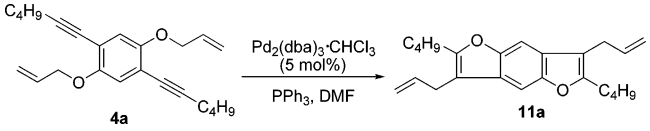
With the optimized reaction conditions in hand, the scope of this reaction was explored (Table 4). Several types of substituents R^1 at the terminal position of the carbon−carbon triple bonds, such as butyl, CH_2OBn, phenyl, and *t*-butyl groups, could be introduced into the products. The substituents R^2 at the 2-position of the allylic halides could be methyl, *n*-butyl, or an electron-withdrawing group such as the ethoxycarbonyl group.

Conclusion

In summary, we have developed an easy and efficient route for the synthesis of multisubstituted benzodifurans by using palladium-catalyzed double annulations of bis(allyloxy)bis(alkynyl)benzenes or bis(alkynyl)dihydroxybenzenes in the presence of allylic halides in good yields. It was also demonstrated that the products **11f**−**i** containing two 1,7-dienes moieties may be further utilized to build two aromatic rings to afford a pentacyclic aromatic compound via a one-pot double RCM and oxidation reaction.

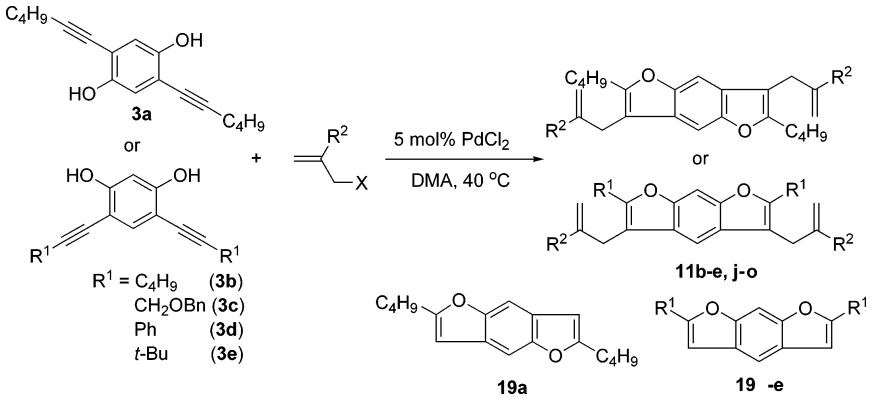
Experimental Section

Pd-Catalyzed Double Cyclization of Bis(allyloxy)bis(alkynyl)benzenes. Cycloisomerization of 4a for the Synthesis of 2,6-Dibutyl-3,7-bisallylbenzo[1,2-*b*:4,5-*b*′]difuran 11a (Typical Procedure A). To a solution of **4a** (70 mg, 0.20 mmol) in DMF (2 mL) was added $Pd_2(dba)_3$·$CHCl_3$ (10 mg, 0.096 mmol) and PPh_3 (10 mg, 0.038 mmol) under Ar. The reaction mixture was stirred for 9 h at 60 °C as monitored by TLC, quenched with water, extracted with Et_2O, washed with brine, and dried over $MgSO_4$. Evaporation and flash column chromatography on silica gel (petroleum ether) gave **11a** (65 mg, 93%) as an oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.38 (s, 1H), 6.02−5.92 (m, 2H), 5.18−5.05 (m, 4H), 3.40 (d, J = 6.3 Hz, 4H), 2.74 (t, J = 7.2 Hz, 4H), 1.77−1.66 (m, 4H), 1.43−1.35 (m, 4H), 0.95 (t, J = 7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 150.7, 135.9, 126.6, 115.5, 111.6, 99.6, 30.5, 28.1, 26.2, 22.3, 13.8; MS (EI) *m*/*z* (%): 350 (67.1), 307 (100.0); IR (neat) ν (cm^{-1}): 2957, 2929, 2872, 1639, 1436; HRMS calcd for $C_{24}H_{31}O_2$: 351.2319; Found: 351.2319.



One-Pot Sequential Double RCM of Tetraenes/Oxidation Reaction. Synthesis of 3,9-Bisbutylbenzo[1,2-*b*:5,4-*b*′]bisbenzofuran 14c (Typical Procedure B). To a solution of **11h** (85 mg, 0.198 mmol) in CH_2Cl_2 (5 mL) was added the second generation

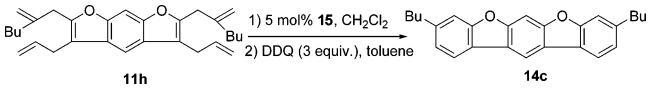
TABLE 4. Double Annulations of Bis(alkynyl)dihydroxybenzenes with Allyl Halides



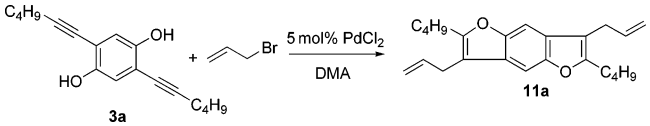
entry	substrate	R^2	X	yield of **11** and **19** (%)	**11**/**19**[a]
1	**3b**	H	Br	45 (**11b**)	>20:1
2	**3c**	H	Br	42 (**11c**)	>20:1
3	**3d**	H	Br	76 (**11d**)	
4	**3e**	H	Br	76 (**11e**)	
5	**3d**	Me	Cl	76 (**11j**)	
6	**3e**	Me	Cl	80 (**11k**)	20:1
7	**3d**	*n*-Bu	Br	78 (**11l**)	
8	**3a**	CO_2Et	Br	61 (**11m**)	
9	**3d**	CO_2Et	Br	66 (**11n**)	
10	**3e**	CO_2Et	Br	71 (**11o**)	

[a] Ratio of **11**/**19** determined by NMR (300 MHz) analysis.

Grubbs catalyst (8 mg, 0.009 mmol) under Ar. After being refluxed with stirring under Ar for 11 h, the reaction was complete as monitored by TLC. Then CH_2Cl_2 was removed by evaporation, which was followed by the addition of toluene (3 mL) and DDQ (139 mg, 0.612 mmol). After being stirred for 4 h at 80 °C, the reaction was complete as monitored by TLC. Evaporation and flash column chromatography on silica gel (petroleum ether) gave **14c** (39 mg, 53%) as a white solid: mp 123−124 °C (Et_2O). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.89 (d, J = 8.1 Hz, 2H), 7.67 (s, 1H), 7.39 (s, 2H), 7.20 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 2H), 2.79 (t, J = 7.8 Hz, 4H), 1.74−1.68 (m, 4H), 1.50−1.38 (m, 4H), 0.98 (t, J = 7.5 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 142.2, 123.4, 121.9, 120.6, 119.8, 111.2, 110.6, 95.2, 36.0, 33.9, 22.3, 14.0; MS (EI) *m*/*z* (%): 370 (58.4), 327 (100.0); IR (neat) ν (cm^{-1}): 2953, 2923, 1608, 1445, 1125; Anal. calcd for $C_{26}H_{26}O_2$: C, 84.29; H, 7.07; Found: C, 83.90; H, 7.30.



Pd-Catalyzed Two-Component Cyclization of Dihydroxydialkynylbenzenes and Allylic Halides. Synthesis of 2,6-Bisbutyl-3,7-bisallylbenzo[1,2-*b*:4,5-*b*′]difuran 11a (Typical Procedure C). To a solution of **3a** (50 mg, 0.185 mmol) in DMA (2 mL) was added allyl bromide (448 mg, 3.70 mmol) and $PdCl_2$ (2 mg, 0.011 mmol) in open air. The reaction mixture was stirred for 3 h at 40 °C, quenched with water, extracted with Et_2O, washed with brine, and dried over $MgSO_4$. Evaporation and flash column chromatography on silica gel (petroleum ether) gave **11a** (48 mg, 74%).



Acknowledgment. Financial support from the Major State Basic Research Development Program (Grant 2006CB806105), National NSF of China (20172060, 200423001, and 20121202), and the Shanghai Municipal Committee of Science and Technology is greatly appreciated.

Supporting Information Available: Experimental procedures and characterization data of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO7016263