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Synthesis of Carbocyclic Aromatic Compounds Using Ruthenium-Catalyzed Ring-Closing Enyne Metathesis

Hidetoshi Takahashi, Kazuhiro Yoshida,* and Akira Yanagisawa*

Department of Chemistry, Graduate School of Science, Chiba University, Yayoi-cho, Inage-ku, Chiba 263-8522, Japan

kyoshida@faculty.chiba-u.jp; ayanagi@faculty.chiba-u.jp

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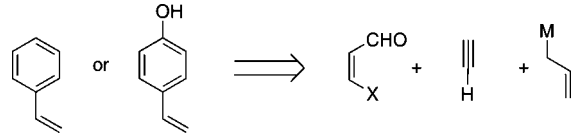

General synthetic methods of substituted carbocyclic aromatic compounds are reported. Ring-closing enyne metathesis (RCEM)/dehydration of 1,5-octadien-7-yn-4-ols **6** and RCEM/tautomerization of 1,5-octadien-7-yn-4-ones **7** furnished a wide variety of substituted styrenes **4** and 4-vinylphenols **8**, respectively. Acyclic precursors **6** and **7** were readily prepared from β-halo-α,β-unsaturated aldehydes **9** or 3-halo-2-propene-1-ols **13** by utilizing combinations of the Sonogashira coupling, allylation, and the Dess−Martin oxidation. The RCEM/dehydration for the synthesis of 1,3,5-tris(1-phenylethenyl)benzene derivative **4r** and the RCEM/RCM/dehydration for the synthesis of 1,1′-binaphthyl derivative **19a** are also presented as applications of this method.

Introduction

Substituted styrenes offer considerable utility as important intermediates in organic chemistry.[1,2] For instance, 4-vinylstyrenes are well-known building blocks of pharmaceuticals,[1c−g] polymer-supported catalysts,[2b] functional polymers,[2c] and calixarenes.[2d] The development of highly reliable and flexible synthetic methods of substituted styrenes is therefore an important subject in organic synthesis. Commonly employed methods for the preparation of styrenes are functional group transformations on existing aromatic rings, such as the Wittig olefination of aryl carbonyl compounds,[3] the transition-metal-catalyzed cross-coupling reaction of aryl halides,[4] the Heck reaction of aryl halides,[5] and the elimination of aryl alcohols to generate a double bond.[6] However, there are a few reports[7] of the construction of benzene rings of styrenes from acyclic precursors despite the fact that unique styrenes can be obtained with this entirely different procedure.

The construction of aromatic rings from acyclic precursors using ruthenium-catalyzed ring-closing olefin metathesis (RCM)[8,9] has recently emerged as an interesting and efficient strategy for preparing aromatic compounds.[10−12] One of the greatest advantages of this strategy is the flexible introduction of various

To whom correspondence should be addressed. Tel: +81-43-290-2790. Fax: +81-43-290-2789.

(1) For examples, see: (a) Fassina, V.; Ramminger, C.; Seferin, M.; Monteiro, A. L. *Tetrahedron* **2000**, *56*, 7403–7409. (b) Fürstner, A.; Thiel, O. R.; Kindler, N.; Bartkowska, B. *J. Org. Chem.* **2000**, *65*, 7990–7995. (c) Winum, J.-Y.; Baghdiguian, S.; Commes, T.; Leydet, A.; Montero, J.-L. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 3529–3532. (d) Perera, R. P.; Wimalasena, D. S.; Wimalasena, K. *J. Med. Chem.* **2003**, *46*, 2599–2605. (e) Snider, B. B.; Grabowski, J. F. *Tetrahedron* **2006**, *62*, 5171–5177. (f) Böehrsch, V.; Blechert, S. *Chem. Commun.* **2006**, 1968–1970. (g) Nagarapu, L.; Paparaju, V.; Satyender, A. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 2351–2354.

(2) (a) For examples, see: *Styrene Polymers in Encyclopedia of Polymer Science and Engineering*, 2nd ed.; Moore, E. R., Ed.; Wiley-Interscience: New York, 1989; Vol. 16, and references therein. (b) Heckel, A.; Seebach, D. *Helv. Chim. Acta* **2002**, *85*, 913–926. (c) Xu, L.; Yokoyama, E.; Satoh, M. *Langmuir* **2005**, *21*, 7153–7160. (d) Yordanova, S.; Miloshev, S.; Berlinova, I.; Diakovski, B. *J. Inclusion Phenom. Macrocycl. Chem.* **2006**, *56*, 337–344.

(3) For recent examples, see: (a) Srikrishna, A.; Babu, R. R.; Ravikumar, P. C. *Synlett* **2007**, 655–657. (b) Tietze, L. F.; Brasche, G.; Grube, A.; Boehnke, N.; Stadler, C. *Chem.—Eur. J.* **2007**, *13*, 8543–8563.

(4) For recent examples, see: (a) Belema, M.; Nguyen, V. N.; Zusi, F. C. *Tetrahedron Lett.* **2004**, *45*, 1693–1697. (b) Zeng, F.; Stehouwer, J. S.; Jarkas, N.; Voll, R. J.; Williams, L.; Camp, V. M.; Votaw, J. R.; Owens, M. J.; Kilts, C. D.; Nemeroff, C. B.; Goodman, M. M. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 3044–3047. (c) Achmatowicz, M.; Chan, J.; Wheeler, P.; Liu, L.; Faul, M. M. *Tetrahedron Lett.* **2007**, *48*, 4825–4829.

(5) For recent examples, see: (a) Kotoku, N.; Kato, T.; Narumi, F.; Ohtani, E.; Kamada, S.; Aoki, S.; Okada, N.; Nakagawa, S.; Kobayashi, M. *Bioorg. Med. Chem.* **2006**, *14*, 7446–7457. (b) Huang, W.-S.; Wang, Y.; Sundaramoorthi, R.; Thomas, R. M.; Wen, D.; Liu, S.; Lentini, S. P.; Das, S.; Banda, G.; Sawyer, T. K.; Shakespeare, W. C. *Tetrahedron Lett.* **2007**, *48*, 7388–7391.

(6) For recent examples, see: (a) Antane, S.; Caufield, C. E.; Hu, W.; Keeney, D.; Labthavikul, P.; Morris, K.; Naughton, S. M.; Petersen, P. J.; Rasmussen, B. A.; Singh, G.; Yang, Y. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 176–180. (b) Nakamura, S.; Sugano, Y.; Kikuchi, F.; Hashimoto, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 6532–6535. (c) Sinha, A. K.; Sharma, A.; Joshi, B. P. *Tetrahedron* **2007**, *63*, 960–965.

(7) For examples, see: (a) Gevorgyan, V.; Yamamoto, Y. *J. Organomet. Chem.* **1999**, *576*, 232–247. (b) Xi, Z.; Li, Z.; Umeda, C.; Guan, H.; Li, P.; Kotora, M.; Takahashi, T. *Tetrahedron* **2002**, *58*, 1107–1117. (c) Gorin, D. J.; Watson, I. D. G.; Toste, F. D. *J. Am. Chem. Soc.* **2008**, *130*, 3736–3737.

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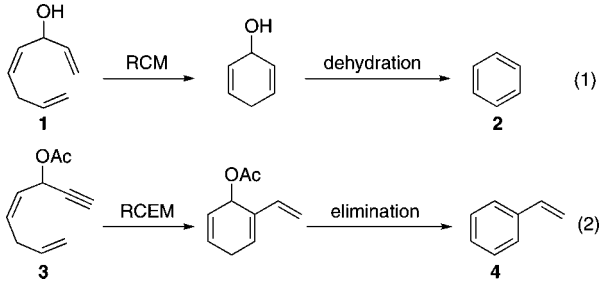
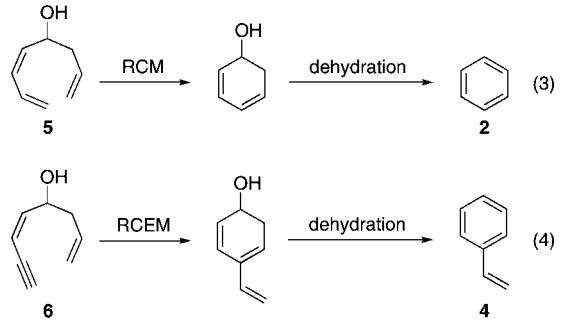
substituents to the aromatic rings. Since modern synthetic organic chemistry offers sufficient flexibility to construct acyclic compounds selectively, the formation of aromatic compounds from acyclic precursors having various substituents makes it possible to obtain a wide variety of aromatic compounds without the formation of inseparable regioisomers.

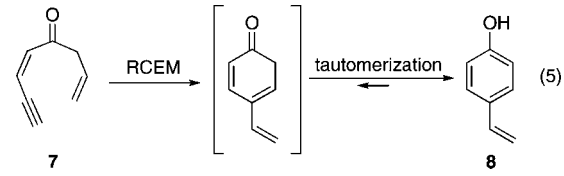
In the past few years, we have devoted much of our effort to this field[13] and reported that benzenes **2** and styrenes **4** can be obtained by RCM/dehydration of 1,4,7-octatrien-3-ols **1** (eq 1)[13b] and ring-closing enyne metathesis (RCEM)[14]/elimination of 3-acetoxy-4,7-octadien-1-ynes **3** (eq 2),[13f] respectively. Although various benzenes and styrenes could be synthesized without the formation of regioisomers, these approaches were limited by the difficulty of preparing **1** and **3**. Further, in the styrene synthesis, the requirement of acyl protection at the propargyl hydroxyl group of the substrate was another disadvantage. Very low conversions were observed in the RCEM with substrates having a free propargyl hydroxyl group, which were the precursors of **3**.



In 2008, we reported an improved and general synthetic approach to the synthesis of benzenes **2** that adopted 1,5,7-octatrien-4-ols **5** instead of **1** as the new acyclic precursors of RCM/dehydration (eq 3).[13e] Because the synthetic routes to **1** show great generality in which cross-coupling with vinyl metal reagents and allylation with allyl metal reagents were employed as carbon−carbon bond forming reactions, a wide variety of substituted benzenes **2** having various functionalities could be synthesized. Based on this background, we expected that the generality of the synthesis of styrenes might likewise be improved by replacing enyne substrates **3** with 1,5-octadien-7-yn-4-ols **6** (eq 4). The analogy of the basic structure of **6** to **5** is expected to lead to the easy and flexible preparation of **6**. In addition, acyl protection of the hydroxyl group of **6** may be unnecessary because the hydroxyl group is not located at the propargyl position of **6**.



It should also be added that the synthesis of 4-vinylphenols **8** by RCEM/tautomerization of 1,5-octadien-7-yn-4-ones **7** is possible (eq 5). Because of the instability of 4,7-octadien-1-yn-3-ones that we tried to prepare by oxidation of the alcohol derivatives of **3**,[13f] we were unable to obtain 2-vinylphenols by RCEM/tautomerization. However, taking into account that a considerable number of the analogues of **7**, which have a similar conjugate (*Z*)-2-en-4-yn-1-one framework, have been reported so far,[15] we have every reason to expect that **7** would be prepared and their conversion to 4-vinylphenols **8** would be achieved.



In this paper, we report the synthesis of styrenes **4** by RCEM/dehydration of **6** and the synthesis of 4-vinylphenols **8** by RCEM/tautomerization of **7**. We describe first the preparation of enyne substrates **6** and **7**, and then the synthesis of the styrenes in detail. We also present applications of the RCEM/dehydration to the synthesis of unique aromatic compounds, 1,3,5-tris(1-phenylethenyl)benzene derivative **4r** and 1,1′-binaphthyl derivative **19a**.

(8) For a comprehensive review, see: (a) *Handbook of Metathesis*; Grubbs, R. H., Ed; Wiley-VCH: Weinheim, Germany, 2003. For reviews, see: (b) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413–4450. (c) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012–3043. (d) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18–29. (e) Hoveyda, A. H.; Zhugralin, A. R. *Nature* **2007**, *450*, 243–251.

(9) For reports on the pharmaceutical application of RCM in multi-kilogram scale (>400 kg of cyclized product), see: (a) Nicola, T.; Brenner, M.; Donsbach, K.; Kreye, P. *Org. Process Res. Dev.* **2005**, *9*, 513–515. (b) Yee, N. K.; Farina, V.; Houpis, I. N.; Haddad, N.; Frutos, R. P.; Gallou, F.; Wang, X.-J.; Wei, X.; Simpson, R. D.; Feng, X.; Fuchs, V.; Xu, Y.; Tan, J.; Zhang, L.; Xu, J.; Smith-Keenan, L. L.; Vitous, J.; Ridges, M. D.; Spinelli, E. M.; Johnson, M.; Donsbach, K.; Nicola, T.; Brenner, M.; Winter, E.; Kreye, P.; Samstag, W. *J. Org. Chem.* **2006**, *71*, 7133–7145. (c) Tsantrizos, Y. S.; Ferland, J.-M.; McClory, A.; Poirier, M.; Farina, V.; Yee, N. K.; Wang, X.-J.; Haddad, N.; Wei, X.; Xu, J.; Zhang, L. *J. Organomet. Chem.* **2006**, *691*, 5163–5171.

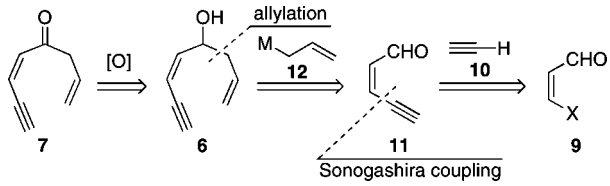
(10) For a review, see: Donohoe, T. J.; Orr, A. J.; Bingham, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 2664–2670.

(11) For reports on the direct synthesis of carbocyclic aromatic compounds using RCM, see: (a) Iuliano, A.; Piccioli, P.; Fabbri, D. *Org. Lett.* **2004**, *6*, 3711–3714. (b) Walker, E. R.; Leung, S. Y.; Barrett, A. G. M. *Tetrahedron Lett.* **2005**, *46*, 6537–6540. (c) Bonifacio, M. C.; Robertson, C. R.; Jung, J.-Y.; King, B. T. *J. Org. Chem.* **2005**, *70*, 8522–8526. (d) Pelly, S. C.; Parkinson, C. J.; Van Otterlo, W. A. L.; De Koning, C. B. *J. Org. Chem.* **2005**, *70*, 10474–10481. (e) Collins, S. K.; Grandbois, A.; Vachon, M. P.; Côté, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 2923–2926. (f) Grandbois, A.; Collins, S. K. *Chem.—Eur. J.* **2008**, *14*, 9323–9329. For reports using RCM/elimination protocol, see: (g) Evans, P.; Grigg, R.; Ramzan, M. I.; Sridharan, V.; York, M. *Tetrahedron Lett.* **1999**, *40*, 3021–3024. (h) Huang, K. S.; Wang, E. C. *Tetrahedron Lett.* **2001**, *42*, 6155–6157. (i) Chen, Y.; Dias, H. V. R.; Lovely, C. J. *Tetrahedron Lett.* **2003**, *44*, 1379–1382. (j) Chen, P.-Y.; Chen, H.-M.; Chen, L.-Y.; Tzeng, J.-Y.; Tsai, J.-C.; Chi, P.-C.; Li, S.-R.; Wang, E.-C. *Tetrahedron* **2007**, *63*, 2824–2828. For reports using the RCM/oxidation protocol, see: (k) Kotha, S.; Mandal, K. *Tetrahedron Lett.* **2004**, *45*, 2585–2588. (l) Ma, S.; Yu, F.; Zhao, J. *Synlett* **2007**, 583–586. (m) Kotha, S.; Shah, V. R.; Mandal, K. *Adv. Synth. Catal.* **2007**, *349*, 1159–1172. For reports using the RCM/tautomerization protocol, see: (n) van Otterlo, W. A. L.; Ngidi, E. L.; Coyanis, E. M.; de Koning, C. B. *Tetrahedron Lett.* **2003**, *44*, 311–313. (o) Toueg, J.; Prunet, J. *Synlett* **2006**, 2807–2811.

(12) For selected recent reports on the synthesis of heterocyclic aromatic compounds using RCM, see: (a) Arisawa, M.; Nishida, A.; Nakagawa, M. *J. Organomet. Chem.* **2006**, *691*, 5109–5121. (b) Donohoe, T. J.; Fishlock, L. P.; Procopiou, P. A. *Chem.—Eur. J.* **2008**, *14*, 5716–5726.

(13) (a) Yoshida, K.; Imamoto, T. *J. Am. Chem. Soc.* **2005**, *127*, 10470–10471. (b) Yoshida, K.; Kawagoe, F.; Iwadate, N.; Takahashi, H.; Imamoto, T. *Chem. Asian J.* **2006**, *1*, 611–613. (c) Yoshida, K.; Horiuchi, S.; Iwadate, N.; Kawagoe, F.; Imamoto, T. *Synlett* **2007**, 1561–1564. (d) Yoshida, K.; Toyoshima, T.; Imamoto, T. *Chem. Commun.* **2007**, 3774–3776. (e) Yoshida, K.; Takahashi, H.; Imamoto, T. *Chem.—Eur. J.* **2008**, *14*, 8246–8261. (f) Yoshida, K.; Shishikura, Y.; Takahashi, H.; Imamoto, T. *Org. Lett.* **2008**, *10*, 2777–2780. (g) Yoshida, K.; Narui, R.; Imamoto, T. *Chem.—Eur. J.* **2008**, *14*, 9706–9713. (h) Yoshida, K.; Toyoshima, T.; Imamoto, T. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 1512–1517. (i) Yoshida, K.; Kawagoe, F.; Hayashi, K.; Horiuchi, S.; Imamoto, T.; Yanagisawa, A. *Org. Lett.* **2009**, *11*, 515–518.

SCHEME 1



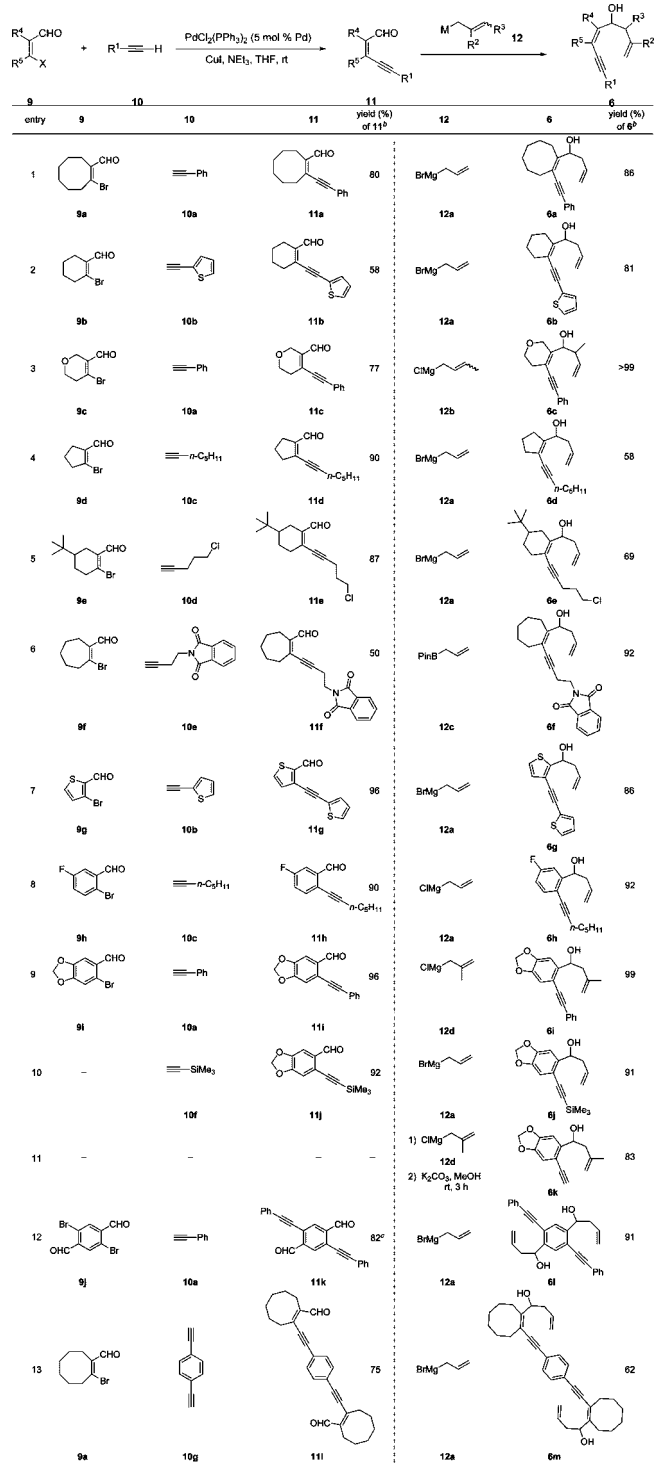
Results and Discussion

The retrosynthetic analysis of **6** and **7** is shown in Scheme 1. The route starts from the Sonogashira coupling[16] between terminal alkynes **10** and β-halo-α,β-unsaturated aldehydes **9**,[17,18] which are well-known and readily prepared building blocks. Then, the allylation of resulting coupling products **11** with allyl metal reagents **12** is expected to yield **6**,[19] which are the precursors of styrenes **4**. Further, the preparation of **7** for the synthesis of 4-vinylphenols **8** is expected to be achieved by oxidizing **6** at the alcohol position.

The results of the Sonogashira coupling between **9** and **10** and the allylation reaction of coupling products **11** with **12** to yield **6** are summarized in Table 1. The Sonogashira coupling was conducted with various **9** and **10** in the presence of $PdCl_2(PPh_3)_2$ (5 mol %), CuI (5 mol %), and NEt_3 (3 equiv) in THF, and the resulting coupling products **11** were obtained in good yields after silica gel chromatography. The following allylation of aldehydes **11** was conducted with readily available allyl Grignard or allylborane reagents without any problems to produce desired enyne substrates **6**. In the case of the preparation of **6k** that has a terminal alkyne, the crude mixture of the allylation of **11j** was treated with K_2CO_3 in MeOH at room temperature to cleave the C−Si bond (Table 1, entry 11).

For the preparation of **6**, we also examined another synthetic route starting from 3-halo-2-propen-1-ols **13** that were prepared by reducing corresponding β-halo-α,β-unsaturated esters[20] (Table 2). The route involves the Sonogashira coupling between **13** and **10**, the oxidation of resulting coupling products **14** to aldehydes **11** with Dess-Martin periodinane, and the allylation of **11** with allyl metal reagents **12** to yield **6**. All Sonogashira coupling reactions were run at room temperature and desired coupling products **14** were obtained in high yields. However, a non-negligible amount of the (*Z*)-stereoisomer of **14a** (*E*/*Z* = 10/1) was produced when the reaction of geometrically pure (*Z*)-**13a** with **10a** was carried out (Table 2, entry 1). The undesired (*Z*)-stereoisomer was removed by gel permeation chromatography at the next oxidation step, because the separa-

TABLE 1. Preparation of 1,5-Octadien-7-yn-4-ols 6, Precursors of Styrenes 4, from β-Halo-α,β-unsaturated Aldehydes 9 by Sonogashira Coupling and Allylation[a]



[a] Sonogashira coupling was carried out with β-halo-α,β-unsaturated aldehyde **9** and terminal alkyne **10** in the presence of $PdCl_2(PPh_3)_2$ (5 mol %), CuI (5 mol %), and NEt_3 (3 equiv) in THF at room temperature for 17−49 h. Allylation was carried out with **11** and allyl metal reagent **12** under various conditions (see the Supporting Information for details). [b] Yield of isolated product after silica gel chromatography. [c] The reaction was carried out at refluxing temperature.

(14) (a) Mori, M. *Top. Organomet. Chem.* **1998**, *1*, 133–154. (b) Poulsen, C. S.; Madsen, R. *Synthesis* **2003**, 1–18. (c) Diver, S. T.; Giessert, A. J. *Chem. Rev.* **2004**, *104*, 1317–1382. (d) Mori, M. *Adv. Synth. Catal.* **2007**, *349*, 121–135.

(15) (a) Kusumoto, T.; Nishide, K.; Hiyama, T. *Chem. Lett.* **1985**, 1409–1410. (b) Kobayashi, S.; Matsui, S.; Mukaiyama, T. *Chem. Lett.* **1988**, 1491–1494. (c) Liu, Y.; Zhong, Z.; Nakajima, K.; Takahashi, T. *J. Org. Chem.* **2002**, *67*, 7451–7456. (d) Jeong, I. H.; Jeon, S. L.; Kim, M. S.; Kim, B. T. *J. Fluorine Chem.* **2004**, *125*, 1629–1638. (e) Irifune, T.; Ohashi, T.; Ichino, T.; Sakai, E.; Suenaga, K.; Uemura, D. *Chem. Lett.* **2005**, *34*, 1058–1059. (f) Casey, C. P.; Strotman, N. A. *J. Org. Chem.* **2005**, *70*, 2576–2581.

(16) For a review, see: Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874–922.

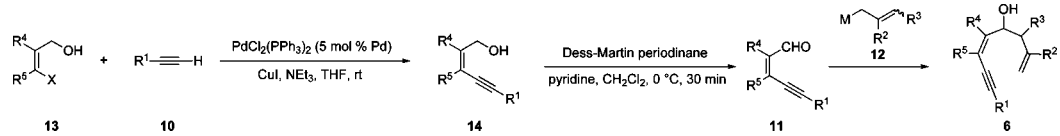
(17) **9a**−**f** and **9j** are known compounds, and **9g**−**i** are commercially available; see the Supporting Information.

(18) For a review, see: Brahma, S.; Ray, J. K. *Tetrahedron* **2008**, *64*, 2883–2896.

(19) For similar synthetic approaches to the construction of the *o*-ethynyl(1-hydroxy-3-butenyl)benzene framework, see: (a) Blanco-Urgoiti, J.; Casarrubios, L.; Domínguez, G.; Pérez-Castells, J. *Tetrahedron Lett.* **2001**, *42*, 3315–3317. (b) Rosillo, M.; Domínguez, G.; Casarrubios, L.; Amador, U.; Pérez-Castells, J. *J. Org. Chem.* **2004**, *69*, 2084–2093. (c) Pérez-Serrano, L.; Dominguez, G.; Pérez-Castells, J. *J. Org. Chem.* **2004**, *69*, 5413–5418. (d) Bajracharya, G. B.; Nakamura, I.; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 892–897. (e) Madu, C. E.; Lovely, C. J. *Org. Lett.* **2007**, *9*, 4697–4700.

(20) These are known compounds; see the Supporting Information.

TABLE 2. Preparation of 1,5-Octadien-7-yn-4-ols 6, Precursors of Styrenes 4, from 3-Halo-2-propen-1-ols 13 by Sonogashira Coupling, Oxidation with Dess−Martin Periodinane, and Allylation[a]



entry	13	10	14	yield (%) of 14[b,c]	11	yield (%) of 11[b,d]	12	6	yield (%) of 6[b]
1	13a	10a	14a	93	11m	80[e]	12b	6n	98
2	13b	10h	14b	81	11n	74	12a	6o	81
3	13c	10i	14c	95	11o	81	12c	6p	78
4	13d	10d	14d	90	11p	95	12a	6q	84

[a] Sonogashira coupling was carried out with 3-halo-2-propen-1-ol **13** and terminal alkyne **10** in the presence of $PdCl_2(PPh_3)_2$ (5 mol %), CuI (5 mol %), and NEt_3 (3 equiv) in THF at room temperature for 12−65 h. Oxidation of **14** to **11** was carried out with Dess−Martin periodinane (2 equiv) and pyridine (4 equiv) in CH_2Cl_2 at 0 °C for 30 min. Allylation was carried out by reacting **11** with allyl metal reagent **12** under various conditions (see the Supporting Information for details). [b] Yield of isolated product after silica gel chromatography. [c] *E*/*Z* ratio (**14a**: *E*/*Z* = 10/1, **14b**−**d**: *E*/*Z* = 1/>20). [d] *E*/*Z* ratio (**11m**: *E*/*Z* = 10/1, **11n**−**p**: *E*/*Z* = 1/>20). [e] The obtained isomers were separated by gel permeation chromatography at this step.

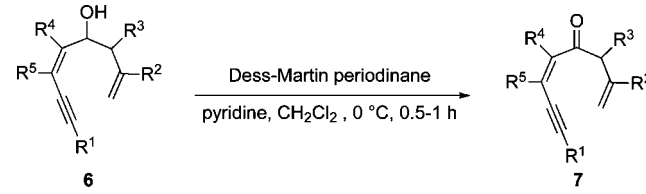
tion of the *E*/*Z*-stereoisomers of **14a** was difficult by silica gel chromatography. The oxidation of **14** with Dess−Martin periodinane and the allylation of **11** with allyl Grignard or allyl borane reagents proceeded without any problems and desired **6** were obtained in high yields.

The Dess−Martin oxidation was employed for the conversion of **6** into **7**, the acyclic precursors of 4-vinylphenols **8** (Table 3). The reaction was carried out in CH_2Cl_2 at 0 °C in the presence of Dess-Martin periodinane and pyridine. To our delight, **7** proved to be stable and isolable, while we failed to obtain 4,7-octadien-1-yn-3-ones by oxidation of the alcohol derivatives of **3**.[13f]

Next, we tried to synthesize substituted styrenes from a wide variety of resulting acyclic precursors **6** and **7** by using RCEM (Tables 4 and 5). Since ethylene often plays significant roles in RCEM,[21] we conducted all RCEM reactions under both nitrogen and ethylene atmospheres and compared the difference between the two reaction conditions.

As can be seen from Table 4, the RCEM/dehydration of **6** successfully furnished a wide variety of substituted styrenes **4** having various functionalities and the RCEM with Grubbs

TABLE 3. Preparation of 1,5-Octadien-7-yn-4-ones 7, Precursors of 4-Vinylphenols 8, from 1,5-Octadien-7-yn-4-ols 6 by Oxidation with Dess−Martin Periodinane[a]

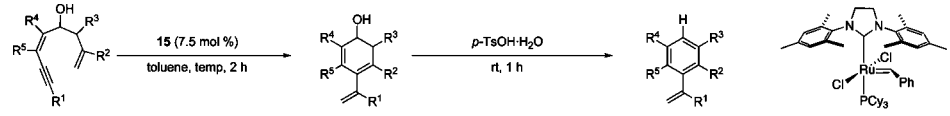


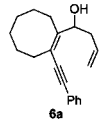
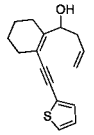
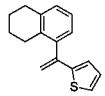
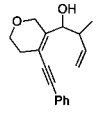
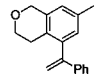
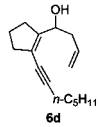
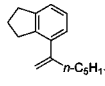
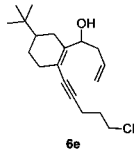
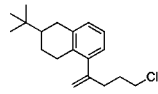
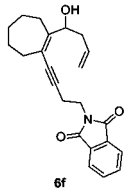
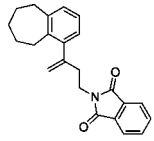
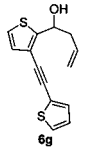
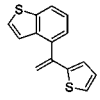
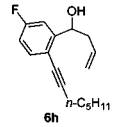
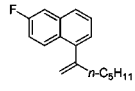
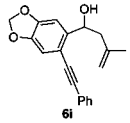
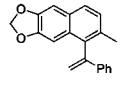
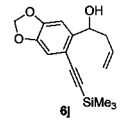
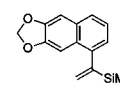
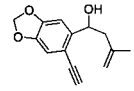
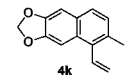
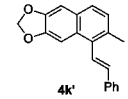
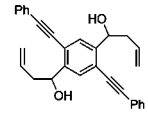
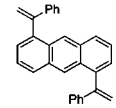
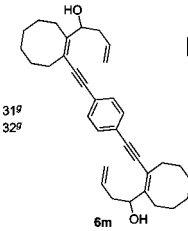
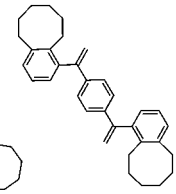
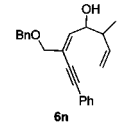
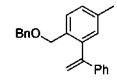
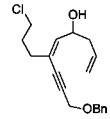
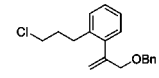
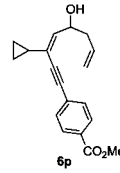
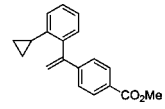
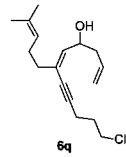
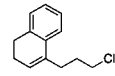
entry	6	7	yield[b] (%)
1	**6a**	**7a**	82
2	**6c**	**7c**	72
3	**6d**	**7d**	45
4	**6e**	**7e**	59
5	**6f**	**7f**	73
6	**6g**	**7 g**	69
7	**6i**	**7i**	60
8	**6m**	**7m**	26
9	**6n**	**7n**	89
10	**6o**	**7o**	63
11	**6p**	**7p**	63
12	**6q**	**7q**	78

[a] The reaction was carried out with 1,5-octadien-7-yn-4-ol **6**, Dess−Martin periodinane (2 equiv), and pyridine (4 equiv) in CH_2Cl_2 at 0 °C for 0.5−1 h. [b] Yield of isolated product after silica gel chromatography.

(21) Mori and co-workers reported the beneficial effects of ethylene atmosphere in RCEM. See: (a) Mori, M.; Sakakibara, N.; Kinoshita, A. *J. Org. Chem.* **1998**, *63*, 6082–6083. For recent examples of the RCEM conducted under ethylene gas, see: (b) Kim, B. G.; Snapper, M. L. *J. Am. Chem. Soc.* **2006**, *128*, 52–53. (c) Kaliappan, K. P.; Ravikumar, V. *J. Org. Chem.* **2007**, *72*, 6116–6126. (d) Yang, Q.; Lai, Y.-Y.; Xiao, W.-J.; Alper, H. *Tetrahedron Lett.* **2008**, *49*, 7334–7336.

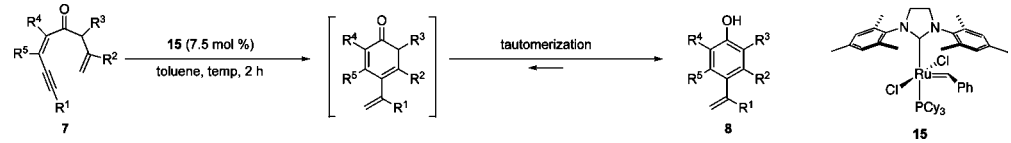
TABLE 4. Synthesis of Styrenes 4 by RCEM/Dehydration of 6[a]

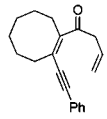
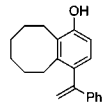
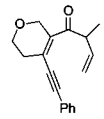
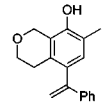
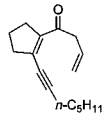
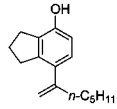
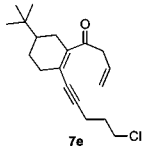
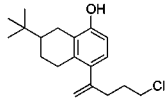
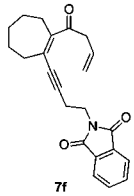
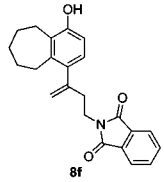
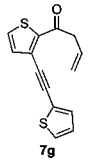
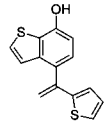
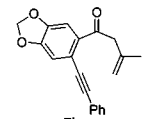
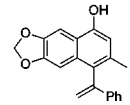
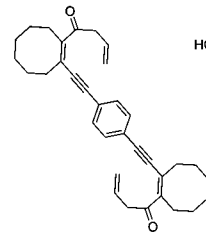
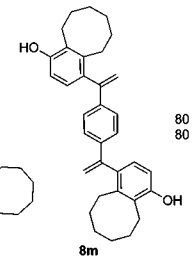
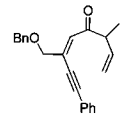
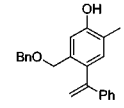
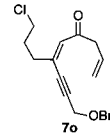
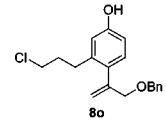
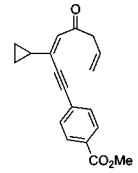
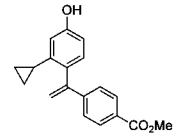
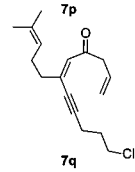
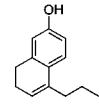


entry	substrate	product	conditions	yield (%)[b]
1	 **6a**	 **4a**	80 °C, under C_2H_4	74
2			80 °C, under N_2	78
3	 **6b**	 **4b**	80 °C, under C_2H_4	84
4			80 °C, under N_2	74
5	 **6c**	 **4c**	80 °C, under C_2H_4	88
6			80 °C, under N_2	28
7[c]	 **6d**	 **4d**	80 °C, under C_2H_4	72
8[c]			80 °C, under N_2	46
9	 **6e**	 **4e**	80 °C, under C_2H_4	88
10			80 °C, under N_2	79
11	 **6f**	 **4f**	80 °C, under C_2H_4	84
12			80 °C, under N_2	54
13	 **6g**	 **4g**	80 °C, under C_2H_4	89
14			80 °C, under N_2	81
15[d,e]	 **6h**	 **4h**	80 °C, under C_2H_4	83
16[d]			80 °C, under N_2	76
17	 **6i**	 **4i**	80 °C, under C_2H_4	0
18			80 °C, under N_2	0
19			100 °C, under C_2H_4	0
20			100 °C, under N_2	0
21	 **6j**	 **4j**	80 °C, under C_2H_4	0[f]
22			80 °C, under N_2	0[f]
23			100 °C, under C_2H_4	0[f]
24			100 °C, under N_2	0[f]
25	 **6k**	 **4k**	80 °C, under C_2H_4	**4k** 29%; **4k'** 5%
26			80 °C, under N_2	**4k** 29%
27[g]			60 °C, under N_2	**4k** 31%; **4k'** 7%
28[g]		 **4k'**	40 °C, under N_2	**4k** 41%; **4k'** 10%
29[g]	 **6l**	 **4l**	80 °C, under C_2H_4	85
30[g]			80 °C, under N_2	62
31[g]	 **6m**	 **4m**	80 °C, under C_2H_4	62
32[g]			80 °C, under N_2	60
33	 **6n**	 **4n**	80 °C, under C_2H_4	84
34			80 °C, under N_2	22
35	 **6o**	 **4o**	80 °C, under C_2H_4	90
36			80 °C, under N_2	68
37	 **6p**	 **4p**	80 °C, under C_2H_4	84
38			80 °C, under N_2	84
39	 **6q**	 **4q**	80 °C, under C_2H_4	88
40			80 °C, under N_2	78

[a] Ring-closing enyne metathesis was carried out with 1,5-octadien-7-yn-4-ol **6** and ruthenium catalyst (**15**, 7.5 mol %) in toluene (0.01 M) for 2 h under ethylene or nitrogen atmosphere (1 atm). The reaction mixture was treated with *p*-toluenesulfonic acid (10 mol %) at room temperature for 1 h. [b] Yield of isolated product after silica gel chromatography. [c] For the dehydration, the reaction mixture after RCEM was treated with silica gel (SiO_2; excess) and stirred for 9 h at room temperature. [d] The reaction was carried out with freshly prepared ruthenium catalyst (**15**, 7.5 mol %). [e] Even if the load of freshly prepared ruthenium catalyst was decreased to 1 mol %, the reaction still efficiently furnished **4h** in 80% yield. [f] Recovered **6j** and an isomer that has the 2,5-octadien-7-yn-4-ol framework were obtained. [g] The reaction was carried out in the presence of ruthenium catalyst (**15**, 15 mol %).

TABLE 5. Synthesis of 4-Vinylphenols 8 by RCEM/Tautomerization of 7[a]



entry	substrate	product	conditions	yield (%)[b]
1			80 °C, under C_2H_4	98
2			80 °C, under N_2	74
3			80 °C, under C_2H_4	95
4			80 °C, under N_2	31
5			80 °C, under C_2H_4	>99
6			80 °C, under N_2	86
7			80 °C, under C_2H_4	95
8			80 °C, under N_2	40
9			80 °C, under C_2H_4	85
10			80 °C, under N_2	64
11			80 °C, under C_2H_4	64
12			80 °C, under N_2	59
13			80 °C, under C_2H_4	0
14			80 °C, under N_2	0
15			100 °C, under C_2H_4	0
16			100 °C, under N_2	0
17[c]			80 °C, under C_2H_4	60
18[c]			80 °C, under N_2	53
19			80 °C, under C_2H_4	88
20			80 °C, under N_2	13
21			80 °C, under C_2H_4	34
22			80 °C, under N_2	72
23			80 °C, under C_2H_4	91
24			80 °C, under N_2	80
25			80 °C, under C_2H_4	67
26			80 °C, under N_2	61
27[d]			80 °C, under C_2H_4	72

[a] Ring-closing enyne metathesis was carried out with 1,5-octadien-7-yn-4-one **7** and ruthenium catalyst (**15**, 7.5 mol %) in toluene (0.01 M) for 2 h under ethylene or nitrogen atmosphere (1 atm). [b] Yield of isolated product after silica gel chromatography. [c] The reaction was carried out in the presence of ruthenium catalyst (**15**, 15 mol %). [d] The reaction was carried out at substrate concentration of 0.1 M.

second-generation catalyst **15**[22] proceeded well without the acyl protection of the hydroxyl group of **6**.[13f,23] The formation of condensed styrenes having five- to eight-membered aliphatic rings **4a**−**f** (Table 4, entries 1−12), 4-vinylbenzothiophene **4g** (Table 4, entries 13 and 14), and 1-vinylnaphthalenes **4h** and **4k** (entries 15, 16, and 25−28) was achieved by the RCEM/dehydration of corresponding enyne substrates **6**. Further, the construction of two rings simultaneously from **6l** and **6m** yielded 1,5-divinylanthracene **4l** (Table 4, entries 29 and 30) and 1,4-bis(1-phenylethenyl)benzene derivative **4m** (Table 4, entries 31 and 32), respectively. Single-ring styrenes **4n**−**p** were also synthesized in good yields without any problems (Table 4, entries 33−38). Applying the tandem RCEM/RCM to **6q** that has a second olefin functionality at the appropriate position led to the construction of two rings and resulted in the formation of 1,2-dihydronaphthalene **4q** as the final product (Table 4, entries 39 and 40).[24]

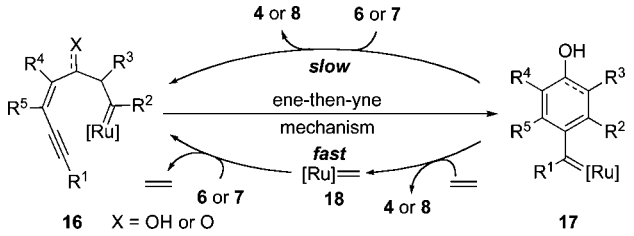
Comparing the difference between nitrogen and ethylene atmospheres revealed that the reactions under ethylene gas proceeded smoothly and gave products in high yields in most runs. Striking differences were observed in the reactions of substrates having an R^3 substituent (Table 4, entries 5, 33 vs entries 6, 34). Substrate **6i** that had substituents at both R^1 and R^2 positions could not be converted into corresponding product

(22) (a) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953–956. (b) Trnka, T. M.; Morgan, J. P.; Sanford, M. S.; Wilhelm, T. E.; Scholl, M.; Choi, T.-L.; Ding, S.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 2546–2558.

(23) For acceleration effect of an allylic hydroxyl group on RCEM, see: Imahori, T.; Ojima, H.; Yoshimura, Y.; Takahata, H. *Chem.—Eur. J.* **2008**, *14*, 10762–10771.

(24) The sequence of the RCEM/RCM/dehydration/DDQ oxidation of **6q** provided 1-(3-chloropropyl)naphthalene in 49% isolated yield.

SCHEME 2



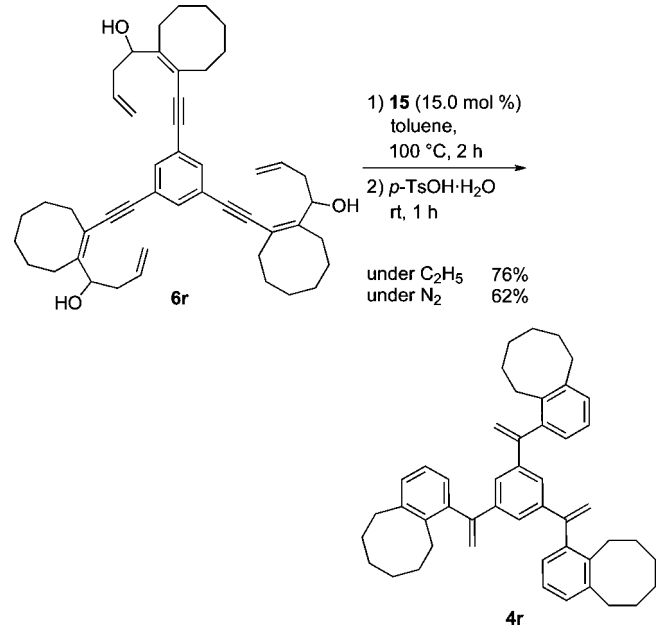
4i at all under nitrogen or ethylene atmosphere (Table 4, entries 17−20). On the other hand, the reaction of **6k** that has a methyl group at R^2 position and a terminal alkynyl group furnished corresponding product **4k** (Table 4, entries 25 and 26). In this case, however, the yields were extremely low and the beneficial effects of ethylene were not observed. Although slight improvement in product yield was attained by lowering temperature and increasing catalyst load, cross-metathesis product **4k′**, which has a phenyl group that was derived from catalyst **15,** was formed in a non-negligible amount and its amount increased as the catalyst load increased (Table 4, entries 27 and 28). Concerning the R^1 position, the introduction of various alkyl and aryl substituents was accomplished successfully. However, substrate **6j** that has a bulky trimethylsilyl group at R^1 position was found to be inactive to RCEM (Table 4, entries 21−24).

The results of RCEM/tautomerization of isolated **7** for the synthesis of 4-vinylphenols **8** are summarized in Table 5. Similar to styrenes **4**, a wide variety of **8** having various functionalities, such as a haloalkyl, a phthalimido, an ester, or a benzyloxy group, were obtained due to the great functional group tolerance of the catalyst. As we had anticipated, the reaction of **7i** that has a methyl group at R^2 position did not proceed at all (Table 5, entries 13−16). The difference in the reactivity of **7** between nitrogen and ethylene atmospheres showed the same tendency as that of **6**. In most runs, the reactions under ethylene gas gave products in high yields and the differences were most prominent in the reactions of substrates having an R^3 substituent (Table 5, entries 3, 19 vs entries 4, 20). One exception was the reaction of **7o** in which product **8o** was obtained in lower yield under ethylene gas than under nitrogen gas (Table 5, entry 21 vs entry 22). The reason for the low yield of the reaction under ethylene gas is the formation of byproduct having structures that were undefined and difficult to assign.

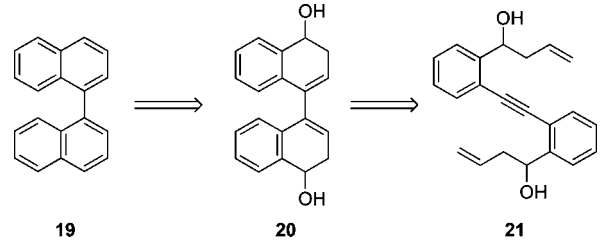
It can be assumed that the sluggishness of the reaction between Ru-alkylidene intermediate **17** and acyclic substrate **6** or **7** in the ene-then-yne mechanism[25] accounts for such a decrease in reactivity under nitrogen gas (Scheme 2). In particular, the presence of the R^3 substituent would hinder this step by steric interactions. In contrast, under ethylene gas, it is possible to interpret that ethylene promotes the formation of **16** from **17** smoothly via **18**, which must be advantageous for the steric hindrance.

This procedure can be applied to the synthesis of highly useful aromatic compounds. 1,3,5-Tris(1-phenylethenyl)benzene is an attractive linking agent for the synthesis of branched polystyrenes.[26] The preparation of this compound was accomplished by the Wittig olefination of 1,3,5-tris(benzoyl)benzene that was prepared by the Friedel−Crafts reaction of benzene with 1,3,5-

SCHEME 3



SCHEME 4



benzenetricarbonyl trichloride. We envisaged that various 1,3,5-tris(1-phenylethenyl)benzene derivatives could be synthesized by the RCEM/dehydration strategy. In fact, the construction of three benzene rings from **6r** by the RCEM/dehydration strategy led to the formation of desired 1,3,5-tris(1-phenylethenyl)benzene derivative **4r** in good yields (Scheme 3).

1,1′-Binaphthyl compounds constitute a class of compounds employed in many research fields, e.g., asymmetric synthesis, molecular recognition, and polydendrimer.[27] Therefore, the development of flexible synthetic methods of these compounds continues to be an active area of research. Our next plan was the synthesis of 1,1′-binaphthyl compounds using the RCEM/dehydration strategy. The retrosynthetic analysis shown in Scheme 4 revealed that 1,1′-binaphthyl compounds **19** could be synthesized by the tandem RCEM/RCM of dienynes **21** followed by the double dehydration of resulting diols **20**. To our delight, combination of the tandem RCEM/RCM with the dehydration of **21a** that was prepared readily by allylation of corresponding dicarboxyaldehyde successfully furnished desired nonsymmetrically substituted 1,1′-binaphthyl derivative **19a** (Scheme 5).

Conclusion

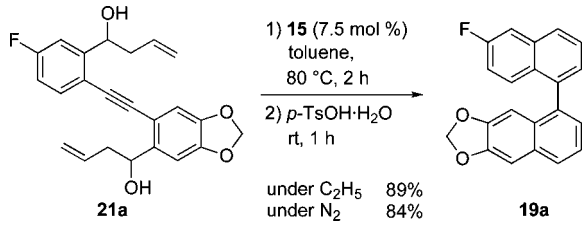
We have synthesized a wide variety of styrenes **4** by the RCEM/dehydration of acyclic precursors **6** that were readily

(25) (a) Lippstreu, J. J.; Straub, B. F. *J. Am. Chem. Soc.* **2005**, *127*, 7444–7457. (b) Lloyd-Jones, G. C.; Margue, R. G.; de Vries, J. G. *Angew. Chem., Int. Ed.* **2005**, *44*, 7442–7447.

(26) (a) Quirk, R. P.; Tsai, Y. *Macromolecules* **1998**, *31*, 8016–8025. (b) Lee, J. S.; Quirk, R. P.; Foster, M. D. *Macromolecules* **2005**, *38*, 5381–5392.

(27) (a) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345–50. (b) Pu, L. *Chem. Rev.* **1998**, *98*, 2405–2494. (c) Kocovský, P.; Vyskocil, S.; Smrcina, M. *Chem. Rev.* **2003**, *103*, 3213–3245. (d) Brunel, J. M. *Chem. Rev.* **2005**, *105*, 857–897.

SCHEME 5



prepared from β-halo-α,β-unsaturated aldehydes **9** or 3-halo-2-propen-1-ols **13** by utilizing highly reliable transformations at all steps. Employing the RCEM/dehydration enabled us to introduce various functionalities to the styrene framework with perfect regiocontrol. Moreover, we could obtain 4-vinylstyrenes **8** by the RCEM/tautomerization of **7** that were prepared by oxidizing **6**. Because the RCEM/tautomerization does not involve any elimination steps, it is a 100% atom-economical process. Obtained **8** are markedly useful building blocks whose hydroxyl and vinyl groups are convertible in many ways. In addition, we have presented the application of the method to the synthesis of unique aromatic compounds, 1,3,5-tris(1-phenylethenyl)benzene derivative **4r** and 1,1′-binaphthyl derivative **19a**. We are currently extending the scope of the methods to the synthesis of other important aromatic compounds and the catalytic asymmetric synthesis of biaryl compounds, including 1,1′-binaphthyl derivatives, by employing homochiral Ru-alkylidene catalysts.

Experimental Section

Procedures for the Preparation of 1-((*Z*)-2-Phenylethynyl-1-cyclooctenyl)-3-buten-1-ol (6a). To a mixture of dichlorobis(triphenylphosphine)palladium (210.6 mg, 0.300 mmol) and β-halo-α,β-unsaturated aldehyde **9a** (1.30 g, 5.99 mmol) in THF (43 mL) was added triethylamine (1.70 mL, 12.2 mmol). After the mixture was stirred for 10 min at room temperature, terminal acetylene **10a** (1.30 mL, 11.8 mmol) and copper iodide (22.9 mg, 0.120 mmol) were added. The resulting mixture was stirred at room temperature for 17 h. The reaction mixture was diluted with saturated aq NH_4Cl and extracted with ethyl acetate three times. The organic layers were combined, washed with brine, and dried over Na_2SO_4. After filtration, the filtrate was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc = 20/1) to give (*Z*)-2-phenylethynyl-1-cyclooctenecarbaldehyde (**11a**) (1.15 g, 4.83 mmol, 80% yield, pale yellow oil): ^{1}H NMR ($CDCl_3$) δ 1.46−1.60 (m, 6H), 1.80−1.90 (m, 2H), 2.45−2.52 (m, 2H), 2.65−2.68 (m, 2H), 7.33−7.39 (m, 3H), 7.46−7.50 (m, 2H), 10.33 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 23.48, 25.81, 26.38, 28.86, 29.72, 33.96, 86.73, 98.96, 122.28, 128.38, 128.99, 131.61, 142.89, 145.77, 192.40; HRMS (FAB) calcd for $C_{17}H_{19}O$ (M^+ + H) 239.1436, found 239.1425. To a stirred solution of **11a** (842 mg, 3.53 mmol) in Et_2O (20 mL) was added allylmagnesium bromide (1.07 M solution in Et_2O, 7.60 mL, 7.06 mmol) at 0 °C and the mixture stirred for 30 min. The mixture was then quenched by addition of saturated aq NH_4Cl, extracted with EtOAc three times, and washed with brine. The organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc = 10/1) to give 1-((*Z*)-2-phenylethynyl-1-cyclooctenyl)-3-buten-1-ol (**6a**) (852 mg, 3.04 mmol, 86% yield, colorless oil): ^{1}H NMR ($CDCl_3$) δ 1.45−1.73 (m, 8H), 1.88 (s, 1H), 2.29−2.46 (m, 6H), 5.12 (dt, *J* = 1.9, 1.0 Hz, 1H), 5.14−5.16 (m, 1H), 5.19−5.21 (m, 1H), 5.89 (ddt, *J* = 17.3, 10.2, 7.1 Hz, 1H), 7.28−7.33 (m, 3H), 7.39−7.42 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 26.00, 26.15, 26.64, 28.44, 31.12, 31.53, 40.48, 73.70, 89.19, 93.41, 117.69, 119.21, 123.74, 127.82, 128.26, 131.24, 135.08, 149.31; HRMS (FAB) calcd for $C_{20}H_{23}O$ (M^+ − H) 279.1749, found 279.1761.

Procedures for the Preparation of (*E*)-6-Benzyloxymethyl-3-methyl-8-phenyl-1,5-octadien-7-yn-4-ol (6n). To a mixture of dichlorobis(triphenylphosphine)palladium (54.7 mg, 0.078 mmol) and ally alcohol **13a** (478 mg, 1.57 mmol) in THF (22 mL) was added triethylamine (660 μL, 4.74 mmol). After the mixture was stirred for 10 min at room temperature, terminal acetylene **10a** (241 mg, 2.37 mmol) and copper iodide (15.0 mg, 0.079 mmol) were added. The resulting mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with saturated aq NH_4Cl and extracted with ethyl acetate three times. The organic layers were combined, washed with brine, and dried over Na_2SO_4. After filtration, the filtrate was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc = 3/1) to give (*E*)-3-benzyloxymethyl-5-phenyl-2-penten-4-yn-1-ol (**14a**) (405 mg,1.46 mmol, 93% yield, brown oil): ^{1}H NMR ($CDCl_3$) δ 1.61 (br s, 1H), 4.13 (d, *J* = 1.2 Hz, 2H), 4.51 (t, *J* = 6.4 Hz, 2H), 4.55 (s, 2H), 6.24 (tt, *J* = 6.8, 1.6 Hz, 1H), 7.24−7.47 (m, 10H). To a stirred suspension of Dess−Martin periodinane (1.24 g, 2.92 mmol) in dichloromethane (18 mL) and pyridine (500 μL, 5.80 mmol) was added **14a** (406 mg, 1.46 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 30 min. The mixture was then diluted with Et_2O and passed through Celite. The residual solid was washed with Et_2O thoroughly. The filtrate was concentrated under reduced pressure. Purification by silica gel flash column chromatography (hexane/EtOAc = 6/1) gave (*E*)-3-benzyloxymethyl-5-phenyl-2-penten-4-ynal (**11m**) (*E*/*Z* = 9/1 mixture: 323 mg, 1.17 mmol, 80% yield, yellow oil). The single isomer was obtained by gel permeation chromatography: ^{1}H NMR ($CDCl_3$) δ 4.30 (d, *J* = 1.9 Hz, 2H), 4.64 (s, 2H), 6.57 (dt, *J* = 8.3, 1.9 Hz, 1H), 7.30−7.44 (m, 8H), 7.48−7.52 (m, 2H), 10.26 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 71.29, 72.91, 82.93, 101.25, 121.39, 127.68, 127.98, 128.52, 128.56, 129.75, 131.92, 132.27, 132.29, 137.22, 143.02, 192.26; HRMS (FAB) calcd for $C_{19}H_{17}O_2$ (M^+ + H) 277.1229, found 277.1237. To a stirred solution of **11m** (59.2 mg, 0.214 mmol) in THF (20 mL) was added crotylmagnesium chloride (0.50 M solution in THF, 860 μL, 0.430 mmol) at 0 °C and the mixture stirred for 30 min. The mixture was then quenched by addition of saturated aq NH_4Cl, extracted with EtOAc three times, and washed with brine. The organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc = 3/1) to give (*E*)-6-benzyloxymethyl-3-methyl-8-phenyl-1,5-octadien-7-yn-4-ol (**6n**) (diastereomeric mixture: 69.8 mg, 0.210 mmol, 98% yield, colorless oil). The following data are for a mixture of two diastereomers (0.5/0.5): ^{1}H NMR ($CDCl_3$) δ 1.08 (d, *J* = 7.0 Hz, 1.5H), 1.11 (d, *J* = 7.0 Hz, 1.5H), 1.93 (br s, 0.5H), 1.99 (br s, 0.5H), 2.37 (sextet, *J* = 7.0 Hz, 0.5H), 2.54 (sextet, *J* = 7.0 Hz, 0.5H), 4.13 (t, *J* = 1.2 Hz, 1.0H), 4.15 (t, *J* = 1.5 Hz, 1.0H), 4.53−4.62 (m, 0.5H), 4.58 (d, *J* = 1.8 Hz, 1.0H), 4.59 (d, *J* = 2.1 Hz, 1.0H), 4.68 (t, *J* = 7.1 Hz, 0.5H), 5.11−5.19 (m, 2.0H), 5.81−5.89 (m, 1.0H), 6.02 (q, *J* = 1.2 Hz, 0.5H), 6.03 (q, *J* = 1.5 Hz, 0.5H), 7.27−7.46 (m, 10.0H); ^{13}C NMR ($CDCl_3$) δ 14.90, 16.07, 43.76, 44.49, 72.04, 72.09, 72.12, 73.42, 85.33, 95.29, 95.47, 116.57, 122.51, 122.86, 122.89, 127.70, 127.75, 128.33, 128.38, 128.49, 131.53, 138.01, 138.54, 139.75, 140.12; HRMS (FAB) calcd for $C_{23}H_{23}O$ (M^+ − OH) 315.1749, found 315.1755.

Procedures for the Preparation of 1-((*Z*)-2-Phenylethynyl-1-cyclooctenyl)-3-buten-1-one (7a). To a stirred suspension of Dess−Martin periodinane (632 mg, 1.49 mmol) in dichloromethane (5 mL) and pyridine (260 μL, 3.02 mmol) was added **6a** (209 mg, 0.746 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 30 min. The mixture was then diluted with Et_2O and passed through Celite. The residual solid was washed with Et_2O thoroughly. The filtrate was concentrated under reduced pressure and purified by silica gel flash column chromatography (hexane/EtOAc = 10/1) to give 1-((*Z*)-2-phenylethynyl-1-cycloocte-

nyl)-3-buten-1-one (**7a**) (171 mg, 0.614 mmol, 82% yield, pale yellow oil): ^{1}H NMR ($CDCl_3$) δ 1.48−1.55 (m, 4H), 1.63−1.68 (m, 2H), 1.75−1.79 (m, 2H), 2.48−2.51 (m, 2H), 2.57−2.60 (m, 2H), 3.84 (dt, J = 7.1, 1.2 Hz, 2H), 5.14 (dq, J = 17.2, 1.5 Hz, 1H), 5.17 (dq, J = 9.8, 1.6 Hz, 1H), 6.05 (ddt, J = 17.3, 10.2, 6.8 Hz, 1H), 7.26−7.36 (m, 3H), 7.42−7.45 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 26.18, 26.38, 28.45, 28.96, 30.30, 34.39, 47.19, 90.19, 97.42, 118.12, 122.92, 128.40, 128.56, 128.68, 131.38, 131.57, 146.61, 202.56; HRMS (FAB) calcd for $C_{20}H_{23}O$ (M^+ + H) 279.1749, found 279.1739.

Procedures for the Preparation of 5,6,7,8,9,10-Hexahydro-1-(1-phenylvinyl)benzo[8]annulene (4a). Under Ethylene Atmosphere. To a solution of **6a** (61.7 mg, 0.220 mmol) in toluene (22.0 mL, 0.01 M) was added 7.5 mol % of catalyst **15** (14.0 mg, 0.0227 mmol) in one portion under nitrogen, and then the system was evacuated carefully and filled with ethylene gas in three cycles. The reaction mixture was heated to 80 °C and stirred for 2 h. After being cooled to room temperature, the reaction mixture was treated with *p*-toluenesulfonic acid (4.2 mg, 0.022 mmol) and stirred for 1 h at room temperature. The mixture was concentrated under reduced pressure and purified by PTLC on silica gel (hexane) to give 5,6,7,8,9,10-hexahydro-1-(1-phenylvinyl)benzo[8]annulene (**4a**); (42.8 mg, 0.163 mmol, 74% yield, colorless oil). **Under Nitrogen Atmosphere.** To a solution of **6a** (78.1 mg, 0.279 mmol) in toluene (27.9 mL, 0.01 M) was added 7.5 mol % of catalyst **15** (17.7 mg, 0.0209 mmol) in one portion under nitrogen. After being stirredfor 2 h at 80 °C, the reaction mixture was treated with *p*-toluenesulfonic acid (5.3 mg, 0.028 mmol) and stirred for 1 h at room temperature. The mixture was concentrated under reduced pressure and purified by PTLC on silica gel (hexane) to give 5,6,7,8,9,10-hexahydro-1-(1-phenylvinyl)benzo[8]annulene (**4a**) (57.2 mg, 0.218 mmol, 78% yield, colorless oil): ^{1}H NMR ($CDCl_3$) δ 1.23−1.40 (m, 6H), 1.68 (m, 2H), 2.59−2.62 (m, 2H), 2.75−2.79 (m, 2H), 5.16 (d, J = 1.2 Hz, 1H), 5.78 (d, J = 1.5 Hz, 1H), 7.04 (dd, J = 7.3, 2.0 Hz, 1H), 7.09−7.17 (m, 2H), 7.21−7.27 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 25.89, 26.28, 28.18, 30.80, 32,39, 32,77, 114.58, 125.71, 126.38, 127.47, 128.19, 128.26, 128.59, 138.59, 141.05, 141.39, 142.23, 149.52; HRMS (FAB) calcd for $C_{20}H_{23}$ (M^+ + H) 263.1800, found 263.1803.

Procedures for the Preparation of (1-(5,6,7,8,9,10-Hexahydro-1-hydroxy-4-benzocyclooctenyl)vinyl)benzene (8a). Under Ethylene Atmosphere. To a solution of **7a** (84.3 mg, 0.303 mmol) in toluene (30.3 mL, 0.01 M) was added 7.5 mol % of catalyst **15** (19.3 mg, 0.0227 mmol) in one portion under nitrogen, and then the system was evacuated carefully and filled with ethylene gas in three cycles. The reaction mixture was heated to 80 °C and stirred for 2 h. The mixture was concentrated under reduced pressure and purified by PTLC on silica gel (hexane/EtOAc = 5/1) to give (1-(5,6,7,8,9,10-hexahydro-1-hydroxy-4-benzocyclooctenyl)vinyl)benzene (**8a**) (82.7 mg, 0.297 mmol, 98% yield, colorless oil). **Under Nitrogen Atmosphere.** To a solution of **7a** (53.2 mg, 0.191 mmol) in toluene (19.1 mL, 0.01 M) was added 7.5 mol % of catalyst **15** (12.2 mg, 0.022 mmol) in one portion under nitrogen. After being stirred for 2 h at 80 °C, the mixture was concentrated under reduced pressure and purified by PTLC on silica gel (hexane/EtOAc = 5/1) to give (1-(5,6,7,8,9,10-hexahydro-1-hydroxy-4-benzocyclooctenyl)vinyl)benzene (**8a**) (39.4 mg, 74% yield, colorless oil): ^{1}H NMR ($CDCl_3$) δ 1.27−1.39 (m, 6H), 1.65−1.73 (m, 2H), 2.56−2.61 (m, 2H), 2.81−2.85 (m, 2H), 4.64 (s, 1H), 5.14 (d, J = 1.7 Hz, 1H), 5.75 (d, J = 1.7 Hz, 1H), 6.67 (d, J = 8.3 Hz, 1H), 6.93 (d, J = 8.1 Hz, 1H), 7.20−7.31 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 24.31, 26.11, 26.44, 28.92, 29.43, 30.91, 112.39, 114.77, 126.44, 127.30, 127.42, 128.15, 128.60, 134.21, 140.83, 141.42, 149.47, 152.32; HRMS (FAB) calcd for $C_{20}H_{22}O$ (M^+) 278.1671, found 278.1671.

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Supporting Information Available: Experimental details, ^{1}H NMR and ^{13}C NMR spectra of new compounds, and ^{1}H NMR spectra of known compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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