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Facile Synthesis of Selenium/Sulfur-Substituted 3-Oxa-bicyclo[4.2.0]octa-1(8),5-diene and Tetrahydro-1*H*-isochromene via Sequential Three-Component Conjugate Addition/ Condensation/Elimination/[2 + 2] or [4 + 2] Cyclization Reactions

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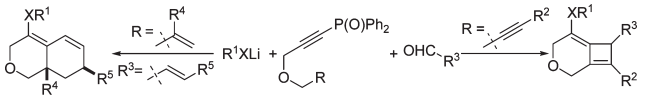

An interesting sequential three-component reaction provides a facile synthesis of selenium/sulfur-substituted 3-oxabicyclo[4.2.0]octa-1(8),5-diene and tetrahydro-1*H*-isochromene from lithium alkylselenolates or alkylthiolates, 1-alkynylphosphine oxides, and aldehydes. The sequential reaction proceeds via a conjugate addition/ condensation/elimination process to form the allene intermediate, which subsequently underwent [2 + 2] or [4 + 2] cyclization reaction to afford bicyclic frameworks.

The synthesis of complex cyclic molecules from simple starting materials by efficient formation of carbon−carbon bonds is of high interest in organic synthesis.[1] Sequential reactions represent one of the most powerful tools for the rapid construction of functionalized polycyclic molecules via a process that often features the formation of multibonds and stereocenters in one pot with high efficiency.[2] Allenes have shown impressive synthetic potentials in organic chemistry[3] and many novel reactions were well established in the past decades.[4] [2+2][5] cycloaddition of ene/yne−allenes provides a convenient route for the construction of cyclobutane and cyclobutene that are difficult to synthesize, while [4 + 2][6] cycloaddition of ene/yne-allenes represents a powerful method for the synthesis of cyclohexene. Recently, sequential reactions in which allenes were generated in situ and underwent subsequent processes have been intensively explored.[7] Our group also established a series of sequential reactions, leading to the efficient synthesis of structurally complex polycycles with 2,3-dihydrofuran units,[8] fused dihydroisobenzofuran derivatives,[9] polysubstituted pyridines, and isoquinolines.[10]

(1) (a) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (b) Negishi, E.; Coperet, C.; Ma, S.; Liou, S.; Liu, F. *Chem. Rev.* **1996**, *96*, 365. (c) Negishi, E. *Pure Appl. Chem.* **1992**, *74*, 323. (d) de Meijere, A.; von Zezschwitz, P.; Bräse, S. *Acc. Chem. Res.* **2005**, *38*, 413.

(2) (a) Ho, T. L. *Tandem Organic Reactions*; John Wiley & Sons: New York, 1992. (b) Tietze, L. F.; Brasche, G.; Gericke, K. M. *Domino Reaction in Organic Synthesis*; Wiley-VCH: Weinheim, 2006. (c) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223. (d) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115. (e) Arns, S.; Barriault, L. *Chem. Commun.* **2007**, 2211. (f) Tietze, L. F.; Modi, A. *Med. Res. Rev.* **2000**, *20*, 304. (g) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7134. (h) Posner, G. H. *Chem. Rev.* **1986**, *86*, 831. (i) Parsons, P. J.; Penkett, C. S.; Shell, A. J. *Chem. Rev.* **1996**, *96*, 195. (j) de Meijere, A.; von Zezschwitz, P.; Nüske, H.; Stulgies, B. *J. Organomet. Chem.* **2002**, *653*, 129. (k) von Zezschwitz, P.; de Meijere, A. *Top. Organomet. Chem.* **2006**, *19*, 49–89.

(3) (a) Patai, S. *The Chemistry of Ketenes, Allenes, and Related Compounds*; John Wiley & Sons: New York, 1980. (b) Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; John Wiley & Sons: New York, 1984. (c) Landor, S. R. *The Chemistry of Allenes*; Academic Press: New York, 1982; Vols. 1−3. (d) Krause, N.; Hashmi, A. S. K. *Modern Allene Chemistry*; Wiley-VCH: Weinheim, 2004; Vols. 1−2.

(4) (a) Ma, S. *Chem. Rev.* **2005**, *105*, 2829. (b) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701. (c) Ma, S. *Acc. Chem. Res.* **2009**, *42*, 1679. (d) Ma, S. *Eur. J. Org. Chem.* **2004**, 1175. (e) Ma, S. *Aldrichim. Acta* **2007**, *40*, 91. (f) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31. (g) Yamamoto, Y.; Radhakrishnan, U. *Chem. Soc. Rev.* **1999**, *28*, 199. (h) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067. (i) Marshall, J. *Chem. Rev.* **2000**, *100*, 3163.

(5) (a) Jiang, X.; Ma, S. *Tetrahedron* **2007**, *63*, 7589. (b) Shen, Q.; Hammond, G. B. *J. Am. Chem. Soc.* **2002**, *124*, 6534. (c) Oh, C. H.; Gupta, A. K.; Park, D. I.; Kim, N. *Chem. Commun.* **2005**, 5670. (d) Brummond, K. M.; Chen, D. *Org. Lett.* **2005**, *7*, 3473. (e) Ohno, H.; Mizutani, T.; Kadoh, Y.; Miyamura, K.; Tanaka, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 5113.

(6) (a) Ma, S.; Lu, P.; Lu, L.; Hou, H.; Wei, J.; He, Q.; Gu, Z.; Jiang, X.; Jin, X. *Angew. Chem., Int. Ed.* **2005**, *44*, 5275. (b) Jiang, X.; Kong, W.; Chen, J.; Ma, S. *Org. Biomol. Chem.* **2008**, *6*, 3606. (c) Padwa, A.; Meske, M.; Murphree, S. S.; Watterson, S. H.; Ni, Z. *J. Am. Chem. Soc.* **1995**, *117*, 7071. (d) Wender, P. A.; Jenkins, T. E.; Suzuki, S. *J. Am. Chem. Soc.* **1995**, *117*, 1843. (e) Padwa, A.; Filipkowski, M. A.; Meske, M.; Watterson, S. H.; Ni, Z. *J. Am. Chem. Soc.* **1993**, *115*, 3776. (f) Kanematsu, K.; Sugimoto, N.; Kawaoka, M.; Yeo, S.; Shiro, M. *Tetrahedron Lett.* **1991**, *32*, 1351.

(7) (a) Braun, R. U.; Ansorge, M.; Müller, T. J. J. *Chem.—Eur. J.* **2006**, *12*, 9081. (b) Braun, B. U.; Zeitler, K.; Müller, T. J. J. *Org. Lett.* **2001**, *3*, 3297. (c) D'Souza, D. M.; Kiel, A.; Herten, D. P.; Müller, T. J. J. *Chem.—Eur. J.* **2008**, *14*, 529. (d) Braun, B. U.; Zeitler, K.; Müller, T. J. J. *Org. Lett.* **2000**, *2*, 4181. (e) D'Souza, D. M.; Rominger, F.; Müller, T. J. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 153. (f) D'Souza, D. M.; Rominger, F.; Müller, T. J. J. *Chem. Commun.* **2006**, 4096. (g) Gao, G. L.; Niu, Y. N.; Yan, Z. Y.; Wang, H. L.; Wang, G. W.; Shaukat, A.; Liang, Y. M. *J. Org. Chem.* **2010**, *75*, 1305.

(8) Shen, R.; Huang, X. *Org. Lett.* **2008**, *10*, 3283.

(9) Shen, R.; Huang, X.; Chen, L. *Adv. Synth. Catal.* **2008**, *350*, 2865.

(10) Sha, F.; Huang, X. *Angew. Chem., Int. Ed.* **2009**, *48*, 3458.

(11) (a) Ma, S.; Hao, X.; Huang, X. *Chem. Commun.* **2003**, 1082. (b) Petrov, M. L.; Radchenko, S. I.; Kupin, V. S.; Petrov, A. A. *J. Org. Chem. USSR* **1973**, *9*, 683. (c) Reich, H. J.; Shah, S. K.; Gold, P. M.; Olson, R. E. *J. Am. Chem. Soc.* **1981**, *103*, 3112. (d) Reich, H. J.; Kelly, M. J. *J. Am. Chem. Soc.* **1982**, *104*, 1119.

(12) (a) Ma, S.; Hao, X.; Huang, X. *Org. Lett.* **2003**, *5*, 1217. (b) Yeo, S. K.; Shiro, M.; Kanematsu, K. *J. Org. Chem.* **1994**, *59*, 1621. (c) Guillerm, G.; Guillerm, D.; Witkowski-Vandenplas, C. *Nucleosides Nucleotides* **2001**, *20*, 685. (d) Narasaka, K.; Hayashi, Y.; Shimadzu, H.; Niihata, S. *J. Am. Chem. Soc.* **1992**, *114*, 8869. (e) Kim, J. T.; Kel'in, A. V.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2003**, *42*, 98. (e) McConachie, L. K.; Schwan, A. L. *Tetrahedron Lett.* **2000**, *41*, 5637.

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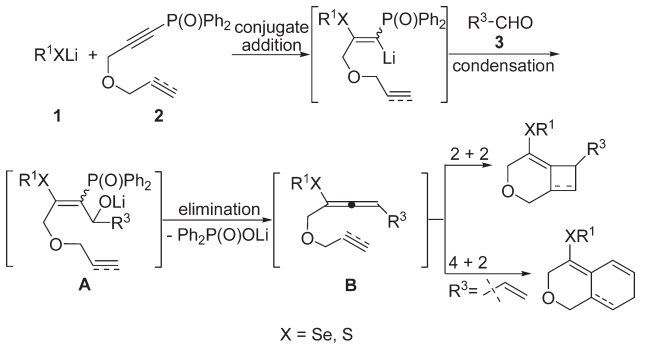
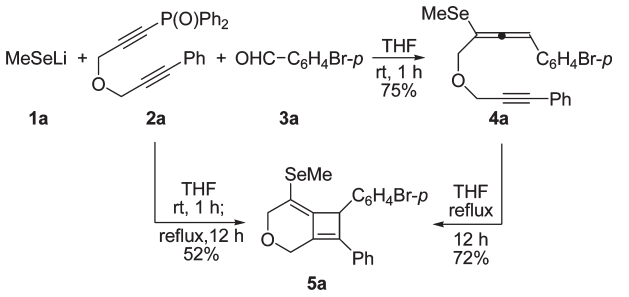
SCHEME 1



Selenium[11]/sulfur[12]-substituted allenes have been used in a wide range of applications in organic chemistry owing to their utility as synthetic intermediates. Recently, our group has reported a novel tandem three-component reaction to afford selenium/sulfur-substituted allenes.[13] In a continuous effort to design sequential reactions via allene intermediates,[14] we envisioned a sequential three-component conjugate addition/condensation/elimination/[2 + 2] or [4 + 2] cycloaddition reaction: the intermediates **A**, which would be generated in situ from conjugate addition of lithium alkylselenolates or alkylthiolates **1** with 1-alkynylphosphine oxides **2** and subsequent reaction with aldehydes **3**, may undergo elimination reaction leading to the allenes **B**. Then an intramolecular [2 + 2] or [4 + 2] cycloaddition reaction may proceed to furnish selenium/sulfur-substituted 3-oxa-bicyclo[4.2.0]octa-1(8),5-diene and tetrahydro-1*H*-isochromene, which are important and useful skeletons in medicinal chemistry (Scheme 1).[15] Apparently, by our strategy three new carbon−carbon bonds and one carbon−selenium/surfur bond would be formed in one pot, and two rings could be efficiently assembled. Furthermore, the vinyl selenide/sufide products are useful intermediates for many transformations.[16] Herein, we report our results on this novel sequential three-component reaction.

We initiated our study by attempting the reaction of **1a**, **2a**, and **3a** (1:1:1) (Scheme 2). After the mixture was stirred at room temperature for 1 h, the reaction gave allene **4a** in 75% yield and no [2 + 2] product **5a** was detected. Fortunately, simply refluxing the solution of **4a** in THF resulted in complete conversion to the desired cycloaddition bicyclic product **5a** in 72% yield. Based on these results, we performed the sequential three-component reaction in one pot. The

SCHEME 2



reaction mixture of **1a**, **2a**, and **3a** (1:1:1) in THF was stirred at room temperature for 1 h, which was directly followed by stirring under reflux for additional 12 h to afford the desired product **5a** in 52% yield.

Further screening of reaction conditions demonstrated that DME was the most suitable solvent for this reaction. We then carried out the reaction using various lithium alkylselenolates or alkylthiolates **1** with 1-alkynylphosphine oxides **2** and aldehydes **3**. As indicated in Table 1, the reactions proceeded smoothly to afford the corresponding 3-oxabicyclo[4.2.0]octa-1(8),5-dienes **5** in moderate to good yields. Both lithium alkylselenolates and alkylthiolates underwent the reaction smoothly (Table 1, entries 1, 5 and 10). R^2 in 1-alkynylphosphine oxides **2** can be a substituted phenyl group (entries 1, 8, and 9). Various aryl and α,β-unsaturated enals **3** worked (entries 1−7 and 11−14).

When R^2 or R^3 was the alkyl group, although allene **4** could be obtained, the [2 + 2] reaction gave a complex mixture (Scheme 3).

Inspired by the above results, we expanded the reaction scope by replacing the triple bond substituted with R^2 in 1-alkynylphosphine oxides **2** with a double bond. However, the allene **4d** obtained from the reaction of **1a**, **6a**, and **3a** gradually decomposed upon heating in refluxing DME for 40 h, and no expected product was found (Scheme 4). Interestingly, when α,β-unsaturated aldehyde **3f** was employed, [4 + 2] reaction occurred to afford tetrahydro-1*H*-isochromene **7a** in 61% yield.

We then carried out the reaction using various lithium alkylselenolates or alkylthiolates **1** with 1-alkynylphosphine oxides **6** and α,β-unsaturated enals **3**, and the results are shown in Table 2.

All products above were afforded as a single stereoisomer, and the stereochemistry of these compounds was established by the NOESY study of **7f** and **7g** (Figure 1 and Supporting Information). Similar stereoselectivity of the intramolecular Diels−Alder reaction of vinylallene has been reported in several cases.[17]

Vinyl selenides are useful intermediates for many transformations in organic chemistry. Therefore, compound **5f**

(13) (a) Huang, X.; Xiong, Z. *Chem. Commun.* **2003**, 1714. (b) Huang, X.; Xiong, Z. *Tetrahedron Lett.* **2003**, *44*, 5913.

(14) (a) Shen, R.; Zhu, S.; Huang, X. *J. Org. Chem.* **2009**, *74*, 4118. (b) Huang, X.; Zhu, S.; Shen, R. *Adv. Synth. Catal.* **2009**, *351*, 3118. (c) Shen, R.; Chen, L.; Huang, X. *Adv. Synth. Catal.* **2009**, *351*, 2833.

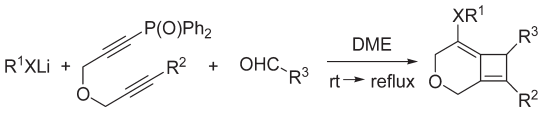
(15) (a) Somnath, M.; Tsutomu, N.; Naoki, A.; Yoshinori, Y. *J. Org. Chem.* **2003**, *68*, 9496. (b) Wang, W. Y.; Li, T. C.; Milbum, R.; Yates, J.; Hinnant, E.; Luzzio, M. J.; Noble, S. A.; Attardo, G. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 1579. (c) Mutter, R.; Martin de la Neva, E. M.; Wills, M. *Chem. Commun.* **2000**, 1675. (d) Yue, D. W.; Della Ca, N.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 3381. (e) Kusama, H.; Sawada, T.; Okita, A.; Shiozawa, F.; Iwasawa, N. *Org. Lett.* **2006**, *8*, 1077. (f) Obika, S.; Kono, H.; Yasui, Y.; Yanada, R.; Takemoto, Y. *J. Org. Chem.* **2007**, *72*, 4462. (g) Villeneuv, K.; Tam, W. *Eur. J. Org. Chem.* **2006**, 5449.

(16) (a) Comasseto, J. V.; Ling, L. W.; Petragnani, N.; Stefani, H. A. *Synthesis* **1997**, 373. (b) Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320. (c) Han, L.-B.; Tanaka, M. *Chem. Commun.* **1999**, 395. (d) Ogawa, A. *J. Organomet. Chem.* **2000**, *611*, 463. (e) Beletskaya, I.; Moberg, C. *Chem. Rev.* **1999**, *99*, 3435. (f) Perin, G.; Lenardão, E. J.; Jacob, R. G.; Panatieri, R. B. *Chem. Rev.* **2009**, *109*, 1277.

(17) (a) Deutsch, E. A.; Snider, B. B. *J. Org. Chem.* **1982**, *47*, 2682. (b) Deutsch, E. A.; Snider, B. B. *Tetrahedron Lett.* **1983**, *24*, 3701. (c) Keck, G. E.; Kachensky, D. F. *J. Org. Chem.* **1986**, *51*, 2487. (d) Gibbs, R. A.; Bartels, K.; Lee, R. W. K.; Okamura, W. H. *J. Am. Chem. Soc.* **1989**, *111*, 3717. (e) Curtin, M. L.; Okamura, W. H. *J. Org. Chem.* **1990**, *55*, 5278. (f) Krause, N. *Liebigs Ann. Chem.* **1993**, 521.

(18) (a) Okamura, H.; Miura, M.; Kosugi, K.; Takei, H. *Tetrahedron Lett.* **1980**, *21*, 87. (b) Martynov, A. V.; Potapov, V. A.; Amosova, S. V.; Makhaeva, N. A.; Beletskaya, I. P.; Hevesi, L. *J. Organomet. Chem.* **2003**, *674*, 101.

TABLE 1. Synthesis of 3-Oxabicyclo[4.2.0]octa-1(8),5-dienes 5[a]

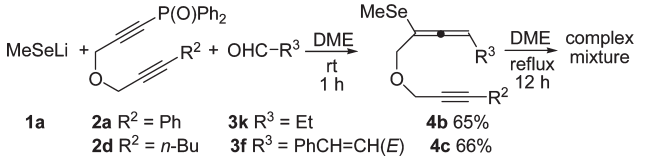


1 2 3 5

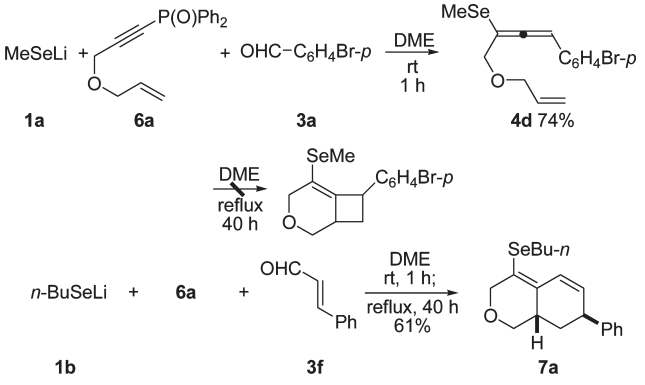
entry	R^1X (1)	R^2 (2)	R^3 (3)	yield of 5 (%)
1	MeSe (**1a**)	Ph (**2a**)	*p*-BrC_6H_4 (**3a**)	59 (**5a**)
2	MeSe (**1a**)	Ph (**2a**)	*p*-ClC_6H_4 (**3b**)	62 (**5b**)
3	MeSe (**1a**)	Ph (**2a**)	*p*-$MeOC_6H_4$ (**3c**)	70 (**5c**)
4	MeSe (**1a**)	Ph (**2a**)	*p*-MeC_6H_4 (**3d**)	65 (**5d**)
5	*n*-BuSe (**1b**)	Ph (**2a**)	*p*-$MeOC_6H_4CH{=}CH(E)$ (**3e**)	55 (**5e**)
6	MeSe (**1a**)	Ph (**2a**)	$PhCH{=}CH(E)$ (**3f**)	52 (**5f**)
7	MeSe (**1a**)	Ph (**2a**)	$MeCH{=}CH(E)$ (**3g**)	40 (**5g**)
8	*n*-BuSe (**1b**)	*p*-MeC_6H_4 (**2b**)	$PhCH{=}CH(E)$ (**3f**)	50 (**5h**)
9	*n*-BuSe (**1b**)	*p*-ClC_6H_4 (**2c**)	$PhCH{=}CH(E)$ (**3f**)	53 (**5i**)
10	MeS (**1c**)	Ph (**2a**)	*p*-BrC_6H_4 (**3a**)	49 (**5j**)
11	MeSe (**1a**)	Ph (**2a**)	*p*-FC_6H_4 (**3h**)	44 (**5k**)
12	MeSe (**1a**)	Ph (**2a**)	*m*-ClC_6H_4 (**3i**)	57 (**5l**)
13	MeS (**1c**)	Ph (**2a**)	Ph (**3j**)	53 (**5m**)
14	MeS (**1c**)	Ph (**2a**)	$PhCH{=}CH(E)$ (**3f**)	42 (**5n**)

[a]Unless otherwise specified, the reaction was carried out using **1** (1.0 equiv), **2** (1.0 equiv), and **3** (1.0 equiv) at rt for 1 h and then under reflux for 8−12 h.

SCHEME 3



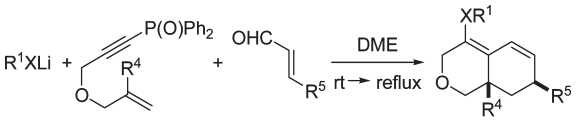
SCHEME 4



was selected for study of the Kumada cross-coupling reaction with Grignard reagent.[18] Under classical conditions of the Kumada coupling reaction, **5f** reacted smoothly with ethylmagnesium bromide at rt in THF to afford the cross-coupling product **8** in 53% yield (Scheme 5).

In conclusion, we have realized a sequential three-component Michael addition/aldol/Horner−Wadsworth−Emmons /[2 + 2] or [4 + 2] cyclization reaction, affording an efficient and stereoselective synthesis of bicyclic skeletons selenium/sulfur-substituted 3-oxa-bicyclo[4.2.0]octa-1(8),5-dienes and tetrahydro-1*H*-isochromenes from readily available lithium alkylselenolates or alkylthiolates, 1-alkynylphosphine oxides, and aldehydes. Furthermore, Kumada cross-coupling reaction of the product vinyl selenide was conducted to show the potential of the products. Experiments designed to further explore the reaction scope are currently underway.

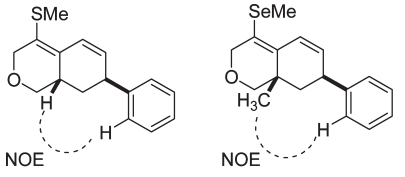
TABLE 2. Synthesis of Tetrahydro-1*H*-isochromenes 7[a]



1 6 3 7

entry	R^1X (1)	R^5 (3)	R^4 (6)	yield of 7 (%)
1	*n*-BuSe (**1b**)	Ph (**3f**)	H (**6a**)	61 (**7a**)
2	*n*-BuSe (**1b**)	*p*-BrC_6H_4 (**3k**)	H (**6a**)	57 (**7b**)
3	*n*-BuSe (**1b**)	*p*-$MeOC_6H_4$ (**3e**)	H (**6a**)	63 (**7c**)
4	*n*-BuS (**1d**)	Ph (**3f**)	H (**6a**)	55 (**7d**)
5	MeSe (**1a**)	Me (**3g**)	H (**6a**)	39 (**7e**)
6	MeS (**1c**)	Ph (**3f**)	H (**6a**)	49 (**7f**)
7[b]	MeSe (**1a**)	Ph (**3f**)	Me (**6b**)	41 (**7g**)

[a]Unless otherwise specified, the reaction was carried out using **1** (1.0 equiv), **6** (1.0 equiv), and **3** (1.0 equiv) at rt for 1 h and then under reflux for 40−50 h. [b]The reaction was carried out in dioxane at rt for 1 h and then under reflux for 48 h.



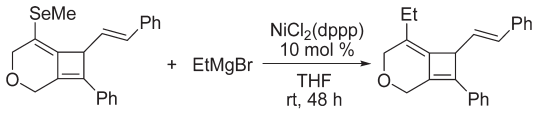
7f 7g

FIGURE 1. NOESY of **7f** and **7g**.

Experimental Section

Typical Procedure for the Synthesis of 3-Oxabicyclo[4.2.0]octa-1(8),5-diene. (See **5a**, Table 1, entry 1 as an example.) To a suspension of Se powder (79 mg, 1 mmol) in DME (5 mL) was

SCHEME 5



5f **8** 53%

added MeLi (0.625 mL, 1 mmol, 1.6 mmol/mL in hexane) under nitrogen atmosphere, and the mixture was stirred at rt for 5 min. Then, the above-formed solution of MeSeLi **1a** was added to a solution of 1-alkynylphosphine oxide **2a** (370 mg, 1 mmol) and aldehyde **3a** (184 mg, 1 mmol) in DME (5 mL) under nitrogen atmosphere, and the mixture was stirred at rt for 1 h and then under reflux for 10 h. After filtration and evaporation, the residue was purified by flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 50:1) to afford **5a** (255 mg, 59%): liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (2H, d, J = 8.4 Hz), 7.22−7.28 (4H, m), 7.15−7.19 (1H, m), 7.07 (2H, d, J = 7.2 Hz), 4.83 (1H, dd, J = 1.6 and 1.2 Hz), 4.77 (1H, dd, J = 15.6 and 1.6 Hz), 4.62 (1H, dd, J = 15.6 and 1.2 Hz), 4.27 (1H, d, J = 15.2 Hz), 4.23 (1H, d, J = 15.2 Hz), 1.91 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 140.0, 139.0, 137.9, 133.0, 131.6, 129.5, 128.6, 127.7, 126.3, 120.7, 108.9, 67.9, 62.5, 54.6, 5.4; MS (m/z) 432 (M^+); IR (neat, cm^{-1}) 2929, 2822, 1592, 1487, 1271, 1071, 1010; HRMS calcd for $C_{20}H_{17}OSeBr$ (M^+) 431.9628, found 431.9640.

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Supporting Information Available: Spectroscopic data for **4a**−**d**, **5a**−**n**, **7a**−**g**, and **8**. NOESY spectra of **7f** and **7g**. Detailed experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.