Synthetic Methods

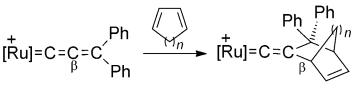
DOI: 10.1002/anie.201102969

Dehydrative Cyclization of Alkynals: Vinylidene Complexes with the C_β Incorporated into Unsaturated Five- or Six-Membered Rings**

María Batuecas, Luz Escalante, Miguel A. Esteruelas, Cristina García-Yebra, Enrique Oñate, and Carlos Saá**

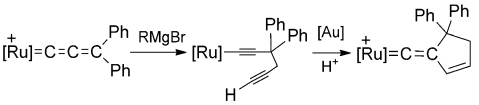
Vinylidene–transition metal complexes are intermediates in a number of synthetically important organic transformations.[1] However, the development of single-step procedures for the preparation of vinylidene complexes with the C_β atom of the C_2 chain incorporated into five- or six-membered rings, substructures commonly found in bioactive natural and nonnatural products, still remains a challenge.[2]

Vinylidene complexes are most often prepared by the tautomerization of terminal alkynes, therefore the majority of vinylidene ligands are monosubstituted;[3] the disubstituted ones are relatively rare. Remarkable findings have shown that heteroatom-substituted internal alkynes can afford disubstituted vinylidenes having a heteroatom on the C_β atom.[4] In addition, we have recently described the preparation of borylvinylidene derivates from alkynyl boryl complexes through a 1,3-boryl shift from the metal center to the C_β atom of the alkynyl ligand.[5] The known dicarbon-disubstituted vinylidenes have been generally prepared by electrophilic addition to neutral alkynyl complexes.[6] Ishii and coworkers have demonstrated that under appropriate conditions it is also possible to form dicarbon-disubstituted vinylidenes from unfunctionalized internal alkynes.[7] Both allenes and alkylidenecyclopropanes have been used to prepare ruthenium[8] and osmium vinylidenes,[9] respectively. Vinylidene ligands having the C_β atom incorporated into a ring are extremely rare and have been prepared by multistep procedures from allenylidene compounds. We have shown that the C_β=C_γ bond of electrophilic allenylidenes undergoes Diels–Alder reactions to afford vinylidenes with the C_β integrated into a ring [Eq. (1); $Cp = \eta^5$-C_5H_5].[10] In contrast Lin and coworkers have reported that the nucleophilic addition of propargyl Grignard reagents to C_γ and subsequent $Au(PR_3)$-catalyzed cyclization of the resulting diyne yields a vinylidene with the C_β incorporated into a five-membered ring [Eq. (2)].[11]



(1)

[Ru] = [RuCp(CO)(P*i*Pr$_3$)] n = 0,1,2



(2)

[Ru] = [RuCp(PPh$_3$)$_2$] R = HC≡CCH$_2$

Functionalized terminal alkynes have proven to be useful for generating valuable organic fragments within the coordination sphere of a transition metal. For instance, the most general synthetic approach to allenylidene complexes employs propargylic alcohols.[12] Those containing hydrogen atoms adjacent to the carbon atom bearing the OH group give alkenylvinylidenes.[13] When the alkynol has a CH_2 spacer between the triple bond and the OH group, 2-oxacycloalkylidene complexes are formed.[14]

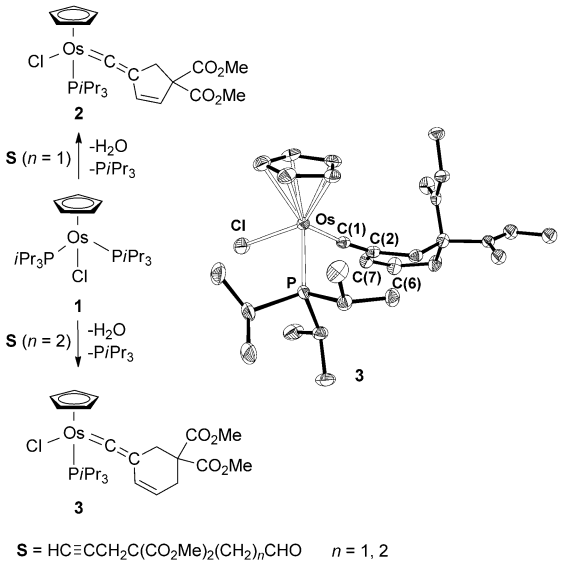
Alkynals are valuable substrates in organic synthesis.[15] Thus, a variety of metal-catalyzed processes involving these molecules have been developed.[16] We have now discovered that terminal alkynals are useful substrates for generating vinylidene complexes with the C_β atom incorporated into a five- or six-membered ring in a single step.

Treatment of toluene solutions of the cyclopentadienyl osmium complex **1** with 1.5 equivalents of 3,3-di(methoxycarbonyl)-5-hexyn-1-al and 4,4-di(methoxycarbonyl)-6-heptyn-1-al for 5 hours at 60 °C produces the displacement of one of the phosphine ligands by the alkynals and their dehydrative cyclization to afford, in a single-step process, the alkenylvinylidene derivatives **2** and **3**, respectively (Scheme 1). These compounds were isolated as red (**2**) and brown (**3**) solids in high yields (86 % and 70 %, respectively). The X-ray structure of **3** proves the formation of the vinylidenes with the C_β atom integrated into a ring. The vinylidene moiety is bonded to the metal in a nearly linear fashion with an Os-C(1)-C(2) angle of 173.7(3)°. The Os–C(1)

[*] M. Batuecas, Prof. M. A. Esteruelas, Dr. C. García-Yebra, Dr. E. Oñate
Departamento de Química Inorgánica—Instituto de Síntesis Química y Catálisis Homogénea (ISQCH)
Universidad de Zaragoza—CSIC, 50009 Zaragoza (Spain)
E-mail: maester@unizar.es
L. Escalante, Prof. C. Saá
Departamento de Química Orgánica—Centro Singular de Investigación en Química Biológica y Materiales Moleculares (CIQUS)
Universidad de Santiago de Compostela
15782 Santiago de Compostela (Spain)
E-mail: carlos.saa@usc.es

[**] Financial support from the MICINN of Spain (project numbers CTQ2008-00810 and CTQ2008-06557), and the Consolider Ingenio 2010 (CSD2007-00006), The Diputacion General de Aragón (E35), Xunta de Galicia, and the European Regional Development Fund (2007/XA084 and INCITE08PXIB 209024PR), and the European Social Fund is acknowledged. M.B. and L.E. thank the Spanish MICINN and Fundación Fundayacucho (Venezuela), respectively, for predoctoral grants.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201102969.

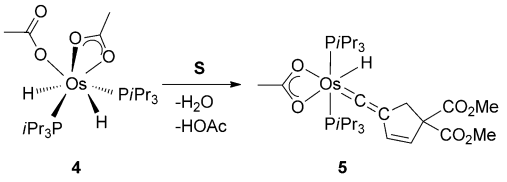


S = HC≡CCH$_2$C(CO$_2$Me)$_2$(CH$_2$)$_n$CHO n = 1, 2

Scheme 1. For the crystal structure of **3**, the thermal ellipsoids are shown at 50% probability.[21]

and C(1)–C(2) bond lengths of 1.832(3) and 1.326(4) Å, respectively, compare well with those found in other osmium vinylidene complexes.[17] In the $^{13}C\{^1H\}$ NMR spectra, the OsC_α resonances appear at $\delta = 284.0$ (**2**) and 290.5 ppm (**3**).

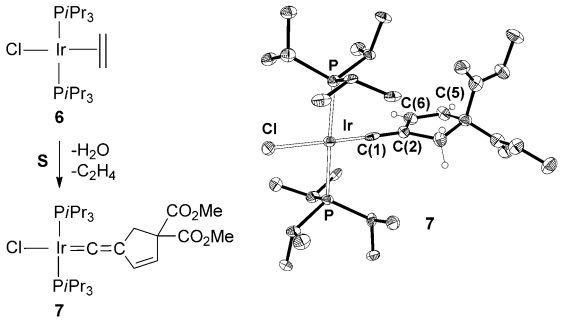
The *i*Pr$_3$P-Os-P*i*Pr$_3$ metal fragment also promotes the dehydrative cyclization of terminal alkynals to afford this type of vinylidene. Treatment of tetrahydrofuran solutions of the dihydride **4** with 1.5 equivalents of 3,3-di(methoxycarbonyl)-5-hexyn-1-al for 2 hours at 50 °C leads to the hydride alkenylvinylidene derivate **5** and acetic acid [Eq. (3)]. Complex **5** was isolated as a dark purple solid in 72% yield. The formation of **5** implies, in addition to the dehydrative cyclization of the alkynal, the reduction of the metal center from Os^{IV} to Os^{II}. The $^{13}C\{^1H\}$ NMR spectrum of this compound shows the OsC_α resonance of the vinylidene at $\delta = 285.9$ ppm. In the ^{1}H NMR spectrum, the hydride signal appears at $\delta = -11.59$ ppm.



(3)

S = HC≡CCH$_2$C(CO$_2$Me)$_2$CH$_2$CHO

This dehydrative cyclization of terminal alkynals is not only promoted by different metal skeletons of an element but also by different metals. The square planar iridium(I) complex **6** reacts with 3,3-di(methoxycarbonyl)-5-hexyn-1-al in tetrahydrofuran at 60 °C to give, after three days, the 16-valence electron alkenylvinylidene derivative **7** in 60% yield along with a minor amount of the carbonyl compound [IrCl(CO)(P*i*Pr$_3$)$_2$] that results from the decarbonylation of the aldehyde. At room temperature the decarbonylation is prevented. However, the formation of the vinylidene is too slow and addition of 20% mol of triflic acid is required as a catalyst. Under these conditions, complex **7** is obtained after five days in almost quantitative yield (93%; Scheme 2).

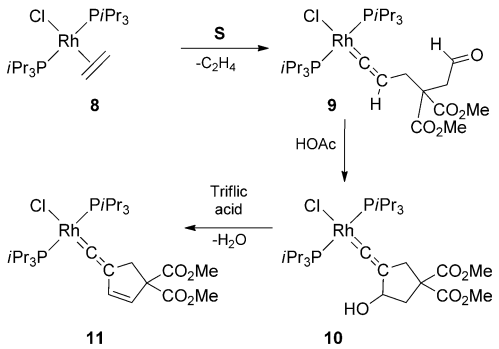


S = HC≡CCH$_2$C(CO$_2$Me)$_2$CH$_2$CHO

Scheme 2. For the crystal structure of **7**, the thermal ellipsoids are shown at 50% probability.[21]

Complex **7** was characterized by X-ray diffraction analysis. The Ir–C(1) and C(1)–C(2) bond lengths of 1.762(9) and 1.353(12) Å, respectively, and the Ir-C(1)-C(2) angle of 178.6(7)° agree well with those reported for other iridium vinylidene complexes.[18] In the $^{13}C\{^1H\}$ NMR spectrum, the IrC_α resonance appears at $\delta = 257.5$ ppm.

The rhodium counterpart is similarly achieved starting from **8** (Scheme 3). In this case, the intermediates of the



S = HC≡CCH$_2$C(CO$_2$Me)$_2$CH$_2$CHO

Scheme 3.

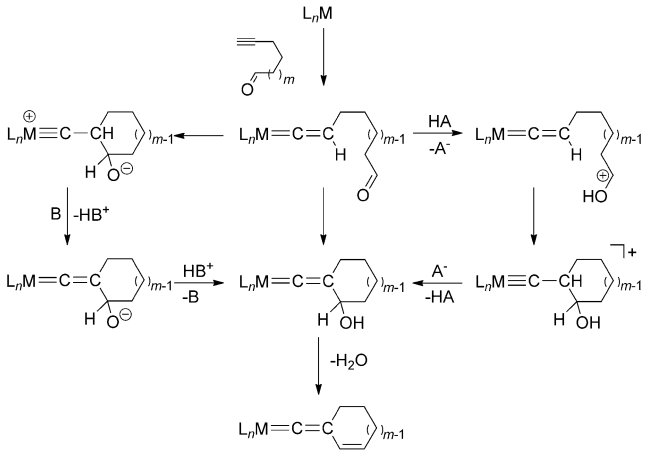
vinylidene formation process have been detected or isolated and fully characterized. The isolation of the intermediates is a consequence of the less-electron-rich character of rhodium, in comparison with osmium and iridium, which increases the activation barrier for the cyclization and dehydration steps.

Complex **8** reacts with 3,3-di(methoxycarbonyl)-5-hexyn-1-al to initially give the monosubstituted vinylidene **9**, which is slowly transformed into **10** as a result of a formal insertion of the C=O bond of the aldehyde substituent into the C_β–H bond. Acetic acid catalyzes this insertion. Whereas the

treatment of tetrahydrofuran solutions of **8** with 1.5 equivalents of the alkynal for 24 hours at 60 °C in the presence of 2.0 equivalents of the acid affords **10** in quantitative yield, a mixture of **9** and **10** in a 3:7 molar ratio is formed in its absence. Characteristic spectroscopic features of **9** are: a double triplet at $\delta = 288.6$ ppm ($J_{C\text{-}Rh} = 58.6$ Hz and $J_{C\text{-}P} = 16.0$ Hz) and a singlet at $\delta = 197.7$ ppm corresponding to RhC_α and the carbonyl group, respectively, in the $^{13}C\{^1H\}$ NMR spectrum; and a singlet at $\delta = 9.42$ ppm and a multiplet at $\delta = 0.15$ ppm assigned to the CHO and $C_\beta H$ protons, respectively, in the ^1H NMR spectrum. Complex **10** was isolated as a dark green solid in 85% yield. In the $^{13}C\{^1H\}$ NMR spectrum the RhC_α resonance of the vinylidene is observed at $\delta = 283.3$ ppm, whereas the C(OH) signal appears at $\delta = 66.7$ ppm. In the ^1H NMR spectrum, the most noticeable feature is the presence of a OH signal at $\delta =$ 2.43 ppm in [D_6]benzene and $\delta = 5.36$ ppm in [D_8]THF.

Complex **10** slowly dehydrates to give **11**, the rhodium counterpart of **7**. The dehydration is catalyzed by triflic acid. At room temperature in the presence of a 10% mol of acid, the transformation is quantitative after 1 hour. Complex **11** is isolated as a green solid in 98% yield. In agreement with other rhodium vinylidene complexes,[19] the $^{13}C\{^1H\}$ NMR spectrum shows the RhC_α resonance at $\delta = 290.0$ ppm ($J_{C\text{-}Rh} =$ 59.2 Hz and $J_{C\text{-}P} = 16.8$ Hz) as a double triplet.

The reactions shown in Schemes 1, 2, and 3, and Equation (3) are particular cases of a general process, which can be rationalized according to that shown in Scheme 4. As



Scheme 4.

expected for terminal alkynes, terminal alkynals react with different types of transition-metal complexes, such as **1**, **4**, **6**, and **8**, to initially give monosubstituted vinylidene intermediates related to **9**. The formal insertion of the C=O bond of the aldehyde substituent into the C_β–H bond of the vinylidene moiety leads to cyclic derivatives related to **10**, which dehydrate to afford the alkenylvinylidenes **2**, **3**, **5**, **7**, and **11**. The insertion step is catalyzed by acids (Os [Eq. (3)], Ir and Rh; Schemes 2 and 3) or alternatively by bases (Scheme 1). It is well known that vinylidene complexes of late transition metals are nucleophilic at C_β and their reactions with electrophiles lead to carbyne derivatives.[20] In the presence of acids, the protonation of the oxygen atom of the aldehyde increases the electrophilicity of the carbonyl carbon atom. This facilitates its electrophilic attack to C_β. The resulting carbyne intermediates subsequently dissociate the $C_\beta H$ proton. The phosphine dissociated during the reactions shown in Scheme 1 seems to facilitate the hydrogen atom migration from C_β to the oxygen atom in the zwitterionic intermediates resulting from the electrophilic attack of the carbonyl group to C_β.

In conclusion, vinylidene complexes with the C_β atom incorporated into unsaturated five- or six-membered rings are easily prepared by dehydrative cyclization of terminal alkynals in the presence of transition-metal compounds.[22]

Received: April 29, 2011
Revised: June 16, 2011
Published online: August 2, 2011

Please note: Minor changes have been made to this manuscript since its publication in *Angewandte Chemie* EarlyView. The Editor.

Keywords: alkynes · cyclizations · iridium · osmium · rhodium

[1] a) C. Bruneau, P. H. Dixneuf, *Angew. Chem.* **2006**, *118*, 2232; *Angew. Chem. Int. Ed.* **2006**, *45*, 2176; b) B. M. Trost, A. McClory, *Chem. Asian J.* **2008**, *3*, 164.
[2] a) B. Heasley, *Eur. J. Org. Chem.* **2011**, 19; b) H. Pellissier, *Adv. Synth. Catal.* **2011**, *353*, 189.
[3] a) M. C. Puerta, P. Valerga, *Coord. Chem. Rev.* **1999**, *193–195*, 977; b) M. A. Esteruelas, A. M. López, M. Oliván, *Coord. Chem. Rev.* **2007**, *251*, 795; c) J. M. Lynam, *Chem. Eur. J.* **2010**, *16*, 8238.
[4] See for example a) T. Miura, N. Iwasawa, *J. Am. Chem. Soc.* **2002**, *124*, 518; b) K. Venkatesan, O. Blacque, T. Fox, M. Alfonso, H. W. Schmalle, S. Kheradmandan, H. Berke, *Organometallics* **2005**, *24*, 920; c) K. Ilg, M. Paneque, M. L. Poveda, N. Rendón, L. L. Santos, E. Carmona, K. Mereiter, *Organometallics* **2006**, *25*, 2230; d) I. de Los Ríos, E. Bustelo, M. C. Puerta, P. Valerga, *Organometallics* **2010**, *29*, 1740.
[5] M. L. Buil, M. A. Esteruelas, K. Garcés, E. Oñate, *J. Am. Chem. Soc.* **2011**, *133*, 2250.
[6] C.-W. Liu, Y.-C. Lin, S.-L. Huang, C.-W. Cheng, Y.-H. Liu, Y. Wang, *Organometallics* **2007**, *26*, 3431.
[7] a) Y. Ikeda, T. Yamaguchi, K. Kanao, K. Kimura, S. Kamimura, Y. Mutoh, Y. Tanabe, Y. Ishii, *J. Am. Chem. Soc.* **2008**, *130*, 16856; b) Y. Mutoh, Y. Ikeda, Y. Kimura, Y. Ishii, *Chem. Lett.* **2009**, *38*, 534.
[8] A. Collado, M. A. Esteruelas, F. López, J. L. Mascareñas, E. Oñate, B. Trillo, *Organometallics* **2010**, *29*, 4966.
[9] R. Castro-Rodrigo, M. A. Esteruelas, A. M. López, F. López, J. L. Mascareñas, M. Oliván, E. Oñate, L. Saya, L. Villarino, *J. Am. Chem. Soc.* **2010**, *132*, 454.
[10] M. Baya, M. L. Buil, M. A. Esteruelas, A. M. López, E. Oñate, J. R. Rodríguez, *Organometallics* **2002**, *21*, 1841.
[11] K.-H. Chen, Y. J. Freng, H.-W. Ma, Y.-C. Lin, Y.-H. Liu, T.-S. Kuo, *Organometallics* **2010**, *29*, 6829.
[12] V. Cadierno, J. Gimeno, *Chem. Rev.* **2009**, *109*, 3512.
[13] V. Cadierno, M. P. Gamasa, J. Gimeno, *Coord. Chem. Rev.* **2004**, *248*, 1627.
[14] See for example: a) C. Bianchini, A. Marchi, N. Mantovani, L. Marvelli, D. Masi, M. Peruzzini, R. Rossi, *Eur. J. Inorg. Chem.* **1998**, 211; b) L. Marvelli, N. Mantovani, A. Marchi, R. Rossi, M. Brugnati, M. Peruzzini, P. Barbaro, I. de Los Rios, V. Bertolasi, *Dalton Trans.* **2004**, 713; c) H. Kopf, C. Pietraszuk, E. Hübner, N. Burzlaff, *Organometallics* **2006**, *25*, 2533.

[15] a) T. J. Tanaka, *J. Synth. Org. Chem. Jpn.* **2005**, *63*, 351; b) R. Blankespoor, *Org. Prep. Proced. Int.* **2010**, *42*,467; c) M. C. Willis, *Chem. Rev.* **2010**, *110*, 725.

[16] See for example: a) R. Shintani, K. Okamoto, Y. Otomaru, K. Ueyama, T. Hayashi, *J. Am. Chem. Soc.* **2005**, *127*, 54; b) H. Tsukamoto, T. Ueno, Y. Kondo, *J. Am. Chem. Soc.* **2006**, *128*, 1406; c) J. A. Varela, C. González-Rodríguez, S. G. Rubín, L. Castedo, C. Saá, *J. Am. Chem. Soc.* **2006**, *128*, 9576.

[17] See for example: a) D. Huang, M. Oliván, J. C. Huffman, O. Eisenstein, K. G. Caulton, *Organometallics* **1998**, *17*, 4700; b) C. Bohanna, M. L. Buil, M. A. Esteruelas, E. Oñate, C. Valero, *Organometallics* **1999**, *18*, 5176; c) T. B. Wen, Y. K. Cheung, J. Yao, W.-T. Wong, Z. Y. Zhou, G. Jia, *Organometallics* **2000**, *19*, 3803; d) R. Castarlenas, M. A. Esteruelas, E. Oñate, *Organometallics* **2000**, *19*, 5454; e) T. B. Wen, S.-Y. Yang, Y.-Z. Zhou, Z. Lin, C.-P. Lau, G. Jia, *Organometallics* **2000**, *19*, 3757; f) R. Castarlenas, M. A. Esteruelas, E. Gutiérrez-Puebla, E. Oñate, *Organometallics* **2001**, *20*, 1545; g) M. Baya, P. Crochet, M. A. Esteruelas, A. M. López, J. Modrego, E. Oñate, *Organometallics* **2001**, *20*, 4291; h) D. G. Gusev, T. Maxwell, F. M. Dolgushin, M. Lyssenko, A. J. Lough, *Organometallics* **2002**, *21*, 1095; i) T. B. Wen, Z. Y. Zhou, G. Jia, *Organometallics* **2003**, *22*, 4947; j) T. B. Wen, Z. Y. Zhou, M. F. Lo, I. D. Williams, G. Jia, *Organometallics* **2003**, *22*, 5217; k) T. B. Wen, W. Y. Hung, Z. Y. Zhou, M. F. Lo, I. D. Williams, G. Jia, *Eur. J. Inorg. Chem.* **2004**, 2837.

[18] See for example: a) A. Höhn, H. Otto, M. Dziallas, H. Werner, *J. Chem. Soc. Chem. Commun.* **1987**, 852; b) H. Werner, M. Schulz, B. Windmüller, *Organometallics* **1995**, *14*, 3659; c) see Ref. [4c].

[19] See for example: a) F. García-Alonso, A. Höhn, J. Wolf, H. Otto, H. Werner, *Angew. Chem.* **1985**, *97*, 401; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 406; b) H. Werner, M. Baum, D. Schneider, B. Windmüller, *Organometallics* **1994**, *13*, 1089; c) D. B. Grotjahn, X. Zeng, A. L. Cooksy, *J. Am. Chem. Soc.* **2006**, *128*, 2798; d) D. B. Grotjahn, X. Zeng, A. L. Cooksy, W. S. Kassel, A. G. DiPasquale, L. N. Zakharov, A. L. Rheingold, *Organometallics* **2007**, *26*, 3385.

[20] See for example: a) M. L. Buil, O. Eisenstein, M. A. Esteruelas, C. García-Yebra, E. Gutiérrez-Puebla, M. Oliván, E. Oñate, N. Ruiz, M. A. Tajada, *Organometallics* **1999**, *18*, 4949; b) see Ref. [17f]; c) M. Baya, M. A. Esteruelas, E. Oñate, *Organometallics* **2001**, *20*, 4875; d) G. Jia, *Coord. Chem. Rev.* **2007**, *251*, 2167.

[21] CCDC 823462 (**3**) and CCDC 823463 (**7**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

[22] **Note added in proof** (September 5, 2011): After publication of this article online in EarlyView (August 2, 2011), we have noted that Davies and co-workers have described the intramolecular cyclization on a ruthenium complex containing an alkynyl ligand with a 4-chlorobutyl substituent to afford a vinylidene fragment with the beta-carbon atom incorporated into a saturated five-membered ring, although the yield of the cyclization and the spectroscopic and structural characterization of the complex were not reported (S. Abbott, S. G. Davies, P. Warner *J. Organomet. Chem.* **1983**, *246*, C65). Based on this cyclization, Lee and co-workers have speculated about the participation of such vinylidene intermediates in the rhodium-catalyzed cycloaddition of 3-haloalkyl-1,6-enynes (J. M. Joo, Ch. Lee *J. Am. Chem. Soc.* **2006**, *128*, 14818; J. M. Joo, R. A. David, Y. Yuan, Ch. Lee *Org. Lett.* **2010**, *12*, 5704).

