Synthesis of Allenes by Palladium-Catalyzed S_N2' Reaction of Indium Organometallics with Propargylic Esters

Ricardo Riveiros, José Pérez Sestelo,* Luis A. Sarandeses*

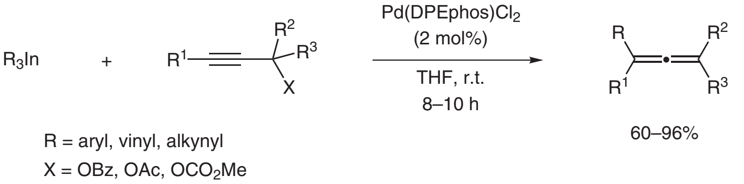
Departamento de Química Fundamental, Universidade da Coruña, 15071 A Coruña, Spain
Fax +34(981)167065; E-mail: qfsarand@udc.es; E-mail: sestelo@udc.es

Received 4 April 2007

PSP No 102

Abstract: Allenes have been efficiently prepared by the reaction of propargylic esters (benzoates, acetates, carbonates) with triorganoindium compounds (R_3In) under palladium catalysis, via an S_N2' rearrangement. The reaction proceeds smoothly at room temperature with a variety of aryl-, alkenyl-, and alkynylindium reagents. The yields obtained are high and the regioselectivity is complete both in the case of terminal and nonterminal propargylic esters.

Key words: allenes, indium organometallics, palladium catalysis, propargylic esters, regioselective reactions



Scheme 1

Introduction

Allenes are attractive building blocks in modern organic chemistry due to their extensive reactivity and axial chirality.[1] They can participate as nucleophiles or electrophiles in different organic transformations and in cycloadditions or metathesis reactions. Additionally, the axial chirality has made possible their use in asymmetric synthesis. The allene functionality is also present in a variety of natural products and pharmacologically active compounds.[2] Therefore, the development of versatile synthetic methods of allenes has gained considerable interest in recent years.

Allenes can be generally prepared from propargyl alcohol derivatives by S_N2' displacement with organocopper species.[3] Additionally, Grignard[4] and organozinc reagents[5] can be also used in S_N2' propargylic substitution reactions under transition metal catalysis. Herein, we report the efficient synthesis of allenes by palladium-catalyzed S_N2' reaction of indium organometallics with propargylic esters (Scheme 1).

Few years ago, we initiated a research program devoted to the study and application of indium organometallics in fundamental organic reactions. As a result, we discovered that triorganoindium reagents (R_3In) can be used in fundamental organic transformations such as the nickel-catalyzed conjugate addition reaction,[6] and the palladium-catalyzed cross-coupling reactions.[7] More recently, we found that R_3In can be regioselectively coupled with allyl halides and esters under palladium catalysis affording the S_N2 product, or, under copper catalysis, affording the S_N2' product.[8] The procedure summarized in Scheme 1 encompasses a new set of reactions in which the reaction of R_3In with propargylic esters, under palladium catalysis, affords allenes in good yields via S_N2' displacement.[9]

Scope and Limitations

We explored the reactivity of triorganoindium reagents towards propargylic substrates under metal catalysis. Under palladium catalysis, we found that the reaction of the propargyl benzoate **1** with triphenylindium (120 mol%) and $Pd(DPEphos)Cl_2$[10] (2 mol%) as catalyst, afforded the allene **5** in 79% yield after eight hours at room temperature in THF (Table 1, entry 1). During our studies we realized that, despite the ability of R_3In in cross-coupling reactions to transfer the three groups attached to indium, stoichiometric amounts of Ph_3In are necessary to totally consume the propargylic ester. When lower amounts of Ph_3In were used, the reaction was not complete due to the formation of biphenyl, a product generated as a consequence of a reductive homodimerization of the nucleophile.

In the reaction we observed that different leaving groups, such as the acetate **2** and carbonate **3**, also reacted effi-

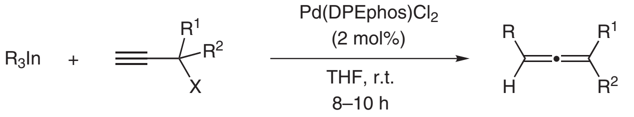
SYNTHESIS 2007, No. 22, pp 3595–3598
Advanced online publication: 08.08.2007
DOI: 10.1055/s-2007-983849; Art ID: Z08707SS

ciently with Ph_3In, affording the allene **5** in similar yields than using benzoate as leaving group (96% and 90% yields, respectively, Table 1, entries 2 and 3).

The versatility of this novel reaction was studied using indium reagents furnished with aryl, alkenyl, and alkynyl groups, and the results are shown in Table 1. The reaction of substituted arylindium reagents such as tri(2-methoxyphenyl)indium with the benzoates **1** and **4** gave aryl allenes **6** and **11** in good yields (Table 1, entries 4 and 9, respectively). For alkenylindium reagents, the reaction of trivinylindium with benzoate **1** also afforded the corresponding alkenyl allene **7** in high yield (Table 1, entry 5). The alkynyl group can also be efficiently transferred from indium reagents as shown in the reaction of tri(phenylethynyl)indium or tris[(trimethylsilyl)ethynyl]indium with benzoates **1** and **4** to give the corresponding allenynes **8**, **9**, **12** and **13** (Table 1, entries 6, 7, 10 and 11). The reactions with alkylindium reagents did not afford the corresponding cross-coupling products in good yields. In these cases it seems that the β-hydride elimination reaction takes place prior to the formation of the carbon–carbon bond by reductive elimination.

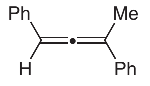
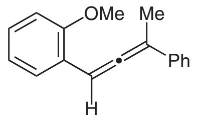
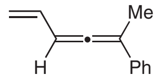
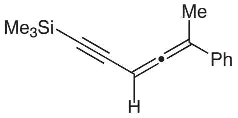
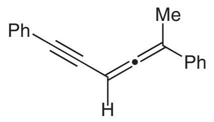
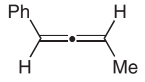
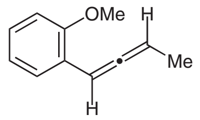
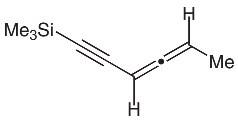
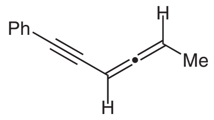
The reactivity of R_3In with nonterminal alkynes was tested using the propargyl benzoate **14** derived from but-3-yn-2-ol.[11] Under the previous conditions reported before,

Table 1 Allenes **5–13** Prepared from Terminal Alkynes



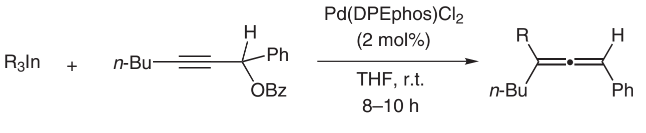
1: R^1 = Ph, R^2 = Me, X = OBz
2: R^1 = Ph, R^2 = Me, X = OAc
3: R^1 = Ph, R^2 = Me, X = OCO_2Me
4: R^1 = Me, R^2 = H, X = OBz

5–13

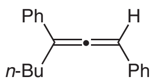
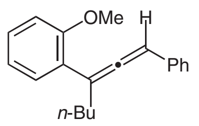
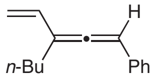
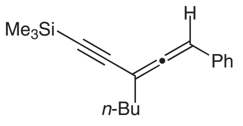
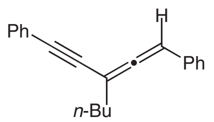
Entry	R	Propargylic ester	Product	Yield (%)[a]
1	Ph	**1**	 **5**	79
2		**2**	**5**	96
3		**3**	**5**	90
4	$2-MeOC_6H_4$	**1**	 **6**	81[b]
5	$CH_2=CH$	**1**	 **7**	85
6	$Me_3SiC≡C$	**1**	 **8**	83
7	PhC≡C	**1**	 **9**	85[c]
8	Ph	**4**	 **10**	80
9	$2-MeOC_6H_4$	**4**	 **11**	60[b]
10	$Me_3SiC≡C$	**4**	 **12**	70
11	PhC≡C	**4**	 **13**	90

[a] Isolated yield.
[b] Reaction performed at reflux.
[c] Reaction performed with $Pd_2dba_3/P(2-furyl)_3$ (1:4, 2 mol%) as catalyst.

Table 2 Allenes **15–19** Prepared from Nonterminal Alkynes



14 **15–19**

Entry	R	Product	Yield (%)[a]
1	Ph	 **15**	88
2	$2-MeOC_6H_4$	 **16**	70[b]
3	$CH_2=CH$	 **17**	75
4	$Me_3SiC≡C$	 **18**	84
5	PhC≡C	 **19**	81

[a] Isolated yield.
[b] Reaction performed at reflux.

the palladium-catalyzed reactions of aryl-, alkenyl- and alkynylindium reagents with **14** proceeded with complete S_N2' regioselectivity (the S_N2 product was not detected in the reaction mixture by NMR spectroscopy). As in the previous examples, the corresponding allenes **15–19** were obtained in good yields (60–82%, Table 2).

In summary, triorganoindium reagents react with propargyl esters under palladium catalysis to afford allenes in good yields and in high regioselectivity. The reaction can be performed using various propargylic esters and triaryl-, trialkenyl-, and trialkynylindium reagents. The reaction proceeds smoothly at room temperature and the scope of the propargylic substitution is comparable with that of other organometallics used in this procedure.

Procedures

All reactions were conducted in flame-dried glassware under argon. NMR spectra were performed in a Bruker Avance 300 (300 MHz for ^{1}H and 75 MHz for ^{13}C) spectrometer in $CDCl_3$ using the residual solvent signal at $\delta = 7.26$ (^{1}H) or $\delta = 77.0$ (^{13}C) as internal standard. DEPT was used to assign carbon types. Low-resolution electron-impact mass spectra were measured on a Thermo Finnigan Trace MS spectrometer at 70 eV. Low-resolution FAB and high-resolution mass spectra were measured on a Thermo Finnigan MAT 95XP spectrometer.[12]

Propargyl acetates and benzoates **1**, **2**, and **4** were prepared from the corresponding commercial alcohols by treatment with acetyl or benzoyl chloride in pyridine, in the presence of a catalytic amount of DMAP.[13] Carbonate **3** was prepared by the reaction of the corresponding lithium alkoxide with methyl chloroformate.[14] Propargyl benzoate **14** was prepared from but-3-yn-2-ol by alkylation [*n*-BuLi (2 equiv), THF, –78 °C, then *n*-BuI, HMPA, THF, r.t.] followed by benzoylation (BzCl, Py, DMAP, CH_2Cl_2).[11]

Triorganoindium Reagents

According to previously reported methods,[7b] triorganoindium compounds were prepared by treatment of the corresponding organolithium or Grignard reagents (3 equiv) with $InCl_3$ (1.1 equiv) in anhyd THF at –78 °C and warming to r.t. In this procedure triphenyl-, tris[(trimethylsilyl)ethynyl]-, and tri(phenylethynyl)indium were prepared from the corresponding organolithium reagents, and trivinylindium and tri(2-methoxyphenyl)indium were prepared from vinylmagnesium bromide and 2-methoxyphenylmagnesium bromide, respectively. All organolithium and Grignard solutions were commercially available and used as received, except (trimethylsilyl)ethynyl- and (phenylethynyl)lithium which were prepared, prior to use, by metalation of (trimethylsilyl)acetylene and phenylacetylene, respectively, with *n*-BuLi in anhyd THF at –78 °C, and warming to r.t.

Palladium-Catalyzed Cross-Coupling Reaction of Propargylic Esters with Indium(III) Organometallics; General Procedure

To a suspension of $Pd(DPEphos)Cl_2$ (14.3 mg, 0.02 mmol) and the appropriate propargylic ester **1–4** (1 mmol) in anhyd THF (7 mL) was added slowly a solution of R_3In (1.2 mmol, ca. 0.24 M in anhyd THF). The resulting solution was stirred at r.t. for 8–10 h and the reaction quenched by the addition of a few drops of MeOH. The mixture was concentrated and the residue was purified by flash chromatography (hexanes) affording, after concentration and high-vacuum drying, the corresponding allenes as colorless to yellowish oils.[15]

Buta-1,2-dienylbenzene (10)[16]

^{1}H NMR ($CDCl_3$): $\delta = 1.78$ (dd, $J = 6.9, 3.0$ Hz, 3 H), 5.53 (dq, $J = 6.9, 6.6$ Hz, 1 H), 6.09 (dq, $J = 6.6, 3.0$ Hz, 1 H), 7.14–7.32 (m, 5 H).

^{13}C NMR ($CDCl_3$): $\delta = 14.1$ (CH_3), 89.6 (CH), 93.9 (CH), 126.6 (3 × CH), 128.5 (2 × CH), 135.1 (C), 206.0 (C).

MS (EI): *m*/*z* (%) = 130 (M^+, 71), 115 [($M^+ - CH_3$), 86], 84 (100).

HRMS (EI): *m*/*z* calcd for $C_{10}H_{10}$: 130.0783; found: 130.0786.

1-(Buta-1,2-dienyl)-2-methoxybenzene (11)[17]

^{1}H NMR ($CDCl_3$): $\delta = 1.78$ (dd, $J = 3.4, 5.9$ Hz, 3 H), 3.85 (s, 3 H), 5.51 (m, 1 H), 6.46–6.54 (m, 1 H), 6.84–6.99 (m, 2 H), 7.13–7.40 (m, 2 H).

^{13}C NMR ($CDCl_3$): $\delta = 14.1$ (CH_3), 55.6 (CH_3), 87.8 (CH), 88.8 (CH), 110.9 (CH), 120.7 (CH), 123.5 (C), 127.7 (CH), 127.7 (CH), 156.0 (C), 206.4 (C).

MS (EI): *m*/*z* (%) = 160 (M^+, 23), 145 [($M^+ - CH_3$), 100].

HRMS (EI): *m*/*z* calcd for $C_{11}H_{12}O$: 160.0888; found: 160.0885.

Hexa-3,4-dien-1-ynyltrimethylsilane (12)[16]

^{1}H NMR ($CDCl_3$): $\delta = 0.19$ (s, 9 H), 1.73 (dd, $J = 3.0, 3.9$ Hz, 3 H), 5.31–5.44 (m, 2 H).

^{13}C NMR ($CDCl_3$): $\delta = -0.1$ (3 × CH_3), 13.5 (CH_3), 75.2 (CH), 88.1 (CH), 95.0 (C), 98.2 (C), 213.5 (C).

MS (EI): *m*/*z* (%) = 150 (M^+, 16), 135 [($M^+ - CH_3$), 100].

HRMS (EI): *m*/*z* calcd for $C_8H_{11}Si$ ($M^+ - CH_3$): 135.0625; found: 135.0622.

Hexa-3,4-dien-1-ynylbenzene (13)[16]

^{1}H NMR ($CDCl_3$): $\delta = 1.77$ (dd, $J = 3.3, 3.8$ Hz, 3 H), 5.41–5.59 (m, 2 H), 7.27–7.38 (m, 3 H), 7.41–7.47 (m, 2 H).

^{13}C NMR ($CDCl_3$): $\delta = 13.7$ (CH_3), 75.3 (CH), 82.7 (C), 88.1 (CH), 89.8 (C), 123.5 (C), 128.0 (CH), 128.2 (2 × CH), 131.4 (2 × CH), 213.1 (C).

MS (EI): *m*/*z* (%) = 154 (M^+, 14), 139 [($M^+ - CH_3$), 9], 84 (100).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{10}$: 154.0777; found: 154.0773.

1,3-Diphenylhepta-1,2-diene (15)[18]

^{1}H NMR ($CDCl_3$): $\delta = 0.95$ (t, $J = 7.1$ Hz, 3 H), 1.41–1.69 (m, 4 H), 2.51–2.68 (m, 2 H), 6.56 (t, $J = 3.0$ Hz, 1 H), 7.21–7.64 (m, 10 H).

^{13}C NMR ($CDCl_3$): $\delta = 13.9$ (CH_3), 22.6 (CH_2), 29.9 (CH_2), 30.1 (CH_2), 97.8 (CH), 110.0 (C), 126.1 (2 × CH), 126.7 (2 × CH), 126.9 (CH), 127.0 (CH), 128.5 (2 × CH), 128.7 (2 × CH), 206.5 (C).

MS (EI): *m*/*z* (%) = 248 (M^+, 6), 219 [($M^+ - C_2H_5$), 6], 206 [($M^+ - C_3H_6$), 100].

HRMS (EI): *m*/*z* calcd for $C_{19}H_{20}$: 248.1560; found: 248.1554.

1-Methoxy-2-(1-phenylhepta-1,2-dien-3-yl)benzene (16)

^{1}H NMR ($CDCl_3$): $\delta = 0.92$ (t, $J = 7.1$ Hz, 3 H), 1.38–1.59 (m, 4 H), 2.53–2.59 (dt, $J = 2.8, 7.4$ Hz, 2 H), 3.82 (s, 3 H), 6.28 (t, $J = 2.8$ Hz, 1 H), 6.85–7.02 (m, 3 H), 7.18–7.45 (m, 6 H).

^{13}C NMR ($CDCl_3$): $\delta = 13.9$ (CH_3), 22.5 (CH_2), 30.2 (CH_2), 32.5 (CH_2), 55.5 (CH_3), 94.5 (CH), 107.3 (C), 111.1 (CH), 120.6 (CH), 126.5 (CH), 126.8 (2 × CH), 126.9 (C), 128.3 (CH), 128.5 (2 × CH), 129.4 (CH), 135.5 (C), 156.9 (C), 205.8 (C).

MS (EI): *m*/*z* (%) = 278 (M^+, 21), 263 [($M^+ - CH_3$), 35], 84 (100).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{22}O$: 278.1671; found: 278.1665.

1-(3-Vinylhepta-1,2-dienyl)benzene (17)

^{1}H NMR ($CDCl_3$): δ = 0.93 (t, *J* = 7.4 Hz, 3 H), 1.35–1.59 (m, 4 H), 2.26–2.33 (m, 2 H), 5.11 (d, *J* = 10.4 Hz, 1 H), 5.29 (d, *J* = 16.5 Hz, 1 H), 6.35 (m, 2 H), 7.20–7.35 (m, 5 H).

^{13}C NMR ($CDCl_3$): δ = 13.9 (CH_3), 22.6 (CH_2), 27.9 (CH_2), 95.8 (CH), 109.3 (C), 113.1 (CH_2), 126.8 (2 × CH), 128.6 (2 × CH), 134.4 (CH), 134.8 (C), 108.6 (C).

MS (EI): *m*/*z* (%) = 198 (M^+, 8), 183 [($M^+ - CH_3$), 6], 141 (100).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{18}$: 198.1409; found: 198.1415.

3-[2-(Phenylethenylidene)hept-1-ynyl]trimethylsilane (18)

^{1}H NMR ($CDCl_3$): δ = 0.20 (s, 9 H), 0.92 (t, *J* = 7.4 Hz, 3 H), 1.34–1.61 (m, 4 H), 2.23–2.29 (m, 2 H), 6.35 (t, *J* = 3.0 Hz, 1 H), 7.21–7.36 (m, 5 H).

^{13}C NMR ($CDCl_3$): δ = 0.0 (3 × CH_3), 13.8 (CH_3), 22.1 (CH_2), 29.8 (CH_2), 33.6 (CH_2), 94.4 (C), 96.3 (C), 96.5 (CH), 99.7 (C), 127.27 (2 × CH), 127.32 (CH), 128.7 (2 × CH), 133.6 (C), 211.8 (C).

MS (EI): *m*/*z* (%) = 268 (M^+, 4), 253 [($M^+ - CH_3$), 27], 211 (100).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{24}Si$: 268.1642; found: 268.1634.

3-Butyl-1,5-diphenylpenta-1,2-dien-4-yne (19)

^{1}H NMR ($CDCl_3$): δ = 0.95 (t, *J* = 7.4 Hz, 3 H), 1.41–1.70 (m, 4 H), 2.33–2.40 (m, 2 H), 6.42 (t, *J* = 2.7 Hz, 1 H), 7.15–7.40 (m, 10 H).

^{13}C NMR ($CDCl_3$): δ = 13.9 (CH_3), 22.1 (CH_2), 30.1 (CH_2), 33.8 (CH_2), 84.2 (C), 91.4 (C), 94.5 (C), 96.2 (CH), 123.5 (C), 127.3 (2 × CH), 127.4 (CH), 128.1 (CH), 128.2 (2 × CH), 128.7 (2 × CH), 131.5 (2 × CH), 133.7 (C), 211.5 (C).

MS (EI): *m*/*z* (%) = 272 (M^+, 11), 257 [($M^+ - CH_3$), 17], 229 (100).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{20}$: 272.1560; found: 272.1553.

Acknowledgment

We are grateful to the Ministerio de Educación y Ciencia (Spain, BQU2003-00301 and CTQ2006-06166), Xunta de Galicia (PGIDIT04PXIC10308PN), and FEDER for financial support. R.R. thanks Xunta de Galicia for an 'Isidro Parga Pondal' contract.

References

(1) *Modern Allene Chemistry*; Krause, N.; Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, **2004**.

(2) Hoffmann-Röder, A.; Krause, N. *Angew. Chem. Int. Ed.* **2004**, *43*, 1196.

(3) For general references, see: (a) Tsuji, J.; Mandai, T. In *Metal-Catalyzed Cross-Coupling Reactions,* 2nd ed.; de Meijere, A.; Diederich, F., Eds.; Wiley-VCH: Weinheim, **2004**, 585. (b) Alexakis, A. *Pure Appl. Chem.* **1992**, *64*, 387. (c) Hoffmann-Röder, A.; Krause, N. In *Modern Allene Chemistry*; Krause, N.; Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, **2004**, 51.

(4) (a) Pasto, D. J.; Hennion, G. F.; Shults, R. H.; Waterhouse, A.; Chou, S.-K. *J. Org. Chem.* **1976**, *41*, 3496. (b) Jeffery-Luong, T.; Linstrumelle, G. *Tetrahedron Lett.* **1980**, *21*, 5019.

(5) Negishi, E.; Liu, F. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley: New York, **2002**, 551.

(6) Pérez, I.; Pérez Sestelo, J.; Maestro, M. A.; Mouriño, A.; Sarandeses, L. A. *J. Org. Chem.* **1998**, *63*, 10074.

(7) (a) Pérez, I.; Pérez Sestelo, J.; Sarandeses, L. A. *Org. Lett.* **1999**, *1*, 1267. (b) Pérez, I.; Pérez Sestelo, J.; Sarandeses, L. A. *J. Am. Chem. Soc.* **2001**, *123*, 4155. (c) Pena, M. A.; Pérez, I.; Pérez Sestelo, J.; Sarandeses, L. A. *Chem. Commun.* **2002**, 2246. (d) Pena, M. A.; Pérez Sestelo, J.; Sarandeses, L. A. *Synthesis* **2003**, 780. (e) Pena, M. A.; Pérez Sestelo, J.; Sarandeses, L. A. *Synthesis* **2005**, 485. (f) Pena, M. A.; Pérez Sestelo, J.; Sarandeses, L. A. *J. Org. Chem.* **2007**, *72*, 1271.

(8) (a) Rodríguez, D.; Pérez Sestelo, J.; Sarandeses, L. A. *J. Org. Chem.* **2003**, *68*, 2518. (b) Baker, L.; Minehan, T. *J. Org. Chem.* **2004**, *69*, 3957. (c) Rodríguez, D.; Pérez Sestelo, J.; Sarandeses, L. A. *J. Org. Chem.* **2004**, *69*, 8136.

(9) Riveiros, R.; Rodríguez, D.; Pérez Sestelo, J.; Sarandeses, L. A. *Org. Lett.* **2006**, *8*, 1403.

(10) (a) DPEphos = bis[*o*-(diphenylphosphino)phenyl] ether. (b) Kranenburg, M.; van der Burgt, Y. E. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Goubitz, K.; Fraanje, J. *Organometallics* **1995**, *14*, 3081. (c) Huang, Z.; Qian, M.; Babinski, D. J.; Negishi, E. *Organometallics* **2005**, *24*, 475.

(11) (a) Rosini, C.; Giacomelli, C.; Salvadori, P. *J. Org. Chem.* **1984**, *49*, 3394. (b) Wang, S.; Zhang, L. *J. Am. Chem. Soc.* **2006**, *128*, 8414.

(12) For general experimental methods, see ref. 8a.

(13) Höffe, G.; Steglich, W.; Vorbrüggen, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 569.

(14) Matsuda, I.; Komori, K.-I.; Itoh, K. *J. Am. Chem. Soc.* **2002**, *124*, 9072.

(15) Spectroscopic and analytical data for allenes **5**–**9** in Table 1 have been previously reported in ref. 9. Spectroscopic and analytical data for allenes **10**–**13** and **15**–**19** are reported herein.

(16) Ruitenberg, K.; Kleijn, H.; Elsevier, C. J.; Meijer, J.; Vermeer, P. *Tetrahedron Lett.* **1981**, *22*, 1451.

(17) Caporusso, A. M.; Zampieri, A.; Aronica, L. A.; Banti, D. *J. Org. Chem.* **2006**, *71*, 1902.

(18) Jansen, A.; Krause, N. *Inorg. Chim. Acta* **2006**, *359*, 1761.