

## Communications to the Editor

### Highly Chemo-, Regio-, and Stereoselective Carbon–Carbon Bond Formation via Migratory Insertion Reaction of Zirconacyclopentene Derivatives and Alkynyl Metals Containing Li and Mg. Novel Synthesis of 1,5-Dienes and 1,5-Enynes

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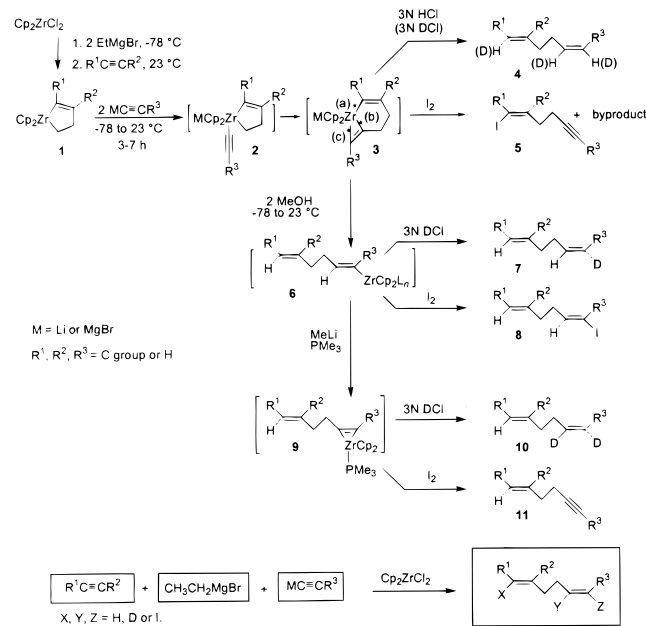
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We wish to report that zirconacyclopentenes (**1**), readily generated in situ from alkynes and  $\text{Cp}_2\text{ZrEt}_2$ ,<sup>2</sup> react with alkynyl metals containing Li or Mg to undergo remarkably chemo-, regio-, and stereoselective carbon–carbon bond-forming transformations summarized in Scheme 1. The results not only provide a novel and efficient synthetic route to a variety of 1,5-dienes and 1,5-enynes but also offer a number of intriguing structural and mechanistic puzzles to be solved.

We earlier reported that the treatment of  $\text{Cp}_2\text{ZrCl}_2$  with 3 equiv of alkynyllithiums generated organozirconiums represented by  $\text{LiCp}_2\text{Zr}(\text{C}\equiv\text{CR})_3$  and that these zirconate species underwent thermal 1,2-migration to give conjugated enynes after protonolysis and conjugated diynes after iodolysis.<sup>3</sup> Although a related migratory insertion was also observed in the reaction of diarylzirconocenes with alkynyllithiums,<sup>3</sup> our attempts to induce similar reactions of zirconocene derivatives containing alkyl groups did not produce clean and useful results. We then turned our attention to the use of cyclic zirconocene derivatives. Whereas the treatment of 3-(*n*-octyl)zirconacyclopentane with 1-octynyllithium merely released 1-decene presumably via known base-induced ring contraction of zirconacyclopentanes<sup>4</sup> without a sign of carbon–carbon bond formation, the corresponding reaction of **1a** ( $\text{R}^1 = \text{R}^2 = n\text{-Bu}$ ) at 23 °C for several hours produced, after the reaction was quenched with 3 N HCl, (5*E*,9*Z*)-6-(*n*-butyl)-5,9-hexadecadiene (**4a**) in 89% isolated yield as a  $\geq 98\%$  isomerically pure compound (entry 1).<sup>5</sup> Quenching the organozirconium product, identified as **3a** ( $\text{M} = \text{Li}$ ) as detailed below, with 3 N DCl in  $\text{D}_2\text{O}$  provided in a comparable yield the 5,9,10-trideuterio derivative of **4a** with  $\geq 95\%$  D incorporation at each of the three deuterated positions (entry 2). It was also feasible to convert **3a**

Scheme 1



into **5a** in 49% yield by treatment with 6 equiv of  $\text{I}_2$ , although this reaction was complicated by the formation of an unidentified byproduct. Little or no compounds obtainable via 1,2-migration of the alkenyl group of the putative zirconate intermediate **2** were detected. The results indicate a highly chemoselective alkyl migration.<sup>6</sup> In these reactions, an alkyne, an ethylene moiety derived from  $\text{EtMgBr}$ , and another alkyne were selectively linked in one pot by the action of  $\text{Cp}_2\text{ZrCl}_2$  in excellent yields, as schematically shown at the bottom of Scheme 1.

The reaction offered additional synthetically attractive but puzzling features. Thus, treatment of **3a** with exactly 2 equiv of  $\text{MeOH}$  ( $-78$  to  $23$  °C) followed by deuteriolysis with 3 N DCl cleanly provided the 10-monodeuterio derivative **7a** in 92% yield by GLC (87% isolated) with  $\geq 95\%$  D incorporation (entry 3), while a methanolysis-iodolysis sequence gave **8a** in 85% NMR yield (74% isolated) (entry 4). These results indicate that  $\text{MeOH}$  selectively protonolyzed the bonds (a) and (b) in preference to (c). Attempts to differentiate (a) and (b) by further limiting the amount of  $\text{MeOH}$  have not led to clean results. The intermediacy of **6** in the conversion of **3** into **7** and **8** was indicated by successive treatment of **3b** ( $\text{R}^1 = \text{R}^2 = n\text{-Bu}$ ,  $\text{R}^3 = \text{Me}$ ,  $\text{M} = \text{MgBr}$ ) with 2 equiv of  $\text{MeOH}$ ,  $\text{MeLi}$  (1.1 equiv), and  $\text{PMe}_3$  (1.5 equiv) which produced in 52% combined NMR yield after 24 h at 23 °C a 2:1 mixture of two apparently isomeric species exhibiting two  $^1\text{H}$  NMR doublets ( $J = 1.7$  Hz) due to coupling with phosphorus at  $\delta$  5.32 and 5.28 ppm, to which the Cp signals of two stereoisomers of **9b** ( $\text{R}^1 = \text{R}^2 = n\text{-Bu}$ ,  $\text{R}^3 = \text{Me}$ ) arising from the position of P relative to the two chain substituents may be assigned in consultation with published NMR data of similar

(6) Chemoselective alkyl migration in preference to alkenyl migration was repeatedly observed since the first observation in the reaction of zirconacyclopentenes with *n*-BuNC (Negishi, E.; Swanson, D. R.; Miller, S. R. *Tetrahedron Lett.* **1988**, 29, 1631). This abnormal chemoselectivity may tentatively be attributed to steric hindrance to ate complexation due to  $\text{R}^1$  which lies in the plane of the zirconacyclopentene ring.

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(5) In addition to  $^1\text{H}$  and  $^{13}\text{C}$  NMR as well as mass spectroscopic data consistent with the assigned structure, an independent synthesis via hydromagnesation of 5-decyne with *i*-BuMgBr and 2%  $\text{Cp}_2\text{TiCl}_2$  (Sato, F. *J. Organomet. Chem.* **1985**, 285, 53–64),  $\text{Li}_2\text{CuCl}_4$ -catalyzed cross coupling with 3-bromopropanal protected with ethylene glycol (Raederstorff, D.; Shu, A. Y. L.; Thompson, J. E.; Djerassi, C. *J. Org. Chem.* **1987**, 52, 2337) and Wittig olefination (Gosney, I.; Rowley, A. G. In *Organophosphorous Reagents in Organic Synthesis*; Cadsyan, J. I. G., Ed.; Academic Press: New York, 1979; Chapter 2) with *n*-HexCH=PPH<sub>3</sub> producing a 9*Z*/8 mixture of the 9*Z* and 9*E* isomers of **4a** firmly identified the product and established its stereoisomeric purity.

**Table 1.** Synthesis of 1,5-Dienes via Migratory Insertion Reaction of Zirconacyclopentene Derivatives with Alkynyllithiums or Alkynylmagnesium Halides<sup>a</sup>

entry	R <sup>1</sup> C≡CR <sup>2</sup>	MC≡CR <sup>3</sup>	method of quenching	product			yield, % <sup>b</sup>
				X	Y	Z	
1	<i>n</i> -BuC≡CBu- <i>n</i>	LiC≡CHex- <i>n</i>	HCl	H	H	H	92(89)
2	<i>n</i> -BuC≡CBu- <i>n</i>	LiC≡CHex- <i>n</i>	DCl	D	D	D	90(87)
3	<i>n</i> -BuC≡CBu- <i>n</i>	LiC≡CHex- <i>n</i>	1. MeOH. <sup>c</sup> 2. DCl	H	H	D	92(87)
4	<i>n</i> -BuC≡CBu- <i>n</i>	LiC≡CHex- <i>n</i>	1. MeOH. <sup>c</sup> 2. I <sub>2</sub> <sup>d</sup>	H	H	I	85(74)
5	<i>n</i> -BuC≡CBu- <i>n</i>	BrMgC≡CMe		H	H	H	91(85)
6	<i>n</i> -BuC≡CBu- <i>n</i>	BrMgC≡CMe	1. MeOH. <sup>c</sup> 2. MeLi 3. PMe <sub>3</sub> . 4. DCl	H	D	D	44
7	<i>n</i> -BuC≡CBu- <i>n</i>	LiC≡CH· (H <sub>2</sub> NCH <sub>2</sub> ) <sub>2</sub>	HCl	H	H	H	90
8	MeC≡CMe	LiC≡CHex- <i>n</i>	HCl	H	H	H	76
9	PhC≡CMe <sup>e</sup>	LiC≡CHex- <i>n</i>	HCl	H	H	H	71
10	EtC≡CEt	BrMgC≡CMe	HCl	H	H	H	89
11	EtC≡CEt	BrMgC≡CMe	1. MeOH. <sup>c</sup> 2. I <sub>2</sub> <sup>d</sup>	H	H	I	92
12	EtC≡CEt	BrMgC≡CMe	1. MeOH. <sup>c</sup> 2. PhI, ZnBr <sub>2</sub> , Cl <sub>2</sub> Pd(PPh <sub>3</sub> ) <sub>2</sub> <sup>f</sup>	H	H	Ph	72
13	<i>n</i> -BuC≡C(CH <sub>2</sub> ) <sub>3</sub> - CH=CH <sub>2</sub> <sup>g</sup>	BrMgC≡CMe	HCl	H	H	H	84 <sup>h</sup>

<sup>a</sup> Zirconacyclopentenes were reacted with 2 equiv of MC≡CR<sup>3</sup> at -78 to 23 °C. <sup>b</sup> By NMR or GLC. The numbers in parentheses are isolated yields. The stereoisomeric purity of each double bond was determined to be ≥98% by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy. <sup>c</sup> 2 equiv of MeOH was used. <sup>d</sup> 3 equiv of I<sub>2</sub> was used. <sup>e</sup> R<sup>1</sup> = Ph, R<sup>2</sup> = Me. <sup>f</sup> 3 equiv of PhI, 3 equiv of ZnBr<sub>2</sub>, and 10 mol % of Cl<sub>2</sub>Pd(PPh<sub>3</sub>)<sub>2</sub> were used. <sup>g</sup> The starting compound is 2-(*n*-butyl)-3,3-bis(η<sup>5</sup>-cyclopentadienyl)-3-zirconabicyclo[3.3.0]oct-1-ene obtained by the reaction of *n*-Bu<sub>2</sub>ZrCp<sub>2</sub> and the indicated enyne. <sup>h</sup> The product is 1-(*E*)-pentylidene-2-(*Z*)-2'-butenylcyclopentane.

compounds.<sup>7</sup> As expected, their deuteration and iodination gave **10b** (Entry 6) and **11b** (R<sup>1</sup> = R<sup>2</sup> = *n*-Bu and R<sup>3</sup> = Me) (Scheme 1).

The experimental results summarized in Table 1 show the potential synthetic utility of the new route to 1,5-dienes and 1,5-enynes. The following observations are particularly noteworthy: (1) Stereoselectivity in the formation of either of the two double bonds of 1,5-dienes is ≥98%. (2) D and I atoms can be selectively introduced in the three available alkenyl positions. (3) The C–Zr bond of **6** can also be utilized to form carbon–carbon bonds via Pd-catalyzed cross coupling, as exemplified by the reaction of

(7) (a) Buchwald, S. L.; Watson, B. T. *J. Am. Chem. Soc.* **1986**, *108*, 7411. (b) Buchwald, S. L.; Lum, R. T.; Dewan, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 7441. (c) Buchwald, S. L.; Watson, B. T.; Huffman, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 2544. (d) Takahashi, T.; Swanson, D. R.; Negishi, E. *Chem. Lett.* **1987**, 623.

**6c** (R<sup>1</sup> = R<sup>2</sup> = Et, R<sup>3</sup> = Me) with PhI, which was doubly catalyzed by ZnBr<sub>2</sub> and Cl<sub>2</sub>Pd(PPh<sub>3</sub>)<sub>2</sub><sup>8</sup> (entry 12).

The results presented above establish beyond any doubt the dienyli moiety of **3** and **6** including the positions of the three Zr–C bonds. Although our attempts to isolate **3** or **6** as pure compounds were not successful, three concentrated samples of **3**, i.e., **3b**, **3d**, and **3e**, yielded <sup>1</sup>H and <sup>13</sup>C NMR data which strongly support our structural assignment of **3**, including (i) the presence of two equivalent Cp groups and (ii) the zirconate representation reflected by the <sup>1</sup>H NMR chemical shift values (δ 5.53–5.64) of the Cp groups. These three samples prepared via solvent evaporation in vacuo have provided the following rather clean and single dominant sets of <sup>1</sup>H and <sup>13</sup>C NMR spectral data which are in excellent agreement with the assigned structures:<sup>9</sup> **3b** (M = MgBr, R<sup>1</sup> = R<sup>2</sup> = *n*-Bu, R<sup>3</sup> = Me): <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>, THF, mesitylene) δ 0.93 (t, *J* = 7.2 Hz, 3 H), 1.06 (t, *J* = 7.2 Hz, 3 H), 1.25–1.5 (m, 8 H), 2.05–2.15 (m, 2 H), 2.25–2.35 (m, 4 H), 2.49 (s, 3 H), 2.59 (t, *J* = 7.3 Hz, 2 H), 5.55 (s, 10 H); <sup>13</sup>C NMR (C<sub>6</sub>D<sub>6</sub>, THF(traces)) δ 14.54, 14.95, 20.22, 23.57, 23.95, 29.17, 32.49, 33.99, 36.84, 37.40, 40.85, 105.32 (10 C), 129.35, 141.73, 160.79, 190.78. **3d** (M = MgBr, R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = Me): <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>, THF) δ 1.89 (s, 3 H), 2.07 (t, *J* = 7 Hz, 2 H), 2.25–2.35 (m, 2 H), 2.29 (s, 3 H), 2.47 (s, 3 H), 5.53 (s, 10 H); <sup>13</sup>C NMR (C<sub>6</sub>D<sub>6</sub>, THF (traces)) δ 17.76, 20.31, 23.10, 29.46, 42.96, 105.40 (10 C), 129.21, 140.0 (br), 152.07, 191.82. **3e** (M = Li, R<sup>1</sup> = R<sup>2</sup> = Et; R<sup>3</sup> = *n*-Hex) + *n*-octynyllithium: <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>, THF-*d*<sub>8</sub> (traces)) δ 0.90 (t, *J* = 7.1 Hz, 3 H), 0.95 (t, *J* = 7.1 Hz, 3 H), 1.15 (t, *J* = 7.6 Hz, 3 H), 1.37 (t, *J* = 7.6 Hz, 3 H), 1.2–1.6 (m, 16 H), 1.8–1.95 (m, 2 H), 1.95–2.45 (m, 6 H), 2.65 (q, *J* = 7.5 Hz, 2 H), 2.85–2.95 (m, 2 H), 5.64 (s, 10 H); <sup>13</sup>C NMR (C<sub>6</sub>D<sub>6</sub>, THF-*d*<sub>8</sub> (traces)) δ 14.30, 14.47, 15.01, 19.19, 22.39, 23.01, 23.34, 25.94, 29.07, 29.15, 29.75, 29.98, 30.87, 31.06, 31.73, 32.52, 35.69, 40.29, 105.60 (10 C), 113.95 (C<sub>sp</sub>), 126.33 (C<sub>sp</sub>), 135.00, 144.36, 159.87, 196.40.

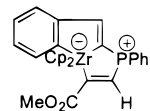
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**Supporting Information Available:** Experimental details (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Miquel, Y.; Igan, A.; Donnadiou, B.; Majoral, J. P.; Pirio, N.; Meunier, P. J. *Am. Chem. Soc.* **1998**, *120*, 3504.