First Demonstration of Helical Chirality in 1,4-Disubstituted (*Z,Z*)-1,3-Dienes: $R_3Si{-}SnR'_3$-Mediated Cyclization of 1,6-Diynes

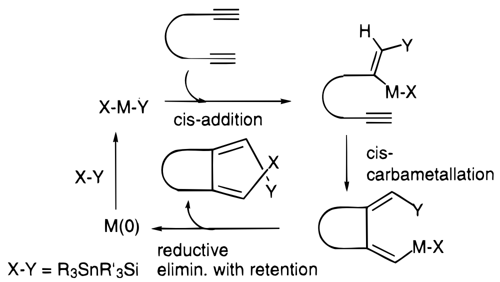
Sandra Gréau, Branko Radetich, and T. V. RajanBabu*

Department of Chemistry, 100 West 18th Avenue
The Ohio State University, Columbus, Ohio 43210

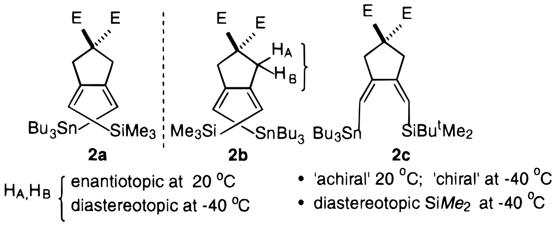
Received May 5, 2000

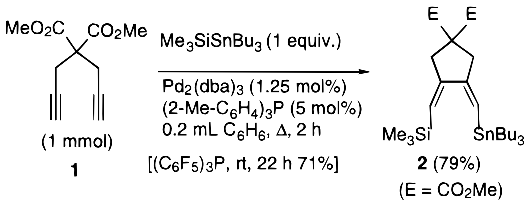
1,2-Bis-alkylidenecycloalkane derivatives prepared from α,*ω*-diynes or eneynes are valuable intermediates in organic synthesis.[1] Catalytic methods which convert diynes to functionalized bis-alkylidene derivatives invariably use bifunctional reagents, X−Y, which can undergo oxidative addition to low-valent transition metals (Scheme 1). Thus, metal-catalyzed cyclization of 1,6-diynes can be accomplished under hydrosilylation,[2a−c] hydrostannylation,[2d] borosilylation,[2e] and borostannylation[2f] conditions. However, an important stereochemical aspect of this reaction, brought about as a necessary consequence of the organometallic reaction mechanisms involved (Scheme 1), viz., the formation of a (*ZZ*)-1,3-diene, has received little attention in the literature. This work addresses this issue in the context of a highly versatile bis-functionalization/cyclization of 1,6-diynes assisted by trialkylsilyltrialkyltin reagents, a class of compounds known to undergo Pd(0)-catalyzed addition to acetylenes with high regio- and stereoselectivity.[3] Sterically demanding silicon and tin substituents impose a nonplanar, therefore, helically chiral structure for such a diene. To the best of our knowledge, helical chirality associated with terminally substituted *(ZZ)*-1,3-dienes has not been disclosed in the literature, even though the first member of this class of compounds has been known for some time.[2f]

Scheme 1. Formation of a Chiral (*Z,Z*)-1,3-Diene from a Diyne



Scheme 2. Enantiomers of **2** at −40 °C





(1)

The structure, stereochemistry, and the fluxional nature of the compound **2** prepared from di-O-methyl dipropargylmalonate (eq 1) were unambiguously established by elemental analysis (C, H) and NMR spectroscopy (^1H, ^{13}C, and ^{119}Sn, COSY, NOESY, DEPT and variable temperature experiments).[4] The ^1H NMR (500 MHz, $CDCl_3$) of **2** is characterized by the following peaks: 0.05 (s, $SiCH_3$, 9 H), 0.85−0.88 (t superimposed on m, $H_2C{-}CH_3$, $SnCH_2$, 15 H, $^2J_{Sn,H}$ satellites), 1.24−1.29 (m, CH_2, 6 H), 1.38−1.44 (m, CH_2, 6 H), 2.66−3.20 (ring CH_2, s, broad, 4 H), 3.69 (s, OCH_3, 6 H), 5.23 (s, Me_3SiCH, 1 H), 5.65 (s, Bu_3SnCH, 1 H, $^1J_{SnH}$ 50 Hz). Irradiation of the olefinic signals at δ 5.23 and 5. 65 causes enhancements of the broad peak centered around δ 2.93 (ring CH_2) which support the *(ZZ)*-assignment of the diene. The extraordinarily broad signals due to the ring methylene hydrogens (at 20 °C: peak width ≈ 0.54 ppm) gave the first indication of a possible fluxional molecule. Upon warming to 50 °C, the peaks resolve into two broad singlets centered around δ 2.97 and 3.01. When a CD_2Cl_2 solution is cooled to −40 °C, two sets of signals appear as AB quartets around δ 3.12 ($\nu_A = 3.10$, $\nu_B = 3.14$, $J_{AB} = 9$ Hz) and at δ 2.72 ($\nu_A = 2.69$, $\nu_B = 2.75$, $J_{AB} = 14$ Hz). Between 20 and −40 °C the changes in the spectrum can be interpreted as arising from two closely spaced AB systems, undergoing A−B exchange, with a coalescence temperature between −10 and −5 °C. At −40 °C, the CO_2Me signals also resolve into two singlets at δ 3.748 and 3.756. The evolution of the two AB quartets for the ring CH_2 group and the doubling of the carbon signals[5] are possible only if the molecule is chiral. Barring a highly unlikely conformational equilibrium involving the cyclopentane, such chirality must have its origin in the helical arrangement of groups in the *(ZZ)*-diene (Scheme 2). Failure of the diene to undergo Diels−Alder reaction with dienophiles including maleic anhydride (150 °C) also supports the unusual nonplanar arrangement of the 1,4-substituents. Another derivative **2c,** with larger Si-substituents exhibits similar behavior including diastereotopic $SiMe_2$ groups, except, as expected, the coalescence temperatures for the diastereotopic hydrogen and carbon signals are approximately 10−15 °C higher.[4]

Cyclizations of a number of other 1,6-diynes were carried out and the results are shown in Table 1. Methyl 2-(2-propynyl)-4-pentynoate **3** gave 66% isolated yield of a product (**4**) which

---

(1) For recent reviews see: (a) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539. (b) Tamao, K.; Kobayashi, K.; Ito, Y. *Synlett* **1992**, 539. (c) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon/Elsevier: Kidlington, 1995; p 741. (d) Negishi, E.-i.; Copéret, C.; Ma, S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365. (e) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635. (f) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 305. (g) Sato, Y.; Nishimata, T.; Mori, M. *Heterocycles* **1997**, *44*, 443. (h) Ogawa, R.; Itoh, K. *J. Org. Chem.* **1998,** *63*, 9610 and references therein. (i) Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 2788.

(2) (a) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 6478. (b) Muraoka, T.; Matsuda, I.; Itoh, K. *Tetrahedron Lett.* **1998,** *39*, 7325. (c) For a recent related reports of hydrosilylation/carbonylation, see: Chatani, N.; Fukumoto, Y.; Ida, T.; Murai, S. *J. Am. Chem. Soc.* **1993**, *115*, 11614; Ojima, I.; Lee, S.-Y. *J. Am. Chem. Soc.* **2000,** *122,* 2385 and references therein. (d) Lautens, M.; Smith, N. D.; Ostrovsky, D. *J. Org. Chem.* **1997**, *62*, 8970. (e) Onozawa, S.; Hatanaka, Y.; Tanaka, M. *J. Chem. Soc., Chem. Commun.* **1997**, 1229. (f) Onozawa, S.; Hatanaka, Y.; Choi, N.; Tanaka, M. *Organometallics* **1997**, *16*, 5389.

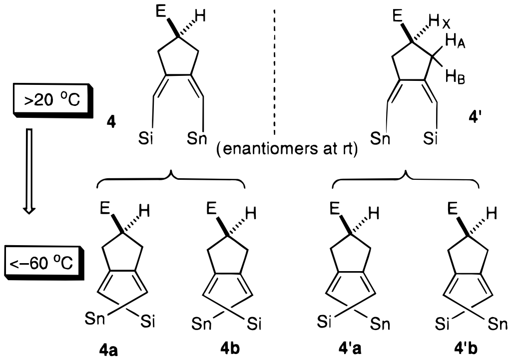
(3) (a) Chenard, B. L.; Laganis, E. D.; Davidson, F.; RajanBabu, T. V. *J. Org. Chem.* **1985**, *50*, 3666. (b) Mitchell, T. N.; Killing, H.; Dicke, R.; Wickenkamp, R. *J. Chem. Soc., Chem. Commun.* **1985**, 345.

(4) See Supporting Information for details, including VT NMR spectra and a discussion of criteria of purity (NMR and HPLC) of key compounds.

(5) The ^{13}C spectrum[4] is characterized by the signals at δ 0.43 (q, $SiCH_3$), 10.71 (t, $SnCH_2$, $^1J_{Sn,C} = 336$ Hz), 13.64 (q, $SnCH_2CH_2CH_2CH_3$), 27.32 (t, $SnCH_2CH_2$, $^2J_{Sn,C} = 59$ Hz), 28.95 (t, $SnCH_2CH_2CH_2$, $^3J_{Sn,C} = 20$ Hz), 44.07 (t, CH_2, 1 C), 44.10 (t, CH_2, 1 C), 52.72 (q, OCH_3, 2 C), 55.05 (s, $C(CO_2Me)_2$, 1 C), 125.57 (d, HCSn, 1 C), 126.21 (d, HCSi, 1 C), 155.34 (s, 1 C), 155.89 (s, 1 C), 172.11 (s, CO). The ^{13}C spectrum also shows the doubling of the CO_2CH_3 and CO_2CH_3 carbons at −40 °C. The ring CH_2 carbons are also better resolved at −40 °C.

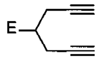
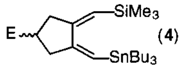
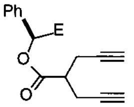
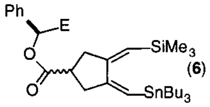
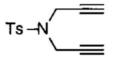
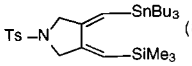
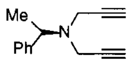
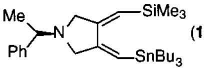
10.1021/ja0015500 CCC: $19.00

Scheme 3. Helical Chirality in **4** at Low Temperature



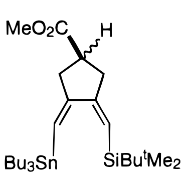
(**4a/4'b** and **4b/4'a** are enantiomeric pairs, -70 °C)

Table 1. Silylstannylation−Cyclization of 1,6-Diynes[a]

entry	substrate	product	isolated yield
1.	**1**	**2a**	71 (79[b])
2.	 (**3**)	 (**4**)	66
3.	 (**5**)	 (**6**)	75
4.	 (**7**)	 (**8**)	77
5.	 (**9**)	 (**10**)	79

[a] See Supporting Information for experimental procedures. [b] Using (2-Me-C_6H_4)$_3$P.

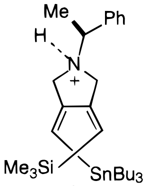
was readily separated on a chiral HPLC column (Chiracel OD, 25 cm × 4.6 mm, 100% hexane, flow rate of 0.1 mL/min. R_t = 37.50, 42.22 min.). As expected, **4** is a highly fluxional molecule. The ring methylenes which appear as two broad doublets ($CDCl_3$) at δ 2.555 and 2.591 (each $\sim J = 8$ Hz) at 27 °C resolves into two ABX patterns at 65 °C (in C_6D_6).[4] The low-temperature spectrum is very complex, yet four sets of ABX patterns are clearly discernible in the spectrum below −40 °C. The temperature-dependent changes in the ^{13}C spectrum of this compound are indeed remarkable,[4] and all of the changes are completely in agreement with the suggested equilibrium between two sets of diastereomers at low temperature (Scheme 3). The corresponding $Bu^t(Me)_2Si-$ derivative **4c** provided the most unequivocal evidence for the equilibration with doubling of the largest number of signals in going from 20 °C to −40 °C. These include, $Si(CH_3)_2$, ring CH_2's, CO_2CH_3 in the proton spectrum, ring CH_2's, ring CH, carbonyl C, SnCH, SiCH in the ^{13}C spectrum, and the Sn signal in the ^{119}Sn spectrum.[4]



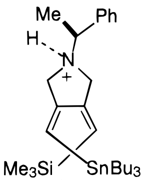
4c

2 enantiomers at rt

2 sets of diastereomers at -40 °C



10a



10b

Diastereomers in the unit cell

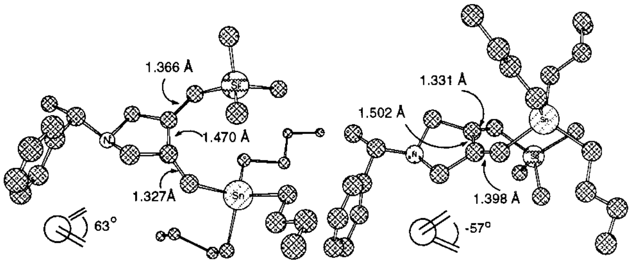


Figure 1. X-ray structures of **10a** and **10b** (cations, H's omitted for clarity).

The reaction conditions are compatible with amino and amido groups, allowing access to functionalized heterocycles (**8**, **10**, entries 4, 5). In VT NMR and nOe experiments,[4] **8** behaves like **2**, in which the equilibration process is slow below −40 °C, resulting in one of the ring CH_2 groups to appear as a true ABq at low temperature. NMR spectra of **10**, prepared from dipropargylamine **9**, are indicative of a single compound (fast N-inversion and helical equilibration remove any potential diastereoisomerism) at room temperature. The low-temperature spectra recorded in CD_3OD are much less resolved compared to the carbocyclic compounds, nonetheless, a mixture of diastereomers is indicated at temperatures below −60 °C. Quaternization of **10** with methyl triflate removes the nitrogen inversion, and a set of diastereomeric triflate salts, characterized by, *inter alia*, a pair of SiCH and SnCH signals, are produced at room temperature.[4]

Finally, a crystalline oxalate salt of the pyrrolidine derivative **10** was found to contain, in its unit cell, two of the four possible diastereomers, in which the diene helicity can be clearly seen. Chem3D renditions of these structures with selected intramolecular distances and angles are shown in Figure 1.[6] The epimerization reaction, observed in the NMR spectra, is apparently frozen in the solid state, permitting isolation of the individual diastereomers.

Acknowledgment. We acknowledge the financial assistance by the U.S. National Science Foundation (CHE-9706766). We thank Dr. Judith C. Gallucci for the X-ray crystallographic analysis.

Supporting Information Available: Experimental procedures for the synthesis of precursors and products listed in Table 1; VT NMR spectra of compounds **2**, **2c**, **4**, **4c**, **6**, **8**, **10**, [**10**-Me]$^+$[OTf]$^-$ and ^1H NMR of **10a/b** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA0015500

---

[6] Because of disorders in the crystal, complete solution of the structure was not possible, even though reliable data on the ammonium ion could be extracted.