Insertion of 1-Chloro-1-lithioalkenes into Organozirconocenes. A Versatile Synthesis of Stereodefined Unsaturated Systems

Aleksandr Kasatkin and Richard J. Whitby*

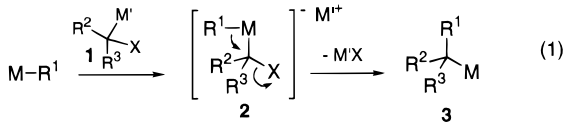
Contribution from the Department of Chemistry, Southampton University, Southampton, HANTS, SO17 1BJ, U.K.

Received March 30, 1999

Abstract: Hydrozirconation of alkenes and alkynes, followed by insertion of 1-halo-1-lithio-1-alkenes, generated in situ by lithium tetramethylpiperidide deprotonation of vinyl halides, affords vinylzirconocene species which may be further elaborated. The method provides easy access to many structures including terminal (3*E*)- and (3*Z*)-1,3-dienes and (3*E*,5*E*)- and (3*Z*,5*E*)-1,3,5-trienes, and internal (*E*,*Z*)-dienes, (*E*,*Z*,*E*)-trienes, and (1*E*,3*Z*)-1,3-dien-5-ynes. Insertion of 2-monosubstituted 1-halo-1-lithio-1-alkenes occurs with clean inversion of configuration of the sp^2-carbenoid carbon. Carbenoids derived by deprotonation of 2,2-disubstituted 1-halo-1-alkenes gave poor stereocontrol probably due to isomerization before insertion into the organozirconium species. Insertion of vinyl carbenoids into alkynylzirconocenes affords terminal (3*E*)- or (3*Z*)-1,3-dien-5-ynes, internal (1*E*,3*Z*)-1,3-dien-5-ynes, and (*Z*)-3-en-1,5-diynes.

Introduction

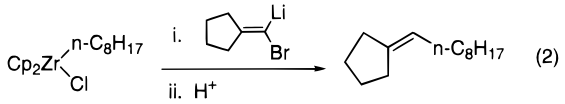
A characteristic of transition metal chemistry is the often facile insertion of components with carbenoid properties (CO, RNC) into carbon−metal bonds to generate a new organometallic with the potential for further elaboration. With the current interest in combinatoric methods, such inherently iterative reactions are of particular relevance to organic synthesis. A recently developed class of such reactions is the insertion of metal carbenoids **1** to afford a new organometallic **3**, probably occurring via 1,2-rearrangement of an intermediate "ate" complex **2** (eq 1).[1−3] Such rearrangements are well-known



(1)

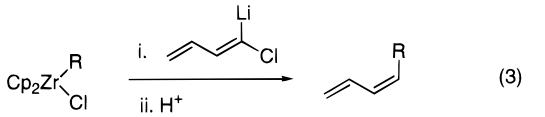
in boron chemistry,[4] and have been reported for several other main group elements.[5,6] We have developed the use of carbenoid insertions in the elaboration of zirconacycles.[7]

Hydrozirconation of alkenes and alkynes with the Schwartz reagent ($Cp_2Zr(H)Cl$, $Cp = C_5H_5$) to give alkyl- and vinylzirconocene chlorides is a well-established synthetic method.[8] To be useful in organic synthesis methods for further elaboration of the organozirconium species are needed. Carbon−carbon bond-forming reactions include carbonylation, isocyanide insertion, and copper-, nickel-, and palladium-catalyzed reactions.[8] A particularly interesting elaboration method is the insertion of α-haloorganolithium species as described above, reported by Negishi.[1] Of particular relevance to the work described herein is the insertion of (1-lithio-1-bromomethylene)cyclopentane, generated by Br/Li exchange from the corresponding dibromide, into *n*-octylzirconocene chloride to give a good yield of nonylidenecyclopentane on acid quench (eq 2).[1]



(2)

We recently reported the insertion of 1-lithio-1-halobutadiene into organozirconocenes providing a stereocontrolled synthesis of terminal dienes, trienes, and dienynes (e.g., eq 3).[9] We now report full details of this work, extension to a wide range of



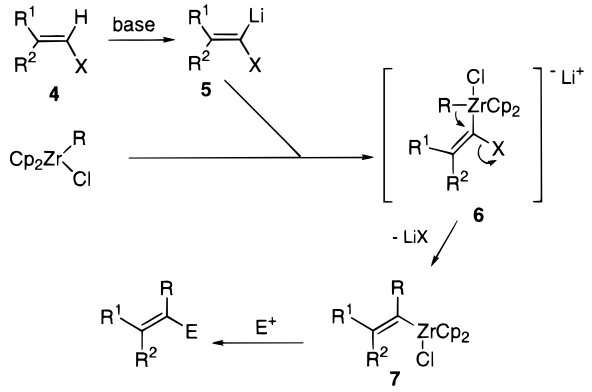
(3)

other vinylcarbenoids, and functionalization of the carbon−zirconium bond present in the initial insertion product. Application to the synthesis of natural products is also described.

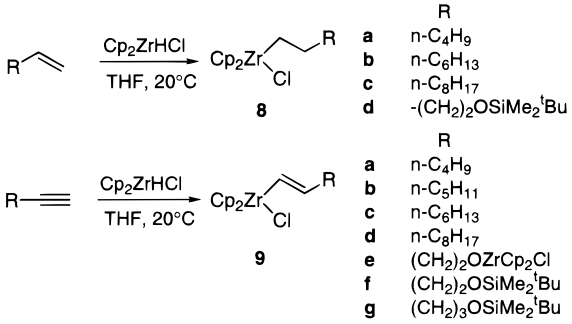
(1) Negishi, E.; Akiyoshi, K.; O'Connor, B.; Takagi, K.; Wu, G. *J. Am. Chem. Soc.* **1989**, *111*, 3089.
(2) Kocienski, P.; Barber, C. *Pure Appl. Chem.* **1990**, *62*, 1933.
(3) Siddure, A.; Rozema, M. J.; Knochel, P. *J. Org. Chem.* **1993**, *58*, 2694.
(4) (a) Matteson, D. S. *Chem. Rev.* **1989**, *89*, 1535. (b) Negishi, E. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, F. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 7, pp 255−363. (c) Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc.* **1967**, *89*, 5086. (d) Birkinshaw, S.; Kocienski, P. *Tetrahedron Lett.* **1991**, *32*, 6961.
(5) Al, Mg, Zn, Cd: (a) Negishi, E.; Akiyoshi, K. *J. Am. Chem. Soc.* **1988**, *110*, 646. Zn: (b) Harada, T.; Katsuhira, T.; Hara, D.; Kotani, Y.; Maejima, K.; Kaji, R.; Oku, A. *J. Org. Chem.* **1993**, *58*, 4897. (c) Harada, T.; Katsuhira, T.; Osada, A.; Iwazaki, K.; Maejima, K.; Oku, A. *J. Am. Chem. Soc.* **1996**, *118*, 11377. Al: (d) Miller, J. A. *J. Org. Chem.* **1989**, *54*, 998. Si: (e) Achmatowicz, B.; Jankowski, P.; Wicha, J.; Zarecki, A. *J. Organomet. Chem.* **1998**, *558*, 227. (f) Matsumoto, K.; Aoki, Y.; Oshima, K.; Utimoto, K.; Rahman, N. A. *Tetrahedron* **1993**, *49*, 8487. Mg: (g) Lima, C.; Julia, M.; Verpeaux, J.-N. *Synlett* **1992**, 133
(6) Li: (a) Topolski, M.; Duraisamy, M.; Rachon, J.; Gawronski, J.; Gawronska, K.; Goedken, V.; Walborsky, H. M. *J. Org. Chem.* **1993**, *58*, 546. (b) Nguyen, T.; Negishi, E. *Tetrahedron Lett.* **1991**, *32*, 5903. (c) Nelson, D. J.; Nagarajan, A. *J. Organomet. Chem.* **1993**, *463*, 1.
(7) Fillery, S. F.; Gordon, G. J.; Luker, T.; Whitby, R. J. *Pure Appl. Chem.* **1997**, *69*, 633. Gordon, G. J.; Whitby, R. J. *Chem. Commun.* **1997**, 1321. Gordon, G. J.; Whitby, R. J. *Chem. Commun.* **1997**, 1045. Tuckett, M. W.; Watkins, W. J.; Whitby, R. J. *Tetrahedron Lett.* **1998**, *39*, 123.
(8) Wipf, P.; Jahn, H. *Tetrahedron* **1996**, *52*, 12853.
(9) Kasatkin, A.; Whitby, R. J. *Tetrahedron Lett.* **1997**, *38*, 4857

10.1021/ja9910208 CCC: $18.00
Published on Web 07/16/1999

Scheme 1



Scheme 2



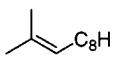
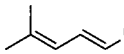
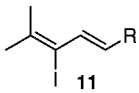
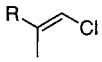
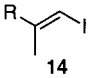
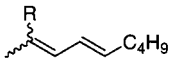
Results and Discussion

Our aim was to extend the insertion of (1-lithio-1-bromomethylidene)cyclopentane into *n*-octylzirconocene chloride reported by Negishi[1] (eq 2) to a range of other vinylcarbenoids **5** and organozirconium species (Scheme 1). In particular we wished to investigate the stereochemistry of the carbenoid insertion. Clean inversion of stereochemistry of the vinyl halide **4** is expected from the proposed mechanism[1] via the "ate" complex **6**, and has been demonstrated with other elements.[2,4c,d,5b,d,6a,b] For experimental ease, and the possibility of generating stereodefined species, we chose to generate the 1-halo-1-lithio-1-alkenyl species **5** by deprotonation of the corresponding vinyl halides **4** in situ.[10] A wide variety of alkyl- and alkenylzirconocene chlorides **8** and **9** used in this work were generated by hydrozirconation[8] of the corresponding alkenes and alkynes (Scheme 2). To our delight, addition of lithium tetramethylpiperidide (LiTMP) to a mixture of 1-chloro-2-methyl-1-propene (**10**) and *n*-octylzirconocene chloride (**8b**) at −90 °C followed by protic quench gave an excellent yield of 2-methyl-2-undecene (Table 1, entry 1). In a similar way insertion into (*E*)-1-octenylzirconocene chloride (**9c**) gave (*E*)-2-methyl-2,4-undecadiene, slightly improved yields being obtained by using 2 equiv of the carbenoid (Table 1, entry 3, cf. 2). Quenching the reaction with iodine gave the iodide **11** in good yield, confirming the intermediate formation of a new vinylzirconocene **7** (Scheme 1), and beginning to demonstrate the key advantage of carbenoid insertion methods for elaboration of organometallics: the product retains the organometallic functionality of the precursor.

Insertion of the carbenoid derived by deprotonation of (*E*)-1-chloro-2-methyl-1-octene (**12**) into either *n*-hexyl- or (*E*)-1-hexenylzirconocene chloride (**8a** and **9a**) gave the expected products **13** and **17** in moderate yield, but with poor stereoselectivity (Table 1, entries 5, 6, and 12). The (*Z*) product is that expected from a 1,2-metalate rearrangement occurring with inversion of the sp^2 carbon, and was the minor isomer! Insertion of the carbenoid derived from (*Z*)-1-chloro-2-methyl-1-octene (**15**) into *n*-hexylzirconocene chloride gave **13** with a good 93:7 *E*:*Z* ratio in favor of the product derived by inversion of the reacting sp^2 center (entry 9). The carbenoids derived from (*E*)- and (*Z*)-1-iodo-2-methyl-1-octene (**14** and **16**) inserted into *n*-hexylzirconocene chloride with predominant inversion to give 27:73 and 75:25 *E*:*Z* ratios respectively of the alkene **13** (Table 1, entries 8 and 11). With short reaction times at low temperature the vinyl iodide carbenoid precursors gave incomplete reaction. Interestingly under these conditions the product **13** was obtained with higher (*Z*)-selectivity from **14** (Table 1, entry 7, cf. 8) but lower (*E*)-selectivity from **16** (Table 1, entry 10, cf. 11). In both cases iodide was recovered from the protonation and had partially lost stereochemical integrity (88:12 and 14:84 *E*:*Z*, respectively). Similarly, the reaction of the carbenoid derived from **14** with (*E*)-1-hexenylzirconocene chloride led to the diene **17** with partial inversion of configuration (Table 1, entry 13). A discussion of the possible causes of the poor stereocontrol observed for the insertion of 2,2-disubstituted 1-lithio-1-haloalkenes follows description of the rest of the preparative results.

We next examined insertion of β-monosubstituted 1-lithio-1-halo-1-alkenes. In general such species are very unstable, 1,2-β-hydride migration with loss of lithium halide to give an

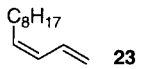
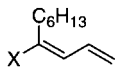
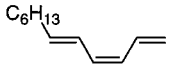
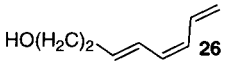
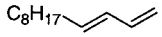
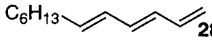
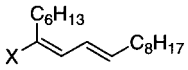
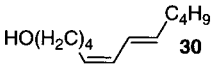
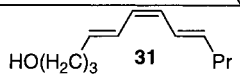
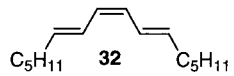
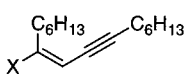
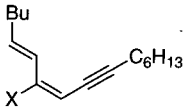
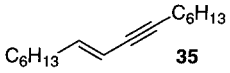
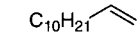
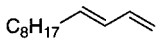
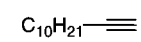
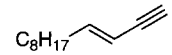
Table 1. Insertions of β,β-Disubstituted Vinyl Carbenoids (Scheme 1, R^1, $R^2 \neq H$; R = *n*-C_6H_{13}.)

Entry	Organo-zirconium	Carbenoid precursor	Cond.[a]	Product[b]	Yield% GC (Isolated)	*E* : *Z*[c]
1	**8b**	 **10**	A		80 (72)	
2	**9c**	**10**	A		73 (67)	
3	**9c**	**10**	B		83 (78)	
4	**9c**	**10**	B[d]	 **11**	86 (72)	
5	**8a**	 **12**	A	 **13**	35	56 : 44
6	**8a**		C		45	63 : 37
7	**8a**	 **14**	A	**13**	23	16 : 84
8	**8a**		C	**13**	61 (61)	27 : 73
9	**8a**	 **15**	C	**13**	70 (65)	93 : 7
10	**8a**	 **16**	A	**13**	11	54 : 46
11	**8a**		C	**13**	57	75 : 25
12	**9a**	**12**	C	 **17**	46	58 : 42
13	**9a**	**14**	D	**17**	63 (62)	25 : 75

[a] A: 1.3 equiv of halide, 1.3 equiv of LiTMP, THF, −90 to −80 °C, 15 min. B: as A but 2 equiv of halide and LiTMP. C: as A, then −60 to −40 °C for 1 h. D: as C but 1.8 equiv of halide and LiTMP. [b] After workup with 2 M HCl(aq) except where stated. [c] Stereochemistry of the trisubstituted alkene, ratio by GC. [d] Quenched with 3 equiv of I_2, then 0 °C, 30 min.

(10) For reviews on 1-lithio-1-haloalkenes see: Braun, M. In *Methoden Org. Chem. (Houbden-Weyl)*, 4th ed.; Thieme: Stuttgart, 1993; Vol. E 19d, pp 291−304. Braun, M. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 430.

Table 2. Insertion of β-Monosubstituted Vinyl Carbenoids (Scheme 1, R^1 and/or R^2 = H)'

Entry	Zr cmp.	Carbenoid	Cond.[a]	E^+	Product[b]	GC Yield % (isolated)
1	**8b**	**18**	A	H^+		33
2	**8b**	**20**	A	H^+	 **23**	83 (76)
3	**8a**	**20**	A	NBS[c]	 **24a** X = Br	61 (62)
4				BuNC[d]	**24b** X = CHO	(70)
5	**9c**	**20**	A	H^+	 **25**	74 (72)
6	**9e**	**20**	A	H^+	 **26**	(65)
7	**9f**	**20**	A	i. H^+, ii. F^-	**26**	(62)
8	**8b**	**19**	A	H^+	 **27**	85 (83) *E* : *Z* 91 : 9
9	**9c**	**19**	A	H^+	 **28**	46 (48) *E*, *E* : *Z*, *E* 86 : 14
10	**8a**	**40d**	B	H^+	 **29a** X = H	82 (82)
11				I_2[e]	**29b** X = I	84 (81)[g]
12				NBS[c]	**29c** X = Br	83 (73)
13				BuNC[d]	**29d** X = CHO	(67)
14	**8d**	**40b**	B	H^+	 **30**	(67)
15	**9g**	**40a**	B	H^+	 **31**	(70)
16	**9b**	**40c**	B	H^+	 **32**	(76)
17	**8a**	**40e**	C	H^+	 **33a** X = H	77 (76)
18				NBS[c]	**33b** X = Br	67 (64)
19	**9a**	**40e**	C	H^+	 **34a** X = H	71 (70)
20				NBS[f]	**34b** X = Br	54 (52)
21	**8a**	**43**	B	H^+	 **35**	17
22	**8c**	**44**	A	H^+	 **36**	55
23	**9d**	**44**	A	H^+	 **27**	38
24	**8c**	**45**	D	H^+	 **37**	83
25	**9d**	**45**	D	H^+	 **38**	79 (78)

[a] A: 1.3 equiv of Li-carbenoid, −90 to −80 °C, 15 min, THF. B: as A but 0.83 equiv of Li-carbenoid. C: as B, then −60 to −40 °C, 40 min. D: as A, then −15 to 20 °C, 2 h. [b] Isomeric purity of products is >95:5 except where stated. [c] 1.5 equiv of NBS, −60 to −40 °C, 1 h. [d] 1.3 equiv of BuNC, 20 °C, 16 h, then 50% HOAc/H_2O, 20 °C, 1 h. [e] 1.5 equiv of I_2, −60 to −40 °C, 1 h. [f] 1.5 equiv of NBS, 20 °C, 30 min. [g] Disubstituted alkene 86:14 *E*:*Z* after purification.

acetylene being facile, and a widely used alkyne synthesis.[11] The rearrangement is much faster with a hydrogen trans to the halide, for example (*E*)- and (*Z*)-1-lithio-1-chloro-2-phenylethene decompose to phenylacetylene at −60 and −110 °C, respectively.[12] The only other reported example of a carbenoid with a hydrogen trans to the halide being formed and trapped is the parent 1-lithio-1-chloroethene.[13] β-Monosubstituted 1-lithio-1-chloro-1-alkenes are also difficult to form by deprotonation (our preferred route to stereospecific species), halogen−lithium exchange from 1,1-dihaloalkenes being preferred.[10,14] However, a few examples of deprotonation have been reported.[10,12,13,15]

Treatment of (*E*)-β-bromostyrene with LiTMP to generate (*E*)-1-bromo-1-lithio-2-phenylethene (**18**) in the presence of *n*-octylzirconocene chloride followed by hydrolysis gave a 33% yield of (*Z*)-1-phenyl-1-decene (Table 2, entry 1) demonstrating clean inversion of the sp^2 center for the first time.

The base-induced elimination of HX from (*E*)- or (*Z*)-1,4-dihalo-2-butene is known to give predominantly (*Z*)- or (*E*)-1-halobutadiene, respectively.[16] We found that treatment of (*E*)- or (*Z*)-1,4-dichloro-2-butene with 2 equiv of LiTMP at −90 °C gave stereoselectively, and in good yield, (*Z*)- or (*E*)-1-chloro-1-lithio-1,3-butadienes (**19** and **20**) via α-deprotonation of the in situ formed 1-chlorobutadienes (Scheme 3). Trapping with benzaldehyde to afford the alcohols **21** and **22** confirmed the formation and stereochemistry of the novel carbenoids.[17] The formation of **19** is notable as the first efficient deprotonation of a (*Z*)-chloroalkene with a proton trans to the chlorine. The use of lithium diisopropylamide instead of LiTMP as the base gave similar results. Treatment of (*E*)- or (*Z*)-1,4-dibromo-2-butene with 2 equiv of LiTMP gave the corresponding (*Z*)- or (*E*)-1-bromo-1-lithio-1,3-butadienes, but the stereoselectivity was lower than for the chloro-substituted case. Reaction of the in situ generated carbenoids **19** and **20** with *n*-octyl- and (*E*)-1-octenylzirconocene chlorides (**8b** and **9c**) followed by acidic workup gave (*E*)- and (*Z*)-1,3-dodecadiene (**27** and **23**), and (3*E*,5*E*)- and (3*Z*,5*E*)-1,3,5-dodecatriene (**28** and **25**), as shown in Table 2 (entries 2, 5, 8, and 9). Workup with DCl/

(11) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769. Villieras, J.; Perriot, P.; Normant, J. F. *Synthesis* **1975**, 458. McIntosh, M. C.; Weinreb, S. M. *J. Org. Chem.* **1993**, *58*, 4823. Tietze, L. F.; Neumann, T.; Kajino, M.; Pretor, M. *Synthesis* **1995**, 1003. Reetz, M. T.; Strack, T. J.; Kanand, J.; Goddard, R. *J. Chem. Soc., Chem. Commun.* **1996**, 733.

(12) Schlosser, M.; Ladenberger, V. *Chem. Ber.* **1967**, *100*, 3893.

(13) (a) Kobrich, G.; Flory, K. *Chem. Ber.* **1966**, *99*, 1773. (b) Shimizu, N.; Shibata, F.; Tsuno, Y. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 777.

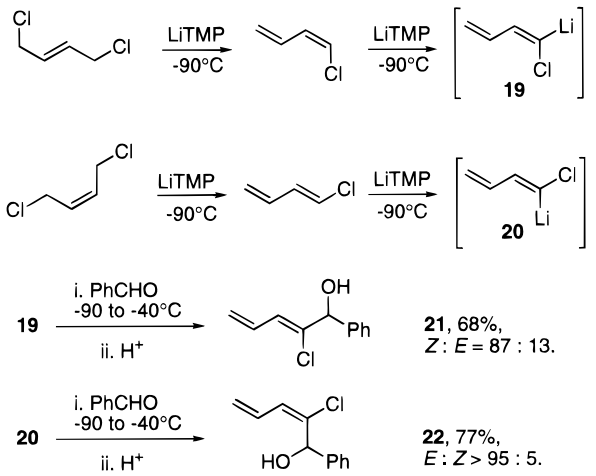
(14) Grandjean, D.; Pale, P. *Tetrahedron Lett.* **1993**, *34*, 1155−1158. Zweifel, G.; Lewis, W.; On, H. P. *J. Am. Chem. Soc.* **1979**, *101*, 5101.

(15) (a) Alami, M.; Crousse, B.; Linstrumelle, G. *Tetrahedron Lett.* **1995**, *36*, 3687. (b) Richardson, S. K.; Jeganathan, A.; Watt, D. S. *Tetrahedron Lett.* **1987**, *28*, 2335.

(16) Heasley, V. L.; Lais, B. R. *J. Org. Chem.* **1968**, *33*, 2571. Keegstra, M. A.; Verkruijsse, H. D.; Andringa, H.; Brandsma, L. *Synth. Commun.* **1991**, *21*, 721. Alexakis, A.; Barthel, A.; Normant, J. F.; Fugier, C.; Leroux, M. *Synth. Commun.* **1992**, *22*, 1839.

(17) The stereochemistry of **21** and **22** follows from the γ-gauche effect in the carbon-13 NMR—the CH(OH) carbons coming at δ_C 77.27 and 70.88 ppm, respectively.

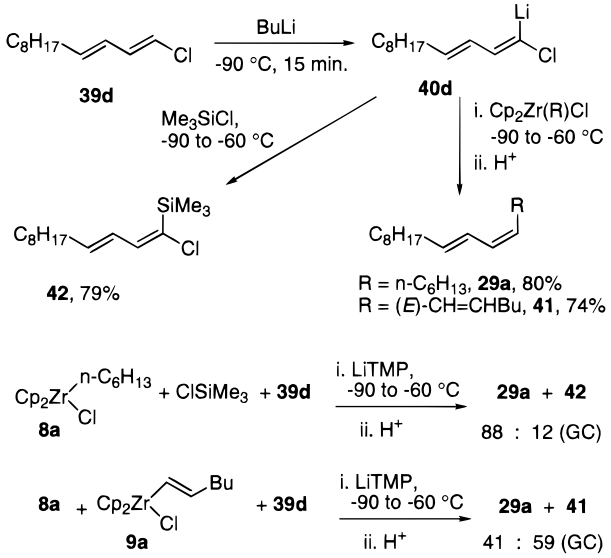
Scheme 3



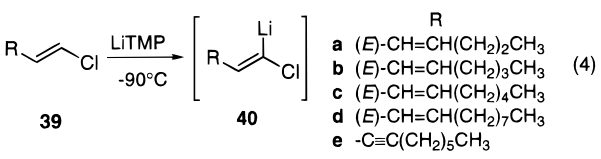
D_2O gave >95% deuterium incorporation at the expected site for a product like **7**. Stereoselectivity was consistent with clean inversion of configuration of the carbenoid sp^2 center, allowing for the isomeric purity of the carbenoids as judged from **21** and **22**. Since both isomeric carbenoids were available, the results prove that the 1,2-metalate rearrangement of vinylzirconate species **6** is stereospecific with inversion, not merely stereoselective. Compounds **25** and **28** are homologues (hexyl rather than pentyl chain) of the galbanolenes—natural products isolated from essential oils of galbanum, and of interest in the perfumery industry.[18] Our synthetic method compares well with the many published routes to these compounds.[19] The incorporation of functional groups is important for further applications of this chemistry so we investigated 3-butyn-1-ol as the hydrozirconation substrate. Reaction of the alcohol with 2.3 equiv of $Cp_2Zr(H)Cl$ followed by 1.3 equiv of the carbenoid **20** and protonolysis gave (3*E*,5*Z*)-3,5,7-octatrien-1-ol (**26**) in good yield and stereoselectivity (Table 2, entry 6). Careful control of the quantity of $Cp_2Zr(H)Cl$ was required to prevent overreduction of the alkyne and subsequent formation of 5,7-octadien-1-ol. Hydrozirconation of 1-*tert*-butyldimethylsiloxy-3-butyne followed by reaction with **20**, hydrolysis, and deprotection with tetrabutylammonium fluoride (TBAF) also gave **26** (entry 7).

To extend the chemistry to nonterminal dienes and trienes we examined the deprotonation and trapping of (*E*,*E*)-4-alkyl-1-chloro-1,3-butadienes. Treatment of the vinyl halides **39a**−**d** with LiTMP in the presence of an organozirconium species gave products consistent with the in situ formation of the novel carbenoid type illustrated by **40a**−**d** (eq 4). Insertion into alkyl- and vinylzirconocene chlorides followed by hydrolysis gave the nonterminal dienes **29a** and **30**, and trienes **31** and **32** with high yields and stereoselectivity (Table 2, entries 10 and 14−16). Diene **30** is the pheromone of *Malascoma disstria*, the forest tent caterpiller,[20] and triene **31** is the ether component of bretonin B.[21] We examined the formation and trapping of the carbenoid **40d** in more detail. Butyllithium is the most widely used base for the deprotonation of vinyl chlorides,[10] and indeed exposure of (*E*,*E*)-1-chloro-1,3-dodecadiene (**39d**) to 1.05 equiv of butyllithium at −90 °C, followed by the addition of *n*-hexyl- or (*E*)-1-hexenylzirconocene chloride (**8a** and **9a**) or chlorotrimethylsilane, gave the expected products (**29a**, **41**, and **42**) in excellent yields (Scheme 4). The relative rates by which the three species trapped the carbenoid were determined by competition experiments. Exposing a 1:1 mixture of *n*-hexylzirconocene chloride and chlorotrimethylsilane to 0.85 equiv of the carbenoid **40d**, generated in situ, gave an 88:12 mixture of the diene **29a** and silylated diene **42**. Likewise a 1:1 mixture of *n*-hexyl- and (*E*)-1-hexenylzirconocene chloride gave a 41:59 mixture of the diene **29a** and triene **41**. The relative rates of trapping of the carbenoid **40d** by chlorotrimethylsilane, **8a**, and **9a** is thus 1:7.3:10.5. Of note is that addition of butyllithium to a mixture of the chloride **39d** and organozirconocene **8a** gave no insertion products, and greater than 90% recovery of the starting chloride, suggesting fast attack of the butyl anion at the metal, and confirming the importance of the use of the nonnucleophilic base LiTMP for in situ deprotonations.

Scheme 4



To allow access to internal (*Z*,*Z*)-dienes and (*Z*,*Z*,*E*)-trienes we examined the insertion of the β-acetylenic carbenoid **40e** (eq 4), previously reported by Alami and Linstrumelle,[15a] into organozirconium species. Reaction of **40e** with **8a** and **9a** worked well to give the enyne **33a** and dienyne **34a** in good yields and excellent stereocontrol (Table 2, entries 17 and 19). Reduction of the alkyne in systems similar to **33a** and **34a** to afford cis alkenes is well-known.[22] Encouraged by the successful



(4)

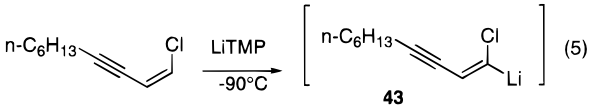
(18) Chretien-Bessiere, Y.; Garnero, J.; Benezet, L.; Peyron, L. *Bull. Soc. Chim. Fr.* **1967**, 97. Naves, Y. R. *Bull. Soc. Chim. Fr.* **1967**, 3152. Moore, R. E.; Mistysyn, J.; Pettus, J. A. *J. Chem. Soc., Chem. Commun.* **1972**, 326. Moore, R. E.; Pettus, J.; Mistysyn, J. *J. Org. Chem.* **1974**, *39*, 2201.

(19) (a) Solladie, G.; Urbano, A.; Stone, G. B. *Synlett* **1993**, 548 and references therein. (b) Alami, M.; Gueugnot, S.; Domingues, E.; Linstrumelle, G. *Tetrahedron* **1995**, *51*, 1209. (c) Furber, M.; Herbert, J. M.; Taylor, R. J. K. *J. Chem. Soc., Perkin Trans. 1* **1989**, 683. (d) Tellier, F.; Descoins, C.; Sauvetre, R. *Tetrahedron* **1991**, *47*, 7767. (e) Hodgetts, K. J.; Saengchantara, S. T.; Wallis, C. J.; Wallace, T. W. *Tetrahedron Lett.* **1993**, *34*, 6321.

(20) For previous synthesis of pheromone **30** see: Rossi, R.; Carpita, A. *Tetrahedron* **1983**, *39*, 287. Gardette, M.; Jabri, N.; Alexakis, A.; Normant, J. F. *Tetrahedron* **1984**, *40*, 2741. Trost, B. M.; Martin, S. J. *J. Am. Chem. Soc.* **1984**, *106*, 4263. Stille, J. K.; Groh, B. L. *J. Am. Chem. Soc.* **1987**, *109*, 813. Huang, Y.-Z.; Shi, L.; Yang, J. *J. Org. Chem.* **1987**, *52*, 3558. Fiandanesse, V.; Marchese, G.; Naso, F.; Ronzini, L.; Rotunno, D. *Tetrahedron Lett.* **1989**, *30*, 243. Tsuboi, S.; Ishii, N.; Sakai, I.; Utaka, M. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1888.

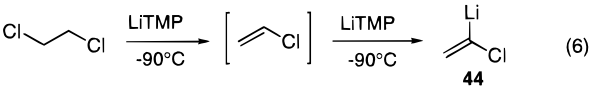
(21) Mancini, I.; Guella, G.; Pietra, F. *Helv. Chim. Acta* **1991**, *74*, 941.

formation of carbenoid **19** we also tried to generate and trap the carbenoid **43** from (*Z*)-1-chlorodec-1-en-3-yne (eq 5).



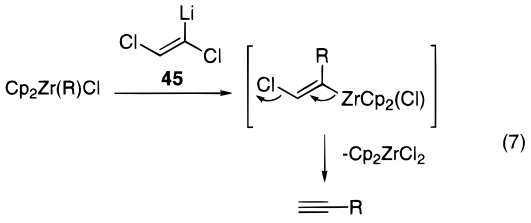
Although Alami and Linstrumelle report failure to trap species such as **43**,[15a] we obtained a low yield of the expected adduct **35** from insertion into *n*-hexylzirconocene chloride (**8a**) (Table 2, entry 21), indicating the great speed with which the zirconium species traps the anion, and the advantages of in situ generation using an amide base.

We next examined the insertion of the parent vinyl carbenoid, 1-chloro-1-lithioethene (**44**). Kobrich found that metalation of vinyl chloride with butyllithium at −110 °C was quantitative,[13a] and **44** has been generated and trapped in situ using LDA/chlorotrimethylsilane at −78 °C.[13b] For convenience we treated a mixture of the organozirconium species **8c** or **9d** and 1, 2-dichloroethane with 2 equiv of LiTMP, vinyl chloride being generated, and metalated in situ (eq 6). Moderate yields of the



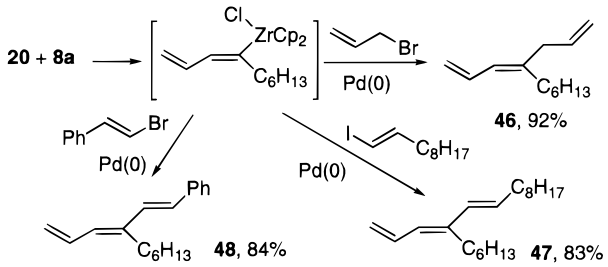
expected terminal alkene **36** and (*E*)-1,3-diene **27** were obtained (Table 2, entries 22 and 23). The later was formed with complete stereocontrol, cf. the alternative route to terminal (*E*)-dienes using carbenoid **19** (Table 2, entry 8).

Finally we examined insertion of (*E*)-1,2-dichloro-1-lithioethene (**45**).[13a] Treatment of a mixture of (*E*)-1,2-dichloroethene and organozirconium species **8c** and **9d** with LiTMP at −90 °C gave rise to the terminal acetylene **37** and enyne **38** in excellent yield (Table 2, entries 24 and 25), presumably via *anti*-elimination of zirconocene dichloride from the intermediate (*E*)-2-chloroalkenylzirconocene chloride (eq 7).



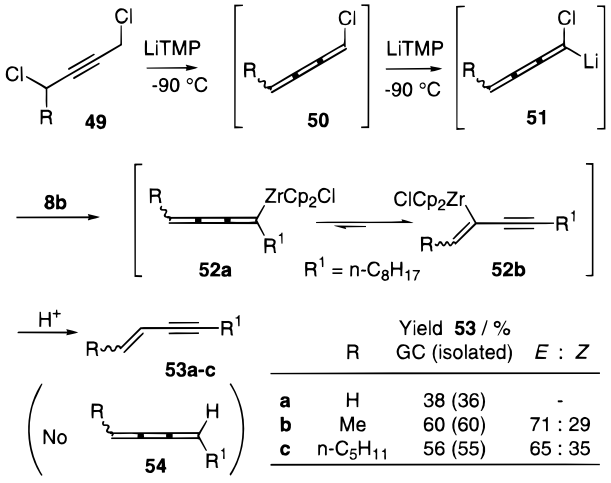
An important feature of the carbenoid insertion route to unsaturated systems described above is the presence of a carbon−zirconium bond in the primary products. Workup with iodine or NBS gave the corresponding vinyl halide in good yield and excellent stereocontrol (Table 2, entries 3, 11, 12, 18, and 20). Formation of bromides was preferred since we found it difficult to avoid some isomerization of the dienyliodide **29b** during workup (>98% *E*,*E* in the crude product by GC, only 86% *E*,*E* after purification). Formation of a new carbon−carbon bond was illustrated by the insertion of *n*-butyl isocyanide,[23] mild acidic workup giving the aldehydes **24b** and **29d** as single geometric isomers (Table 2, entries 4 and 13). Carbon−carbon bond formation was also achieved by palladium-catalyzed

Scheme 5[a]



[a] Reaction conditions: 0.8 equiv of halide, 1.0 equiv of $ZnCl_2$, 5 mol % [$Pd(PPh_3)_2Cl_2$ + $2PPh_3$ + 2EtMgBr], THF, 20 °C, 16 h.

Scheme 6



	R	Yield **53** / % GC (isolated)	*E* : *Z*
a	H	38 (36)	-
b	Me	60 (60)	71 : 29
c	n-C_5H_{11}	56 (55)	65 : 35

coupling with vinyl or allyl halides[24] to give the products **46**−**48** with >95:5 stereopurity (Scheme 5).

Prompted by our successful in situ formation of **19** and **20**, we examined the generation of unusual 1-lithio-1-chloro-1,2,3-triene carbenoids **51** from 1,4-dichloro-2-alkynes **49** on treatment with 2 equiv of LiTMP (Scheme 6).[25] Trapping with *n*-octylzirconocene chloride (**8b**) presumably gave the intermediate **52**, which underwent regioselective protonation to afford enynes **53a**−**c**. It is interesting that the 1,2,3-triene product **54** which could also be formed was not observed. In the nonterminally substituted cases (**53b** and **53c**) a mixture of double bond stereoisomers was formed, favoring the trans isomer. We believe that the regio- and stereochemistry of the protonated products **53a**−**c** is best explained by the intermediate zirconium species existing in the enyne form **52b**, this protonating on the carbon carrying the zirconium with retention of configuration. It is known that hydrolysis of 2-metallo-1,3-dienes gives 1,3-dienes, rather than the 1,2-dienes which would result from reaction with allylic rearrangement.[26] The stereochemistry of the alkene component of **53b,c** thus derives from the initial elimination of hydrogen chloride to afford **50**, predominantly as the cis isomer.

(22) Boland, W.; Schroer, N.; Sieler, C.; Feigel, M. *Helv. Chim. Acta* **1987**, *70*, 1025. Also refs 19b,d.

(23) Negishi, E.; Swanson, D. R.; Miller, S. R. *Tetrahedron Lett.* **1988**, *29*, 1631. Buchwald, S. L.; LaMaire, S. J. *Tetrahedron Lett.* **1987**, *28*, 295.

(24) Negishi, E.; Okukado, N.; King, A. O.; Van Horn, D. E.; Spiegel, B. I. *J. Am. Chem. Soc.* **1978**, *100*, 2254. Matsushita, H.; Negishi, E. *J. Am. Chem. Soc.* **1981**, *103*, 2882. Negishi, E.; Takahashi, T.; Baba, S.; Van Horn, D. E.; Okukado, N. *J. Am. Chem. Soc.* **1987**, *109*, 2393.

(25) We can find no previous reports on elimination of 1,4-dihalo-2-alkynes. For elimination/metalation of $R^1R^2CXC{\equiv}CCH_2X$ to afford $R^1R^2C{=}C{=}C{=}CMX$ (M = Li, Na; X = OR, SR) see: Montijn, P. P.; Van Boom, J. H.; Brandsma, L.; Arens, J. F. *Recl. Trav. Chim.* **1967**, *86*, 115. Mantione, R.; Alves, A.; Montijn, P. P.; Wildschut, G. A.; Bos, H. J. T.; Brandsma, L. *Recl. Trav. Chim.* **1970**, *89*, 97. Visser, R. G.; Bos. H. J. T.; Brandsma, L. *Recl. Trav. Chim.* **1981**, *100*, 34.

(26) Okamoto, S.; Sato, H.; Sato, F. *Tetrahedron Lett.* **1996**, *37*, 8865 and references therein.

Scheme 7

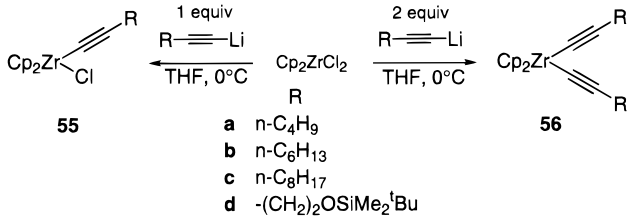
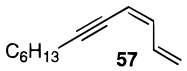
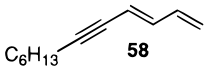
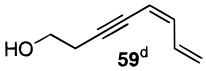
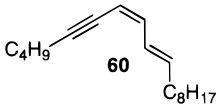
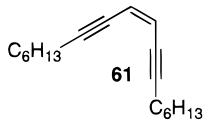
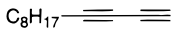


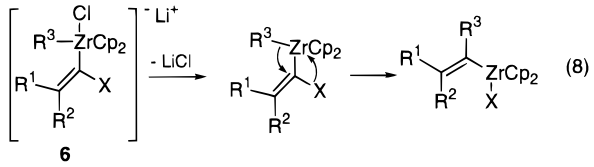
Table 3. Insertions into Alkynyl Zirconocenes (Scheme 1, R = C≡CR)

Entry	Zr cmp.	Carbenoid	Conditions[a]	Product[b]	GC Yield % (isolated)[c]
1	**56b**	**20**	B	 **57**	74 (72) *E* : *Z* = 7 : 93
2	**56b**	**20**	A	**57**	56 *E* : *Z* = 9 : 91
3	**55b**	**20**	B	**57**	55 *E* : *Z* = 13 : 87
4	**56b**	**19**	C	 **58**	(64) *E* : *Z* = 96 : 4
5	**56d**	**20**	C	 **59**[d]	(61) *E* : *Z* = 5 : 95
6	**55a**	**40d**	B	 **60**	(56)
7	**56b**	**40e**	C	 **61**	(42)
8	**56c**	**45**	D	 **62**	22 (19)

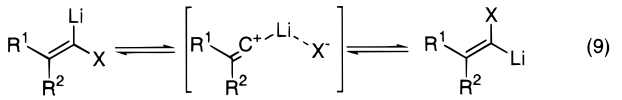
[a] A: 1.3 equiv of Li-carbenoid, THF, −90 to −80 °C, 15 min. B: as A, then 1 h at −30 °C. C: as A, then 1 h at −50 °C. D: as A, then 2 h at −15 to 20 °C. [b] After workup with 2 M HCl(aq). [c] Based on Cp_2ZrCl_2. [d] After desilylation with TBAF.

With the above methods we can synthesize most geometric isomers of terminal and nonterminal dienes and trienes. To complete the scope we needed access to systems which might be considered derived from a (*Z*)-alkenylzirconocene. Unfortunately these are only accessible in a few special cases (from zirconacycles),[27] so we examined insertions into alkynyl zirconocenes. Di(1-octynyl)zirconocene (**56b**) was readily prepared in situ from the lithiated alkyne and zirconocene dichloride (Scheme 7).[28] Treatment with 1.3 equiv of the lithium carbenoid **20** followed by aqueous workup gave (*Z*)-1,3-dodecadien-5-yne (**57**) in good yield (72%) based on Cp_2ZrCl_2 but only 36% yield based on the alkyne (Table 3, entry 1). To obtain the high yield it was found necessary to warm the reaction mixture to −20 °C before quenching (Table 3, entry 1, cf. 2). Use of 2 equiv of the carbenoid did not increase the yield of **57** implying that only one of the two alkyne moieties in **56b** reacts. Addition of 1 equiv of lithiated 1-octyne to zirconocene dichloride gave predominantly (1-octynyl)zirconocene chloride (**55b**, Scheme 7). The reaction of **55b** with the carbenoid **20** followed by protonolysis gave **57** in an improved yield of 55% based on the alkyne (Table 3, entry 3). In similar fashion reaction of **19** with **56b** gave (*E*)-1,3-dodecadien-5-yne (**58**) in reasonable yield, and good stereoselectivity. Use of 1-*tert*-butyldimethylsiloxy-3-butyne as the acetylenic component and **20** as the carbenoid gave (*Z*)-5,7-octadien-3-yn-1-ol (**59**) after deprotection. Reduction of 1,3-dien-5-ynes to (5*Z*)-1,3,5-trienes with activated zinc is well-known.[22] In the case of **58** this leads to a homologue (*n*-hexyl- rather that *n*-pentyl-saturated chain) of the major galbanolene used in the perfumery industry.[18] Coupling of 1-hexynylzirconocene chloride (**55a**) with the dienyl carbenoid **40d** gave a good yield of the internal (*E*,*Z*)-dienyne **60**, and provides potential access to (*E*,*Z*,*Z*) conjugated trienes. Coupling of the dialkynylzirconocene **56b** with the carbenoid **40e** gave the (*Z*)-3-en-1,5-diyne **61**, a motif characteristic of the enediyne antitumor compounds.[29] Finally, reaction of the dialkynylzirconocene **56c** with lithiated (*E*)-1,2-dichloroethene (**45**) gave rise to the terminal diyne **62**.

Mechanism of the Insertion Reaction and Reasons for Loss of Stereochemistry of β,β-Disubstituted Vinyl Carbenoids. For the insertion of β-monosubstituted 1-halo-1-lithioalkenes the clean inversion of configuration of the sp^2 center strongly supports a concerted 1,2-migration mechanism as shown in Scheme 1. The speed of the insertion and the fact that zirconacycles work wel,[7,30] suggest that rearrangement is of an "ate" complex as shown in eq 1 and Scheme 1; however, we cannot disprove initial loss of halide to afford a neutral zirconocene species which undergoes a diotropic rearrangement (eq 8).[31]



For the insertion of β,β-disubstituted vinyl carbenoids the results given in Table 1 indicate either that the insertion does not occur by the concerted stereospecific mechanism suggested in Scheme 1 or that isomerization is occurring before rearrangement. In the later case it may be the lithium carbenoid, or an organozirconium intermediate, that isomerizes. Kobrich observed rapid isomerization below −85 °C of (*Z*)- to (*E*)-1-chloro-1-lithio-2-phenylpropene.[32] Similar loss of stereochemical integrity of 2,2-disubstituted 1-lithio-1-haloalkenes generated by deprotonation has been described by Walborsky and attributed to "metal assisted ionization" (eq 9).[6a,33] Harada reported



the rapid isomerization of 1-lithio-1-bromoalkenes derived by Br/Li exchange, and proved the mechanism to be via rapid reversible halogen/lithium exchange with unreacted dibromide.[34]

(27) Aoyagi, K.; Kasai, K.; Kondakov, D. Y.; Hara, R.; Suzuki, N.; Takahashi, T. *Inorg. Chim. Acta* **1994**, *220*, 319. Suzuki, N.; Kondakov, D. Y.; Kageyama, M.; Kotora, M.; Hara, R.; Takahashi, T. *Tetrahedron* **1995**, *51*, 4519. Hara, R.; Liu, Y. H.; Sun, W. H.; Takahashi, T. *Tetrahedron Lett.* **1997**, *38*, 4103.

(28) Erker, G.; Froemberg, W.; Benn, R.; Mynott, R.; Angermund, K.; Krueger, C. *Organometallics* **1989**, *8*, 911.

(29) Nicolaou, K. C.; Smith, A. L. *Acc. Chem. Res.* **1992**, *25*, 497.

(30) Fillery, S. M.; Kasatkin, A.; Whitby, R. J. Unpublished results.

(31) Erker, G.; Petrenz, R.; Kruger, C.; Lutz, F.; Weiss, A.; Werner, S. *Organometallics* **1992**, *11*, 1646. Kasai, K.; Liu, Y. H.; Hara, R.; Takahashi, T. *Chem. Commun.* **1998**, 1989.

(32) Kobrich, G.; Ansari, F. *Chem. Ber.* **1967**, *100*, 2011.

(33) Nelson, D. J.; Matthews, M. K. G. *J. Organomet. Chem.* **1994**, *469*, 1.

(34) Harada, T.; Katsuhira, T.; Hattori, K.; Oku, A. *Tetrahedron* **1994**, *50*, 7987.

Scheme 8

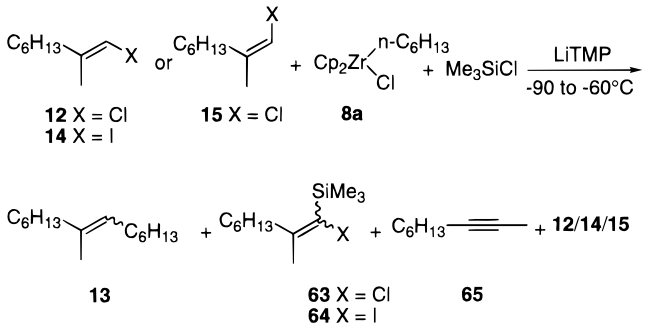
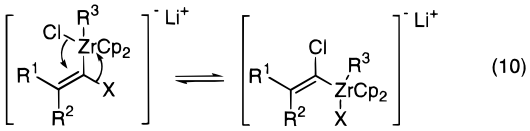


Table 4. Competition and Isomerization Results for β,β-Disubstituted Carbenoids (Scheme 8)[a]

entry	halide	**8a**, equiv	$ClSiMe_3$, equiv	% composition of products[b] **13** (*E*:*Z*)[c]	**63**/**64** (*E*:*Z*)[c]	**65**	halide
1	**12**		1.1		44 (75:25)	41	15
2	**15**		1.1		40 (25:75)	38	22
3	**12**	1.2	1.2	31 (47:53)	14 (92:8)	19	36
4	**15**	1.2	1.2	72 (96:4)	3 (−)	10	15
5	**14**		1.1		100 (>95:5)	0	0
6	**14**	1.2	1.2	10 (34:66)	90 (85:15)	0	0

[a] Conditions: 1 equiv of halide, 1.1 equiv of LiTMP, THF, −90 to −60 °C, 1 h. [b] Combined yield (GC) was >95% in all cases. [c] *E*:*Z* ratios by GC for **13** and **64**, by NMR of the crude product for **63**.

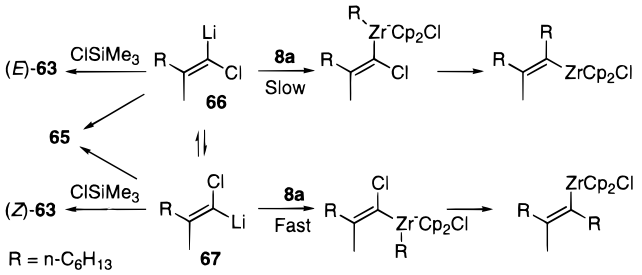
For isomerization on the zirconium, a diotropic rearrangement of an intermediate zirconate species is possible (eq 10).[31]



(10)

To probe the mechanisms of loss of stereochemical integrity we examined the formation/trapping of the carbenoids derived from (*E*)- and (*Z*)-1-chloro-2-methyloctenes **12** and **15** (Scheme 8). Lithiation of **12** and **15** with an in situ trap of chlorotrimethylsilane gave the vinyl silanes **63** in around 40% yield, and with around 50% loss of stereochemical integrity (Table 4, entries 1 and 2). In each case around 40% of 2-nonyne (**65**) derived by Fritsch−Buttenberg−Wiechell rearrangement[11] was also formed. The results show that the rate of isomerization of the lithiated vinyl chlorides in the absence of a zirconium species is around half both their rate of trapping by $ClSiMe_3$ and decomposition to **65**. For the two stereoisomers **12** and **15** the ratio of isomerization to rearrangement rates is similar. In further experiments LiTMP was added to a mixture of the vinyl chloride **12** or **15**, chlorotrimethylsilane, and *n*-hexylzirconocene chloride (**8a**) to give the products shown in Table 4 (entries 3 and 4) after protic workup. At first sight the much greater loss of stereochemical integrity of the zirconium trapped product **13** compared to the silylated product **63** obtained from lithiated **12** (Table 4, entry 3) indicates isomerization on the metal. However, the relative amounts of zirconium and trimethylsilyl trapped products in entries 3 and 4, and the reduced amount of rearrangement product **65** in the second case, are consistent with **8a** trapping lithiated **15** (**67**) around 10 times faster than lithiated **12** (**66**) (Scheme 9). The greater steric hindrance of the *n*-hexyl chain compared with a methyl group to approach of the very bulky zirconium electrophile provides a reasonable explanation. Given the much faster trapping of **67** compared with **66** by **8a** the experimental results are consistent with the loss of stereochemical integrity arising from rapid interconversion of **66** and **67** (Scheme 9). The slight increase in stereochemical purity of **13** formed from **15** in the presence (Table 4, entry 4) rather than absence (Table 1, entry 9) of chlorotrimethylsilane is consistent with the model. The chlorotrimethylsilane removes around a third of the **66** formed by isomerization of **67**, without competing significantly with **8a** for **67**. The increase in stereochemical purity of the silane product **63** derived from **12** in the presence rather than absence of **8a** (Table 4, entry 3, cf. 1) is also consistent with the model. The zirconium species **8a** traps most of the organolithium **67** formed by isomerization of **66** reducing the formation of (*Z*)-**63**.

Scheme 9



In preparative experiments the vinyl iodides **14** and **16** both gave around 50% loss of stereochemical integrity in the formation of **13** (Table 1, entries 8 and 11). Deprotonation/chlorotrimethylsilane trap of **14** gave (*E*)-**64** with no isomerization or rearrangement to **65** (Scheme 8, Table 4, entry 5). Competitive trapping of lithiated **14** with **8a** and chlorotrimethylsilane showed the later to be around 9 times faster than the former. The result is in marked contrast to the analogous vinyl chloride **12**, and consistent with the much larger size of the halogen and bulky zirconium electrophile. Under the conditions used in the preparative experiments we believe that isomerization of the lithiated vinyliodide via "metal assisted ionization" (eq 9) is the most likely explanation for the loss of stereochemical integrity. The recovery of partially isomerized iodide from reactions stopped early (Table 1, entries 7 and 10) provides evidence that the isomerization occurs prior to 1,2-metalate rearrangement on the zirconium. No vinyl chloride **12** or **15** was detected in the products providing strong evidence against a diotropic rearrangement (as eq 10) of a zirconate intermediate as the mechanism of isomerization. Our failure to observe either the 1,1-bis-iodide or 2-methyl-1-octene by GC in reactions of **14** or **16** argues against fast I/Li exchange. Addition of the vinyl halide **14** slowly to premixed **8a** and LiTMP gave the same results as the usual addition order, again suggesting that I/Li exchange is not the mechanism of isomerization.

The clean inversion of configuration of lithiated β-monosubstituted vinyl halides observed on reaction with organozirconocenes is best explained by much slower rates of isomerization of the carbenoid compared with β,β-disubstituted examples. In the "metal assisted ionization" mechanism for carbenoid isomerization (eq 9) it is reasonable that β-alkyl substituents will stabilize the cationic component of the dipolar intermediate more than β-hydrogens. Furthermore, there should be greater relief of steric strain accompanying the ionization of the β,β-disubstituted lithiated vinyl halides compared with the monosubstituted analogues.

Conclusion

2-Alkenyl- or 2-alkynyl-1-lithio-1-haloalkenes insert stereospecifically into alkyl-, terminal alkenyl-, and alkynylzirconocene chlorides to give new organozirconium species which

may be further elaborated. 2,2-Dialkylsubstituted 1-lithio-1-haloalkenes also insert, but stereochemistry of the vinyl halide precursor is partially lost, probably via "metal assisted ionization". 1-Lithio-1-chloroethene inserts, but in moderate yield. The insertion of (*E*)-1,2-dichloro-1-lithioethylene is followed by 1,2-elimination of zirconocene chloride to give a terminal alkyne.

Experimental Section

Materials. $Cp_2Zr(H)Cl$ (Schwartz reagent) was purchased from Aldrich. 1-Chloro-2-methyl-1-propene (**10**), (*E*)- and (*Z*)-1,4-dichloro-2-butene, β-bromostyrene (*E*:*Z* = 91:9), (*E*)-1,2-dichloroethylene, 1,2-dichloroethane, and 1,4-dichloro-2-butyne purchased from a commercial source were distilled and stored under argon. (*E*)-1-Iodo-2-methyl-1-octene (**14**),[35] (*E*,*E*)-1-chloro-1,3-nonadiene (**39c**),[19b] (*E*)-1-chloro-1-decene-3-yne (**39e**),[36] 1,4-dichloro-2-pentyne,[37] and (*E*)-1-iodo-1-decene[38] were prepared according to procedures described in the literature.

(*E*)-1-Chloro-2-methyl-1-octene (**12**) was prepared by the reaction of 1-octyne with Me_3Al[35] followed by the treatment of the crude reaction mixture with *N*-chlorosuccinimide (0 to 20 °C, 3 h). ^{1}H NMR δ 0.89 (t, J = 7.2 Hz, 3H), 1.20−1.45 (m, 8H), 1.77 (s, 3H), 2.08 (t, J = 7.3 Hz, 2H), 5.80 (s, 1H). ^{13}C NMR δ 14.07, 16.34, 22.58, 27.46, 28.76, 31.63, 37.09, 111.60, 138.97. IR 3071, 2928, 2857, 1639, 1466, 1378, 1309, 1180, 1111, 856, 788, 771, 724 cm^{-1}. Anal. Calcd for $C_9H_{17}Cl$: C, 67.28; H, 10.66; Cl, 22.06. Found: C, 67.33; H, 10.70; Cl, 22.46.

(*Z*)-1-Iodo-2-methyl-1-octene (**16**) was prepared by the reaction of propyne with $C_6H_{13}MgBr\cdot CuBr$ followed by iodinolysis.[39] ^{1}H NMR δ 0.85 (m, 3H), 1.20−1.45 (m, 8H), 1.82 (s, 3H), 2.15 (m, 2H), 5.75 (s, 1H). ^{13}C NMR δ 14.26, 22.77, 23.44, 27.09, 29.14, 31.87, 38.83, 73.94, 148.01. IR 3052, 2923, 2855, 1616, 1464, 1377, 1270, 1146, 762, 723, 676 cm^{-1}. HRMS calcd for $C_9H_{17}I$ 252.0375, found 252.0371.

(*Z*)-1-Chloro-2-methyl-1-octene (**15**) was prepared by treatment of the iodide **16** with CuCl in *N*-methylpyrrolidinone (130 °C, 2 h).[40] ^{1}H NMR δ 0.85 (m, 3H), 1.20−1.45 (m, 8H), 1.65 (s, 3H), 2.12 (t, J = 7.3 Hz, 2H), 5.68 (s, 1H). ^{13}C NMR δ 14.24, 20.95, 22.76, 26.89, 29.16, 31.86, 31.96, 111.39, 139.10. Anal. Calcd for $C_9H_{17}Cl$: C, 67.28; H, 10.66; Cl, 22.06. Found: C, 67.41; H, 10.72; Cl, 22.24.

(*E*,*E*)-1-Chloro-1,3-dodecadiene (**39d**) was prepared by $Ni(PPh_3)_4$ catalyzed cross-coupling reaction of (*E*)-$C_8H_{17}CH{=}CHAl(i\text{-}Bu)_2$.[19b] ^{1}H NMR δ 0.85 (t, J = 7.2 Hz, 3H), 1.15−1.40 (m, 12H), 2.00 (m, 2H), 5.63 (dt, J = 15.8, 7.3 Hz, 1H), 5.89 (dd, J = 15.8, 10.3 Hz, 1H), 6.00 (d, J = 14.2 Hz, 1H), 6.33 (dd, J = 14.2, 10.3 Hz, 1H). ^{13}C NMR δ 14.09, 22.67, 29.05, 29.19, 29.28, 29.44, 31.88, 32.65, 118.18, 126.01, 133.86, 136.30. IR 3063, 3014, 2923, 2853, 1643, 1583, 1466, 975, 822, 722 cm^{-1}. Anal. Calcd for $C_{12}H_{21}Cl$: C, 71.80; H, 10.54; Cl, 17.66. Found: C, 72.43; H, 10.73; Cl, 17.83. (*E*,*E*)-1-Chloro-1,3-heptadiene (**39a**)[41] and (*E*,*E*)-1-chloro-1,3-octadiene (**39b**)[42] were prepared similarly.

(*Z*)-1-Chloro-1-decen-3-yne was prepared by the treatment of (*Z*)-1,2-dichloroethylene with 1-octyne in the presence of $BuNH_2$ and Pd−Cu catalyst.[19b] ^{1}H NMR δ 0.92 (t, J = 7.3 Hz, 3H), 1.25−1.60 (m, 8H), 2.41 (m, 2H), 5.85 (d, J = 7.4 Hz, 1H), 6.30 (d, J = 7.4 Hz, 1H). ^{13}C NMR δ 14.03, 19.65, 22.54, 28.47, 28.48, 31.31, 74.61, 99.43, 112.51, 126.68. IR 3085, 2931, 2858, 2215, 1624, 1591, 1466, 1429, 1334, 1133, 850, 818, 721 cm^{-1}. Anal. Calcd for $C_{10}H_{15}Cl$: C, 70.37; H, 8.86; Cl, 20.77. Found: C, 70.51; H, 8.75; Cl, 21.03.

1,4-Dichloro-2-nonyne was prepared from 2-nonyn-1,4-diol by treatment with $SOCl_2$ in the presence of 2,4,6-collidine.[37] ^{1}H NMR δ 0.80 (m, 3H), 1.15−1.45 (m, 6H), 1.78 (m, 2H), 4.02 (d, J = 1.7 Hz, 2H), 4.41 (m, 1H). IR 2956, 2860, 2220, 1466, 1430, 1263, 1164, 704, 649 cm^{-1}. Anal. Calcd for $C_9H_{14}Cl_2$: C, 55.97; H, 7.31; Cl, 36.72. Found: C, 55.94; H, 7.16; Cl, 36.69.

General Procedure for the Reaction of Lithium Carbenoids with Organozirconium Compounds. (A) Preparation of Alkenylzirconium Reagents. To a stirred suspension of $Cp_2Zr(H)Cl$ (0.402 g, 1.56 mmol) in THF (12.0 mL) was added 1-alkene or 1-alkyne (1.30 mmol). The mixture was stirred at 20 °C for 1 h to give a clear yellow solution of **8** or **9**, respectively. After the mixture was cooled to −90 °C 1-chloro- or 1-iodo-1-alkene (1.69 mmol), 1-chloro-1,3-diene (1.08 mmol), or 1-chloro-1-en-3-yne (1.08 mmol) was added followed by a solution of LiTMP (1.69 or 1.08 mmol, 0.7 M in THF, freshly formed from TMP and 1 equiv of BuLi at 0 °C). The reaction mixture was stirred at −90 to −80 °C for 15 min (for other conditions see Tables 1−3) to give a solution of the alkenylzirconium reagent ready for the next reaction.

The lithium carbenoids **19**, **20**, **44**, and **51** were generated from (*E*)- and (*Z*)-1,4-dichloro-2-butene (0.211 g, 1.69 mmol), 1,2-dichloroethane (0.167 g, 1.69 mmol), and substituted 1,4-dichloro-2-butynes (1.69 mmol), respectively, by using 2.0 equiv of LiTMP (4.83 mL, 0.7 M in THF, 3.38 mmol). The alkynylzirconium compounds **55** and **56** were prepared in solution by treatment of 1-alkyne (1.3 mmol) with BuLi (0.52 mL, 2.5 M in hexane, 1.30 mmol) in THF (12.0 mL) at −20 °C followed by addition of Cp_2ZrCl_2 (0.380 g, 1.30 mmol or 0.190 g, 0.65 mmol) and stirring at 0 °C for 2 h.

(B) Hydrolysis. To the solution of the alkenylzirconium reagent prepared above was added 2 M HCl (aq) (8.0 mL) at −80 °C. The mixture was warmed to room temperature and stirred for 30 min. After extraction with ether (12 mL) the organic layer was washed with 2 M HCl (aq) (10 mL), saturated $NaHCO_3$(aq) (10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (40−60 petroleum ether).

(*E*)-2-Methyl-2,4-undecadiene (entries 2 and 3 in Table 1). ^{1}H NMR δ 0.90 (t, J = 6.9 Hz, 3H), 1.25−1.45 (m, 8H), 1.76 (s, 3H), 1.79 (s, 3H), 2.09 (m, 2H), 5.58 (dt, J = 15.4, 7.7 Hz, 1H), 5.82 (d, J = 9.9 Hz, 1H), 6.26 (dd, J = 15.4, 9.9 Hz, 1H). IR 3020, 2950, 2825, 2650, 1615, 1464, 1375, 960, 878 cm^{-1}. HRMS calcd for $C_{22}H_{22}$ 166.1722, found 166.1721.

7-Methyl-7-tetradecene (**13**, entries 8 and 9 in Table 1). ^{13}C NMR δ 14.27, 22.84, 23.44, 27.81, 28.05, 28.96, 29.31, 30.12, 31.75, 31.86, 125.43, 135.55 (*Z*-isomer); 14.27, 16.00, 22.84, 27.91, 27.96, 28.96, 29.02, 29.89, 31.81, 31.84, 39.74, 124.71, 135.27 (*E*-isomer). ^{1}H NMR and IR spectral data were in good agreement with those described in the literature for both (*Z*)-**13** and (*E*)-**13**.[43] An authentic sample of (*E*)-**13** was prepared by the reaction of (*E*)-$C_6H_{13}C(Me){=}CHI$ (**14**) with $C_6H_{13}ZnCl$ (THF, 20 °C, 5 mol % $Pd(PPh_3)_4$).[44]

8-Methyl-5,7-tetradecadiene (**17**, entry 13 in Table 1). ^{1}H NMR δ 0.82 (m, 6H), 1.15−1.40 (m, 12H), 1.67 (s, 3H), 1.90−2.10 (m, 4H), 5.56 (dt, J = 14.7, 7.0 Hz, 1H), 5.80 (d, J = 11.0 Hz, 1H), 6.24 (dd, J = 14.7, 11.0 Hz, 1H) (5*E*,7*Z*-isomer); 1.65 (s, 3H), 5.58 (dt, J = 14.7, 7.0 Hz, 1H), 6.26 (dd, J = 14.7, 11.0 Hz, 1H) (5*E*,7*E*-isomer). ^{13}C NMR δ 14.12, 14.27, 22.41, 23.82, 28.31, 29.40, 31.95, 32.38, 32.73, 125.43, 126.56, 132.30, 137.23 (5*E*,7*Z*-isomer); 14.12, 14.27, 16.62, 22.45, 22.80, 28.03, 29.22, 31.95, 32.78, 40.02, 124.62, 126.79, 132.45, 136.93 (5*E*,7*E*-isomer). IR 3016, 2955, 2821, 2653, 1619, 1464, 1376, 960, 874 cm^{-1}. HRMS calcd for $C_{15}H_{28}$ 208.2191, found 208.2195. An authentic sample of the (5*E*,7*E*)-**17** was prepared by the reaction of (*E*)-$C_6H_{13}C(Me){=}CHI$ (**14**) with (*E*)-$BuCH{=}CHZr(Cl)Cp_2$ (THF, 20 °C, 5 mol % $Pd(PPh_3)_4$).[24]

(*Z*)-1-Phenyl-1-decene (entry 1 in Table 2). An authentic sample of the title compound was prepared by reduction of 1-phenyl-1-decyne.[45] Its NMR spectral data were in good agreement with those described in the literature.[46]

(35) Negishi, E.; Van Horn, D. E.; Yoshida, T. *J. Am. Chem. Soc.* **1985**, *107*, 6639.
(36) Negishi, E.; Okukado, N.; Lovich, S. F.; Luo, F.-T. *J. Org. Chem.* **1984**, *49*, 2629.
(37) Montijn, P. P.; Brandsma, L.; Arens, J. F. *Recl Trav. Chim.* **1967**, *86*, 129.
(38) Suseela, Y.; Periasamy, M. *J. Organomet. Chem.* **1993**, *450*, 47.
(39) Hoffmann, R. W.; Schlapbach, A. *Lieb. Ann. Chem.* **1990**, 1243.
(40) Commercon, A.; Normant, J.; Villieras, J. *J. Organomet. Chem.* **1975**, *93*, 415.
(41) Zhang, X.; Schlosser, M. *Tetrahedron Lett.* **1993**, *34*, 1925.
(42) Ratovelomanana, V.; Linstrumelle, G. *Tetrahedron Lett.* **1984**, *25*, 6001.
(43) Obayashi, M.; Utimoto, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1760.
(44) Negishi, E.; Valente, L. F.; Kobayashi, M. *J. Am. Chem. Soc.* **1980**, *102*, 3298.
(45) Kauffmann, T.; Rauch, E.; Schulz, J. *Chem. Ber.* **1973**, *106*, 1612.

(3*Z*,5*E*)-1,3,5-Dodecatriene (**25**, entry 5 in Table 2). ^{1}H NMR δ 0.88 (t, J = 6.8 Hz, 3H), 1.25−1.45 (m, 8H), 2.17 (m, 2H), 5.12 (d, J = 10.3 Hz, 1H), 5.21 (d, J = 16.9 Hz, 1H), 5.77 (dt, J = 15.1, 7.0 Hz, 1H), 5.90 (dd, J = 10.7, 10.3 Hz, 1H), 5.99 (dd, J = 10.7, 10.3 Hz, 1H), 6.52 (dd, J = 15.1, 10.3 Hz, 1H), 6.82 (ddd, J^1 = 16.9, J^2, J^3 = 10.3 Hz, 1H). ^{13}C NMR δ 14.26, 22.78, 29.09, 29.40, 31.90, 33.14, 117.27, 125.66, 127.89, 130.45, 132.43, 137.04. IR 3027, 2956, 2855, 1688, 1640, 1618, 1466, 1439, 1378, 973, 941, 900, 724, 645 cm^{-1}. HRMS calcd for $C_{12}H_{20}$ 164.1565, found 164.1567.

(3*E*,5*Z*)-3,5,7-Octatrien-1-ol (**26**, entries 6 and 7 in Table 2). The crude *tert*-butyldimethylsilyl-protected alcohol prepared by the reaction of **9f** with **20** followed by hydrolysis with saturated aqueous NH_4Cl was dissolved in THF (5.0 mL). To the solution was added Bu_4NF (1.30 mL, 1.0 M in THF, 1.30 mmol) and the reaction mixture was stirred for 2 h at room temperature. After concentration under reduced pressure the residue was dissolved in ether (10.0 mL), the solution was washed with 2 M HCl (aq) (2.0 mL), dried over $MgSO_4$, and concentrated again. Purification of the residue by column chromatography (silica gel, 40−60 petroleum ether−EtOAc, 2:1) gave the title alcohol (0.100 g, 62% yield). ^{1}H NMR δ 1.61 (br s, 1H), 2.35 (dt, J^1, J^2 = 6.3 Hz, 2H), 3.62 (m, 2H), 5.15 (d, J = 10.3 Hz, 1H), 5.23 (d, J = 16.9 Hz, 1H), 5.73 (dt, J = 15.1, 7.3 Hz, 1H), 5.93 (dd, J = 10.7, 10.3 Hz, 1H), 6.00 (dd, J = 10.7, 10.3 Hz, 1H), 6.62 (dd, J = 15.1, 10.3 Hz, 1H), 6.81 (ddd, J^1 = 16.9 Hz, J^2, J^3 = 10.3 Hz, 1H). ^{13}C NMR δ 36.44, 62.05, 117.94, 128.36, 128.88, 129.60, 131.72, 132.02. IR 3416, 2930, 1640, 1440, 1109, 1046, 976 cm^{-1}. HRMS calcd for $C_8H_{12}O$ 124.0888, found 124.0887.

(3*E*,5*E*)-1,3,5-Dodecatriene[47] (**28**, entry 9 in Table 2). ^{1}H NMR δ 0.82 (t, J = 6.8 Hz, 3H), 1.15−1.40 (m, 8H), 2.02 (m, 2H), 5.05 (d, J = 9.9 Hz, 1H), 5.19 (d, J = 16.9 Hz, 1H), 5.75 (dt, J = 15.1, 7.0 Hz, 1H), 6.08 (dd, J = 15.1, 10.3 Hz, 1H), 6.14 (dd, J = 14.7, 10.3 Hz, 1H), 6.23 (dd, J = 14.7, 9.6 Hz, 1H), 6.38 (ddd, J = 16.9, 9.9, 9.6 Hz, 1H). ^{13}C NMR δ 14.26, 22.79, 29.05, 29.40, 31.90, 33.01, 116.32, 130.24, 131.11, 133.80, 136.35, 137.35.

(7*Z*,9*E*)-7,9-Octadecadiene[48] (**29a**, entry 10 in Table 2). ^{1}H NMR δ 0.88 (t, J = 6.8 Hz, 6H), 1.30 (m, 20H), 2.15 (m, 4H), 5.32 (dt, J = 10.7, 7.7 Hz, 1H), 5.67 (dt, J = 15.1, 7.0 Hz, 1H), 5.96 (dd, J = 11.0, 10.7 Hz, 1H), 6.32 (dd, J = 15.1, 11.0 Hz, 1H). ^{13}C NMR δ 14.25, 22.81, 22.84, 27.86, 29.12, 29.42, 29.45, 29.58, 29.65, 29.88, 31.92, 32.06, 33.05, 125.76, 128.75, 130.23, 134.82.

(4*E*,6*Z*,8*E*)-4,6,8-Dodecatrien-1-ol[21] (**31**, entry 15 in Table 1). For deprotection the reaction mixture after addition of 2 M HCl (aq) was stirred overnight at room temperature and then treated as described above. ^{1}H NMR δ 0.80 (t, J = 7.7 Hz, 3H), 1.32 (m, 2H), 1.50 (br s, 1H), 1.62 (m, 2H), 2.00 (m, 2H), 2.13 (m, 2H), 3.56 (t, J = 6.8 Hz, 2H), 5.70 (dt, J = 14.7, 7.4 Hz, 1H), 5.72 (dt, J = 15.1, 7.0 Hz, 1H), 5.87 (m, 2H), 6.52 (m, 2H). ^{13}C NMR δ 13.89, 22.65, 29.37, 32.38, 35.18, 62.58, 125.96, 126.56, 127.40, 128.26, 134.30, 135.79.

(6*E*,8*Z*,10*E*)-6,8,10-Hexadecatriene[49] (**32**, entry 16 in Table 2). ^{1}H NMR δ 0.89 (t, J = 7.3 Hz, 3H), 1.25−1.45 (m, 12H), 2.13 (m, 4H), 5.72 (dt, J = 15.1, 7.7 Hz, 2H), 5.86 (m, 2H), 6.47 (dd, J = 15.1, 8.6 Hz, 2H). ^{13}C NMR δ 14.20, 22.70, 29.22, 31.61, 33.10, 125.90, 127.77, 135.69.

(*Z*)-7-Hexadecen-9-yne (**33a**, entry 17 in Table 2). ^{13}C NMR δ 14.21, 14.25, 19.68, 22.74, 28.71, 29.02, 30.18, 31.53, 31.84, 94.59, 109.42, 142.82. ^{1}H NMR and IR spectral data were in good agreement with those described in the literature.[50]

(5*E*,7*Z*)-5,7-Hexadecadien-9-yne (**34a**, entry 19 in Table 2). ^{1}H NMR δ 0.90 (t, J = 6.8 Hz, 6H), 1.30−1.60 (m, 12H), 2.16 (m, 2H), 2.40 (td, J = 7.5, 1.7 Hz, 2H), 5.32 (d, J = 10.3 Hz, 1H), 5.86 (dt, J = 15.4, 7.0 Hz, 1H), 6.28 (dd, J = 11.0, 10.3 Hz, 1H), 6.57 (dd, J = 15.4, 11.0 Hz, 1H). ^{13}C NMR δ 14.07, 14.21, 19.86, 22.45, 22.75, 28.76, 28.97, 31.44, 31.53, 32.74, 77.97, 96.37, 107.55, 127.89, 138.17, 139.30. IR 3022, 2928, 2856, 2212, 1686, 1638, 1465, 1377, 1327, 1119, 980, 956 cm^{-1}. HRMS calcd for $C_{16}H_{26}$ 218.2035, found 218.2036.

(*E*)-7-Hexadecen-9-yne (**35**, entry 21 in Table 2). An authentic sample of the title compound was prepared by the reaction of (*E*)-1-iodo-1-octene with 1-octyne in the presence of CuI.[51] Its NMR spectral data were in good agreement with those described in the literature.[51]

(*E*)-3-Dodecen-1-yne (**38**, entry 25 in Table 2). ^{1}H NMR δ 0.89 (t, J = 6.8 Hz, 3H), 1.25−1.45 (m, 12H), 2.13 (m, 2H), 2.78 (d, J = 1.7 Hz, 1H), 5.47 (d, J = 15.8 Hz, 1H), 6.25 (dt, J = 15.8, 6.9 Hz, 1H). IR spectral data were in good agreement with those described in the literature.[52]

1-Dodecen-3-yne (**53a**, Scheme 6). ^{1}H NMR δ 0.90 (t, J = 6.8 Hz, 3H), 1.25−1.60 (m, 12H), 2.30 (td, J = 7.5, 1.7 Hz, 2H), 5.38 (d, J = 10.2 Hz, 1H), 5.57 (d, J = 17.1 Hz, 1H), 5.80 (dd, J = 17.1, 10.2 Hz, 1H). IR spectral data were in good agreement with those described in the literature.[53]

2-Tridecen-4-yne[54] (**53b**, Scheme 6). ^{1}H NMR δ 0.89 (t, J = 6.9 Hz, 3H), 1.25−1.60 (m, 12H), 1.76 (d, J = 7.0 Hz, 3H), 2.28 (td, J = 7.3, 1.7 Hz, 2H), 5.47 (d, J = 15.8 Hz, 1H), 6.06 (dq, J = 15.8, 7.0 Hz, 1H) (*E*-isomer); 1.86 (d, J = 6.6 Hz, 3H), 2.36 (td, J = 7.3, 1.7 Hz, 2H), 5.89 (dq, J = 10.7, 6.6 Hz, 1H) (*Z*-isomer). ^{13}C NMR δ 14.26, 18.59, 19.47, 22.82, 29.01, 29.07, 29.28, 29.36, 32.00, 79.23, 88.71, 111.23, 138.06 (*E*-isomer); 15.84, 19.68, 110.54, 136.98 (*Z*-isomer).

6-Heptadecen-8-yne (**53c**, Scheme 6). ^{1}H NMR δ 0.92 (m, 6H), 1.25−1.60 (m, 18H), 2.08 (m, 2H), 2.36 (td, J = 7.3, 1.7 Hz, 2H), 5.45 (d, J = 15.8 Hz, 1H), 6.08 (dt, J = 15.8, 6.9 Hz, 1H) (*E*-isomer); 2.32 (m, 4H), 5.55 (d, J = 10.7 Hz, 1H), 5.80 (dt, J = 10.7, 6.9 Hz, 1H) (*Z*-isomer). ^{13}C NMR δ 14.04, 14.10, 14.13, 19.36, 19.53, 22.51, 22.67, 22.70, 28.52, 28.59, 28.86, 28.89, 28.94, 29.13, 29.15, 29.20, 29.25, 30.00, 31.29, 31.43, 31.85, 32.93, 79.16, 88.71, 94.45, 109.28, 109.76, 142.65, 143.38 (*E*- and *Z*-isomers). IR 2950, 2200, 1450, 1000 cm^{-1}. HRMS calcd for $C_{17}H_{30}$ 234.2348, found 234.2345.

(*Z*)-1,3-Dodecadien-5-yne (**57**, entry 1 in Table 3). ^{1}H NMR δ 0.88 (t, J = 6.8 Hz, 3H), 1.25−1.60 (m, 8H), 2.38 (m, 2H), 5.24 (d, J = 9.6 Hz, 1H), 5.35 (d, J = 16.9 Hz, 1H), 5.47 (d, J = 10.8 Hz, 1H), 6.33 (dd, J^1, J^2 = 10.8 Hz, 1H), 6.88 (ddd, J = 16.9, 10.8, 9.6 Hz, 1H). ^{13}C NMR δ 14.20, 19.82, 22.71, 28.75, 28.91, 31.50, 77.59, 97.32, 110.77, 119.48, 134.28, 139.26. HRMS calcd for $C_{12}H_{18}$ 162.1409, found 162.1407.

(*Z*)-5,7-Octadien-3-yn-1-ol (**59**, entry 5 in Table 3). The crude *tert*-butyldimethylsilyl-protected alcohol from the reaction of **56d** with **20** followed by hydrolysis with saturated aqueous NH_4Cl was treated with Bu_4NF as described above for **26** to afford the title compound. ^{1}H NMR δ 1.96 (br s, 1H), 2.60 (m, 2H), 3.69 (t, J = 6.4 Hz, 2H), 5.27 (d, J = 10.3 Hz, 1H), 5.37 (d, J = 17.3 Hz, 1H), 5.47 (d, J = 10.7 Hz, 1H), 6.36 (dd, J^1, J^2 = 10.7 Hz, 1H), 6.85 (ddd, J = 17.3, 10.7, 10.3 Hz, 1H). ^{13}C NMR δ 24.19, 61.30, 79.38, 93.07, 110.05, 120.26, 134.05, 140.17. IR 3420, 2930, 2215, 1640, 1440, 1109, 1046, 990, 910 cm^{-1}. HRMS calcd for $C_8H_{10}O$ 122.0732, found 122.0723.

(7*Z*,9*E*)-7,9-Octadecadien-5-yne (**60**, entry 6 in Table 3). ^{1}H NMR δ 0.90 (m, 6H), 1.25−1.60 (m, 16H), 2.15 (m, 2H), 2.41 (m, 2H), 5.32 (d, J = 10.3 Hz, 1H), 5.83 (dt, J = 15.4, 7.7 Hz, 1H), 6.30 (dd, J^1, J^2 = 10.3 Hz, 1H), 6.58 (dd, J = 15.4, 10.3 Hz, 1H). ^{13}C NMR 13.78, 14.26, 19.55, 22.15, 22.83, 29.28, 29.42, 29.63, 31.09, 32.04, 33.07, 77.95, 96.30, 107.53, 127.84, 138.24, 139.32. IR 3021, 2925, 2852, 2211, 1686, 1638, 1464, 1430, 1377, 1326, 980, 957, 743 cm^{-1}. HRMS calcd for $C_{18}H_{30}$ 246.2348, found 246.2350.

(*Z*)-9-Octadecen-7,11-diyne (**61**, entry 7 in Table 3). ^{1}H NMR δ 0.80 (t, J = 6.8 Hz, 6H), 1.20−1.55 (m, 16H), 2.32 (t, J = 7.5 Hz, 4H), 5.66 (s, 2H). ^{13}C NMR δ 14.23, 19.95, 22.72, 28.71, 28.83, 31.56, 78.40, 98.11, 119.07. IR 3027, 3043, 2956, 2917, 2851, 2216, 1685, 1581, 1438, 1400, 1376, 749 cm^{-1}. HRMS calcd for $C_{18}H_{28}$ 244.2191, found 244.2195.

Spectral data for 2-methyl-2-undecene[55] (entry 1 in Table 1), (*Z*)-

(46) Periasamy, M.; Prasad, A. S. B.; Suseela, Y. *Tetrahedron* **1995**, *51*, 2743.
(47) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918.
(48) Bestmann, H. J.; Vostrowsky, O.; Paulus, H.; Billmann, W.; Stransky, W. *Tetrahedron Lett.* **1977**, 121.
(49) Stewart, S. K.; Whiting, A. *Tetrahedron Lett.* **1995**, *36*, 3925.
(50) Carlton, L.; Read, G. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1631.
(51) Ogawa, T.; Kusume, K.; Tanaka, M.; Hayami, K.; Suzuki, H. *Synth. Commun.* **1989**, *19*, 2199.
(52) Rodin, J. O.; Leaffer, M. A.; Silverstein, R. M. *J. Org. Chem.* **1970**, *35*, 3152.
(53) Petrov, A. A.; Kupin, B. S.; Yakovleva, T. V.; Mingaleva, K. S. *Zh. Obshch. Khim.* **1959**, *29*, 3732.
(54) Hamada, T.; Daikai, K.; Irie, R.; Katsuki, T. *Tetrahedron: Asymmetry* **1995**, *6*, 2441.
(55) Hernandez, D.; Larson, G. L. *J. Org. Chem.* **1984**, *49*, 4285.

and (*E*)-1,3-dodecadiene[56] (**23** and **27**, entries 2 and 8 in Table 2), (5*Z*,7*E*)-5,7-dodecadien-1-ol[20] (**30**, entry 14 in Table 2), (*E*)-1,3-dodecadien-5-yne[57] (**58**, entry 4 in Table 3), and 1,3-dodecadiyne[58] (**62**, entry 8 in Table 3) were in good agreement with those described in the literature.

(C) Iodinolysis. To the solution of the alkenylzirconium reagent prepared above (see A) was added a solution of iodine (1.5 or 3.0 equiv) in THF (2.5 mL) at −80 °C. The mixture was stirred at −60 to −40 °C over 1.5 h or stirred at 0 °C for 30 min and quenched by addition of saturated aqueous $Na_2S_2O_3$ (8.0 mL). After being stirred at room temperature for 30 min and extracted with ether (12 mL) the organic layer was washed with brine (10 mL), 2 M HCl (aq) (10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (40−60 petroleum ether) to afford an alkenyl iodide.

(*E*)-2-Methyl-3-iodo-2,4-undecadiene (**11**, entry 4 in Table 1). ^{1}H NMR δ 0.89 (m, 3H), 1.25−1.50 (m, 8H), 2.02 (s, 3H), 2.10 (s, 3H), 2.21 (m, 2H), 5.93 (m, 2H). ^{13}C NMR δ 14.26, 21.15, 22.76, 29.07, 29.61, 31.86, 32.45, 32.67, 100.51, 128.39, 138.65, 139.36. HRMS calcd for $C_{12}H_{21}I$ 292.0688, found 292.0710.

7-Iodo-7,9-octadecadiene (**29b**, entry 11 in Table 2). ^{1}H NMR δ 0.90 (m, 6H), 1.20−1.55 (m, 20H), 2.08 (m, 2H), 2.50 (t, J = 7.7 Hz, 2H), 5.67 (dt, J = 15.1, 7.0 Hz, 1H), 6.15 (dd, J = 15.1, 11.0 Hz, 1H), 6.74 (d, J = 11.0 Hz, 1H) (7*E*,9*E*-isomer); 5.41 (dt, J = 10.6, 7.0 Hz, 1H), 6.10 (m, 1H), 7.03 (d, J = 11.0 Hz, 1H) (7*E*,9*Z*-isomer). ^{13}C NMR δ 14.25, 22.75, 22.83, 28.13, 29.25, 29.33, 29.43, 29.59, 31.79, 32.03, 32.84, 39.16, 104.74, 125.71, 136.57, 140.83 (7*E*,9*E*-isomer); 27.83, 29.82, 107.50, 123.63, 133.50, 136.28 (7*E*,9*Z*-isomer). HRMS calcd for $C_{18}H_{33}I$ 376.1627, found 376.1618.

(D) Brominolysis. To the solution of the alkenylzirconium reagent prepared above (see A) was added *N*-bromosuccinimide (1.5 equiv) at −80 °C. The mixture was stirred at −60 to −40 °C over 1 h or stirred at 20 °C for 30 min and hydrolyzed by addition of 2 M HCl (aq) (8.0 mL). After being stirred at room temperature for 30 min and extractive workup as described above the crude product was purified by column chromatography on silica gel (40−60 petroleum ether) to afford an alkenyl bromide.

(*E*)-4-Bromo-1,3-decadiene (**24a**, entry 3 in Table 2). ^{1}H NMR δ 0.88 (m, 3H), 1.30 (m, 6H), 1.59 (m, 2H), 2.58 (t, J = 7.7 Hz, 2H), 5.11 (d, J = 8.8 Hz, 1H), 5.23 (d, J = 16.2 Hz, 1H), 6.42 (ddd, J = 16.2, 11.0, 8.8 Hz, 1H), 6.52 (d, J = 11.0 Hz, 1H). ^{13}C NMR δ 14.20, 22.70, 28.32, 31.72, 36.24, 118.06, 130.66, 131.52, 132.91. IR 2926, 2836, 1719, 1631, 1466, 1377, 1174, 1127, 1068, 982, 908, 725 cm^{-1}. HRMS calcd for $C_{10}H_{17}Br$ 216.0514, found 216.0519.

(7*E*,9*E*)-7-Bromo-7,9-octadecadiene (**29c**, entry 12 in Table 2). ^{1}H NMR δ 0.82 (m, 6H), 1.22 (m, 18H), 1.50 (m, 2H), 1.98 (m, 2H), 2.45 (t, J = 7.7 Hz, 2H), 5.68 (dt, J = 15.1, 7.0 Hz, 1H), 6.08 (dd, J = 15.1, 11.0 Hz, 1H), 6.44 (d, J = 11.0 Hz, 1H). ^{13}C NMR δ 14.24, 22.73, 22.82, 28.29, 28.33, 29.28, 29.31, 29.42, 29.59, 31.76, 32.02, 32.99, 36.09, 124.95, 127.27, 132.46, 136.29. IR 2930, 2860, 1680, 1633, 1459, 1377, 1075, 970, 888, 725 cm^{-1}. HRMS calcd for $C_{18}H_{33}Br$ 328.1766, found 328.1764.

(*E*)-7-Bromo-7-hexadecen-9-yne (**33b**, entry 18 in Table 2). ^{1}H NMR δ 0.83 (t, J = 6.9 Hz, 6H), 1.15−1.50 (m, 16H), 2.21 (td, J = 7.5, 1.7 Hz, 2H), 2.60 (t, J = 7.9 Hz, 2H), 5.80 (t, J = 1.7 Hz, 1H). ^{13}C NMR δ 14.23, 19.70, 22.72, 27.91, 28.20, 28.70, 31.48, 31.69, 37.74, 76.94, 95.51, 113.10, 139.95. IR 2930, 2860, 2220, 1680, 1633, 1459, 1375, 1070, 870, 725 cm^{-1}. HRMS calcd for $C_{16}H_{27}Br$ 298.1296, found 298.1281.

(5*E*,7*E*)-7-Bromo-5,7-hexadecadien-9-yne (**34b**, entry 20 in Table 2). ^{1}H NMR δ 0.91 (m, 6H), 1.30−1.65 (m, 12H), 2.25 (m, 2H), 2.38 (td, J = 7.5, 1.7 Hz, 2H), 5.90 (br s, 1H), 6.24 (dt, J = 14.7, 7.0 Hz, 1H), 6.63 (d, J = 14.7 Hz, 1H). ^{13}C NMR δ 14.06, 14.21, 19.92, 22.48, 22.74, 28.69, 28.74, 31.33, 31.50, 32.34, 77.45, 98.23, 112.17, 125.66, 133.66, 140.72. IR 2952, 2854, 2207, 1702, 1632, 1464, 1431, 1377, 1323, 1084, 956, 821, 733 cm^{-1}. HRMS calcd for $C_{16}H_{25}Br$ 296.1140, found 296.1135.

(E) Reaction with Butyl Isocyanide. To the solution of the alkenylzirconium reagent prepared above (see A) was added butyl isocyanide (1.3 equiv). The reaction mixture was warmed to 20 °C and stirred at room temperature for 16 h. The resulting solution was cooled to −78 °C, and 50% HOAc (aq) (5.0 mL) was added. After being warmed to room temperature and stirred for 1 h, water (6.0 mL) was added and the mixture was extracted with ether (2 × 10 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (3 × 10 mL) and brine (10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 40−60 petroleum ether−EtOAc, 10:1) to afford an aldehyde.

(*E*)-2-Hexyl-2,4-pentadienal (**24b**, entry 4 in Table 2). ^{1}H NMR δ 0.78 (m, 3H), 1.20 (m, 8H), 2.27 (t, J = 7.7 Hz, 2H), 5.50−5.75 (m, 2H), 6.65−6.85 (m, 2H), 9.44 (s, 1H). ^{13}C NMR δ 14.19, 22.71, 24.34, 29.28, 29.40, 31.74, 126.44, 132.04, 143.28, 148.86, 195.19. IR 2927, 2857, 2712, 1681, 1630, 1461, 1428, 1366, 1230, 1087, 1004, 930, 870, 726 cm^{-1}. HRMS calcd for $C_{11}H_{18}O$ 166.1358, found 166.1357.

(2*E*,4*E*)-2-Hexyl-2,4-tridecadienal (**29d**, entry 13 in Table 2). ^{1}H NMR δ 0.80 (m, 6H), 1.15−1.45 (m, 20H), 2.10−2.30 (m, 4H), 6.23 (dt, J = 15.1, 7.0 Hz, 1H), 6.50 (dd, J = 15.1, 11.0 Hz, 1H), 6.78 (d, J = 11.0 Hz, 1H), 9.38 (s, 1H). ^{13}C NMR δ 14.23, 22.75, 22.81, 24.26, 28.90, 29.23, 29.36, 29.38, 29.55, 31.79, 32.00, 33.60, 125.91, 140.86, 146.20, 149.77. IR 2930, 2880, 1680, 1631, 1458, 1371, 1209, 1180, 1087, 1005, 973, 729 cm^{-1}. HRMS calcd for $C_{19}H_{34}O$ 278.2610, found 278.2613.

(F) Cross-Coupling with Alkenyl and Allyl Halides. To the solution of the alkenylzirconium reagent prepared according to the general procedure (see **A**) by the reaction of **8a** with **20** and warmed to room temperature was added anhydrous zinc chloride (0.57 mL, 2.3 M in THF, 1.30 mmol). After the mixture was stirred for 15 min at 20 °C, allyl bromide (0.126 g, 1.04 mmol), (*E*)-*β*-bromostyrene (0.190 g, 1.04 mmol), or (*E*)-1-iodo-1-decene (0.277 g, 1.04 mmol) was added followed by a solution of Pd catalyst [preformed by the treatment of $PdCl_2(PPh_3)_2$ (0.037 g, 0.052 mmol) and PPh_3 (0.027 g, 0.104 mmol) with EtMgBr (0.052 mL, 2.0 M in ether, 0.104 mmol) in THF (2.0 mL) at 20 °C]. The reaction mixture was stirred overnight at room temperature and hydrolyzed by the addition of 2 M HCl (aq) (8.0 mL). After extraction with ether (12 mL) the organic layer was washed with 2 M HCl (aq) (10 mL) and saturated aqueous $NaHCO_3$ (10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (40−60 petroleum ether).

(*E*)-4-Hexyl-1,3,6-heptatriene (**46**, Scheme 5). ^{1}H NMR δ 0.91 (m, 3H), 1.25−1.50 (m, 8H), 2.18 (t, J = 7.7 Hz, 2H), 2.83 (d, J = 6.9 Hz, 2H), 5.00−5.18 (m, 4H), 5.75−5.85 (m, 1H), 5.88 (d, J = 10.5 Hz, 1H), 6.61 (ddd, J^1= 17.3 Hz, J^2, J^3 = 10.5 Hz, 1H). ^{13}C NMR δ 14.25, 22.78, 28.67, 29.46, 30.92, 31.89, 41.81, 115.39, 116.37, 126.45, 133.25, 136.57, 142.46. IR 3079, 3002, 2953, 2924, 2855, 1634, 1596, 1466, 1429, 1377, 986, 912, 897 cm^{-1}. HRMS calcd for $C_{13}H_{22}$ 178.1722, found 178.1727.

(3*E*,5*E*)-4-Hexyl-1,3,5-tetradecatriene (**47**, Scheme 5). ^{1}H NMR δ 0.82 (m, 6H), 1.15−1.40 (m, 20H), 2.07 (m, 2H), 2.26 (t, J = 7.7 Hz, 2H), 5.09 (d, J = 9.9 Hz, 1H), 5.21 (d, J = 16.6 Hz, 1H), 5.75 (dt, J = 15.4, 7.0 Hz, 1H), 5.96 (d, J = 11.0 Hz, 1H), 5.99 (d, J = 15.4 Hz, 1H), 6.67 (ddd, J = 16.6, 11.0, 9.9 Hz, 1H). ^{13}C NMR δ 14.26, 22.81, 22.84, 27.32, 29.37, 29.45, 29.67, 29.70, 31.90, 32.05, 33.26, 116.60, 129.21, 130.56, 133.36, 133.42, 141.06. IR 3081, 3014, 2923, 2854, 1614, 1465, 1377, 1146, 984, 962, 897 cm^{-1}. HRMS calcd for $C_{20}H_{36}$ 276.2817, found 276.2829.

(3*E*,5*E*)-4-Hexyl-6-phenyl-1,3,5-hexatriene (**48**, Scheme 5). ^{1}H NMR δ 0.88 (t, J = 6.8 Hz, 3H), 1.25−1.60 (m, 8H), 2.50 (t, J = 7.8 Hz, 2H), 5.23 (d, J = 9.9 Hz, 1H), 5.35 (d, J = 16.9 Hz, 1H), 6.25 (d, J = 11.0 Hz, 1H), 6.66 (d, J = 16.2 Hz, 1H), 6.76 (ddd, J = 16.9, 11.0, 9.9 Hz, 1H), 6.80 (d, J = 16.2 Hz, 1H), 7.25−7.50 (m, 5H). ^{13}C NMR δ 14.32, 22.85, 27.21, 29.70, 29.76, 31.93, 118.09, 126.52, 127.43, 127.80, 132.43, 132.50, 133.35, 137.87, 140.96. IR 3078, 3021, 2925, 2854, 1620, 1493, 1465, 1446, 1416, 1072, 984, 957, 899, 829 cm^{-1}. HRMS calcd for $C_{18}H_{24}$ 240.1878, found 240.1879.

(56) Baudin, J. B.; Hareau, G.; Julia, S. A.; Lorne, R.; Ruel, O. *Bull. Soc. Chim. Fr.* **1993**, *130*, 856.

(57) Mitsudo, T.; Nakagawa, Y.; Watanabe, K.; Hori, Y.; Misawa, H.; Watanabe, H.; Watanabe, Y. *J. Org. Chem.* **1985**, *50*, 565.

(58) Miller, J. A.; Zweifel, G. *Synthesis* **1983**, 128.

Reaction of the Lithium Carbenoids 19 and 20 with Benzaldehyde (Scheme 3). To a solution of (*Z*)-1,4-dichloro-2-butene (0.150 g, 1.20 mmol) in THF (12 mL) was added dropwise a solution of LiTMP (3.43 mL, 0.7 M in THF, 2.40 mmol, freshly formed from TMP and 1 equiv of BuLi at 0 °C) at −90 °C. The reaction mixture was stirred for 15 min at −90 °C to afford **1**, then benzaldehyde (0.165 g, 1.56 mmol) was added and the mixture was allowed to warm to −40 °C over 1 h. After hydrolysis with 2 M HCl (aq) (8.0 mL) and extraction with ether (3 × 5 mL), the organic layer was washed with 2 M HCl (aq) (10 mL) and saturated aqueous $NaHCO_3$ (10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 40−60 petroleum ether−EtOAc, 3:1) to give (*E*)-2-chloro-1-phenyl-2,4-pentadien-1-ol (**22**) (0.180 g, 77% yield). ^{1}H NMR δ 2.40 (br s, 1H), 5.30 (d, J = 9.4 Hz, 1H), 5.39 (d, J = 16.3 Hz, 1H), 5.97 (s, 1H), 6.48 (d, J = 9.4 Hz, 1H), 6.72 (ddd, J^1 = 16.3 Hz, J^2, J^3 = 9.4 Hz, 1H), 7.39 (m, 5H). ^{13}C NMR δ 70.88, 121.10, 125.88, 128.14, 128.62, 130.02, 130.95, 137.23, 140.07. IR 3377, 1493, 1448, 1050, 1011, 984, 917, 696, 657 cm^{-1}. Anal. Calcd for $C_{11}H_{11}ClO$: C, 67.87; H, 5.70; Cl, 18.21. Found: C, 67.73; H, 5.66; Cl, 18.60.

In a similar way the reaction of **19** generated from (*E*)-1,4-dichloro-2-butene and LiTMP with benzaldehyde gave the mixture (87:13) of (*Z*)-2-chloro-1-phenyl-2,4-pentadien-1-ol (**21**) and **22** in 68% yield. **21**: ^{1}H NMR δ 2.70 (br s, 1H), 5.32 (s, 1H), 5.35 (d, J = 9.4 Hz, 1H), 5.41 (d, J = 16.3 Hz, 1H), 6.58 (d, J = 9.4 Hz, 1H), 6.72 (ddd, J^1 = 16.3 Hz, J^2, J^3 = 9.4 Hz, 1H), 7.39 (m, 5H). ^{13}C NMR δ 77.27, 121.47, 126.42, 126.87, 128.50, 128.70, 131.59, 136.30, 140.14.

Generation of the Lithium Carbenoid 40d by the Reaction of (*E*,*E*)-1-Chloro-1,3-dodecadiene (39d) with BuLi (Scheme 4). To a solution of **39d** (0.15 g, 0.75 mmol) in THF (10.0 mL) was added BuLi (0.30 mL, 2.5 M in hexane, 0.75 mmol) at −90 °C. The mixture was stirred at −90 °C for 15 min to give a clear yellow solution of **40d**. Me_3SiCl (0.098 g, 0.90 mmol) was added, and the mixture was warmed to −60 °C over 1 h and hydrolyzed with 2 M HCl (aq) (6.0 mL). After extraction with petroleum ether (10 mL) the organic layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (40−60 petroleum ether) to give 1-chloro-1-trimethylsilyl-1,3-dodecadiene (**42**, 0.161 g, 79% yield) as only one (presumably 1*E*,3*E*) stereoisomer. ^{1}H NMR δ 0.29 (s, 9H), 0.91 (m, 3H), 1.25−1.45 (m, 12H), 2.10 (m, 2H), 5.74 (dt, J = 15.1, 7.0 Hz, 1H), 6.20 (dd, J = 15.1, 11.4 Hz, 1H), 6.93 (d, J = 11.4 Hz, 1H). ^{13}C NMR δ −0.21, 14.25, 22.81, 29.08, 29.29, 29.42, 29.56, 32.02, 32.94, 126.15, 136.82, 138.57, 143.55. IR 2925, 2854, 1638, 1561, 1466, 1250, 965, 868, 842, 757, 644 cm^{-1}. Anal. Calcd for $C_{15}H_{29}ClSi$: C, 66.01; H, 10.71; Cl, 12.99; Si, 10.29. Found: C, 66.21; H, 10.69; Cl, 12.78; Si, 10.21.

In a similar way the reaction of **40d** with the zirconium reagents **8a**, and **9a** afforded (7*Z*,9*E*)-7,9-octadecadiene (**29a**) and (5*E*,7*Z*,9*E*)-5,7,9-octadecatriene (**41**) in 80 and 74% yield, respectively. **41**: ^{1}H NMR δ 0.91 (m, 6H), 1.25−1.50 (m, 16H), 2.17 (m, 4H), 5.71 (dt, J = 15.1, 7.0 Hz, 2H), 5.86 (m, 2H), 6.50 (dd, J = 15.1, 8.8 Hz, 2H). ^{13}C NMR δ 14.10, 14.26, 22.45, 22.84, 29.44, 29.56, 29.65, 31.69, 32.06, 32.81, 33.15, 125.92, 127.76, 135.58, 135.66. IR 3025, 2922, 1688, 1639, 1463, 1378, 1341, 1132, 986, 963, 886, 841, 739 cm^{-1}. HRMS calcd for $C_{18}H_{32}$ 248.2504, found 248.2505.

Trapping the Lithium Carbenoids Generated from 12 and 14 with Me_3SiCl (Table 4, entries 1, 5). To a solution of (*E*)-1-chloro-2-methyl-1-octene (**12**, 0.12 g, 0.75 mmol) and Me_3SiCl (0.090 g, 0.825 mmol) in THF (10.0 mL) was added LiTMP (1.18 mL, 0.7 M in THF, 0.825 mmol, freshly prepared from TMP and BuLi) at −90 °C. The mixture was slowly warmed to −60 °C over 1 h and hydrolyzed by addition of 2 M HCl (aq) (6.0 mL). After the usual extractive workup the residue was dried under vacuum (0.5 mmHg, 20 °C, 3 h) to remove 2-nonyne and the unreacted **12**. 1-Chloro-1-trimethylsilyl-2-methyl-1-octene (**63**, 0.066 g, 38% yield) was isolated as the mixture (75:25) of (*E*)- and (*Z*)-isomers. ^{1}H NMR δ 0.28 (s, 9H), 0.91 (m, 3H), 1.25−1.45 (m, 8H), 1.92 (s, 3H), 2.15 (m, 2H) (*E*-isomer); 1.83 (s, 3H), 2.30 (m, 2H) (*Z*-isomer). ^{13}C NMR δ 0.61, 14.20, 20.68, 22.75, 29.08, 29.44, 31.91, 36.95, 130.22, 149.05 (*E*-isomer); 0.45, 21.04, 27.15, 36.50, 148.45 (*Z*-isomer). IR 2927, 2857, 1601, 1466, 1408, 1371, 1250, 901, 841, 758, 693, 632 cm^{-1}. HRMS calcd for $C_{12}H_{25}ClSi$ 232.1414, found 232.1416. For confirmation of the stereochemistry (*E*)-**63** was prepared independently by the reaction of the corresponding (*E*)-iodide **64** (see below) with CuCl (*N*-methylpyrrolidinone, 130 °C, 1.5 h) with complete retention of the configuration.[40]

In a similar way treatment of (*E*)-1-iodo-2-methyl-1-octene (**14**) and Me_3SiCl with LiTMP afforded (*E*)-1-iodo-1-trimethylsilyl-2-methyl-1-octene (**64**) in 95% yield as only one stereoisomer. ^{1}H NMR δ 0.29 (s, 9H), 0.92 (m, 3H), 1.25−1.50 (m, 8H), 2.08 (s, 3H), 2.32 (m, 2H). ^{13}C NMR δ 2.16, 14.05, 22.58, 29.08, 29.22, 31.71, 32.50, 38.01, 107.57, 156.49. IR 2957, 2926, 2856, 1641, 1588, 1466, 1407, 1369, 1260, 1097, 1019, 877, 839, 805, 758, 626 cm^{-1}. HRMS calcd for $C_{12}H_{25}ISi$ 324.0770, found 324.0768. For confirmation of the stereochemistry the product was treated with BuLi (ether, −60 °C, 10 min) followed by hydrolysis to give (*Z*)-1-trimethylsilyl-2-methyl-1-octene whose spectral data were in good agreement with those described in the literature.[59]

Acknowledgment. We thank the EPSRC (grant GR/K19907) for a postdoctoral award to A.K. R.J.W. thanks Pfizer central research, Glaxo-Wellcome, and Zeneca for generous uncommitted support.

JA9910208

(59) Snider, B. B.; Karras, M.; Conn, R. S. E. *J. Am. Chem. Soc.* **1978**, *100*, 4624. For the (*E*)-isomer, see: Chatani, N.; Amishiro, N.; Morii, T.; Yamashita, T.; Murai, S. *J. Org. Chem.* **1995**, *60*, 1834.