Asymmetric Synthesis of *cis*-1,2-Dialkenyl-Substituted Cyclopentanes via (−)-Sparteine-Mediated Lithiation and Cycloalkylation of a 9-Chloro-2,7-nonadienyl Carbamate

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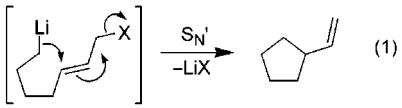
Herein we report our comprehensive results in enantioselective cyclopentane synthesis via stereogenic allyllithium compounds. The described cycloalkylation reaction starts with a (−)-sparteine-mediated asymmetric deprotonation of the 2,7-alkadienyl carbamate **7e** and leads to the enantioenriched (80% ee) and diastereomerically pure (dr = 99:1) *cis*-1,2-divinyl-cyclopentane **8**, by a subsequent cyclization and elimination of lithium chloride. The reaction mechanism has been investigated by silylation and lithiodestannylation experiments and was found to represent a completely regioselective *anti*-$S_N'S_E'$-reaction. Trapping of the vinyllithium intermediate **12** with various electrophiles under retention of the configuration at the double bond extends the field of application for this cyclization. We also applied this reaction as the key step in the enantioselective synthesis of (+)-dihydromultifidene (**17**).

Introduction

The allylic substitution of a leaving group by a carbon nucleophile is one of the most important reactions in organic synthesis. In almost every allylic substitution reaction transition metals, such as copper[1] and palladium,[2] are involved. Simple main-group organometallics are rarely used in allylic substitutions,[3] because in intermolecular reactions the regioselectivity becomes a major problem, giving rise to product mixtures resulting from S_N2 and S_N2' reactions.[4] In intramolecular variants these difficulties could be overcome by the different cyclization rates in both competing mechanistic pathways. Due to the fast formation of five-membered rings,[5] the cyclopentane synthesis[6] is strongly favored in these reactions (eq 1).



(1)

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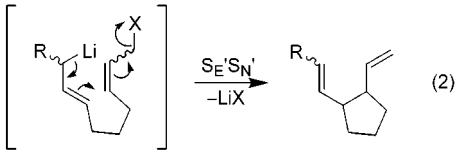
In the examples previously published, alkoxides were used as leaving groups and a lithium alkanide **1**, which was generated by tin−lithium exchange, was utilized as nucleophile.[7,8] An enantioselective cycloallylation reaction mediated by an external ligand has not been reported so far.[9]

Results and Discussion

Herein we report our entire efforts in cyclopentane synthesis by carbocyclization of allyllithium compounds (eq 2).[10] Particularly challenging in this reaction is the control of both regioselectivities, in respect of the allylic



(2)

2

leaving group and of the allyl anion.[11] Out of the four possible regioselective reaction pathways, eq 2 only shows the desired γ,γ'-regioselective bond formation. Since, in addition, we wanted to realize this cyclization in an enantioselective fashion, by control of an external ligand, we chose a deprotonation by a chirally modified butyllithium as the initial reaction to generate the organo-

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(1) Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135.

(2) (a) Trost, B. M.; van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (b) Helmchen, G.; Pfaltz, A. *Acc. Chem. Res.* **2000**, *33*, 336. (c) Reiser, O. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 547−550.

(3) Review: Magid, R. M. *Tetrahedron* **1980**, *36*, 1901−1930.

(4) (a) Yanagisawa, A.; Yasue, K., Yamamoto, H. *Synlett* **1996**, 842−844. (b) Yanagisawa, A.; Yamamoto H. In *Active Metals*; Fürstner, A., Ed.; VCH: Weinheim, 1995; pp 61−84. (c) Yanagisawa, A.; Hibino, H.; Habaue, S.; Hisada, Y.; Yamamoto, H. *J. Org. Chem.* **1992**, *57*, 6386-6387.

(5) Eliel, E. L.; Wilen, S. H. In *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; pp 675−685.

(6) Recent reviews about the synthesis of 3−eight-membered carbocycles: (a) Hartley, R. C.; Caldwell, S. T. *J. Chem. Soc., Perkin Trans. 1* **2000**, 477−501; (b) Molander, G. A. *Acc. Chem. Res.* **1998**, *31*, 603−609.

(7) Synthesis of pyrrolidines: Coldham, I.; Hufton, R.; Rathmell, R. E. *Tetrahedron Lett.* **1997**, *38*, 7617−7620.

(8) Synthesis of racemic tetrahydrofurans: (a) Broka, C. A.; Shen T. *J. Am. Chem. Soc.* **1989**, *111*, 2981−2984; (b) Broka, C. A.; Lee, W. J.; Tong S. *J. Org. Chem.* **1988**, *53*, 1336−1338.

(9) (a) For an enantioselective 5-*exo*-*tet*-cyclization see: Serino, C.; Stehle, N.; Park, Y. S.; Florio, S.; Beak, P. *J. Org. Chem.* **1999**, *64*, 1160−1165. (b) Review about enantioselective carbolithiations: Marek, I.; *J. Chem. Soc., Perkin Trans. 1* **1999**, 535−544.

(10) For a preliminary communication of our work, see: Deiters, A.; Hoppe, D. *Angew. Chem.* **1999**, *111*, 529−532; *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 546−548.

(11) We could solve this problem for intramolecular reactions, it still exists in intermolecular variants (see ref 4). For enantioselective cyclononadiene syntheses by an intramolecular α,α'-coupling, see: (a) Deiters, A.; Fröhlich, R.; Hoppe, D. *Angew. Chem.* **2000**, *112*, 2189−2192; *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 2105−2107. (b) Deiters, A.; Mück-Lichtenfeld, C.; Fröhlich, R.; Hoppe, D. *Org. Lett.* **2000**, *2*, 2415−2418.

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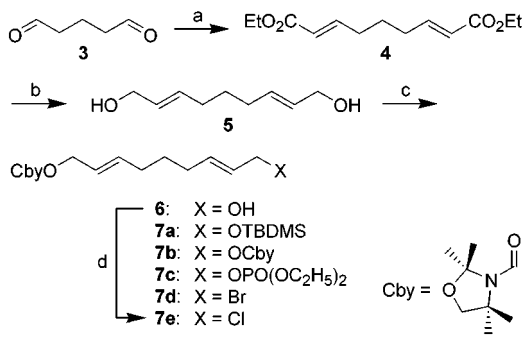
Scheme 1. Synthesis of the Cyclization Precursors[a]



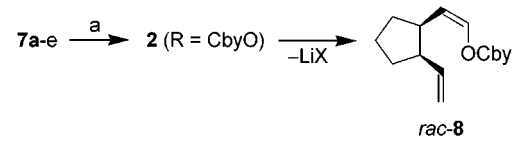
[a] Reagents and conditions: (a) $EtO_2CCH_2PO(OEt)_2$, K_2CO_3, H_2O, 35%; (b) DIBAH, toluene, 92%; (c) NaH, CbyCl, THF, 39% of **6**, 22% of **7b**, 19% of **5**; (d) LiCl, *n*-BuLi, CH_3SO_2Cl, THF, 90%.

lithium species **2**.[12] Due to this, the R group must acidify the protons in α-position and has to stabilize the lithium compound **2**. We used the 2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyl group (R = CbyO), developed in our laboratories, because of its easy introduction and its facile cleavage.[13] As leaving group we investigated a silyloxide (**7a**, X = OTBDMS), a carbamate (**7b**, X = OCby), a phosphate (**7c**, X = $OPO(OEt)_2$),[14] bromide (**7d**, X = Br), and chloride (**7e**, X = Cl).[15] The straightforward synthesis of the precursor **7e** is depicted in Scheme 1.

It started with commercially available glutaric dialdehyde (**3**) which was subjected to a Horner−Wadsworth−Emmons reaction[16] in aqueous solution. The diester **4**[17] was reduced to the diol **5**[18] using DIBAH at −78 °C. Carbamoylation of the sodium alkoxide of **5** with CbyCl furnished the carbamate **6**, which was subsequently chlorinated to yield the cyclization precursor **7e**. Complete diastereomeric purity of the cyclization precursors was verified by GLC analysis; the (*E*)-geometry of the double bonds was confirmed by the ^{1}H NMR coupling constants of the olefinic protons of the symmetrical dienes **4** (15.7 Hz) and **7b** (15.2 Hz).

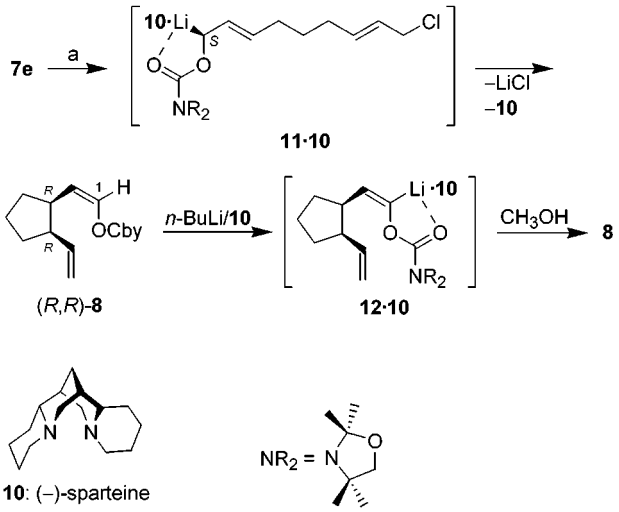
Cyclization of the Allylic Chloride 7e. The deprotonation of the carbamates **7a**−**e** was carried out in diethyl ether at −78 °C by slow addition of 1.1 equiv of *n*-butyllithium/TMEDA (**9**). In case of **7a**−**d** at −78 °C no cyclization reaction took place. In the case of **7a** the substrate was completely reisolated, but analysis of the crude reaction mixtures of **7b** and **7c**, in addition, showed some unidentified minor products. Although several side-reactions are conceivable,[19] the precursor **7e** was efficiently deprotonated in the α-position by means of

Scheme 2[a]



[a] Reagents and conditions: (a) *n*-BuLi, TMEDA (**9**), Et_2O, −78 °C.

Scheme 3. Enantioselective Cyclization[a]



[a] Reagents and conditions: (a) *n*-BuLi, (−)-sparteine (**10**), solvent, temp, time (see Table 1).

Table 1. (−)-Sparteine-Mediated Enantioselective Cyclization

entry	base (equiv)	solvent	temp, °C	time, h	yield, %	er	ee, %
1	1.1	ether	−78	24	64	75:25	50
2	1.1	toluene	−78	7	50	83:17	66
3	1.6	toluene	−88	6	80	88:12	76
4	2.2	toluene	−90	2	90	90:10	80
5	1.8[a]	toluene	−86	7	9	80.5:19.5	61
6	2.2[b]	toluene	−78	2	76	83:17	66
7	2.2[c]	ether	−78	2	71	80:20	60

[a] 0.1 equiv of (−)-sparteine were used. [b] 1.2 equiv of (−)-sparteine were used. [c] 2.2 equiv of LiCl were added.

n-BuLi/TMEDA (**9**) in the presence of the allyl chloride moiety. The intermediate allyllithium species **2** (R = OCby, X = Cl) reacted smoothly, with elimination of LiCl, to furnish the divinylcyclopentane *rac*-**8** (68%, dr = 99:1), even at −78 °C (Scheme 2).[20]

The diastereomeric ratio of *cis*-**8** was determined by GLC, the relative configuration was established by NOE measurements, and the (*Z*)-geometry of the enol carbamate moiety is based on the small olefinic coupling constant (6.5 Hz). By employing the chiral diamine (−)-sparteine (**10**) as ligand for the butyllithium, instead of the achiral TMEDA (**9**), one of the enantiotopic α-protons was abstracted preferentially, which led to the enantioenriched allyllithium species (1*S*)-**11·10**. The subsequent cyclization at −78 °C in Et_2O furnished diastereomerically pure (*R*,*R*)-**8** in 64% yield (Scheme 3, Table 1, entry

(12) Reviews: (a) Hoppe, D.; Hense, T. *Angew. Chem.* **1997**, *109*, 2376−2410; *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2282−2316. (b) Beak, P.; Basu, A.; Gallagher, D. J.; Park, Y. S.; Thayumanavan, S. *Acc. Chem. Res.* **1996**, *29*, 552−560.

(13) (a) Bebber, J. von; Ahrens, H.; Fröhlich, R.; Hoppe, D. *Chem. Eur. J.* **1999**, *5*, 1905−1916. (b) Hintze, F.; Hoppe, D. *Synthesis* **1992**, 1216−1218.

(14) Syntheses of allylic phosphates: S.-I. Murahashi, Y. Taniguchi, Y. Imada, Y. Tanigawa *J. Org. Chem.* **1989**, *54*, 3292−3303.

(15) For syntheses of allylic chlorides see ref 3.

(16) Reviews about Horner−Wadsworth−Emmons reactions: (a) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863−927. (b) Wadsworth, W. S., Jr. *Org. React. (N.Y.)* **1977**, *25*, 73−253.

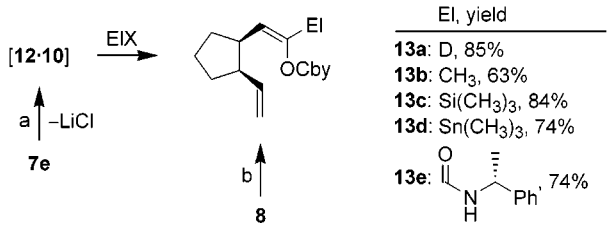
(17) Synthesis of **4**: Villieras, J.; Raumbaud, M.; Graff, M. *Synth. Commun.* **1986**, *16*, 149−156.

(18) For a different synthesis of **5**, see: (a) Iriye, R.; Toya, T.; Makino, J.; Aruga, R.; Doi, Y. *Agric. Biol. Chem.* **1988**, *52*, 989−996. (b) Lennon, P.; Rosenblum, M. *J. Am. Chem. Soc.* **1983**, *105*, 1233−1241.

(19) Possible side-reactions of the allyl chloride moiety are an intermolecular substitution with *n*-BuLi, a halogen−lithium exchange or a deprotonation in α-position to the chloro atom.

(20) Unfortunately, the application of this reaction was not possible in the synthesis of substituted cyclohexanes (ref 35).

Scheme 4[a]



[a] Reagents and conditions: (a) *n*-BuLi, (−)-sparteine (**10**), toluene, −90 °C, 2 h; (b) *n*-BuLi, TMEDA, Et_2O, −78 °C, ElX.

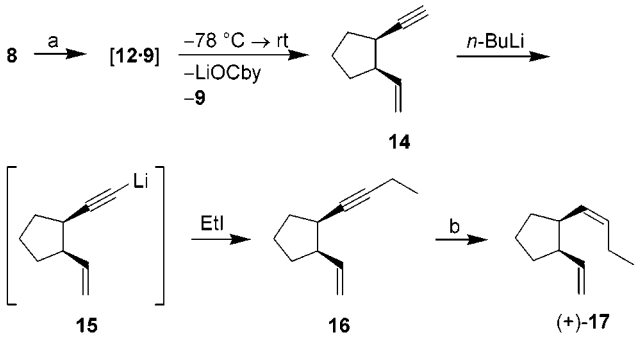
1), in an enantiomeric ratio (er) of 75:25 (50% ee). By using toluene as nonpolar solvent (Table 1, entry 2), the er could be increased to 83:17 (66% ee) and through lowering the reaction temperature to −90 °C (Table 1, entry 4) a further enhancement up to *er* = 90:10 (80% ee) was possible. An increase of the amount of *n*-BuLi/(−)-sparteine led to higher yields (Table 1, entries 2−4); when employing 2.2 equiv of the chiral base, (*R*,*R*)-**8** was obtained in the excellent yield of 90%.

The necessity for using at least 2 equiv of *n*-BuLi can be explained by the formation of the vinyllithium compound **12·10**. The vinylic proton at the 1-positon in **8** has a similar acidity compared to that of the allylic α-protons in **7e** and, owing to the high cyclization rate, **7e** and **8** are competing for the butyllithium. A quantitative formation of **12·10** was possible with 2 equiv of base. This is also the reason, why the reaction could not be accomplished with catalytic amounts of (−)-sparteine (Table 1, entry 5), because in **12·10** the lithium alkenide is still chelated by the diamine. However, a smooth reaction proceeded when using 2.2 equiv of *n*-BuLi and 1.2 equiv of (−)-sparteine without loss in yield and stereoselectivity (Table 1, entry 6).

The subsequent formation of **12·10** from **7e** provides the opportunity to perform a multistep one-pot procedure by trapping the intermediate **12·10** with several electrophiles to generate the functionalized cyclopentanes **13a**−**e** (Scheme 4). The substitution products **13a**−**e** are also accessible from **8** via **12·9**, which is equivalent to a two-step process starting from **7e**. The configurative stability of **12** was examined by reprotonation and deuteriolysis, as well.

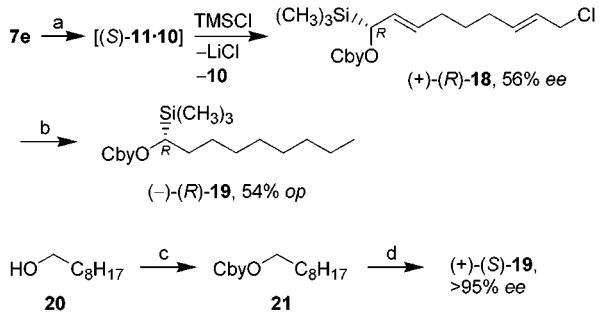
Investigation of the Cyclization Mechanism. To determine the absolute configuration and to demonstrate a synthetic application of this cycloallylation reaction, (*R*,*R*)-**8** was transformed into the natural compound derivative (+)-dihydromultifidene (**17**, Scheme 5).[21] The reaction sequence starts with a vinylic lithiation of **8** to **12·9** at −78 °C. Then, the carbenoide[22] **12** was allowed to warm to room temperature, which initiated a Fritsch−Buttenberg−Wiechell rearrangement.[23] The formed alkyne **14** was lithiated by a second equiv of butyllithium and the lithium acetylide **15** could be alkylated with EtI to yield the alkyne **16**. The synthesis was completed by a Lindlar hydrogenation to the (*Z*)-alkene (+)-**17**.[24] A

Scheme 5. Synthesis of (+)-Dihydromultifidene[a]



[a] Reagents and conditions: (a) *n*-BuLi (2 equiv), TMEDA, THF, −78 °C, 65%; (b) H_2, 1 atm, Lindlar catalyst, quinoline, pentane, 76%. The lithium cation in **15** is complexed by TMEDA and/or THF.

Scheme 6[a]



[a] Reagents and conditions: (a) *n*-BuLi, (−)-sparteine, toluene, −78 °C; (b) H_2, Pd/C, NaOAc, MeOH, 90%; (c) CbyCl, NaH, THF, 90%; (d) 1. *s*-BuLi, (−)-sparteine, Et_2O, −78 °C; 2. TMSCl, 80%.

comparison of the sense of the optical rotation with a previously reported value[21a] clearly establishes the (*R*,*R*)-configuration of (+)-**17** and hence the (*R*,*R*)-configuration of **8**.

For proposing a likely mechanism of this enantioselective cycloallylation reaction, knowledge of the absolute configurations of **8** and of the lithiated intermediate **11·10** is required. The configuration of the latter has been determined by transformation of **11·10** into the allylic silane (*R*)-**18** and a subsequent hydrogenation of the double bonds and simultaneous hydrogenolytic cleavage of the chlorine atom to produce (−)-(*R*)-**19**. The enantiomer (+)−(*S*)-**19** has been synthesized in a highly enantioenriched form from the saturated alcohol **20** via the alkyl carbamate **21** by using our *s*-BuLi/(−)-sparteine method (Scheme 6).[25] By comparison of the sense of the optical rotations, (−)-**19** and thus (+)-**18** could be assigned the (*R*)-configuration. Silylations of allyllithium compounds generally proceed under inversion of the configuration,[26] hence (1*S*)-**11·10** was the intermediate that led to (*R*,*R*)-**8**.

Time-dependent silylations of (*S*)-**11·10** and lithiodestannylation experiments gave deeper insights into the

(21) Multifidene is an attracting pheromone of the brown algae *Cutleria multifida*. (a) Boland, W.; Mertes, K.; Jaenicke, L.; Müller, D. G.; Fölster, E. *Helv. Chim. Acta* **1983**, *66*, 1905−1913; (b) Jaenicke, L.; Boland, W. *Angew. Chem.* **1982**, *94*, 655−724; *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 643−712.

(22) Review: Braun, M. *Angew. Chem.* **1998**, *110*, 444−465; *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 430−451.

(23) Kocienski, P.; Dixon, N. J. *Synlett* **1989**, 52−54; (b) Kocienski, P.; Barber, C. *Pure Appl. Chem.* **1990**, *62*, 1933−1940.

(24) Review on semihydrogenation of triple bonds: Marvell, E. N.; Li, T. *Synthesis* **1973**, 457−468.

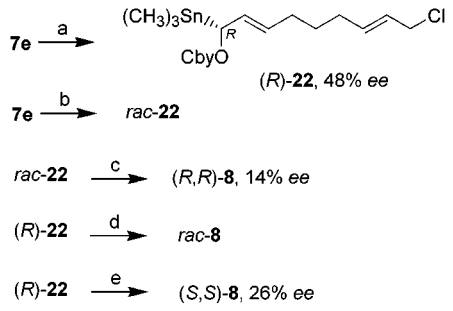
(25) Hoppe, D.; Paetow, M.; Hintze, F. *Angew. Chem.* **1993**, *105*, 430−432; *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 394−396. In all known cases, deprotonation of saturated *O*-carbamates with *s*-BuLi/**10** furnished the (*S*)-configurated lithium species, which reacted under retention of the configuration with the electrophile; see also ref 12a.

(26) (a) Behrens, K.; Fröhlich, R.; Meyer, O.; Hoppe, D. *Eur. J. Org. Chem.* **1999**, 2397−2403. (b) Paulsen, H.; Graeve, C.; Hoppe, D. *Synthesis* **1996**, 141−144.

Table 2. Time-Dependent Silylation

entry	time, min	yield of (*R*)-**18, %** (% ee)	yield of **8**, %
1	0	70 (56)	0
2	15	22 (46)	30
3	30	13 (34)	43

Scheme 7[a]



[a] Reagents and conditions: (a) 1. *n*-BuLi, (−)-sparteine, toluene, −78 °C; 2. $(CH_3)_3SnCl$, 7%; (b) *s*-BuLi, TMEDA, $(CH_3)_3SnCl$, toluene, −78 °C, 15%; (c) *n*-BuLi, (−)-sparteine, toluene, −78 °C, 94%; (d) 1. *n*-BuLi, TMEDA, toluene, −78 °C, 90%; (e) see c, 100%.

mechanism. Silylations after 15 and 30 min showed a decrease in the enantiomeric excess of (*R*)-**19** (Table 2). Compared to the high ee in (*R*,*R*)-**8** this, together with the observed lithiation of **8** to **12**, suggests a very fast cyclization step. To gain more information about the reaction mechanism, we also performed lithiodestannylation experiments using the allyltin compound **22**, which has been synthesized both in racemic and in enantioenriched form (Scheme 7). The synthesis of *rac*-**22** was problematic, because the injection of a hexane solution of Me_3SnCl to the reaction mixture a few minutes after lithiation did not furnish *rac*-**22**, due to the very high cyclization rate when TMEDA was employed as ligand. Therefore the tin electrophile was added in situ and *s*-BuLi/TMEDA[27] was used as the base, which afforded *rac*-**22** in 15% yield. Since the cyclization is a little slower using (−)-sparteine as diamine, addition of Me_3SnCl to the reaction mixture after 5 min yielded (*R*)-**22** (7%, 48% ee).[28] Lithiodestannylation of *rac*-**22** with *n*-BuLi in the presence of (−)-sparteine in toluene at −78 °C furnished (*R*,*R*)-**8** in nearly quantitative yield, with an ee of 14%. This can be explained with a slight kinetic resolution[29] in the cyclization step, but it cannot count for the high ee's observed in **8** under deprotonation conditions. Treatment of (*R*)-**22** (48% ee) with *n*-BuLi/**9** led to *rac*-**8** in 90% yield. Probably, the stereochemical information was lost on the stage of the TMEDA-complexed allyllithium compound **11·9**, because TMEDA-complexed lithium alkanides have proved to be much more configuratively labile than the corresponding (−)-sparteine complexes.[30a,b] Therefore a similar experiment was carried out with (−)-sparteine as diamine, which furnished (*S*,*S*)-**8** (26% ee) in quantitative yield.[30] These results reveal, that the sense of stereoinformation found in the cyclization product (*R*,*R*)-**8** is, as expected, defined in the deprotonation step.

This information, together with the (1*S*)-configuration of the allyllithium compound **11·10** and the configuration of the cyclopentane **8** (1*R*,2*R*; *cis* arrangement of the side chains; (*Z*)-configuration of the vinyl carbamate unit) enables us to decide for one of the three possible cyclization pathways (Scheme 8): Deprotonation of **7e** leads to the (1*S*)-configured allyllithium species **11·10** in the 1-*endo*-conformation.[31] In the previously proposed lithium ene-mechanism[10,32] **11** passes through the transition state **C**, in which the lithium cation is involved in the six-membered ring. Therefore this reaction must proceed with retention of the configuration, eventually leading to the enantiomeric cyclopentane (*S*,*S*)-**8**. However, the observed formation of (*R*,*R*)-**8** suggests that the cycloalkylation has to proceed in an *anti*-S_E' fashion in respect of the lithium-bearing allylic moiety. Here, two different transition states are possible: **A** with a chairlike conformation and **B** with a boatlike conformation. Both of them benefit from a favorable HOMO/LUMO-interaction of the parallel oriented allyl moieties. **A**, which would furnish the *trans*-substituted cyclopentane (*R*,*S*)-**8**, holds a more strained trimethylene bridge than **B**,[33] hence the reaction pathway via transition state **B** has the lower activation energy. Presumably the high charge separation in **B** is compensated by coordination of "free" lithium cations, because previous addition of LiCl to the reaction mixture led to slightly higher ee's (Table 1, entry 7). Therefore this cyclization can be classified as a regio-, diastereo-, and enantioselective intramolecular *anti*-$S_E'S_N'$-reaction.

Cyclization of a Configurationally Stable Allyllithium Compound. This mechanism is in contrast to our previously proposed one,[10] which includes an inversion of the configuration at the lithium-bearing carbon atom prior to the cyclization step. Therefore we wanted to gain further evidence by the use of a allyllithium derivative, which is definitely configurationally stable under the reaction conditions. In our laboratories, lithiated α-methyl-substituted allylic carbamates (**23·9**, CH_3 for $Si(CH_3)_3$) were found to be configuratively stable at −78 °C.[34] The application of an α-methyl cyclization precursor was difficult, due to the slow deprotonation, which led to decomposition of the allyl chloride moiety, and the instability of the cyclization product **13b** under the basic reaction conditions.[35] Therefore we employed lithiated α-silyl allylcarbamates (like **23·9**) as new configurationally stable enantioenriched allyllithium com-

(27) A strong and sterical demanding base, such as *s*-BuLi has the advantage of deprotonating the allylic carbamate faster and reacting slower with Me_3SnCl compared to the use of *n*-BuLi.

(28) Here, no in situ trapping was applied, because the use of *s*-BuLi led to a lower enantiomeric enrichment in **8** (30% ee, Et_2O, −78 °C) than *n*-BuLi (50% ee, Et_2O, −78 °C).

(29) Review on dynamic kinetic resolution: Caddick, S.; Jenkins, K. *Chem. Soc. Rev.* **1996**, 447−456.

(30) Other examples of inversion of the configuration by means of stannylation (inversion) and lithiodestannylation (retention) in heterosubstituted allyl and benzyl compounds: (a) Weisenburger, G. A.; Beak, P. *J. Am. Chem. Soc.* **1996**, *118*, 12218−12219. (b) Weisenburger, G. A.; Beak, P. *J. Am. Chem. Soc.* **1996**, *118*, 3757−3758. (c) Derwing, C.; Hoppe, D. *Synthesis* **1996**, 149−154. (d) Carstens, A.; Hoppe, D. *Tetrahedron* **1994**, *50*, 6097−6108.

(31) Review: Schlosser, M.; Desponds, O.; Lehmann, R.; Moret, E.; Rauchschwalbe, G. *Tetrahedron* **1993**, *49*, 10175−10203.

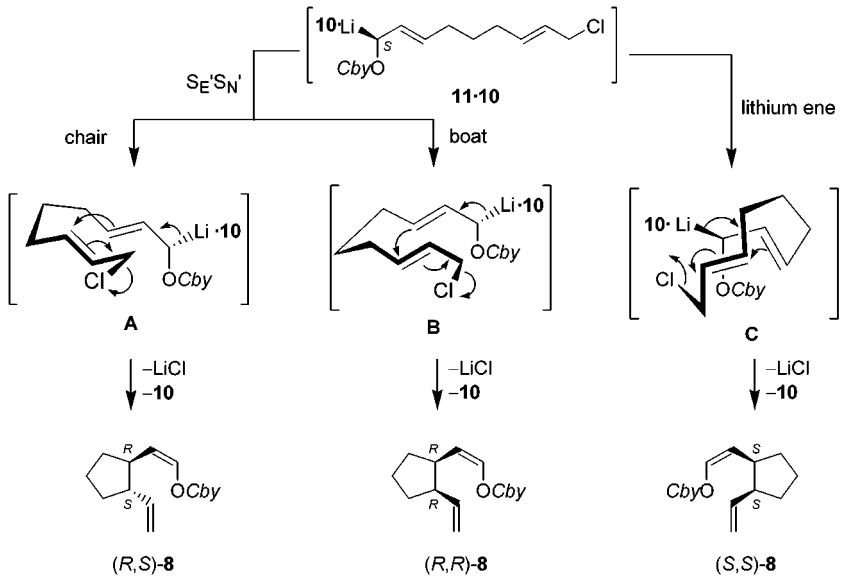
(32) Review on metallo ene-reactions: Oppolzer, W. *Angew. Chem.* **1989**, *101*, 39−53; *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 38−52. (b) Recent example of a lithium ene-reaction: Cheng, D.; Knox, K. R.; Cohen, T. *J. Am. Chem. Soc.* **2000**, *122*, 412−413.

(33) The same reasoning was used in the explanation of *cis*-selective ene-reactions: Oppolzer, W.; Snieckus, V. *Angew. Chem.* **1978**, *90*, 506−516; *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476−486.

(34) (a) Schwark, J.-R.; Hoppe, D. *Synthesis* **1990**, 291−294. (b) Krämer, T.; Hoppe, D. *Tetrahedron Lett.* **1987**, *28*, 5149−5152. (c) Krämer, T.; Hoppe, D. *Angew. Chem.* **1986**, *28*, 5149−5152; *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 160−162.

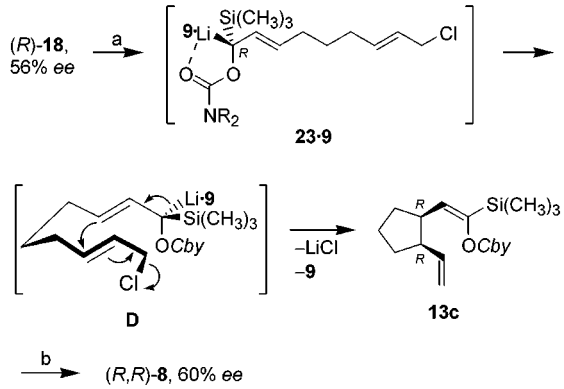
(35) Deiters, A. Ph.D. Thesis, 2000, University of Münster.

Scheme 8. Possible Cyclization Pathways[a]



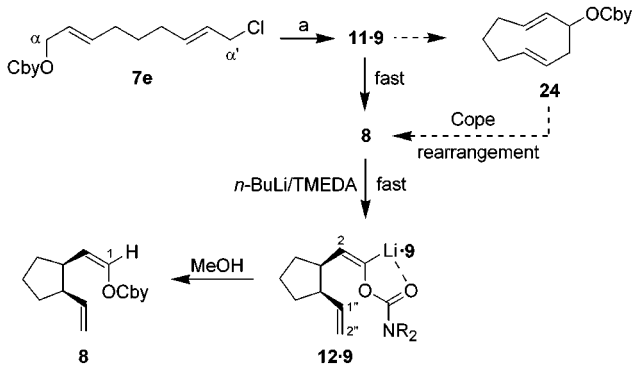
[a] The chelate of the carbonyl group with the lithium cation is omitted for the sake of clearness.

Scheme 9. Cyclization of (*R*)-18[a]



[a] Reagents and conditions: (a) *n*-BuLi, TMEDA (**9**), Et_2O, −78 °C, 40%; (b) TBAF, THF, room temperature, 87%.

Scheme 10[a]



[a] Reagents and conditions: (a) *n*-BuLi, TMEDA (**9**), THF-d_8 −80 °C.

pounds.[36] The cyclization precursor (*R*)-**18** (56% ee) was already synthesized in previous experiments and was subjected to *n*-BuLi/TMEDA (2.0 equiv) at −78 °C in Et_2O. After 8.5 h (*R*,*R*)-**13c** was obtained in 40% yield and 39% of **18** were reisolated (Scheme 9). The low yield of **13c** suggests a lower cyclization rate, due to the steric hindrance of the trimethylsilyl group. The ee of **13c** was determined by GLC on a chiral stationary phase to 60% after desilylation to **10**,[37] which is equivalent to 100% chirality transfer from (*R*)-**18** to (*R*,*R*)-**13c**.[38] The absolute configuration found in the cyclization product (*R*,*R*)-**13c**, together with the (*R*)-configuration of **18**, again suggests an antarafacial coupling reaction via the transition state **D** and gives another evidence for the mechanism described in Scheme 8.

NMR Experiment of the Cyclization Reaction. In contrast to the proposed cyclization mechanism, an α,α′-coupling of **11** to the cyclononadiene **24** and a subsequent Cope rearrangement to **8** is also conceivable.[39] To ensure a direct formation of **8**, we monitored the lithiation and cyclization of **7e** with *n*-BuLi/TMEDA in THF-d_8 at −80 °C by ^{1}H NMR. Here, the typical signals of **7e** for H-1 (4.60 ppm) and H-9 (4.11 ppm) vanished immediately and the characteristic signals of **8** for H-2 (4.43−4.53 ppm), H-2″ (4.75−4.93 ppm) and H-1″ (5.58−5.68) appeared. The signal for the proton at the 1-position was not visible, indicating the fast vinylic lithiation to **11**. However, after addition of methanol, the typical doublet (J = 4.6 Hz) for H-1 at 7.07 ppm occurred (Scheme 10). These results suggest that no Cope rearrangement, but the expected direct formation of **8** from **11** takes place.

Conclusion

In summary we developed a novel intramolecular regio-, diastereo-, and enantioselective allylation reaction, based on a *n*-BuLi/(−)-sparteine-mediated deprotonation of an allylic carbamate, which furnished 1,2-dialkenyl-

(36) Preliminary investigations of an enantioenriched lithiated α-silyl-cinnamyl carbamate showed a fast deprotonation and a remarkable degree of configurative stability (see ref 35).

(37) Crowley, P. J.; Percy, J. M.; Stansfield, K. *Tetrahedron Lett.* **1996**, *37*, 8237−8240.

(38) The discrepancy of the ee values of (*R*)-**18** and **13c** is due to the different determination methods (^{1}H NMR shift experiment and GLC on a chiral stationary phase).

(39) Reviews on [3,3]-sigmatropic rearrangements: (a) Bennet, G. B. *Synthesis* **1977**, 589−606. (b) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227−232.

substituted cyclopentanes in good to excellent yields. Further functionalization and transformation of the vinyl carbamate moiety[40] was demonstrated, and an application of this reaction was found in the stereoselective synthesis of (+)-dihydromultifidene. The cyclization mechanism was investigated to be an intramolecular *anti*-$S_E'S_N'$ substitution reaction, by determination of the (1*S*)-configuration of the lithiated intermediate and of the (*R*,*R*)-configuration of the cyclization product. Silylation, stannylation, and lithiodestannylation experiments and employing a configurationally stable allyllithium compound in the cycloallylation gave deeper insights into the cyclization mechanism. This new concept of deprotonation of an allylic carbamate in the presence of an allyl chloride moiety gives us additional opportunities in the development of synthetic methods using enantioenriched lithium alkenides.[11a,11b,41]

Experimental Section

General Methods. The doubling of some signals in the NMR spectra occurs as a result of the *E*/*Z* isomerism of the carbamate group; these signals are separated by slashes. (−)-Sparteine (**10**) is commercially available (Aldrich) and was stored under argon; TMEDA (**9**) was distilled from CaH_2 and kept under argon. *n*-BuLi was received as a 1.6 M solution in hexane from Acros and *s*-BuLi as a 1.4 M solution in cyclohexane/hexane (92:8) from Fluka; the latter was titrated before use.[42] Reactions with air and moisture sensitive reagents were performed in dried glassware with dry solvents, freshly distilled before use. The flash chromatography was performed with an excess pressure of 1 bar on silica gel (Merck, mesh 40−63 μm).[43] GLC was performed on a 25 m HP1 column at an oven temperature of 50 °C for 1 min and then 10 °C/min to 290 °C, and the final temperature was kept for 10 min (HP1) or on a 25 m HP1701 column at an oven temperature of 50 °C for 1 min and then 10 °C/min to 260 °C, and the final temperature was kept for 10 min (HP1701). For GLC on a chiral stationary phase a 30 m BetaDex 120TM column (Supelco) was used in an isothermic fashion; the main enantiomer is marked by an asterix.

(2*E*,7*E*)-2,7-Nonadiene-1,9-diol (5). The diester **4** (1.50 g, 6.2 mmol, 1.0 equiv) was dissolved in THF (6 mL), cooled to −78 °C, and was slowly treated with DIBAH (36 mL, 36.0 mmol, 5.8 equiv, 1 M solution in toluene). After 4 h stirring at −78 °C, methanol (5 mL) and water (5 mL) were added, and the reaction mixture was carefully warmed to room temperature. Then it was stirred for further 30 min, was filtered over $MgSO_4$ (25 g), the precipitate was rinsed with Et_2O (150 mL), and the filtrate was concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (ether/pentane 1:1 → ether) and **5** (887 mg, 92%) was obtained as colorless oil. The analytical data were identical to those found in the literature.[18]

(2*E*,7*E*)-9-Hydroxy-2,7-nonadienyl 2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carboxylate (6) and (2*E*,7*E*)-(2,7-Nonadiene-1,6-diyl) 1,9-Bis(2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate) (7b). The diol **5** (1.10 g, 7.1 mmol, 1.0 equiv) was added to a suspension of NaH (311 mg, 7.8 mmol, 1.1 equiv, 60% suspension in mineral oil) in THF (15 mL). After stirring for 1 h, a solution of 2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyl chloride (CbyCl, 1.35 g, 7.1 mmol, 1.1 equiv) in THF (10 mL) was injected and the reaction mixture was heated to 70 °C for 48 h. Then, sat. NH_4Cl (aq, 5 mL) and water (5 mL) were added, the layers were separated, and the aqueous phase was extracted with ether (5 × 30 mL). The combined organic phases were dried ($MgSO_4$), and the solvents were removed in vacuo. The crude product was purified by flash chromatography on silica gel (ether/pentane 1:5 → ether) yielding the carbamate **6** (866 mg, 39%) as colorless oil, the dicarbamate **7b** (712 mg, 22%) as a highly viscous oil, and the substrate **5** (210 mg, 19%). When only 0.25 equiv of CbyCl was used, the formation of **7b** could be successfully supressed. **6.** R_f = 0.15 (ether/pentane 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.36/1.42 (s, 6H), 1.46−1.56 (m, 8H), 1.76 (s, broad, 1H), 2.02−2.11 (m, 4H), 3.72 (s, 2H), 4.08 (d, J = 3.8 Hz, 2H), 4.52 (d, J = 6.0 Hz, 2H), 5.53−5.79 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.1/25.2/26.5, 28.3, 59.6/60.5, 63.5, 65.0, 76.0/76.3, 94.8/95.7, 124.9, 129.4, 132.3, 135.0, 153.0. IR (neat, cm^{-1}): 3435 (broad, OH), 1698 (C=O). MS (EI): m/z = 311 [3%, M$^+$], 296 [18%, (M − CH_3)$^+$]. Anal. Calcd for $C_{17}H_{29}NO_4$ (311.42): C, 65.57; H, 9.39; N, 4.50. Found: C, 65.55; H, 9.47; N, 4.69. **7b.** t_R = 25.3 min (HP 1). R_f = 0.44 (ether/pentane 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.36/1.42 (s, 12H), 1.46−1.59 (m, 14H), 2.07 (quin, J = 6.7 Hz, J = 7.1 Hz, 4H), 3.72 (s, 4H), 4.53 (d, J = 5.9 Hz, 4H), 5.58 (dt, J = 5.9, J = 15.2 Hz, 2H), 5.74 (dt, J = 15.2 Hz, J = 6.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (not all signals were visible) 24.1/25.3/26.5, 28.2, 31.4, 59.7/60.5, 65.0, 76.1/76.3, 94.8/95.8, 125.0, 135.0, 151.9/152.5. IR (neat, cm^{-1}) 1701 (C=O). MS (EI): m/z = 466 [3%, M$^+$], 294 [100%, (M − OCby)$^+$]. Anal. Calcd for $C_{28}H_{42}N_2O_6$ (466.61): C, 64.35; H, 9.07; N, 6.00. Found: C, 64.29; H, 8.83; N, 6.14.

(2*E*,7*E*)-9-Chloro-2,7-nonadienyl 2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carboxylate (7e). Dry LiCl (1.09 g, 25.6 mmol, 4.0 equiv) and **6** (2.00 g, 6.4 mmol, 1.0 equiv) were suspended in THF (50 mL) and cooled to −78 °C. After addition of *n*-BuLi (5.2 mL, 8.3 mmol, 1.3 equiv, 1.6 M solution in hexane), the reaction mixture was stirred for 10 min and methanesulfonyl chloride (1.47 g, 12.8 mmol, 2.0 equiv) was injected. The suspension was allowed to warm to room temperature overnight, and the reaction was quenched by addition of H_2O (10 mL). After separation of the layers, the aqueous phase was extracted with Et_2O (3 × 50 mL), the combined organic phases were dried ($MgSO_4$), and the solvents were evaporated. The crude product was purified by flash chromatography on silica gel (ether/pentane 1:10 → 2:5), yielding **7e** (1.55 g, 73%) as a colorless liquid. t_R = 19.5 min (HP1). R_f = 0.20 (ether/pentane 1:5). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.40−1.68 (m, 14H), 2.14 (q, J = 7.1 Hz, 4H), 3.79 (s, 2H), 4.08 (dd, J = 6.8 Hz, J = 0.8 Hz, 2H), 4.59 (d, J = 5.9 Hz, 2H), 5.61−5.74 (m, 2H), 5.75−5.87 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.1/25.3/26.5, 28.0, 31.2, 31.4, 45.2, 59.7/60.5, 65.0, 76.1/76.3, 94.8/95.8, 125.1, 126.4, 134.8, 135.4, 152.5. IR (neat, cm^{-1}): 1696 (C=O). MS (EI): m/z 329 [1%, M$^+$], 294 [100%, (M − Cl)$^+$]. Anal. Calcd for $C_{17}H_{28}ClNO_3$ (329.86): C, 61.90; H, 8.56; N, 4.25. Found: C, 61.91; H, 8.68; N, 4.38.

Typical Procedure for the Enantioselective Cyclization. [1*Z*,2(1*R*,2*R*)]-2-(2-Vinylcyclopentyl)ethenyl 2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carboxylate (8). The chloride **7e** (1.70 g, 5.10 mmol, 1.0 equiv) and (−)-sparteine (2.70 g, 11.3 mmol, 2.2 equiv) were dissolved in toluene (30 mL) and cooled to −90 °C. After slow addition of *n*-BuLi (7.1 mL, 11.3 mmol, 2.2 equiv, 1.6 M solution in hexane), the solution was stirred for 2 h. CH_3OH (3 mL) and NH_4Cl (aq, 3 mL) were added, and the reaction mixture was allowed to warm to room temperature The organic layer was separated, the aqueous phase was extracted with Et_2O (3 × 100 mL), the combined organic phases were dried over $MgSO_4$, and the solvents were removed in vacuo. The crude product was purified by flash chromatography on silica (ether/pentane 1:5), yielding 1.35 g (90%) of (*R*,*R*)-**8** as a colorless oil. The ee was determinded to 80% by GLC on a BetaDex 120 column. t_R = 16.6 min (HP1). t_R = 87.7 min, 89.8 min* (Beta-DexTM 120, 150 °C). R_f = 0.29 (ether/pentane 1:5). $[\alpha]^{20}_D$ = +53.8 (c = 1.00, $CHCl_3$, 80% ee). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.21−1.65 (m, 14H), 1.76−1.85 (m, 4H), 2.52−2.68 (m, 1H), 2.97−3.15 (m, 1H), 3.77 (s, 2 H), 4.70 (dd, J = 6.5 Hz, J = 9.6 Hz, 1H), 4.95−5.03 (m, 2H), 5.72−

(40) For several reactions of this masked carbonyl group see: Peschke, B. Ph.D. Thesis, 1991, University of Kiel. See also ref 23.

(41) An application of this concept in pyrrolidine synthesis could be accomplished recently: Deiters, A.; Wibbeling, B.; Hoppe, D. *Adv. Synth. Catal.* **2001**, *1*, 181−183.

(42) (a) Lin, H.-S.; Paquette, L. A. *Synth. Commun.* **1994**, *24*, 2503−2506. (b) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1871−1880.

(43) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1979**, *44*, 2923−2924.

5.84 (m, 1H), 6.96 (d, J = 6.5 Hz, 1H).^{13}C NMR (75 MHz, $CDCl_3$): δ 23.2/23.9/25.5, 26.7, 30.8, 32.3, 40.0, 48.0, 60.1/60.9, 76.1/76.4, 95.2/96.1, 112.7/112.8, 114.3, 133.9/134.0, 139.9, 149.3/150.1. IR (neat, cm^{-1}): 1716 (C=O). MS (EI): m/z 293 [0.5, M$^+$], 278 [4, (M − CH_3)$^+$]. Anal. Calcd for $C_{17}H_{27}NO_3$ (293.40): C, 69.59; H, 9.28; N, 4.77. Found: C, 69.19; H, 9.21; N, 4.79. In the other cyclization reactions, depicted in Table 1, 50−100 mg of **7e** were used.

[1*Z*,2(1*R*,2*R*)]-1-(Trimethylsilyl)-2-(2-vinylcyclopentyl)-ethenyl 2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carboxylate (13c). According to the typical procedure for the enantioselective cyclization−substitution sequence, **7e** (100 mg, 0.30 mmol, 1.0 equiv) was treated with (−)-sparteine (316 mg, 1.35 mmol, 4.5 equiv), *n*-BuLi (0.75 mL, 1.20 mmol, 4.0 equiv, 1.6 M solution in hexane), and TMSCl (163 mg, 1.50 mmol, 5.0 equiv) in toluene (4 mL) at −90 °C. The described workup procedure and a subsequent purification of the crude product by flash chromatography on silica gel (ether/pentane 1:5) furnished **13c** in 84% yield (92 mg) as a colorless liquid. The enantiomeric excess was determined to 80% after desilylation to **10**. **13c**. t_R = 20.3 min (HP1701). R_f = 0.60 (ether/pentane 1:5). $[\alpha]^{20}_D$ = +28.2 (c = 1.85, $CHCl_3$, 80% ee). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.12 (s, 9H), 1.42/1.56 (s, 12H), 1.50−1.93 (m, 6H), 2.54−2.64 (m, 1H), 2.90−3.05 (m, 1 H), 3.74 (s, 2H), 4.90−5.01 (m, 2H), 5.27 (d, 1 H, J = 9.3 Hz), 5.66−5.82 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −0.9, 23.2, 23.9/25.0/25.1/26.4, 30.6, 31.5, 40.2, 47.7, 59.6/60.5, 76.0/76.2, 94.7/95.7, 113.9, 131.5, 139.7, 151.0, 153.9. IR (neat, cm^{-1}): 1701 (C=O). MS (EI): m/z 365 [6%, M$^+$], 350 [30%, (M − CH_3)$^+$]. Anal. Calcd for $C_{20}H_{35}NO_3Si$ (365.58): C, 65.71; H, 9.65; N, 3.83. Found: C, 65.64; H, 9.96; N, 4.18.

Typical Procedure for the Lithiation and Substitution of 8. [1*Z*,2(1*R*,2*R*)]-1-(Trimethylstannyl)-2-(2-vinylcyclopentyl)ethenyl 2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carboxylate (13d). The cyclopentane **8** (38 mg, 0.13 mmol, 1.0 equiv, 70% ee) and TMEDA (18 mg, 0.16 mmol, 1.2 equiv) were dissolved in THF (3 mL) and cooled to −78 °C. *n*-BuLi (0.09 mL, 0.14 mmol, 1.1 equiv, 1.6 M solution in hexane) was injected slowly and after stirring for 1 h Me_3SnCl (0.26 mL, 0.26 mmol, 2.0 equiv, 1 M solution in hexane) was added. The reaction was stirred for further 90 min and was subsequently quenched by addition of CH_3OH (0.5 mL) and sat. NH_4Cl (aq, 0.5 mL). After warming up the reaction mixture to room temperature, it was poured into Et_2O (70 mL) and dried ($MgSO_4$), and the solvents were removed in vacuo. The crude product was purified by flash chromatography on silica gel (ether/pentane 1:10 → 1:5) furnishing **13d** (44 mg, 74%) as a colorless oil and 7 mg (18%) of the substrate **8**. t_R = 18.64 min (HP1). R_f = 0.57 (ether/pentane 2:5). $[\alpha]^{20}_D$ = +7.1 (c = 0.49, $CHCl_3$).[44] ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.13 (s, 9H), 1.42/1.56 (s, 12H), 1.50−1.93 (m, 6H), 2.54−2.67 (m, 1H), 3.08−3.25 (m, 1H), 3.75 (s, 2H), 4.81 (d, J = 6.4 Hz, 1H), 4.91−5.02 (m, 2H), 5.69−5.84 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −6.5, 23.3, 24.0/25.1/25.4/26.6/26.7, 30.8, 32.4, 41.0, 48.0, 59.9/60.8, 76.2, 95.0/96.0, 114.0, 126.4/126.6, 140.2, 151.5/152.2, 154.1. IR (neat, cm^{-1}): 1680 (C=O). MS (EI): m/z 442 [67, (M(^{120}Sn) − CH_3)$^+$], 440 [48, (M(^{118}Sn) − CH_3)$^+$], 438 [27, (M(^{116}Sn) − CH_3)$^+$]. Anal. Calcd for $C_{20}H_{35}NO_3Sn$ (456.19): C, 52.66; H, 7.73; N, 3.07. Found: C, 52.96; H, 8.12; N, 3.32.

(1*R*,2*R*)-1-(But-1-ynyl)-2-vinylcyclopentane (16). The cyclopentane **8** (300 mg, 1.02 mmol, 1.0 equiv, 80% ee) and TMEDA (357 mg, 3.07 mmol, 3.0 equiv) were dissolved in THF (8 mL) and cooled to −78 °C. Then *n*-BuLi (1.92 mL, 3.07 mmol, 3.0 equiv, 1.6 M solution in hexane) was added, and the reaction mixture was stirred for 90 min at −78 °C before it was warmed to room-temperature After stirring for 2.5 h at this temperature, the solution was cooled to 0 °C and treated with EtI (638 mg, 4.09 mmol, 4.0 equiv). The reaction mixture was stirred for 12 h at 40 °C and then cooled to ambient temperature, and sat. $NaHCO_3$ (aq, 2 mL) was injected. The layers were separated, the aqueous phase was extracted with pentane (4 × 20 mL), and the combined organic layers were dried with $MgSO_4$. After evaporation of the solvents, the crude product was purified by flash chromatography on silica gel (pentane). The alkyne **16** (98 mg, 65%) was obtained as a colorless, strongly smelling liquid. t_R = 9.0 min (HP1701). R_f = 0.29 (pentane). $[\alpha]^{20}_D$ = +24.2 (c = 1.43, pentane).[44] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.10 (t, J = 7.5 Hz, 3H), 1.15−1.90 (m, 6H); 2.15 (dq, J = 7.5 Hz, J = 2.4 Hz, 2H), 2.42−2.57 (m, 1H), 2.70−2.86 (m, 1H), 4.96−5.09 (m, 2H), 5.91−6.04 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.5, 14.1, 23.1, 27.7, 33.1, 36.1, 47.9, 80.6, 84.2, 114.0, 140.5. MS (EI): m/z 148 [2%, M$^+$], 133 [25%, (M − CH_3)$^+$]. HRMS calcd for $C_{11}H_{16}$ (148.24): 148.1251 (M$^+$). Found: 148.1214 (M$^+$).

(+)-3,4-Dihydromultifidene (17). Lindlar's catalyst (5% $Pd/CaCO_3$/Pb, 30 mg) was placed in a 50 mL round-bottom flask and was flushed three times with H_2. Then, pentane (25 mL), quinoline (2 drops), and **16** (100 mg, 0.68 mmol, 80% ee) were added, and the suspension was strirred under a balloon pressurized with hydrogen. After 3 h a complete conversion was detected by GLC. Filtration through silica gel and removal of the solvent in vacuo furnished the crude product, which was purified by flash chromatography on silica gel (pentane) yielding (+)-**17** (78 mg, 76%). The analytical data were identical with those reported in the literature.[21a] $[\alpha]^{20}_D$ = +50.0, $[\alpha]^{20}_D$ = +52.0 (c = 0.39, pentane, corrected to 100% ee).[44] These optical rotations agree well with the literature value: $[\alpha]^{20}_D$ = +55.8 (c = 2.56, pentane, 100% ee).[21a]

(1*R*,2*E*,7*E*)-9-Chloro-1-(trimethylsilyl)-nona-2,7-dienyl 2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carboxylate (18). The chloride **7e** (100 mg, 0.30 mmol, 1.0 equiv), (−)-sparteine (106 mg, 0.45 mmol, 1.5 equiv), and TMSCl (49 mg, 0.45 mmol, 1.5 equiv) were dissolved in toluene (4 mL), cooled to −78 °C, and treated with *n*-BuLi (0.29 mL. 0.45 mmol, 1.5 equiv, 1.6 M solution in hexane). After stirring for 90 min at this temperature, CH_3OH (0.5 mL) and sat. NH_4Cl (aq, 0.5 mL) were added, the reaction mixture was warmed to room temperature and was poured into Et_2O (70 mL). After drying with $MgSO_4$ and evaporation of the solvents, the crude product was purified by flash chromatography on silica gel (ether/pentane 1:5) yielding **18** as colorless liquid (85 mg, 70%). The enantiomeric excess was determined to 56% by a ^{1}H NMR shift experiment with **18** (20 mg) and $Eu(hfc)_3$ (40 mg) in $CDCl_3$ (0.7 mL). Here, the $Si(CH_3)_3$ signal splits to two new signals at δ_A 0.39 ppm* and δ_B 0.65 ppm. t_R = 20.9 min (HP1). R_f = 0.30 (ether/pentane 1:5). $[\alpha]^{20}_D$ = +11.7 (c = 0.73, $CHCl_3$, 56% ee). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.05 (s, 9H), 1.31−1.59 (m, 14H), 1.97−2.09 (m, 4H), 3.71 (s, 2H), 3.99 (dd, J = 6.9 Hz, J = 0.7 Hz, 2H), 5.03 (d, J = 5.0 Hz, 1H), 5.42−5.78 (m, 4H).^{13}C NMR (75 MHz, $CDCl_3$): δ −3.6, 24.1/24.3/25.4/26.6/26.9, 28.6, 31.3, 31.8, 45.3, 59.5/60.8, 70.3, 76.2/76.4, 94.7/96.0, 126.3, 127.7, 128.8, 135.7, 152.8. IR (neat, cm^{-1}): 1697 (C=O). MS (EI): m/z = 366 [40%, (M − Cl)$^+$]. Anal. Calcd for $C_{20}H_{36}ClNO_3Si$ (402.04): C, 59.75; H, 9.02; N, 3.48. Found: C, 59.65; H, 9.05; N, 3.74. **18** has also been synthesized by injection of TMSCl 15 min (22%, 46% ee) and 30 min (13%, 34% ee) after addition of *n*-BuLi.

(1*R*)-1-(Trimethylsilyl)nonyl 2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carboxylate ((*R*)-19). The silane **18** (47 mg, 0.12 mmol, 1.0 equiv, 56% ee), the hydrogenation catalyst (100 mg, 10% Pd on charcoal), and sodium acetate (100 mg, 1.20 mmol, 10.0 equiv) were suspended in CH_3OH (10 mL). After stirring for 6 h under a balloon pressurized with hydrogen, the reaction mixture was filtered over silica gel. Without purification (*R*)-**19** was obtained in 90% yield (40 mg). $[\alpha]^{20}_D$ = −3.9 (c = 0.26, $CHCl_3$, 55% op).

(1*S*)-1-Trimethylsilyl-nonyl 2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carboxylate ((*S*)-19). The carbamate **21** (300 mg, 1.0 mmol, 1.0 equiv) and (−)-sparteine (469 mg, 2.0 mmol, 2.0 equiv) were dissolved in Et_2O and cooled to −78 °C. After slowly addition of *s*-BuLi (1.3 mL, 1.50 mmol, 1.5 equiv, 1.15 M solution in hexane/cyclohexane) and stirring for 4 h at this temperature, TMSCl (326 mg, 3.0 mmol, 3.0 equiv) was injected and the reaction mixture was allowed to warm to room temperature overnight. Sat. NH_4Cl (aq, 3 mL) was added, the layers were separated, and the aqueous phase was extracted

(44) The enantiomeric excess has not been determined; since **12·9** is configuratively stable, the enantiomeric excess in the substitution product should be the same like in the substrate **8**.

with ether (3 × 30 mL). The combined organic phases were dried with $MgSO_4$, and the solvents were removed in vacuo. Purification of the crude product by flash chromatography on silica gel (ether/pentane 1:10 → 1:5) yielded **19** (297 mg, 80%) as a colorless liquid. t_R = 21.0 min (HP1701). R_f = 0.47 (ether/pentane 1:5). $[\alpha]^{20}_D$ = +7.07 (*c* = 2.08, $CHCl_3$, 95% ee). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.04 (s, 9H), 0.86 (t, *J* = 6.8 Hz, 3 H), 1.20−1.65 (m, 26H), 3.70 (s, 2H), 4.68 (dd, *J* = 10.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −3.3, 14.0, 22.6, 24.3/25.5/26.6, 27.1, 29.2, 29.5, 31.2, 31.8, 59.4/60.5, 68.8, 76.2, 94.6/95.9, 152.7. IR (neat, cm^{-1}): 1693 (C=O). MS (EI): *m*/*z* = 371 [2%, M^+], 356 [9%, $(M - CH_3)^+$]. Anal. Calcd for $C_{20}H_{41}NO_3Si$ (371.63): C, 64.64; H, 11.12; N, 3.77. Found: C, 64.63; H, 11.18; N, 4.04.

(1*R*,2*E*,7*E*)-9-Chloro-1-(trimethylstannyl)nona-2,7-dienyl 2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carboxylate ((*R*)-22). Enantioselective Synthesis. 7e (200 mg, 0.61 mmol, 1.0 equiv) and (−)-sparteine (256 mg, 1.09 mmol, 1.8 equiv) were dissolved in toluene (10 mL), cooled to −78 °C, and treated with *n*-BuLi (0.57 mL, 0.91 mmol, 1.5 equiv, 1.6 M solution in hexane). After 5 min $(CH_3)_3SnCl$ (1.52 mL, 1.52 mmol, 2.5 equiv, 1 M solution in hexane) was injected, and after 30 min the reaction was quenched with CH_3OH (1 mL) and sat. NH_4Cl (aq, 2 mL). The layers were separated, the aqueous phase was extracted three times with ether (20 mL), the combined organic phases were dried ($MgSO_4$), and the solvents were removed in vacuo. After purification of the crude product by flash chromatography on silica gel (ether/pentane 1:10 → 1:5), (*R*)-**22** was obtained in 16% yield (49 mg). Other isolated compounds were **13d** (19 mg, 7%), **8** (95 mg, 53%), and **7e** (36 mg, 18%). The enantiomeric excess of **22** was determined to 48% by an ^{1}H NMR shift experiment with **22** (20 mg) and Eu(hfc)$_3$ (40 mg) in $CDCl_3$ (0.7 mL). Here, the Sn-$(CH_3)_3$ signal splits up in two new signals at δ_A 0.44 ppm* and δ_B 0.65 ppm. $[\alpha]^{20}_D$ = −9.5 (*c* = 0.40, $CHCl_3$, 48% ee).

Typical Procedure for a Cyclization by Lithiodestannylation. The carbamate *rac*-**22** (20 mg, 0.04 mmol, 1.0 equiv) and (−)-sparteine (19 mg, 0.08 mmol, 2.0 equiv) were dissolved in toluene (3 mL) and cooled to −78 °C. Then, *n*-BuLi was added dropwise (0.05 mL, 0.08 mmol, 2.0 equiv, 1.6 M solution in hexane), and the reaction mixture was stirred for 90 min at this temperature. After addition of CH_3OH (0.2 mL) and sat. NH_4Cl (aq, 0.2 mL), the reaction mixture was warmed to room temperature, diluted with Et_2O (20 mL), and dried with $MgSO_4$. The crude product, obtained after evaporation of the solvents, was purified by flash-chromatography on silica gel (ether/pentane 1:5) yielding (*R*,*R*)-**8** (11 mg, 94%, er = 57:43, 14% ee).

Lithiodestannylation of the Enantioenriched Allyltin Compound (*R*)-22. TMEDA as Ligand. According to the typical procedure for the lithiodestannylation (*R*)-**22** (15 mg, 0.03 mmol, 1.0 equiv, 48% ee), TMEDA (7 mg, 0.06 mmol, 2.0 equiv), and *n*-BuLi (0.04 mL, 0.06 mmol, 2.0 equiv, 1.6 M solution in hexane) were reacted in toluene (2 mL) at −78 °C for 1 h. After workup and purification of the crude product by flash chromatography on silica gel (ether/pentane 1:5) *rac*-**8** (8 mg, 90%) was obtained. **(−)-Sparteine as Ligand.** According to the typical procedure for lithiodestannylation, (*R*)-**22** (15 mg, 0.03 mmol, 1.0 equiv, 48% ee), (−)-sparteine (21 mg, 0.09 mmol, 3.0 equiv), and *n*-BuLi (0.04 mL, 0.06 mmol, 2.0 equiv, 1.6 M solution in hexane) were reacted in toluene (2 mL) at −78 °C for 1 h. After workup and purification of the crude product by flash chromatography on silica gel (ether/pentane 1:5) (*S*,*S*)-**8** (9 mg, 100%. 26% ee) was obtained.

Lithiation and Cyclization of (*R*)-18. The allylsilane (*R*)-**18** (65 mg, 0.16 mmol, 1.0 equiv, 56% ee) and TMEDA (38 mg, 0.32 mmol, 2.0 equiv) were dissolved in Et_2O (3 mL) and cooled to −78 °C. After dropwise addition of *n*-BuLi (0.20 mL, 0.32 mmol, 2.0 equiv), the reaction mixture was stirred for 8.5 h. Then CH_3OH (0.5 mL) and sat. NH_4Cl (0.5 mL) were added, the reaction mixture was warmed to room temperature, and it was poured into Et_2O (70 mL) and was dried with $MgSO_4$. After evaporation of the solvents, the crude product was purified by flash chromatography on silica gel (ether/pentane 1:10 → 1:6) yielding **13c** (24 mg, 40%) and **7e** (24 mg, 39%). The enantiomeric excess of **13c** (60% ee) was determined by GLC on a BetaDex 120TM column after desilylation to **8**. A comparison with another sample of **8** showed the (*R*,*R*)-configuration for **13c**.

Desilylation of the Substituted Cyclopentane 13c. The vinylsilane **13c** (33 mg, 0.09 mmol, 1.0 equiv) was dissolved in THF (2 mL) and TBAF (0.27 mL, 0.27 mmol, 3.0 equiv, 1 M solution in THF) was added. The reaction mixture has been stirred for 90 min and was quenched by addition of sat. NH_4Cl (aq, 2 mL). The layers were separated, the aqueous phase was extracted with Et_2O (3 × 10 mL), the combined organic layers were dried with $MgSO_4$, and the solvents were removed in vacuo. Purification of the crude product by flash chromatography on silica gel (ether/pentane 1:10) yielded **8** (23 mg, 87%).

NMR Experiment of the Cyclization. In a flame-dried NMR tube, TMEDA (11 mg, 0.18 mmol, 2.3 equiv) and **7e** (20 mg, 0.08 mmol, 1.0 equiv) were dissolved in THF-d_8 (0.7 mL), and cooled to −78 °C. *n*-BuLi (0.11 mL, 0.18 mmol, 2.3 equiv, 1.6 M solution in hexane) was added dropwise, the reaction mixture was shaken, and the NMR tube was immediately put into the NMR spectrometer (360 MHz), which had been cooled to −80 °C. Identical ^{1}H NMR spectra were measured in intervals of 10 min, showing the typical signals of **12**, as described in the discussion part. After adding methanol (0.1 mL) at −78 °C, the ^{1}H NMR spectrum was identical with this of **8**.

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Supporting Information Available: Additional prescriptions and characterizations; ^{1}H NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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