Chiral organometallic reagents. Part XXIII.[1] On the stereochemistry of the carbolithiation reaction of vinyl sulfides

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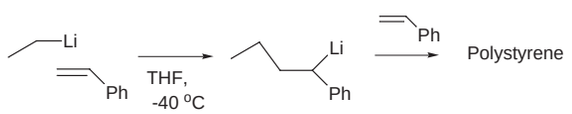
The intramolecular carbolithiation of vinyl sulfides at −105 °C in THF has been found to be stereospecific regarding the formation of the new carbon–carbon bond and non stereospecific regarding the formation of the new carbon–lithium bond. The resulting α-durylthioalkyllithium compounds are configurationally stable at −105 °C and epimerize at −90 °C.

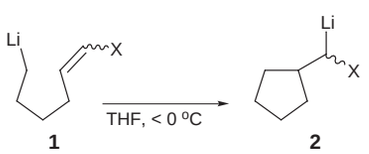
Introduction

The carbolithiation reaction of alkenes, *i.e.* the addition of an organolithium compound across a C–C double bond[2] is the key step in the anionic polymerisation of alkenes (Scheme 1).[3]



Scheme 1

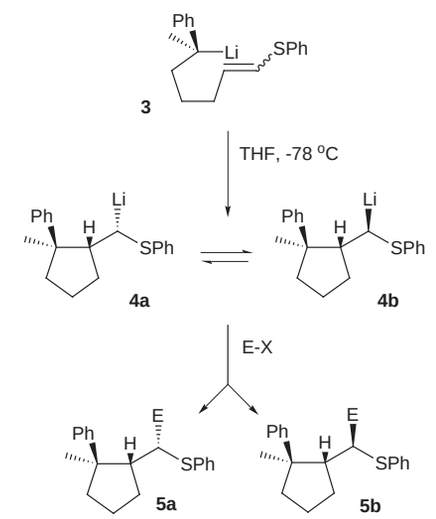
The intramolecular version had been studied as a route to carbo- and heterocycles with a defined substitution pattern. For a review see refs. 4–7. The most simple intramolecular carbolithiation reaction, that of **1** (X = H) to give **2** proceeds in ether as solvent at +23 °C with a half-life of minutes (Scheme 2).[8,9]



Scheme 2

Both intra- and intermolecular carbolithiation reactions are facilitated by phenyl,[3,9,10] silicon,[9,11] sulfur,[12,13] chlorine,[14] or seleno[15] substituents X in **1** which stabilize a negative charge. But stabilization of charge by a heteroatom is not the only decisive factor: the lithium cation as well plays a key role in the carbometallation of alkenes, because cyclization does not occur with the alkali metal analogs of **1** (Na, K, Rb, Cs).[16] An interaction of the lithium with the olefinic p bond[17] has been postulated.[9] On the other hand, solvation of the lithium by basic additives such as TMEDA has been noted to facilitate the carbolithiation reaction.[6,7,9,13,14,18,19] Intramolecular solvation of the lithium, *i.e.* complexation assisted carbolithiation allows the carbolithiation reaction to proceed under much milder conditions than in the absence of such assisting substituents.[5,19,20] This suggests that detachment of the lithium cation from the migration origin contributes to the activation barrier. In consequence, carbolithiation reactions may be realized at temperatures as low as −110 °C, if the lithium atom at the migration origin is in a benzylic or allylic position,[21] a situation that merges with the metallo–ene reaction.[22]

The ability to carry out carbolithiation reactions at low temperatures becomes important in the following context: carbolithiation in a substrate **1** in which X is not a hydrogen atom creates a new stereogenic center, the lithium bearing carbon atom. The issue of the stereochemistry of the carbolithiation reaction had not been addressed before, since so far the organolithium compounds generated were found to be configurationally labile at the temperatures required to effect the carbolithiation reaction. A typical case is the intramolecular carbolithiation of **3**, which leads predominantly to the cyclized compound **4**.[23] On trapping with various electrophiles the diastereomer ratio of the α-substituted alkylsulfides **5** depends on the nature of the electrophile, an indication that a Curtin–Hammett situation prevails, *i.e.* that epimerization of the organolithium compound **4** is more rapid than trapping to give **5** (Scheme 3). Therefore, any information regarding the stereochemical course of the carbolithiation reaction is lost.

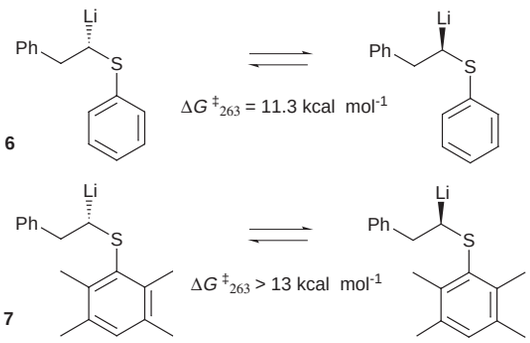


E-X =		
CD_3OD	90	10
CO_2	85	15
CH_3I	72	28
CH_2=CH-CH_2Br	60	40

Scheme 3

This result is in line with other observations regarding the configurational lability of α-arylthioalkyllithium compounds.[24]

In fact, we had determined the racemization barrier for the lithium compound **6** in THF–cyclohexane to be 11.3 kcal mol^{-1} at −10 °C, which corresponds to a half-life for enantiomerization of *ca*. 1 s at −78 °C.[25] We noted however, that the barrier to racemization is significantly higher for the α-durylthio-derivative **7**† (Scheme 4).[25]

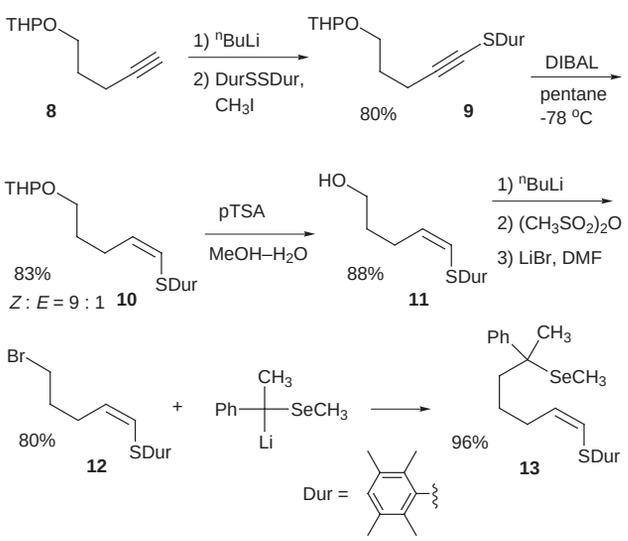


Scheme 4

In this case, this barrier is high enough to render organolithium compounds of type **7** configurationally stable at temperatures of −105 °C, this would create a chance to determine the stereochemistry of the carbolithiation reaction. We report here the details of a study on the intramolecular carbolithiation of **20** and **29**, the *S*-duryl analogs of **3**. For a preliminary communication see ref. 26.

Preparation of starting materials

In order to reveal the details of the carbolithiation process compounds **13** and **19** with both a *Z*- and an *E*-geometry of the vinyl sulfide bond were desired. Synthesis in the *Z*-series commenced with the protected pentynol **8** (Scheme 5).[27] Lithiation



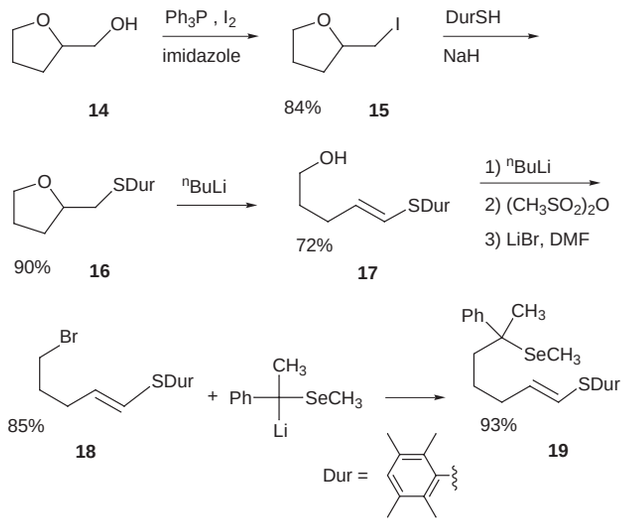
Scheme 5

and quenching with *S*-methylated diduryl disulfide[28] furnished **9** in 80% yield. This procedure avoids the formation of durylthiolate, which might add to the alkyne **9** formed.

Reduction of the alkyne **9** with DIBAL gave the vinyl sulfide **10** with a 9:1 *Z*:*E* selectivity. The THP group was removed and the alcohol **11** was converted to the bromo compound **12**. Finally, the methylselenobenzyl moiety was incorporated by nucleophilic substitution.[23] The product **13** had a 87:13 *Z*:*E* ratio.

† Duryl = 2,3,5,6-tetramethylphenyl.

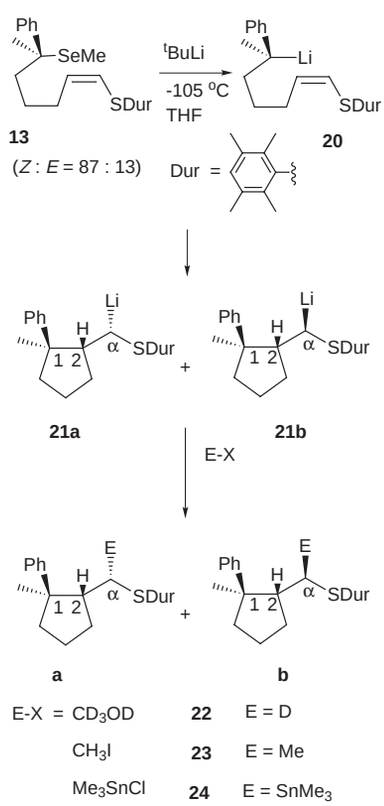
The synthesis in the *E*-series started with the tetrahydrofurfuryl alcohol **14**. This was converted *via* the iodide **15** to the duryl thioether **16**. Butyllithium initiated the ring opening[23,29] to give the vinyl sulfide **17** with a >98% *E*-selectivity (Scheme 6). Conversion to the *E*-durylthio compound **19** was effected as described for the *Z*-series.



Scheme 6

The carbolithiation reaction

The lithium compound **20** may be generated by a selenium–lithium exchange reaction[23] on **13**. This exchange may be effected at −105 °C in THF by the addition of **13** to precooled *tert*-butyllithium in pentane in a two compartment reaction vessel.[30] After quenching with precooled CD_3OD in THF after 10 minutes the sulfides **22** could be isolated in 71% yield (Scheme 7).

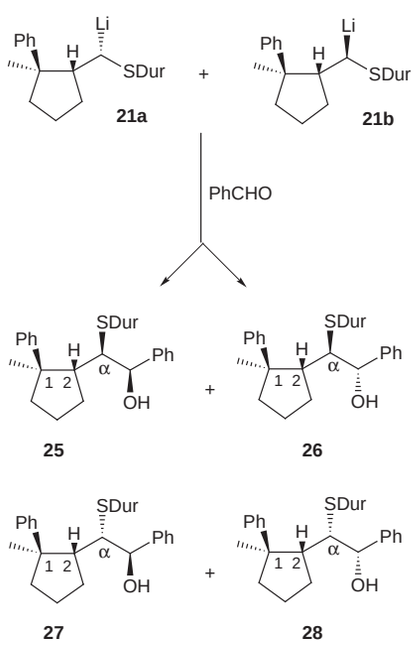


Scheme 7

^{2}D-NMR revealed a diastereomer ratio of 88:12. Both diastereomers of **22** have[23] the same relative configuration at C-1 and C-2 as indicated (*cf*. the crystal structures of **23b** and **24a** reported below). The coupling constants between the protons at C-α and the proton at C-2 suggest that the major isomer (2.4 Hz) is **22a** and the minor isomer (11.1 Hz) **22b**. MM3 calculations with MACROMODEL[31] and Boltzmann averaging over the local conformer population produce coupling constants of 2.9 and 11.1 Hz for **22a** and **22b**. These calculations support the assumption that **22** should populate predominantly a conformation in which the sulfur is antiperiplanar to the quaternary center at C-1, *i.e.* Φ C-1–C-2–C-α–S ≈ 180 °C.

When the lithium compounds **21** were quenched after 30 min by addition of CH_3I a 90:10 mixture of the methylated compounds **23** was obtained. The minor diastereomer **23b** could be obtained in crystalline form, allowing the assignment of the relative configuration by X-ray structure analysis. After generation of the lithium compounds **21** in THF + 4 equivalents of TMEDA at −108 °C quenching with Me_3SnCl after 20 min resulted in 87% of stannylated compound **24**. NMR-analysis indicated a 85:15 ratio of diastereomers. The major diastereomer **24a** was obtained in crystalline form and its structure was confirmed by X-ray structure analysis.

These results verify that **20** cyclizes in THF in such a manner that the phenyl at C-1 and the hydrogen atom at C-2 are in a *cis*-arrangement on the cyclopentane ring, as inferred from previous studies.[23] Finally, the organolithium compounds **21** have also been trapped by addition to benzaldehyde after 30 min at −106 °C, resulting in a 30:60:5:5 mixture of the adducts **25**–**28** (Scheme 8).

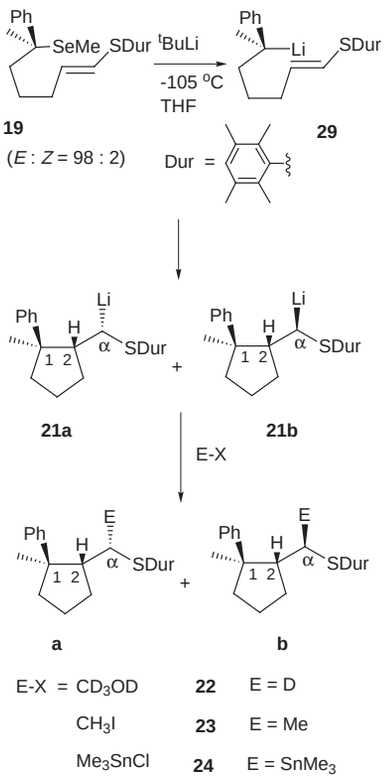


Scheme 8

The structures of the major adducts **25** and **26** were confirmed by X-ray structural analysis. No assignment was made in the cases of **27** and **28**.

Stereochemistry of the carbolithiation reaction

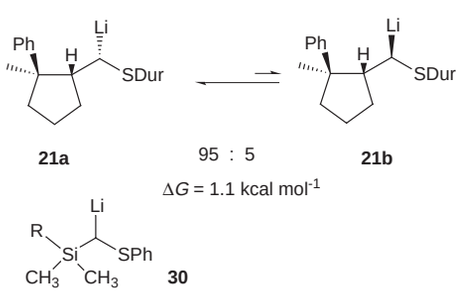
Prima facie all of the above results can be interpreted in terms of a concerted *syn*-addition of the carbon–lithium bond in **20** (*Z*:*E* = 87:13) to give the lithium compounds **21a** and **21b** in a *ca*. 87:13. The situation is, however, more complex. This became evident on studying the carbolithiation of the corresponding *E*-isomer **29** (Scheme 9).



Scheme 9

The lithium compound **29** was generated from the selenoether **19** (*E*:*Z* = 98:2). Quenching with CD_3OD furnished the thioethers **22** in a 59:41 ratio. The same diastereomer ratio was recorded after quenching of **21** with methyl iodide or trimethyltin chloride. This led us to an extensive series of experiments in order to clarify the stereochemistry of the carbolithiation reaction. Selected examples are given in Table 1.

Entries 1 and 2, as well as 3–7 show that the ratio of diastereomeric deuteration products **22** is independent of the time between the initiation of the carbolithiation and trapping. Since the *Z*-(**20**) and the *E*-(**29**) starting materials give rise to different product ratios, the formation of the products is clearly kinetically controlled and reflects the stereochemistry of the carbolithiation process. An equilibration between **21a** and **21b** becomes possible at temperatures above −100 °C (Scheme 10), *cf*. Table 1, the entries 20–27.



Scheme 10

The equilibrium between **21a** and **21b** is rapidly established at −78 °C (Table 1, entries 20–23) and lies 95:5 on the side of **21a**. The equilibration may be followed at −90 °C by quenching with CD_3OD at different time intervals. The half-life for epimerisation at −90 °C in THF is 20 min ($k = 5.4 \pm 0.2 \times 10^{-4}$ s^{-1}). Practically the same rate constant ($5.2 \pm 0.1 \times 10^{-4}$ s^{-1}) is obtained when **21b** is generated by lithiodestannylation of **24b** with 3 equivalents of methyllithium in THF at −90 °C, followed by quenching with CD_3OD, *cf*. Fig. 1.

Equilibration of **21a** and **21b** is facilitated by the addition of

Table 1

Entry	−*T*/°C	Solvent	Substrate *E*:*Z*	Electrophile	Time/min	Products **22**–**24** Yield (%)	**a**:**b**
1	−105	THF	13:87	CD_3OD	10		88:12
2	−105	THF	13:87	CD_3OD	60	71	88:12
3	−107	THF	98:2	CD_3OD	5.5		41:59
4	−107	THF	98:2	CD_3OD	10		41:59
5	−104	THF	98:2	CD_3OD	20		41:59
6	−105	THF	98:2	CD_3OD	30	70	41:59
7	−105	THF	98:2	CD_3OD	60		44:56
8	−106	THF	98:2	CD_3OD	15 + 30		41:59
9	−106	THF	13:87	CH_3I	30		90:10
10	−104	THF	98:2	CH_3I	20		43:57
11	−108	THF + 4 TMEDA	15:85	Me_3SnCl	20	70	85:15
12	−106	THF	94:6	Me_3SnCl	20	88	35:65
13	−106	THF + 4 TMEDA	94:6	Me_3SnCl	20	37	38:62
14	−106	THF + 4 HMPT	94:6	Me_3SnCl	10	46	33:67
15	−107	THF + 4 HMPT	15:85	CD_3OD	15	42	86:14
16	−104	THF + 1 HMPT	98:2	CD_3OD	20	67	41:59
17	−105	THF + 4 HMPT	98:2	CD_3OD	5		36:64
18	−103	Pentane + 1 THF	98:2	CD_3OD	50	82	42:58
19	−102	Pentane + 4 THF	98:2	CD_3OD	60	70	39:61
20	−78	THF	13:87	CD_3OD	90		94:6
21	−78	THF	13:87	CD_3OD	840	65	95:5
22	−78	THF	13:87	CH_3I	90		94:6
23	−78	THF	98:2	CD_3OD	90	82	94:6
24	−90	THF	98:2	CD_3OD	5		47:53
25	−90	THF	98:2	CD_3OD	10		53:47
26	−90	THF	98:2	CD_3OD	20		67:33
27	−90	THF	98:2	CD_3OD	30		76:24

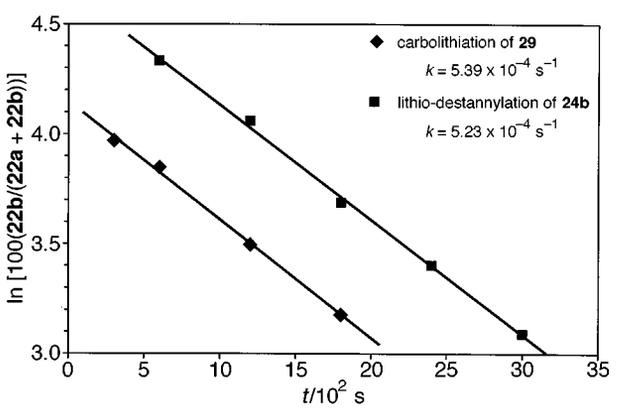


Fig. 1 Equilibration of **21a** ⟸⟹ **21b** when generated from either **29** or **24b** at −90 °C in THF.

4 equivalents of HMPT, such that it occurs already slowly at −108 °C with a half-life of *ca.* 2 h ($k = 9.2 \pm 1.0 \times 10^{-5}$ s^{-1}). Reich reported several cases in which addition of HMPT raised the enantiomerization barrier of the lithium compound **30**.[32] It is therefore not obvious why HMPT should lower the epimerization barrier of α-thioalkyllithium compounds **21**, a barrier which is probably governed by a rotation barrier in the case of the α-durylthio compound.[25]

Coming back to the kinetically controlled carbolithiation: its stereochemical outcome does not—or only to an insignificant extent—depend on the presence of HMPT (Table 1, entries 14–17) or TMEDA (entries 11–13). The "standard" results were obtained even when the reaction was run in pentane with as little as one equivalent of THF present (entries 18, 19).

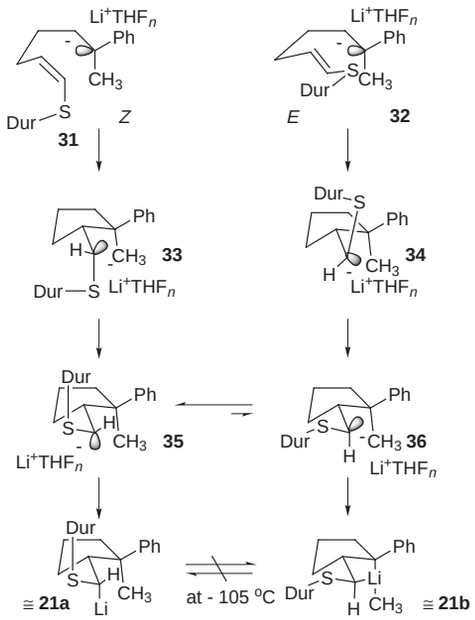
Discussion

In an attempt to integrate the puzzling set of data into a consistent picture, we assume that the carbolithiation is initiated by detachment of the lithium cation from the migration origin, *i.e.* by formation of a contact ion pair **31** from **20** and **32** from **29** (Scheme 11).

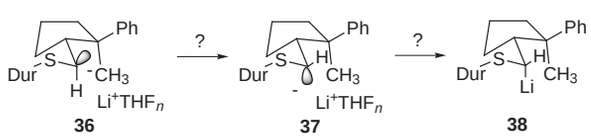
Carbon–carbon bond formation is attained most readily from a conformation in which the *S*-duryl bond is parallel to the π-lobes of the double bond. This facilitates stabilization of the incipient negative charge at C_α by hyperconjugation into the σ*-orbital of the *S*-duryl bond, *cf.* the formation of **33** from **31** and of **34** from **32**. The anions **33** and **34** are thereby generated in a high energy conformation, in which the C_α–S bond and the C-1–methyl or C-1–phenyl bond have a *syn*-pentane interaction. The anion **33** should therefore relax by rotation around the C-2–C-α bond into the more stable conformation **35**. Likewise anion **34** should relax to the conformation **36**. Association of the lithium cation should then give **21a** from **35** and **21b** from **36**. While the lithium compounds **21** do not interconvert under the reaction conditions, a stereochemical leak must occur before the lithium compounds **21** are generated.

A scenario to be discussed is a stereo-equilibration between the contact ion pairs **35** and **36**, an idea we initially discounted.‡ This equilibrium involves both inversion of con-

‡ For a while[26] we entertained the notion, that the two distinct ion pairs **34** and **36** do not interconvert under the low temperature reaction conditions. Inversion at the carbanionic C_α atom should nevertheless be fast.[33] The ensuing collapse of the contact ion pairs **35** and **36** would have to be non stereospecific in this scenario to account for the lack of stereoretention in the overall carbolithiation reaction. This somehow implies, that the lithium compound **21a** would be generated in two different rotameric states, **21a** and **38** respectively, depending on whether it is formed from **35** (to give **21a**) or after inversion at carbon from **33** to **37** (to give **38**) (Scheme 12). **38** and **21a** differ with respect to the conformation of the C_α–S bond and should interconvert only slowly at the reaction temperature on account on the high barrier to rotation about this bond.[25] If there were two atropoisomeric lithium compounds **21a** and **38** involved, they would be expected to show a different simple diastereoselectivity on reaction with an aldehyde. This notion was the reason to carry out the trapping experiments with benzaldehyde, which led to the four adducts **25**–**28**. That is, we wanted to use the simple diastereoselectivity, the *syn–anti* ratio **25**:**26** as the fingerprint of the species that is being trapped by benzaldehyde. The product ratio **25**/**26** obtained starting from either the *Z*-series (**13**) or from the *E*-series (**19**) turned out to be identical (33:67 in both cases)! This rendered the notion of the formation of two distinct atropoisomeric lithium compounds **21a** from **20** and **38** from **29** unlikely.



Scheme 11



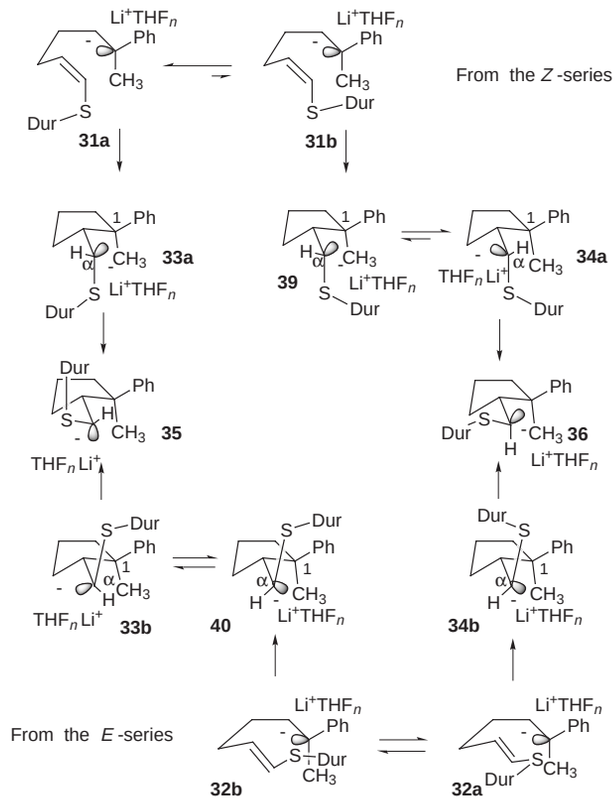
Scheme 12

figuration at the carbanion carbon *and* rotation about the C_α–S bond,[25] the latter being the slow step. This notion implies that stereo-equilibration is more facile in the contact ion pairs **35** and **36** than in the lithium compounds **21a** and **21b**, a situation we considered as unlikely earlier.[25] However, this notion leads to a consistent interpretation of the carbolithiation results presented here: the finding that the equilibration between **21a** and **21b** becomes more rapid in the presence of HMPT, suggests that conversion of **21a** back to the contact ion pair **35** and that of **21b** to the contact pair **36** leads to epimerization. This implies that equilibration at the contact ion pair stage (**35**, **36**) is more rapid than that of the lithium compounds **21**.

The carbolithiation reaction of the lithio compounds **20** and **29** is not under thermodynamic control, because the thermodynamic ratio of the cyclized products **21a**:**21b** = 95:5 is not reached. The overall stereochemistry of the carbolithiation process in the cyclization of either the *Z*-(**20**) or the *E*-(**29**) lithium compounds depends rather on a competition between the collapse of the ion pairs **35** and **36** to the lithium compounds **21** and an equilibration between the ion pairs **35** and **36**. In the case that ion pair collapse would be much faster than equilibration, the carbolithiation should be stereospecific, *i.e.* **20** would give **21a** and **29** would give **21b**. In the case that ion pair collapse would be much slower than equilibration between the ion pairs **35** and **36**, the carbolithiation would be stereoconvergent, giving the same diastereomer ratio of **21a** to **21b** irrespective of the starting material **20** or **29**.

The fact that the result of this competition, *i.e.* the stereoselectivity attained is essentially independent of the presence or absence of HMPT and related lithium coordinating agents, suggests that the competition involves the contact ion pairs rather than solvent separated ion pairs. Apparently the negative charge in the anions **35** and **36** is mostly localized. Therefore, the coulombic force which would be involved in the stoichiometric formation of a solvent separated ion pair is too large to be overcome by a low concentration of HMPT under the reaction conditions.

Another scenario that does not require an equilibration between the stereoisomeric ion pairs **35** and **36**, can also account for the observations. Here, the assumption is made that as soon as there is an α-durylthiocarbanion formed, there is no longer a >60° rotation possible about the C_α–S bond. This scenario then connects the stereochemical leakage of the carbolithiation reaction directly with the carbon–carbon bond forming step: as illustrated for the *Z*-series, the starting anion **31** may react from two conformers **31a** and **31b** regarding the C_α–S bond, a Curtin–Hamett situation (Scheme 13). Carbon–



Scheme 13

carbon bond formation generates then the anions **33a** and **39**. Anion **33a** has the more stable *anti*-arrangement of the carbanion lone pair and the *S*-duryl bond. It relaxes to **35** by rotation about the C_2–C_α bond as discussed before. Anion **39** with a *syn*-arrangement of the lone pair and the *S*-duryl bond rapidly inverts to the more stable stereoisomer **34a** which then leads by rotation of the C_α–C_2 bond to **36**. This means that the stereoselectivity of the carbolithiation reaction would be determined in the carbon–carbon bond-forming step by selecting the rotamers **31a** and **31b**. The stereoselectivity obtained would imply the transformation of **31a** to **33a** to be more favored than that of **31b** into **39**.

For the *E*-series a similar argument involves the rotamers (with respect to the C_α–S bond) **32a** and **32b**. Selection in the carbon–carbon bond forming process leads to the anions **34b** and **40**. The *syn* (lone pair/*S*-duryl bond) anion **40** inverts to the more stable **33b** which gives eventually **35**. The *anti* (lone pair/S-duryl bond) anion **34b** leads to **36**. The observed stereoselectivity would then require a significant contribution of the reaction *via* **32b** to **40**. The steric destabilisation in the process can be viewed as being smaller than in the corresponding conversion of **31b** into **39**. This scenario gives a picture which is consistent with the experimental results, but as in all mechanistic studies it cannot be considered as established. An equilibration between the ion pairs **35** and **36** as in the first scenario would have to be postulated anyway at higher temperatures to account for the epimerization and the acceleration of the latter process by HMPT.

Even if we have not found experiments by which these two

scenarios can be distinguished, we have shown that the intramolecular carbolithiation of a vinyl sulfide is not a synchronous *syn*-addition. Rather the formation of the carbon–carbon bond precedes the formation of the carbon–lithium bond. Epimerization occurs at the stage of an intermediate, which is energetically higher than the resulting organolithium compound **21**. The discussion is tentative regarding the nature of this intermediate (solvent separated ion pair or contact ion pair). A related situation has been encountered by Bickelhaupt [35] during the formation of Grignard reagents. The insights into the mechanism of the carbolithiation reaction have been gained by changing from an α-*phenyl*thioalkyllithium moiety **4** to an α-*duryl*thioalkyllithium one (**21**), the epimerization barrier of which was found to be higher by *ca*. 2 kcal mol^{-1}.

Experimental

All temperatures quoted are uncorrected. Temperatures around −100 °C were determined with a GTH 215 precision digital thermometer of Fa. Greisinger, Regenstauf, Germany. ^{1}H NMR, ^{13}C NMR: Bruker ARX-200, AC-300, AMX-500. HRMS: Varian MAT-95S. Boiling range of petroleum ether: 40–60 °C. pH 7 buffer: mixture of sat. aqueous $NaHCO_3$ and sat. aqueous NH_4Cl solutions (1/1 v/v). Flash chromatography: Silica gel Si60 (40–63 μm; E. Merck AG, Darmstadt). Analytical gas chromatography: Siemens Sichromat 3 with a 30 m × 0.3 mm quartz capillary column with DB 5, He (1 bar).

1. 1-(2,3,5,6-Tetramethylphenylthio)-5-(tetrahydro-2*H*-pyran-2-yloxy)pent-1-yne (9)

A 1.57 M solution of n-butyllithium in hexane (29.5 mL, 46.3 mmol) was added to a solution of 5-(tetrahydro-2*H*-pyran-2-yloxy)pent-1-yne (**8**) (7.58 g, 45.1 mmol) in THF (250 mL) at 0 °C. After 60 min a mixture of di(2,3,5,6-tetramethylphenyl) disulfide (18.7 g, 56.6 mmol) and methyl iodide (3.50 mL, 56.2 mmol) in THF (200 mL), aged for 90 min,[28] was added within 2 h. The resulting mixture was stirred for 12 h and treated with sat. aqueous NH_4Cl solution (50 mL) and water (150 mL). The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 100 mL). The combined organic phases were washed with brine (100 mL), dried with Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (petroleum ether–*tert*-butyl methyl ether = 100 : 1 to 50 : 1, 1% NEt_3) to give the thioether **9** (12.0 g, 36.0 mmol, 80%): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.44–1.85 (m, 8H), 2.25 (s, 6H), 2.38 (t, J = 7.0 Hz, 2H), 2.51 (s, 6H), 3.43 (ddd, J = 9.8, 6.2, 6.2 Hz, 1H), 3.38–3.50 (m, 1H), 3.78 (ddd, J = 9.8, 6.3, 6.3 Hz, 1H), 3.73–3.88 (m, 1H), 4.52–4.58 (m, 1H), 6.97 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.9, 18.2, 19.4, 20.7, 25.4, 28.9, 30.6, 62.0, 65.8, 68.7, 90.9, 98.7, 131.0, 132.5, 134.5, 137.5. $C_{20}H_{28}O_2S$ (332.5): calcd. C, 72.24; H, 8.49. Found: C, 72.01, H, 8.46%.

2. (1*Z*)-1-(2,3,5,6-Tetramethylphenylthio)-5-(tetrahydro-2*H*-pyran-2-yloxy)pent-1-ene (10)

A solution of DIBAL in petroleum ether (1.00 M, 30.0 mL, 30.0 mmol) was added at −18 °C within 100 min to a solution of the alkyne **9** (5.96 g, 17.9 mmol) in petroleum ether (150 mL). The mixture was stirred for 1 h at 0 °C and for 21 h at room temperature and transferred to NaOH solution (2.0 M, 300 mL). The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 200 mL). The combined organic phases were dried with Na_2SO_4, concentrated *in vacuo* and purified by flash chromatography (pentane–*tert*-butyl methyl ether = 30 : 1, 2% NEt_3) to give 5.00 g (14.9 mmol, 83%) of the vinyl sulfide **10** (E : Z = 10 : 90 by ^{1}H NMR). **10**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49–1.93 (m, 6H), 1.79 (ddt, all J = 7.0 Hz, 2H), 2.25 (s, 6H), 2.30–2.43 (m, 2H), 2.45 (s, 6H), 3.47 (ddd, J = 9.7, 6.7, 6.7 Hz, 1H), 3.46–3.58 (m, 1H), 3.83 (ddd, J = 9.7, 6.7, 6.7 Hz, 1H), 3.85–3.96 (m, 1H), 4.60–4.66 (m, 1H), 5.57 (dt, J = 9.3, 6.9 Hz, 1H), 5.67 (d, J = 9.5 Hz, 1H), 6.99 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.3, 19.6, 20.7, 25.5, 25.6, 29.1, 30.7, 62.2, 66.9, 98.8, 127.1, 127.7, 132.0, 133.6, 134.2, 138.0. $C_{20}H_{30}O_2S$ (334.5): calcd. C, 71.81; H, 9.04. Found: C, 71.65; H, 9.03%.

3. (4*Z*)-5-(2,3,5,6-Tetramethylphenylthio)pent-4-en-1-ol (11)

To a solution of **10** (4.93 g, 14.7 mmol) in dry methanol (200 mL) was added water (4.0 mL) and toluene-*p*-sulfonic acid monohydrate (100 mg, 0.53 mmol). The mixture was stirred for 17 h, treated with K_2CO_3 (250 mg) and added to *tert*-butyl methyl ether (500 mL) and water (250 mL). The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 100 mL). Evaporation of the solvent *in vacuo* and purification of the residue by flash chromatography (pentane–*tert*-butyl methyl ether = 3 : 1, 1% NEt_3) gave 3.22 g (12.9 mmol, 88%) of **11** (E : Z = 12 : 88 by ^{1}H NMR). **11**: mp (non-recrystallized product) 45–47 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.72–1.80 (m, 3H), 2.25 (s, 6H), 2.36 (ddt, J = 7.3, 7.3, 1.2 Hz, 2H), 2.42 (s, 6H), 3.73 (t, J = 6.5 Hz, 2H), 5.56 (dt, J = 9.3, 7.3 Hz, 1H), 5.68 (dt, J = 9.3, 1.3 Hz, 1H), 6.96 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.3, 20.7, 25.2, 31.9, 62.4, 127.3, 127.6, 132.0, 133.3, 134.3, 138.0. $C_{15}H_{22}OS$ (250.40): calcd. C, 71.95; H, 8.86. Found: C, 71.74; H, 8.80%.

4. (1*Z*)-5-Bromo-1-(2,3,5,6-tetramethylphenylthio)pent-1-ene (12)

A solution of methanesulfonic anhydride (2.19 g, 12.6 mmol) in THF (15 mL) was cooled to −50 °C and treated with a solution of n-butyllithium in hexane (1.95 M, 0.60 mL, 1.2 mmol) to deprotonate any methanesulfonic acid present. In a separate vessel a solution of n-butyllithium in hexane (1.95 M, 3.60 mL, 7.02 mmol) was added to a solution of **11** (1.71 g, 6.83 mmol) in THF (20 mL) at −50 °C. The resulting solution was transferred *via* cannula into the first solution. The reaction mixture was allowed to reach −15 °C within 4 h. An aqueous buffer (pH = 7, 50 mL) was added, the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 50 mL). The combined organic phases were dried with Na_2SO_4 and concentrated *in vacuo*.

The residue was taken up in DMF (15 mL). Lithium bromide (1.30 g, 15.0 mmol) was added while cooling with a water bath. After 20 h a 4 : 2 : 1 mixture of water, sat. aqueous $NaHCO_3$ solution and sat. aqueous NH_4Cl solution (70 mL) and *tert*-butyl methyl ether (50 mL) were added. The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 50 mL). The combined organic phases were dried with Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (pentane) to give 1.72 g (5.49 mmol, 80%) of the bromide **12** (E : Z = 14 : 86 by ^{1}H NMR, GC). **12**: ^{1}H NMR (200 MHz, C_6D_6): δ = 1.70 (tt, all J = 7.0 Hz, 2H), 2.10 (s, 6H), 2.30 (ddt, J = 7.2, 7.2, 1.2 Hz, 2H), 2.47 (s, 6H), 3.03 (t, J = 6.9 Hz, 2H), 5.23 (dt, J = 9.3, 7.2 Hz, 1H), 5.68 (dt, J = 9.3, 1.3 Hz, 1H), 6.86 (s, 1H). ^{13}C NMR (50 MHz, C_6D_6): δ = 18.5, 20.8, 27.8, 32.4, 32.8, 126.0, 129.0, 132.5, 133.8, 134.5, 138.3. $C_{15}H_{21}BrS$ (313.30): calcd. C, 57.51, H, 6.76. Found: C, 57.60; H, 6.68%.

5. (1*Z*)-1-(2,3,5,6-Tetramethylphenylthio)-6-methylseleno-6-phenylhept-1-ene (13)

To a solution of 1,1-bis(methylseleno)-1-phenylethane (1.45 g, 4.96 mmol) in THF (15 mL) was added a solution of n-butyllithium in hexane (1.95 M, 2.30 mL, 4.49 mmol) at −85 °C. After stirring for 30 min a solution of the bromo compound **12** (1.60 g, 5.11 mmol) in THF (10 mL) was added within 5 min. The mixture was allowed to reach −45 °C within 2 h. Water (10 mL) was added, the phases were separated and

the aqueous phase was extracted with petroleum ether (3 × 20 mL). The combined organic phases were dried with Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (petroleum ether to petroleum ether–*tert*-butyl methyl ether 40:1) to give 1.87 g (4.33 mmol, 96%) of the selenium ether **13** (*E*:*Z* = 13:87 by ^{1}H NMR) as a colourless oil. **13**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26–1.42 (m, 1H), 1.47–1.65 (m, 1H), 1.76 (s, Se-sat.: *J* = 10.6 Hz, 3H), 1.90 (s, Se-sat.: *J* = 9.0 Hz, 3H), 2.09 (ddd, *J* = 13.6, 12.2, 4.7 Hz, 1H), 2.23–2.41 (m, 3H), 2.28 (s, 6H), 2.45 (s, 6H), 5.51 (dt, *J* = 9.3, 7.1 Hz, 1H), 5.68 (dt, *J* = 9.3, 1.2 Hz, 1H), 6.99 (s, 1H), 7.18–7.25 (m, 1H), 7.29–7.38 (m, 2H), 7.49–7.56 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 3.2, 18.3, 20.7, 24.6, 26.3, 29.0, 42.3, 46.6, 126.1, 126.8, 127.3, 127.7, 128.0, 132.0, 133.6, 134.2, 138.0, 145.3. $C_{24}H_{32}SSe$ (431.54): calcd. C, 66.80; H, 7.47. Found C, 66.68; H, 7.62%.

6. 2-Iodomethyltetrahydrofuran (15)

A solution of tetrahydrofurfuryl alcohol **14** (5.00 g, 48.9 mmol) in THF (150 mL) was treated with triphenylphosphine (14.4 g, 54.9 mmol), iodine (14.0 g, 55.2 mmol) and imidazole (3.74 g, 54.9 mmol). The mixture was stirred for 140 min and concentrated *in vacuo*. The residue was purified by flash-chromatography (petroleum ether–*tert*-butyl methyl ether 40:1) to give 8.73 g (41.2 mmol, 84%) of the iodo compound **15**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.55–1.69 (m, 1H), 1.79–2.13 (m, 3H), 3.16 (dd, *J* = 9.9, 6.6 Hz, 1H), 3.21 (dd, *J* = 9.9, 5.2 Hz, 1H), 3.73–3.82 (m, 1H), 3.86–4.00 (m, 2H). *cf*. ref. 34 ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.3, 26.0, 31.8, 68.8, 78.4.

7. 2-(2,3,5,6-Tetramethylphenylthiomethyl)tetrahydrofuran (16)

To a suspension of NaH (2.29 g, 76.3 mmol, 80% in paraffin oil) in THF (300 mL) was added 2,3,5,6-tetramethylthiophenol (13.0 g, 78.2 mmol) in small portions at 0 °C. After stirring for 3 h at room temperature a solution of tetrahydrofurfuryl iodide **15** (15.5 g, 73.3 mmol) in DMF (30 mL) was added. The mixture was stirred for an additional 2 h and treated with water (200 mL). The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 100 mL). The combined organic phases were dried with Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (pentane–*tert*-butyl methyl ether 25:1) to give 16.6 g (66.2 mmol, 90%) of the thioether **16** as a white solid: mp 28–29 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.58–1.68 (m, 1H), 1.81–1.96 (m, 2H), 1.97–2.10 (m, 1H), 2.23 (s, 6H), 2.51 (s, 6H), 2.61 (dd, *J* = 12.7, 7.2 Hz, 1H), 2.81 (dd, *J* = 12.7, 5.8 Hz, 1H), 3.69–3.78 (m, 1H), 3.84–3.95 (m, 2H), 6.93 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.4, 20.8, 25.7, 31.0, 41.0, 68.1, 78.1, 131.8, 134.0, 134.2, 138.5. $C_{15}H_{22}OS$ (250.40): calcd. C, 71.95; H, 8.86. Found C, 71.84; H, 8.70%.

8. (4*E*)-5-(2,3,5,6-Tetramethylphenylthio)pent-4-en-1-ol (17)

To a solution of 2-durylthiomethyltetrahydrofuran **16** (5.54 g, 22.1 mmol) in THF (60 mL) was added dropwise (!) a solution of n-butyllithium in hexane (1.95 M, 11.9 mL, 23.2 mmol) at −18 °C within 165 min. After 30 min pH 7 buffer solution (80 mL) was added, the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 50 mL). The combined organic phases were dried with Na_2SO_4 and concentrated *in vacuo*. Recrystallization of the residue from n-hexane (70 mL) gave 4.00 g (16.0 mmol, 72%) of the alcohol **17** (*E*:*Z* > 98:2 by GC). **17**: mp 88 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.52–1.65 (m, 3H), 2.11 (dt, all *J* = 7.0 Hz, 2H), 2.26 (s, 6H), 2.42 (s, 6H), 3.59 (t, *J* = 6.4 Hz, 2H), 5.18 (dt, *J* = 14.9, 7.0 Hz, 1H), 5.86 (d, *J* = 14.8 Hz, 1H), 6.98 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.9, 20.7, 29.0, 32.2, 62.1, 123.8, 126.8, 131.1, 132.3, 134.3, 138.6. $C_{15}H_{22}OS$ (250.40): calcd. C, 71.95; H, 8.86. Found C, 71.70; H, 8.64%.

9. (1*E*)-5-Bromo-1-(2,3,5,6-tetramethylphenylthio)pent-1-ene (18)

The bromo compound **18** was prepared from methanesulfonic anhydride (5.02 g, 28.8 mmol), n-butyllithium (1.95 M in hexane, 8.90 mL, 17.4 mmol), alcohol **17** (3.93 g, 15.7 mmol) and lithium bromide (2.93 g, 33.7 mmol) as described in experiment 4. The reaction furnished 4.18 g (13.3 mmol, 85%) of **18** (*E*:*Z* = 98:2 by GC). **18**: mp 44–46 °C. ^{1}H NMR (300 MHz, C_6D_6): δ = 1.33–1.44 (m, 2H), 1.82 (ddt, *J* = 7.2, 7.2, 1.2 Hz, 2H), 2.11 (s, 6H), 2.50 (s, 6H), 2.89 (t, *J* = 6.7 Hz, 2H), 5.02 (dt, *J* = 14.9, 7.1 Hz, 1H), 5.80 (dt, *J* = 14.8, 1.3 Hz, 1H), 6.88 (s, 1H). ^{13}C NMR (75 MHz, C_6D_6): δ = 18.2, 20.8, 31.2, 32.4, 32.6, 124.9, 125.5, 131.5, 132.9, 134.6, 138.9. $C_{15}H_{21}BrS$ (313.30): calcd. C, 57.51; H, 6.76. Found C, 57.53; H, 6.64%.

10. (1*E*)-1-(2,3,5,6-Tetramethylphenylthio)-6-methylseleno-6-phenylhept-1-ene (19)

1,1-Bis(methylseleno)-1-phenylethane (3.88 g, 13.3 mmol), n-butyllithium (8.40 mL, 12.9 mmol, 1.54 M in hexane) and the bromo compound **18** (4.28 g, 13.6 mmol) were allowed to react as described in experiment 5 to give 5.21 g (12.1 mmol, 93%) of the selenoether **19** (*E*:*Z* = 98:2 by ^{1}H NMR). **19**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08–1.22 (m, 1H), 1.28–1.44 (m, 1H), 1.72 (s, Se-Sat.: *J* = 10.5 Hz, 3H), 1.84 (s, Se-Sat.: *J* = 8.8 Hz, 3H), 1.94 (ddd, *J* = 13.6, 12.3, 4.6 Hz, 1H), 2.03 (dddd, *J* = 7.0, 7.0, 7.0, 1.1 Hz, 2H), 2.12–2.24 (m, 1H), 2.29 (s, 6H), 2.45 (s, 6H), 5.11 (dt, *J* = 14.9, 7.0 Hz, 1H), 5.84 (dt, *J* = 14.8, 1.3 Hz, 1H), 7.02 (s, 1H), 7.17–7.24 (m, 1H), 7.27–7.36 (m, 2H), 7.41–7.47 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 3.2, 18.0, 20.8, 24.8, 26.2, 32.9, 42.1, 46.6, 123.6, 126.1, 126.8, 127.2, 128.0, 131.2, 132.3, 134.3, 138.7, 145.2. $C_{24}H_{32}SSe$ (431.54): calcd. C, 66.80; H, 7.47. Found C, 66.66; H, 7.40%.

11. 1-Methyl-1-phenyl-2-[1′-deutero-1′-(2,3,5,6-tetramethylphenylthio)methyl]cyclopentane (22)

Representative procedure (Table 1, entries 1–8, 15–21, 23–27). In a typical experiment a solution of **13** (1.0 mL, 0.20 mmol of a 0.20 M stock solution in THF, *E*:*Z* = 13:87) was transferred to the top compartment of a two-compartment reaction vessel,[30] cooled to −105 °C and added to a precooled solution of *tert*-butyllithium in pentane (1.70 M, 0.15 mL, 0.26 mmol). The mixture was stirred for 60 min and treated with CD_3OD (0.15 mL, 3.7 mmol). After 45 min aqueous buffer solution (pH = 7, 10 mL) and *tert*-butyl methyl ether (10 mL) were added. The mixture was allowed to reach room temperature, extracted with *tert*-butyl methyl ether (3 × 15 mL), dried with Na_2SO_4 and concentrated *in vacuo*. After determination of the diastereoisomer ratio by ^{2}H NMR spectroscopy (**22a**:**22b** = 88:12) the crude material was purified by flash chromatography (pentane) to give 48 mg (71%) of **22** as a colourless oil.

Important deviations from this procedure: entry 8: a solution of **19** (20 mM stock solution in THF, 10.0 mL, 0.20 mmol) was added to a precooled mixture of *tert*-butyllithium in pentane (1.70 M, 0.20 mL, 0.34 mmol) and THF (4.0 mL) within 15 min; entries 15–17: HMPA was added to the stock solution of either **13** or **19** before adding to the solution of *tert*-butyllithium; entries 18,19: a mixture of **19** (0.10 M stock solution in pentane) and THF was used; entries 24–27: a solution of **19** was added to the solution of *tert*-butyllithium at −107 °C and warmed up to −90 °C as fast as possible (about 30 s). $C_{23}H_{29}DS$ (339.6): calcd. C, 81.36; H + D, 8.90. Found C, 81.24; H + D, 8.99%.

Compound **22a**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.16 (s, 3H), 1.56–1.65 (m, 1H), 1.71–1.92 (m, 4H), 2.18–2.23 (m, 1H), 2.23 (s, 6H), 2.25–2.31 (m, 1H), 2.41 (s, 6H), 2.69 (br d, *J* = 2.0 Hz, 1H), 6.94 (s, 1H), 7.14–7.17 (m, 3H), 7.20–7.25 (m, 2H).

^{2}H NMR (77 MHz, $CHCl_3$): $\delta = 2.38$ (br s, 1D). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 18.3$, 20.1, 20.8, 21.7, 30.3, 36.9 (t, $J = 21$ Hz), 43.0, 48.5, 48.8, 125.5, 125.8, 128.0, 131.6, 134.1, 134.2, 138.5, 148.6.

Compound **22b**: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.16$ (s, 3H), 1.56–1.65 (m, 1H), 1.71–1.92 (m, 4H), 2.18–2.23 (m, 1H), 2.23 (s, 6H), 2.25–2.31 (m, 1H), 2.34 (br d, $J = 11.2$ Hz, 1H), 2.14 (s, 6H), 6.94 (s, 1H), 7.14–7.17 (m, 3H), 7.20–7.25 (m, 2H). ^{2}H NMR (77 MHz, $CHCl_3$): $\delta = 2.74$ (br s, 1D).

12. 1-Methyl-1-phenyl-2-[1′-(2,3,5,6-tetramethylphenylthio)-ethyl]cyclopentane (23)

Representative procedure (Table 1, entries 9, 10, 22). In a typical experiment a solution of **13** (2.0 mL, 0.40 mmol of a 0.20 M stock solution in THF, $E:Z = 13:87$) was transferred to the top compartment of a two-compartment reaction vessel,[30] cooled to −78 °C and added to a precooled 1.70 M solution of *tert*-butyllithium in pentane (0.28 mL, 0.48 mmol). The mixture was stirred for 90 min and treated with a solution of methyl iodide (0.25 mL, 4.0 mmol) in THF (2.0 mL). After 3 h the reaction mixture was worked up as described for experiment 11. The diastereoisomer ratio was determined by ^{1}H NMR spectroscopy (**23a**:**23b** = 94:6). The crude material was purified by flash chromatography (petroleum ether–*tert*-butyl methyl ether 100:1) to give 115 mg (82%) of **23**. $C_{24}H_{32}S$ (352.58): calcd. C, 81.76; H, 9.15. Found C, 81.46; H, 9.17%.

Compound **23a**: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.14$ (d, $J = 6.8$ Hz, 3H), 1.33 (s, 3H), 1.64–1.74 (m, 1H), 1.76–1.85 (m, 3H), 1.89–1.99 (m, 1H), 2.04–2.14 (m, 1H), 2.20 (s, 6H), 2.29 (s, 6H), 2.32 (ddd, $J = 10.7$, 7.3, 3.8 Hz, 1H), 2.94 (dq, $J = 6.8$, 3.9 Hz, 1H), 6.91 (s, 1H), 7.11–7.17 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 18.3$, 18.4, 20.6, 20.9, 21.8, 25.8, 42.4, 44.1, 48.6, 54.5, 125.2, 125.9, 127.8, 131.6, 133.5, 133.8, 139.1, 148.9.

Compound **23b**: This diastereoisomer was separated from a 43:57 mixture of **23a**:**23b** by crystallization from hexane.§ Mp 101–102 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.50$ (d, $J = 6.6$ Hz, 3H), 1.33 (s, 3H), 1.69–1.96 (m, 4H), 1.97–2.10 (m, 1H), 2.23 (s, 6H), 2.44–2.54 (m, 2H), 2.47 (s, 6H), 2.91 (dq, $J = 9.8$, 6.5 Hz, 1H), 6.92 (s, 1H), 7.13–7.20 (m, 1H), 7.27–7.34 (m, 2H), 7.41–7.47 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 18.6$, 18.8, 20.8, 20.9, 22.1, 30.5, 46.7, 47.8, 48.5, 56.0, 125.3, 126.0, 128.0, 131.6, 133.6, 133.9, 139.1, 149.9.

13. 1-Methyl-1-phenyl-2-[1′-(2,3,5,6-tetramethylphenylthio)-1′-trimethylstannylmethyl]cyclopentane (24)

Representative procedure (Table 1, entries 11–14). A solution of **19** (1.0 mL, 0.20 mmol of a 0.20 M stock solution in THF, $E:Z = 94:6$) was transferred to the top compartment of a two-compartment reaction vessel,[30] cooled to −106 °C and added to a precooled 1.70 M solution of *tert*-butyllithium in pentane (0.15 mL, 0.26 mmol). The mixture was stirred for 20 min and treated with a precooled solution of trimethyltin chloride (1.0 mL, 1.0 mmol of a 1.0 M stock solution in THF). After 3.5 h the reaction mixture was worked up as described for experiment 11. The diastereoisomer ratio was determined by ^{1}H NMR spectroscopy (**24a**:**24b** = 35:65). The crude material was purified by flash chromatography (pentane) to give 37 mg (37%) of **24**. The diastereoisomers of **24** have been separated by repeated flash chromatography.

Important deviations from this procedure: entries 11, 13: TMEDA was added to the stock solution of either **13** or **19** before adding to the solution of *tert*-butyllithium; entry 14: HMPA was added to the stock solution of **19** before adding to the solution of *tert*-butyllithium.

Compound **24a**:§ mp 90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.29$ (s, Sn-sat.: $J = 52.9/50.8$ Hz, 9H), 1.11 (s, 3H), 1.45–1.85 (m, 5H), 2.15 (s, 6H), 2.20–2.29 (m, 1H), 2.22 (s, 6H), 2.34–2.49 (m, 1H), 2.55 (d, $J = 1.1$ Hz, Sn-sat.: $J = 50.7$ Hz, 1H), 6.62–6.70 (m, 2H), 6.84–7.01 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = -6.8$ (Sn-sat.: $J = 330/316$ Hz), 18.2, 20.9, 21.0, 22.1, 32.1 (Sn-sat.: $J = 35$ Hz), 34.2 (Sn-sat.: $J = 339/324$ Hz), 43.0, 48.2, 54.9 (Sn-sat.: $J = 7$ Hz), 124.8, 125.3, 127.6, 131.6, 133.8, 134.7, 138.8, 148.1. $C_{26}H_{38}SSn$ (501.36): calcd. C, 62.29; H, 7.64. Found C, 62.34; H, 7.70%.

Compound **24b**: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = -0.17$ (s, Sn-sat.: $J = 52.2/50.1$ Hz, 9H), 1.16 (s, 3H), 1.59–1.88 (m, 4H), 1.94–2.12 (m, 2H), 2.20 (s, 6H), 2.44 (s, 6H), 2.61 (ddd, $J = 10.5$, 7.5, 3.1 Hz, 1H), 2.96 (d, $J = 3.2$ Hz, Sn-sat.: $J = 48.5$ Hz, 1H), 6.87 (s, 1H), 7.13–7.21 (m, 1H), 7.26–7.34 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = -8.1$, 19.0, 20.7, 20.8, 21.7, 28.5, 32.4, 42.5, 50.1, 55.5, 125.5, 126.1, 128.1, 131.2, 134.1, 137.5, 137.9, 149.0. $C_{26}H_{38}SSn$ (501.36): calcd. C, 62.29; H, 7.64. Found C, 61.99; H, 7.60%.

14. 1-Methyl-1-phenyl-2-[2′-hydroxy-1′-(2,3,5,6-tetramethyl-phenylthio)-2′phenylethyl]cyclopentane (25–28)

Representative procedure. A solution of **19** (2.0 mL, 0.30 mmol of a 0.15 M stock solution in THF, $E:Z = 97:3$) was transferred to the top compartment of a two-compartment reaction vessel,[30] cooled to −106 °C and added to a precooled 1.60 M solution of *tert*-butyllithium in pentane (0.25 mL. 0.40 mmol). The mixture was stirred for 30 min and treated with a precooled solution of benzaldehyde (1.5 mL, 1.5 mmol of a 1.0 M stock solution in THF). After 45 min the reaction mixture was worked up as described for experiment 11. The diastereoisomer ratio was determined by ^{1}H NMR spectroscopy [**25**:**26**:(**27** or **28**):(**28** or **27**) = 13.5:26.9:34.1:25.6]. The crude material was purified by flash chromatography (pentane–*tert*-butyl methyl ether 40:1) to give 92 mg (69%) of the product mixture. Repeated flash chromatography separated the diastereoisomers **25** and (**27** or **28**) and gave a mixture of **26** and (**28** or **27**).

After equilibration of the lithium compound **21** at −78 °C in another experiment the diastereoisomers **25**, **26**, (**27** or **28**) and (**28** or **27**) were obtained in a ratio of 30.6:63.5:*ca.* 3:*ca.* 3.

The analogous reaction of the corresponding *Z*-vinyl sulfide **13** resulted in the diastereoisomers **25**, **26**, (**27** or **28**) and (**28** or **27**) in a ratio of 30.5:59.2:*ca.* 5.5:*ca.* 4.8.

The relative configurations of the diastereoisomers **25** and **26** were determined by crystal structure analysis.§ The relative configurations of the diastereoisomers **27** and **28** are unknown.

Compound **25**: mp 163–164 °C. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.49$ (s, 3H), 1.66–1.72 (m, 1H), 1.77–1.85 (m, 1H), 1.86–1.97 (m, 2H), 1.91 (s, 6H), 1.99 (s, 6H), 2.05–2.14 (m, 1H), 2.33 (ddd, $J = 11.8$, 7.1, 2.8 Hz, 1H), 2.36–2.43 (m, 1H), 2.60 (d, $J = 6.8$ Hz, 1H), 3.23 (br d, $J = 2.5$ Hz, 1H), 5.22 (br d, $J = 6.7$ Hz, 1H), 6.67 (s, 1H), 6.97–7.00 (m, 2H), 7.02–7.09 (m, 4H), 7.13–7.17 (m, 2H), 7.25–7.28 (m, 2H). ^{13}C NMR (75 MHz, C_6D_6): $\delta = 18.2$, 20.7, 20.9, 22.1, 27.4, 44.1, 49.1, 54.3, 55.6, 72.8, 125.5, 125.6, 125.9, 126.8, 128.2, 131.96, 132.01, 133.9, 138.9, 144.3, 148.2; one aromatic signal is masked by the C_6D_6 triplet. $C_{30}H_{36}OS$ (444.68): calcd. C, 81.03; H, 8.16. Found C, 80.77; H, 8.34%.

Compound **26**: this diastereoisomer was obtained as a 95:5 mixture of **26** and (**28** or **27**). mp 159–160 °C. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.84$–0.96 (m, 1H), 1.48–1.61 (m, 4H), 1.53 (s, 3H), 1.78–1.88 (m, 1H), 2.17 (s, 6H), 2.41 (s, 6H), 2.60 (d, $J = 2.4$ Hz, 1H), 2.77–2.84 (m, 1H), 3.37 (dd, $J = 9.5$, 1.8 Hz, 1H), 4.25 (br s, 1H), 6.84 (s, 1H), 7.09–7.12 (m, 2H), 7.13–

§ Full crystallographic details for compounds **23b**, **24a**, **25** and **26**, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc.*, *Perkin Trans. 2*, available *via* the RSC web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 188/152. See http://www.rsc.org/suppdata/p2/1999/183/ for crystallographic files in .cif format.

7.21 (m, 2H), 7.22–7.27 (m, 2H), 7.29–7.33 (m, 2H), 7.50–7.53 (m, 2H). ^{13}C NMR (75 MHz, C_6D_6): δ = 18.7, 19.5, 20.8, 22.9, 31.5, 46.5, 48.9, 50.2, 58.1, 73.0, 125.8, 125.9, 126.7, 126.8, 128.1, 128.2, 132.3, 133.7, 134.4, 138.8, 143.8, 149.8. $C_{30}H_{36}OS$ (444.68): calcd. C, 81.03; H, 8.16. Found C, 80.85; H, 7.98%.

Compound **27** or **28**: mp 114–115 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.51 (s, 3H), 1.53–1.59 (m, 1H), 1.70–1.89 (m, 3H), 2.13–2.19 (m, 2H), 2.21 (s, 6H), 2.33–2.37 (m, 1H), 2.51 (s, 6H), 2.65 (d, J = 1.3 Hz, 1H), 2.98 (br s, 1H), 4.03 (br s, 1H), 6.69–6.72 (m, 2H), 6.75–6.78 (m, 2H), 6.91 (s, 1H), 6.91–6.99 (m, 3H), 7.03–7.13 (m, 3H). ^{13}C NMR (75 MHz, C_6D_6): δ = 19.1, 20.8, 21.2, 22.1, 26.8, 42.6, 48.0, 49.4, 53.9, 74.1, 125.3, 125.9, 126.1, 126.6, 128.2, 128.3, 132.4, 132.5, 134.6, 139.1, 141.7, 147.3. $C_{30}H_{36}OS$ (444.68): calcd. C, 81.03; H, 8.16. Found C, 81.06; H, 8.26%.

Compound **28** or **27**: this diastereoisomer was obtained as a 49 : 51 mixture of (**28** or **27**) and **26**. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.50 (s, 3H), 1.72–1.85 (m, 4H), 2.02 (s, 6H), 2.15 (d, J = 7.7 Hz, 1H), 2.25 (s, 6H), 2.26–2.31 (m, 1H), 2.85–2.91 (m, 1H), 3.61 (dd, J = 9.7, 1.6 Hz, 1H), 4.47 (br d, J = 7.3 Hz, 1H), 6.58 (s, 1H), 6.85–6.89 (m, 1H), 6.92–6.97 (m, 4H), 7.14–7.20 (m, 1H), 7.29–7.33 (m, 2H), 7.47–7.49 (m, 2H); one signal at *ca*. 1.55 ppm is masked by **26**. ^{13}C NMR (75 MHz, C_6D_6): δ = 19.0, 19.4, 20.7, 22.0, 30.0, 46.4, 48.8, 53.1, 57.7, 72.9, 125.3, 126.0, 126.1, 126.4, 127.1, 128.7, 131.6, 133.9, 137.4, 142.8, 148.9. $C_{30}H_{36}OS$ (444.68): calcd. C, 81.03; H, 8.16. Found [**26** : (**28** or **27**) = 51 : 49] C, 81.17; H, 7.92%.

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