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Intramolecular Carbolithiation of 2,6-Dilithio-1,6-heptadienes: An Experimental and Theoretical Study

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Abstract: 2,6-Dilithio-1,6-heptadienes **3** undergo intramolecular carbolithiation in Et_2O/*N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) at the lithiated double bonds to afford 1,2-bis(lithiomethyl)cyclopentenes **5**. Reaction of these dianions with electrophiles affords a number of 1,2-difunctionalized cyclopentene derivatives **7**–**10**. The ease of carbolithiation of 2,6-dilithio-1,6-heptadiene (**3a**) compared to that of 2-lithio-1,6-heptadiene (**14**) has been studied experimentally. A series of ab initio molecular-orbital calculations on the course of the reaction were carried out and the results were compared to those for the corresponding intramolecular carbolithiation of an isolated double bond. The Li–C interactions found in the transition state by this theoretical study support a carbolithiation pathway for the cyclization of 2,6-dilithio-1,6-heptadienes.

Keywords: ab initio calculations · carbanions · carbolithiation · cyclization · cyclopentenes

Introduction

Although simple alkenes are not generally thought of as sites of nucleophilic attack, the formation of ring systems by anionic cyclization of olefinic alkyl-,[1] aryl-,[2] and vinyllithium compounds[3] is an interesting synthetic transformation and provides a regiospecific and highly stereoselective route to five-membered carbocycles and heterocycles.[4] Moreover, enantioselective reactions of this kind[5] can be carried out with enantiomerically enriched secondary lithium derivatives[6] or by enantiofacially selective cycloisomerization of achiral olefinic organolithiums in the presence of chiral ligands.[7]

The observed regioselectivities and stereoselectivities of the intramolecular addition of a C–Li bond to an unactivated alkene could be rationalized by recourse to a transition-state model that resembles a cyclohexane chair in which substituents preferentially occupy pseudoequatorial positions. Ab initio molecular-orbital calculations carried out by Bailey et al. reveal that the regio- and stereochemistry of the isomerization of substituted 5-hexen-1-yllithium compounds is a consequence of an energetically favorable coordination of the lithium atom of the substrate with the remote π bond.[8] Lithiophilic Lewis bases, such as THF, *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA), and *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine (PMDTA), have been found to increase the rate of cyclization of olefinic organolithium compounds, and such additives do not reduce the high stereoselectivity of these processes.[8]

One of the major drawbacks of intramolecular carbolithiation of unactivated alkenes is that they are limited to terminal double bonds (i.e. the alkenyl trap may only be monosubstituted or 1,1-disubstituted). However, it has been possible to obtain cyclized products for 1,2-disubstituted alkenes when the formed alkyllithium product is substituted with a leaving group in a β position leading to an elimination reaction of the organolithium.[9] Also, terminally substituted 5-hexenyllithiums bearing a moderately activating group, such as phenyl, trimethylsilyl,[10] arylthio,[11] tributyl-

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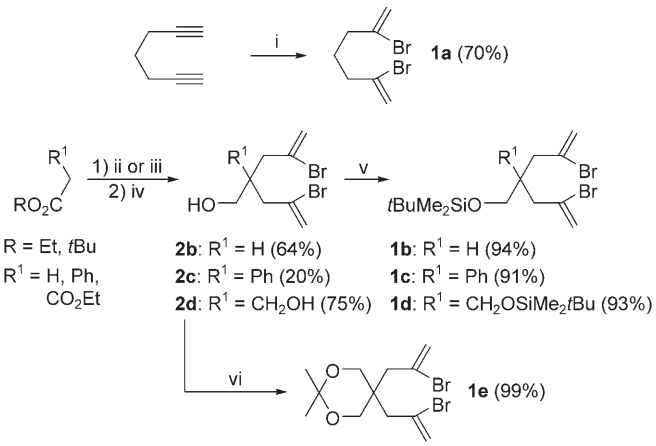
Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author. Calculated total energies and Cartesian coordinates of all minima and transition structures **18**, **TS1**, **19**, **20**, **TS2**, **21**, **22**, **TS3**, **23**, **24**, **TS4**, and **25**.

tin,[3d] alkenyl, or alkynyl,[12] undergo totally regiospecific 5-*exo*-cyclization reactions.

In recent years, we have developed an intramolecular carbolithiation reaction of lithiated double bonds, a conceptually new process that expands the scope of this kind of reaction.[13] Initially, we described how *N*,*N*-bis(2-lithioallyl)-amines, derived from readily prepared *N*,*N*-bis(2-bromoallyl)amines, cyclize efficiently to afford 3,4-bis(lithiomethyl)-dihydropyrrole derivatives that could be trapped with electrophiles leading to functionalized *N*-heterocycles in good yields. Until now, this new process was limited to *N*,*N*-bis(2-lithioallyl)amines and to *N*-2-lithioallyl-2-lithioanilines. Herein, we report that this cyclization is general with respect to the moiety of the starting material and that simple 2,6-dilithio-1,6-heptadienes undergo this kind of process efficiently. Moreover, we have carried out ab initio molecular orbital calculations on the parent system, 2,6-dilithio-1,6-heptadiene, and compared the results to those obtained for 2-lithio-1,6-heptadiene.

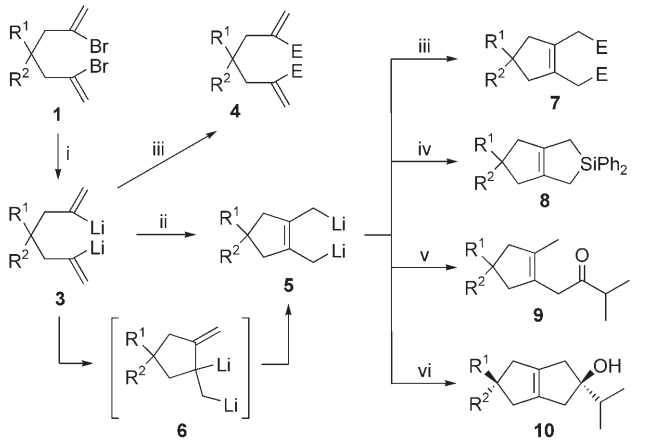
Results and Discussion

Preparation of 2,6-dibromo-1,6-heptadienes 1: To test whether intramolecular carbolithiation of lithiated double bonds is a general process with regard to the dilithiated starting product, we first synthesized some 2,6-dibromo-1,6-heptadienes **1** by means of known methodologies (Scheme 1). The parent 2,6-dibromo-1,6-heptadiene (**1a**) was prepared by double hydrobromination of 1,6-heptadiyne with tetraethylammmonium hydrogen dibromide in CH_2Cl_2 (Scheme 1).[14] Double alkylation of *tert*-butyl acetate, phenyl acetate, or diethyl malonate with 2,3-dibromopropene, followed by reduction with $LiAlH_4$ afforded alcohols **2b–d** in overall moderate-to-good yields (Scheme 1). Subsequent protection of the hydroxyl groups gave dienes **1b–d** in almost quantitative yield. Alternatively, protection of **2d** by ketalization afforded quantitatively dibromodiene **1e** (Scheme 1).



Scheme 1. Synthesis of 2,6-dibromo-1,6-heptadienes **1**. Reagents and conditions: i) $(Et_4N)^+HBr_2^-$ (2 equiv), CH_2Cl_2, 40 °C; ii) for **2b** and **2c**: 1) LDA, −78 to 20 °C; 2) $BrCH_2C(Br)=CH_2$ (1 equiv), −40 °C to reflux; iii) for **2d**: $BrCH_2C(Br)=CH_2$ (2 equiv), K_2CO_3 (4 equiv), MeCOEt, reflux; iv) $LiAlH_4$, Et_2O, 0 to 20 °C; v) *t*$BuMe_2SiCl$, 1*H*-imidazole, DMF, 20 °C; vi) $Me_2C(OMe)_2$ (excess), PPTS (cat.), 20 °C to reflux. LDA: lithium diisopropylamide; PPTS: pyridinium *p*-toluene sulfonate.

Intramolecular carbolithiation of 2,6-dilithio-1,6-heptadienes 3: Treatment of 2,6-dibromo-1,6-heptadienes derivatives **1** with *t*BuLi (4 equiv) in diethyl ether at −78 °C led to the expected dianions **3**, which were characterized by deuteriolysis or treatment with chlorotrimethylsilane to give compounds **4** (Scheme 2 and Table 1, entries 1–3). Although these anions are stable in an ethereal solution at −78 °C, on addition of TMEDA they reacted with a number of different electrophiles (D_2O, silicon chlorides, tin chlorides, and 3-pentanone) to afford the functionalized cyclopentene derivatives **7** and **8** (Scheme 2 and Table 1, entries 4–14). The for-



Scheme 2. Intramolecular carbolithiation of 2,6-dilithio-1,6-heptadienes **3**. Reagents and conditions: i) *t*BuLi (4 equiv), Et_2O, −78 °C; ii) TMEDA (4 equiv), −78 to 20 °C; iii) 1) E^+ (2.2 equiv), −78 to 20 °C, 2) H_2O; iv) 1) Ph_2SiCl_2 (1 equiv), −78 to 20 °C, 2) H_2O; v) 1) *i*$PrCO_2Et$ (1 equiv), −78 °C, 2) MeOH, −78 to 20 °C; vi) 1) *i*$PrCO_2Et$ (1 equiv), −78 to 20 °C, 2) H_2O.

Abstract in Spanish: *Los 2,6-dilitio-1,6-heptadienos **3** experimentan en Et_2O/TMEDA la reacción de carbolitiación intramolecular de un doble enlace litiado, generando los 1,2-bis(litiometil)ciclopentenos **5**. La reacción de estos dianiones con electrófilos permite la preparación de varios derivados de ciclopenteno 1,2-difuncionalizados **7–10**. Se han realizado experimentos para comparar la facilidad de carbolitiación del 2,6-dilitio-1,6-heptadieno (**3a**) con respecto a la del 2-litio-1,6-heptadieno (**14**). También se han llevado a cabo una serie de cálculos con orbitales moleculares, de tipo ab initio, sobre el transcurso de la reacción y se ha comparado ésta con la correspondiente carbolitiación intramolecular de un doble enlace aislado. Las interacciones Li–C encontradas en el estado de transición con este estudio teórico apoyan que la ciclación de los 2,6-dilitio-1,6-heptadienos tenga lugar mediante un proceso de carbolitiación.*

Table 1. Preparation of functionalized products **4**, and **7**–**10**.

Entry	Diene	R^1	R^2	E^+/MCl_2	Product	E/M	Yield [%][a]
1	**1a**	H	H	Me_3SiCl	**4a**	$SiMe_3$	89
2	**1b**	H	CH_2OSi[b]	MeOD	**4b**	D	93
3	**1d**	CH_2OSi[b]	CH_2OSi[b]	MeOD	**4c**	D	91
4	**1a**	H	H	Me_3SiCl	**7a**	$SiMe_3$	82
5	**1a**	H	H	Et_2CO	**7b**	$Et_2C(OH)$	77
6	**1b**	H	CH_2OSi[b]	D_2O	**7c**	D	90
7	**1b**	H	CH_2OSi[b]	Bu_3SnCl	**7d**	$SnBu_3$	83
8	**1b**	H	CH_2OSi[b]	$B(OMe)_3$[c]	**7e**	OH	64
9	**1c**	Ph	CH_2OSi[b]	D_2O	**7f**	D	92
10	**1d**	CH_2OSi[b]	CH_2OSi[b]	D_2O	**7g**	D	90
11	**1d**	CH_2OSi[b]	CH_2OSi[b]	Bu_3SnCl	**7h**	$SnBu_3$	81
12	**1d**	CH_2OSi[b]	CH_2OSi[b]	$B(OMe)_3$[c]	**7i**	OH	67
13	**1e**	-$CH_2OC(Me)_2OCH_2$-		Et_2CO	**7j**	$Et_2C(OH)$	81
14	**1a**	H	H	Ph_2SiCl_2	**8a**	$SiPh_2$	80
15	**1a**	H	H	$iPrCO_2Et$[d]	**9a**	–	67
16	**1a**	H	H	$iPrCO_2Et$[e]	**10a**	–	72
17	**1b**	H	CH_2OSi[b]	$iPrCO_2Et$[d]	**9b**	–	50
18	**1b**	H	CH_2OSi[b]	$iPrCO_2Et$[e]	**10b**	–	52[f]
19	**1d**	CH_2OSi[b]	CH_2OSi[b]	$iPrCO_2Et$[d]	**9c**	–	65
20	**1d**	CH_2OSi[b]	CH_2OSi[b]	$iPrCO_2Et$[e]	**10c**	–	50

[a] Yield of isolated product based on starting dibromides **1**. [b] CH_2OSi=CH_2OSiMe_2tBu. [c] After the treatment of dianions **5b**, and **5d** with trimethyl borate, the resulting mixtures were oxidized in situ with alkaline hydrogen peroxide at 20 °C. [d] Carried out at −78 °C. [e] Carried out from −78 °C to room temperature. [f] Obtained as a 1:1 mixture of diastereoisomers.

mation of these compounds seems to point to 1,2-bis(lithiomethyl)cyclopentene derivatives **5** as intermediates. This transformation, which involves the cycloisomerization of vinyllithium to allyllithium moieties and the formation of a new C−C double bond, could be explained by assuming that the first step is an intramolecular carbolithiation of one vinyllithium moiety by the other one to afford a methylenecyclopentane moiety such as **6**. Finally, these probable intermediates could undergo an allylic rearrangement to give dianions **5** (Scheme 2). Interestingly, different groups R^1 and R^2 (alkyl, aryl, hydrogen) are tolerated at the central position of the starting diene moiety, which indicates that the process is general with respect to the structure of the starting material.

In a study of the reactivity of the new organolithium compounds generated after the carbolithiation reactions, we also reported that treatment of 2,5-dihydro-3,4-bis(lithiomethyl)-1-(4-methylphenyl)-1*H*-pyrrole derivatives with different carboxylic esters gave rise to β,γ-unsaturated ketones or bicyclic alcohols, depending on the reaction conditions.[15] To check whether this behavior was the same in the case of the corresponding 1,2-bis(lithiomethyl)cyclopentene derivatives **5**, we reacted some of these dianions **5** with ethyl isobutyrate. Treatment of dianions **5a**, **5b**, and **5d** with such a carboxylic ester (1 equiv) at −78 °C afforded, after 1 h and further hydrolysis with MeOH at this temperature, the β,γ-unsaturated ketones **9**. Moreover, the addition of the ester at −78 °C, stirring of the reaction mixture overnight at room temperature, and aqueous hydrolysis led to 1,2,3,4,5,6-hexahydro-2-hydroxypentalene derivatives **10** (Scheme 2 and Table 1, entries 15–20). We have thus shown that the reactivity of these 1,2-bis(lithiomethyl)cyclopentene derivatives **5** with carboxylic esters is similar to that observed with the corresponding 3,4-bis(lithiomethyl)dihydropyrroles, and that monocyclic ketones or bicyclic alcohols can be prepared in a selective manner, depending on the reaction conditions.

Effects on the cyclization rate: The role played by TMEDA in this intramolecular carbolithiation process is shown in Table 2. When TMEDA was added to the ethereal solution of intermediates **3**, cyclization was complete in 50 min at room temperature for all the dianions derived from dibromides **1a**–**e** (Table 2, entry 1). Moreover, the cyclizations were monitored by GC-MS analysis of aliquots quenched with MeOD at different temperatures. For **3a**, we found that the cyclization process begins at about −20 °C in the presence of TMEDA; however, this reaction takes place very slowly, and carbolithiation at 0 °C required 90 min to go to completion (Table 2, entry 2). However, in the absence of TMEDA, the reaction does not take place below room temperature (Table 2, entry 3) and even at 20 °C the cyclization rate was much slower than in the presence of the diamine (6 h were necessary to complete the reaction; Table 2, entry 4). Thus, the addition of TMEDA allows the reaction to proceed at lower temperatures and more quickly,

Table 2. Effect of TMEDA and the dibromide **1** moiety on the cyclization rate.

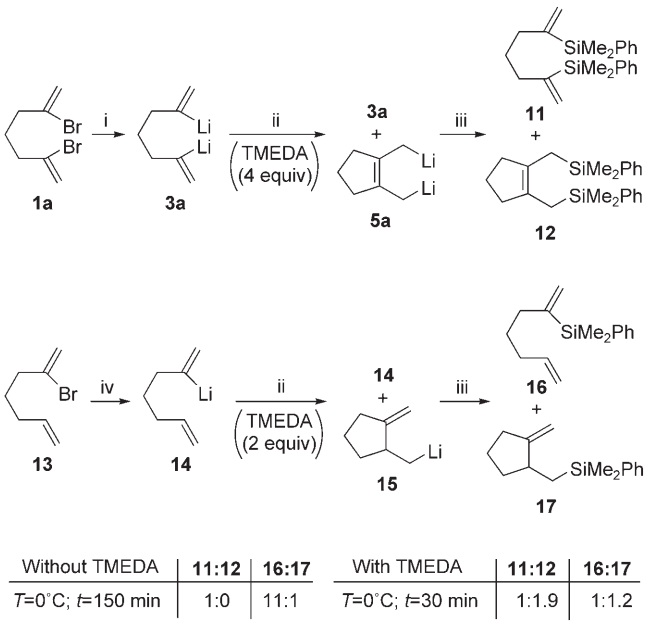
Entry	Diene	TMEDA	T [°C]	t [min]	**4/7** ratio[a]
1	**1a–e**	yes	20	50	0/1
2	**1a**	yes	0	90	0/1
3	**1a**	no	0	150	1/0
4	**1a**	no	20	360	0/1
5	**1a**	no	20	50	9/1
6	**1b**	no	20	50	2/1
7	**1d**	no	20	50	1/5

[a] Ratio determined by ^1H NMR analysis.

which indicates that this lithium-coordinating diamine has a strong accelerating effect. Table 2 also shows the effect of substituents (R^1 and R^2) at the central carbon of the dibromodienes **1** on the cyclization rate. Compounds **1a**, **1b**, and **1d** were reacted in the absence of TMEDA, and the reaction mixture was quenched after 50 min at room temperature with deuterium oxide or chlorotrimethylsilane. When the starting material was diene **1a** ($R^1=R^2=H$), a 9:1 mixture of uncyclized (**4a**) and cyclized products (**7a**) was obtained (Table 2, entry 5). Diene **1b** ($R^1=H$, $R^2=CH_2OSiMe_2tBu$) gave a 2:1 mixture of the corresponding deuteriated diene **4b** and the cyclopentene derivative **7c** (Table 2, entry 6). Dibromodiene **1d** ($R^1=R^2=CH_2OSiMe_2tBu$) gave a 1:5 mixture of the linear product **4c** and the corresponding cyclized product **7g** (Table 2, entry 7). These results indicate that the presence of substituents at C4 in the starting 1,6-heptadienes **1** increases the cyclization rate. This effect is more pronounced with diene **1d** in which two substituents are present. The acceleration of the cyclization reaction indicates that the substitution of alkyl groups for hydrogen atoms on the carbons in the chain linking the two reactive centers allows a more efficient approach between the vinyllithium moieties in the corresponding dilithiated derivatives **3**. This "*gem*-dialkyl effect"[16] has been explained by the compression of the internal angle ("Thorpe–Ingold effect"),[17] by the reactive rotamer effect,[18] and by the "facilitated transition" hypothesis.[19]

Comparative study of the intramolecular carbolithiation of 2,6-dilithio-1,6-heptadiene (3a) and 2-lithio-1,6-heptadiene (14): To compare the ease of cyclization in the intramolecular carbolithiation of a lithiated double bond with the corresponding intramolecular carbolithiation of an isolated double bond, by a vinyllithium in both cases, we carried out two parallel reactions with dibromide **1a** and monobromide **13** under identical conditions of temperature and reaction time. Dienes **1a** and **13** were treated with *t*BuLi (4 equiv for **1a** and 2 equiv for **13**) in Et_2O at −78 °C. The resulting solutions of dianion **3a** and monoanion **14** were warmed to 0 °C and stirred at this temperature for 150 min. After the mixture was cooled to −78 °C, chlorodimethylphenylsilane (2 equiv for dibromide **1a** and 1 equiv for monobromide **13**) was added to afford compound **11** in the first case, and a 11:1 mixture of compounds **16** and **17** in the second case (Scheme 3).[20] This result shows that the intramolecular carbolithiation process for an isolated double bond begins at a lower temperature than that of a lithiated double bond.

However, when the same set of experiments was carried out in the presence of TMEDA (4 equiv for dianion **3a** and 2 equiv for monoanion **14**) we observed a different result. When the cyclizations of **3a** and **14** were carried out with TMEDA at 0 °C, the ratio of the cyclized product **12** derived from dianion **3a** is greater than the ratio of cyclized product **17** derived from monoanion **14** (Scheme 3).[21] Moreover, it is interesting to note that for both **3a** and **14**, the addition of TMEDA gave a higher ratio of cyclized products than the reactions without the diamine. This leads to the conclusion

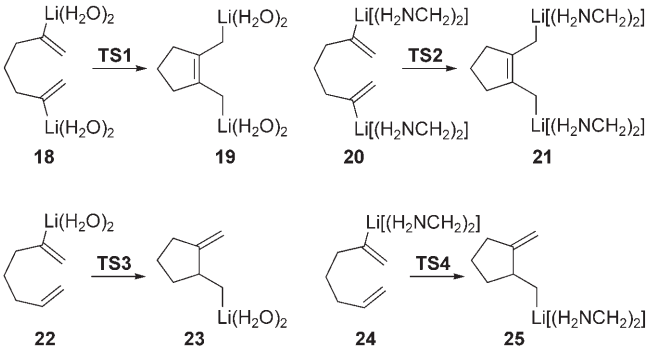


Without TMEDA	11:12	16:17	With TMEDA	11:12	16:17
T=0°C; t=150 min	1:0	11:1	T=0°C; t=30 min	1:1.9	1:1.2

Scheme 3. Comparative intramolecular carbolithiation of dianion **3a** and monoanion **14**. Reagents and conditions: i) *t*BuLi (4 equiv), Et_2O, −78 °C; ii) −78 to *T* [°C], *t* [min]; iii) 1) $Me_2PhSiCl$, −78 to 20 °C, 2) H_2O; iv) *t*BuLi (2 equiv), Et_2O, −78 °C.

that the addition of TMEDA increases the rate of carbolithiation of both lithiated and isolated double bonds, but interestingly this acceleration is greater for lithiated double bonds. In an effort to probe the factors responsible for these differences in the rates of cyclization of both kinds of substrates and also to increase our understanding of the carbolithiation reaction of lithiated double bonds, we carried out a series of ab initio molecular-orbital calculations on the course of these reactions.

Computational details: All ab initio calculations on lithiated compounds solvated with two water or one ethylenediamine molecules per lithium atom (Scheme 4) were carried out with the Gaussian 98 program package.[22] The molecular geometries were first optimized without any molecular symmetry constraints at the HF/6-31+G(d) level of theory. The optimized structures were characterized as minima or saddle



Scheme 4. Lithiated model compounds **18**–**25** for ab initio calculations.

points (representing transition structures) by the evaluation of force constants. Single-point calculations were carried out at the MP2/6-31+G(d) and MP2/6-311+G(2df) level of theory to introduce electron correlation and basis set effects into the energy estimation. For a complementary modeling of the solvation effect, single-point calculations were carried out with the Onsager model, as implemented within a self-consistent reaction field (SCRF) method in Gaussian 98, with a dielectric constant of Et_2O ($\varepsilon = 4.34$).

Theoretical results: The relative energies of **18**, **TS1**, **19**, **20**, **TS2**, **21**, **22**, **TS3**, **23**, **24**, **TS4**, and **25** (Scheme 4) are given in Tables 3 and 4. We first tried to mimic the different behavior observed when the reaction is carried out without or with TMEDA. According to our calculations, the cyclic model **19** is the most stable structure at all the computed levels. The water/dilithiated model **18** should be 35.1 kcal mol^{-1} more stable than **TS1** at the HF/6-31+G(d) level (Table 3). Inclusion of correlation gives a value of 24.4 kcal mol^{-1}, [MP2/6-31+G(d)], which supposes a relative stabilization for the transition structure **TS1** compared to **18**. The same tendency is predicted with the improved basis set 6-311+G(2df) at the MP2 level ($\Delta H = 23.4$ kcal mol^{-1}). However, the solvation effect calculated with the Onsager model appears to have little influence because it gave a value of 24.6 kcal mol^{-1} [MP2/6-31+G(d)+SCRF]. To obtain a more accurate energy difference, we considered that the Gibb free energy and SCRF correction to the MP2/6-31+G(d) energy should be additive: our best level of calculation [MP2/6-311+G(2df)+SCRF] indicated an energy barrier of 24.3 kcal mol^{-1} (Table 3). To account for the faster cyclization of dianion **3a** versus monoanion **14** in the presence of TMEDA, we decided to carry out a similar theoretical study with the ethylenediamine/dilithiated model **20**. The energy barrier at the MP2/6-311+G(2df)+SCRF level for the ethylenediamine/dilithiated model **TS2**, was calculated to be 17.4 kcal mol^{-1}, which indicates that conversion from **20** to **21** should be quicker than conversion from **18** to **19** at the same temperature. Indeed, this is observed experimentally: cyclization of dibromides **1** ($T = 20\,^{\circ}C$, $t = 50$ min) is more effective in the presence than in the absence of TMEDA (Table 2, entry 1 vs. entries 5–7). The latter requires a reaction time of 360 min to obtain the same result (Table 2, entry 1 vs. entry 4).

This result may be explained by looking at the optimized geometries. Figure 1 shows a computer plot of the structures

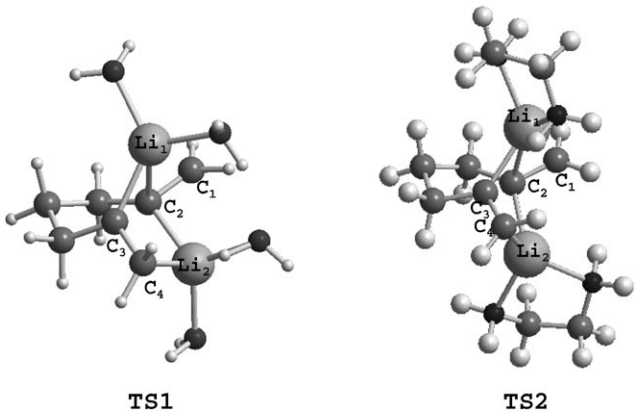


Figure 1. Computer plot of the HF/6-31+G(d)-optimized structures for **TS1**, and **TS2**. Selected bond lengths [Å] for model **TS1**: Li_1–C_1 2.551, Li_1–C_2 2.391, Li_1–C_3 2.071, Li_1–C_4 2.986, Li_2–C_1 2.614, Li_2–C_2 2.093, Li_2–C_3 2.357, Li_2–C_4 2.109, C_1–C_2 1.344, C_2–C_3 2.058, C_3–C_4 1.470. For model **TS2**: Li_1–C_1 2.244, Li_1–C_2 2.263, Li_1–C_3 2.106, Li_1–C_4 2.953, Li_2–C_1 2.893, Li_2–C_2 2.143, Li_2–C_3 2.259, Li_2–C_4 2.128, C_1–C_2 1.374, C_2–C_3 1.912, C_3–C_4 1.411.

Table 3. Calculated relative energies [kcal mol^{-1}] for solvated dilithiated minima **18**–**21** and transition structures **TS1** and **TS2**.[a]

	18	TS1	19	20	TS2	21
HF/6-31+G(d)	0.0	+35.1	−14.7	0.0	+33.8	−11.7
MP2/6-31+G(d)	0.0	+24.4	−30.2	0.0	+15.7	−28.0
MP2/6-31+G(d)+SCRF	0.0	+24.6	−30.0	0.0	+17.7	−25.7
MP2/6-311+G(2df)	0.0	+23.4	−32.9	0.0	+12.9	−30.8
MP2/6-311+G(2df)+SCRF[b]	0.0	+24.3	−30.4	0.0	+17.4	−26.4

[a] All calculations at the HF/6-31+G(d)-optimized geometries. [b] Based on MP2/6-311+G(2df) energies and modified by additive corrections obtained from Gibb free energies [thermochemical analysis at the HF/6-31+G(d) level for $T = 298$ K] and MP2/6-31+G(d)+SCRF.

Table 4. Calculated relative energies [kcal mol^{-1}] for solvated monolithiated minima **22**–**25** and transition structures **TS3** and **TS4**.[a]

	22	TS3	23	24	TS4	25
HF/6-31+G(d)	0.0	+25.5	−9.0	0.0	+25.8	−8.6
MP2/6-31+G(d)	0.0	+14.7	−13.4	0.0	+12.0	−13.9
MP2/6-31+G(d)+SCRF	0.0	+14.1	−14.8	0.0	+12.3	−15.5
MP2/6-311+G(2df)	0.0	+13.7	−13.8	0.0	+10.6	−14.4
MP2/6-311+G(2df)+SCRF[b]	0.0	+12.4	−15.0	0.0	+11.7	−14.7

[a] All calculations at the HF/6-31+G(d)-optimized geometries. [b] Based on MP2/6-311+G(2df) energies and modified by additive corrections obtained from Gibb free energies [thermochemical analysis at the HF/6-31+G(d) level for $T = 298$ K] and MP2/6-31+G(d)+SCRF.

of **TS1** and **TS2** optimized at the HF/6-31+G(d) level of theory. The bond lengths in **TS1** [Li_1–C_2 2.391 Å, Li_1–C_3 2.071 Å, Li_2–C_2 2.093 Å, Li_2–C_3 2.357 Å, and Li_2–C_4 2.109 Å] and in **TS2** [Li_1–C_1 2.244 Å, Li_1–C_2 2.363 Å, Li_1–C_3 2.106 Å, Li_2–C_2 2.143 Å, Li_2–C_3 2.259 Å, and Li_2–C_4 2.128 Å] represent typical values for Li–C interactions. This seems to indicate that Li–C interactions complete the lithium coordination sphere. In addition, if we consider the C–C distances, it can be observed that the geometry of transition state **TS2** has a closer resemblance to the cyclic product (C_1–C_2 1.374 Å, C_2–C_3 1.912 Å, and C_3–C_4 1.411 Å)

than that of **TS1** (C_1–C_2 1.344 Å, C_2–C_3 2.058 Å, and C_3–C4 1.470 Å), which explains the lower energy barrier for the former.

For the monolithiated structures, Table 4 and Figure 2 show the calculated energies for **22**–**25**, **TS3**, and **TS4** as

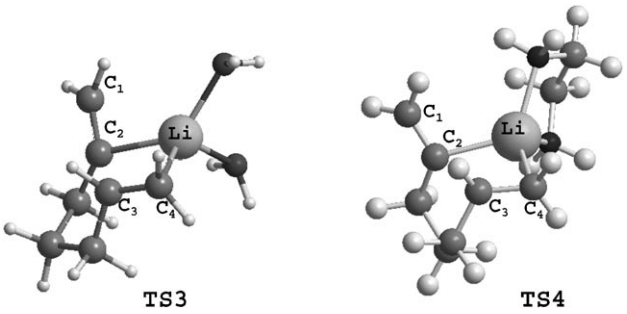


Figure 2. Computer plot of the HF/6-31+G(d)-optimized structures for **TS3**, and **TS4**. Selected bond lengths [Å] for model **TS3**: Li–C_1 2.621, Li–C_2 2.150, Li–C_3 2.334, Li–C_4 2.118, C_1–C_2 1.331, C_2–C_3 2.121, C_3–C_4 1.405. For model **TS4**: Li–C_1 2.870, Li–C_2 2.163, Li–C_3 2.334, Li–C_4 2.109, C_1–C_2 1.329, C_2–C_3 2.092, C_3–C_4 1.408.

well as the selected geometrical parameters for **TS3** and **TS4**, respectively. The energy values deserve a comment. At the MP2/6-311+G(2df)+SCRF level, the energy barrier for the water/dilithiated **TS1** model is 11.9 kcal mol^{-1} higher than that obtained for **TS3**. This energy gap should be enough to cause different experimental behaviors. This was indeed observed for both reactions described in Scheme 3. For the reaction at $T=0$ °C ($t=150$ min), cyclization was observed for the monolithiated compound, **14**, but not for its dilithiated counterpart, **3a**.[23] Thus, there is excellent agreement between the experimental and theoretical results. On the other hand, the barrier for dilithiated **TS2** is 5.7 kcal mol^{-1} higher than that calculated for ethylenediamine/monolithiated **TS4** at the same level of calculation. Therefore, the conversion from **24** to **25** should be quicker than the conversion from **20** to **21** at the same temperature. However, our experiments showed that cyclization of dianion **3a** was quicker than cyclization of monoanion **14** in the presence of TMEDA (Scheme 3). Although the theory is not in agreement with the experimental outcome in this case, our calculations have shown that the presence of a diamine solvating the dianion has a large stabilization effect and explains the facile carbolithiation of lithiated double bonds. If we compare the calculated values for **TS1** and **TS2** at the MP2/6-31+G(d)+SCRF level, a decrease of about 7 kcal mol^{-1} is observed when the calculation is performed with the diamine-solvated dianion model. However, looking at the calculated values for monoanion models **TS3** and **TS4**, the C_2–C_3 distance is almost identical (2.121 and 2.092 Å, respectively, Figure 2) and, consistently, only a stabilization of 0.7 kcal mol^{-1} is observed.

Conclusion

In conclusion, we have shown that intramolecular carbolithiation of lithiated double bonds is not restricted to bis(2-lithioallyl)amines and that this reaction thus is general for 2,6-dilithio-1,6-heptadienes moieties. In addition, ab initio molecular-orbital calculations reveal that the transition state for this process presents typical values for Li–C interactions, thus supporting a carbolithiation pathway for this reaction. We also showed, both experimentally and theoretically, that this carbolithiation of lithiated double bonds is slightly slower than the corresponding carbolithiation of isolated double bonds. Interestingly, we found that the accelerating effect of TMEDA as cosolvent in these reactions is greater for carbolithiation of lithiated double bonds than for carbolithiation of isolated double bonds.

Experimental Section

General: All reactions were carried out under a nitrogen atmosphere in oven-dried glassware with magnetic stirring. Temperatures are reported as bath temperatures. Et_2O and THF were continuously refluxed and freshly distilled from sodium under nitrogen. CH_2Cl_2 was distilled over P_2O_5. TMEDA was refluxed over potassium under nitrogen using benzophenone as indicator, and distilled under reduced pressure. Solvents used in extraction and purification were distilled prior to use. TLC was performed on Al-backed plates coated with silica gel 60 with F_{254} indicator; the chromatograms were visualized under UV light (254 nm) and/or by staining with a Ce/Mo reagent, anisaldehyde, or phosphomolybdic acid solution and subsequent heating. R_f values refer to silica gel. Flash column chromatography was carried out on silica gel 60, 230–400 mesh. Melting points (uncorrected) were obtained on a Büchi–Tottoli apparatus with open capillary tubes. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova-400, Varian Mercury-plus 300, or Varian Gemini VXR-200 spectrometers. ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s: singlet, brs: broad singlet, d: doublet, t: triplet, dd: doublet of doublets, dt: doublet of triplets, q: quartet, qt: quintet, sept: septet, m: multiplet), coupling constants (J in Hz) and integration. Chemical shifts (δ) are given as ppm relative to the residual solvent peak ($CDCl_3$ 7.16/76.95 ppm). FT-IR spectra were recorded on a Nicolet Impact 410 spectrometer. Low-resolution electron-impact mass spectra (EI-LRMS) were obtained at 70 eV on a HP 5987 A instrument or Micromass Autospec spectrometer and only the molecular ions and/or base peaks in the spectra are given. The intensities are reported as a percentage relative to the base peak after the corresponding m/z value. High-resolution mass spectra (HRMS) were obtained with a Micromass Autospec spectrometer. Elemental analyses were carried out with Perkin Elmer and LECO elemental analyzers. All commercially available reagents were used without further purification, unless otherwise indicated, and were purchased from Aldrich Chemical Co. or Acros Organics. *t*BuLi was used as a 1.5 M solution in pentane, and *n*BuLi was used as 1.6 M or 2.5 M solutions in hexane.

2,6-Dibromo-1,6-heptadiene (1a): This compound was prepared by hydrobromination of 1,6-heptadiyne following an established procedure.[14] HBr, generated by adding PBr_3 (5.23 mL, 55 mmol) dropwise to water (2.97 mL, 165 mmol), was bubbled through $Et_4N^+Br^-$ (31.50 g, 150 mmol) in CH_2Cl_2 (150 mL) at 0 °C. The weight of the resulting solution showed that 10.12 g of HBr (125 mmol) had been absorbed by the $Et_4N^+Br^-$ solution. 1,6-Heptadiyne (7.16 mL, 62.5 mmol) was added. The mixture was heated at 40 °C overnight and then cooled to 0 °C. Et_2O (300 mL) was added, and the mixture was filtered. Vacuum distillation (94–95 °C/20 Torr) gave 11.11 g (70 %) of **1a** as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=5.59$ (dt, $J=1.7$ and 1.1 Hz, 2H), 5.43 (d, $J=1.7$ Hz, 2H), 2.44 (dq, $J=7.3$ and 1.1 Hz, 4H), 1.84 ppm (qt, $J=7.3$ Hz,

2H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 133.5, 117.2, 39.7, 25.8 ppm; LRMS (70 eV, EI): *m*/*z* (%): 175 (8) $[M-Br+2]^+$, 173 (8) $[M-Br]^+$, 93 (100); elemental analysis calcd (%) for $C_7H_{10}Br_2$ (254.0): C 33.11, H 3.97; found: C 33.05, H 3.96.

2,6-Dibromo-4-(*tert*-butyldimethylsilyloxymethyl)-1,6-heptadiene (1b): A solution of LDA (100 mmol), prepared by addition of *n*BuLi (40 mL, 100 mmol) over a solution of *i*Pr$_2$NH (14.0 mL, 100 mmol) in dry THF (40 mL) at 0 °C, was added dropwise to a solution of *tert*-butyl acetate (12.14 mL, 90 mmol) in THF (40 mL) under nitrogen at −78 °C. When addition was complete, the cooling bath was removed, and the mixture was stirred at room temperature for 15 min. After cooling to −40 °C, a solution of 2,3-dibromopropene (20.0 g, 100 mmol) in THF (10 mL) was added. The reaction mixture was then heated to reflux for 8 h. Water (40 mL) was added and the mixture was transferred to a separatory funnel. The organic layer was separated and the aqueous phase was extracted with Et$_2$O (2×20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was removed under vacuum to afford 19.5 g (92%) of *tert*-butyl 4-bromo-4-pentenoate, which was not purified. Alkylation of the crude product with 2,3-dibromopropene under the same reaction conditions as before afforded 24.77 g (85%) of *tert*-butyl 4-bromo-2-(2-bromoallyl)-4-pentenoate. The crude product was dissolved in Et$_2$O (20 mL), and the solution was added dropwise to a suspension of $LiAlH_4$ (2.68 g, 70.4 mmol) in Et$_2$O (70 mL) at 0 °C. The reaction mixture was stirred for 24 h at room temperature. The mixture was hydrolyzed by pouring it over ice. The organic compound was extracted with EtOAc (3×30 mL). After usual work-up, the crude product was subjected to column chromatography (hexane/EtOAc) to afford 16.39 g (82%) of 4-bromo-2-(2-bromoallyl)-4-pentenol (**2b**) as a colorless oil. R_f = 0.26 (hexane/EtOAc, 3:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.67–5.63 (m, 2H), 5.51–5.46 (m, 2H), 3.70–3.58 (m, 2H), 2.64–2.26 (m, 5H), 1.72–1.62 ppm (br s, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 132.2, 118.6, 62.4, 41.9, 36.7 ppm; LRMS (70 eV, EI): *m*/*z* (%): 205 (10) $[M-Br+2]^+$, 203 (10) $[M-Br]^+$, 83 (100). A mixture of **2b** (14.20 g, 50 mmol), *t*BuMe$_2$SiCl (9.0 g, 60 mmol) and 1*H*-imidazole (8.42 g, 125 mmol) in DMF (75 mL) was stirred under nitrogen overnight. Addition of water was followed by extraction with CH_2Cl_2 (3×30 mL). The combined organic layers were dried over Na_2SO_4, and the solvents were removed under vacuum to afford 18.71 g (94%) of 2,6-dibromo-4-(*tert*-butyldimethylsilyloxymethyl)-1,6-heptadiene (**1b**) as a colorless oil. R_f = 0.30 (hexane); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.62–5.58 (m, 2H), 5.48–5.44 (m, 2H), 3.55 (d, *J* = 3.4 Hz, 2H), 2.64–2.19 (m, 5H), 0.88 (s, 9H), 0.02 ppm (s, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 132.7, 118.3, 61.8, 42.1, 36.6, 25.8, 18.1, −5.6 ppm; LRMS (70 eV, EI): *m*/*z* (%): 343 (2) $[M-t\text{Bu}+4]^+$, 341 (4) $[M-t\text{Bu}+2]^+$, 339 (2) $[M-t\text{Bu}]^+$, 105 (100).

2,6-Dibromo-4-(*tert*-butyldimethylsilyloxymethyl)-4-phenyl-1,6-heptadiene (1c): A solution of LDA (44 mmol), prepared by addition of *n*BuLi (17.6 mL, 44 mmol) over *i*Pr$_2$NH (6.16 mL, 44 mmol) in dry THF (25 mL) at 0 °C, was added dropwise to a solution of ethyl phenyl acetate (6.56 g, 40 mmol) in THF (25 mL) under nitrogen at −78 °C. The mixture was stirred at this temperature for 1 h before addition of a solution of 2,3-dibromopropene (8 g, 40 mmol) in THF (20 mL). After 15 min, the cooling bath was removed and the reaction was stirred for 4 h at room temperature. The mixture was quenched with water, and the organic compound was extracted with EtOAc (3×30 mL). After usual work-up, the crude product was subjected to column chromatography (hexane/EtOAc) to afford ethyl 4-bromo-2-phenyl-4-pentenoate (10.4 g, 92%) as a colorless oil. R_f = 0.50 (hexane/EtOAc, 5:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.36–7.26 (m, 5H), 5.54–5.50 (m, 1H), 5.39–5.35 (m, 1H), 4.25–3.94 (m, 3H), 3.21 (dd, *J* = 7.8 and 14.4 Hz, 1H), 2.81 (dd, *J* = 14.4 and 7.8 Hz, 1H), 1.21 ppm (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 172.2, 137.4, 130.4, 128.5, 127.6, 127.3, 118.9, 60.7, 49.6, 44.8, 13.9 ppm; LRMS (70 eV, EI): *m*/*z* (%): 203 (100) $[M-Br]^+$. A solution of LDA (40.4 mmol) in THF (20 mL) was added dropwise to a solution of ethyl 4-bromo-2-phenyl-4-pentenoate (10.4 g, 36.8 mmol) in dry THF (20 mL) at −78 °C. After stirring the mixture for 1 h at this temperature, a solution of 2,3-dibromopropene (7.36 g, 36.8 mmol) in THF (10 mL) was added dropwise and stirring at low temperature was continued for 15 min. The cooling bath was removed, and the mixture was heated to reflux for 15 h before addition of water. Extraction and work-up afforded a mixture of unreacted initial compound and ethyl 4-bromo-2-(2-bromoallyl)-2-phenyl-4-pentenoate. Distillation under vacuum gave 5.2 g (18.4 mmol) of the initial compound. Without further purification, the residue of ethyl 4-bromo-2-phenyl-4-pentenoate (5.91 g, 14.7 mmol, 40%) was reduced with $LiAlH_4$ (0.56 g, 14.7 mmol) in dry THF (20 mL) under nitrogen. After the reaction mixture was stirred for 24 h at room temperature, the reaction was quenched by pouring the mixture into ice. The organic compound was extracted with EtOAc (3×30 mL). After usual work-up, the crude product was purified by column chromatography (hexane/EtOAc) to afford 4-bromo-2-(2-bromoallyl)-2-phenyl-4-penten-1-ol (**2c**, 2.84 g, 54%) as a clear brown oil. R_f = 0.36 (hexane/EtOAc, 4:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.40–7.17 (m, 5H), 5.48–5.43 (m, 2H), 5.31–5.25 (m, 2H), 4.13 (d, *J* = 5.6 Hz, 2H), 3.08 (d, *J* = 15.4 Hz, 2H), 2.98 (d, *J* = 15.4 Hz, 2H), 2.33 ppm (t, *J* = 5.6 Hz, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 141.3, 128.1, 127.7, 126.7, 126.5, 121.4, 47.4, 46.4 ppm; LRMS (70 eV, EI): *m*/*z* (%): 331 (1) $[M-CH_2OH+4]^+$, 333 (2) $[M-CH_2OH+2]^+$, 331 (1) $[M-CH_2OH]^+$, 91 (100). A mixture of **2c** (2.84 g, 7.9 mmol), *t*BuMe$_2$SiCl (1.2 g, 9.52 mmol), and 1*H*-imidazole (1.33 g, 19.83 mmol) in DMF (12 mL) was stirred under nitrogen overnight. After water was added (20 mL), the mixture was extracted with CH_2Cl_2 (3×20 mL), the combined organic layers were dried over anhydrous Na_2SO_4, and the solvents were removed under vacuum to afford 2,6-dibromo-4-(*tert*-butyldimethylsilyloxymethyl)-4-phenyl-1,6-heptadiene (**1c**, 3.41 g, 91%) as a colorless oil. R_f = 0.35 (hexane); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.42–7.16 (m, 5H), 5.46–5.41 (m, 2H), 5.30–5.25 (m, 2H), 4.08 (s, 2H), 3.10 (d, *J* = 15.4 Hz, 2H), 2.97 (d, *J* = 15.4 Hz, 2H), 0.92 (s, 9H), 0.05 ppm (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 141.7, 128.4, 128.0, 126.8, 126.4, 120.8, 63.9, 47.16, 46.7, 25.8, 18.1, −5.6 ppm; LRMS (70 eV, EI): *m*/*z* (%): 419 (1) $[M-t\text{Bu}+4]^+$, 417 (2) $[M-t\text{Bu}+2]^+$, 415 (1) $[M-t\text{Bu}]^+$, 73 (100).

2,6-Dibromo-4,4-bis(*tert*-butyldimethylsilyloxymethyl)-1,6-heptadiene (1d): A mixture of diethyl malonate (8.0 g, 50 mmol), 2,3-dibromopropene (20 g, 100 mmol), and anhydrous K_2CO_3 (30.43 g, 220 mmol) in 2-butanone (100 mL) was heated to reflux for 48 h.[24] The mixture was filtered, and the filtrate was concentrated under vacuum. The resulting crude product was dissolved in Et$_2$O (30 mL) and then added dropwise to a suspension of $LiAlH_4$ (3.76 g, 100 mmol) in dry Et$_2$O (100 mL) at 0 °C. When the addition was complete, the ice bath was removed and the mixture was stirred at room temperature for 16 h. The reaction was quenched by pouring it into ice. After filtration, the organic product was extracted with EtOAc (3×30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was removed under vacuum. The crude product was subjected to flash column chromatography (hexane/EtOAc 3:1) to give 2,2-bis(2-bromoallyl)-1,3-propanediol (**2d**, 11.70 g, 75%) as a white solid. M.p. 56–58 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.73–5.69 (m, 2H), 5.61–5.58 (m, 2H), 3.69 (s, 4H), 3.12 (s, 2H), 2.67 ppm (s, 4H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 127.8, 122.0, 65.3, 43.6, 42.7 ppm; LRMS (70 eV, EI): *m*/*z* (%): 235 (12) $[M-Br+2]^+$, 233 (12) $[M-Br]^+$, 95 (100). A mixture of **2d** (7.8 g, 25 mmol), *t*BuMe$_2$SiCl (9.0 g, 60 mmol) and 1*H*-imidazole (8.42 g, 125 mmol) in DMF (75 mL) was stirred under nitrogen at room temperature overnight. Water was added, and the mixture was extracted with CH_2Cl_2 (3×40 mL). The combined organic layers were washed with water (5×30 mL) and dried over anhydrous Na_2SO_4. The solvents were removed under vacuum to afford **1d** (12.6 g, 93%) as a colorless oil. R_f = 0.76 (hexane); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.70–5.67 (m, 2H), 5.60–5.57 (m, 2H), 3.61 (s, 4H), 2.73 (s, 4H), 0.90 (s, 18H), 0.04 ppm (s, 12H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 128.9, 121.2, 63.8, 45.1, 42.3, 25.8, 18.1, −5.6 ppm; LRMS (70 eV, EI): *m*/*z* (%): 73 (100).

5,5-Bis(2-bromoallyl)-2,2-dimethyl-[1,3]-dioxane (1e): A solution of 2,2-bis(2-bromoallyl)-1,3-propanediol (**2d**, 1.56 g, 5 mmol), prepared as described above, and a catalytic amount of PPTS in 2,2-dimethoxypropane (15 mL) was stirred for 3 h at room temperature and heated to reflux for 1 h. Excess 2,2-dimethoxypropane was evaporated to afford **1e** (1.77 g, 100%) as a yellow oil. R_f = 0.45 (hexane/EtOAc, 10:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.75 (s, 2H), 5.65 (s, 2H), 3.81 (s, 4H), 2.82 (s, 4H), 1.42 ppm (s, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 127.6, 122.1, 97.8, 65.9, 43.2, 36.6, 23.7 ppm; LRMS (70 eV, EI): *m*/*z* (%): 341 (14) $[M-CH_3+4]^+$, 339 (30) $[M-CH_3+2]^+$, 415 (16) $[M-CH_3]^+$, 43 (100).

2-Bromo-1,6-heptadiene (13): This compound was prepared following an established procedure.[25] Colorless oil. $R_f=0.52$ (hexane); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=5.85$–5.74 (m, 1H), 5.58–5.56 (m, 1H), 5.41–5.39 (m, 1H), 5.06–4.96 (m, 2H), 2.43 (t, $J=7.6$ Hz, 2H), 2.12–2.03 (m, 2H), 1.66 ppm (qt, $J=7.6$ Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=137.9$, 134.3, 116.6, 105.5, 40.6, 32.3, 26.9 ppm; elemental analysis calcd (%) for $C_7H_{11}Br$ (175.1): C 48.02, H 6.33; found: C 47.95, H 6.35.

General procedure for the preparation of dienes 4: A solution of the corresponding starting dibromodiene **1** (1 mmol) in dry Et_2O (10 mL) was treated with *t*BuLi (2.67 mL, 4 mmol) at −78 °C under nitrogen. After the reaction mixture was stirred for 30 min at this temperature, deuterium oxide (excess) or chlorotrimethylsilane (240 mg, 2.2 mmol) was added to the solution. The cooling bath was removed to allow the mixture to reach room temperature. The mixture was quenched with water and extracted with EtOAc (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the solvents were removed under vacuum. The resulting residue was purified by column chromatography (silica gel, hexane) to afford **4a**–**c**.

2,6-Bis(trimethylsilyl)-1,6-heptadiene (4a): Reaction of **1a** (254 mg, 1 mmol) with *t*BuLi (2.67 mL, 4 mmol) was followed by addition of chlorotrimethylsilane (240 mg, 2.2 mmol). Work-up as above yielded **4a** (214 mg, 89%) as a colorless oil. $R_f=0.60$ (hexane); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=5.57$–5.55 (dt, $J=3.0$ and 1.5 Hz, 2H), 5.33–5.30 (dt, $J=3.0$ and 1.0 Hz, 2H), 2.16–2.10 (m, 4H), 1.57–1.48 (m, 2H), 0.08 ppm (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=152.2$, 123.8, 36.0, 28.5, −1.4 ppm; LRMS (70 eV, EI): *m*/*z* (%): 240 (1) $[M]^+$, 73 (100); HRMS (EI): *m*/*z*: calcd for $C_{13}H_{28}Si_2$: 240.1730; found: 240.1724.

4-(*tert*-Butyldimethylsilyloxymethyl)-2,6-dideuterio-1,6-heptadiene (4b): Reaction of **1b** (398 mg, 1 mmol) with *t*BuLi (2.67 mL, 4 mmol) was followed by addition of deuterium oxide (excess). Work-up as above yielded **4b** (225 mg, 93%) as a colorless oil. $R_f=0.36$ (hexane); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=5.00$ (s, 4H), 3.48 (d, $J=5.6$ Hz, 2H), 2.20–1.95 (m, 4H), 1.72–1.55 (m, 1H), 0.89 (s, 9H), 0.03 ppm (s, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=136.7$ (t, $J=23.4$ Hz), 115.8, 64.5, 40.2, 34.8, 25.9, 18.2, −5.5 ppm; LRMS (70 eV, EI): *m*/*z* (%): 18h5 (14) $[M-t\text{Bu}]^+$, 75 (100); elemental analysis calcd (%) for $C_{14}H_{26}D_2OSi$ (242.5): C 69.35, H/D 12.47; found: C 69.22, H/D 12.51.

4,4-Bis(*tert*-butyldimethylsilyloxymethyl)-2,6-dideuterio-1,6-heptadiene (4c): Compound **1c** (543 mg, 1 mmol) was treated with *t*BuLi (2.67 mL, 4 mmol) before adding deuterium oxide (excess) to the mixture. Work-up as above afforded **4c** (352 mg, 91%) as a colorless oil. $R_f=0.64$ (hexane); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=5.03$ (s, 4H), 3.32 (s, 4H), 1.96 (s, 4H), 0.89 (s, 18H), 0.02 ppm (s, 12H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=134.2$ (t, $J=23.0$ Hz), 117.1, 63.8, 43.1, 35.0, 25.9, 18.2, −5.6 ppm; LRMS (70 eV, EI): *m*/*z* (%): 329 (2) $[M-t\text{Bu}]^+$, 147 (100); anal. calcd (%) for $C_{21}H_{42}D_2O_2Si_2$ (386.8): C 65.22, H/D 11.99; found: C 65.05, H/D 11.96.

Intramolecular carbolithiation of 2,6-dilithio-1,6-dienes 3: **General procedure for the preparation of cyclopentene derivatives 7 and 8**: TMEDA (0.6 mL, 4 mmol) was added at −78 °C to a solution of the corresponding dianion **3** (1 mmol), which was generated by reaction of the corresponding dibromodiene **1** (1 mmol) with *t*BuLi (2.67 mL, 4 mmol), as described above. The resulting mixture was stirred for 15 min at this temperature, then the cooling bath was removed to allow the reaction to reach room temperature. Stirring was continued for 50 min. The ethereal solution of the resulting dianion **5** was cooled to −78 °C, and 2.2 equiv (2.2 mmol) of an electrophile (deuterium oxide, chlorotributyltin, trimethylborate, 3-pentanone, or chlorotrimethylsilane) or 1 equiv (1 mmol) of dichlorodiphenylsilane was added. The mixture was allowed to reach room temperature and stirring was continued for 3 h. The mixture was hydrolyzed with water and extracted with EtOAc (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The solvents were removed under vacuum and the resulting residue was purified by flash column chromatography to yield functionalized cyclopentenes **7** and **8**.

1,2-Bis(trimethylsilylmethyl)cyclopentene (7a): Reaction of **1a** (254 mg, 1 mmol) with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol) was followed by addition of chlorotrimethylsilane (0.28 mL, 2.2 mmol). Work-up as above yielded **7a** (197 mg, 82%) as a colorless oil. $R_f=0.75$ (hexane); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=2.22$ (t, $J=7.4$ Hz, 4H), 1.70 (qt, $J=7.4$ Hz, 2H), 1.43 (s, 4H), 0.00 ppm (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=129.5$, 38.2, 22.3, 19.1, −0.7 ppm; LRMS (70 eV, EI): *m*/*z* (%): 240 (20) $[M]^+$, 73 (100); HRMS (EI): *m*/*z*: calcd for $C_{13}H_{28}Si_2$: 240.1730; found: 240.1738.

1,2-Bis(2-ethyl-2-hydroxybutyl)cyclopentene (7b): Reaction of **1a** (254 mg, 1 mmol) with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol) was followed by addition of 3-pentanone (189 mg, 2.2 mmol). Work-up as above yielded **7b** (207 mg, 77%) as a colorless oil. $R_f=0.22$ (hexane/EtOAc 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=2.40$ (t, $J=7.3$ Hz, 4H), 2.27 (s, 4H), 2.19 (br s, 2H), 1.76 (qt, $J=7.3$ Hz, 2H), 1.49 (q, $J=7.2$ Hz, 8H), 0.87 ppm (t, $J=7.2$ Hz, 12H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=136.4$, 75.0, 38.7, 37.8, 31.3, 23.0, 8.1 ppm; LRMS (70 eV, EI): *m*/*z* (%): 87 (100); elemental analysis calcd (%) for $C_{17}H_{32}O_2$ (268.4): C 76.06, H 12.02; found: C 75.93, H 11.98.

4-(*tert*-Butyldimethylsilyloxymethyl)-1,2-bis(deuteriomethyl)cyclopentene (7c): Reaction of **1b** (398 mg, 1 mmol) with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol) was followed by addition of deuterium oxide (excess). Work-up as above yielded **7c** (218 mg, 90%) as a colorless oil. $R_f=0.25$ (hexane); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.46$ (d, $J=6.4$ Hz, 2H), 2.42–2.30 (m, 3H), 2.06–1.95 (m, 2H), 1.56 (s, 4H), 0.90 (s, 9H), 0.05 ppm (s, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=129.5$, 67.6, 41.2, 37.8, 25.9, 18.3, 13.4 (t, $J=19.5$ Hz), −5.3 ppm; LRMS (70 eV, EI): *m*/*z* (%): 185 (24) $[M-t\text{Bu}]^+$, 109 (100); elemental analysis calcd (%) for $C_{14}H_{26}D_2OSi$ (242.5): C 69.35, H/D 12.47; found: C 69.46, H/D 12.43.

4-*tert*-Butyldimethylsilyloxymethyl-1,2-bis(tributylstannylmethyl)cyclopentene (7d): Reaction of **1b** (398 mg, 1 mmol) with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol) was followed by addition of tributyltin chloride (0.61 mL, 2.2 mmol). Work-up as above yielded **7d** (679 mg, 83%) as a colorless oil. $R_f=0.33$ (hexane); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.46$ (d, $J=6.8$ Hz, 2H), 2.37–2.20 (m, 3H), 2.02–1.89 (m, 2H), 1.60 (s, 4H), 1.55–1.38 (m, 12H), 1.36–1.19 (m, 12H), 0.99–0.70 (m, 39H), 0.04 ppm (s, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=128.0$, 67.9, 41.3, 38.0, 29.2, 27.4, 25.9, 18.3, 13.7, 10.8, 9.8, −5.3 ppm.

4-*tert*-Butyldimethylsilyloxymethyl-1,2-bis(hydroxymethyl)cyclopentene (7e): Reaction of **1b** (398 mg, 1 mmol) with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol) was followed by addition of trimethylborate (0.26 mL, 22 mmol).at −78 °C. After the mixture was stirred for 30 min at this temperature, the cooling bath was removed, and stirring was continued for 1 h at room temperature. The mixture was cooled to 0 °C and a solution of NaOH (1.33 mL of a 3 M solution in water, 4 mmol) and H_2O_2 (0.4 mL of a solution 10 M in water, 4 mmol) was added dropwise. The resulting mixture was heated to reflux for 30 min. Work-up as above yielded **7e** (174 mg, 64%) as a white solid. M.p. 38–40 °C (hexane); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.17$ (d, $J=12.8$ Hz, 2H), 4.12 (d, $J=12.8$ Hz, 2H), 3.48 (d, $J=7.6$ Hz, 2H), 3.42 (br s, 2H), 2.59–2.49 (m, 2H), 2.48–2.37 (m, 1H), 2.24–2.14 (m, 2H), 0.87 (s, 9H), 0.03 ppm (s, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=136.7$, 66.8, 58.9, 38.0, 37.8, 25.8, 18.2, −5.3 ppm; elemental analysis calcd (%) for $C_{14}H_{28}O_3Si$ (272.5): C 61.72, H 10.36; found: C 61.59, H 10.38.

4-*tert*-Butyldimethylsilyloxymethyl-1,2-bis(deuteriomethyl)-4-phenylcyclopentene (7f): Compound **1c** (474 mg, 1 mmol) was treated with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol). Addition of deuterium oxide (excess) followed by work-up as above yielded **7f** (293 mg, 92%) as a white solid. M.p. 56–58 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=$ 7.31–7.12 (m, 5H), 3.47 (s, 2H), 2.64 (d, $J=14.6$ Hz, 2H), 2.54 (d, $J=$ 14.6 Hz, 2H), 1.60 (s, 4H), 0.79 (s, 9H), −0.23 ppm (s, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=148.5$, 129.1, 127.5, 127.4, 125.3, 71.4, 49.8, 47.0, 25.8, 18.2, 13.5 (t, $J=19.3$ Hz), −5.9 ppm; LRMS (70 eV, EI): *m*/*z* (%): 261 (51) $[M-t\text{Bu}]^+$, 186 (100); elemental analysis calcd (%) for $C_{20}H_{30}D_2OSi$ (318.6): C 75.40, H/D 10.76; found: C 75.57, H/D 10.80.

4,4-Bis(*tert*-butyldimethylsilyloxymethyl)-1,2-bis(deuteriomethyl)cyclopentene (7g): Compound **1d** (543 mg, 1 mmol) was treated with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol) before addition of deuterium oxide (excess). Work-up as above afforded **7g** (348 mg, 90%) as a colorless oil. $R_f=0.45$ (hexane); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=$ 3.44 (s, 4H), 2.01 (s, 4H), 1.54 (s, 4H), 0.88 (s, 18H), 0.02 ppm (s, 12H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=128.8$, 65.8, 46.6, 46.9, 25.9, 18.3, 13.5 (t, $J=19.1$ Hz), −5.5 ppm; LRMS (70 eV, EI): *m*/*z* (%): 329 (2)

$[M-t\mathrm{Bu}]^+$, 122 (100); elemental analysis calcd (%) for $C_{21}H_{42}D_2O_2Si_2$ (386.8): C 65.22, H/D 11.99; found: C 65.46, H/D 12.03.

4,4-Bis(*tert*-butyldimethylsilyloxymethyl)-1,2-bis(tributylstannylmethyl)-cyclopentene (7h): Compound **1d** (543 mg, 1 mmol) was treated with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol). Addition of tributyltin chloride (0.61 mL, 2.2 mmol) and work-up as above yielded **7h** (780 mg, 81%) as a colorless oil. $R_f=0.63$ (hexane); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.44$ (s, 4H), 1.97 (s, 4H), 1.58 (s, 4H), 1.55–1.20 (m, 24H), 0.95–0.77 (m, 48H), 0.03 ppm (s, 12H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=127.3$, 65.8, 46.5, 44.0, 29.2, 27.4, 25.9, 18.3, 13.7, 10.8, 9.8, −5.5 ppm.

4,4-Bis(*tert*-butyldimethylsilyloxymethyl)-1,2-bis(hydroxymethyl)cyclo-pentene (7i): Reaction of **1d** (543 mg, 1 mmol) with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol) was followed by addition of trimethylborate (0.26 mL, 2.2 mmol).at −78°C. After the mixture was stirred for 30 min at this temperature, the cooling bath was removed and stirring was continued for 1 h at room temperature. The mixture was cooled to 0°C, and a solution of NaOH (1.33 mL of a 3 M solution in water, 4 mmol) and H_2O_2 (0.4 mL of a solution 10 M in water, 4 mmol) was added dropwise. The resulting mixture was heated to reflux for 30 min. Work-up as above yielded **7i** (279 mg, 67%) as a white solid. M.p. 86–88°C (hexane); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=4.19$ (s, 4H), 3.47 (s, 4H), 2.22 (s, 4H), 2.09 (brs, 1H), 1.62 (brs, 1H), 0.87 (s, 18H), 0.02 ppm (s, 12H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=136.0$, 65.4, 59.1, 46.9, 40.7, 25.8, 18.2, −5.5 ppm; elemental analysis calcd (%) for $C_{21}H_{44}O_4Si_2$ (416.7): C 60.52, H 10.64; found: C 60.31, H 10.67.

2,3-Bis(2-ethyl-2-hydroxybutyl)-8,8-dimethyl-7,9-dioxaspiro[4,5]-2-decene (7j): Compound **1e** (354 mg, 1 mmol) was treated with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol). Addition of 3-pentanone (189 mg, 2.2 mmol) and work-up as above yielded **7j** (313 mg, 81%) as a white solid. M.p. 84–86°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=3.65$ (s, 4H), 2.53 (brs, 2H), 2.33 (s, 4H), 2.21 (s, 4H), 1.46 (q, $J=7.6$ Hz, 8H), 1.40 (s, 6H), 0.83 ppm (t, $J=7.6$ Hz, 12H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=$ 134.1, 97.7, 74.9, 69.2, 45.8, 39.8, 37.8, 31.4, 23.7, 8.1 ppm; LRMS (70 eV, EI): *m*/*z* (%): 353 (3) $[M-CH_3]^+$, 87 (100); elemental analysis calcd (%) for $C_{22}H_{40}O_4$ (368.6): C 71.70, H 10.94; found: C 71.48, H 10.98.

2,2-Diphenyl-1,2,3,4,5,6-hexahydro-2-silapentalene (8a): Compound **1a** (254 mg, 1 mmol) was treated with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol). Addition of dichlorodiphenylsilane (253 mg, 1 mmol) and work-up as above yielded **8a** (221 mg, 80%) as a white solid. M.p. 81–83°C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.64$–7.59 (m, 4H), 7.47–7.38 (m, 6H), 2.33 (t, $J=7.2$ Hz, 4H), 2.10 (qt, $J=7.2$ Hz, 2H), 1.77 ppm (s, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=141.9$, 136.6, 134.5, 129.3, 127.8, 34.4, 24.9, 15.5 ppm; LRMS (70 eV, EI): *m*/*z* (%): 276 (31) $[M]^+$, 183 (100); HRMS (EI): *m*/*z* calcd for $C_{19}H_2Si$: 276.1334; found: 276.1324.

General procedure for the preparation of carbonyl derivatives 9: The suspension of the corresponding dianion **5**, generated by reaction of the corresponding starting diene **1** (1 mmol) with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol) as described above, was treated with ethyl isobutyrate (1 mmol) at −78°C. The mixture was stirred for 1 h at this temperature. It was then quenched with MeOH and extracted with EtOAc (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was removed under vacuum and the resulting residue was purified by flash column chromatography (silica gel, hexane/EtOAc, 25:1) to yield the monocyclic ketones **9**.

1-Methyl-2-(3-methyl-2-oxobutyl)cyclopentene (9a): Diene **1a** (254 mg, 1 mmol) was treated with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol). Addition of ethyl isobutyrate (116 mg, 1 mmol) followed by work-up as above gave **9a** (111 mg, 67%) as a colorless oil. $R_f=0.32$ (hexane/EtOAc, 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.15$ (s, 2H), 2.62 (sept, $J=7.0$ Hz, 1H), 2.32–2.20 (m, 4H), 1.75 (qt, $J=7.5$ Hz, 2H), 1.62 (s, 3H), 1.04 ppm (d, $J=7.0$ Hz, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=212.8$, 135.4, 128.1, 41.0, 39.8, 38.2, 36.4, 21.5, 18.2, 14.0 ppm; LRMS (70 eV, EI): *m*/*z* (%): 166 (48) $[M]^+$, 71 (100); HRMS (EI): *m*/*z*: calcd for $C_{11}H_{18}O$: 166.1358; found: 166.1352; elemental analysis calcd (%) for $C_{11}H_{18}O$ (166.3): C 79.46, H 10.91; found: C 79.30, H 10.92.

4-*tert*-Butyldimethylsilyloxymethyl-1-methyl-2-(2-oxo-2-isopropyl)cyclo-pentene (9b): Reaction of **1b** (398 mg, 1 mmol) with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol) followed by addition of ethyl isobutyrate (116 mg, 1 mmol) and work-up as above yielded **9b** (155 mg, 50%) as a colorless oil. $R_f=0.19$ (hexane/EtOAc, 25:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.46$-3.44 (m, 2H), 3.14 (s, 2H), 2.63 (sept, $J=$ 7.0 Hz, 1H), 2.46–2.31 (m, 3H), 2.18–1.95 (m, 2H), 1.62 (s, 3H), 1.07 (d, $J=7.0$ Hz, 6H), 0.87 (s, 9H), 0.02 ppm (s, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=212.6$, 134.3, 127.0, 67.1, 41.1, 39.8, 39.3, 37.8, 25.9, 18.2, 14.0, −5.4 ppm; LRMS (70 eV, EI): *m*/*z* (%): 253 (27) $[M^+$-*t*Bu], 107 (100); elemental analysis calcd (%) for $C_{18}H_{34}O_2Si$ (310.6): C 69.62, H 11.04; found: C 69.49, H 11.07.

4,4-Bis(*tert*-butyldimethylsilyloxymethyl)-1-methyl-2-(2-oxo-2-isopropyl)-cyclopentene (9c): Diene **1d** (543 mg, 1 mmol) was treated with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol). Addition of ethyl isobutyrate (116 mg, 1 mmol) and work-up as above afforded **9c** (296 mg, 65%) as a colorless oil. $R_f=0.19$ (hexane/EtOAc, 25:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.43$ (s, 4H), 3.11 (s, 2H), 2.64 (sept, $J=6.8$ Hz, 1H), 2.08 (s, 2H), 2.03 (s, 2H), 1.60 (s, 3H), 1.06 (d, $J=6.8$ Hz, 6H), 0.86 (s, 18H), 0.01 ppm (s, 12H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=212.7$, 133.7, 126.3, 65.6, 46.9, 43.7, 42.0, 41.3, 39.6, 25.8, 18.3, 14.2, −5.5 ppm; LRMS (70 eV, EI): *m*/*z* (%): 397 (53) $[M-t\mathrm{Bu}]^+$, 71 (100); elemental analysis calcd (%) for $C_{25}H_{50}O_3Si_2$ (454.8): C 66.02, H 11.08; found: C 65.87, H 11.11.

General procedure for the preparation of hydroxylic derivatives 10: The suspension of the corresponding dianion **5**, generated by reaction of the corresponding starting diene **1** (1 mmol) with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol) as described above, was treated with ethyl isobutyrate (1 mmol) at −78°C. The mixture was allowed to reach room temperature and was then stirred overnight. The mixture was hydrolyzed with water and extracted with EtOAc (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was removed under vacuum, and the resulting residue was purified by flash column chromatography (silica gel, hexane/EtOAc, 15:1) to afford the bicyclic alcohols **10**.

2-Isopropyl-1,2,3,4,5,6-hexahydropentalen-2-ol (10a): Reaction of **1a** (254 mg, 1 mmol) with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol) was followed by addition of ethyl isobutyrate (116 mg, 1 mmol). Work-up as above yielded **10a** (120 mg, 72%) as a colorless oil. $R_f=0.27$ (hexane/AcOEt, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=2.40$ (d, $J=$ 15.2 Hz, 2H), 2.29–2.14 (m, 6H), 2.10 (d, $J=15.2$ Hz, 2H), 1.81 (sept, $J=$ 6.8 Hz, 1H), 1.61 (brs, 1H), 0.95 ppm (d, $J=6.8$ Hz, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=142.9$, 90.5, 43.1, 37.3, 29.6, 27.3, 17.3 ppm; LRMS (70 eV, EI): *m*/*z* (%): 166 (28) $[M]^+$, 71 (100); HRMS (EI): *m*/*z*: calcd for $C_{11}H_{18}O$: 166.1358; found: 166.1361.

5-(*tert*-Butyldimethylsilyloxymethyl)-2-isopropyl-1,2,3,4,5,6-hexahydro-pentalen-2-ol (10b): Reaction of diene **1b** (398 mg, 1 mmol) with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol) was followed by addition of ethyl isobutyrate (116 mg, 1 mmol). Work-up as above yielded **10b** as a 1:1 mixture of diastereoisomers $\mathbf{10b_1}$ and $\mathbf{10b_2}$ (162 mg, 52% combined yield for the two diastereoisomers).

$\mathbf{10b_1}$: Colorless oil. $R_f=0.23$ (hexane/EtOAc, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.55$ (d, $J=7.2$ Hz, 2H), 2.86–2.74 (m, 1H), 2.45–2.34 (m, 2H), 2.31–2.20 (m, 2H), 2.11–1.93 (m, 4H), 1.79 (sept, $J=6.8$ Hz, 1H), 1.63 (brs, 1H), 0.93 (d, $J=6.8$ Hz, 6H), 0.88 (s, 9H), 0.04 ppm (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=141.5$, 90.1, 67.5, 44.6, 43.2, 37.3, 32.8, 25.9, 18.3, 17.3, −5.3 ppm; LRMS (70 eV, EI): *m*/*z* (%): 292 (8) $[M-H_2O]^+$, 161 (100).

$\mathbf{10b_2}$: Colorless oil. $R_f=0.16$ (hexane/EtOAc, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.54$ (d, $J=7.2$ Hz, 2H), 2.89–2.78 (m, 1H), 2.43–2.27 (m, 4H), 2.17–2.03 (m, 2H), 1.96–1.85 (m, 2H), 1.80 (sept, $J=6.9$ Hz, 1H), 1.62 (brs, 1H), 0.94 (d, $J=6.9$ Hz, 6H), 0.88 (s, 9H), 0.04 ppm (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=141.6$, 90.1, 67.3, 44.7, 43.2, 37.3, 32.9, 25.9, 18.3, 17.3, −5.3 ppm; LRMS (70 eV, EI): *m*/*z* (%): 310 (1) $[M]^+$,107 (100); HRMS (EI): *m*/*z*: calcd for $C_{18}H_{34}O_2Si$: 310.2328; found: 310.2317.

5,5-Bis(*tert*-butyldimethylsilyloxymethyl)-2-isopropyl-1,2,3,4,5,6-hexahy-dropentalen-2-ol (10c): Compound **1d** (543 mg, 1 mmol) was treated with *t*BuLi (2.67 mL, 4 mmol) and TMEDA (0.6 mL, 4 mmol). Addition

of ethyl isobutyrate (116 mg, 1 mmol) and work-up as above afforded **10c** (227 mg, 50%) as a colorless oil. R_f=0.16 (hexane/EtOAc, 25:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=3.52 (s, 2H), 3.48 (s, 2H), 2.42–2.33 (m, 2H), 2.11–1.88 (m, 6H), 1.79 (sept, J=6.7 Hz, 1H), 1.64 (br s, 1H), 0.93 (d, J=6.7 Hz, 6H), 0.88 (s, 9H), 0.87 (s, 9H), 0.03 (s, 6H), 0.02 ppm (s, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=140.6, 89.9, 65.9, 54.7, 43.4, 37.3, 35.8, 25.8, 18.2, 17.3, −5.5 ppm; LRMS (70 eV, EI): m/z (%): 397 (2) $[M-t\mathrm{Bu}]^+$, 159 (100); HRMS (EI): m/z: calcd for $C_{21}H_{41}O_3Si_2$ $[M-t\mathrm{Bu}]^+$: 397.2594; found: 397.2582.

Comparative study of the intramolecular carbolithiation of 2,6-dilithio-1,6-heptadiene 3a and 2-lithio-1,6-heptadiene 14: A solution of dibromodiene **1a** (254 mg, 1 mmol) in dry Et_2O (10 mL) was treated with 4 equiv of *t*BuLi (2.67 mL, 4 mmol) at −78°C under nitrogen. The reaction mixture was stirred for 30 min at this temperature. Depending on the experiment, at this point TMEDA (0.60 mL, 4 mmol) was added at −78°C and the resulting mixture was stirred for a further 15 min at low temperature. The cooling bath was removed to allow the reaction to reach 0°C. The mixture was stirred for another 30 min if TMEDA had been added or it was stirred for 150 min if TMEDA had not been added (see Scheme 3). The mixture was cooled to −78°C, and chloro(dimethyl)phenylsilane (376 mg, 2.2 mmol) was added to the solution. The cooling bath was removed to allow the mixture to reach room temperature. The mixture was quenched with water and extracted with EtOAc (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvents were removed under vacuum. The resulting residue was purified by column chromatography (silica gel, hexane) to afford a mixture (see Scheme 3) of products **11** and **12** 281 mg (77%) in the experiment with TMEDA and 303 mg (83%) without TMEDA.

2,6-Bis(dimethylphenylsilyl)-1,6-heptadiene (11):[26] Colorless oil. R_f= 0.28 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.53–7.48 (m, 4H), 7.40–7.33 (m, 6H), 5.64–5.60 (m, 2H), 5.40–5.37 (m, 2H), 2.10–2.04 (m, 4H), 1.48–1.39 (m, 2H), 0.35 ppm (s, 12H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=150.1, 138.3, 133.8, 128.8, 127.6, 125.7, 35.7, 28.1, −3.0 ppm; LRMS (70 eV, EI): m/z (%): 364 (1) $[M]^+$, 135 (100); elemental analysis calcd (%) for $C_{23}H_{32}Si_2$ (364.7): C 75.75, H 8.84; found: C 75.54, H 8.87.

1,2-Bis(dimethylphenylsilylmethyl)cyclopentene (12):[26] Colorless oil. R_f=0.32 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.51–7.47 (m, 6H), 7.36–7.31 (m, 6H), 2.09 (t, J=7.4 Hz, 4H), 1.65–1.57 (m, 6H), 0.25 ppm (s, 12H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=140.0, 133.4, 129.7, 128.7, 127.6, 38.2, 22.3, 18.3, −2.2 ppm; LRMS (70 eV, EI): m/z (%): 364 (18) $[M]^+$, 135 (100); HRMS (EI): m/z: calcd for $C_{23}H_{32}Si_2$: 364.2043; found: 364.2056.

Parallel to this, a solution of bromodiene **13** (175 mg, 1 mmol) in dry Et_2O (10 mL) was treated with two equivalents of *t*BuLi (1.33 mL, 2 mmol) at −78°C under nitrogen. The reaction mixture was stirred for 30 min at this temperature. Depending on the experiment, at this point TMEDA (0.30 mL, 2 mmol) was added at −78°C and the resulting mixture was stirred for another 15 min at low temperature. The cooling bath was removed to allow the mixture to reach 0°C. Stirring was continued for 30 min if TMEDA had been added or for 150 min if TMEDA had not been added (see Scheme 3). The mixture was cooled to −78°C, and chloro(dimethyl)phenylsilane (188 mg, 1.1 mmol) was added to the solution. The cooling bath was removed to allow the mixture to reach room temperature. The mixture was quenched with water and extracted with EtOAc (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the solvents were removed under vacuum. The resulting residue was purified by column chromatography (silica gel, hexane) to afford 171 mg (74%, with TMEDA) or 180 mg (78%, without TMEDA) as a mixture (see Scheme 3) of products **16** and **17** as a colorless oil, R_f=0.39 (hexane).

2-Dimethylphenylsilyl-1,6-heptadiene (16): ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.59–7.48 (m, 2H), 7.36–7.24 (m, 3H), 5.78–5.65 (m, 2H), 5.43–5.36 (m, 1H), 4.98–4.85 (m, 2H), 2.14 (t, J=7.6 Hz, 2H), 2.02–1.97 (m, 2H), 1.43 (qt, J=7.6 Hz, 2H) 0.39 ppm (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=159.5, 150.1, 138.4, 133.9, 128.9, 127.7, 125.9, 114.4, 35.4, 33.3, 28.1, −2.9 ppm.

1-Dimethylphenylsilylmethyl-2-methylenecyclopentane (17): ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.59–7.48 (m, 2H), 7.36–7.24 (m, 3H), 4.82 (s, 1H), 4.77 (s, 1H), 2.37–2.23 (m, 3H), 1.86–1.80 (m, 1H), 1.73–1.62 (m, 1H), 1.45–1.40 (m, 1H), 1.22 (dd, J=14.8, 3.6 Hz, 1H) 1.16–1.03 (m, 1H),0.72 (dd, J=14.8, 11.2 Hz, 1H), 0.30 ppm (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=138.7, 133.5, 128.8, 127.7, 126.0, 103.5, 40.3, 35.3, 32.2, 23.9, 20.7, −2.0, −2.3 ppm.

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[20] When the solutions of dianion **3a** and monoanion **14** were stirred at 11–16 °C for 60 min, a 17:1 mixture of compounds **11** and **12** and a 5:1 mixture of compounds **16** and **17** were obtained after treatment of the corresponding mixtures of dianions **3a** and **5a** and monoanions **14** and **15** with chlorodimethylphenylsilane. The ratio of the cyclized product from the carbolithiation of an isolated double bond is thus higher than the ratio of the cyclized product from the carbolithiation of a lithiated double bond.
[21] The cyclization of both **3a** and **14** starts at much lower temperature in the presence of TMEDA than in its absence. At about −20 °C, a 3.2:1 ratio of **11**:**12** was obtained from **3a** and a 4.4:1 ratio of **16**:**17** was obtained from **14**. This tendency was maintained when both cyclizations were performed at a slightly higher temperature (≈ −10 °C): 1:1 ratio for **11**:**12** and 2.5:1 for **16**:**17**.
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[23] Also, at $T = 11$–16 °C and $t = 60$ min (see ref. [20]), the ratio of the cyclized product from **14** is higher than the ratio of the cyclized product from **3a**.
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[26] Compounds **11** and **12** were prepared independently according to the procedure to prepare compounds **4** and **7**, respectively.

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