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Alkylative Carbocyclization of ω-Iodoalkynyl Tosylates with Alkynyllithium Compounds Through a Carbenoid-Chain Process Leading to (1-Iodoprop-2-ynylidene)tetrahydrofurans and -cyclopropanes

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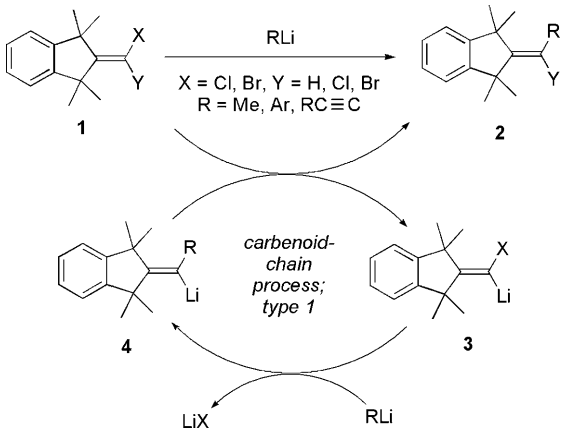
Abstract: Alkylative carbocyclization reactions of ω-iodoalkynyl tosylates with alkynyllithium compounds to give products with incorporated iodine atoms are described. Slow addition of 2-(3-iodoprop-2-ynyloxy)ethyl tosylates to 1-alkynyllithium compounds in tetrahydrofuran at 40 °C followed by additional stirring at this temperature gives (*Z*)-3-(1-iodoprop-2-ynylidene)tetrahydrofurans stereoselectively in good to moderate yields. Under similar conditions at 0 °C, 4-iodobut-1-ynyl tosylates react with 1-alkynyllithium compounds to give (1-iodoprop-2-ynylidene)cyclopropanes. The carbocyclization reactions are proposed to proceed through a new carbenoid-chain process involving the *exo* cyclization of a lithium acetylide intermediate and the vinylic substitution of the resulting TsO,Li-cycloalkylidenecarbenoids (Ts = tosyl) by 1-alkynyllithium compounds.

Keywords: alkynes · carbenoids · cyclization · iodine · lithium

Introduction

Carbenoids carrying both a metal cation and a nucleofugal group on the same carbon exhibit characteristic ambiphilic reactivities.[1] They have been exploited extensively in synthetic transformations as reactive intermediates.[2–6] Recently, the scope of carbenoid-mediated reactions has been broadened further by the development of carbon–carbon bond-forming reactions that proceed through a novel carbenoid-chain mechanism.[7,8]

Knorr and co-workers reported a facile and clean reaction of 2-(halomethylidene)indanes **1** (X = Cl, Br, Y = H, Cl, Br) with organolithium compounds, which led to a formal substitution product **2** (Scheme 1).[7] It was shown clearly that the reaction occurs through an alkylidenecarbenoid-chain mechanism (type 1), which involves generation of carbenoid **3** (either by deprotonation (Y = H) or by halogen/lithium exchange (Y = Cl, Br) with RLi (initiation step)), followed by a fast vinylic substitution of **3** by RLi to form alkenyllithium **4**,[9] and the rate-limiting transfer of Y (= H, Cl, Br) from substrate **1** to **4** with formation of product **2**, and with regeneration of carbenoid **3** to close the chain cycle.



Scheme 1. Vinylic substitution 2-(halomethylidene)indanes through a type 1 carbenoid-chain process.

Recently, we reported an efficient, atom-economical carbocyclization reaction of ω-iodo- and 1,ω-diiodo-1-alkynes **5a**,**b**, which led to cycloisomerization products **6a**,**b** (Scheme 2).[8] For example, treatment of iodoalkyne **5a** (Y = H, Z = O, $n = 1$) with a catalytic amount of LDA affords the **6a** (Y = H, Z = O, $n = 1$). The cycloisomerization reaction proceeds through a carbenoid-chain mechanism (type 2) that is different from Knorr's type 1 process. Iodoalkyne **5a**

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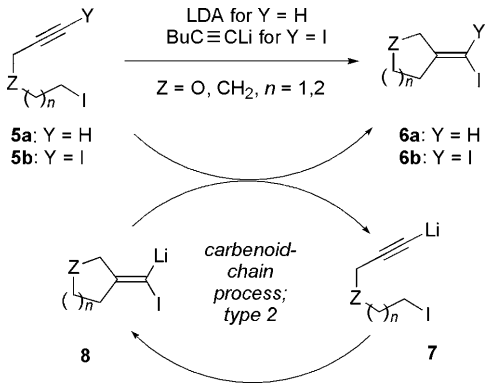
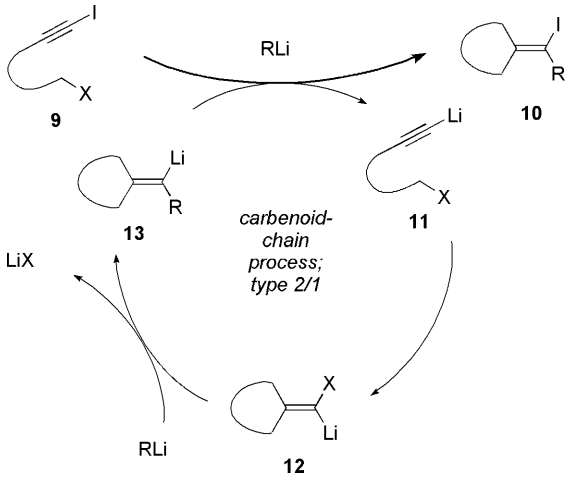


Scheme 2. Cycloisomerization through a type 2 carbenoid-chain process. LDA = lithium diisopropylamide.

is deprotonated by LDA to give lithium acetylide **7** (initiation step). In the chain cycle, acetylide **7** undergoes facile *exo* cyclization at the β position of the acetylide moiety to generate I,Li-alkylidenecarbenoid **8**,[10] which is protonated by **5a** to give product **6a**, with simultaneous regeneration of acetylide **7**. The type 2 carbenoid-chain process is also responsible for the cycloisomerization of diiodoalkyne **5b** (Y = I, Z = O, CH_2, n = 1,2) to give diiodomethylene derivatives **6b** (Y = I, Z = O, CH_2, n = 1,2). The reaction is initiated by the I/Li exchange reaction of **5b** with 1-hexynyllithium (0.2–0.4 equiv) to give acetylide **7**. The chain cycle, in this case, closes by iodination of carbenoid **8** by **5b** to produce **6b**.

There might be many variants of the carbenoid-chain process, other than type 1 and 2, that could be exploited to bring about unprecedented synthetic transformations. It occurred to us that the combination of the type 1 and 2 carbenoid-chain processes would provide a novel alkylative carbocyclization reaction of iodoalkyne **9** with organolithium compounds, which would afford the iodine-atom-retained product **10** (Scheme 3). Thus, the I/Li exchange reaction of iodoalkyne **9** with RLi generates lithium acetylide **11** with a



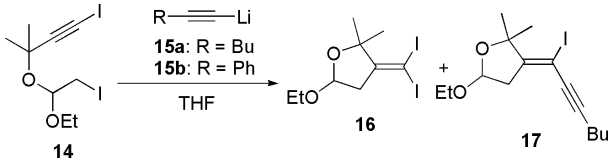
Scheme 3. Possible alkylative carbocyclization through a type 2/1 carbenoid-chain process.

leaving group X. *Exo* cyclization of **11** followed by vinylic substitution of the resulting cycloalkylidene carbenoid **12** with RLi would produce alkenyllithium intermediate **13**, which would then be iodinated by **9** to give product **10** together with regeneration of acetylide intermediate **11**.

Herein, we report the alkylative carbocyclization of ω-iodoalkynyl tosylates with alkynyllithium compounds to afford 3-(1-iodoprop-2-ynylidene)tetrahydrofurans and (1-iodoprop-2-ynylidene)cyclopropanes. The reaction is proposed to proceed through a new carbenoid-chain process involving the *exo* cyclization of a lithium acetylide intermediate and the vinylic substitution of the resulting TsO,Li-cycloalkylidenecarbenoids by the alkynyllithium compounds.

Results and Discussion

Reaction of 2-(3-iodoprop-2-ynyloxy)ethyl iodide 14 with alkynyllithium compounds: We reported recently that diiodoalkyne **14** undergoes a cycloisomerization reaction through a type 2 carbenoid-chain process upon treatment with 1-hexynyllithium (**15a**; 0.2 equiv) in THF at 40 °C for 2 h or at 0 °C for 22 h to give 3-(diiodomethylene)tetrahydrofuran **16** in high yield (Scheme 4).[8d] In anticipation that



Scheme 4.

an alkylidenecarbenoid intermediate could be trapped by **15a** before undergoing iodination by **14**, reactions were carried out by slowly adding a solution of **14** (0.5 mmol, 1.0 M) in THF to **15a** (1.1–6 equiv), which was prepared from 1-hexyne and *n*BuLi (1.6 M in hexane) in THF (1 mL) (Table 1). Reactions at 40 °C gave **17** diastereoselectively in moderate yields together with cycloisomerization product **16** (Table 1, entries 1, 2, 4, and 5). Neither the rate at which **14** was added nor the concentration of **15a** had a significant influence on the yield of **17**, or on the **17**/**16** ratio. Prolonged reaction time led to the disappearance of **16**, but resulted in a decreasing yield of **17** (Table 1, entry 3). The reaction at 0 °C gave cycloisomerization product **16** in high yield without the formation of **17** (Table 1, entry 6). When the reaction was carried out with phenylethynyllithium (**15b**), product **16** was obtained as a sole product even at 40 °C (Table 1, entry 7).

It is likely that the reactions at 40 °C proceeded mainly through an initial type 2 process followed by the conversion of the resulting product **16** to **17** through an independent type 1 process. It was demonstrated previously that 3-(diiodomethylene)tetrahydrofurans such as **16** undergo a reversible iodine/lithium exchange reaction with **15a** at 0 °C to gen-

Table 1. Reaction of diiodoalkyne **14** with 1-hexynyllithium (**15a**).[a]

Entry	**15** ([equiv])	T [°C]	t [h] [b]	[c]	Products; yield [%] **17**	Z/E[d]	**16**
1	**15a** (1.1)	40	0.5	1	53	4.8:1	21
2	**15a** (2)	40	0.5	1.5	57	2.3:1	31
3	**15a** (2)	40	0.5	19	28	10:1	<1
4	**15a** (2)	40	2	0.5	48	2.8:1	19
5	**15a** (6)	40	4	0.5	60	3.6:1	3
6	**15a** (2)	0	2	0.5	0	–	85
7	**15b** (2)	40	2	0.5	0	–	85

[a] Reactions were carried out by slowly adding a solution of **14** (0.5 mmol, 1.0 M) in THF to **15a**,**b** prepared by treatment of the corresponding 1-alkyne with *n*BuLi (1.6 M in hexane) in THF (1 mL). [b] Time for slow addition. [c] Time for further stirring after the slow addition. [d] Determined by a capillary GC analysis.

Table 2. Alkylative carbocyclization of 2-(3-iodoprop-2-ynyloxy)ethyl tosylate **18a** with 1-hexynyllithium (**15a**).[a]

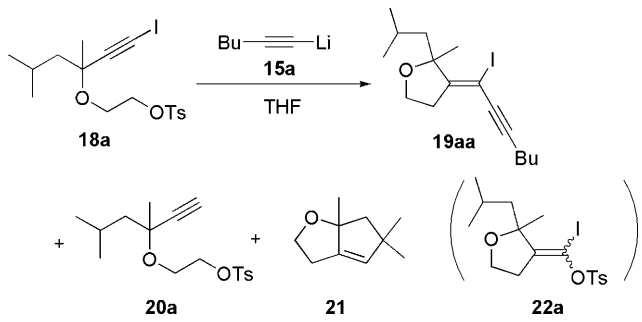
Entry	**15a** [equiv]	T [°C]	t [h] [b]	[c]	Products; yield [%] **19aa**	Z/E[d]	**21**
1[e]	2	0 to RT	2	4	17	3.2:1	25
2	2	40	2	0.5	31	4.8:1	20
3	4	40	4	1	66	5.7:1	5
4	4	RT	4	3	58	6.1:1	10
5	6	40	4	0.5	69	8.4:1	<1

[a] Reactions were carried out by slowly adding a solution of **18a** (0.5 mmol, 1.0 M) in THF to **15a** prepared by treatment of 1-hexyne with *n*BuLi (1.6 M in hexane) in THF (1 mL). [b] Time for slow addition. [c] Time for further stirring after the slow addition. [d] Determined by a capillary GC analysis. [e] After the addition of **18a** at 0 °C, the reaction mixture was stirred for 2 h at 0 °C and then for 2 h at room temperature.

erate the corresponding I,Li-alkylidenecarbenoids.[8d] Judging from the exclusive formation of **16** in recorded in entries 6 and 7 in Table 1, the I,Li-carbenoid derived from **16** did not undergo vinylic substitution by **15a** at 0 °C or by **15b** and 40 °C.

Reaction of 2-(3-iodoprop-2-ynyloxy)ethyl tosylates 18 with alkynyllithium compounds: We expected that TsO,Li-alkylidenecarbenoid **12** (X = OTs), with the more electronegative TsO group, would be more reactive toward organolithium compounds than I,Li-carbenoid **12** (X = I) (Scheme 3). We therefore turned our attention to the reaction of iodoalkynyl tosylate **9** (X = OTs).

2-(3-Iodoprop-2-ynyloxy)ethyl tosylate **18a** was chosen as a substrate (Scheme 5). Reactions were carried out with **15a** under conditions similar to those used for **14**. A solution of

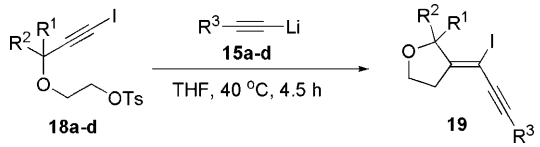


Scheme 5.

18a (0.5 mmol, 1 M) in THF was added over 2 h to **15a** (2 equiv) at 0 °C. GC analysis of quenched aliquots of the reaction mixture, taken immediately after the slow addition as well as after stirring for a further 2 h, showed only the formation of alkynyl tosylate **20a**. However, stirring for an additional 2 h at room temperature led to 3-(1-iodoprop-2-ynylidene)tetrahydrofuran **19aa** (Z/E = 3.2:1) in 17% yield (entry 1 in Table 2). In this reaction, bicyclic product **21** (25%), derived from intramolecular 1,5-C–H insertion of the corresponding alkylidenecarbenoid,[10b] and alkynyl tosylate **20a** (24%) were also formed. The formation of α-iodovinyl tosylate **22a**, which would arise from a type 2 carbenoid process, was not detected.

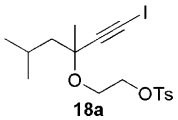
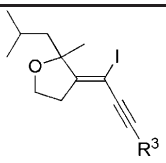
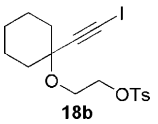
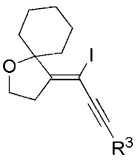
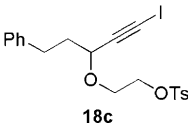
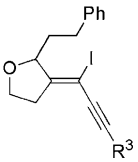
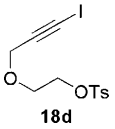
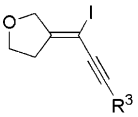
The formation of **20a** indicates the formation of a lithium acetylide derived from **18a** that is stable at 0 °C, but slowly undergoes *exo* cyclization at room temperature. To facilitate the *exo* cyclization step, the reaction was examined at 40 °C. Thus, the addition of **18a** to **15a** (2 equiv) at 40 °C for 2 h followed by further stirring for 0.5 h afforded **19aa** (31%) and **21** (20%) (Table 2, entry 2). When the addition time was extended to 4 h, and the concentration of **15a** was increased to 4 equiv, the yield of **19aa** increased with a concomitant decrease of **21** (Table 2, entry 3). Under similar conditions, the reaction at room temperature did not improve the result (Table 2, entry 4). By using 6 equiv of **15a**, the optimum yield of **19aa** (69%) was obtained with good selectivity (Z/E = 8.4:1), and with very little formation of **21** (Table 2, entry 5).

To clarify the scope of the alkylative carbocyclization, reactions were carried out between iodoalkynyl tosylates **18a–d** and alkynyllithium **15a–d** under the optimal conditions (Scheme 6, Table 3). The 1-(iodoethynyl)cyclohexyl derivative **18b** reacted with **15a** to give spirocyclic product **19ba** in 65% yield with high Z selectivity (Table 3, entry 3). Reaction of **18b** with phenylethynyllithium (**15b**), 1-naphthylethynyllithium (**15c**), and trimethylsilylethynyllithium (**15d**) also afforded the corresponding spirocyclic products **19** with Z selectivity in good to moderate yields (Table 3, entries 4–6). In the reaction with **15d**, a partial desilylation of the initial product **19bd′** (R^3 = $SiMe_3$) was observed (Table 3, entry 6). The crude products were treated with K_2CO_3 in methanol at reflux and isolated as **19bd** (R^3 = H). The efficiency of the alkylative carbocyclization reaction was influenced by the substitution pattern of the substrates. In com-



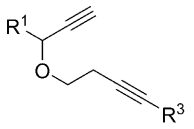
Scheme 6.

Table 3. Alkylative carbocyclization of 2-(3-iodoprop-2-ynyloxy)ethyl tosylates **18** with alkynyllithium compounds **15**.[a]

Entry	Iodoalkyl tosylate	Alkynyllithium	Product		Yield [%]	Z/E[b]
1	 **18a**	**15a**; R^3=Bu		**19aa**	69	8.4:1
2		**15b**; R^3=Ph		**19ab**	63	5.1:1
3	 **18b**	**15a**; R^3=Bu		**19ba**	65	14:1
4		**15b**; R^3=Ph		**19bb**	72	7.8:1
5		**15c**; R^3=1-naph		**19bc**	72	7.9:1
6[c]		**15d**; R^3=Me_3Si		**19bd** (R^3=H)	60	>20:1
7[d]	 **18c**	**15a**; R^3=Bu		**19ca**	50	7.3:1
8[d]		**15b**; R^3=Ph		**19cb**	35	4.1:1
9[d]	 **18d**	**15a**; R^3=Bu		**19da**	24	1.9:1

[a] Reactions were carried out at 40°C by adding a solution of **18** (0.5 mmol, 1.0 M) in THF for 4 h to **15** (6.0 equiv) prepared by treatment of the corresponding alkyne with *n*BuLi (1.6 M in hexane) in THF (1 mL). The reaction mixture was stirred further for 0.5 h before workup. [b] Determined by a capillary GC or ^{1}H NMR spectroscopic analysis. [c] The crude products were treated with K_2CO_3 in MeOH. [d] The corresponding diynes **23** were obtained in 25, 5, and 40% yield in entries 7, 8, and 9, respectively.

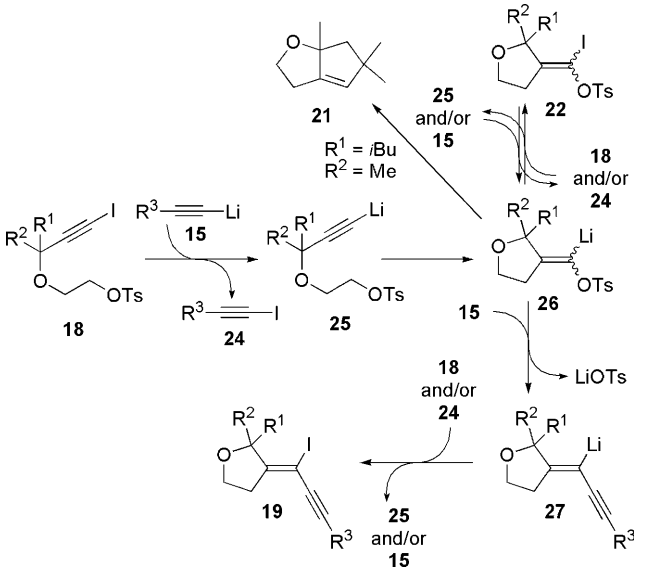
parison with *gem*-disubstituted derivatives **18a**,**b**, mono-substituted **18c** reacted with **15a**,**b** to give the corresponding products **19** in lower yields (Table 3, entries 7 and 8). The reaction of a nonsubstituted tosylate (**18d**) was much less efficient (Table 3, entry 9). In these reactions, the formation of diyne by-product **23** was observed .



23ca: R^1 = $PhCH_2CH_2$, R^3 = Bu
23cb: R^1 = $PhCH_2CH_2$, R^3 = Ph
23da: R^1 = H, R^3 = Bu

In all reactions examined, *Z* isomers of **19** were formed as the major diastereomers. The degree of selectivity was influenced both by the substitution pattern of tosylates **18** and by the structure of alkynyllithium compounds **15**. In general, higher *Z* selectivity was observed for tosylates with sterically demanding substituents R^1 and R^2. The selectivity in the reaction with **15a** decreased in the order of **18b**, **18a**, **18c**, and **18d** (Table 3, entries 3, 1, 7, and 9). As illustrated in entries 3–6 in Table 3, arylethynyllithium **15b** and **15c** exhibited lower selectivity than **15a** and **15d**.

The formation of alkylative carbocyclization products **19** from iodohexynyl tosylates **18** and 1-alkynyllithium **15** can be rationalized by invoking a mechanism involving a type 2/1 carbenoid-chain process (Scheme 7). An acetylide intermediate **25**, first formed by iodine–lithium exchange reaction of **18** with **15**, undergoes *exo* cyclization at 40°C to generate TsO,Li-alkylidenecarbenoid **26**. Then, carbenoid **26** undergoes vinylic substitution by **15** to give alkenyllithium **27**, which is iodinated by substrate **18** to give product **19**, with concurrent regeneration of acetylide **25**. Compound **19** is also produced by the iodination of alkenyllithium **27** with iodoalkyne **24**, formed by the reaction of **18** and **15**. Concurrently, compound **24** is converted into **15**, the reaction of which with **18** leads to the regeneration of **25**.



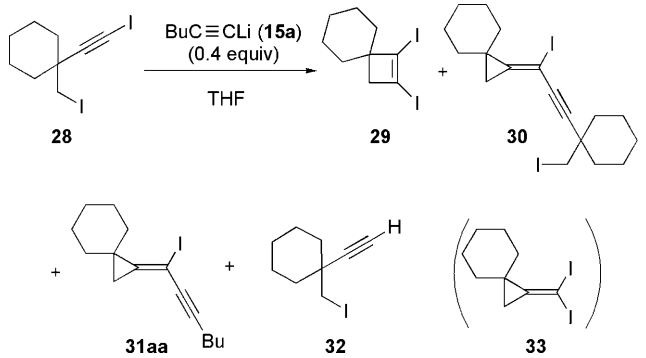
Scheme 7. Type 2/1 carbenoid chain mechanism for alkylative carbocyclization of iodohexynyl tosylates **18**.

In contrast to the reaction of diiodoalkyne **14** (Scheme 4), formation of the cycloisomerization by-product **22** was not detected in the reaction of iodoalkynyl tosylate **18**. Since **22** was not accumulated in the reaction, it is unlikely that **19** was produced through an independent type 1 chain process

via **22**. However, this does not necessarily exclude the possibility that a portion of carbenoid **26** is reversibly converted into **22** through iodination by **18** and/or **20** (Scheme 7).

While *exo* cyclization of lithium acetylide **25**, with a TsO group, was less facile than that with an iodine atom (see above), the resulting TsO,Li-alkylidenecarbenoid **26** is more reactive in the vinylic substitution reaction by alkynyllithium **15** than I,Li-alkylidenecarbenoids. Thus, phenylethynyllithium **15b** reacted smoothly with iodoalkynyl tosylates **18** to give the corresponding products **19** (Table 3, entries 2, 4, and 8) whereas it did not afford alkylative cyclization product **17** in the reaction with **14** (Table 1, entry 7). The enhanced reactivity of carbenoid **26** can be understood by considering that the carbenoid carbon becomes more electron deficient with the attachment of the electronegative TsO group. The electron-deficient character of **26** might also be responsible for the formation of 1,5-C–H insertion by-product **21** in the reaction of **18a** at the lower concentrations of **15a** (Table 2, entries 1 and 2). In the reaction of **18c**,**d**, diynes **23** were obtained as by-products (Table 3, entries 7–9). As shown in our previous work,[8d] the *exo* cyclization of lithium acetylide **25** is accelerated by *gem*-disubstitution at the propargylic position. Without the geminal substituents, acetylides derived from **18c**,**d** underwent the cyclization more slowly than those derived from *gem*-disubstituted **18a**,**b**. For these substrates, substitution by lithium acetylides **15** occurred concurrently to give by-products **23**.

Reaction of 1,4-diiodobut-1-yne 28 with a catalytic amount of 1-hexynyllithium (15a): Upon treatment with **15a** (0.2–0.4 equiv) at 40 °C in THF, diiodoalkynes **5b** (Y = I, Z = O, CH_2, n = 1,2) undergo cycloisomerization reactions through a type 2 carbenoid-chain mechanism to afford diiodomethylene derivatives **6b** (Y = I, Z = O, CH_2, n = 1,2) (Scheme 2).[8d] On the other hand, attempted cycloisomerization of 1,4-diiodobut-1-yne **28** with **15a** (0.4 equiv) did not afford the anticipated (diiodomethylene)cyclopropane **33** (Scheme 8, Table 4). Reaction at 0 °C for 4 h in THF afforded 1,2-diiodocyclobutene **29** (23%), dimeric methylenecyclopropane **30** (49%), and (1-iodoprop-2-ynylidene)cyclopropane **31aa** (3%) (Table 4, entry 1). Methylenecyclopropanes **30** and **31aa** were obtained with high Z selectivity.



Scheme 8.

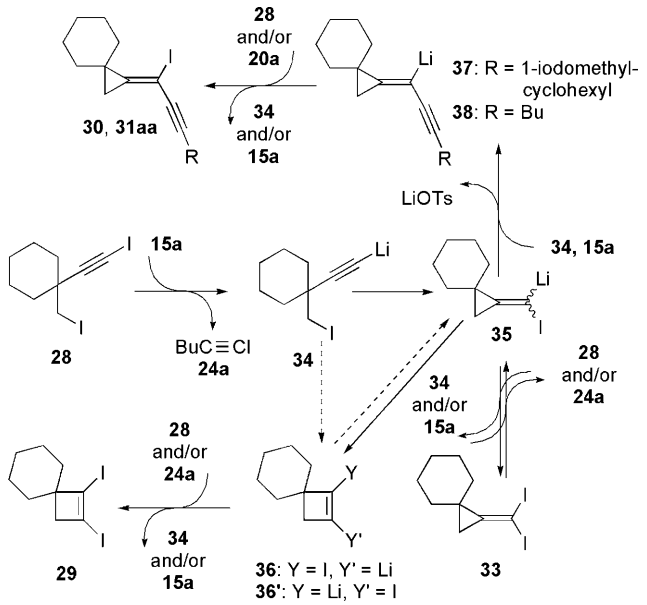
Table 4. Reaction of 1,4-diiodobut-1-yne **28** with 1-hexynyllithium (**15a**).[a]

Entry	T [°C]	Products; yield [%]		
		29	**30**[b,c]	**31aa**[b]
1	0	23	49	3
2	−20	20	62	8
3[d,e]	−80	0	20	0
4[f]	−20	5	72	4

[a] Unless otherwise noted, reactions were carried out with **28** (1 mmol) and **15a** (0.4 equiv) in THF (2 mL) for 4 h. [b] $Z/E >$ 10:1. [c] The yields were calculated by dividing the molar amounts of **29** by 0.5 mmol, or 1/2 of the molar amount of substrate **28**. [d] The reaction was carried out for 23 h. [e] Iodoalkyne **32** and starting material **28** were obtained in 25 and 45% yield, respectively. [f] The reaction was carried out in DME.

Even at −20 °C, compound **28** was consumed completely within 4 h (Table 4, entry 2). The relative yield of methylenecyclopropane products (**30**+**31aa**) increased from 69% (Table 4, entry 1) to 78% under these conditions. Although the reaction became sluggish at −80 °C, compound **30** was produced selectively in 20% yield after 23 h together with iodoalkyne **32** (25%). In addition, 45% of the starting material **28** was recovered (Table 4, entry 3). Reaction in dimethoxyethane (DME) at −20 °C afforded **30** as the major product in relatively high yield (Table 4, entry 4).

The formation of methylenecyclopropanes **30** and **31aa** implies the generation of I,Li-cyclopropylidenecarbenoid **35** through the *exo* cyclization of lithium acetylide **34** (Scheme 9). Thus, the vinylic substitution of **35** by **34** and **15a** gave alkenyllithium intermediates **37** and **38**, which were subsequently iodinated with **28** and/or 1-iodo-1-hexyne (**24a**) to give **30** and **31aa**, respectively. The formation of diiodocyclobutene **29** could conceivably occur through the Fritsch–Buttenberg–Wiechell rearrangement[11,1e] of carbenoid **35** and subsequent iodination of the resulting β-iodocy-

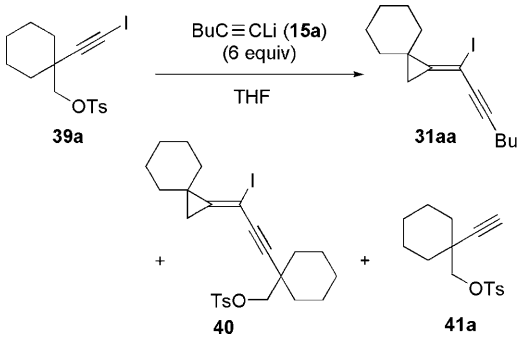


Scheme 9. Plausible mechanism for formation of **29**, **30**, and **31aa** from diiodobutyne **28**.

clobutenyllithium intermediates **36** and/or **36′** with **28** and/or **24a**.[12,13] Alternatively, compounds **36** and/or **36′** would be formed directly from **34** by *endo* cyclization,[14] although such a pathway is less likely because the formation of **29** was totally suppressed in the reaction at −80 °C (Table 4, entry 3).

In contrast to the efficient five- and six-membered ring cycloisomerization reactions observed for diiodoalkynes **5b** (Y = I, Z = O, CH_2, n = 1,2), the reaction of diiodobutyne **28** under similar conditions afforded a mixture of **29**, **30**, and **31aa** without the formation of (diiodomethylene)cyclopropane **33**. The high reactivity of I,Li-cyclopropylidenecarbenoid **35** might be responsible for the unsuccessful cycloisomerization of **28** to give **33** through a type 2 chain process. Judging from the selective formation of **30** reported in Table 4, entry 3, carbenoid **35** underwent vinylic substitution by **34** even at −80 °C. At higher temperature, compound **35** also underwent Fritsch–Buttenberg–Wiechell rearrangement.

Reaction of 4-iodobut-1-ynyl tosylates 39 with alkynyllithium compounds 15: The high reactivity of cyclopropylidenecarbenoids observed in the attempted cycloisomerization reaction of **28** prompted us to examine the alkylative carbocyclization of iodoalkynyl tosylate **39a** (Scheme 10). The reaction was first examined under the conditions optimized for iodoalkynyl tosylates **18**. Thus, addition of **39a** over 4 h to 1-hexynyllithium (**15a**) (6 equiv) in THF at 40 °C followed by further stirring for 1.5 h afforded alkylative carbocyclization product **31aa** in 57% yield with high Z selectivity (Z/E = 10:1) along with dimeric by-product **40** (24%) (Table 5, entry 1). By carrying out the reaction at 0 °C, the yield of **31aa** was improved to 63% with considerable suppression of **40** (Table 5, entry 2). Reaction at −20 °C, however, resulted in the formation of butynyl tosylate **41a** as the major product (76%), indicating that the *exo* cyclization of the corresponding acetylide intermediate became sluggish at this temperature (Table 5, entry 3). As was observed in the reaction of diiodoalkyne **28** (Table 3, entry 4), the yield of **40** increased noticeably by using DME as a solvent (Table 5, entry 4). On the other hand, the addition of tetramethylethylenediamine (TMEDA; 6 equiv) did not affect the ratio of **31aa** and **40** (Table 5, entry 5).



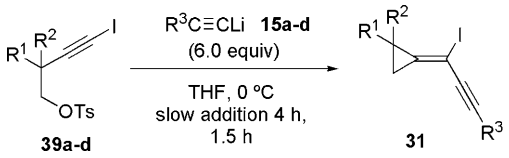
Scheme 10.

Table 5. Alkylative carbocyclization of iodobutynyl tosylate **39a** with 1-hexynyllithium (**15a**).[a]

Entry	T [°C]	Products; yield [%]		
		31aa	Z/E[b]	**40**[c,d]
1	40	57	10:1	24
2	0	63	16:1	8
3[e,f]	−20	5	17:1	–
4[g]	0	39	8.0:1	45
5[h]	0	52	10:1	12

[a] Unless otherwise noted, reactions were carried out by slowly adding a solution of **39a** (0.5 mmol, 0.5 M) in THF to **15a** (6 equiv) prepared by treatment of 1-hexyne with *n*BuLi (1.6 M in hexane) in THF (2 mL). The reaction mixture was stirred further for 1.5 h before workup. [b] Determined by ^{1}H NMR spectroscopic analysis. [c] $Z/E > 10:1$. [d] The yields were calculated by dividing the molar amounts of **40** by 0.25 mmol, or 1/2 of the molar amount of substrate **39a**. [e] The reaction mixture was stirred for 2.5 h before workup. [f] Alkynyl tosylate **41a** was obtained in 76% yield. [g] The reaction was carried out in DME. [h] TMEDA (6 equiv) was added to **15a** in THF.

Methylenecyclopropanes have broad utility for the rapid construction of complex molecular frameworks by virtue of their high strain energy.[15] To clarify the scope of the alkylative carbocyclization reaction, which leads to the synthetically useful methylenecyclopropane derivatives,[16,7] the reactions of several iodobutynyl tosylates **39a–d** with alkynyllithium compounds **15a–c** were examined under the conditions of entry 2 in Table 5 (Scheme 11).

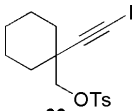
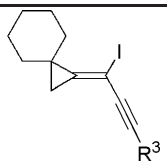
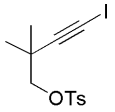
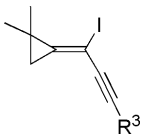
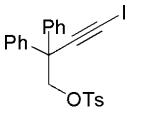
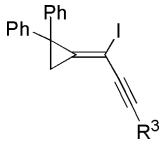
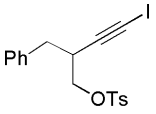
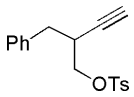


Scheme 11.

As summarized in Table 6, iodobutynyl tosylates **39a–c** with *gem*-disubstitution at the propargyl position reacted smoothly at 0 °C with **15 a–c** to give the corresponding (prop-2-ynylidene)cyclopropanes **31** in good to moderate yields. On the other hand, the reaction of mono-substituted **39d** with **15a** afforded butynyl tosylate **41d** without the formation of a carbocyclization product, which indicates that the *exo* cyclization of the corresponding mono-substituted acetylide intermediate is slow at 0 °C (Table 6, entry 11).

In the reaction of **39a** with **15a–d**, the Z isomers of **31** were obtained as the major products (Table 6, entries 1–3). The Z selectivity was higher for the reaction with alkynyllithium **15a** than with arylethynyllithium **15b,c**. The trend in stereoselectivity is similar to that observed in the reaction of iodohexynyl tosylates **14** (Table 2). Z selectivity was also observed (albeit somewhat diminished) for dimethyl derivative **39b** (Table 6, entries 6 and 7). While moderate Z selectivity was observed in the reaction of diphenyl derivative **39c** with

Table 6. Alkylative carbocyclization reaction of iodobutynyl tosylates **39** with **15**.[a]

Entry	Iodoalkyl tosylate	Alkynyllithium		Product	Yield [%]	Z/E[b]
1	 **39a**		**15a**	**31aa**; R^3 = Bu	63	16:1
2			**15b**	**31ba**; R^3 = Ph	54	4.9:1
3[c]			**15c**	**31ac**; R^3 = 1-naph	80	3.0:1
4[c,d]			**15c**	**31ac**	73	1:1.1
5[c,e]			**15c**	**31ac**	59	1.0:1
6[f]	 **39b**		**15a**	**31ba**; R^3 = Bu	37	1.4:1
7			**15c**	**31bc**; R^3 = 1-naph	75	1.4:1
8	 **39c**		**15a**	**31ca**; R^3 = Bu	45	1.7:1
9			**15b**	**31cb**; R^3 = Ph	69	1:2.4
10			**15c**	**31cc**; R^3 = 1-naph	65	1.3.0
11	 **39d**		**15a**	**41d**	35	–

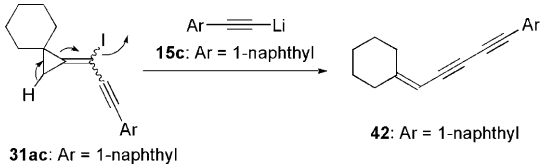
[a] Unless otherwise noted, reactions were carried out by adding a solution of **39a--d** (0.5 mmol) in THF (1 mL) to a solution of 1-alkynyllithium **15a--d** (3 mmol) in THF (2 mL) during 4 h at 0 °C. The reaction mixture was stirred for a further 1.5 h before workup. [b] Determined by ^{1}H NMR spectroscopy. [c] Enediyne **42** was obtained in 9, 13, and 30% yield in entries 3, 4, and 5, respectively. [d] Further stirring for 3 h. [e] Further stirring for 4 h. [f] Slow addition over 1 h.

15a (Table 6, entry 8), reactions with arylethynyllithium **15b**,**c** afforded the *E* isomers as major products (Table 6, entries 10 and 11).

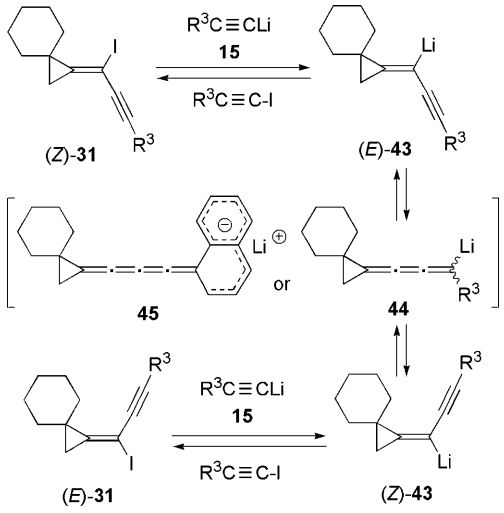
In the reaction of **39a** with **15c**, the *Z*/*E* ratio of product **31ac** varied with reaction times. Thus, under the standard reaction conditions, in which the reaction mixture was stirred for a further 1.5 h after the slow addition of **39a**, a 3.0:1 mixture of (*Z*)- and (*E*)-**31ac** was obtained (Table 6, entry 3). Extension of the additional stirring time to 3 or 4 h resulted in the formation of a approximately 1:1 mixture of the isomers (Table 6, entries 4 and 5), which suggests that isomerization occurs between (*Z*)- and (*E*)-**31ac**. In these reactions, formation of by-product enediyne **42** was observed. The by-product is most probably produced by the ring-opening reaction of **31ac**, which itself is induced by deprotonation of the cyclopropane-ring proton by **15c** (Scheme 12). The yield of **42** increased with longer reaction times, counterbalancing the decrease in yield of **31ac** (Table 6, entries 3–5). Isomerization between (*Z*)- and (*E*)-**31ac** under the present reaction conditions was confirmed by carrying out a separate isomerization experiment on the pure *Z* isomer: upon treatment with **15c** (6 equiv) in THF at 0 °C for 2 h, compound (*Z*)-**31ac** underwent isomerization to give a 1.2:1 mixture of (*Z*)- and (*E*)-**31ac** in 77% yield.

Isomerization between (*Z*)- and (*E*)-**31ac** most probably occurred via alkenyllithium (*E*)- and (*Z*)-**43** (R^3 = 1-naphthyl), which are formed by I/Li exchange of **31ac** with **15c** (Scheme 13).[8d] Butatrienyllithium **44** (R^3 = 1-naphthyl), or the more delocalized structure **45**, might be responsible for the interconversion between (*E*)- and (*Z*)-**43** (R^3 = 1-naphthyl).

The observed decrease in *Z* selectivity in order from **31aa** to **31ab** to **31ac** (Table 6, entries 1–3) can be rationalized by assuming a relatively high kinetic selectivity for *Z*, which is reduced to varying degrees by isomerization. In the reaction with **15a**, high *Z* selectivity was observed even at 40 °C (Table 5, entry 1), which indicates that isomerization is slow, if not negligible. Interconversion between (*E*)- and (*Z*)-**43** (R^3 = Bu) is less favorable due to the instability of butatrienyllithium **44** (R^3 = Bu), which is devoid of aromatic conjugation. In the reaction with **15b**, reduction in the initial kinetic *Z* selectivity of **31ab** via **44** (R^3 = Ph) might be less extensive than that of **31ac**, which results in a *Z*/*E* ratio in be-



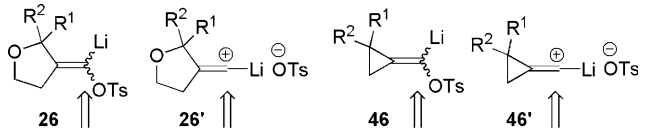
Scheme 12.



Scheme 13. Isomerization of (*Z*)- and (*E*)-**31ac** via alkenyllithium (*E*)- and (*Z*)-**43**.

tween those of **31aa** and **31ac**. Reaction of diphenyl derivative **39c** with arylethynyllithium **15b**,**c** gave the corresponding products **31cb** and **31cc** with moderate *E* selectivity (Table 6, entries 9 and 10). The *E* selectivity might be the result of extensive isomerization of the kinetically favorable *Z* isomers to the *E* isomers. Support for the thermodynamic preference for the *E* isomer was obtained by ab initio molecular orbital calculations (HF/3-21G*)[18,19] of (*E*)- and (*Z*)-**31cb**, which showed that the *E* isomer is 1.25 kcal mol^{-1} more stable than the *Z* isomer.[20,21] In the alkylative carbocyclization of iodohexynyl tosylates **18**, *Z* selectivities were slightly lower with arylethynyllithium **15b**,**c** than with alkynyllithium **15a**. It is possible that initial kinetic *Z* selectivities would be reduced to some extent by the analogous isomerization.

The reactions with 1-hexynyllithium **15a** provide us with information on the stereochemistry of nucleophilic substitution of the alkylidenecarbenoid intermediate[9d,1e] with minimum influence of the subsequent isomerization. In the reactions of both **18** and **39**, compound **15a** exhibited higher *Z* selectivity for the substrates with sterically more demanding groups at the propargylic position. Irrespective of the *E,Z* geometry of TsO,Li-alkylidenecarbenoids **26** and **46**, for which no experimental information is available, the general trend in stereoselectivity is consistent with the preferential attack of **15a** from the less hindered side of alkylidenecarbenoids **26** and **46** or, more probably, their dissociated forms, **26′** and **46′** (Scheme 14).



Scheme 14. Possible rationale for the *Z* selectivity.

Determination of *E*,*Z*-stereochemistry: Although most of the 3-(1-iodoprop-2-ynylidene)tetrahydrofurans **19** were obtained as oils, the major isomer (*Z*)-**19bc** was recrystallized from hexane to give suitable crystals for X-ray crystallographic analysis, which showed unequivocal *Z* geometry (Figure 1). The stereochemistry of other products (**19**), as well as that of **17**, was assigned based on consistent trends in ^{13}C NMR chemical-shift differences between *Z* and *E* isomers (Table 7 in the Supporting Information). Stereochemical assignments for the 3-(1-iodoprop-2-ynylidene)cyclopropanes **31** were also based on X-ray analysis and consistent trends in ^{13}C NMR chemical-shift differences between *Z* and *E* isomers (Table 8 in the Supporting Information). Recrystallization of a 1:2.4 mixture of (*Z*)- and (*E*)-**31cb** from hexane gave crystals of the minor *Z* isomer suitable for X-ray analysis, which allowed *Z* geometry to be unambiguously established (Figure 2).

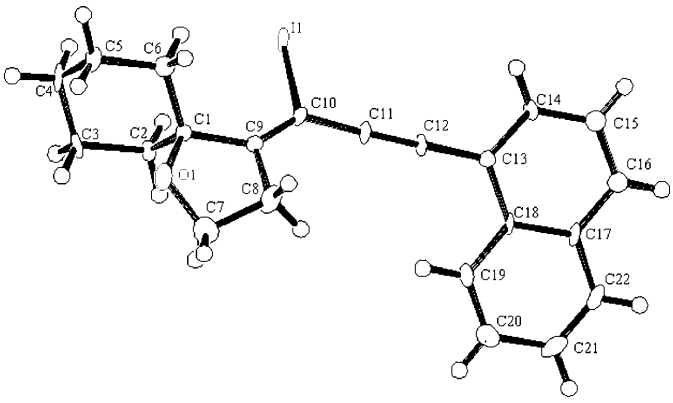


Figure 1. ORTEP diagram of (*Z*)-**19bc**.

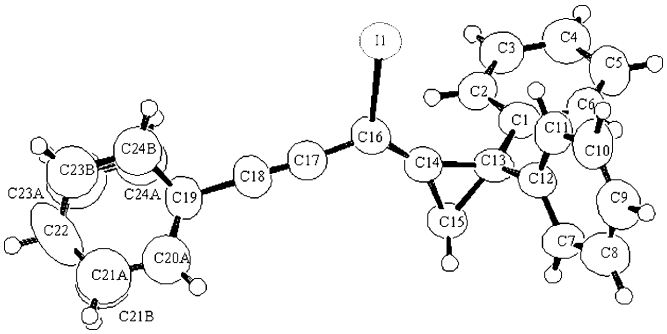


Figure 2. ORTEP diagram of (*Z*)-**31cb**.

Conclusion

We have described a new alkylative carbocyclization reaction of ω-iodoalkynyl tosylates with alkynyllithium compounds to give products with incorporated iodine atoms. Treatment of 2-(3-iodoprop-2-ynyloxy)ethyl tosylates with 1-alkynyllithium compounds in THF at 40 °C provided (*Z*)-3-(1-iodoprop-2-ynylidene)tetrahydrofurans stereoselectively in good to moderate yields. 4-Iodobut-1-ynyl tosylates underwent alkylative carbocyclization with 1-alkynyllithium compounds at 0 °C to give (1-iodoprop-2-ynylidene)cyclopropanes. In this reaction, high *Z* selectivity was observed when the kinetically favorable *Z* isomers were not prone to isomerizing to the thermodynamically more stable *E* isomers. We propose that these reactions proceed through a new carbenoid-chain process involving *exo* cyclization of a lithium acetylide intermediate and vinylic substitution of the resulting TsO,Li-cycloalkylidenecarbenoid by 1-alkynyllithium compounds.

Experimental Section

General: NMR spectra were recorded on a Bruker DRX-500 spectrometer (500 MHz for ^{1}H and 125.8 MHz for ^{13}C). Proton chemical shifts are reported in ppm (δ) using residual $CHCl_3$ ($\delta = 7.26$ ppm) or C_6D_6 ($\delta =$

7.24 ppm) in deuterated solvents as the internal standard. Carbon chemical shifts are reported relative to the internal standard $CDCl_3$ ($\delta=$ 77.0 ppm) or C_6D_6 ($\delta=128.0$ ppm). MS measurements were conducted with a JEOL JMS-700 instrument. X-ray analysis was conducted with a Rigaku AFC7R diffractometer with filtered $Cu_{K\alpha}$ radiation and a rotating anode generator at 213 K. GC analyses were performed with a capillary column (OV-1, 30 m). Flash column chromatography was performed by using silica gel (Wakogel C-300). THF, DME, and toluene were dried and distilled over sodium benzophenone ketyl. CH_2Cl_2 and triethylamine were dried and distilled over CaH_2. Acetone was dried and distilled over K_2CO_3. 1-Hexyne, phenylacetylene, 1-ethynylnaphthalene, trimethylsilylacetylene, and $BF_3{\cdot}OEt_2$ were distilled before use. Other commercially available reagents were used without further purification. Reactions were performed under an argon atmosphere unless otherwise noted.

5-Ethoxy-3-(1-iodohept-2-ynylidene)-2,2-dimethyltetrahydrofuran (17) (Table 1, entry 5): *n*BuLi (1.6 M in hexane; 1.94 mL, 3.1 mmol) was added to a solution of 1-hexyne (0.34 mL, 3.0 mmol) in THF (1 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 15 min. Compound **14**[8d] (0.204 g, 0.50 mmol) in THF (0.5 mL) was added to the resulting mixture of **15a** in THF at 40 °C over 4 h with a syringe pump. After stirring for a further 0.5 h at 40 °C, the reaction mixture was poured into water and extracted with ethyl acetate (3×30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by flash chromatography (3–5% diethyl ether in hexane) to give, in order of elution, **17** (0.109 g, 65%) and **16** (5.7 mg, 3%) ($Z/E=3.6$:1).[8d] The *Z* isomer was isolated by recycling gel permeation chromatography (JAI LC-908 equipped with JAIGEL-1H and −2H columns, toluene as an eluent). (*Z*)-**17**: ^{1}H NMR (500 MHz, C_6D_6): $\delta=0.82$ (3H, t, $J=7.1$ Hz), 1.13 (3H, t, $J=7.1$ Hz), 1.26–1.35 (4H, m), 1.63 (3H, s), 1.82 (3H, s), 2.17 (2H, br t, $J=6.4$ Hz), 2.91 (1H, dd, $J=5.4$ and 17.4 Hz), 3.24–3.34 (2H, m), 3.81 (1H, m), 4.90 ppm (1H, d, $J=5.4$ Hz); ^{13}C NMR (125.8 MHz, C_6D_6): $\delta=13.6$, 15.2, 19.2, 22.1, 26.5, 27.0, 30.8, 44.8, 60.9, 62.3, 83.5, 84.7, 95.5, 100.5, 158.9 ppm; MS (EI), *m*/*z* (%): 362 (31) $[M]^+$, 250 (68), 99 (100); HRMS (EI): calcd for $C_{15}H_{23}IO_2$: 362.0743; found 362.0748. (*Z*)- and (*E*)-**17** (1:1): ^{1}H NMR (500 MHz, C_6D_6): $\delta=0.81$ (3H for *Z* and *E* isomer, t, $J=7.1$ Hz), 1.13 (3H for *Z* isomer, t, $J=7.1$ Hz), 1.15 (3H for *E* isomer, t, $J=7.1$ Hz), 1.28–1.33 (4H for *Z* and *E* isomer, m), 1.63 (3H for *Z* isomer, s), 1.73 (3H for *E* isomer, s), 1.82 (3H for *Z* isomer, s), 1.88 (3H for *E* isomer, s), 2.12 (2H for *E* isomer, t, $J=$ 6.6 Hz), 2.17 (2H for *Z* isomer, br t, $J=6.4$ Hz), 2.76 (1H for *E* isomer, dd, $J=5.5$ and 18.2 Hz), 2.91 (1H for *Z* isomer, dd, $J=5.4$ and 17.4 Hz), 2.96 (1H for *E* isomer, d, $J=18.2$ Hz), 3.25–3.32 (1H for *E* isomer and 2H for *Z* isomer, m), 3.81 (1H for *Z* and *E* isomer, m), 4.90 (1H for *Z* isomer, d, $J=5.4$ Hz), 4.97 ppm (1H for *E* isomer, d, $J=5.4$ Hz); ^{13}C NMR (125.8 MHz, C_6D_6): $\delta=13.52$, 15.20, 19.34, 22.18, 26.8, 27.6, 30.5, 49.9, 62.33, 65.0, 81.5, 83.8, 97.9, 100.3, 161.3 ppm for *E* isomer, 13.58, 15.18, 19.22, 22.08, 26.5, 27.0, 30.8, 44.8, 60.9, 62.29, 83.5, 84.7, 95.5, 100.5, 158.9 ppm for *Z* isomer; MS (EI): *m*/*z* (%): 362 (14) $[M]^+$, 58 (100); HRMS (EI): calcd for $C_{15}H_{23}IO_2$: 362.0743; found: 362.0748.

Typical procedure for alkylative carbocyclization of iodohexynyl tosylates 18 with alkynyllithium compounds 15

*3-(1-Iodohept-2-ynylidene)-2-isobutyl-2-methyltetrahydrofuran (**19aa**) (Table 3, entry 1)*: *n*BuLi (1.6 M in hexane; 1.94 mL, 3.1 mmol) was added to a solution of 1-hexyne (0.34 mL, 3.0 mmol) in THF (1 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 15 min. Iodoalkynyl tosylate **18a** (0.224 g, 0.50 mmol) in THF (0.5 mL) was added to the resulting mixture of **15a** in THF at 40 °C over 4 h with a syringe pump. After stirring for 30 min at 40 °C, the reaction mixture was poured into water and extracted three times with ethyl acetate (3×30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by flash chromatography (1–2% diethyl ether in hexane) to give **19aa** (0.117 g, 65%; $Z/E=8.4$:1): ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=$ 0.94 (9H for *E* and *Z* isomer, m), 1.37 (3H for *Z* isomer, s), 1.38 (3H for *E* isomer, s), 1.38–1.57 (5H for *Z* and *E* isomer, m), 1.64 (1H for *E* isomer, dd, $J=5.3$ and 14.8 Hz), 1.74 (1H for *Z* and *E* isomer, sept, $J=$ ca. 6.3 Hz), 1.93 (1H for *E* isomer, dd, $J=5.3$ and 14.8 Hz), 2.02 (1H for *Z* isomer, dd, $J=5.3$ and 14.7 Hz), 2.43 (2H for *Z* and *E* isomer, t, $J=$ 7.0 Hz), 2.62–2.75 (2H for *Z* and *E* isomer, m), 2.80 (1H for *Z* isomer, td, $J=8.5$ and 17.0 Hz), 2.92 (1H for *Z* isomer, ddd, $J=4.2$, 6.7, and 17.0 Hz), 3.74 (1H for *Z* isomer, dt, $J=6.8$ and 8.6 Hz), 3.75–3.95 (2H for *Z* and *E* isomer, m), 3.85 ppm (1H for *Z* isomer, dt, $J=4.2$ and 8.6 Hz); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 13.6, 19.2, 21.9, 23.0, 24.0, 24.3, 24.7, 30.7, 38.7, 44.9, 60.6, 63.1, 82.9, 86.4, 95.1, 159.6 ppm for *Z* isomer, 13.5, 19.4, 22.1, 23.5, 23.9, 24.5, 24.6, 30.3, 43.5, 45.5, 62.7, 64.5, 80.9, 85.7, 97.7, 161.8 ppm for *E* isomer; MS (EI): *m*/*z* (%): 361 (<1) $[M]^+$, 349 (54), 303 (100), 58 (85); HRMS (EI): calcd for $C_{16}H_{25}OI$: 360.0950; found: 360.0960.

Typical procedure for reaction of 1,4-diiodobut-1-yne 28 with a catalytic amount of 1-hexynyllithium (15a)

*1,2-Diiodospiro[3.5]non-1-ene (**29**) (Table 4, entry 1)*: *n*BuLi (1.6 M in hexane; 0.48 mL, 0.77 mmol) was added to a solution of 1-hexyne (0.082 mL, 0.71 mmol) in THF (2.1 mL) at 0 °C. The resulting solution was stirred at 0 °C for 15 min to give a 0.27 M solution of **15a**. Compound **15a** (0.74 mL, 0.20 mmol) was added to a solution of **28** (185 mg, 0.495 mmol) in THF (0.7 mL) at 0 °C. The resulting solution was stirred at 0 °C for 4 h. The mixture was poured into water (10 mL) and extracted with diethyl ether (3×30 mL). The combined organic layers were washed with brine, dried (Mg_2SO_4), and concentrated in vacuo. The residue was purified by flash chromatography (hexane) to give, in order of elution, **29** (43 mg, 23%) and **30** (53 mg, 49%). **29**: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=$ 1.17 (1H, m), 1.25–1.39 (4H, m), 1.50–1.53 (2H, m), 1.62 (1H, m), 1.74–1.77 (2H, m), 2.81 ppm (2H, s); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta=23.7$, 25.1, 34.4, 52.9, 59.4, 99.4, 117.6 ppm; MS (EI): *m*/*z* (%): 374 (4) $[M]^+$, 247 (5), 120 (3), 58 (100); HRMS (EI): calcd for $C_9H_{12}I_2$; 373.9028; found: 373.9022. **30**: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=1.11$ (1H, m), 1.25–1.32 (4H, m), 1.32 (2H, s), 1.40–1.48 (3H, m), 1.58–1.67 (6H, m), 1.71–1.79 (4H, m), 1.87 (2H, br d, $J=12.1$ Hz), 3.27 ppm (2H, s); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta=20.2$, 23.1, 23.5, 25.2, 25.7, 25.9, 30.4, 32.1, 37.6, 38.0, 55.0, 84.7, 92.2, 151.4 ppm; MS (EI), *m*/*z* (%): 494 (2) $[M]^+$, 367 (16), 240 (100); HRMS (EI): calcd for $C_{18}H_{24}I_2$: 493.9967; found: 493.9970.

Typical procedure for alkylative carbocyclization of iodobutynyl tosylates 39 with alkynyllithium compounds 15

*1-(1-Iodohept-2-ynylidene)spiro[2.5]octane (**31aa**) (Table 6, entry 1)*: *n*BuLi (1.6 M in hexane; 1.94 mL, 3.1 mmol) was added to a solution of 1-hexyne (0.34 mL, 3.0 mmol) in THF (2 mL) at 0 °C. The resulting solution was stirred at 0 °C for 15 min. Iodobutynyl tosylate **39a** (209 mg, 0.50 mmol) in THF (1 mL) was added to the resulting solution of **15a** in THF at 0 °C over 4 h with a syringe pump. The resulting solution was stirred at 0 °C for 1.5 h. The mixture was poured into water (10 mL) and extracted with Et_2O (3×30 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (0–20% ethyl acetate in hexane) to give, in order of elution, **31aa** (103 mg, 63% yield, $Z/E=16$:1) and **40** (11 mg, 8%). **31aa**: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.92$ (3H for *Z* and *E* isomer, t, $J=$ 7.3 Hz), 1.03 (2H for *E* isomer, s), 1.26 (2H for *Z* and *E* isomer, m), 1.31 (2H for *Z* isomer, s), 1.35–1.82 (12H for *Z* and *E* isomer, m), 2.37 ppm (2H for *Z* and *E* isomer, t, $J=7.1$ Hz). ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta=13.6$, 19.18, 21.96, 23.0, 25.2, 25.85, 30.2, 30.5, 32.0, 55.8, 81.0, 90.6, 150.3 for *Z* isomer, 13.6, 19.16, 21.92, 24.2, 25.91, 26.00, 30.5, 34.6, 37.1, 59.9, 81.4, 90.4, 153.2 ppm; MS (EI), *m*/*z* (%): 328 (7) $[M]^+$, 201 (22), 58 (100); HRMS (EI): calcd for $C_{15}H_{21}I$: 328.0688; found: 328.0684. **40**: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.91$ (1H, m), 1.14 (1H, m), 1.25–1.80 (20H, m, including s (2H) at 1.29), 2.45 (3H, s), 3.84 (2H, s), 7.34 (2H, d, $J=8.2$ Hz), 7.81 ppm (2H, d, $J=8.2$ Hz); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 21.7, 22.4, 23.1, 25.2, 25.5, 25.8, 30.3, 32.0, 33.6, 38.0, 54.7, 76.0, 84.6, 90.5, 128.0, 129.8, 132.8, 144.7, 151.7 ppm; MS (EI): *m*/*z* (%): 538 (<1) $[M]^+$, 239 (38), 149 (100); HRMS (EI): calcd for $C_{25}H_{31}O_3SI$: 538.1039; found: 538.1055.

X-ray analysis of (*Z*)-19b,c: Single crystals suitable for X-ray analysis were obtained by recrystallization from hexane as colorless prisms. Crystal dimensions: 0.60×0.50×0.50 mm^3. Crystal data: $C_{22}H_{21}OI$; $M=428.31$; monoclinic; space group $P2_1/a$ (no. 14); $a=17.523(8)$, $b=7.512(2)$, $c=$ 14.123(4) Å; $\beta=96.42(3)°$; $V=1847.5(10)$ Å^3; $Z=4$; $\rho_{calcd}=1.540$ g cm^{-3}; $F(000)=856$; reflections collected/unique 4445/3267 ($R_{int}=0.134$). The structure was solved by direct methods (SHELXL-97) and refined by

full-matrix least-squares methods on F^2 with 188 parameters. $R_1 = 0.0651$ ($I > 2\sigma(I)$), $wR_2 = 0.1786$, goodness of fit (GOF) = 1.159; max./min. residual density 2.66/−2.55 e Å^3.

X-ray analysis of (*Z*)-31cb: Single crystals suitable for X-ray analysis were obtained by recrystallization from hexane as colorless prisms. Crystal dimensions: 0.30 × 0.20 × 0.20 mm^3. Crystal data: $C_{24}H_{17}I$; $M = 432.30$; monoclinic; space group $P2_1/n$ (no. 14); $a = 12.708(8)$, $b = 27.602(15)$, $c = 6.251(3)$ Å; $\beta = 95.44(4)°$; $V = 2182.7(20)$ Å^3; $Z = 4$; $\rho_{calcd} = 1.315$ g cm^{-3}; $F(000) = 856$; reflections collected/unique 5380/3872 ($R_{int} = 0.388$). The structure was solved by direct methods (SHELXL-97) and refined by full-matrix least-squares methods on F^2 with 224 parameters. $R_1 = 0.1444$ ($I > 2\sigma(I)$), $wR_2 = 0.3228$, GOF = 1.243; max./min. residual density 0.93/−3.54 e Å^3.

CCDC-774472 (**19b,c**) and 774473 (**31b,c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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[20] The calculated relative energy (1.25 kcal mol^{-1}) corresponds to a thermodynamic *E*/*Z* ratio of 10:1 at 0 °C.

[21] Calculations were also performed for spirocyclic product **31ab** to gain information on the thermodynamic stability of the *E* and *Z* isomers. The calculations showed that two stable structures, with respect to the conformation of the cyclohexane ring, exist for each isomer. Calculated relative energies are 0 and 0.33 kcal mol^{-1} for conformers 1 and 2 of (*E*)-**31ab**, respectively, and 0.40 and 1.30 kcal mol^{-1} for conformers 1 and 2 of (*Z*)-**31ab**, which corresponds to a calculated thermodynamic *E*/*Z* ratio of 2.7:1 at 0 °C.

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