

Novel cyclization reaction of 1, ω -diiodo-1-alkynes without the loss of iodine atoms†

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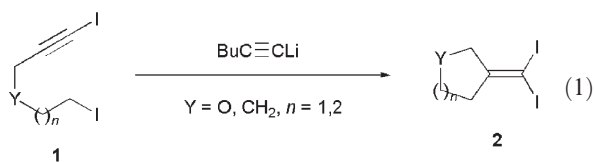
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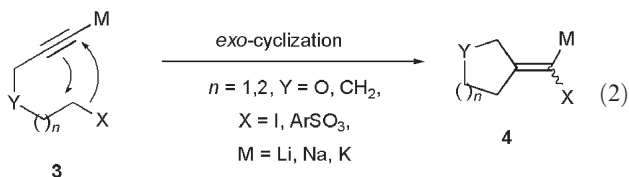
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In the presence of 1-hexynyllithium (0.2–0.6 equiv.), 1, ω -diiodo-1-alkynes undergo a new type of cyclization reaction without the loss of two iodine atoms to afford (diiodomethylene)cycloalkanes.

Organoiodine compounds are efficient and versatile electrophilic reagents, frequently utilized in carbon–carbon bond forming reactions. In their reactions, the substrate iodine atom is usually lost as an iodide salt and not incorporated into the product. Carbon–carbon bond forming reactions that give products with incorporation of the iodine atom would provide a useful means for constructing complex carbon frameworks through a subsequent bond forming reaction of the iodine-containing products.¹ Herein, is reported a new type of cycloisomerization in which 1, ω -diiodo-1-alkynes **1** are transformed into (diiodomethylene)cycloalkanes **2** without the loss of two iodo functional groups (eqn. (1)).



Although metal acetylides generally react at the α -carbon with electrophiles, it has recently been disclosed that those bearing a leaving group at an appropriate position undergo *exo*-cyclization at the β -position to generate alkylidene carbenoids **4** (eqn. (2)).^{2,3} Most recently, a LDA-catalyzed cycloisomerization of iodoalkyne **5** has been developed by using the *exo*-cyclization of a lithium acetylide (eqn. (3)).⁴ In this reaction, initial lithiation of **5** by LDA and the *exo*-cyclization of the resulting acetylide **3** (M = Li, $n = 1$, Y = O, X = I) generates the corresponding carbenoid **4**, which undergoes deprotonation of the starting iodoalkyne **5** to yield cycloisomerization product **6** with simultaneous regeneration of intermediate **3**.

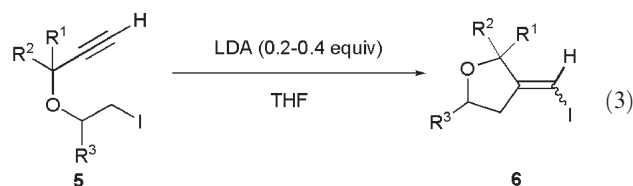


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† Electronic Supplementary Information (ESI) available: Typical reaction procedure and characterization data for products in Table 2. See DOI: 10.1039/b516515f



If the same intermediate **3** is generated by an iodine/lithium exchange reaction of diiodoalkynes **1** with an appropriate organolithium compound, carbenoid intermediate **4**, formed by *exo*-cyclization, will react with diiodoalkyne **1** to give cycloisomerization product **2**. Indeed, when diiodoalkyne **1a** was treated with 0.2 equiv. of butyllithium in THF at 40 °C, the corresponding cycloisomerization product **2a** was obtained in 69% yield (Table 1, entry 1). Although an increase in the amount of butyllithium resulted in a lower yield of **2a** (Table 1, entry 2), an improvement in the yield of **2a** was realized by using 1-hexynyllithium as an initiator. Thus, in the presence of 0.2 equiv. of 1-hexynyllithium in THF at 40 °C, **1a** cyclized to give **2a** in 85% yield (Table 1, entry 4). Decreasing further the amount of the initiator decreased the product yield, together with the recovery (16%) of the starting diiodide (Table 1, entry 3). No cyclization was observed in diethyl ether under otherwise similar conditions (Table 1, entry 5).

The scope of the cycloisomerization was investigated for other diiodoalkynes (Table 2). In the presence of 0.2 equiv. of 1-hexynyllithium, 2-(3-iodo-2-propynyloxy)ethyl iodides **1a–g** underwent smooth cyclization within 2 h at 40 °C to give 3-(diiodomethylene)tetrahydrofurans **2a–g** in high yield (Table 2, entries 1–7). Although LDA-catalyzed cycloisomerization of iodoalkynes (eqn. 3) was not applicable to either six-membered

Table 1 Cycloisomerization of diiodoalkyne **1a**^a

Entry	RLi	Equiv.	2a yield (%)
1	BuLi	0.2	69
2	BuLi	0.4	48
3	C ₄ H ₉ C≡CLi	0.1	61 ^b
4	C ₄ H ₉ C≡CLi	0.2	85
5 ^c	C ₄ H ₉ C≡CLi	0.2	— ^d

^a Unless otherwise noted, reactions were carried out in THF (0.5 M) at 40 °C for 2–6 h. ^b **1a** was recovered in 16% yield. ^c The reaction was carried out in diethyl ether. ^d **1a** was recovered in 77% yield.

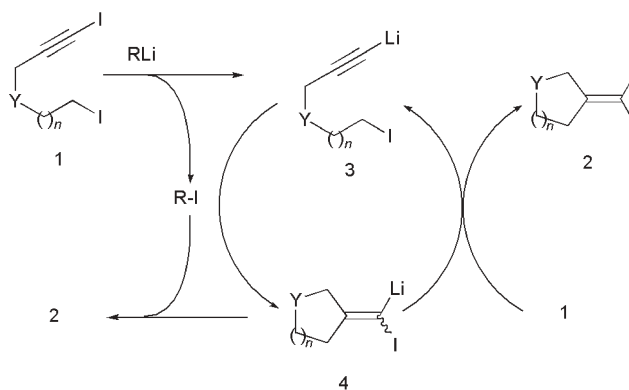
Table 2 Cycloisomerization of diiodoalkynes **1a–k**^a

Entry	Diiodoalkyne	Product	Isolated yield (%)
1		1a ; Y = OEt	2a 85
2		1b ; Y = H	2b 86
3		1c ; Y = OEt	2c 80
4		1d ; Y = H	2d 87
5		1e	2e 88
6		1f ; Y = OEt	2f 68
7		1g ; Y = H	2g 81
8 ^b		1h	2h 41
9 ^c		1i	2i 39
10 ^b		1j	2j 43
11 ^b		1k	2k 50

^a Unless otherwise noted, reactions were carried out by using 0.2 equiv. of 1-hexynyllithium at 40 °C for 2–4 h. ^b 0.4 equiv. of 1-hexynyllithium was used. ^c 0.6 equiv. of 1-hexynyllithium was used.

ring formation or carbocycle formation,⁴ cycloisomerization of homologous diiodides **1h,i** and diiodohexynes **1j,k** proceeded by using 0.4–0.6 equiv. of 1-hexynyllithium to give the corresponding tetrahydropyran derivatives **2h,i** and cyclopentane derivatives **2j,k**, respectively, in moderate yields (Table 2, entries 8–11).

A plausible mechanism for the present cycloisomerization reaction is depicted in Scheme 1. The initiation step involves regioselective iodine/lithium exchange of diiodoalkyne **1** at the acetylenic carbon by the organolithium compound (RLi). The lithium acetylide **3** thus generated undergoes *exo*-cyclization to give carbenoid **4**, which in turn undergoes iodine/lithium exchange with **1** to give product **2**, with simultaneous generation of **4**.

**Scheme 1** Proposed chain mechanism for the cycloisomerization of **1**.

According to this mechanism, stoichiometric conversion of **1** into the product would be achieved only when carbenoid **4** undergoes iodination, not only by **1**, but also by RI, which is formed in the initiation step. The observation that the yield of **2a** decreased with an increasing amount of butyllithium (Table 1, entries 1 and 2) implies that iodobutane does not serve as an iodine donor toward carbenoid **4**. On the other hand, 1-iodo-1-hexyne, generated from 1-hexynyllithium, can undergo a facile exchange reaction with **4**, thus leading to the high yield formation of **2**.

In comparison with the cycloisomerization reaction of iodoalkynes **5** (eqn. 3), the reaction of diiodoalkynes **1** proceeded more efficiently, realizing higher yields of the products. The less efficient nature of the reaction of iodoalkynes is most probably due to the decomposition of unstable carbenoid intermediate **4** to the corresponding carbenes by the elimination of the lithium iodide, which occurs competitively with proton abstraction to form cycloisomerization product **6**. Halogen/lithium exchange by organolithium compounds is known to be much faster than proton abstraction.⁵ A rapid transformation of labile carbenoid **4** by iodine/lithium exchange into the product might be responsible for the higher efficiency of the cycloisomerization reaction of diiodides.

Notes and references

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