Catalytic Cycloisomerization of Unsaturated Organoiodides

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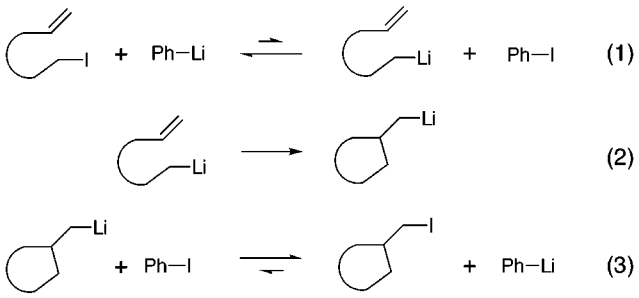
Catalytic quantities of phenyllithium (PhLi) have been found to initiate novel 5-exo cycloisomerization of a variety of structurally diverse unsaturated organoiodides. The isomerization reaction appears to be a process of broad synthetic utility for the preparation of iodomethyl-substituted five-membered rings. Primary, secondary, tertiary, or aryl iodides tethered to a suitably positioned carbon−carbon π-bond are converted cleanly to their cyclic isomers in good to excellent yield (i.e., 70−90%) by simply allowing a hydrocarbon−MTBE solution of the iodide to stand in the presence of a small quantity of PhLi at an appropriate temperature. The mechanism of the cycloisomerization was found to be substrate dependent: unsaturated aryl and primary alkyl iodides undergo isomerization via a three-step cascade (eqs 1−3) mediated by two reversible lithium−iodine exchange reactions bracketing an irreversible 5-exo cyclization of an unsaturated organolithium; unsaturated secondary and tertiary alkyl iodides apparently isomerize via a radical-mediated atom transfer process initiated by homolytic fragmentation of the ate-complex generated upon attack of PhLi on the iodine atom of the substrate.

We recently reported that the reversible nature of the lithium−iodine exchange reaction may be exploited to effect clean isomerization of 6-iodo-1-hexene to (iodomethyl)cyclopentane upon treatment of the unsaturated alkyl iodide with a catalytic quantity of phenyllithium (PhLi).[1] This novel cycloisomerization apparently involves three discrete steps as illustrated below (eqs 1−3).[1] Thus, the unsaturated alkyllithium initially generated by reversible exchange[2,3] between the iodide precursor and PhLi (eq 1) undergoes irreversible cyclization (eq 2)[4,5] prior to reconversion to a cyclic iodide and regeneration of PhLi (eq 3). Provided that the final equilibrium represented by eq 3 lies far to the right, the net isomerization is catalytic in PhLi.

Prompted by the potential synthetic utility of a process that serves to convert an unsaturated organoiodide to its cyclic isomer in a highly atom-economical fashion,[6] we have investigated the scope of PhLi-initiated cycloisomerization as a route to iodomethyl-substituted five-membered rings. Herein we report that such isomerizations appear to be of general utility: a catalytic quantity of PhLi is indeed capable of effecting cycloisomerization of a variety of structurally diverse unsaturated alkyl and aryl iodides. However, as detailed below, the mechanism of the process is substrate dependent and it is sometimes more complex than that suggested by the three-step sequence outlined in eqs 1−3.



Results and Discussion

Aryl Iodides Bearing a Pendant Unsaturation. The possibility of effecting cycloisomerization of an aryl iodide with a pendant carbon−carbon π-bond was explored with *N*,*N*-diallyl-2-iodoaniline (**1**) as a typical substrate. Prior art has demonstrated that the organolithium derived from **1** undergoes clean, rapid 5-exo cyclization at temperatures above ∼ −20 °C in the presence of *N*,*N*,*N*′*N*′-tetramethylethylenediamine (TMEDA) to deliver [(1-allyl-3-indolinyl)methyl]lithium in high yield.[7] It might be anticipated that **1** would be a good substrate for PhLi-initiated cycloisomerization via the exchange-mediated sequence discussed above: not only is the initial exchange equilibrium between PhLi and **1** (eq 1) likely to be more favorable than that between PhLi and an alkyl iodide,[2,3] the [(1-allyl-3-indolinyl)methyl]-lithium generated upon cyclization (eq 2) may be converted to product by exchange with either PhI (eq 3) or the starting material (**1**).

As expected, cycloisomerization of **1** to give 1-allyl-3-iodomethylindoline (**2**) was readily accomplished, as illustrated below, by simply allowing an approximately

(1) Bailey, W. F.; Carson, M. W. *J. Org. Chem.* **1998**, *63*, 361.
(2) Applequist, D. E.; O'Brien, D. F. *J. Am. Chem. Soc.* **1963**, *85*, 743.
(3) (a) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon Press: New York, 1974. (b) Bailey, W. F.; Patricia, J. J. *J. Organomet. Chem.* **1988**, *352*, 1. (c) Wakefield, B. J. *Organolithium Methods*; Pergamon Press: New York, 1988. (d) Wardell, J. L. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon Press: New York, 1982; Vol. 1, p 43. (e) Jones, R. G.; Gilman, H. *Chem. Rev.* **1954**, *54*, 835. (f) Gilman, H.; Jones, R. G. *Org. React. (N. Y.)* **1951**, *6*, 339.
(4) Bailey, W. F.; Patricia, J. J.; DelGobbo, V. C.; Jarret, R. M.; Okarma, P. J. *J. Org. Chem.* **1985**, *50*, 1999.
(5) Bailey, W. F.; Khanolkar, A. D.; Gavaskar, K.; Ovaska, T. V.; Rossi, K.; Thiel, Y.; Wiberg, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 5720 and references therein.
(6) (a) Trost, B. M. *Science* **1991**, *254*, 1471. (b) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259.
(7) (a) Zhang, D.; Liebeskind, L. S. *J. Org. Chem.* **1996**, *61*, 2594. (b) Bailey, W. F.; Jiang, X.-L. *J. Org. Chem.* **1996**, *61*, 2596. (c) Bailey, W. F.; Carson, M. W. *Tetrahedron Lett.* **1997**, *38*, 1329.

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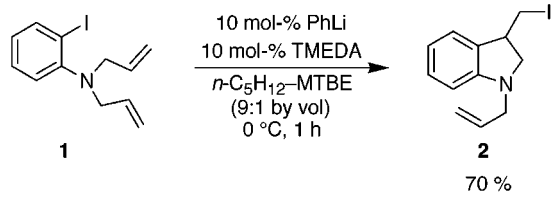
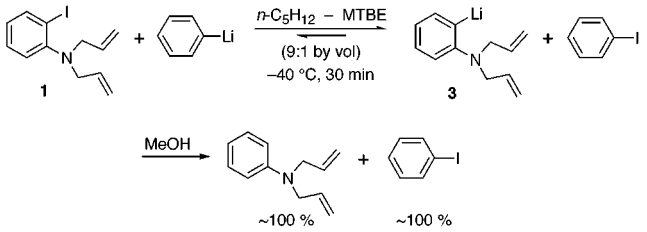
0.1 M solution of **1** in dry and deoxygenated *n*-pentane−MTBE (9:1 by vol) to stand under argon in the presence of 10 mol % of both PhLi and TMEDA for 1 h at 0 °C. GC analysis of the crude reaction mixture revealed that **2** had been produced in 87% yield; the somewhat labile iodide was isolated as analytically pure material in 70% yield. It should be noted, as detailed elsewhere,[1] although the conversion of **1** to **2** requires, in principle, only a trace of PhLi to initiate the reaction sequence (eqs 1−3), it is our experience that it is exceedingly difficult, in practice, to avoid premature termination of an exchange-mediated cycloisomerization through inadvertent quench of organolithium intermediates by proton abstraction from solvent or adventitious moisture when very small quantities of initiator are used.

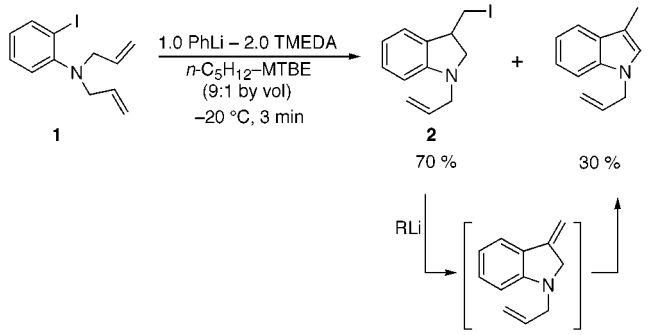


The PhLi-initiated isomerization of **1** to **2** is undoubtedly mediated by the exchange−cyclization−exchange cascade outlined above (eqs 1−3). Indeed, as shown below, addition of a full molar equivalent of PhLi to a solution of **1** in *n*-pentane−MTBE (9:1 by vol) effects virtually complete exchange within minutes at −40 °C to give iodobenzene and [2-(*N*,*N*-diallylamino)phenyl]-lithium (**3**); quench of such a reaction mixture with MeOH affords *N*,*N*-diallylaniline and iodobenzene in essentially quantitative yield. Apparently, the *ortho*-amino substituent present in **3**, which is known to stabilize an adjacent carbon−metal bond,[8] is responsible for this highly one-sided exchange equilibrium. As expected,[7] no cyclic product was detected when the exchange between **1** and PhLi was established in the absence of TMEDA at temperatures below −20 °C.



Although cycloisomerization of **1** to **2** may be accomplished at temperatures as low as −40 °C in the presence of a full equivalent of PhLi and TMEDA, significant benefit derives from conducting the transformation, albeit more slowly, using only a catalytic quantity of the aryllithium initiator at 0 °C. While a higher initial concentration of PhLi leads to a faster overall isomerization, the presence of excess organolithium−TMEDA in such reaction mixtures may result in dehydrohalogenation of the alkyl iodide product (**2**). For example, as illustrated in Scheme 1, treatment of a solution of **1** in *n*-pentane−MTBE (9:1 by vol) with 1 equiv of PhLi and 2 equiv of TMEDA at −20 °C leads within 3 min to consumption of the starting iodide and formation of an

Scheme 1



approximately 70/30 mixture of **2** and 1-allyl-3-methylindole. Not surprisingly, a longer reaction time or a larger initial concentration of PhLi leads to a larger proportion of indole in the product mixture. The indole is most likely generated, as summarized in Scheme 1, by base-catalyzed isomerization of the 3-methylene species produced upon loss of HI from **2**. As a practical matter, dehydrohalogenation of the product is not a major side reaction when a catalytic quantity of PhLi−TMEDA is used, as described above, to initiate the cycloisomerization of **1** to **2**; the favorable position of the initial exchange equilibrium leading to **3** (eq 1), followed by the rapid unimolecular cyclization of **3** (eq 2) in the presence of TMEDA at 0 °C,[7] allows the cycloisomerization sequence to proceed essentially to completion before the inherently slower bimolecular elimination reaction becomes a problem.

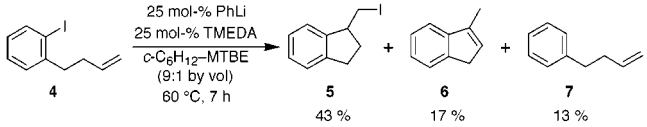
Dehydrohalogenation can be a potentially serious complication when the cyclization step (eq 2) of the exchange-mediated cycloisomerization is sluggish. To the extent that the alkyl iodide product is consumed by reaction with an organolithium, the dehydrohalogenation also removes a portion of the initiator and/or the initially generated aryllithium needed to complete the cycloisomerization. In short, dehydrohalogenation serves to terminate the isomerization sequence (eqs 1 and 3) when the cyclization step (eq 2) is slow.

Just such behavior is apparent in the PhLi-initiated conversion of 2-iodo-1-(3-butenyl)benzene (**4**) to 1-iodomethylindan (**5**) illustrated below. Cyclization of [2-(3-butenyl)phenyl]lithium, the organolithium derived from **4**, which was first reported over a decade ago by Woosley and co-workers,[9] is considerably less facile than is the ring closure of **3** discussed above. Moreover, the lithium−iodine exchange equilibrium (eq 1) between **4** and PhLi to give [2-(3-butenyl)phenyl]lithium and PhI is much less favorable than the comparable exchange involving **1**.[10] As a result, the cycloisomerization of **4** to **5** requires more forcing conditions (elevated temperature and considerably more initiator) than does the conversion of **1** to **2**. Thus, when a solution of **4** in scrupulously dry, oxygen-free cyclohexane−MTBE (9:1 by vol) containing 25 mol % of both PhLi and TMEDA was heated at 60 °C for 7 h under an atmosphere of pure argon, the product mixture consisted of **5** (43%) as well as 3-methylindene (**6**, 17%), 4-phenyl-1-butene (**7**, 13%), and recovered **4** (27%). Clearly, the dehydrohalogenation reaction, which is unavoidable at the elevated temperature needed to effect

(8) (a) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879. (b) Gschwend, H. W.; Rodriguez, H. R. *Org. React. (N. Y.)* **1979**, 1.

(9) (a) Ross, G. A.; Koppang, M. D.; Bartak, D. E.; Woolsey, N. F. *J. Am. Chem. Soc.* **1985**, *107*, 6742. (b) Koppang, M. D.; Ross, G. A.; Woolsey, N. F.; Bartak, D. E. *J. Am. Chem. Soc.* **1986**, *108*, 1441.

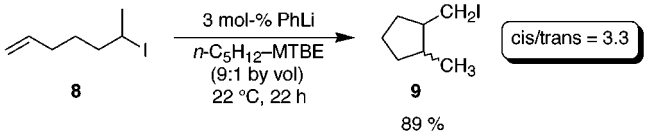
cyclization of the aryllithium derived from **4**, is responsible for formation of both **6** and **7**. Perhaps more importantly, no active organolithium remains in the reaction mixture after 7 h at 60 °C and the isomerization sequence is effectively terminated. Of course, additional PhLi may be used to complete the consumption of **4** but this expedient also results in consumption of product iodide (**5**) by conversion to **6**. Although the PhLi-initiated cycloisomerization of **4** is slow and results in modest yields of **5**, the transformation most likely involves the three-step, exchange-mediated sequence outlined above (eqs 1−3).



Unsaturated Secondary Alkyl Iodides. In light of the facile PhLi-initiated cycloisomerization of 6-iodo-1-hexene and related systems bearing a primary alkyl iodide,[1] it was of interest to determine whether a secondary alkyl iodide incorporating a 5-hexenyl unit would behave analogously. At the inception of the exploratory phase of this study it was recognized that lithium−iodine exchange between an aryllithium and a secondary alkyl iodide to give a secondary alkyllithium and an aryl iodide is a highly unfavorable process;[2,3] conventional wisdom suggests that the more probable outcome from reaction of a secondary halide with an organolithium would be elimination.[3] Thus, it seemed unlikely that the exchange-mediated cascade (eqs 1−3) would prove useful for the cycloisomerization of a secondary substrate.

Despite these reservations, the reaction of 6-iodo-1-heptene (**8**) with PhLi was investigated. Remarkably, and quite unexpectedly, treatment of a 0.5 M solution of **8** in *n*-pentane−MTBE (9:1 by vol) with as little as 3 mol % of PhLi for 22 h at room temperature effects almost complete isomerization of the substrate to 2-iodomethyl-1-methylcyclopentane (*cis*-**9** and *trans*-**9**); as shown below, the cyclic product was isolated in 89% yield as a 3.3/1 mixture of the cis and trans isomers. Given the small amount of PhLi needed to initiate the cycloisomerization depicted below, it is important to note that control experiments, conducted in the absence of PhLi but under otherwise identical conditions, demonstrated that there is no reaction in the absence of the aryllithium. Moreover, the cycloisomerization of **8** proceeds at a comparable rate both in the dark as well as in ambient light.

In view of the fact that 1-methyl-5-hexenyllithium, the organolithium derived from **8**, is known to cyclize with a very distinct preference for the trans-stereochemistry[3b]



(viz., trans/cis > 30),[11−13] it seems improbable that the PhLi-initiated conversion of **8** to **9** involves cyclization of the organolithium. The cis-rich stereochemistry of the product mixture is, however, highly suggestive of the intermediacy of a 1-methyl-5-hexenyl radical.[14,15] Indeed, the stereochemical outcome of a reaction mediated by cyclization of the 1-methyl-5-hexenyl radical is well-known: kinetic studies by Ingold's group have demonstrated that the product composition is temperature dependent and Arrhenius parameters characterizing both the cis- and trans-modes of ring closure are available.[15] In view of the apparent involvement of the 1-methyl-5-hexenyl radical in the PhLi-initiated cycloisomerization of **8**, the isomeric composition of the 2-iodomethyl-1-methylcyclopentane product (*cis*-**9** and *trans*-**9**) should be temperature dependent and quantitatively predictable.[16] Agreement of experimental cis/trans ratios with product composition predicted on the assumption that stereochemistry is controlled by cyclization of the 1-methyl-5-hexenyl radical would provide strong evidence for the putative radical intermediate. To this end, a series of experiments were conducted in which solutions of **8** in hydrocarbon−MTBE (9:1 by vol) were treated with PhLi at several temperatures between −20 and 60 °C. The results of these experiments are summarized in Table 1.

At the outset it should be noted that the isomerizations reported in Table 1 were conducted by using a full molar equivalent of PhLi so as to increase the overall rate of the cycloisomerization: analogous results were obtained when catalytic quantities of PhLi were employed for several of the experiments but reaction times were then much longer. Cursory inspection of the data presented in Table 1 demonstrates that there is a very good correlation between the observed isomeric composition and that calculated on the assumption that the cycloisomerization reaction is mediated by cyclization of the 1-methyl-5-hexenyl radical. The small variation in the

(10) In striking contrast to the favorable exchange equilibrium established when *N*,*N*-diallyl-2-iodoaniline (**1**) is treated with PhLi, the lithium−iodine exchange between **4** and PhLi gives very little [2-(3-butenyl)phenyl]lithium and PhI. The apparent equilibrium constant (K_{obs}) for this exchange [2-iodo-1-(3-butenyl)benzene (**4**) + PhLi ⇌ [2-(3-butenyl)phenyl]lithium + PhI] in *n*-pentane−MTBE (9:1 by vol) was determined at −40 °C following the method introduced by Applequist and O'Brien[2] and detailed in our previous report.[1] The unexpectedly small apparent equilibrium constant for the exchange between **4** and PhLi ($K_{obs} = (8 \pm 5) \times 10^{-3}$) may have a profound effect on the overall rate of the exchange-mediated cycloisomerization of **4** to **5** since there is very little [2-(3-butenyl)phenyl]lithium generated when PhLi is used to initiate the isomerization. In a larger sense, the differing behavior of aryl iodides **1** and **4** when treated with PhLi at low temperature suggests that there is much yet to be learned about the factors affecting lithium−halogen exchange equilibria.

(11) Bailey, W. F.; Nurmi, T. T.; Patricia, J. J.; Wang, W. *J. Am. Chem. Soc.* **1987**, *109*, 2442.

(12) Ashby, E. C.; Pham, T. N. *J. Org. Chem.* **1987**, *52*, 1291.

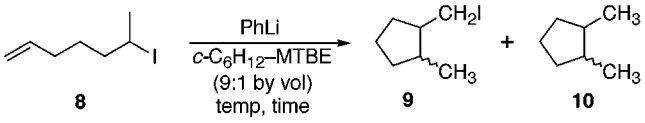
(13) It might be noted that other 6-hepten-2-yl organometallics also cyclize with a high degree of preference for the trans stereochemistry. Cyclization of Grignard reagents derived from 6-halo-1-heptenes invariably produce a preponderance of the trans-isomer (trans/cis > 10; for a review, see: Hill, E. A. *J. Organomet. Chem.* **1975**, *91*, 123) and ring closure of 1-methyl-5-hexenylsodium has been reported to give the trans-product (see: Garst, J. F.; Hines, J. B., Jr. *J. Am. Chem. Soc.* **1984**, *106*, 6433).

(14) Brace, N. O. *J. Org. Chem.* **1967**, *32*, 2711.

(15) Lusztyk, J.; Maillard, B.; Deycard, S.; Lindsay, D. A.; Ingold, K. U. *J. Org. Chem.* **1987**, *52*, 3509.

(16) The rapid 5-exo cyclization of the 1-methyl-5-hexenyl radical is highly cis-selective. Ingold's group has studied the kinetics of this cyclization over a broad range of temperatures (ca. −30 °C to 100 °C) and Arrhenius parameters for both cis- and trans-modes of ring closure are available from this work.[15] The "Best Arrhenius Parameters" reported in Table 2 of ref 15 for cyclization of the 1-methyl-5-hexenyl radical to give the cis-isomer (viz., cis: $\log A = 9.79 \pm 0.24$; $E_a = 6.50 \pm 0.26$ kcal/mol) and the trans-isomer (viz., trans: $\log A = 9.92 \pm 0.26$; $E_a = 7.44 \pm 0.29$ kcal/mol) may be used to predict the relative proportions of cis and trans product that would result at a given temperature from a radical-mediated cycloisomerization of 6-iodo-1-heptene (**8**) initiated by PhLi. On the reasonable assumption that cyclization of the 1-methyl-5-hexenyl radical is irreversible under the conditions used for the cycloisomerization, the isomeric composition of the product mixture is given by: $\text{cis/trans} = k_c/k_t = 0.741 \times e^{473/T}$. The predicted product ratios appear in the last column of Table 1.

Table 1. Cycloisomerization of 6-Iodo-1-heptene (8)[a]



8 9 10

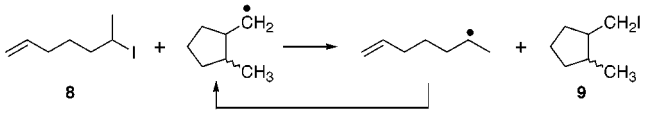
			products, % yield[b]				
entry	temp, °C	time, h	8	10	9	cis/trans[c]	predicted cis/trans[d]
1	−20[e]	3	27.2	0.3	71.0	4.5	4.8
2		6	12.7	0.7	84.7	4.7	
3		9	8.4	1.2	88.6	4.6	
4	0	0.33	24.4	2.0	73.3	3.7	4.2
5		1	6.4	2.9	93.3	3.9	
6		3	1.7	3.1	95.2	3.9	
7	20	0.5	3.5	4.3	86.3	3.4	3.7
8		1	1.6	4.8	91.9	3.4	
9		2	0.6	7.4	84.8	3.5	
10	40	0.25	2.5	6.1	93.0	3.1	3.4
11		0.5		7.7	92.9	3.1	
12	60	0.10	1.8	5.4	88.5	2.9	3.1
13		0.15	0.3	10.3	87.0	3.0	
14		0.33		14.4	80.6	2.9	

[a] Unless otherwise indicated, 0.1 M solutions of 6-iodo-1-heptene (**8**) in cyclohexane−MTBE (9:1 by vol) containing 1 M equiv of PhLi were stirred under an atmosphere of argon at the specified temperature for the indicated time before the addition of water or methanol. [b] Yields were determined by capillary GC by using internal standards (typically *n*-heptane and *n*-decane) and correction for detector response; stereoisomers were assumed to have identical detector response. [c] Ratio of *cis*-**9** + *cis*-**10**/*trans*-**9** + *trans*-**10**. [d] Proportions of cis and trans isomeric products expected from cyclization of the 1-methyl-5-hexenyl radical at the temperature of the experiment; see ref 16. [e] A solvent system composed of *n*-pentane−MTBE (9:1 by vol) was used for experiments conducted at −20 °C.

experimental ratios at a given nominal temperature are most likely the result of systematic error in our temperature control. Nonetheless, the results of these experiments provide compelling evidence, albeit indirect, for generation and cyclization of a secondary radical in the course of the isomerization of **8**.

The results summarized in Table 1 also serve to demonstrate that the PhLi-initiated conversion of **8** to **9** is a very clean process. The absence (i.e., <1%) of any products attributable to dehydrohalogenation is noteworthy: despite the fact that a full equivalent of PhLi was used in these conversions, there is no evidence of HI elimination from either the secondary iodide (**8**) or the product (**9**). Indeed, the only byproducts detected in the reaction mixtures were small and variable amounts of 1,2-dimethylcyclopentanes (*cis*-**10** and *trans*-**10**) derived from formal reduction of the product iodide.[17] Moreover, very little of **10** is produced when the isomerization is conducted at lower temperatures (Table 1, entries 1−6), while at higher temperatures, the isomerization of **8** to **9** is complete well before significant quantities of **10** are generated (Table 1, entries 7−14).

Given that the 1-methyl-5-hexenyl radical is an intermediate in the PhLi-initiated transformation of **8** to **9**, the rearrangement most likely involves a radical-mediated atom transfer cyclization process.[18,19] This well-characterized chain reaction may be initiated by even trace amounts of the 1-methyl-5-hexenyl radical (vide infra).[18,19] The effectively irreversible[18] iodine atom transfer cyclization sequence, which is depicted in abbreviated form below, would serve to rapidly convert the unsaturated secondary alkyl iodide to cyclic product.



8 9

Generation of the 1-methyl-5-hexenyl radical from **8** in more traditional ways has been demonstrated to effect cyclization of **8** to **9** by both Brace (who used AIBN to initiate the conversion)[14] and Curran's group (initiation with hexabutylditin and sunlamp irradiation).[19] In light of these precedents, it seems quite reasonable to propose that the PhLi-initiated transformation of **8** to **9** discussed above is the result of inadvertent initiation of the atom transfer cyclization chain by a phenyl radical or a radical impurity in the PhLi reagent. While one cannot exclude such a possibility, there are two additional experimental observations, admittedly anecdotal, that mitigate against this supposition. (1) The PhLi-initiated rearrangement of **8** to **9** does not seem to be affected, either in terms of rate or product composition, by the source of the initiator: both commercial (Aldrich, FMC) PhLi in cyclohexane−diethyl ether (produced from chlorobenzene) and the reagent prepared in situ from bromobenzene in pure diethyl ether by low-temperature lithium−halogen exchange with *t*-BuLi[20] give entirely analogous results. (2) The presence of 1 equiv of cumene, an effective scavenger of the phenyl radical,[21] has no effect on the isomerization of **8** to **9**: allowing a 0.1 M solution of both **8** and cumene in cyclohexane−MTBE (9:1 by vol) containing 1 equiv of PhLi to stand for 1 h at 20 °C afforded **9** (93.6%, cis/trans = 3.4) and **10** (5.5%) in good accord with the result obtained in the absence of cumene (cf. Table 1, entry 8).

Be that as it may, the behavior of the 3-oxa analogue of **8**, 3-(2-iodopropyloxy)propene (**11**), upon treatment with PhLi demonstrates that the role of the organolithium initiator is far from trivial. At the outset, it was expected that **11** would undergo reaction with PhLi in a fashion analogous to **8** since the secondary radical derived from **11** is known to cyclize some 10 times more rapidly than does the 1-methyl-5-hexenyl radical derived from **8**.[22] In that event, addition of 1 M equiv of PhLi to an approximately 0.1 M solution of **11** in cyclohexane−MTBE (9:1 by vol) at 0 °C resulted in complete consumption of both **11** and PhLi within 15 min, but there was no evidence of the expected cycloisomerization product. Rather, as illustrated below, reaction of **11** with PhLi affords essentially 100% yields of the lithium salt of allyl alcohol (assayed as the alcohol), propene (assayed by GC-

(17) It might be noted in this connection that lithium−iodine exchange between the primary alkyl iodide products, *cis*-**9** and *trans*-**9**, and excess PhLi present in reaction mixtures may account for small quantities of 1,2-dimethylcyclopentanes (*cis*-**10** and *trans*-**10**) detected in these experiments. Previous work has demonstrated, however, that the apparent equilibrium constant for such an exchange is negligibly small.[1]

(18) (a) Curran, D. P.; Chen, M.-H.; Kim, D. *J. Am. Chem. Soc.* **1986**, *108*, 2489. (b) Newcomb, M.; Curran, D. P. *Acc. Chem. Res.* **1988**, *21*, 206. (c) Curran, D. P. *Synthesis* **1988**, 417 and 489. (d) Curran, D. P.; Fevig, T. L.; Jasperse, C. P. *Chem Rev.* **1991**, *91*, 1237. (e) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*; VCH Publishers: New York, 1995.

(19) Curran, D. P.; Kim, D. *Tetrahedron Lett.* **1986**, *27*, 5821.

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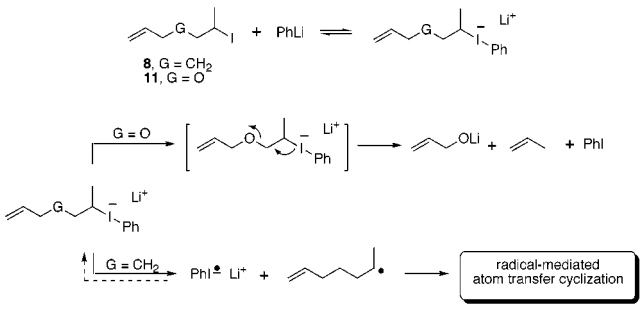
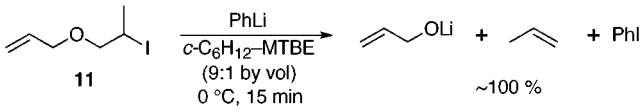
(21) Kryger, R. G.; Lorand, J. P.; Stevens, N. R.; Herron, N. R. *J. Am. Chem. Soc.* **1977**, *99*, 7589 and references therein.

(22) Beckwith, A. L. J.; Blair, I.; Phillipou, G. *J. Am. Chem. Soc.* **1974**, *96*, 1613.

Scheme 2



MS), and iodobenzene. This unexpected result is totally inconsistent with inadvertent initiation of an atom transfer cyclization by phenyl radical or trace impurities in the reaction medium since such a scenario would have resulted in cycloisomerization of **11** rather than the observed fragmentation. Indeed, the fragmentation of **11** upon treatment with PhLi is characteristic of generation of an electron-rich center at the iodine-bearing carbon and expulsion of the allyloxy nucleofuge from the β-position.



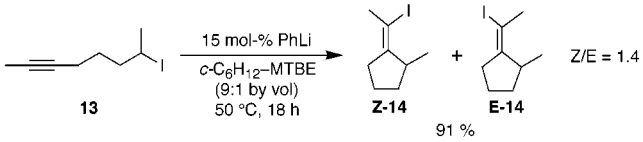
The disparate behavior of substrates **8** and **11** upon treatment with PhLi may be reconciled if one postulates, as depicted in Scheme 2, that the initial event in each instance involves reversible attack of the organolithium on the iodine atom of the substrate to give a 10-I-2 "ate-complex". Just such a species has been implicated as an intermediate in the lithium−iodine exchange reaction (**12**, eq 4);[3,23,24] the iodine ate complex generated in the reaction of iodobenzene with PhLi (**12**, R = R′ = Ph) has been detected spectroscopically[25] and its perfluoro analogue (**12**, R = R′ = C_6F_5) has been crystallized as a stable TMEDA adduct.[26]

$$R{-}I + Li{-}R' \rightleftharpoons [R{-}I{-}R']^{-}Li^{+} \rightleftharpoons R{-}Li + I{-}R' \quad (4)$$

It seems reasonable to expect rapid expulsion of the allyloxy anion from the electron-rich ate-complex generated from **11** (Scheme 2) prior to completion of the exchange reaction and this fragmentation nicely accounts for the behavior of this substrate when treated with PhLi. The behavior of **8** when treated with PhLi is also consistent with reversible generation of an ate-complex if it is realized that the complex need not lead to an exchange: indeed, as noted above, there is no evidence for the production of 1-methyl-5-hexenyllithium in the reaction of **8** with PhLi. Rather, the observed chemistry is consistent with homolytic fragmentation of the long,[26] and apparently weak, carbon−iodine bond in the putative ate-complex derived from **8** to give the 1-methyl-5-hexenyl radical and the radical anion of iodobenzene. Such C−I bond homolysis may well be a relatively rare event but, as illustrated in Scheme 2 and discussed explicitly above, formation of even trace amounts of the 1-methyl-5-hexenyl radical will invariably result in a very rapid radical-mediated atom transfer cyclization to give cis-rich **9**.[18,19]

The intermediacy of a 10-I-2 complex may well be a common feature of all reactions of PhLi with unsaturated organoiodides. This assumption serves to unify the ostensibly dissimilar mechanisms of PhLi-initiated cycloisomerization of a variety of substrates. The exchange-mediated cycloisomerizations (eqs 1−3) of unsaturated aryl iodides such as **1** and **4**, as well as primary alkyl iodides such as 6-iodo-1-hexene,[1] most likely involve reversible generation of ate-complexes in the course of the lithium−iodine interchange steps (i.e., **12**, eq 4).[3,23,24] When the exchange between PhLi and the iodide substrate is highly unfavorable, as is certainly the case for secondary alkyl iodides such as **8**,[2,3] the ate complex may fragment homolytically to initiate a radical-mediated isomerization. In short, from the prospective of mechanism, all of the cycloisomerizations discussed above (as well as those to be introduced below) may be viewed as proceeding from a common elementary step—reversible attack of the PhLi on the iodine atom of the substrate.

Regardless of the mechanistic details, it is clear that even small amounts of PhLi are sufficient to initiate cycloisomerization of suitably constituted organoiodides. The process is not confined to substrates bearing a pendant olefinic unit: as illustrated below, treatment of an approximately 0.5 M solution of 7-iodo-2-octyne (**13**) in dry, deoxygenated cyclohexane−MTBE (9:1 by vol) with 15 mol % of PhLi for 18 h at 50 °C effects clean 5-exo cycloisomerization of the acetylenic alkyl iodide. The cyclic product (**14**) was isolated in 91% yield as a mixture of diastereoisomers (Z/E = 1.4).[27] This efficient isomerization is almost certainly the result of a PhLi-initiated, radical-mediated atom transfer process[18,19] and the mixture of diastereoisomers that results is consistent with cyclization of the 1-methyl-5-heptynyl radical.[28]



Unsaturated Tertiary Alkyl Iodides. Prior art suggests that treatment of a tertiary alkyl iodide with an organolithium should result in dehydroiodination of the iodide.[3] The lithium−iodine exchange between a primary alkyl iodide and *t*-BuLi is, in fact, driven to completion by rapid reaction of excess of *t*-BuLi with the cogenerated *t*-BuI.[20] However, in view of the ease with which tertiary alkyl radicals participate in atom transfer

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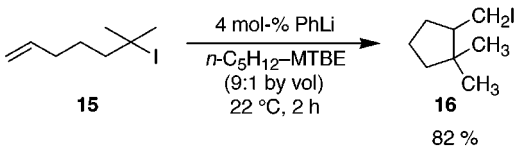
(27) The configuration of the major diastereoisomer (*Z*-**14**) produced upon cycloisomerization of **13** was established by conversion of the vinylic iodides to a mixture of *E*- and *Z*-1-ethylidene-2-methylcyclopentane with retention of configuration at the vinylic carbon (2.2 *t*-BuLi in *n*-pentane−MTBE (9:1 by vol) at −78 °C for 10 min followed by MeOH quench). The major product of the cycloisomerization (*Z*-**14**) gave *E*-1-ethylidene-2-methylcyclopentane whose NMR spectrum was identical to that reported for an authentic sample (see: Negishi, E.-I.; Swanson, D. R.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1987**, *28*, 917).

(28) It might be noted that 5-exo cyclization of acetylenic alkyllithiums is a stereoselectively syn-process, see: Bailey, W. F.; Ovaska, T. V. *J. Am. Chem. Soc.* **1993**, *115*, 3080.

cyclization reactions,[18,19] and given the apparent ability of PhLi to initiate such processes, it seemed worthwhile to attempt cycloisomerization of an unsaturated tertiary iodide. The base sensitive 6-iodo-6-methyl-1-heptene (**15**) system, used by Curran and Kim in their pioneering studies of the radical-mediated atom transfer cyclization,[19] was chosen as a representative substrate.

As shown below, simply stirring a 0.5 M solution of **15** in scrupulously dry and deoxygenated *n*-pentane−MTBE (9:1 by vol) containing as little as 3 mol % of PhLi for 2 h at room temperature produces 2-iodomethyl-1,1-dimethylcyclopentane (**16**) in 82% isolated yield. This result leaves little doubt that PhLi-initiated cycloisomerization of unsaturated organoiodides is of broad utility.

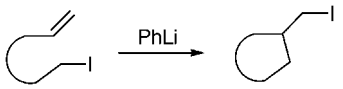


15 **16** 82 %

Conclusions

The chemistry detailed above represents a considerable extension in scope of the novel PhLi-initiated cycloisomerization of 5-hexenyl iodides disclosed in our preliminary report.[1] The results presented herein demonstrate that primary, secondary, tertiary, or aryl iodides tethered to a suitable positioned carbon−carbon π-bond may be converted to their cyclic isomers in good to excellent yield by simply stirring a solution of the iodide in the presence of a catalytic quantity of PhLi. The mechanism of the isomerization was found to be substrate dependent: the PhLi-initiated 5-exo cycloisomerization of aryl and (presumably) primary iodides involves a three-step cascade (eqs 1−3) mediated by a series of lithium−iodine exchange equilibria (eq 1 and 3) bracketing an irreversible cyclization step (eq 2); isomerization of secondary and tertiary substrates apparently entails a radical-mediated atom transfer process initiated by homolytic fragmentation of an ate-complex. Both mechanistic scenarios share an ate-complex intermediate or transition state as a common feature.

In short, PhLi-initiated 5-exo cycloisomerization, depicted below, appears to be a process of broad synthetic utility for the preparation of iodomethyl-substituted five-membered rings. The isomerization reaction is operationally simple, approaches near total atom economy, and appears to be a general phenomenon for a variety of structurally diverse unsaturated organoiodides.



Experimental Section

General Procedures. Spectroscopic and chromatographic procedures, methods used for the purification of reagents and solvents, and precautions regarding the manipulation of organolithiums have been previously described.[5] It is to be noted that all reagents (starting halides, internal standard, and solvents) used in the PhLi-initiated cycloisomerizations that had not been freshly distilled under argon were rendered essentially oxygen-free before use by bubbling dry, deoxygenated argon gas through the neat liquid for at least 5 min before use: failure to follow this rather stringent protocol may result in incomplete isomerization due to consumption of PhLi through reaction with adventitious oxygen. The concentrations of commercial solutions (Aldrich) of phenyllithium (PhLi) in cyclohexane−diethyl ether (7:3 by vol) were determined immediately prior to use by the method of Watson and Eastham.[29] Product mixtures were analyzed by capillary GC on one of the following columns: (1) a 25-m × 0.2-mm × 0.33-μm film thickness, cross-linked, phenyl methyl (5%) silicone column or (2) a 25-m × 0.2-mm × 0.33-μm film thickness, cross-linked, methyl silicone gum column.

Standard procedures were employed for the preparation of 6-hepten-2-ol from 4-pentenyllithium[20] and acetaldehyde in 90% yield; the known alcohol[30] was then converted, via the mesylate, to the known 6-iodo-1-heptene (**8**)[30] in 62% yield. In an analogous fashion, the known 2-methyl-6-hepten-2-ol[15,31] was prepared from 4-pentenyllithium[20] and acetone in 79% yield.

***N,N*-Diallyl-2-iodoaniline (1).** A mixture of 4.81 g (22.0 mmol) of 2-iodoaniline, 16.0 mL (0.185 mol) of allyl bromide, 9.26 g (87.3 mmol) of sodium carbonate, and 100 mL of DMF was heated at reflux for 4 h. The mixture was allowed to cool to room temperature, inorganic salts were removed by filtration, and the solid was washed with a generous portion of diethyl ether (ca. 100 mL). The combined filtrate and washings were poured into 200 mL of water, the layers were separated, and the aqueous layer was extracted with three 60-mL portions of diethyl ether. The combined organic extracts were washed with water, dried ($MgSO_4$), and concentrated by rotary evaporation. Kügelrohr distillation of the residue afforded 5.83 g (89%) of the iodide: bp (bath temp) 105 °C (0.3 mm); ^{1}H NMR ($CDCl_3$) δ 3.60−3.62 (m, 4 H), 5.07−5.17 (m, 4 H), 5.78−5.84 (m, 2 H), 6.75 (m, 1 H), 7.00 (dd, J = 7.98, 1.52 Hz, 1 H), 7.23−7.27 (m, 1 H), 7.84 (dd, J = 7.88, 1.56 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 56.14, 117.71, 124.21, 125.60, 125.89, 128.44, 134.82, 139.95, 151.78. Anal. Calcd for $C_{12}H_{14}NI$: C, 48.18; H, 4.72; N, 4.68. Found: C, 48.15; H, 4.88; N, 4.84.

1-(3-Butenyl)-2-iodobenzene (4). A solution of 4.63 g (21.9 mmol) of 2-bromo-1-(3-butenyl)benzene[9a] in 40 mL of diethyl ether and 70 mL of *n*-pentane was cooled to −78 °C and 28.0 mL of a 1.73 M solution of *t*-BuLi (48.4 mmol) in pentane were added dropwise over a 10-min period. The resulting mixture was stirred at −78 °C for an additional 10 min and then was allowed to warm and stand at room temperature for ca. 1 h to remove residual *t*-BuLi.[20] The cloudy, yellow solution was recooled to −78 °C and a saturated solution of iodine in diethyl ether was added dropwise until an orange color persisted in the reaction mixture. The orange mixture was stirred at −78 °C for 5 min before the addition of 50 mL of 10% aqueous sodium thiosulfate, the cooling bath was then removed, and the slurry was allowed to warm to room temperature. The resulting mixture was washed with 50 mL of water, dried ($MgSO_4$), and concentrated under reduced pressure. Kügelrohr distillation of the residue gave 5.15 g (91%) of the iodide: bp (bath temp) 90 °C (1 mm) [lit.[32] bp 130−132 °C (19 mm)]; ^{1}H NMR ($CDCl_3$) δ 2.30−2.37 (m, 2 H), 2.77−2.81 (m, 2 H), 4.98−5.09 (m, 2 H), 5.83−5.93 (m, 1 H), 6.87 (td, J = 7.58, 1.89 Hz, 1 H), 7.19 (dd, J = 7.58, 1.89 Hz, 1 H), 7.25 (td, J = 7.58, 1.27 Hz, 1 H), 7.80 (dd, J = 7.58, 1.27 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 34.13, 40.22, 100.54, 115.22, 127.72, 128.24, 129.43, 137.49, 139.46, 144.29.

1-(2-Propenoxy)-2-propanol. Neat allyl alcohol, 13.5 mL (0.198 mol), was slowly added to a suspension of 4.80 g (0.200 mol) of oil-free sodium hydride in 100 mL of dry THF and 50 mL of dry HMPA and the resulting mixture was heated at reflux for 3 h. The alcoholate solution was allowed to cool to room temperature and 5.72 g (0.130 mol) of propylene oxide (freshly distilled from $CaSO_4$) was then added over a 20-min period. The resulting mixture was stirred for 30 min at room

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(30) Ashby, E. C.; DePriest, R. N.; Goel, A. B.; Wenderoth, B.; Pham, T. N. *J. Org. Chem.* **1984**, *49*, 3545.
(31) (a) Colonge, J.; Lasfargues, P. *Bull. Soc. Chim. Fr.* **1962**, 177. (b) Surzur, J.-M.; Teissier, P. *Bull. Soc. Chim. Fr.* **1970**, 3060.
(32) Beckwith, A. L. J.; Gara. W. B. *J. Chem. Soc., Perkin Trans. 2* **1975**, 795.

temperature then heated at reflux for 4 h before cautious addition of 50 mL of water and 75 mL of 3 M aqueous hydrochloric acid. The aqueous layer was extracted with diethyl ether, and the combined organic extracts were washed successively with water, aqueous sodium bicarbonate, and brine, then dried ($MgSO_4$), and concentrated under reduced pressure. Vacuum distillation of the residue afforded 4.17 g (28%) of the known alcohol:[33] bp 66−70 °C (25 mm); ^{1}H NMR ($CDCl_3$) δ 1.11−1.13 (m, 3 H), 2.37 (br, s, 1 H), 3.19−3.24 (m, 1 H), 3.39−3.43 (m, 1 H), 3.95−4.01 (m, 3 H), 5.14−5.28 (m, 2 H), 5.83−5.93 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 18.59, 66.26, 72.05, 75.69, 117.08, 134.44.

3-(2-Iodopropyloxy)propene (11). Following the general procedure of Crossland and Servis,[34] 4.00 g (34.5 mmol) of 1-(2-propenoxy)-2-propanol was converted to its mesylate. The crude mesylate was added to a solution of 15.5 g (0.104 mol) of anhydrous sodium iodide in 150 mL of dry acetone and the resulting mixture was stirred for 36 h at room temperature and then for 10 h at gentle reflux. Standard workup yielded 1.59 g (20% from the alcohol) of the iodide: ^{1}H NMR ($CDCl_3$) δ 1.88 (d, J = 6.87 Hz, 3 H), 3.41 (A portion of ABX, J_{AB} = 10.34 Hz, J_{AX} = 7.34 Hz, 1 H), 3.71 (B portion of ABX, J_{AB} = 10.34 Hz, J_{BX} = 6.02 Hz, 1 H), 4.01−4.05 (m, 2 H), 4.15−4.23 (m, 1 H), 5.16−5.30 (m, 2 H), 5.84−5.93 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 24.29, 24.74, 71.81, 77.15, 117.35, 134.38; HRMS calcd for $C_6H_{11}OI$ 225.9854, found 225.9852.

6-Heptyn-2-ol. A suspension of 8.65 g (0.360 mol) of oil-free sodium hydride in 125 mL of 1,3-diaminopropane (freshly distilled from sodium) was stirred at 70 °C for 1.5 h. The brown mixture was then cooled to 55 °C and 5.02 g (44.7 mmol) of 4-heptyn-2-ol in 25 mL of 1,3-diaminopropane were added dropwise. The resulting reddish-brown mixture was stirred at 55 °C for 3.5 h and then cooled to 0 °C before cautious, successive addition of 50 mL of water and 300 mL of 10% aqueous hydrochloric acid. The brown solution was then continually extracted with 350 mL of diethyl ether for 22 h; the ethereal extract was washed with water, dried ($MgSO_4$), and concentrated by rotary evaporation. Kügelrohr distillation of the orange residue afforded 2.70 g (54%) of the alcohol: bp (bath temp) 80−90 °C (13 mm) [lit.[35] bp 75−77 °C (12 mm)]; ^{1}H NMR ($CDCl_3$) δ 1.13 (d, J = 6.18 Hz, 3 H), 1.47−1.59 (m, 4 H), 1.90 (t, J = 2.67 Hz, 1 H), 2.10 (br, s, 1 H), 2.13−2.17 (m, 2 H), 3.72−3.77 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 18.22, 23.35, 24.54, 30.02, 67.24, 68.39, 84.26.

6-Octyn-2-ol. A solution of lithium amide in ammonia was prepared from 0.62 g (89 mmol) of lithium rod and 50 mg of ferric nitrate nonahydrate in 100 mL of liquid ammonia at −33 °C and 4.65 g (41.4 mmol) of 6-heptyn-2-ol was added dropwise over a 20 min period. Neat iodomethane, 7.49 g (52.7 mmol), was then added and the ammonia was allowed to evaporate overnight. Aqueous ammonium chloride solution (5 g/80 mL) was added to the resulting semisolid, the mixture was extracted with five 40-mL portions of diethyl ether, and the combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Kügelrohr distillation of the residue yielded 4.28 g (82%) of the alcohol: bp 103−106 °C (12 mm) [lit.[36] bp 92 °C (10 mm)]; ^{1}H NMR ($CDCl_3$) δ 1.16 (d, J = 6.02 Hz, 3 H), 1.46−1.58 (m, 5 H, including OH), 1.74 (t, J = 2.56 Hz, 3 H), 2.09−2.14 (m, 2 H), 3.78 (apparent six-line pattern, J = 6.02 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 3.33, 18.60, 23.42, 25.17, 38.31, 67.57, 75.70, 78.92.

7-Iodo-2-octyne (13). Following the general procedure of Crossland and Servis,[34] 4.10 g (32.5 mmol) of 6-octyn-2-ol was converted to its mesylate. The crude mesylate was added to a solution of 14.6 g (97.3 mmol) of anhydrous sodium iodide in 150 mL of dry acetone and the resulting mixture was stirred for 22 h at room temperature and then for 3 h at gentle reflux. Standard workup gave 5.99 g (78% from the alcohol) of the iodide:^{1}H NMR ($CDCl_3$) δ 1.51−1.75 (m, 6 H), 1.84−1.89 (m, 1 H), 1.90 (d, J = 6.84 Hz, 3 H), 2.10−2.14 (m, 2 H), 4.11−4.19 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 3.42, 17.85, 28.92, 29.06, 29.62, 41.83, 76.00, 78.37; HRMS calcd for $C_8H_{13}I$ 236.0062, found 236.0061.

6-Iodo-6-methyl-1-heptene (15). Neat bis(trimethylsilyl)-trifluoroacetamide (BSTFA), 5.90 mL (22.2 mmol), was added dropwise over ∼5 min period to a solution of 2.37 g (18.5 mmol) of 2-methyl-6-hepten-2-ol[15,31] in 40 mL of dry DMF. The mixture was stirred at 95−100 °C for 5 h and excess BSTFA was then destroyed by the addition of 40 mL of water. The aqueous layer was extracted with three 10-mL portions of pentane; the combined organic extracts were washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. Kügelrohr distillation of the residue afforded 3.00 g (81%) of **2-methyl-2-trimethylsilyloxy-6-heptene**: bp (bath temp) 105−110 °C (25 mm); ^{1}H NMR ($CDCl_3$) δ 0.08 (s, 9 H), 1.18 (s, 6 H), 1.23−1.25 (m, 2 H), 2.00−2.03 (m, 4 H), 4.90−5.01 (m, 2 H), 5.75−5.85 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 2.60, 23.74, 29.84, 34.24, 44.34, 73.91, 114.24, 139.12. The silyl ether was converted to the title iodide in portions as needed. Neat iodotrimethylsilane (freshly distilled from copper powder), 0.710 mL (4.99 mmol), was added dropwise via syringe over a 5-min period to a solution of 0.791 g (3.95 mmol) of the silyl ether in 10 mL of dry benzene and the resulting yellow solution was stirred for 30 min at room temperature. The contents of the flask were then partitioned between 30 mL of water and 30 mL of pentane, the aqueous layer was extracted with three 5-mL portions of pentane, and the combined pink organic extracts were washed successively with cold 10-mL portions of saturated, aqueous sodium bicarbonate, 10% aqueous sodium thiosulfate, water, and brine, then dried ($MgSO_4$), and concentrated by rotary evaporation to give 0.861 g (92%) of the known[19] title iodide: ^{1}H NMR ($CDCl_3$) δ 1.55−1.61 (m, 4 H), 1.90 (s, 6 H), 2.06−2.10 (m, 2 H), 4.93−5.04 (m, 2 H), 5.77−5.84 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 27.72, 33.34, 38.05, 49.86, 52.24, 114.90, 138.31. The base-labile iodide was stored in a freezer under argon and used within a few hours of preparation.

Cycloisomerization of *N*,*N*-Diallyl-2-iodoaniline (1) to 1-Allyl-3-iodomethylindoline (2). A 25-mL, one-necked, round-bottomed flask, equipped with a Teflon-coated magnetic stir bar and capped with a septum, was flame dried under an atmosphere of argon. The flask was charged with 0.294 g (0.983 mmol) of *N*,*N*-diallyl-2-iodoaniline (**1**), 0.260 mL of a 0.393 M solution of TMEDA (0.102 mmol) in MTBE, 9.0 mL of *n*-pentane, and 1.0 mL of MTBE. The solution was cooled to 0 °C and 0.060 mL of a 1.65 M solution of PhLi (0.099 mmol) in cyclohexane−diethyl ether (7:3 by volume) was added in one portion. The resulting light yellow solution was stirred at 0 °C for 1 h under a positive pressure of argon before the addition of water (1 mL). The contents of the flask were partitioned between 25 mL of pentane and 10 mL of water, the layers were separated, and the organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel (1% ethyl acetate−2% triethylamine−hexanes) gave 0.204 g (70%) of the title iodide: R_f = 0.29; ^{1}H NMR ($CDCl_3$) δ 3.16−3.23 (m, 2 H), 3.44−3.60 (m, 3 H), 3.69−3.71 (m, 2 H), 5.18−5.29 (m, 2 H), 5.82−5.91 (m, 1 H), 6.48 (d, J = 7.89 Hz, 1 H), 6.66 (dt, J = 7.38, 0.96 Hz, 1 H), 7.07−7.24 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 10.04, 43.75, 51.33, 59.95, 107.84, 117.58, 117.67, 123.99, 128.68, 131.03, 133.58, 151.92; HRMS calcd for $C_{12}H_{14}NI$ 299.0171, found 299.0179.

Cycloisomerization of 1-(3-Butenyl)-2-iodobenzene (4). A solution of 0.333 g (1.29 mmol) of 1-(3-butenyl)-2-iodobenzene (**4**) in 13.5 mL of *n*-pentane and 1.5 mL of MTBE, containing 0.820 mL of a 0.391 M solution of TMEDA (0.320 mmol) in MTBE, was warmed to 60 °C under argon and 0.190 mL of a 1.71 M solution of PhLi (0.325 mmol) in cyclohexane−diethyl ether (7:3 by volume) was added in one portion. The resulting light yellow solution was stirred at 60 °C for 7 h under a positive pressure of argon before the addition of water (1 mL). The organic layer was washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. GC analy-

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(34) Crossland, R. K.; Servis, K. L. *J. Org. Chem.* **1970**, *35*, 3195.
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sis on column (1) using temperature programming (100 °C for 5 min, 10 °C/min to 250 °C for 10 min), as well as GC/MS analysis, revealed that the product mixture contained, in order of elution, (3-butenyl)benzene (**7**, 13%), 3-methylindene (**6**, 17%), 1-(3-butenyl)-2-iodobenzene (**4**, 27%), and 1-iodomethylindan[37] (**5**, 43%). Products were identified by comparison of their mass spectra with those reported for authentic samples.[37,38]

Cycloisomerization of 6-Iodo-1-heptene (8) to *cis*- and *trans*-2-Iodomethyl-1-methylcyclopentane (9). A solution of 1.12 g (5.00 mmol) of 6-iodo-1-heptene (**8**) in 9.0 mL of *n*-pentane and 1.0 mL of MTBE was stirred at room temperature under argon and 0.075 mL of a 1.93 M solution of PhLi (0.14 mmol) in cyclohexane−diethyl ether (7:3 by volume) was added in one portion. The resulting yellow solution was then stirred at 22 °C for 22 h under a positive pressure of argon. Water (1 mL) was added to the reaction mixture, the layers were separated, and the organic layer was washed with brine and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure afforded 0.995 g (89%) of the known iodides[14] as a mixture of isomers (*cis*/*trans* = 3.3). The diastereoisomers were separated by preparative GC on a 10-ft, 10% SE−30 on Anakrom A (60/80 mesh) column at 122 °C and were identified on the basis of the following spectroscopic properties. ***cis*-2-Iodomethyl-1-methylcyclopentane (*cis*-9)**: ^{1}H NMR ($CDCl_3$) δ 0.80 (d, J = 7.12 Hz, 3 H), 1.28−1.40 (m, 2 H), 1.59−1.84 (m, 4 H), 2.07−2.17 (m, 1 H), 2.21−2.31 (m, 1 H), 3.33 (A portion of ABX, J_{AB} = 9.47 Hz, J_{AX} = 8.08 Hz, 1 H), 3.39 (B portion of ABX, J_{AB} = 9.47 Hz, J_{BX} = 7.84 Hz, 1 H); ^{13}C NMR ($CDCl_3$) 9.51, 14.07, 22.79, 30.79, 33.37, 36.74, 46.76. ***trans*-2-Iodomethyl-1-methylcyclopentane (*trans*-9)**: ^{1}H NMR ($CDCl_3$) δ 0.97 (d, J = 6.24 Hz, 3 H), 1.20−1.37 (m, 2 H), 1.46−1.62 (m, 4 H), 1.86−1.92 (m, 2 H), 2.97 (A portion of ABX, J_{AB} = 9.51 Hz, J_{AX} = 7.58 Hz, 1 H), 3.49 (B portion of ABX, J_{AB} = 9.51 Hz, J_{BX} = 4.02 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.84, 19.09, 22.96, 33.69, 35.27, 40.75, 49.47.

Reaction of 3-(2-Iodopropyloxy)propene (11) with PhLi. A solution of 67.7 mg (0.299 mmol) of 3-(2-iodopropyloxy)propene (**11**) in 2.7 mL of cyclohexane and 0.3 mL of MTBE containing 46.3 mg (0.326 mmol) of *n*-decane (internal standard) was cooled to 0 °C, and 0.180 mL of a 1.93 M solution of PhLi (0.347 mmol) in cyclohexane−diethyl ether (7:3 by volume) was added dropwise. The resulting solution was stirred at 0 °C for 15 min before addition of just enough saturated, aqueous ammonium chloride to form a clear organic layer, which was dried ($MgSO_4$). GC analysis on column (1) using temperature programming (30 °C for 16 min, 50 °C/min to 100 °C for 1 min, 10 °C/min to 250 °C for 5 min), as well as GC/MS analysis, revealed that the reaction had produced allyl alcohol (∼100%), iodobenzene (∼100%), and propene (characterized by GC/MS). Reaction products were identified by comparison of their GC retention times and mass spectra with those of authentic samples; the yields of iodobenzene and allyl alcohol were corrected for detector response under the conditions of the analysis using samples of pure product and standard.

Cycloisomerization of 7-Iodo-2-octyne (13) to *Z*- and *E*-2-(1-Iodoethylidene)-1-methylcyclopentane (14). A solution of 0.576 g (2.44 mmol) of 7-iodo-2-octyne (**13**) in 4.5 mL of cyclohexane and 0.5 mL of MTBE was warmed to 50 °C under argon and 0.260 mL of a 1.40 M solution of PhLi (0.364 mmol) in cyclohexane−diethyl ether (7:3 by volume) was added in one portion. The resulting light yellow solution was stirred at 50 °C for 18 h under a positive pressure of argon. Water (1 mL) was then added to the reaction mixture and the organic layer was washed with brine and dried (Na_2SO_4). Removal of the solvent under reduced pressure gave 0.530 g (91%) of the vinyl iodides as a mixture of diastereoisomers (Z/E = 1.4):[27] ^{1}H NMR ($CDCl_3$, mixture of diastereoisomers) δ 0.97 (d, J = 7.16 Hz, 3 H), 1.03 (d, J = 7.79 Hz, 3 H), 1.44−1.90 (m, 8 H), 2.19−2.47 (m, 10 H), 2.61−2.68 (m, 1 H), 2.79−2.86 (m, 1 H); ^{13}C NMR ($CDCl_3$, mixture of diastereoisomers) δ 18.30, 19.34, 23.01, 25.10, 30.12, 30.45, 30.65, 33.55, 36.19, 37.19, 40.73, 45.09, 86.36, 89.05, 152.61, 153.60. Anal. Calcd for $C_8H_{13}I$: C, 40.70; H, 5.55; I, 53.75. Found: C, 40.85; H, 5.55.

Cycloisomerization of 6-Iodo-6-methyl-1-heptene (15) to 2-Iodomethyl-1,1-dimethylcyclopentane (16). A solution of 0.835 g (3.52 mmol) of 6-iodo-6-methyl-1-heptene (**15**) in 6.3 mL of *n*-pentane and 0.7 mL of MTBE was stirred at room temperature under argon and 0.080 mL of a 1.93 M solution of PhLi (0.15 mmol) in cyclohexane−diethyl ether (7:3 by volume) was added in one portion. The resulting light yellow solution was stirred at 22 °C for 2 h under a positive pressure of argon before the addition of 1 mL of water. The organic layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure to yield 0.686 g (82%) of the known[19] iodide: ^{1}H NMR ($CDCl_3$) δ 0.75 (s, 3 H), 1.01 (s, 3 H), 1.33−1.63 (m, 4 H), 1.84−1.92 (m, 2 H), 2.07−2.16 (m, 1 H), 2.56 (A portion of ABX, J_{AX} = 11.52 Hz, J_{AB} = 9.22 Hz, 1H), 3.64 (B portion of ABX, J_{AB} = 9.22 Hz, J_{BX} = 3.76 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 9.02, 20.17, 21.18, 28.14, 32.55, 41.87, 42.77, 52.93.

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