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Cyclization of Aryllithiums Tethered to Methylenecycloalkanes: Stereoselective Synthesis of 4*a*-Substituted *cis*-Hexahydrofluorenes

William F. Bailey,* Tahir Daskapan,† and Sriram Rampalli

Department of Chemistry, The University of Connecticut, Storrs, Connecticut 06269-3060

bailey@uconn.edu

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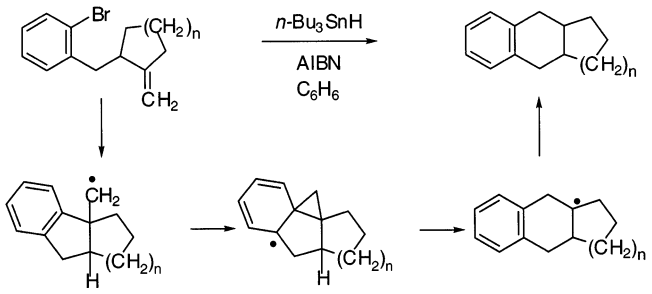
The cyclization of an aryllithium tethered to a methylenecycloalkane, generated from 2-(*o*-bromobenzyl)-1-methylenecycloalkanes **1**, **2**, and **3** by low-temperature lithium−bromine exchange, has been found to be a kinetically slow but thermodynamically favorable process that proceeds at a convenient rate in an exclusively 5-exo fashion when solutions of the aryllithium in *n*-heptane−di-*n*-butyl ether (9:1 v/v) are warmed to 45 °C. The cyclization affords stereoisomerically pure cis-fused products (**7** and **8**) when the methylenecycloalkane is five- or six-membered but it is less stereoselective when the methylenecycloalkane is seven-membered. The ring-closure of the aryllithium derived from 2-(*o*-bromobenzyl)-1-methylenecyclohexane (**2**) provides an experimentally convenient route to stereoisomerically pure 4*a*-substituted *cis*-hexahydrofluorenes in 60−90% isolated yield.

Some time ago, Ghatak and co-workers reported that cyclization of the aryl radical derived from various 2-(*o*-bromobenzyl)-1-methylenecycloalkanes proceeds exclusively in a 6-endo fashion as depicted below.[1,2] More recently, Ishibashi's group presented convincing evidence suggesting that formation of the 6-endo products was actually the result of a rapid 5-exo cyclization followed by a neophyl rearrangement.[3,4] Be that as it may, it occurred to us that the behavior of the aryllithium derived from such substrates would provide a rather stringent test of the scope of the intramolecular cyclization of olefinic organolithiums.[5]



It was anticipated that cyclization of an aryllithium generated from a 2-(*o*-bromobenzyl)-1-methylenecycloalkane would proceed in a 5-exo fashion. What was unclear at the inception of this study was whether such cyclization would be more rapid than the myriad of other processes, such as proton abstraction from solvent or intramolecular proton transfer, that could consume the organolithium. Indeed, while quaternary centers have been constructed by cyclization of various olefinic alkyllithiums,[6] the creation of a quaternary center via cyclization of a relatively stable aryllithium to give a less stable primary alkyllithium appears not to have been investigated. Herein we report that cyclization of aryllithiums tethered to methylenecycloalkanes is an exclusively 5-exo process that proceeds at a convenient rate at elevated temperatures. The method provides a expedient and highly steroselective route to 4*a*-substituted *cis*-hexahydrofluorenes.

Results and Discussion

The previously reported 2-(*o*-bromobenzyl)-1-methylenecycloalkanes (**1**−**3**)[2,3] required for this study were easily prepared, as illustrated in Scheme 1, by alkylation of the potassium enolate of the appropriate cycloalkanone in THF with *o*-bromobenzyl bromide followed by Wittig olefination. Authentic samples of the corresponding 2-benzyl-1-methylenecycloalkanes (**4**−**6**)[2,3] were gener-

† On leave from the Department of Chemistry, Ankara University.

(1) Pal, S.; Mukherjee, M.; Podder, D.; Mukherjee, A. K.; Ghatak, U. R. *J. Chem. Soc., Chem. Commun*. **1991**, 1591.

(2) Pal, S.; Mukhopadhyaya, J. K.; Ghatak, U. R. *J. Org, Chem*. **1994**, *59*, 2687.

(3) Ishibashi, H.; Kobayashi, T.; Nakashima, S.; Tamura, O. *J. Org. Chem*. **2000**, *65*, 9022.

(4) Ishibashi, H.; Kobayashi, T.; Takamasu, D. *Synlett* **1999**, 1286.

(5) For reviews, see: (a) Bailey, W. F.; Ovaska, T. V. Mechanisms of Importance in Synthesis. In *Advances in Detailed Reaction Mechanisms*; Coxon, J. M., Ed.; JAI Press: Greenwich, CT, 1994; Vol. 3, pp 251−273. (b) Mealy, M. M.; Bailey, W. F. *J. Organomet. Chem*. **2002**, *646*, 59. (c) Clayden, J. *Organolithiums: Selectivity for Synthesis*; Pergamon Press: New York, 2002; pp 293−335.

(6) See, for example: (a) Bailey, W. F.; Rossi, K. *J. Am. Chem. Soc.* **1989**, *111*, 765. (b) Krief, A.; Barbeaux, P. *Synlett* **1990**, 511. (c) Bailey, W. F.; Khanolkar, A. D. *J. Org. Chem*. **1990**, *55*, 6058. (d) Bailey, W. F.; Khanolkar, A. D. *Tetrahedron* **1991**, *47*, 7727. (e) 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. (f) Cooke, M. P., Jr. *J. Org. Chem*. **1993**, *58*, 2910. (g) Coldham, I.; Fernàndez, J. C.; Price, K. N.; Snowden, D. J. *J. Org. Chem*. **2000**, *65*, 3788. (h) Deng, K.; Bensari, A.; Cohen, T. *J. Am. Chem. Soc.* **2002**, *124*, 12106.

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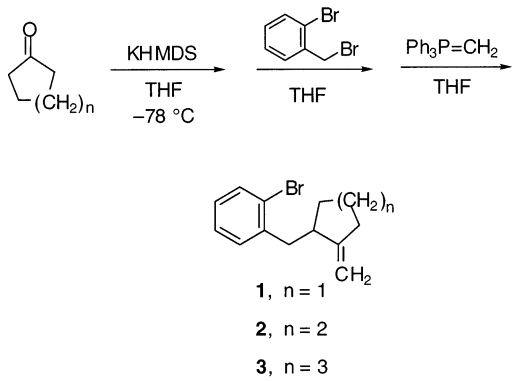
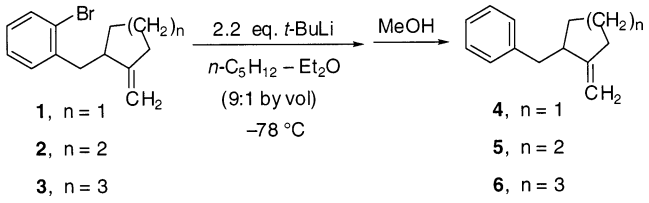
SCHEME 1



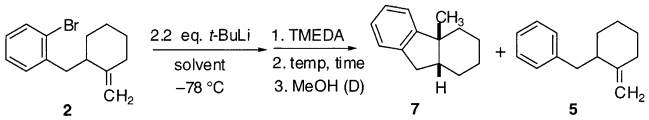
ated in virtually quantitative yield from 2-(*o*-bromobenzyl)-1-methylenecycloalkanes, as shown below, by low-temperature lithium−bromine exchange with *tert*-butyllithium (*t*-BuLi)[7] followed by quench of the aryllithium with methanol.



The behavior of aryllithiums generated from 2-(*o*-bromobenzyl)-1-methylenecycloalkanes was explored in a series of experiments involving the 2-(*o*-bromobenzyl)-1-methylenecyclohexane substrate (**2**). Initially, the aryllithium was generated at −78 °C by addition of 2.2 molar equiv of *t*-BuLi to an approximately 0.1 M solution of bromide **2** in dry, oxygen-free *n*-pentane−diethyl ether (9:1 v/v). Dry TMEDA (2.2 equiv) was then added, and the organolithium solution was allowed to warm and stand at room temperature under an atmosphere of argon for various periods of time. Cursory inspection of the results of a representative series of such experiments (Table 1, entries 1−3) reveals that 5-exo cyclization of the aryllithium derived from **2** is highly stereoselective: *cis*-1,2,3,4,4*a*,9*a*-hexahydro-4*a*-methylfluorene[8] (**7**) is the exclusive cyclic product after quench with MeOH; 2-benzyl-1-methylenecyclohexane (**5**) constitutes the balance of the reaction product. The data also indicate that the cyclization is very slow indeed:[9] the isomerization proceeds to only ∼90% completion when reaction mixtures are allowed to stand for 4.5 h at room temperature (Table 1, entry 3).

Since both the aryllithium and the primary alkyllithium formed upon cyclization appear to be persistent over the course of these experiments, as adjudged by the significant incorporation of deuterium upon quench of reaction mixtures with MeOD (Table 1), it seemed appropriate to attempt to increase the rate of the sluggish

TABLE 1. Exploratory Cyclizations of Aryllithium Derived from 2[a]



entry	solvent	temp, °C	time, min	product ratios[b] (% d_1)[c] 7	5
1	*n*-C_5H_{12}−Et_2O (9:1 v/v)	22	60	34 (89)	66 (85)
2			120	61 (85)	39 (82)
3			270	89 (70)	11 (70)
4	*n*-C_7H_{16}−MTBE (9:1 v/v)	40	30	78 (82)	17[d] (75)
5		45	45	87 (73)	4[e] (80)
6	*n*-C_7H_{16}−*n*-Bu_2O (9:1 v/v)	45	45	95 (85)	5 (41)

[a] The aryllithium was generated at −78 °C by addition of 2.2 equiv of *t*-BuLi in heptane to a solution of bromide **2** in the indicated solvent. TMEDA was added at −78 °C, the cooling bath was then removed, and the mixture was allowed to stand at the specified temperature for a period of time before the addition of an excess of oxygen-free MeOH or MeOD. [b] Ratios were determined by capillary GC. [c] Percent incorporation of deuterium (GC/MS analysis) upon quench with MeOD. [d] Product mixture contained 5% of a $C_{15}H_{20}$ isomer. [e] Product mixture contained 9% of a $C_{15}H_{20}$ isomer.

isomerization by warming reaction mixtures. The fact organolithiums readily abstract protons from both ethers[10] and TMEDA[11] at elevated temperatures is a potential difficulty with this approach. However, we had previously observed that the ether solvent, rather than the (presumably) complexed TMEDA, is generally responsible for protonation when solutions of organolithiums are warmed above ambient temperature[12] and it was anticipated that the small amount of ether in the solvent system would lessen the possibility of unwanted protonation.[13]

To this end, the aryllithium was generated from **2** at −78 °C in dry, oxygen-free *n*-heptane−MTBE (9:1 v/v) by lithium−bromine exchange, using *t*-BuLi in *n*-heptane. Dry TMEDA (2.2 equiv) was then added, and the organolithium solution was warmed and held at 40−45 °C for 30−45 min under a positive pressure of argon to effect cyclization. The results of these experiments (Table 1, entries 4 and 5) demonstrate that, as expected, the isomerization is significantly faster at elevated temperature. Unfortunately, although proton abstraction from solvent appears minimal, a $C_{15}H_{20}$ isomer of unknown structure, possibly formed by methyl transfer from MTBE to the alkyllithium product at the elevated temperature,[10] was noted as a byproduct. The use of di-*n*-butyl ether in place of MTBE in the solvent system obviated production of this byproduct: warming a solution of the aryllithium in *n*-heptane−di-*n*-butyl ether (9:1 v/v) to 45° for 45 min afforded 95% of isomerically pure **7** (Table 1, entry 6).

(7) (a) Bailey, W. F.; Punzalan, E. P. *J. Org. Chem.* **1990**, *55*, 5405. (b) Negishi, E.; Swanson, D. R.; Rousset, C. J. *J. Org. Chem.* **1990**, *55*, 5404.

(8) Barrow, C. J.; Bright, S. T.; Coxon, J. M.; Steel, P. J. *J. Org. Chem.* **1989**, *54*, 2542.

(9) By way of comparison, the half-time for cyclization of the parent 5-hexenyllithium in the presence of TMEDA is ∼6 min at −30 °C. See: Bailey, W. F.; Carson, M. W. *J. Org. Chem.* **1998**, *63*, 361.

(10) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon Press: New York, 1974.

(11) Kohler, F. H.; Hertkorn, N.; Blumel, J. *Chem. Ber.* **1987**, *120*, 2081.

(12) Bailey, W. F.; Khanolkar, A. D.; Gavaskar, K. V. *J. Am. Chem. Soc.* **1992**, *114*, 8053.

(13) Since, as noted elsewhere,[7] it is necessary to conduct the lithium−bromine exchange in a solvent system that contains a dialkyl ether, it is not possible to prepare the aryllithium in good yield in a pure hydrocarbon solvent.

SCHEME 2

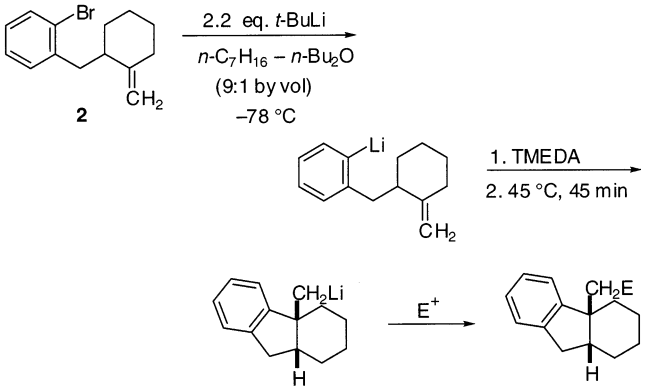
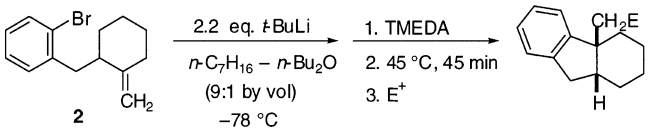


TABLE 2. Preparation of 4*a*-Substituted *cis*-Hexahydrofluorenes (Scheme 2)[a]

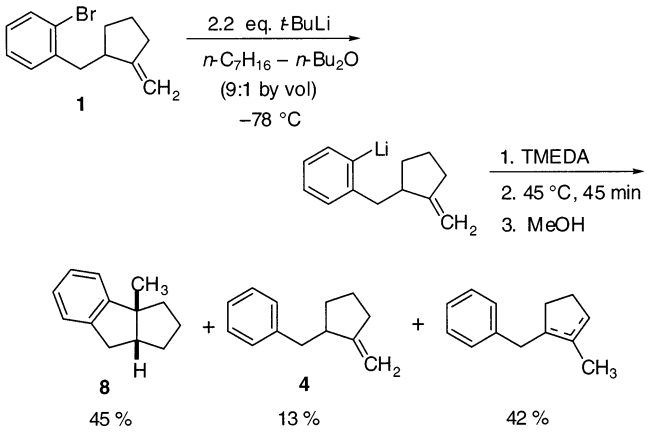


entry	E	E−	yield,[b] %
1	CH_3OH	H	91
2	D_2O	D	78[c]
3	Cl_3CCCl_3	Cl	65
4	PhSSPh	SPh	70
5	CH_2O	CH_2OH	62

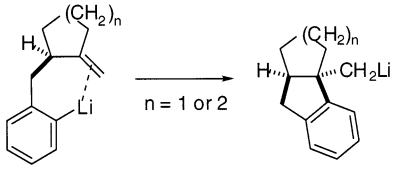
[a] The aryllithium was generated at −78 °C by addition of 2.2 equiv of *t*-BuLi in *n*-heptane to a solution of bromide **2** in *n*-heptane−di-*n*-butyl ether (9:1 v/v), TMEDA (2.2 equiv) was added at −78 °C, the cooling bath was then removed, and the mixture was allowed to warm and stand at +45 °C for 45 min before the addition of an excess of the electrophile. [b] Isolated yield of chromatographically pure product. [c] Determined by GC/MS analysis of the product.

Given the preliminaries outlined above, conditions for the preparation of 4*a*-substituted *cis*-hexahydrofluorenes were readily established (Scheme 2). Thus, addition of 2.2 molar equiv of *t*-BuLi under argon at −78 °C to a 0.1 M solution of **2** in scrupulously dry and oxygen-free *n*-heptane−di-*n*-butyl ether (9:1 v/v) generated the aryllithium. TMEDA (2.2 equiv) was then added and the reaction mixture was allowed to warm to room temperature, and was then heated in an oil-bath under a positive pressure of dry argon at 45 °C for 45 min to complete the ring-closure. As demonstrated by the results presented in Table 2, the 5-exo cyclization product may be trapped by addition of any of a variety of electrophiles to give stereoisomerically pure 4*a*-substituted *cis*-hexahydrofluorenes in 60−90% isolated yield. It might be noted that product isolation is a simple matter since the only other components of the reaction mixture are fairly minor quantities of hydrocarbons generated by inadvertent quench of the organolithiums by proton abstraction from solvent or adventitious moisture.

The aryllithiums derived from the remaining 2-(*o*-bromobenzyl)-1-methylenecycloalkanes (**1** and **3**) were somewhat less well behaved when subjected to the reaction conditions described above. Thus, as shown below, the methylenecyclopentane substrate generated from **1** was found to cyclize in an exclusively 5-exo fashion to give, following methanol quench, 45% (36% isolated yield) of stereoisomerically pure *cis*-tetrahydro-3*a*-methylcyclopenta[*a*]indene[3] (**8**). However, in this instance, the majority of the reaction product consisted of three isomeric alkenes: GC/MS analysis revealed the presence of 2-benzyl-1-methylenecyclopentane (**4**) as a minor product (13%) and two trisubstituted alkenes (42%) that were not further characterized. Apparently, under the conditions used to drive the cyclization of the aryllithium derived from **1**, abstraction of an allylic proton from the substrate to give an allyllithium, which finds ample literature precedent,[10] effectively competes with the ring-closure.



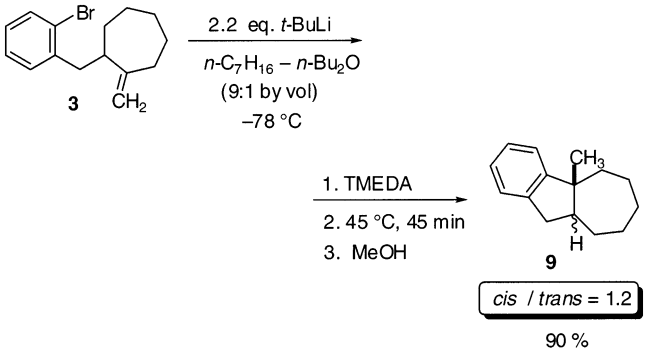
As noted above, 5-exo cyclization of the aryllithiums generated from bromides **1** and **2** leads exclusively to cis-fused products **7** and **8**. This stereochemical outcome is undoubtedly enforced by the fairly rigid geometry of the transition state for the ring-closure[14] and the conformational constraints of these substrates. Thus, as indicated below, coordination of the lithium atom with the methylene π-bond exocyclic to a tethered cyclopentane or cyclohexane ring can only occur on the face that is syn-disposed to the aryl substituent.



In light of the inherent conformational flexibility of the 2-(*o*-bromobenzyl)-1-methylenecycloheptane (**3**) substrate, it is perhaps not surprising that ring-closure of the corresponding aryllithium is much less stereoselective than is the analogous cyclization of an aryllithium tethered to a five- or six-membered ring. Indeed, as illustrated below, the aryllithium prepared from **3** by lithium−bromine exchange cyclizes readily at +45 °C in the presence of TMEDA to give octahydro-5*a*-methylcy-

(14) It should be noted that the lithium atom is intimately involved in the cycloisomerization of unsaturated organolithiums and 5-hexenyllithium is unique among the 5-hexenylalkalis in it ability to undergo facile cyclization; see: Bailey, W. F.; Punzalan, E. R. *J. Am. Chem. Soc.* **1994**, *116*, 6577. Molecular orbital calculations indicate the stereochemical course of these formally anionic cyclizations is a consequence of a transition state for the process in which the lithium atom is coordinated to the remote π-bond.[6d] Indeed, intramolecular coordination of the lithium atom with the remote π-bond in the ground state of 5-hexenyllithium has been experimentally confirmed; see: Rölle, T.; Hoffmann, R. W. *J. Chem. Soc., Perkin Trans. 2* **1995**, 1953.

clohepta[*a*]indene (**9**) in 90% isolated yield as an approximately 55:45 mixture of *cis*-**9** and *trans*-**9**, respectively. Comparison of the ^{1}H and ^{13}C NMR spectra of the product mixture with those reported by Ishibashi for the cis- and trans-isomers of **9** confirmed the stereochemical assignment.[3]



In summary, cyclization of an aryllithium tethered to a 2-(*o*-bromobenzyl)-1-methylenecycloalkane is a kinetically slow but thermodynamically favorable process that proceeds in an exclusively 5-exo fashion to afford stereoisomerically pure cis-fused product (**7** and **8**) when the methylenecycloalkane is five- or six-membered, but it is less stereoselective when the methylenecycloalkane is seven-membered. As demonstrated by the results summarized in Table 1, this simple methodology provides an experimentally convenient and highly steroselective route to 4*a*-substituted *cis*-hexahydrofluorenes.

Experimental Section

General Procedures. The concentration of commercial solutions of *t*-BuLi in *n*-heptane was determined immediately prior to use by the method of Watson and Eastham.[15] Di-*n*-butyl ether and diethyl ether were freshly distilled under dry nitrogen from sodium/benzophenone; *n*-heptane was distilled from sodium/benzophenone/tetraglyme; *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) was purified by distillation under nitrogen from calcium hydride. All bromides used to prepare organolithiums were rendered essentially oxygen-free before use by bubbling dry, deoxygenated argon gas through the neat liquid for at least 5 min before use.

2-(*o*-Bromobenzyl)cyclopentanone. A solution of KHMDS in 60 mL of THF, prepared under nitrogen at room temperature from 2.00 g (0.050 mol) of oil-free potassium hydride and 13.20 mL (0.062 mol) of 1,1,1,3,3,3-hexamethyldisilazane, was cooled to −78 °C, 3.50 g (0.042 mol) of freshly distilled cyclopentanone was added, and the mixture was stirred at −78 °C for 1 h before dropwise addition of a solution of 15.6 g (0.062 mol) of *o*-bromobenzyl bromide in 30 mL of anhydrous THF. The reaction mixture was stirred for a further 20 min at −78 °C and then allowed to warm and stir at room temperature overnight before addition of 150 mL of 10% aqueous HCl. The organic layer was separated, the aqueous layer was extracted with ether, and the combined organic layers were washed with water and brine, dried (Na_2SO_4), and concentrated by rotary evaporation. The residue was chromatographed on silica gel (10% EtOAc−hexane, R_f 0.30) to give 4.83 g (46%) of the known ketone[2] as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.55−1.74 (m, 2 H), 1.93−2.12 (m, 3 H), 2.30−2.36 (m, 2 H), 2.51 (dd, J = 13.7, 9.5 Hz, 1 H), 3.13 (dd, J = 13.7, 3.8 Hz, 1 H), 7.15−7.34 (m, 4 H). An analogous procedure was used to prepare 2-(*o*-bromobenzyl)cyclohexanone and 2-(*o*-bromobenzyl)cycloheptanone as detailed in the Supporting Information.

2-(*o*-Bromobenzyl)-1-methylenecyclopentane (1). A suspension of 8.20 g (23.0 mmol) of methyl(triphenyl)phosphonium bromide and 2.58 g (23.0 mmol) of potassium *tert*-butoxide in 75 mL of anhydrous THF was stirred at room temperature for 1 h before addition of a solution of 4.83 g (19.2 mmol) of 2-(*o*-bromobenzyl)cyclopentanone in 25 mL of anhydrous THF. The reaction mixture was stirred at room temperature for 7 h, solvent was then removed by rotary evaporation, the viscous residue was triturated with pentane, and the suspension was eluted with pentane from a short column of silica gel. Concentration of the eluent afforded 2.10 g (44%) of the known[2] title compound as a viscous oil: ^{1}H NMR ($CDCl_3$) δ 1.41−1.44 (m, 1 H), 1.55−1.60 (m, 1 H), 1.71−1.80 (m, 2 H), 2.41−2.44 (m, 2 H), 2.60 (dd, J = 13.4, 10.0 Hz, 1 H), 2.80 (m, 1 H), 3.11 (dd, J = 13.4, 5.0 Hz, 1 H), 4.90 (apparent s, 1 H), 4.98 (apparent s, 1 H), 7.06 (td, J = 7.9, 3.8 Hz, 1 H), 7.20−7.23 (m, 2 H), 7.56 (d, J = 7.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 24.09, 32.46, 33.23, 41.00, 44.00, 105.07, 124.84, 127.15, 127.58, 131.23, 132.82, 140.75, 155.82. An analogous procedure was used to prepare 2-(*o*-bromobenzyl)-1-methylenecyclohexane (**2**) and 2-(*o*-bromobenzyl)-1-methylenecycloheptane (**3**) as detailed in the Supporting Information.

2-Benzyl-1-methylenecyclopentane (4). A solution of 162 mg (0.65 mmol) of 2-(*o*-bromobenzyl)-1-methylenecyclopentane (**1**) in 5.8 mL of dry *n*-pentane and 0.7 mL of diethyl ether was cooled to −78 °C (dry ice−acetone) under an atmosphere of dry and oxygen-free argon and 1.09 mL of a 2.02 M solution of *t*-BuLi in *n*-heptane (2.20 mmol) was added dropwise by syringe. The mixture was stirred at −78 °C for 15 min, 1 mL of oxygen-free methanol was added, and the flask was allowed to warm to room temperature. The reaction mixture was diluted with ether, washed with water, dried ($MgSO_4$), and concentrated by careful rotary evaporation to give 105 mg (95%) of the known hydrocarbon[2] as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.31−1.37 (m, 3 H), 1.51−1.57 (m, 1 H), 1.72−1.81 (m, 2 H), 2.35−2.42 (m, 2 H), 2.48 (dd, J = 13.4, 9.8 Hz, 1H), 2.68 (m, 1 H), 2.98 (dd, J = 13.4, 5.1 Hz, 1 H), 4.88 (apparent s, 1 H), 4.97 (apparent s, 1 H), 7.21−7.34 (m, 5 H). An analogous procedure was used to prepare 2-benzyl-1-methylenecyclohexane (**5**) and 2-benzyl-1-methylenecycloheptane (**6**) as detailed in the Supporting Information.

General Procedure for the Preparation of 4*a*-Substituted *cis*-Hexahydrofluorenes (Scheme 2). An approximately 0.1 M solution of 2-(*o*-bromobenzyl)-1-methylenecyclohexane (**2**) in anhydrous *n*-heptane−di-*n*-butyl ether (9:1 v/v) was cooled to −78 °C under argon and a 2.2 molar equiv of *t*-BuLi in heptane was added dropwise via syringe. The reaction mixture was stirred for an additional 15 min at −78 °C, 2.2 molar equiv of dry, deoxygenated TMEDA was added via syringe, the cooling bath was removed, and the pale-yellow reaction mixture was allowed to warm to room temperature. The flask was transferred to an oil bath that had been warmed to +45 °C and the mixture was stirred, under a positive pressure of argon, for 45 min. The reaction mixture was then recooled to −78 °C, an excess (typically 1.1 equiv) of the appropriate electrophile (Table 2) was added, and the resulting mixture was then allowed to warm to room temperature and worked up in the usual manner.

***cis*-1,2,3,4,4a,9a-Hexahydro-4a-methylfluorene (7, Table 2, entry 1).** A solution of (*cis*-hexahydrofluorenyl-4a-methyl)-lithium, prepared from 265 mg (1.00 mmol) of 2-(*o*-bromobenzyl)-1-methylenecyclohexane (**2**) as described above, was quenched with dry, oxygen-free methanol. The product mixture was diluted with ether, washed with several portions of water, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (pentane, R_f 0.40) and the eluent was washed with small portions of cold, concentrated sulfuric acid until the acid layer remained clear to remove traces of 2-benzyl-1-methylenecyclohexane (**5**). After being washed with water and 10% aqueous sodium bicarbonate, the solution was dried ($MgSO_4$) and

(15) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

concentrated to afford 170 mg (91%) of the known[8] title compound: ^{1}H NMR ($CDCl_3$) δ 1.34 (3H, s), 1.37−1.60 (m, 6 H), 1.72−1.79 (m, 2 H), 2.16 (quintet, J = 6.4 Hz, 1 H), 2.73 (dd, J = 15.4, 7.19 Hz, 1 H), 2.96 (dd, J = 15.4, 7.0 Hz, 1 H), 7.18−7.36 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 22.20, 22.90, 25.74, 26.82, 35.40, 35.64, 45.30, 46.33, 121.62, 125.21, 125.93, 126.14, 142.40, 152.66. The deuterated material (Table 2, entry 2) was prepared in an analogous fashion, using D_2O to quench the product organolithium.

***cis*-1,2,3,4,4a,9a-Hexahydro-4a-(chloromethyl)fluorene (Table 2, entry 3).** A solution of (*cis*-hexahydrofluorenyl-4a-methyl)lithium, prepared as described above from 314 mg (1.18 mmol) of 2-(*o*-bromobenzyl)-1-methylenecyclohexane (**2**), was recooled to −78 °C and a solution of 308 mg (1.30 mmol) of hexachloroethane in 5.0 mL of dry pentane was added. The reaction mixture was allowed to warm to room temperature, diluted with ether, washed with several portions of water, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (pentane, R_f 0.27) to give 170 mg (65%) of the known[3] title compound: ^{1}H NMR ($CDCl_3$) δ 1.15−1.22 (m, 2 H), 1.27−1.33 (m, 1 H), 1.48−1.56 (m, 2 H), 1.69−1.74 (m, 1 H), 1.83 (ddd, J = 14.3, 10.6, 3.8 Hz, 1 H), 1.95−2.00 (m, 1 H), 2.42−2.49 (m, 1 H), 2.50 (dd, J = 15.5, 3.5 Hz, 1 H), 3.02 (dd, J = 15.5, 6.4 Hz, 1 H), 3.52 (AB-pattern, J_{AB} = 11.0 Hz, 2 H), 7.19−7.26 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 21.91, 23.60, 28.50, 30.05, 36.40, 41.41, 51.22, 52.32, 123.20, 125.85, 126.26, 127.20, 143.10, 146.16.

***cis*-1,2,3,4,4a,9a-Hexahydro-4a-((phenylthio)methyl)-fluorene (Table 2, entry 4).** A solution of (*cis*-hexahydrofluorenyl-4a-methyl)lithium, prepared as described above from 306 mg (1.16 mmol) of 2-(*o*-bromobenzyl)-1-methylenecyclohexane (**2**), was recooled to −78 °C and a solution of 278 mg (1.27 mmol) of diphenyl disulfide in 6.0 mL of dry pentane was added. The reaction mixture was allowed to warm to room temperature, diluted with ether, washed with several portions of water, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (pentane to remove excess $(PhS)_2$ (R_f 0.05) followed by 2% EtOAc−hexane, R_f 0.55) to give 238 mg (70%) of the known[3] title compound: ^{1}H NMR ($CDCl_3$) δ 1.17−1.27 (m, 2 H), 1.33−1.36 (m, 1 H), 1.46−1.54 (m, 2 H), 1.67−1.71 (m, 1 H), 1.76 (ddd, J = 13.9, 10.3, 3.7 Hz, 1 H), 1.97−2.02 (m, 1 H), 2.48−2.51 (m, 1 H), 2.52 (dd, J = 14.9, 4.1 Hz, 1 H), 3.00 (dd, J = 15.1, 6.4 Hz, 1 H), 3.14 (AB-pattern, J_{AB} = 12.4 Hz, 2 H), 7.13−7.23 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 22.12, 23.51, 28.24, 32.30, 36.40, 42.90, 44.33, 50.53, 122.90, 125.60, 125.70, 126.20, 126.80, 128.75, 129.10, 138.25, 142.83, 148.11.

***cis*-2-(1,2,3,4,4a,9a-Hexahydrofluoren-4a-yl)ethanol (Table 2, entry 5).** A solution of (*cis*-hexahydrofluorenyl-4a-methyl)lithium, prepared as described above from 238 mg (0.90 mmol) of 2-(*o*-bromobenzyl)-1-methylenecyclohexane (**2**), was recooled to −78 °C and a stream of formaldehyde gas (generated by heating dry paraformaldehyde and passing the gas through a tube filled with dry $CaCl_2$) was bubbled through the reaction mixture for approximately 3 min. The reaction mixture was allowed to warm to room temperature, diluted with ether, washed with several portions of water, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (60% EtOAc−hexane, R_f 0.27) to give 120 mg (62%) of the known[3] alcohol: ^{1}H NMR ($CDCl_3$) δ 1.21−37 (m, 4 H), 1.41−1.52 (m, 3 H), 1.66−1.69 (m, 1 H), 1.77 (ddd, J = 14.0, 8.9, 6.1 Hz, 1 H), 1.77−1.88 (m, 1 H), 1.96−2.01 (ddd, J = 14.0, 8.9, 5.84 Hz, 1 H), 2.20 (br quintet, J = 6.3 Hz, 1 H), 2.55 (dd, J = 15.5, 5.1 Hz, 1 H), 2.98 (dd, J = 15.5, 6.7 Hz, 1 H), 3.54 (ddd, J = 10.2, 9.06, 5.9 Hz, 1 H), 3.62 (ddd, J = 10.2, 9.06, 6.2 Hz, 1 H), 7.09−7.3 (m, 3 H), 7.36 (br d, J = 6.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.00, 23.20, 27.65, 33.85, 36.16, 41.00, 44.00, 48.12, 59.86, 122.46, 125.70, 126.03, 126.30, 142.97, 149.30.

***cis*-1,2,3,3a,8,8a-Tetrahydro-3a-methylcyclopenta[*a*]indene (8).** A solution of 274 mg (1.09 mmol) of 2-(*o*-bromobenzyl)-1-methylenecyclopentane (**1**) in 9.0 mL of dry *n*-heptane and 1.0 mL of di-*n*-butyl ether was cooled to −78 °C under an atmosphere of dry, oxygen-free argon and 1.20 mL of a 2.02 M solution of *t*-BuLi in *n*-heptane (2.42 mmol) was added dropwise by syringe. The reaction mixture was stirred for an additional 15 min at −78 °C, 256 mg (2.20 mmol) of dry, deoxygenated TMEDA was added via syringe, the cooling bath was removed, and the pale-yellow reaction mixture was allowed to warm to room temperature. The flask was transferred to an oil bath that had been warmed to +45 °C and the mixture was stirred, under a positive pressure of argon, for 45 min. The reaction mixture was quenched with MeOH and then allowed to cool to room temperature. The solution was diluted with ether, washed with several portions of water, and dried ($MgSO_4$). GC/MS analysis [25-m × 0.2-mm × 0.33-μm cross-linked phenyl methyl (5%) silicone capillary column] of the crude reaction mixture revealed the presence of the title compound (vide infra, 45%) as well as 2-benzyl-1-methylenecyclopentane (**4**; 13%) and two isomeric alkenes (42%) that were not further characterized. The solution was concentrated at reduced pressure, the residue was purified by flash chromatography on silica gel (pentane, R_f 0.39), and the eluent was washed with small portions of cold, concentrated sulfuric acid until the acid layer remained clear to remove traces of alkenes. After being washed with water and 10% aqueous sodium bicarbonate, the solution was dried ($MgSO_4$) and concentrated to afford 67.0 mg (36%) of the known[3] title compound: ^{1}H NMR ($CDCl_3$) δ 1.34 (s, 3 H), 1.40−1.46 (m, 2 H), 1.60−1.63 (m, 1 H), 1.69−1.76 (m, 1 H), 1.89−2.00 (m, 2 H), 2.37 (m, 1 H), 2.61 (dd, J = 16.6, 2.9 Hz, 1 H), 3.21 (dd, J = 16.6, 8.8 Hz, 1 H), 7.14−7.26 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 26.20, 29.40, 35.23, 38.60, 42.00, 50.10, 56.50, 123.12, 124.44, 126.22, 126.61, 142.71, 152.15.

***cis*- and *trans*-1,2,3,4,5,5a,10,10a-Octahydro-5a-methylcyclohepta[*a*]indene (9).** A solution of 418 mg (1.50 mmol) of 2-(*o*-bromobenzyl)-1-methylenecycloheptane (**3**) in 13.5 mL of dry *n*-hexane and 1.5 mL of di-*n*-butyl ether was cooled to −78 °C under an atmosphere of dry, oxygen-free argon and 1.64 mL of a 2.02 M solution of *t*-BuLi in *n*-heptane (3.30 mmol) was added dropwise by syringe. The reaction mixture was stirred for an additional 15 min at −78 °C, 384 mg (3.30 mmol) of dry, deoxygenated TMEDA was added via syringe, the cooling bath was removed, and the pale-yellow reaction mixture was allowed to warm to room temperature. The flask was transferred to an oil bath that had been warmed to +45 °C and the mixture was stirred, under a positive pressure of argon, for 45 min. The reaction mixture was worked up as described above for the preparation of **8** to give 270 mg (90%) of the previously reported[3] title compounds as an approximately 1.2:1.0 mixture of cis- and trans-isomers, respectively: ^{1}H NMR ($CDCl_3$) [mixture of isomers] δ 1.07 (s), 1.25 (s), 1.3−1.97 (m), 2.2−2.24 (m), 2.40−2.50 (m), 2.61−2.7 (m), 2.81 (dd, J = 15.3, 7.5 Hz), 3.23 (dd, J = 16.3, 9.1 Hz), 7.01−7.2 (m); ^{13}C NMR ($CDCl_3$) [*cis*-**9**] δ 24.23, 28.50, 30.10, 31.33, 32.90, 39.10, 39.30, 48.20, 51.00, 122.81, 124.20, 126.12, 126.35, 141.83, 152.81; [*trans*-**9**] δ 20.20, 26.25, 26.62, 26.90, 27.80, 38.03, 40.70, 49.10, 50.56, 121.92, 124.06, 126.00, 126.30, 141.90, 155.07.

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Supporting Information Available: Preparation and characterization of compounds **2**, **3**, **5**, and **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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