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Carbenoid Chain Reactions through Proton, Deuteron, or Bromine Transfer from Unactivated 1-Bromo-1-alkenes to Organolithium Compounds[#]

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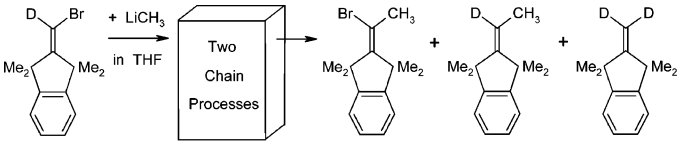

H,D isotope-dependent molar ratios

The deceptively simple vinylic substitution reactions $Alk_2C{=}CA{-}Br + RLi \rightarrow Alk_2C{=}CA{-}R + LiBr$ (A = H, D, or Br) occur via an alkylidenecarbenoid chain mechanism (three steps) without transition metal catalysis. 2-(Bromomethylidene)-1,1,3,3-tetramethylindan ($Alk_2C{=}CH{-}Br$, **2a**) is deprotonated (step 1) by phenyllithium (PhLi) to give the Br,Li-alkylidenecarbenoid $Alk_2C{=}CLi{-}Br$ (**3**). In the ensuing chain cycle, **3** and PhLi (step 2) form the observable alkenyllithium intermediate $Alk_2C{=}CLi{-}Ph$ that characterizes the carbenoid mechanism in Et_2O and is able to propagate the chain (step 3) through deprotonation of **2a**, furnishing carbenoid **3** and the product $Alk_2C{=}CH{-}Ph$. The related 2-(dibromomethylidene)-1,1,3,3-tetramethylindan ($Alk_2C{=}CBr_2$, **2c**) and methyllithium (MeLi) generate carbenoid **3** (step 1), which incorporates MeLi (step 2) to give $Alk_2C{=}CLi{-}CH_3$, which reacts with **2c** by bromine transfer producing $Alk_2C{=}CBr{-}CH_3$ and carbenoid **3** (step 3). PhC≡CLi cannot carry out step 1, but MeLi can initiate (step 1) the carbenoid chain cycle (steps 2 and 3) of **2c** with PhC≡CLi leading to $Alk_2C{=}CBr{-}C{\equiv}C{-}Ph$. Reagent **2a** may perform both proton and bromine transfer toward $Alk_2C{=}CLi{-}CH_3$, feeding two coupled carbenoid chain processes in a ratio that depends on the solvent and on a primary kinetic H/D isotope effect.

Introduction

An organolithium compound RLi confronted with 2-(bromomethylidene)-1,1,3,3-tetramethylindan (**2a**)[1] may choose between several reaction modes (Scheme 1): (i) the Br/Li interchange reaction leading to the formation of **1a**, as observed[2] with *n*-butyllithium, (ii) the α-deprotonation mode generating the short-lived Br,Li-alkylidenecarbenoid[3,4] **3** and its descendants, and (iii) other modes which might be thought to generate the "normal" products **6** obtained from **2a** in the present investigations. The deceptively simple relationship between **6** and **2a** may, for example, suggest an addition−rotation−elimination (ARE)[5] mechanism involving a nucleophilic attack[6,7] of RLi at C^{α} of **2a**. However, it will be reported here that RLi = CH_3Li and **2a** can form **4a** and **5c** also (as depicted in Scheme 1) along with the "normal" product **5a** of type **6**. The formation of **5c,** in particular, may appear surprising because the possible byproduct RBr = CH_3Br (Scheme 1) cannot be expected to produce major portions of **5c** (from **3**?) or **5a** (from **1a**?) under the reaction conditions, as will be explained in section 3.

Previous investigations[6] of the related chloromethylidene reagents **7** and **8** (Scheme 1) have refuted the ARE[5] and several other[7] mechanisms, revealing instead carbenoid chain processes

[#] Sterically Congested Molecules, 19. Part 18: ref 6.

(1) Syntheses of the reagents **2a**, **2b**, and **2c** are outlined in section 4 of Results and Discussion.

(2) Knorr, R.; Freudenreich, J.; Polborn, K.; Nöth, H.; Linti, G. *Tetrahedron* **1994**, *50*, 5845−5860.

(3) Carbenoids carry both a metal cation and a nucleofugal group at the same carbon atom: Köbrich, G. *Angew. Chem.* **1972**, *84*, 557−570 and first footnote therein; *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 473−485.

(4) Nomenclature: Stang, P. J. *Acc. Chem. Res.* **1982**, *15*, 348−354.

(5) Rappoport, Z. *Acc. Chem. Res.* **1992**, *25*, 474−479, and cited literature.

(6) Knorr, R.; Pires, C.; Behringer, C.; Menke, T.; Freudenreich, J.; Rossmann, E. C.; Böhrer, P. *J. Am. Chem. Soc.* **2006**, *128*, 14845−14853.

(7) Depicted in Scheme 1 of ref 6.

10.1021/jo070623w CCC: $37.00
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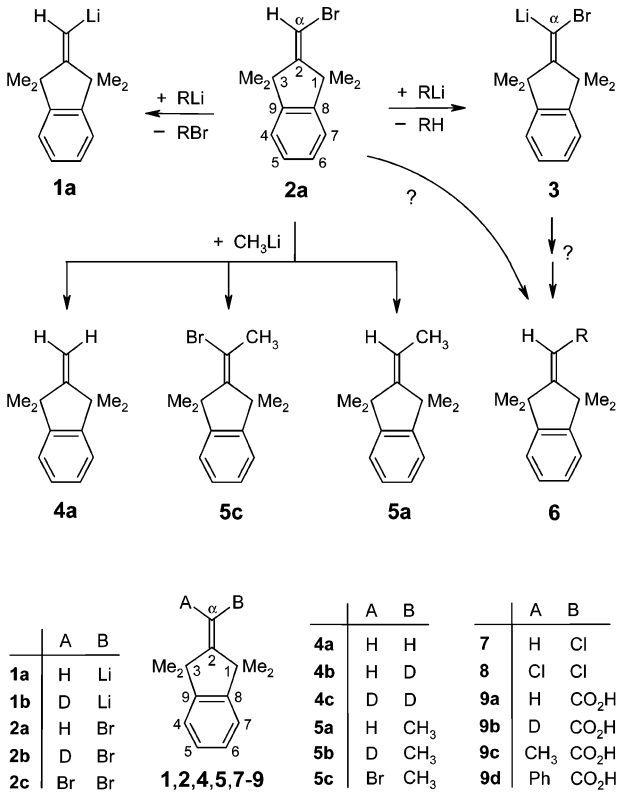
SCHEME 1



	A	B
1a	H	Li
1b	D	Li
2a	H	Br
2b	D	Br
2c	Br	Br

	A	B
4a	H	H
4b	H	D
4c	D	D
5a	H	CH_3
5b	D	CH_3
5c	Br	CH_3

	A	B
7	H	Cl
8	Cl	Cl
9a	H	CO_2H
9b	D	CO_2H
9c	CH_3	CO_2H
9d	Ph	CO_2H

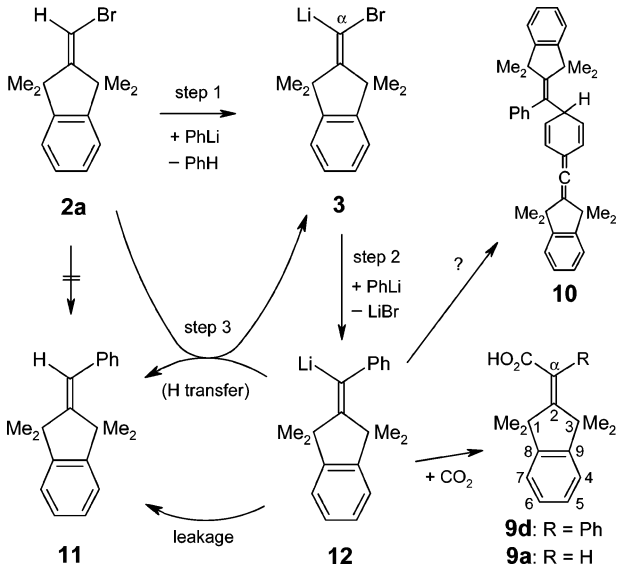
which involved either α-deprotonation (of **7**) or Cl/Li interchange reactions (of **8**). By use of the developed[6] criteria (stoichiometry, observability of intermediates or their detection through trapping with CO_2 to give acids **9**, and kinetic H/D isotope effects, as applicable), it will be inquired here about the feasibility of the carbenoid chain pathway (**2a**−**c** + RLi → **3** → **6**) for RLi = phenyllithium, CH_3Li, and PhC≡CLi. Because most of the results are presented within the running text for the sake of instantaneous deductions, these results are reiterated for reference in the same order in Table S1 of the Supporting Information. The 1,1,3,3-tetramethyl-2-indanylidene model system facilitated these investigations for several reasons: Some of the conceivable[8] side-reactions of the alkylidenecarbenoid **3** or its precursors are suppressed, and the six-proton NMR singlets of 1,1-Me_2 and 3,3-Me_2 provide distinctive and easily spotted marks for detecting the products in situ even on a rather small scale (≈0.1 mmol).

Results and Discussions

1. Phenyllithium (RLi = PhLi) with Reagent 2a: Chain Propagation through Proton Transfer. Scheme 2 presents the alkylidenecarbenoid chain mechanism[6] of PhLi with **2a** as an example. The initiating step 1 employs PhLi as a base to deprotonate reagent **2a**[1] with formation of the carbenoid **3,** which is then substituted[8] in step 2 by PhLi acting as a nucleophile to form the alkenyllithium intermediate **12**. At this point, the carbenoid process may halt, with 2 equiv of PhLi consumed per **2a** (2:1 stoichiometry), and might be recognized by carboxylation which would convert **12** to **9d**. However, the carbenoid chain mechanism may append step 3 in which intermediate **12** is protonated by reagent **2a** to give the final

(8) Knorr, R. *Chem. Rev.* **2004**, *104*, 3795−3849.

SCHEME 2



product **11** of type **6**. This proton transfer would generate carbenoid **3** without participation of PhLi, so that further repetitions of the step 2/step 3 cycle might convert reagent **2a** to product **11** with a total consumption of only (a little more than) 1 equiv of PhLi. Thus the characterizing stoichiometry of PhLi/**2a** should normally be found between 1:1 (chain) and 2:1 (nonchain carbenoid) depending on chain interruptions due to an eventual depletion of reagent **2a** or due to a "leakage" (Scheme 2) from **12** to **11** through protonation by sources other than **2a** (for example, the solvent). Note that a perfect chain, consisting of steps 2 and 3, would leave essentially no residual chain carrier **12** from which to obtain the acid **9d**.

In practice, a run with PhLi (2.1 equiv, 0.24 M) in Et_2O solution at room temperature was almost completed in 20 min. The in situ ^1H NMR spectrum showed residual PhLi, the product[9] **11**, the known[6,10] intermediate **12**, and residual reagent **2a** in the molar ratio 64:15:67:18. The observation of **12** (67%) establishes a predominant course via carbenoid **3** with efficient trapping of **3** by PhLi (fast step 2), because an alternative formation of **12** by deprotonation of **11** was never detected. The increasing PhLi/**2a** ratio (from 2.1:1 to 64:18) is compatible with the formation of **11** from **12** through the chain propagation step 3 (which consumes only reagent **2a**). The observed coexistence of PhLi, **2a**, and **12** implies that both steps 1 and 3 occur slowly. In view of the 15:67 ratio of **11**/**12**, the steps can then be ranked[11] with respect to their rates (rapidity of the flux of material) as $2 \gg 1 \gtrsim 3$. The known[9] allenic "dimer" **10** emerged very slowly through an unknown process after the consumption of reagent **2a**. The final carboxylative workup with solid CO_2 after 44 h furnished the acids **9d**[9] (7% yield),[12] **9a**[2] (≤1% yield), and benzoic acid (from 0.1 equiv of surviving PhLi), showing that not all of intermediate **12** was destroyed

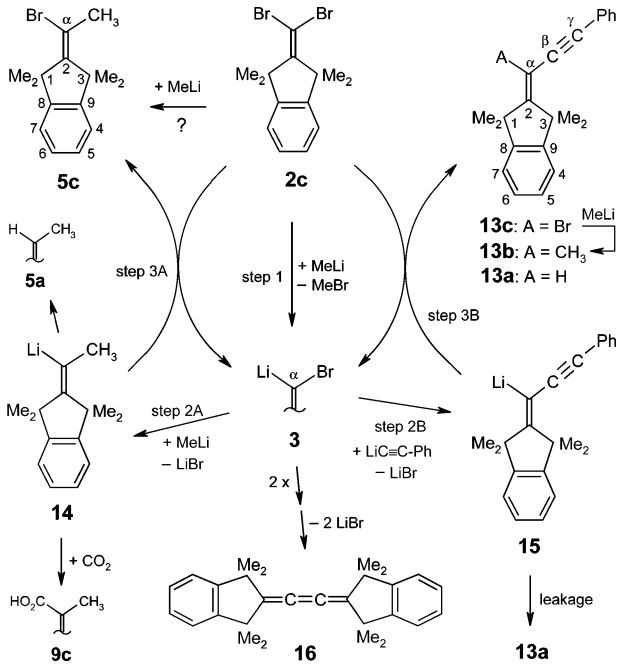
(9) Knorr, R.; Lattke, E.; Räpple, E. *Liebigs Ann. Chem.* **1980**, 1207−1215.

(10) Knorr, R.; Hoang, T. P.; Nöth, H.; Linti, G. *Organometallics* **1992**, *11*, 2669−2673.

(11) With the assumption that the substitution step 2 with LiBr elimination is practically irreversible. To be successful, step 2 must occur more rapidly than the decomposition of the alkylidenecarbenoid which is usually[8] fast at room temperature.

(12) Most of the yields were determined in small-scale runs (0.1−1 mmol) under nonoptimized conditions.

SCHEME 3



by "leakage" during that long period of time. The nonacidic fraction contained mainly **11**, some allenic "dimer" **10**, and a trace of olefin **4a**. The tiny portions of **4a** and **9a** observed demonstrate that PhLi hesitated to perform a Br/Li interchange with **2a** to give **1a**.

In THF solution, product **11** was almost the only tetramethylindan derivative generated from **2a** with PhLi (1 equiv) within less than 15 min at room temperature (no acids, no residual **2a**, no allenic "dimer" **10**, not more than a trace of **4a**). Thus, chain propagation by proton transfer to **12** (step 3) was presumably more efficient in THF than in Et_2O, judging from the clean 1:1 stoichiometry and other parallel results observed earlier[6] for the carbenoid chain processes of PhLi with the dichloro reagent **8**.

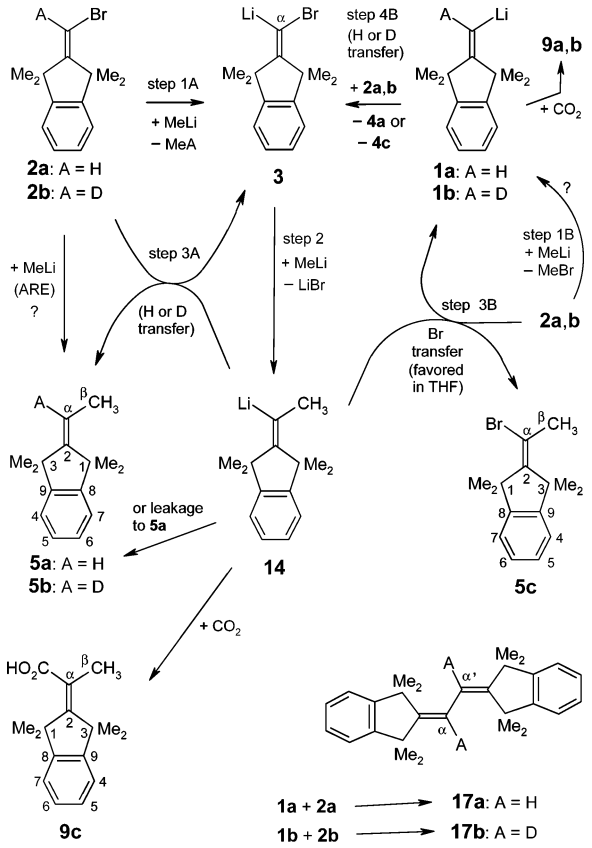
2. Methyllithium (RLi = MeLi) with Reagent 2c: Chain Propagation through Bromine Transfer. The reaction of MeLi (0.34 M) in diethyl ether with reagent **2c**[1] (0.083 M) was complete in 4 min at room temperature and required 1.0 equiv of MeLi to produce **5c** exclusively (Scheme 3). The in situ ^{1}H NMR spectra showed no trace of the leakage product **5a**, and carboxylation afforded no acid **9c** (to be expected from chain carrier **14**). All this accords with an efficient chain process (step rates ranking[11] as 2A and 3A $\gg$ 1), but could it not equally well be explained with a direct conversion (**5c** ← **2c**) through some other[7] mechanism, considering that **2c** is obviously much more reactive than the dichloro reagent[6] **8** toward MeLi? Such direct (non-carbenoid) pathways to **5c** should not be influenced by the presence of PhC≡CLi (which did not interact with **2c** for over more than 4 h). But PhC≡CLi (2.0 equiv) was incorporated (steps 2B and 3B of the carbenoid chain B) as soon as MeLi (0.1 equiv) was added at −70 °C, which induced the consumption of ≈70% of **2c** in <5 min at room temperature, at which point the chain reaction stopped because the chain carrier **15** had been converted to the leakage product **13a**. One restart with a second small batch of MeLi (0.1 equiv) sufficed for the total conversion of **2c**, and carboxylative workup afforded **5c** (4% yield with respect to **2c**), **13c** (71%), **13b** (2%), and **13a** (6%) but no **5a** and no acids other than PhC≡CCO_2H (from residual PhC≡CLi). The constitution of **13c** was confirmed through its easy conversion to the known[6] alkyne **13b** with MeLi. This run established that at least some portion of **2c** and MeLi had generated an intermediate (**3**) that could choose to react either with MeLi (steps 2A and 3A) to give **5c** or (preferentially) with PhC≡CLi to produce **13a**−**c** via steps 2B and 3B (in analogy with the behavior[6] of the dichloro reagent **8**). A complete exclusion of non-carbenoid routes (**5c** ← **2c**)[7] would have to be based on evidence for a *decelerated*[13] consumption of **2c** in the presence of PhC≡CLi, but such evidence was not obtained here because **2c** was always consumed too rapidly.

In THF solution, the interaction of MeLi with **2c** (started at −70 °C) furnished the "butatriene" **16** as a major product in less than 7 min at room temperature. Because **16** results from self-substitution at C^α of carbenoid **3** ("dimerization"),[14] this indicated that the Br/Li interchange step 1 of Scheme 3 was sufficiently fast to build up a relatively high concentration of **3** and that the subsequent "dimerization" could keep pace with step 2A. The amount of MeBr (step 1) corresponding to **16** (including some ethane formed from MeBr with MeLi) and no trace of residual **2c** or MeLi were detected through ^{1}H NMR in situ, which displayed the products MeBr + **16** + **5c** + **5a** in the molar ratio 67:36:26:2. The leakage product **5a** together with a trace of the acid **9c** (isolated after carboxylation) revealed that at least some of the chain carrier **14** had survived in the presence of MeBr up to 3 h. Employment of an excess of MeLi led to almost the same molar ratio (0:35:26:4), except that MeBr was converted completely to ethane within 14 min, so that close to 2 equiv of MeLi were consumed. The quantities of MeBr (or ethane) and **5c**, resulting from fast Br/Li interchange reactions, suggest the rankings[11] of the step rates to be 1 $\gtrsim$ 3A and 2A $\approx$ carbenoid dimerization, which amounts to a disturbed chain process. Clearly, it was preferable to use the undisturbed chain process in Et_2O solution where **5c** was formed exclusively because step 1 was not obtrusive.

3. MeLi with Reagents 2a and 2b: Two Chains Sharing Step 2. The monobromide **2a** (0.10 M) in diethyl ether consumed roughly 1 equiv of MeLi (1.0 M) with a first $t_{1/2} \approx$ 20 min at room temperature.[15] Carboxylative workup after 3.3 h furnished the acid **9c** (Scheme 4, 16% yield, seemingly uncontaminated by the acid **9a**[2,16]), along with the proton transfer product **5a** (85% yield) which was not contaminated by the product **5c** (<2%) of bromine transfer.[12] The exclusive formation of substitution products (**5a** and **9c**), obtained in a quantitative yield, implies that step 2 of Scheme 4 occurred much more rapidly than step 1A. Step 1A was not much slower than step 3A, however, because 16% of the intermediate **14** (trapped as **9c**) had accumulated owing to a shortage of reagent **2a** caused by step 1A. Hence the ranking[11] of step rates can be inferred to be 2 $\gg$ 3A > 1A. The predominance of the alkylidenecarbenoid chain process followed from the ≈1:1 stoichiometry in combination with a distinct (at least 7-fold) deuterium-induced rate-depression[15] for reagent **2b**[1] (0.10 M) reacting with MeLi (1.36 M). Accordingly, the almost-isotope-independent step 2 cannot be rate-limiting.[11] In consequence

(13) See the comments to Scheme 5 of ref 6.
(14) pp 3817−3818 and 3843 of ref 8.
(15) All $t_{1/2}$ values in this work are meant to convey semiquantitative rate information only and to point at primary kinetic isotope effects in reactions of **2b**. They cannot be used to quantitate k_H/k_D ratios because $t_{1/2}$ increases with decreasing initial concentrations [RLi].
(16) Knorr, R.; von Roman, T.; Freudenreich, J.; Hoang, T. P.; Mehlstäubl, J.; Böhrer, P.; Stephenson, D. S.; Huber, H.; Schubert, B. *Magn. Reson. Chem.* **1993**, *31*, 557−565.

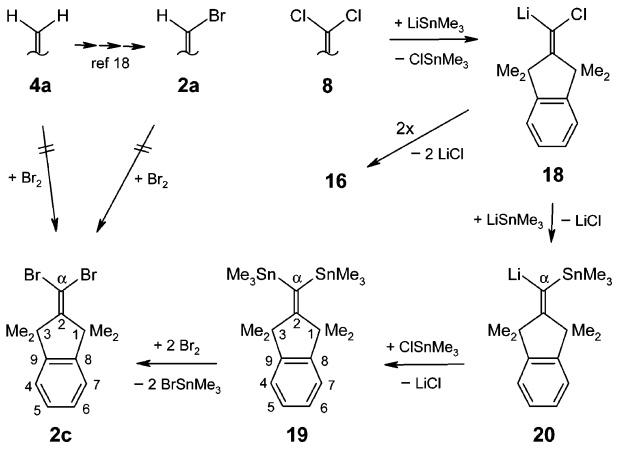
SCHEME 4



of this decelerated consumption of **2b** (steps 1A and 3A), the bromine transfer from **2b** to **14** (in step 3B, without C−D bond scission and, hence, almost isotope-independent) became detectable through the appearance of small amounts of both **5c** and the α,α-dideuterated olefin **4c**, the latter being formed via step 4B and identified through its ^{13}C NMR quintet for C$^{\alpha}$ ($^{1}J_{CD}$ = 23.8 Hz). Both chains A and B share step 2 which connects the chain carriers **3** and **14**. Notice that chain B employs three (instead of two) steps (2, 3B, and 4B) and requires only 0.5 equiv of MeLi per mol of **2a** or **2b** because the latter two reagents are consumed in both step 3B and step 4B, while MeLi is incorporated only through step 2. According to the NMR analyses in situ, the H/D ratio in products **5a**/**5b** increased slowly from 19:72 in the early stage to 43:48 in the end (>3 h), because of the leakage reaction of intermediate **14**, affording the final product ratio **5a**/**5b**/**5c**/**4c**/**4b** = 43:48:5:3:1. Strictly speaking, a slow process with an alternative mechanism,[7] confined to transforming **2b** to **5b** directly, might have participated in this retarded run, but such an alternative pathway would then be unable to contribute significantly to the much faster conversion of **2a** to **5a** observed above.

In THF solution, reagent **2a** (0.26 M) vanished within the warm up period of 12 min (or within 1 h at −70 °C) and consumed 0.9 equiv of MeLi (0.65 M, added at −70 °C). Reagent **2b** (0.26 M) reacted with a longer first $t_{1/2} \approx 5$ min[15] (establishing the carbenoid route) and required only 0.7 equiv of MeLi (0.58 M initially), which points to the carbenoid chain B (as anticipated above). This primary kinetic H/D isotope effect excludes step 2 as rate-limiting,[11] so that the step rates can be ranked as 2 ≫ 3B ≈ 3A > 1A in consideration of the following evidence. The final in situ ^{1}H NMR spectra observed with **2a** showed the presence of **5a**, **5c**, **4a**, and the butadiene-type side-

SCHEME 5



product **17a**[17] in a 45:27:21:7 ratio, whereas the corresponding product ratio **5b**/**5c**/**4c**/**17b** = 13:44:40:3 was detected in the run with **2b**. Hence the retardation of D transfer to **14** in step 3A had increased the portion of Br transfer in step 3B (affording more **5c** and **4c**). The leakage products **5a** and **4b** were not present immediately after the consumption of **2b**, but they were found after a total of 65 min at room temperature when carboxylative workup afforded a nonacidic fraction with the product ratio **5a**/**5b**/**5c**/**4c**/**17b**/**4b** = 6:14:39:32:4:5 accompanied by an acid fraction containing the fully (>99.5%) C$^{\alpha}$-deuterated acid **9b** (11% yield) but no **9c**. This delayed formation of **5a** in the run with **2b** disclosed a transitory minor accumulation of intermediate **14** and its subsequent leakage reaction, while the absence of acid **9c** testified to a shorter lifetime of **14** in THF than in Et_2O solution (where 16% of **9c** had been found). The more stable secondary chain carrier **1b** (trapped as **4b** + **9b**) was accumulated because of the deuterium-induced deceleration of step 4B, as compared to the run with **2a** whose carboxylation after 81 min had furnished only a trace of the acid **9a** and no **9c**. A part of **1b** may have been generated through the almost-isotope-independent step 1B (in analogy with **1a** ← **2a** in Scheme 1), but the byproduct MeBr cannot have formed major portions of both **5c** (from **3**) and **5a**,**b** (from **1a**,**b**) because such isotope-independent processes would not explain the observed variations of the product pattern correctly.

4. Syntheses of the Reagents 2b and 2c. The published[18] method of preparing **2a** (Scheme 5) via epoxidation of **4a** and "nucleophilic bromination" was utilized to obtain the deuterated monobromide **2b** from **4c**. The dibromide **2c** cannot be made by electrophilic bromination[19] of **4a** (because of methyl migration)[18] or of **2a**, and several other approaches[19] were also futile. A successful route to **2c** started from the dichloro reagent **8** which was inert toward LiSn(*n*-Bu)$_3$ but reacted readily when added to a sufficiently concentrated solution of LiSnMe$_3$[20−22] in THF to give **19,** whose constitution was supported by the

(17) The side product **17a** and its formation (which was suppressed in a run at −70 °C) from the reaction of **1a** with **2a** or with the chloroalkene **7** will be analyzed (together with **17b**) in a later publication.

(18) Knorr, R.; Freudenreich, J.; von Roman, T.; Mehlstäubl, J.; Böhrer, P. *Tetrahedron* **1993**, *49*, 8837−8854.

(19) Details are given in the Supporting Information.

(20) Tamborski, C.; Ford, F. E.; Soloski, J. E. *J. Org. Chem.* **1963**, *28*, 237−239.

(21) Kitching, W.; Olszowy, H.; Waugh, J.; Doddrell, D. *J. Org. Chem.* **1978**, *43*, 898−906.

(22) Reich, H. J.; Reich, I. L.; Yelm, K. E.; Holladay, J. E.; Gschneidner, G. *J. Am. Chem. Soc.* **1993**, *115*, 6625−6635.

characteristic magnitude[23] of the $^{119}Sn/^{117}Sn$ coupling constant $^2J = 653$ Hz. This vinylic substitution reaction is thought to begin with the generation of carbenoid **18** and to proceed via **20**; indeed, the carbenoid "dimerization" product **16** was formed as a troublesome side product if the addition of **8** to $LiSnMe_3$ was not carefully controlled or if $LiSnMe_3$ was added to **8**. In contrast, the treatment of acyclic 1,1-dichloroalkenes with $LiSnMe_3$ had been reported[24] to produce alkynes instead of trimethylstannylated alkenes, presumably via acyclic Cl,Li-alkylidenecarbenoids (corresponding to **18**) which rearranged[8] too fast. In the case of **18**, this rearrangement would expand the five-membered ring with little driving force and is therefore retarded (which was one of the reasons for us to utilize indan derivatives). Careful titration of pure **19** with elemental bromine in CCl_4 solution furnished pure **2c** without any rearrangement products.

Conclusions

Fully developed carbenoid chain processes (with step rate rankings[11] "2 and 3 ≫ 1" and a 1:1 stoichiometry) occur less frequently in the bromoalkene (**2a**−**c**) system than with the less reactive, analogous 1-chloro-1-alkenes[6] **7** and **8**. This is so because the chains of **2a**−**c** may become disturbed by an overly fast step 1 (up to carbenoid "dimerization") or by a sluggish propagation step 3. In the latter (nonchain carbenoid) situation which requires up to 2 equiv of RLi per reagent **2**, the accumulated intermediate $Alk_2C{=}CLi{-}R$ may, for preparative purposes, be quenched by protonation or with a Br transfer source, as applicable, immediately after the total conversion of a reagent **2**. In the former case (fast step 1), the 1-bromoalkene reagent should be added slowly to a concentrated solution of RLi kept at −70 °C in order to increase the rate of RLi with the carbenoid **3** (substitution step 2) and to avoid the imminent carbenoid decomposition. The clean course of these processes depends also on the inability of intermediate $Alk_2C{=}CLi{-}R$ (unless R = H, compare **17** in Scheme 4) to attack its parent alkylidenecarbenoid (**3**) at C^α. For a contrasting example, the corresponding intermediates $R{-}(CH_2)_j{-}M$ (M = Li[25,26] or Mg halide[27]), generated from $R{-}(CH_2)_{j-1}{-}M$ ($j \geq 1$) through substitution at a saturated carbenoid $BrCH_2M$, not only have to propagate their (supposed) chain reactions by Br transfer from CH_2Br_2 to re-create $BrCH_2M$ but also have to compete for substitution at $BrCH_2M$ with the residual portions of all of their ancestors $R{-}(CH_2)_i{-}M$ ($0 \leq i < j$), thus creating homologated intermediates and eventually affording (by Br transfer) unwelcome product mixtures $R{-}(CH_2)_k{-}Br$. Earlier reported side products such as $Me_2C{=}CBr{-}CH_3$ (obtained[28] from $Me_2C{=}CBr_2$ and MeLi) or $(CH_2)_3C{=}CBr{-}Ph$ (from $(CH_2)_3C{=}CBr_2$ and PhLi[29]) suggest that the alkylidenecarbenoid chain mechanism with Br transfer may not be confined to the sterically shielded reagents **2a**−**c**.

Reagent **2a** preferred to transfer its α-proton (rather than its Br) onto PhLi or MeLi in both Et_2O and THF solutions and onto the corresponding alkenyllithium intermediates **12** (observable by NMR in Et_2O) or **14**. On the other hand, **2a** and *n*-BuLi performed only[2] the Br/Li interchange reaction to give **1a** in both Et_2O (at +25 °C) and THF solutions (at −70 °C). The propensity of **14** for proton transfer was less marked in THF than in Et_2O and sufficiently small to permit the bromine abstraction from **2b** in competition with deuteron transfer, because the latter was handicapped by a sizable primary kinetic H/D isotope effect (which established the carbenoid pathway). Thus the product pattern became isotope-dependent in both Et_2O and THF, confirming the proposed coupling of two carbenoid chain processes (Scheme 4). These peculiar Et_2O/THF solvent effects are thought to depend on the unknown transition state solvation in steps 1 and 3; hence, they cannot be explained at this time. More examples with ramifications and some limitations of the carbenoid chain mechanism will be reported separately.

Experimental Section

General Remarks. Organolithium compounds were handled under a stream of dry argon cover gas. Experiments in NMR tubes (5 mm) were performed with nondeuterated solvents (≈0.7 mL, containing ≈0.04 mL of C_6D_{12} if required as a "lock substance"), allowing product analyses to be carried out in situ before workup. Concentrations were estimated by comparison with the ^1H NMR integral of a sealed capillary filled with pure $ClCH_2C{\equiv}N$ ($\delta_H \approx 3.9$) or of the low-field ^{13}C satellites of the solvents. Hydrogen versus deuterium distributions were determined by pairwise integrations of the baseline separated ^{13}C NMR absorptions having sufficiently large isotope-induced shift differences $^n\Delta$ ($n > 1$, so as to obviate NOE differences), with the machine parameters set for maximum resolution (for example, number of points $np = 160000$ (^1H at 400 MHz) or 524288 (^{13}C), and acquisition times $at \approx 13$ s). Commercially available solutions of methyllithium ($\delta_H \approx -2$) in Et_2O, containing LiBr, of *n*-butyllithium in hexanes ($\delta_H \approx -0.75$ in benzene) and of *tert*-butyllithium (*t*-BuLi) in pentane, were used. The Br/Li interchange reaction with the ensuing β-elimination of HBr (*t*-BuLi + ArBr → *t*-BuBr + ArLi, then *t*-BuLi + *t*-BuBr → *t*-BuH + LiBr + $Me_2C{=}CH_2$) was employed in ethereal solvents to prepare solutions of phenyllithium ($\delta_H \approx 8.0$ for two *o*-H) from bromobenzene.

2-(Bromomethylidene)-1,1,3,3-tetramethylindans (2a and 2b). These were prepared along the lines described in ref 18. Residual =CH NMR absorptions (^1H, s δ 6.16; ^{13}C, δ 100.0) could not be detected for the α-D derivative **2b**.

2-(Dibromomethylidene)-1,1,3,3-tetramethylindan (2c). (a) A solution of pure 2-[bis(trimethylstannyl)methylidene]-1,1,3,3-tetramethylindan (**19**, 35 mg, 0.068 mmol) in CCl_4 (0.40 mL), contained in an NMR tube, was titrated at −25 °C with a CCl_4 solution (1 M) of elemental bromine. ^1H NMR control spectra revealed the intermediate formation of 2-[bromo(trimethylstannyl)-methylidene]-1,1,3,3-tetramethylindan with δ (200 MHz, CCl_4) +0.45 (s, $^2J(^{119}Sn) = 54$ Hz, $1SnMe_3$) and 1.43 and 1.70 (2 s, 2 + 2 1-/3-CH_3). The final byproduct $BrSnMe_3$ had δ 0.75 (s) with $^2J(^{119}Sn) = 57$ Hz ($SnMe_3$); it diminished on overtitration to give CH_3Br (δ 2.63) and Br_2SnMe_2 (δ 1.35 with $^2J(^{119}Sn) = 66$ Hz). The mixture was diluted with Et_2O (10 mL) and 2 M NaOH, and the aqueous layer was extracted with Et_2O (2×). The combined ethereal phases were washed until neutral, dried over Na_2SO_4, and concentrated to give practically pure **2c** as a colorless powder (21 mg, 89%). The purification and spectra of **2c** are described in the sequel.

(b) The imminent destannylation of **19** by recrystallization from hot ethanol suggested to employ incompletely purified specimens of **19**, most often contaminated with small amounts of the "butatriene" **16**. A CCl_4 solution (10 mL) of **19** (912 mg, 1.78 mmol) was stirred in an ice bath during the slow titration with a

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CCl_4 solution (0.97 M) of elemental bromine. The end point was reached when the red color of bromine persisted for more than 60 s. Overtitration consumed first an eventual admixture of the "butatriene" **16** (recommended) and then the byproduct $BrSnMe_3$ (see above) with formation of MeBr and Br_2SnMe_2 (not desirable). After we confirmed by ^{1}H NMR the complete formation of **2c**, the whole mixture was concentrated in vacuo (with due attention to the toxicity of volatile tin compounds) and then dissolved in boiling ethanol (slow dissolution). Weakly soluble contaminants (such as **16**) were removed by filtration, and part of the ethanol was distilled off until a first fraction of pure **2c** (233 mg, 38%) crystallized slowly as transparent, glimmer-like leaflets: mp 177−179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.65 (s, 4 1-/3-CH_3),[16] 7.13 (m, 4-/7-H), 7.25 (m, 5-/6-H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 27.5 (qq, ^1J = 127.5 Hz, ^3J = 4.5 Hz, 4 1-/3-CH_3), 52.3 (unresolved m, $C^{1,3}$), 82.2 (sharp s, C^α), 122.4 (dm, ^1J = 156 Hz, $C^{4,7}$), 127.5 (ddd, ^1J = 159 Hz, ^3J = 7 Hz, $C^{5,6}$), 148.8 (blurred t, $^3J \approx 7$ Hz, $C^{8,9}$), 160.4 (unresolved m, C^2), assigned[16] by comparison with (dibromomethylidene)-cyclobutane;[29] IR (KBr): 2990, 2961, 2926, 2864, 1576, 1487, 1455, 1362, 802, 756, and 737 cm^{-1}. Anal. Calcd for $C_{14}H_{16}Br_2$ (344.1): C, 48.87; H, 4.69. Found: C, 48.72; H, 4.62. Brominated "butatriene" (**16**·Br_2) accumulated in the mother liquors: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.63, 1.65, 1.72, and 1.82 (4 s, 4 1-/3-CH_3).

2-Methylidene-1,1,3,3-tetramethylindan (4a). See compound **6** in ref 18.

2-Ethylidene-1,1,3,3-tetramethylindans (5a and 5b). Described in ref 6.

2-(1-Bromoethylidene)-1,1,3,3-tetramethylindan (5c). (a) From 2c: The dibromide **2c** (137 mg, 0.40 mmol) was added under argon cover gas to the contents of an NMR tube containing MeLi (1.22 mmol) in Et_2O (0.88 mL) at −70 °C. The stoppered tube was shaken vigorously at room temperature for rapid mixing of the reactants. The first ^{1}H NMR spectrum, recorded after 3 min, showed that reagent **2c** had vanished with consumption of 1 equiv of MeLi, generating **5c** as the only product. The tube was emptied into 0.2 M HCl (5 mL) and rinsed with Et_2O and water. The Et_2O extracts were washed with distilled water until neutral, dried over Na_2SO_4, and concentrated to provide crude **5c** (104 mg, 93%), the purification of which was remarkably difficult: Colorless **5c** crystallized very slowly from methanol (0.5 mL); the first crop was washed with cold methanol (−18 °C, 2×), then recrystallized from pentane (0.3 mL) at −18 °C, separated from the supernatant, and dried first in a stream of N_2 gas and then in vacuo over P_4O_{10} and chipped paraffin wax: mp 131−132.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.53 (s, 2 3-CH_3), 1.63 (s, 2 1-CH_3), 2.61 (s, α-CH_3), 7.12 (m, 4-H), 7.14 (m, 7-H), and 7.22 (m, 5-/6-H), assigned by the NOESY correlations α-CH_3 ↔ 3-CH_3 ↔ 4-H and 1-CH_3 ↔ 7-H; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 28.1 (qq, ^1J = 127.5 Hz, ^3J = 4.3 Hz, 2 1-CH_3), 29.0 (sharp q, ^1J = 129.1 Hz, α-CH_3), 29.5 (qq, ^1J = 127.5 Hz, ^3J = 4.3 Hz, 2 3-CH_3), 49.7 (m, C^3), 50.1 (m, C^1), 117.1 (q, ^2J = 7.3 Hz, C^α), 122.2 and 122.6 (2 dm, ^1J = 156 Hz, $C^{4,7}$), 127.2 and 127.3 (2 dd, ^1J = 160 Hz, ^3J = 8 Hz, $C^{5,6}$), 149.3 (m, C^9), 150.0 (m, C^8), 154.2 (m, C^2), assigned by ^{1}H/^{13}C heterocorrelation and the selective {^{1}H} decouplings {3-CH_3} → C^3 (narrowed) and C^9 (t), {1-CH_3} → C^1 and C^8 (both narrowed), {α-CH_3} → C^α (s); IR (KBr): 2981, 2960, 2925, 2863, 1637, 1591, 1486, 1456, 1364, 1086, 1018, 757 cm^{-1}; MS (GC/EI, 70 eV) *m*/*z* (%) 280.1 (1.5) and 278.1 (1.5, M^+), 265.1 (100) and 263.1 (98.3, $M^+ - CH_3$), 199.2 (57, $M^+ - Br$). Anal. Calcd for $C_{15}H_{19}Br$ (279.2): C, 64.52; H, 6.86. Found: C, 64.65; H, 6.97.

(b) **From 2a at −70 °C**: A solution of monobromide **2a** (200 mg, 0.754 mmol) in anhydrous THF (10.0 mL) was stirred at −70 °C under argon cover gas during the addition of MeLi (1.80 mmol) in Et_2O (1.46 mL). The mixture was stirred for 1 h at −70 °C, then poured onto solid CO_2, warmed up, and dissolved in Et_2O and 2 M NaOH. The acidified NaOH layer furnished the known[2] acid **9a** (29 mg, 17%). The Et_2O phases were washed until neutral, dried over $MgSO_4$, and concentrated to provide a partly solidifying oil containing **5a** (13% yield), **5c** (31%), and the terminal olefin **4a** (10%). Thus the lowered temperature had the effects of suppressing the formation of the butadiene-type side-product **17a** and of accumulating the intermediate **1a** which was trapped as **9a** (of which only a trace had been produced in the run conducted at room temperature).

2-(1,1,3,3-Tetramethyl-2-indanylidene)acetic Acid (9a). Described in ref 2.

2-(1,1,3,3-Tetramethyl-2-indanylidene)propanoic Acid (9c). The preparation of the pure acid **9c** by carboxylation of the short-lived alkenyllithium **14** was difficult, because **14** reacted faster with proton sources (leakage) than it could be generated from bromoalkene **5c** with either MeLi in THF or *n*-BuLi in Et_2O at room temperature. The successful preparation consisted in adding **5c** (≈0.5 mmol as a product mixture with the olefins **4a** and **5a**) in Et_2O (5 mL) slowly over 2 min to a solution of *tert*-butyllithium (*t*-BuLi, 4.30 mmol) in pentane (5.00 mL) stirred at −70 °C, so that **14** was generated in the presence of *t*-BuLi in excess which scavenged the coproduct *t*-BuBr of the Br/Li interchange reaction. This mixture was stirred for 5 min more at −70 °C, then poured onto solid CO_2, warmed up, and dissolved in Et_2O and pure water. The alkaline aqueous layer was acidified and extracted with Et_2O. The latter Et_2O extract was washed until neutral, dried over Na_2SO_4, and concentrated to provide a mixture of *t*-$BuCO_2H$ and the acid **9c** (97:3). Pure **9c** (weakly soluble, colorless needles, 42 mg, ≈34%) was isolated through two crystallizations from boiling petroleum ether (80−110 °C): mp 220−221.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.55 (s, 2 1-CH_3), 1.57 (s, 2 3-CH_3), 2.19 (s, α-CH_3), 7.13 (m, 7-H), 7.16 (m, 4-H), 7.23 (m, 5-H), 7.25 (m, 6-H), assigned through the NOESY correlations α-CH_3 ↔ 3-CH_3 ↔ 4-H and 1-CH_3 ↔ 7-H ↔ 6-H; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 18.35 (sharp q, ^1J = 128.9 Hz, α-CH_3), 29.11 (qq, ^1J = 127.5 Hz, ^3J = 4.5 Hz, 2 3-CH_3), 30.23 (qq, ^1J = 127.5 Hz, ^3J = 4.5 Hz, 2 1-CH_3), 48.08 (m, C^1), 48.31 (m, C^3), 122.18 (dm, qq, ^1J = 156 Hz, C^4), 122.19 (dm, ^1J = 156 Hz, C^7), 122.83 (sharp q, ^3J = 6.5 Hz, C^α), 127.16 (ddd, ^1J = 159.7 Hz, ^3J = 7.4 Hz, ^4J = 1.2 Hz, C^5), 127.29 (ddd, ^1J = 159.7 Hz, ^3J = 7.4 Hz, ^4J = 1.2 Hz, C^6), 149.09 (m, C^9), 149.71 (m, C^8), 159.79 (m, C^2), 177.2 (sharp q, ^3J = 4.4 Hz, CO_2H), assigned in accord with the C−H couplings through ^{1}H/^{13}C heterocorrelations and through the following hetero-multiple-bond correlations (HMBC): α-CH_3 ↔ C^α (^2J), 1-CH_3 ↔ C^1 (^2J), and 3-CH_3 ↔ C^3 (^2J), in addition to the ^3J connections C^8 ↔ 1-CH_3 ↔ C^2 ↔ 3-CH_3 ↔ C^9, 1-CH_3 ↔ 1-CH_3, 3-CH_3 ↔ 3-CH_3, C^2 ↔ α-CH_3 ↔ CO_2H, 4-H ↔ C^6, 5-H ↔ C^7, 6-H ↔ C^4, and 7-H ↔ C^5; FT-IR (diamond, ATR) 3200−2500 (vbr O−H), 1682 (s, C=O), 1281, 1252, and 759 (vs) cm^{-1}. Anal. Calcd for $C_{16}H_{20}O_2$ (244.3): C, 78.65; H, 8.25. Found: C, 78.26; H, 8.24.

2-Phenyl-2-(1,1,3,3-tetramethyl-2-indanylidene)acetic Acid (9d). Described in ref 11.

2-(3-Phenyl-2-propyn-1-ylidene)-1,1,3,3-tetramethylindan (13a). Described in ref 6.

2-(1-Methyl-3-phenyl-2-propyn-1-ylidene)-1,1,3,3-tetramethylindan (13b). Described in ref 6.

2-(1-Bromo-3-phenyl-2-propyn-1-ylidene)-1,1,3,3-tetramethylindan (13c). Addition of MeLi (0.118 mmol) in Et_2O (0.085 mL) to a solution of phenylacetylene (0.013 mL, 0.118 mmol) in Et_2O (0.60 mL) under argon cover gas led to the quantitative formation of PhC≡CLi (^{1}H NMR in situ δ 7.32, dm, 2 *o*-H). Reagent **2c** (20 mg, 0.058 mmol) was added but did not react with PhC≡CLi in the course of 4.5 h. Then the chain process was started at −70 °C by injection of a tiny batch of MeLi (0.004 mL, 0.006 mmol), which ceased to consume **2c** at ≈70% conversion after <5 min at room temperature. Injection of a further batch of 0.004 mL of the MeLi solution completed the consumption of **2c**. The mixture remained unchanged over 8 days at −18 °C and was then poured onto solid CO_2. The usual separation with Et_2O/NaOH as above afforded ≤1 mg of PhC≡CCO_2H along with 18 mg of a nonacidic product mixture containing **5c** (4%), **13c** (71%), **13b**[6] (2%), and **13a**[6] (6%). **13c** crystallized in colorless tufts with mp 117−118 °C (cooled ethanol); ^{1}H NMR (600 MHz, $CDCl_3$, numbering of Scheme 3) δ

1.68 (s, 2 1-CH_3), 1.71 (s, 2 3-CH_3), 7.17 (m, 4-/7-H), 7.26 (m, 5-/6-H), 7.37 (m, 2 *m*-H and 1 *p*-H), and 7.50 (m, 2 *o*-H); ^{13}C NMR (150.8 MHz, $CDCl_3$) δ 27.5 (qq, ^1J = 127 Hz, ^3J = 4.5 Hz, 2 1-CH_3), 28.3 (qq, ^1J = 127 Hz, ^3J = 4.5 Hz, 2 3-CH_3), 50.9 (m, C^1), 51.2 (m, C^3), 88.3 (sharp s, C^β), 95.6 (sharp s, C^α), 95.8 (t, ^3J = 5.5 Hz, C^γ), 122.3 and 122.5 (2 dm, ^1J = 158 Hz, $C^{4,7}$), 122.6 (m, C^i), 127.47 and 127.48 (2 dd, ^1J = 160 Hz, $C^{5,6}$), 128.5 (2 dm, $^1J \approx$ 162 Hz, 2 C^m), 128.8 (dt, ^1J = 161 Hz, ^3J = 7.6 Hz, C^p), 131.2 (dm, $^1J \approx$ 164 Hz, 2 C^o), 148.6 (m, C^9), 149.2 (m, C^8), 167.0 (m, C^2), assigned by comparison of 1-/3-CH_3 with **13a**[6] and by HMBC (with window at 8 Hz) showing the ^2J correlations 1-CH_3 ↔ C^1 and 3-CH_3 ↔ C^3 in addition to the ^3J correlations 1-*C*H_3 ↔ 1-CH_3 ↔ C^8, 3-*C*H_3 ↔ 3-CH_3 ↔ C^9, 4-/7-H ↔ $C^{5,6}$, 5-/6-H ↔ $C^{4,7}$, *m*-H ↔ C^i, C^γ ↔ *o*-H ↔ C^p, *p*-H ↔ C^o; MS (GC/DEI, 70 eV) *m*/*z* (%) 366.2 (7.5) and 364.2 (8.1, M^+), 285.2 (83.6, M^+ − Br), 199.2 (100). The constitution was confirmed through treatment with MeLi in THF solution which furnished **13b**.

1,2-Bis(1,1,3,3-tetramethyl-2-indanylidene)ethene (16). The separation of this "butatriene" derivative from the product mixture was straightforward, by leaching with boiling ethanol (5−10 mL/g of material) which left transparent blocks of **16**: mp 238−240 °C (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 (s, 8 1-/3-CH_3), 7.23 and 7.27 (AA′BB′ system, 2 C_6H_4); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 31.0 (qq, ^1J = 127.4 Hz, ^3J = 4.6 Hz, 8 1-/3-CH_3), 48.5 (unresolved, 4 $C^{1,3}$), 122.7 (dm, ^1J = 156 Hz, 4 $C^{4,7}$), 127.2 (ddd, ^1J = 159 Hz, ^3J = 7 Hz, 4 $C^{5,6}$), 137.9 (m, 2 C^2), 148.9 (m, 4 $C^{8,9}$), 153.8 (sharp s, 2 C^α); IR (KBr): 3019, 2954, 2915, 2852, 1585, 1481, 1454, 1356, 1024, 744 (vs), and 502 cm^{-1}; MS (EI, 70 eV) *m*/*z* (%) 368 (43), 353 (100), 338 (21), 323 (14), 196 (52). Anal. Calcd for $C_{28}H_{32}$ (368.6): C, 91.25; H, 8.75. Found: C, 90.90; H, 8.47. **16** is insoluble in methanol.

2-[Bis(trimethylstannyl)methylidene]-1,1,3,3-tetramethylindan (19). The olive-colored solution of $LiSnMe_3$ in THF (<17 mL), obtained[19] from 11.8 mmol of $ClSnMe_3$, was cooled to −70 °C under argon cover gas with stirring. (The green color[30] may disappear but will return during the following operation.) A solution of the 1,1-dichloroalkene **8** (1.00 g, 3.92 mmol) in THF (10 mL) was added from a pressure-equalizing dropping funnel over a period of no less than 15 min. (The inverse mode of adding $LiSnMe_3$ to **8** promoted the formation of "butatriene" **16** as a troublesome side product.) Stirring was continued for 30 min at −70 °C and then for 60 min at room temperature. The reaction mixture was recooled to −70 °C, and the excess of $LiSnMe_3$ was quenched with methanol (3 mL). The mixture was diluted with Et_2O and distilled water, and the Et_2O layer was washed until neutral, dried over Na_2SO_4, and concentrated to deliver a partially solidifying, pale yellow oil (2.29 g) containing only **19** and nonaromatic methyltin compounds. The recrystallization from preheated ethanol (10 mL) should be performed rapidly, so to avoid the partial ethanolysis which would form the mono(trimethylstannyl) derivative. The colorless glistening flakes of **19** (1.62 g, 81%) were obtained analytically pure: mp 123.5−125 °C (ethanol); ^{1}H NMR (400 MHz, $CDCl_3$) δ +0.32 (s, ^{119}Sn satellites ^2J = 50.1 Hz, 2 $SnMe_3$), 1.41 (s, ^{119}Sn satellites $|^5J_{cis} + {}^5J_{trans}|$ = 3.5 Hz, 4 1-/3-CH_3), 7.14 and 7.21 (AA′MM′ system, C_6H_4); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ −1.34 (qm, ^1J = 128.3 Hz, $^3J \approx$ 1 Hz, $^1J(^{119}Sn)$ = 323 Hz, $^3J(^{119}Sn)$ = 9.2 Hz, 2 $SnMe_3$), 31.3 (qq, ^1J = 126.7 Hz, ^3J = 4.4 Hz, $^4J(^{119}Sn$, trans?) = 10.8 Hz, $^4J(^{119}Sn$, cis?) ≈ 3 Hz, 4 1-/3-CH_3), 50.7 (unresolved m, $^3J(^{119}Sn$, trans) = 92.7 Hz, $^3J(^{119}Sn$, cis) = 43.4 Hz, $C^{1,3}$), 122.7 (dm, ^1J = 155 Hz, $C^{4,7}$), 126.8 (ddd, ^1J = 159.3 Hz, ^3J = 7.4 Hz, $C^{5,6}$), 130.6 (br s, C^α), 150.3 (unresolved, $C^{8,9}$), 183.1 (unresolved, C^2); ^{119}Sn NMR (100.75 MHz, $CDCl_3$, external standard $SnMe_4$) δ −44.8 (s, $^1J(^{13}CH_3)$ = 323.5 Hz, $^2J(^{117}Sn)$ = 653 Hz, $SnMe_3$); IR (KBr): 3001, 2963, 2922, 2863, 1596, 1357, and 762 (vs) cm^{-1}. Anal. Calcd for $C_{20}H_{34}Sn_2$ (511.9): C, 46.93; H, 6.69. Found: C, 47.17; H, 6.69.

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Supporting Information Available: Tabular survey of reaction conditions and products; further attempts toward reagent **2c**; preparation of trimethylstannyllithium. This material is available free of charge via the Internet at http://pubs.acs.org.

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