Reaction of $(CH_3)_3SnNa$ and Ph_3MLi (M = C, Si, Ge, Sn) with 6-Bromo-1-heptene: Are Intermediate 1-Methyl-5-Hexenyl Radicals Involved?[1]

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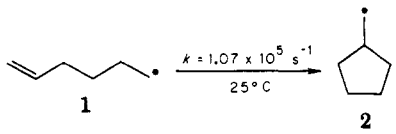
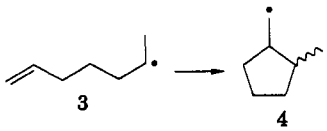
Collective observations lead to the conclusion that the formation of (2-methylcyclopentyl)methyl-derived products cannot be considered as prima facie evidence for the intermediacy of 1-methyl-5-hexenyl radicals during the alkylation of $(CH_3)_3SnNa$, Ph_3SiLi, and Ph_3GeLi by 6-bromo-1-heptene.

The cyclization of the 5-hexenyl radical, 1, is a well-documented process that occurs with a rate constant of ca 1.07×10^5 s^{-1} (at 25 °C).[2,3] As a consequence of this



1 2 (1)

behavior, the 5-hexenyl system has become a standard probe, diagnostic of the intermediacy of (kinetically) free alkyl radicals.[3] The related 1-methyl-5-hexenyl system, 3, has been less studied; however, the rate of cyclization of 3 is known to be essentially the same as that observed for 1, i.e., $k \approx 1 \times 10^5$ s^{-1}.[4] It follows from a consideration

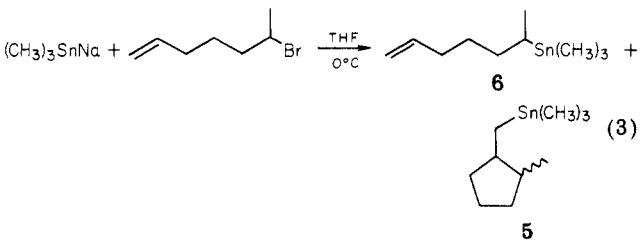


3 4 (2)

of the magnitude of these rate constants that the rearrangement of 1 and 3 is $\gtrsim 10^4$ times too slow to compete with geminate coupling processes which are generally recognized to proceed with effective rate constants $k_{effective} \gtrsim 10^{10}$ s^{-1}.[3c] Indeed, the virtue of both the 5-hexenyl and the 1-methyl-5-hexenyl systems as diagnostic probes in the elucidation of reaction mechanism rests squarely on the understanding that their characteristic rearrangement occurs during the time that the parent radical is kinetically free. By comparison, the loss of configuration associated with alkyl radical center occurs primarily within the parent solvent cage and is complete for kinetically free radicals.[5] It follows, therefore, that under equivalent circumstances, the extent to which the rearrangement of 3 → 4 takes place, can (at most) equal but never exceed the extent of racemization associated with the equivalent reaction involving a radical generated from a chiral precursor.

Results and Discussion

In this vein, the recent observations and proposals of Ashby and DePriest[6] and the related findings of Kitching and co-workers[7] are noteworthy. Both groups examined the reaction of $(CH_3)_3SnM$ with 6-bromo-1-heptene. The former authors reported (for M = Na) a 71% (absolute) yield of the cyclic product 5 and a 4% (absolute) yield of the unrearranged compound 6 while the latter authors reported this same reaction (for M = Li) affords a 48% (absolute) yield of 5 and a 12% (absolute) yield of 6. On this basis both groups concluded that alkylation proceeds through the general intermediacy of 1-methyl-5-hexenyl radicals.



(3)

Ashby and DePriest also examined the corresponding reaction of $(CH_3)_3SnNa$ with optically active 2-bromooctane and observed, as previously noted by other investigators,[8] that this alkylation proceeds with overall *net* (~50% in their hands) inversion of configuration at carbon. However, in contrast to earlier studies[8] which concluded that the stereoselectivity associated with this process results from a partitioning between S_N2 and a one-electron-transfer process (the latter process resulting in the production of free 2-octyl radicals that in turn yield racemic product), these authors proposed that inversion of configuration results from an electron-transfer process followed by a carbon–tin bond-forming step involving a stereospecific reaction between $(CH_3)_3Sn\cdot$ and the resulting 2-octyl radical, all within the same solvent cage. These conclusions pose a dilemma. Specifically, they require that a significant fraction ($\gtrsim$33%) of the production of 5 must occur in the same solvent cage in which the electron-transfer step takes place.[9] However, since 1-methyl-5-hexenyl radicals do not have time to cyclize under such conditions, cyclization under these circumstances cannot be invoked as prima facie evidence for the intermediacy of 1-methyl-5-hexenyl radicals.

Further evidence that 5 does not constitute prima facie evidence for the intermediacy of 1-methyl-5-hexenyl radicals in eq 3 is recognized in the caveats posed by two

(1) Supported by the National Science Foundation, Grant 80-17045, and DOE, Contract DE-AS05-80-ER-1062.

(2) Schmid, P.; Griller, D.; Ingold, K. U. *Int. J. Chem. Kinetc.* **1979**, *11*, 333. Lal, D.; Griller, S.; Ingold, K. U. *Ibid.* **1974**, *96*, 6355.

(3) (a) Garst, J. F.; Smith, C. D. *J. Am. Chem. Soc.* **1976**, *98*, 1520 and references therein. (b) Wilt, J. W. In "Free Radicals"; Kochi, J. K., ed.; Wiley-Interscience: New York, 1973; Vol. 1, Chapter 8. (c) Noyes, R. M. *Prog. React. Kinet.* **1961**, *1*, 129.

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

(5) Greene, F. D.; Berwick, M. A.; Stowell, J. C. *J. Am. Chem. Soc.* **1970**, *92*, 867. Kopecky, K. R.; Gillan, T. *Can. J. Chem.* **1969**, *47*, 2371.

(6) Ashby, E. C.; DePriest, R. *J. Am. Chem. Soc.* **1982**, *104*, 6144.

(7) Kitching, W.; Olszowy, H. A.; Harvey, K. *J. Org. Chem.* **1982**, *47*, 1893.

(8) San Filippo, J., Jr.; Silbermann, J. *J. Am. Chem. Soc.* **1981**, *103*, 5588; **1982**, *104*, 2831.

(9) The normalized yields of 5 and 6 (Table I) are, respectively, 88% and 12%. Since ~50% of the total yield of coupling product (i.e., 5 + 6) must occur (according to ref 6) within the same solvent cage as the rate-limiting electron-transfer step, it follows (assuming all or less than all of 6 is also derived in this initial solvent cage) that a *minimum* of (50–12)/88 or 33% of 5 must also be formed in this initial solvent cage.

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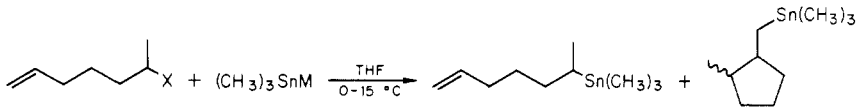
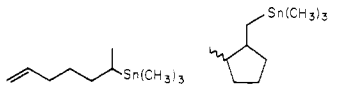
Table I. Reactions of 6-Halohept-1-ene with $(CH_3)_3SnNa$ and Ph_3MLi (M = C, Si, Ge, Sn) in THF



entry	M	X	additive	order of additn	yield,[a] % 	cis/trans	ref
1	Na	Cl		inverse	55 (62) 33 (38)	1.5	6
2	Na	Br		normal	4 (12) 71 (88)	3.7	6
3	Na	Br		inverse	11 (13) 72 (87)	3.2	6
4	Na	Br	DCPH[b]	inverse	1 (7) 14 (93)	3.7	6
5	Na	Br		normal	(6) (94)		c
6	Na	Br		inverse	(32) (68)		c
7	Li	Br		normal	12 (21) 48 (79)	2.8	7

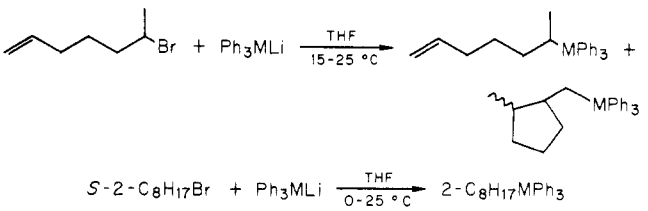
[a] Absolute yields; relative yields are in parentheses. [b] Dicyclohexylphosphine. [c] This work.

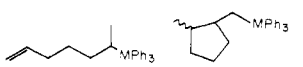
additional observations: (i) the finding that the closely related rearrangement of **1** → **2** does not occur during the corresponding reaction of 6-bromohex-5-ene[7,10] (more sensitive probes[11,12] suggest that ca. 20% of the carbon–tin coupling product afforded by the reaction of $(CH_3)_3SnM$ with primary bromides arises via a pathway consistent with a free radical process) and (ii) the finding (entries 2 and 3, Table II) that the extent of rearrangement observed during the reaction of both Ph_3SiM and Ph_3GeM with 6-bromo-1-heptene exceeds the extent of racemization associated with the corresponding reaction between these same reagents and optically active 2-bromooctane.

The reaction of $(CH_3)_3SnNa$ with 6-halo-1-heptene exhibits other qualities that are inconsistent with the intermediacy of 1-methyl-5-hexenyl radicals. Thus, prior studies[4] have established that the cis–trans ratio of the cyclic product produced from **3** is invariant: cis/trans = 2.3. Moreover, this value is, as it should be, independent of reaction conditions (i.e., solvent, concentration, additives, and leaving group). By contrast, the cis/trans ratios seen in Table I range between 1.5 and 3.7 and, in addition, are substantially influenced by the presence of the additive dicyclohexylphosphine and the nature of the leaving group.

Collectively, these findings vitiate the conclusions of Ashby and DePriest[6] along with the corollary conclusions of Kitching, Kuivila, and co-workers.[7,13] They do not, however, offer a clear explanation to the origin(s) of the cyclic products produced in the reaction of 6-bromo-1-heptene with $(CH_3)_3SnM$, Ph_3SiLi, and Ph_3GeLi. A number of speculative possibilities suggest themselves, including the likelihood that rearrangement originates through the agency of (i) olefin activation initiated by metal coordination, (ii) the intermediacy of the corresponding radical anion, or (iii) a breakdown in the principles (extrapolated from the 6-halo-1-hexene systems) which provide the basis for the interpretations associated with reactions of the 6-halo-1-hexene system. With respect to ii, the existence of such intermediate species has been suggested on the basis of physical studies;[14a] however,

Table II. A Comparison of the Reactions of 2-Bromohept-6-ene and (*S*)-2-Octyl Bromide with Ph_3MLi (M = C, Si, Ge, Sn)



entry	M	order of additn	yield,[a] % 	ee,[c] %	ref
1	C	normal	>99 <1	94	b
		inverse	>99 <1	97	b
2	Si	normal	11 89	24	b
		inverse	37 63	50	b
3	Ge	normal	66 34	85	b
		inverse	84 16	99	b
4	Ge	normal	68 (18) 32 (9)		7
5	Sn	normal	>99 <1	98	b
6	Sn	normal	>99 (83) <1		7

[a] Relative yields; absolute yields are in parentheses. [b] This work; see also ref 16. [c] Reference 16. ee = entantiometric excess.

demanding chemical evidence has been lacking.[14b] Still, the limited observations cited above which indicate that these cyclizations exhibit a dependency on both additives and the nature of the leaving group, together with similar influences noted in related reactions,[8,16] are all consistent with this formulation. Whatever the origin(s) of this unique rearrangement, both physical and chemical studies will be required to delineate its nature and hopefully establish its usefulness as a diagnostic probe.

Finally, the data in Table I raise the additional question of the origin of the discrepancies between the product yields (cf. entries 2–5) and stereoselectivities[15] observed for purportedly equivalent reactions carried out in three

(10) Newcomb, M.; Courtney, A. R. *J. Org. Chem.* **1980**, *45*, 1707.
(11) Bock, P. L.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 2826.
(12) San Filippo, J., Jr.; Silbermann, J.; Fagan, P. J. *J. Am. Chem. Soc.* **1978**, *100*, 4834.
(13) Kuivila, H. G.; Alnajjar, M. S. *J. Am. Chem. Soc.* **1982**, *104*, 6146.
(14) (a) Mishra, S. P.; Neilson, G. W.; Symons, M. C. R. *J. Chem. Soc., Faraday*, **1974**, *70*, 1280. Symons, M. C. R. *J. Chem. Soc. Chem. Commun.* **1977**, 408. Hasegawa, A.; Williams, F. *Chem. Phys. Lett.* **1977**, *45*, 275. Riederer, H.; Hüttermann, J.; Symons, M. C. R. *J. Chem. Soc., Chem. Commun.* **1978**, 313. (b) However, see: Garst, J. F.; Roberts, R. D.; Pacifici, J. A. *J. Am. Chem. Soc.* **1977**, *99*, 3528 and references therein.

(15) The authors in ref 6 and 13 report the reaction of optically active 2-bromooctane with $(CH_3)_3SnNa$ proceeds with ~50–60% net inversion. By comparison, we recently reported[8] that the same reaction occurs with a stereoselectivity (depending on conditions) ranging from ~30% to 100% net inversion. In light of these differences, we have reexamined this reaction. Within experimental error we observed the same stereochemical consequences we had previously reported.
(16) Lee, K.-W.; San Filippo, J., Jr. *Organometallics* **1982**, *1*, 1496.

independent laboratories. In noting similar behavior in their extensive investigations of the reactions of R_3SnM, Pereyre and Quintard[17] reported a correlation between the history of such reagents and their chemical behavior. The general significance of this finding remains to be determined but it cannot be overlooked in any mechanistic investigation involving these reagents.

Experimental Section

General Methods. All reactions involving organometallic compounds were performed under an atmosphere of prepurified nitrogen. Tetrahydrofuran (THF) was distilled under nitrogen from lithium aluminum hydride immediately prior to use. Triphenylmethyl chloride and triphenylmethane (Aldrick Chemical Co.), triphenyltin chloride (Alfa Inorganics), hexaphenyldisilane (Silar Labs.), triphenylgermanium chloride (Alfa Inorganics), and hexaphenyldigermane (Orgmet, Inc.) were all employed without further purification. Lithium metal (200-μm dispersion, 50% by weight in mineral oil) was purchased from Lithium Corp. of America.

Melting points and boiling points are uncorrected. Infrared spectra were determined in sodium chloride cell on a Perkin-Elmer Model 727B grating spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Varian FT-80 spectrometer; chemical shifts are reported in parts per million from tetramethylsilane (Me_4Si). Optical rotations were recorded on neat liquids in an 0.1-dm cell or as solutions employing a 1-dm cell. Rotations were determined on a Perkin-Elmer Model 141 spectropolarimeter at 589 nm.

GLPC and HPLC analyses were performed, respectively, on a Hewlett-Packard 5750 and Waters Associates Model 6000A chromatographs equipped with a Hewlett-Packard Model 3380-A electronic integrator. Reported yields are estimated to have an error range of ±2%. Quantitation was achieved by using internal standard techniques with response factors obtained from authentic samples. Mass spectra were recorded on a Hewlett-Packard 5985 GC/MS. A Vacuum Atmospheres inert atmosphere glovebox was used to transfer all air- and moisture-sensitive solids.

6-Bromo-heptene was prepared according to the procedure of Kitching.[7]

Inverse-Addition Reaction of Triphenylmethyllithium (Prepared from Triphenylmethane) with 6-Bromo-1-heptene (Typical Procedure). Into a flame-dried, nitrogen-flushed 40-mL centrifuge tube equipped with Teflon-coated magnetic stirrer bar were added *n*-butyllithium (1.6 M in pentane, 2.5 mL, 4.0 mmol) and THF (5 mL) by syringe, and the solution was chilled to −78 °C. Triphenylmethane (1.231 g, 5.04 mmol) in THF (10 mL) was slowly added by syringe. The temperature was slowly increased to 25 °C. A solution of 6-bromo-1-heptene (0.708 g, 4.00 mol) was placed in a 100-mL, three-necked, flame-dried, nitrogen-flushed flask equipped with a Teflon-coated magnetic stirrer bar and a 30-mL Kontes slow-addition funnel. The solution of triphenylmethyllithium was filtered through 70–100-μm fritted-glass filter into a Kontes slow-addition funnel. Addition was carried out over a 2-h period; this mixture was then stirred an additional 0.5 h at 25 °C and finally quenched with water. The resulting mixture was extracted with pentane and the organic layer dried ($MgSO_4$), filtered, and concentrated; the combined alkylated product mixture was then collected from HPLC prior to isomer analysis by GLPC. 6-(Triphenylmethyl)-1-heptane: a sample, collected from GLPC, exhibited the following spectral properties ^1H NMR (δ, CCl_4) 0.8 (d, 3 H), 1.0–2.3 (m, 6 H), 3.3 (m, 1 H), 4.7–5.2 (m, 2 H), 5.3–6.1 (m, H), 6.9–7.5 (m, 15 H); mass spectrum (70 eV), *m/e* (relative intensity) 245 (2.2), 244 (21.0), 243 (100), 166 (4.0), 165 (35.5). No difference in reactivity was observed when the equivalent reaction was performed with triphenylmethyllithium prepared by reaction of triphenylmethyl chloride with lithium dispersion.

Normal-Addition Reaction of 6-Bromo-1-heptene with Triphenylsilyllithium (Prepared from Triphenylsilyl Chloride) (Typical Procedure). After several rinses with dry pentane in a glovebox to remove its mineral oil coating, lithium (0.140 g, 20.2 mmol) was placed in a flame-dried, 40-mL centrifuge tube equipped with a Teflon-coated magnetic stirrer bar and capped with a rubber septum. THF (5 mL) was added by syringe. The centrifuge tube was placed in a water bath (25 °C), and a solution of triphenylsilyl chloride (1.240 g, 4.20 mmol) in THF (10 mL) was added through a cannula. The resulting dark brown solution was allowed to stir for 2 h and then transferred by cannula into a 70–100-μm fritted-glass filter and thence into a 100-mL, three-necked, flame-dried, nitrogen-flushed flask equipped with a Teflon-coated magnetic stirrer bar and a 30-mL Kontes slow-addition funnel stoppered with a rubber septum containing a solution of 6-bromo-1-heptene (0.708 g, 4.00 mmol) in THF (10 mL). Addition was carried out over a 2-h period, and the resulting mixture was allowed to stir for an additional 3 h before quenching with water (10 mL). The organic layer was extracted three times with 50-mL portions of pentane, and the combined extracts were dried ($MgSO_4$). The resulting crude product mixture was concentrated, and that fraction corresponding to the alkylated product mixture was collected from HPLC. GLPC analysis of this mixture provided an accurate product isomer distribution.

Normal-Addition Reaction of 6-Bromo-1-heptene with Triphenylsilyllithium (Prepared from Hexaphenyldisislane) and Triphenylgermyllithium (Prepared from Hexaphenylidigermane) (Typical Procedure). In a glovebox, lithium dispersion was rinsed three times with dry pentane to remove its mineral oil coatings. Hexaphenyldisilane (1.142 g, 2.20 mmol) were placed in a flame-dried, 40-mL centrifuge tube equipped with a Teflon-coated magnetic stirrer bar. The vessel was capped with a rubber septum and removed from the glovebox. THF (15 mL) was added by syringe and the mixture stirred for 3 h at room temperature. The resulting dark brown solution was transferred by cannula through a 70–100-μm fritted-glass filter into a 100-mL, three-necked, flame-dried, nitrogen-flushed flask equipped with a Teflon-coated magnetic stirrer bar and a 30-mL Kontes slow-addition funnel stoppered with a rubber septum and charged with a solution of 6-bromo-1-heptene (0.708 g, 4.00 mmol) in THF (10 mL) at 25 °C. Addition was accompanied by efficient stirring and was carried out over a 2-h period after which the resulting solution was stirred an additional 3 h at 25 °C before adding water (10–20 mL). This mixture was extracted with pentane and the organic layer dried ($MgSO_4$) and filtered. The resulting crude product mixture was concentrated and that fraction corresponding to the alkylated product mixture was collected from HPLC. Analysis of this mixture by GLPC provided an accurate product isomer distribution. The spectral properties of each respective isomer were equivalent to those reported by Kitching.[7]

Normal-Addition Reaction of Me_3SnNa with 6-Bromo-1-heptene (Typical Procedure). Sodium (50% dispersion in paraffin, 0.20 g, 8.7mmol) was placed in a flame-dried, 40-mL centrifuge tube equipped with a Teflon-coated magnetic stirrer bar and capped with a rubber septum in a nitrogen glovebox. The dispersion was washed with dry pentane to remove the paraffin. Dry THF (10 mL) was added by syringe followed by the addition of hexamethylditin (0.684 g, 2.08 mmol), and the mixture was allowed to stir for 1 h at room temperature at which time it was centrifuged and the supernatant transferred via cannula through a 70–100-μm fritted-glass filter into a 30-mL Kontes slow-addition funnel. This solution was then added to a cooled (0 °C) solution of 6-bromo-1-heptene (0.710, 4.01 mmol) in THF (10 mL) over a 0.5-h period, and the mixture was allowed to stir an additional 2 h at 0 °C before quenching with water (10 mL). The organic layer was extracted with pentane, then dried ($MgSO_4$), and concentrated. The yields of the three alkylation products were determined by GLPC on a 12-ft column of SE-30 at 110 °C. Individual product isomers were isolated by GLPC. Their respective spectral properties were equivalent to those reported by Kitching.[7]

Registry No. Triphenylmethyllithium, 733-90-4; triphenylsilyllithium, 791-30-0; triphenylgermyllithium, 3839-32-5; trimethylstannylsodium, 16643-09-7; 6-bromo-1-heptene, 38334-98-4; triphenylmethane, 519-73-3; 6-(triphenylmethyl)-1-heptene, 85282-61-7; triphenylsilyl chloride, 76-86-8; hexaphenyldisilane, 1450-23-3; hexaphenyldigermane, 2816-39-9; hexamethylditin, 661-69-8.

(17) Pereyre, M.; Quintard, J.-P. *Pure Appl. Chem.* 1981, *53*, 2401.