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SUPPRESSING THE CYCLIZATION OF (1-METHYL-5-HEXENYL)SODIUM

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SUMMARY: In reactions of 1-methyl-5-hexenyl chloride and bromide with sodium metal and sodium naphthalene in DME and THF, the cyclization of (1-methyl-5-hexenyl)sodium is suppressed by added tert-butylamine. Since the cyclization of 1-methyl-5-hexenyl radical does not appear to be affected, this demonstrates the practicality of using the 1-methyl-5-hexenyl group as a probe for radical intermediates in the presence of tert-butylamine.

5-Hexenyl and a wide variety of related ("5-hexenylic") radicals cyclize, many with known first-order rate constants in the range 10^5-10^7 s^{-1}.[1] This has stimulated extensive application of 5-hexenylic groups as qualitative and quantitative probes for alkyl radical intermediates in reactions. When alkyl anions are plausible intermediates also, it is essential that they not cyclize or that anion and radical cyclizations be distinguishable.

A myth that "5-hexenyl anions don't cyclize" seems to have arisen as a generalization of reports of insignificant or slow anion cyclizations under particular conditions,[2] despite published warnings to the contrary.[3] Citing apparent inconsistencies in the data of several workers, Lee and San Filippo concluded 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" in reactions of (trimethylstannyl)alkalies with 1-methyl-5-hexenyl halides in ethers.[4] This view was confirmed by evidence presented by Garst and Hines that (1-methyl-5-hexenyl)sodium cyclizes significantly when it is formed in reductions of 1-methyl-5-hexenyl halides in ethers by sodium metal or sodium naphthalene.[5] Also, surprisingly rapid cyclizations of 5-hexenylic lithiums have been reported recently.[6]

There is a critical need for methods of validating 5-hexenylic probes for radical intermediates by identifying anion cyclization (or its absence) or eliminating it. The present experiments were inspired by carbanion trapping in other contexts.[7] tert-Butylamine has been reported to be an effective trap for alkylsodiums in ethers,[7a] so we have tested its efficacy as a trap for (1-methyl-5-hexenyl)sodium generated in reductions of 1-methyl-5-hexenyl chloride and bromide by sodium metal and sodium naphthalene.

1-Methyl-5-hexenyl provides a favorable test case because the stereochemistries of anion and radical cyclizations differ markedly.[5] Thus, cyclized product stereochemistry serves as an indicator of the nature of the cyclization, allowing consistency checks on the effects of added tert-butylamine. For radical cyclization at room temperature, the 1,2-dimethylcyclopentanes that result ulitmately have a cis/trans ratio near four; for anion cyclization (sodium counterion), the same ratio is less than one.

Reactions of 1-methyl-5-hexenyl chloride or bromide, in DME and THF, with sodium metal or sodium naphthalene, in the absence or presence of *tert*-butylamine, were examined. Product mixtures were analyzed by GC for 1-heptene, 1,2-dimethylcyclopentanes, and 2-heptenes.[8] The presence or absence of GC peaks assigned tentatively to dimers $C_{14}H_{26}$ was noted also.

The dimer peaks appear only in GC traces of reactions of sodium metal in the absence of excess *tert*-butylamine; they are not present for reactions of sodium metal in the presence of *tert*-butylamine nor for reactions of excess sodium naphthalene, whether or not *tert*-butylamine is present.

The absolute yields of monomeric reduction products from reactions of sodium naphthalene are in or near the 30-50% range that is expected on the basis of previous work; alkylation of the napthalene nucleus competes with reduction.[2a,9] For sodium metal reactions, the yields range more widely, mostly 20-70%, reflecting alkyl dimer formation and incomplete reaction. Relative yields of C_7 reduction products are given in Tables I and II.

Table I. Relative Yields of Monomeric Reduction Products of Reactions of 1-Methyl-5-hexenyl Chloride or Bromide in DME or THF with Sodium Metal at Room Temperature.

expt	sol	hal	[RX]	[*t*-BuNH$_2$]	1-heptene	1,2-dimethylcyclopentanes	(cis/trans)	2-heptenes
20	DME	Cl	0.046 M	none	40%	33%	(0.32)	26%
19	DME	Br	0.061	none	47	38	(0.45)	15
14	THF	Br	0.029	none	26	61	(0.86)	13
129	DME	Cl	0.046	0.13 M	99	1	----	0
131	DME	Br	0.032	0.093	91	1	----	8
132	THF	Br	0.037	0.27	89	3	----	9

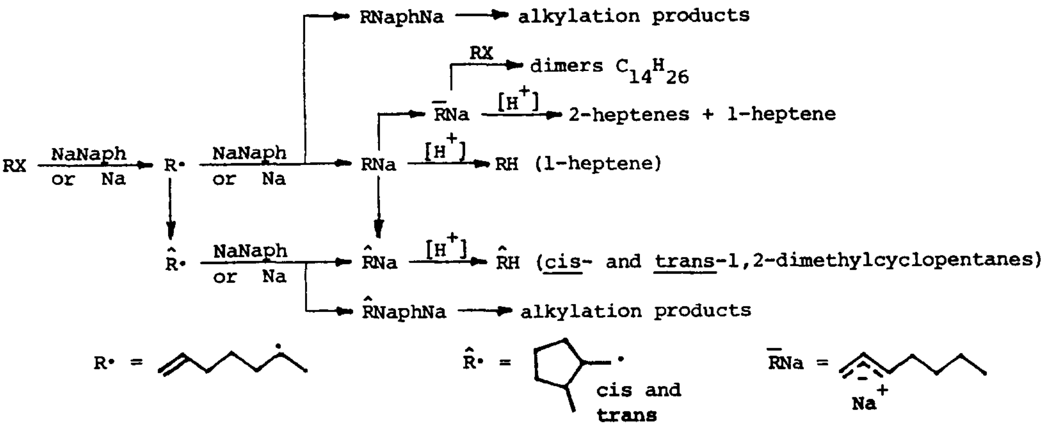
Methylcyclohexane, if any, is included with *cis*-1,2-dimethylcyclopentane. We assume that it is negligible, since five-membered ring cyclizations are overwhelmingly favored for 1-methyl-5-hexenyl radical and anion cyclizations in other cases. See literature cited on this point in reference 5.

Table II. Relative Yields of Monomeric Reduction Products of Reactions of 1-Methyl-5-hexenyl Chloride or Bromide in DME or THF with Sodium Naphthalene at Room Temperature.

expt	sol	hal	[RX]	[*t*-BuNH$_2$]	1-heptene	1,2-dimethylcyclopentanes	(cis/trans)	2-heptenes
38	DME	Cl	0.051 M	none	38%	32%	(0.62)	30%
39	DME	Br	----	none	39	50	(2.1)	11
33	THF	Cl	0.028	none	20	45	(0.92)	35
32	THF	Br	0.046	none	19	76	(2.8)	5
133	DME	Cl	0.024	0.035 M	86	15	(4.4)	0
132	DME	Br	0.021	0.031	71	29	(3.8)	0
139	THF	Cl	0.020	0.029	88	12	(4.9)	0
138	THF	Br	0.016	0.024	68	33	(3.8)	0

Methylcyclohexane, if any, is included with *cis*-1,2-dimethylcyclopentane. See footnote to Table I. Excess sodium naphthalene (0.1-0.4 M) was used.

Products are believed to arise according to the mechanism of Scheme I, which is well established for reactions of sodium naphthalene and plausible for those of sodium metal.[2a,3,5,8] The addition of an acid such as *tert*-butylamine will accelerate protonation steps, thereby suppressing the reactions that compete with protonation. Thus, if *tert*-



Scheme I. Mechanisms of Reductions of 1-Methyl-5-hexenyl Halides by Sodium and Sodium Naphthalene (NaNaph).

butylamine is a sufficiently reactive proton donor, its addition will suppress anion cyclization, 2-heptene formation, and dimer formation, leaving 1-heptene formation as well as _cis_- and _trans_-1,2-dimethylcyclopentane formation through radical cyclization only. If anion isomerizations are important in the absence of _tert_-butylamine, its addition is expected to decrease the extent of cyclization, raise the 1,2-dimethylcyclopentane cis/trans ratio to four, suppress 2-heptene and enhance 1-heptene formation, and suppress dimer formation.

All of these effects are clear in the data. For sodium metal reactions, excess _tert_-butylamine nearly eliminates 1,2-dimethylcyclopentanes, suggesting that radical cyclization is negligible. For sodium naphthalene reactions, 2-heptenes are eliminated by added _tert_-butylamine, but the yields of 1,2-dimethylcyclopentanes are merely diminished. As expected, the cis/trans ratios of the residual 1,2-dimethylcyclopentanes are near four, corresponding to pure radical cyclization.

If radical cyclization is negligible in the sodium metal reactions, then the 1,2-dimethylcyclopentane cis/trans ratios for those reactions in the absence of _tert_-butylamine are those for pure anion cyclization. The is the first clear evidence of this point.

This data presented here provide strong new support for the mechanism of Scheme I, including anion cyclization. More important, they provide a demonstration of the trapping technique for validating a 5-hexenylic probe for radical intermediates.[9]

The carbanion trapping method for validating 5-hexenylic probes is applicable to many reactions and probes, including those for which radical and anion cyclizations give indistinguishable products, provided that sufficiently accurate quantitative product analyses are prossible. Like all other methods that involve additives to reaction mixtures, this one suffers from the possibility that the additive could influence the reaction in ways other than that which is desired.[10] This must always be guarded against.

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References and Footnotes

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(8) Methods were described in reference 5 and in Garst, J. F.; Barbas, J. T. *J. Am. Chem. Soc.* **1974**, *96*, 3239. Analyses were by GC using one of two columns: 5'x1/8" 10% Na_2SO_4/alumina at 160°, or 6'x1/8" *n*-octane/Porasil C at 110°.

(9) (a) Trapping electrochemically generated 2-(3-butenyl)phenyl anions by water (D_2O), thereby suppressing anion cyclization, was demonstrated recently by Koppang, M. D.; Ross, G. A.; Woolsey, N. F.; Bartak, D. E. *Abstracts, 190th ACS National Meeting*, September, 1985, paper ORGN 120. (b) *tert*-Butylamine was employed recently as a carbanion trap with several 5-hexenylic probes in studies of reactions of (trimethylstannyl)sodium with primary alkyl halides. No clear instances of suppression of anion cyclization were reported, although in some cases *tert*-butylamine had other effects on product distributions. Ashby, E. C.; Su, W.-Y.; Pham, T. N. *Organometallics* **1985**, *4*, 1493.

(10) We see evidence for alkene isomerization in a few experiments. Unassigned GC peaks appear in the 2-heptene region. These may represent 3-heptenes. In control experiments, we added 1-hexene to reaction mixtures. Usually it is not isomerized, but when very large concentrations of *tert*-butylamine and long reaction times are used (in sodium metal reactions), GC peaks corresponding to 2-hexenes appear. Isomerization of 1-heptene to 2-heptenes could be the source of the small residual amounts of 2-heptenes reported for some experiments with *tert*-butylamine in Table I.

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