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Free Radical Intermediates in the Reaction of Neophyllithium with Oxygen[1]

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Abstract: Neophyllithium (**1**) has been oxidized in solution by reaction with molecular oxygen at very low, controlled, rates. When autoxidation is carried out at 25° in *n*-pentane or *n*-heptane solution, a significant fraction of the reaction products contain the benzyldimethylcarbinyl moiety; these products strongly implicate neophyl free radical as an intermediate. In hydrocarbon solutions containing tetrahydrofuran or triethylamine, and in pure diethyl ether solution, formation of these products is largely suppressed. Neophyllithium is tetrameric in *n*-pentane at concentrations of 0.07 *N* but dimeric in diethyl ether at similar concentrations ($\sim$0.10 *N*); vapor pressure studies establish that **1** coordinates strongly with tetrahydrofuran, but weakly with triethylamine and diethyl ether. Correlation of product distributions with the composition of the aggregates of **1** inferred from these physical studies indicates that the unsolvated tetrameric aggregates of neophyllithium autoxidize in major part by a path involving free neophyl radicals, while the solvated dimeric aggregates autoxidize predominantly by a path not involving free alkyl radicals.

The reaction of organolithium and -magnesium compounds with molecular oxygen is important as a synthetically useful method of converting these reagents to alcohols and as an almost ubiquitous side reaction in their preparation and handling.[3-5] These autoxidation reactions,[4-9] as well as those of organometallic derivatives of aluminum,[10,11] boron,[10,12] and other

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(2) E. B. Hershberg Fellow, 1965–1966; National Institutes of Health Predoctoral Fellow, 1966–1967.
(3) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Englewood Cliffs, N. J., 1954, Chapter 20; T. G. Brikina and V. A. Shustunov, *Russ. Chem. Rev.*, 35, 613 (1966); T. G. Brikina and V. A. Shustunov, "Reactions of Organometallic Compounds with Oxygen and Peroxides," translated by A. G. Davies, Iliffe Books, Ltd., London, 1969.
(4) H. Hock, H. Kropf, and F. Ernst, *Angew. Chem.*, **71**, 541 (1959).
(5) G. Sosnovsky and J. H. Brown, *Chem. Rev.*, **66**, 529 (1966).
(6) C. W. Porter and C. Steele, *J. Amer. Chem. Soc.*, **42**, 2650 (1920).
(7) C. Walling and S. A. Buckler, *ibid.*, 77, 6032 (1955).
(8) H. Hock and F. Ernst, *Chem. Ber.*, 92, 2716, 2723, 2732 (1959).
(9) C. F. Cullis, A. Fish, and R. T. Pollard, *Proc. Roy. Soc. Ser. A*, **298**, 64 (1967).
(10) M. D. Carabine and R. G. W. Norrish, *ibid.*, **296**, 1 (1967); A. G. Davies, K. U. Ingold, B. P. Roberts, and R. Tudor, *J. Chem. Soc., B*, 698 (1971); A. G. Davies in "Organometallic Peroxides," Vol. 2, D. Swern, Ed., Interscience New York, N. Y., 1971, Chapter 4.

metals,[5,8,10] are believed to occur in two distinct, and mechanistically unrelated steps: first, 1 equiv of organometallic compound is converted to an intermediate metal hydroperoxide by reaction with oxygen; and second, this hydroperoxide is reduced to alcohol by reaction with a second equivalent of the organometallic reagent. This general scheme has found convincing support in the isolation of respectable yields of hydro-

$$\text{R-M} \xrightarrow{O_2} \text{R-O-O-M} \quad (1)$$

$$\text{R-O-O-M} + \text{RM} \longrightarrow 2\text{ROM} \quad (2)$$

peroxides from the autoxidation of alkyllithium and -magnesium reagents under carefully controlled conditions,[3-7] and by observation that Grignard and organolithium reagents reduce hydroperoxides to alcohols, and peresters to ethers (*inter alia*), under reaction conditions similar to those encountered in the autoxidation reactions.[4-11]

Current interest in the mechanism of autoxidation of organolithium and -magnesium compounds is centered about the detailed nature of the conversion of these reagents to hydroperoxide salts (eq 1). Direct reaction of an organometallic compound with ground state ($^3\Sigma_g^-$) oxygen has been considered unlikely since the hydroperoxide would be formed in a high-energy triplet electronic configuration, if electron spin angular momentum is conserved during the reaction.[13] Mechanistic studies by Russell and coworkers have established that the most common pathway for the autoxidation of *weakly basic, resonance stabilized* carbanions is a free radical chain reaction.[13,14] The evidence concerning the intermediacy of free alkyl radicals in autoxidation of *strongly basic* organolithium or -magnesium reagents is less extensive, although the products observed on autoxidation of the Grignard reagents from 5-hexenyl bromide[15] and α,α-diphenylallylcarbinyl[16] bromide suggest radical intermediates. A three-step radical chain mechanism has been proposed[13-15] for the conversion of organometallic compounds (assumed to be monomeric) to hydroperoxide salts that is consistent with these data (eq 3–5). The chain

$$\text{RM} + O_2 \longrightarrow \text{R}\cdot + \text{MO}_2 \quad (3)$$

$$\text{R}\cdot + O_2 \longrightarrow \text{ROO}\cdot \quad (4)$$

$$\text{ROO}\cdot + \text{RM} \longrightarrow \text{ROOM} + \text{R}\cdot \quad (5)$$

transfer step (eq 5) could occur either *via* electron transfer[13,14] or displacement.[15]

Two different free radical chain mechanisms for hydroperoxide salt formation can be written when aggregated rather than monomeric covalent organometallic compounds are considered (illustrated here with alkyllithium tetramers).[17] A scheme analogous to previously proposed mechanisms[13,14] would yield a free alkyl radical intermediate by carbon–metal bond cleavage following electron transfer from the aggregate (eq 6–8). If the oxidized aggregate were

$$(\text{RLi})_4 + O_2 \longrightarrow \text{R}\cdot + \text{R}_3\text{Li}_4^+ + O_2\cdot^- \quad (6)$$

$$\text{R}\cdot + O_2 \longrightarrow \text{ROO}\cdot \quad (7)$$

$$\text{ROO}\cdot + (\text{RLi})_4 \longrightarrow (\text{ROO})\text{R}_3\text{Li}_4 + \text{R}\cdot \quad (8)$$

not to fragment before reacting further, hydroperoxide salt might be formed without the intermediacy of a free alkyl radical (eq 9–12).[18] The chain transfer

$$(\text{RLi})_4 + O_2 \longrightarrow (\text{RLi})_4\cdot^+ + O_2\cdot^- \quad (9)$$

$$(\text{RLi})_4\cdot^+ + O_2 \longrightarrow \text{ROO}\cdot + \text{R}_3\text{Li}_4^+ \quad (10)$$

$$\text{ROO}\cdot + (\text{RLi})_4 \longrightarrow \text{ROO}^- + (\text{RLi})_4\cdot^+ \quad (11)$$

$$\text{ROO}^- + \text{R}_3\text{Li}_4\cdot^- \longrightarrow (\text{ROO})\text{R}_3\text{Li}_4 \quad (12)$$

step in this reaction (eq 11) would occur by electron transfer. Reasonable structural precedents for the proposed partially oxidized aggregates exist. R_3Li_4^- has been observed in mass spectrometric studies[19] and complexes of methyl radical with lithium halide have been observed in low-temperature matrix ir studies.[20] The essential difference between the two pathways is that the first involves a free alkyl radical intermediate and the second does not.

We have explored the importance of free radicals as intermediates in the autoxidation of organolithium compounds by examining the reaction of oxygen with neophyllithium (**1**). There are a number of reasons for choosing neophyllithium for study. It can be prepared in high purity, free of lithium halides or alkoxides, and it is soluble in hydrocarbon solvents.[21] Thus, the autoxidation of **1** can be studied in pure hydrocarbon solutions as well as *mixtures* of hydrocarbon and donor solvents. This flexibility in choice of solvent is of particular importance in light of the well-documented change in the reactivity of alkyllithium solutions that may accompany changes in the solvent composition.[17,22] The characteristic rearrangement of the neophyl radical to the dimethylbenzylcarbinyl radical is a particularly well-understood process.[21,23] The fact that the 1,2-aryl migration is *not* concerted with formation of the neophyl radical, and occurs only subsequent to the formation of a discrete classical neophyl radical, is of particular pertinence to this work.[24] Neophyllithium itself does not rearrange to benzyldimethyl-

(11) E. Miller and T. Topel, *Chem. Ber.*, **72**, 273 (1939); S.-O. Lawesson and N. C. Yang, *J. Amer. Chem. Soc.*, **81**, 4230 (1959); H. J. Jacobsen, E. H. Larsen, and S.-O. Lawesson, *Rel. Trav. Chim. Pays-Bas*, **82**, 791 (1963); S.-O. Lawesson, C. Frisell, D. Z. Denny, and D. B. Denny, *Tetrahedron*, **19**, 1229 (1963).

(12) P. J. Krusic and J. K. Kochi, *J. Amer. Chem. Soc.*, **91**, 3942 (1969).

(13) G. A. Russell, *et al.*, *Advan. Chem. Ser.*, **No. 51**, 112 (1965).

(14) G. A. Russell, *et al.*, *ibid.*, **No. 75**, 174 (1968).

(15) R. C. Lamb, P. W. Ayers, M. K. Toney, and J. F. Garst, *J. Amer. Chem. Soc.*, **88**, 4261 (1966); C. Walling and A. Ciorfari, *ibid.*, **92**, 6609 (1970).

(16) M. E. Howden, A. Maercker, J. Burdon, and J. D. Roberts, *ibid.*, **88**, 1732 (1966); see also W. E. Parham, R. W. Davenport, and J. K. Reinhard, *J. Org. Chem.*, **35**, 2661 (1970).

(17) One-electron oxidation of organolithium aggregates has been discussed previously: G. C. Serettas and J. F. Eastham, *J. Amer. Chem. Soc.*, **88**, 5668 (1966); W. H. Glaze, C. M. Selman, A. L. Ball, Jr., and L. E. Bray, *J. Org. Chem.*, **34**, 641 (1969), and references in each.

(18) A number of obvious variations on this scheme could be proposed.

(19) G. E. Hartwell and T. L. Brown, *Inorg. Chem.*, **5**, 1257 (1966); J. Berkowitz, D. A. Bafus, and T. L. Brown, *J. Phys. Chem.*, **65**, 1380 (1961).

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(22) C. G. Eberhardt and W. A. Butte, *J. Org. Chem.*, **29**, 2928 (1964); F. A. Settle, M. Haggerty, and J. F. Eastham, *J. Amer. Chem. Soc.*, **86**, 2076 (1964); P. D. Bartlett, C. V. Goebel, and W. P. Weber, *ibid.*, **91**, 7425 (1969), and references in each.

(23) Reviews: R. Kh. Freidlina, *Advan. Free-Radical Chem.*, **1**, 211 (1965); C. Walling in "Molecular Rearrangements," Part I, P. de Mayo, Ed., Wiley, New York, N. Y., 1963, p 407 ff; R. Kh. Freidlina, V. N. Yost, and M. Ya. Khorlina, *Russ. Chem. Rev.*, **31**, 1 (1962).

(24) C. Ruchardt and R. Hecht, *Chem. Ber.*, **98**, 2460 2471 (1965); C. Ruchardt, *ibid.*, **94**, 2599, 2609 (1961); C. Ruchardt and S. Eicher, *ibid.*, **95**, 1921 (1962).

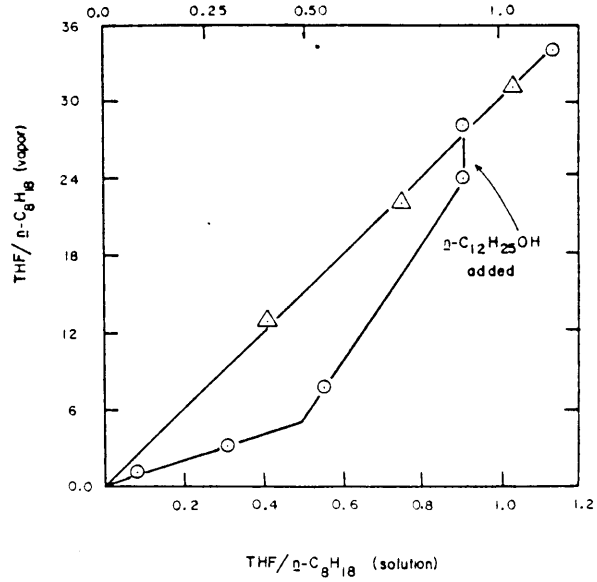

Figure 1. Vapor pressure–composition data used to examine the interaction between tetrahydrofuran (**1**) (THF) and neophyllithium in *n*-pentane solution at ambient temperature. Data obtained in the presence of ~0.07 **1** are indicated by ○; those obtained in the absence of organolithium reagent are indicated by △. The axes represent the ratios of the areas due to THF and *n*-octane (an inert glpc standard) in glpc traces of aliquots taken from the solution containing **1** and from the vapor over the solution. 1-Dodecanol was added to the solution to quench the **1** at the indicated point.

carbinyllithium under the reaction conditions encountered in the autoxidation reactions.[21] Finally, the neophyl radical rearrangement is sufficiently slow[21] ($k < 10^5$ sec^{-1} at 100°) that rearrangement cannot compete with reactions taking place within a solvent cage.[25] Thus, observation of rearranged products in reactions of neophyllithium can be simply interpreted in terms of classical free radicals, without concern for aryl participation in radical formation, or for details and timing of the processes leading to escape of the radical from the solvent cage in which it is initially formed.

Results

Preparation and Properties of Neophyllithium. Neophyllithium was prepared by transmetalation of dineophylmercury with lithium metal and was recrystallized from *n*-pentane solution at −78°.[21] Neophyllithium dissolves readily in diethyl ether and tetrahydrofuran (THF) but is only soluble to the extent of *ca.* 0.1 *N* in *n*-pentane. Hydrolysis of representative samples of recrystallized material yielded *tert*-butylbenzene quantitatively; neophyl alcohol was detected in less than 0.1% yield. Reaction of **1** with lithium *tert*-butyl peroxide in ether solution at room temperature gave neophyl alcohol in 90% yield. No product derived from the benzyldimethylcarbinyl moiety could be detected in either experiment. Thus, the neophyllithium used in the autoxidation studies was free of benzyldimethylcarbinyllithium and of neophyl and benzyldimethylcarbinyl alkoxides.

The extent of aggregation of neophyllithium in *n*-pentane was determined by isothermal distillation at room temperature. Two determinations of the apparent molecular weight yielded degrees of association *n* of 3.80 and 3.94 at a concentration of **1** of *ca.* 0.07 *N*. Although the rate of reaction of neophyllithium with diethyl ether at room temperature was sufficiently rapid that isothermal distillation yielded unreliable values for the molecular weight, isothermal distillation experiments could be carried out at −20° without significant competition from ether cleavage. The degrees of association determined in this solvent at a neophyllithium concentration of *ca.* 0.10 *N* are 2.00 and 2.06.[26] Thus, neophyllithium is tetrameric in *n*-pentane, but apparently dimeric in diethyl ether. Other sterically crowded organolithium reagents are tetrameric or dimeric in hydrocarbon solutions and many organolithium reagents form smaller aggregates in donor solvents.[27]

The ability of neophyllithium to form complexes with donor solvents was determined by measuring the vapor composition over pentane solutions of **1** containing added donor solvent and a small amount of *n*-octane (as an internal glpc standard).[28] Comparison of the partitioning of triethylamine or diethyl ether between an *n*-pentane solution and the atmosphere over the solution indicated the presence of 0.07 *N* **1** in solution had no influence on the apparent vapor pressure of these donors and demonstrated that any complexes formed between neophyllithium and these donors must be weak. Similar measurements made using tetrahydrofuran as the donor clearly demonstrated the formation of a complex of approximate stoichiometry $[(RLi)_2 \cdot THF]_n$ (Figure 1).[29] Thus, qualitatively, **1** coordinates strongly with tetrahydrofuran, but weakly with diethyl ether and triethylamine.

Oxidation in Hydrocarbon Solvents. Reaction of neophyllithium in a hydrocarbon solution with oxygen, followed by hydrolysis, yields a number of products whose relative yields depend primarily on the temperature and rate of addition of oxygen. Rapid addition of oxygen to a solution of **1** at room temperature

$$\underset{\mathbf{1}}{(PhC(CH_3)_2CH_2Li)_4} \xrightarrow[2.\ H_2O]{1.\ O_2,\ 25^\circ} \underset{\mathbf{2}}{PhC(CH_3)_3} + \underset{\mathbf{3}}{PhCH_2CH(CH_3)_2} + \underset{\mathbf{4}}{PhCH_2C(CH_3){=}CH_2} + \underset{\mathbf{5}}{PhCH{=}C(CH_3)_2} + \underset{\mathbf{6}}{PhC(CH_3)_2OH} + \underset{\mathbf{7}}{PhCH_2C(CH_3)_2OH} + \underset{\mathbf{8}}{PhC(CH_3)_2CH_2OH} + \underset{\mathbf{9}}{PhC(CH_3)_2CH_2CH_2C(CH_3)_2Ph} + \underset{\mathbf{10}}{PhC(CH_3)_2CH_2C(CH_3)_2CH_2Ph} + \underset{\mathbf{11}}{PhCH_2C(CH_3)_2C(CH_3)_2CH_2Ph}$$

results in formation of neophyl alcohol (**8**) as the only oxygen-containing product. Under these conditions, the availability of oxygen in solution is presumably

(25) R. M. Noyes, *Progr. React. Kinet.*, **1**, 120 (1961).

(26) In one experiment the isothermal distillation apparatus was opened under a nitrogen atmosphere after equilibrium had been attained and the neophyllithium was quenched with 1,2-dibromoethane. Glpc analysis indicated a 90% yield of neophyl bromide.

(27) H. L. Lewis and T. L. Brown, *J. Amer. Chem. Soc.*, **92**, 4664 (1970); P. West, R. Waack, and J. I. Purmot, *ibid.*, **92**, 840 (1970); W. H. Glaze and C. H. Freeman, *ibid.*, **91**, 7198 (1969); G. E. Hartwell and A. Allerhand, *ibid.*, **93**, 4415 (1971).

(28) R. Waack, M. A. Doran, and P. E. Stevenson, *ibid.*, **88**, 2109 (1966).

(29) Plots similar to that in Figure 1 were obtained in experiments carried out to test the experimental technique using 0.05 *N* *n*-butyllithium in *n*-pentane and ether or triethylamine. These plots confirm the existence of complexes of approximate stoichiometry $(n\text{-BuLi})_2 \cdot TEA$ and $(n\text{-BuLi})_2 \cdot OEt_2$ inferred from analogous studies using more concentrated solutions (see the Experimental Section).[22]

Table I. The Influence of Oxygen Addition Rate and Reaction Temperature on Product Yields (%) in Oxidation of Neophyllithium[a]

Solvent	n-Pentane			n-Heptane			
Temp, °C	25	25	25	25	25	45	70
Oxygen addn rate (ml/hr)	29	5.5	3.1	3.1[b]	3.1[b]	3.1	3.1
Product							
$C_6H_5C(CH_3)_3$ (2)	8.4	12.4	12.2	26.0		31.6	34.7
$C_6H_5CH_2CH(CH_3)_2$ (3)	0.5	1.3		0.7	24.0	0.8	1.5
$C_6H_5CH_2C(CH_3)=CH_2$ (4)	0.6	1.5	<0.2	1.0		1.2	2.0
$C_6H_5CH=C(CH_3)_2$ (5)	0.1	0.4	<0.1	0.9	0.2	0.8	3.4
$C_6H_5C(CH_3)_2OH$ (6)[c]	0.8	0.4		0.7	0.4	0.8	0.5
$C_6H_5CH_2C(CH_3)_2OH$ (7)	7.9	8.5	10.1	6.1	5.4	6.5	4.6
$C_6H_5C(CH_3)_2CH_2OH$ (8)	66.3	52.9	49.3	54.0	53.1	42.5	27.2
R–R[d] (9)	17.7	12.3	12.4	12.7	15.2	8.9	3.9
R–R′[d] (10)	0.9	1.9	2.5	1.3	1.4	1.9	1.8
R′–R′[d] (11)	0.4	0.3	0.4	<0.2	<0.2	0.2	0.4
Product balance, %	103.7	91.9	95.9	103.4	99.7	95.2	80.0
% rearrangement in							
dimeric hydrocarbons	5.0	8.6	10.8	4.9	4.2	10.5	21
alcohols	10.6	13.8	17.0	10.1	9.2	13.3	14.5
Dimer/alcohols	0.26	0.24	0.26	0.23	0.28	0.22	0.19

[a] 10 ml of 0.05 *N* solution of neophyllithium was oxidized in the flask diagrammed in Figure 2. Yields are based on organometallic component and are estimated to be accurate to ±3% (relative). [b] Duplicate experiments. The extent to which they resemble one another is typical of the reproducibility encountered in this work. [c] Characterized by glpc retention time only. [d] R refers to neophyl; R′ refers to benzyldimethylcarbinyl.

relatively high.[30] Since the rate of reaction of simple alkyl radicals with oxygen is close to diffusion controlled,[31] 1,2-phenyl migration in any neophyl radicals formed under these conditions would not be expected to compete with scavenging of the neophyl radicals by oxygen. In order to provide reaction conditions in which the rearrangement of an intermediate neophyl radical could compete with this scavenging, the steady-state concentration of oxygen in the solution was reduced to a low value by slowly introducing this reagent into a nitrogen atmosphere above a vigorously stirred solution of **1** from a capillary inlet (Figure 2). Products obtained in representative reactions carried out using these conditions are given in Table I. For comparison, this table also includes product distributions observed at higher oxygen addition rates, and at higher temperatures.

In practice, the reproducibility of the product yields obtained in these experiments was only fair: variable (<15%) amounts of adventitious hydrolysis (but *not* of oxidation) apparently accompanied manipulation of **1** during the course of the experiments, and consequently the *absolute* yield data derived from these oxidations varied. In order to minimize ambiguities in interpretation arising from this uncertainty in the relative quantities of **1** consumed by reaction with oxygen and by unintended reaction with water, Table I includes three parameters derived from the product yields: the "percentage rearrangement" in the dimeric hydrocarbons and the alcohols (defined as 100(0.5 **10** + **11**)/(**9** + **10** + **11**) and 100(**7**)/(**7** + **8**), respectively, where, *e.g.*, **10** indicates the yield of compound **10**), and the ratio of the yields of dimeric products to alcohols. In principle, each of these quantities should be independent of small variations in the amount of adventitious hydrolysis occurring during an experiment; in practice,

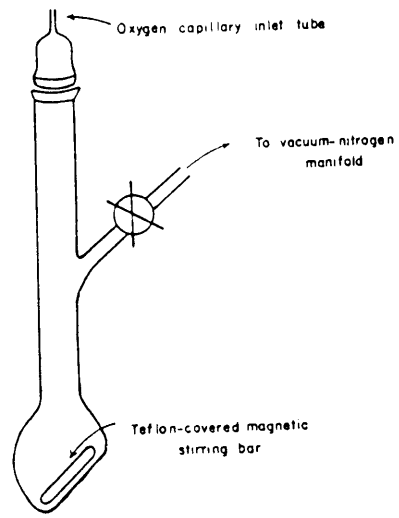

Figure 2. The flask used to carry out the autoxidation experiments. This flask was constructed from a 100-ml Kjedahl flask, modified by addition of a capillary inlet tube for introduction of oxygen, and by beveling the bottom of the flask, to improve the efficiency of stirring.

although they were not completely reproducible, they did provide a more stable basis for interpretation than the raw yields. Nonetheless, the small unexplained residual variation in the results of these oxidation reactions is sufficient that qualitative trends in the data of Table I should be considered more significant than an individual datum from any one experiment.

Control experiments in which the lithium salt of neopentyl alcohol was added to pentane solutions of **1** prior to autoxidation established that alkoxides have negligible effect on the product distribution. The ratio of dimers to alcohols is also unaffected by changes in the reaction temperature and oxygen addition rate.

Oxidation of 1 in the Presence of Coordinating Bases. The addition of small amounts of THF, triethylamine, or diethyl ether to pentane solutions of **1** caused a simultaneous increase in the ratio of dimers to alcohols and a decrease in the percentage rearrangement in the alcohols (Table II). Plots of the change of these

(30) The mole fractions of oxygen saturated ether, *n*-hexane, and *n*-heptane at 25° are 1.98×10^{-3}, 1.93×10^{-3}, and 1.97×10^{-3}, respectively: J. C. Gjaldbaek, *Acta Chem. Scand.*, 6, 623 (1952).

(31) G. A. Russell in "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., Interscience, New York, N. Y., 1962, p 107; see also P. D. Bartlett, R. E. Pincock, J. H. Rolston, W. G. Schindel and L. A. Singer, *J. Amer. Chem. Soc.*, 87, 2590 (1965).

Table II. Influence of Added Tetrahydrofuran, Triethylamine, or Diethyl Ether on the Products of Oxidation of Neophyllithium in *n*-Pentane[a]

Base/$C_6H_5C(CH_3)_2CH_2Li$[b]	Product, % (THF) 0.0[c]	0.25	0.50	1.0	2.0
Monomeric hydrocarbons[g]	21.2	20.4	31.6	22.5	34.9
$C_6H_5CH_2C(CH_3)_2OH$ (7)	10.1	5.0	1.8	1.4	0.7
$C_6H_5C(CH_3)_2CH_2OH$ (8)	49.3	44.4	34.2	37.3	30.1
RR (9)[h]	12.4	20.0	22.5	27.8	26.4
RR′(10)[h,i]	2.5	4.2	4.8	5.1	5.4
R′R′ (11)[h,i]	0.4	0.6	0.3	0.3	0.4
Product balance, %	95.9	94.6	95.2	94.4	98.5
% rearrangement in					
Dimers	11	11	10	9	10
Alcohols	17.0	10.1	5.0	3.6	2.3
Dimers/alcohols	0.26	0.50	0.77	0.86	1.05

[a] 10 ml of 0.05 *N* solution of **1** was oxidized at room temperature with an oxygen addition rate of 3.1 ml/hr, unless otherwise noted. [b] Millimoles of TEA, THF, or diethyl ether/mmol of **1** in solution. [c] 192 mmol of ether/mmol of **1** corresponds to a solution of **1** in ether with no pentane present. [d] Oxygen addition rate 11 ml/hr. [e] Oxygen addition rate 29 ml/hr. [f] Oxygen addition rate rapid (>50 ml/min). [g] No

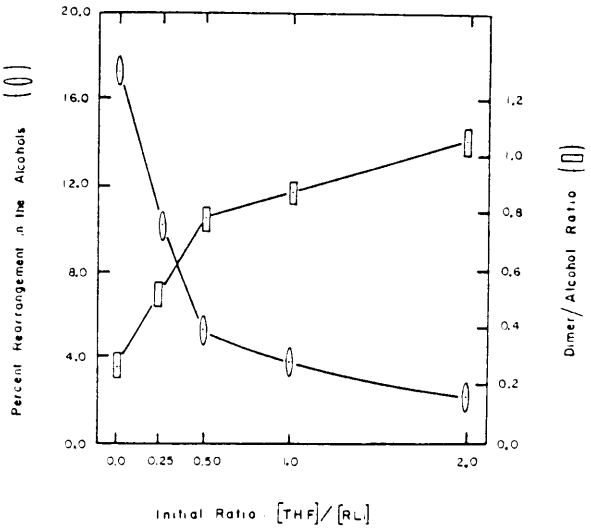

Figure 3. The influence of added THF on the products obtained on autoxidation of neophyllithium in *n*-pentane solution. The two vertical axes represent the per cent rearrangement in the alcohols and dimer/alcohol ratio, respectively (Table II), observed in the autoxidation as a function of the initial ratio of concentrations of added THF to neophyllithium. The initial concentration of **1** was 0.05 *N* in each experiment.

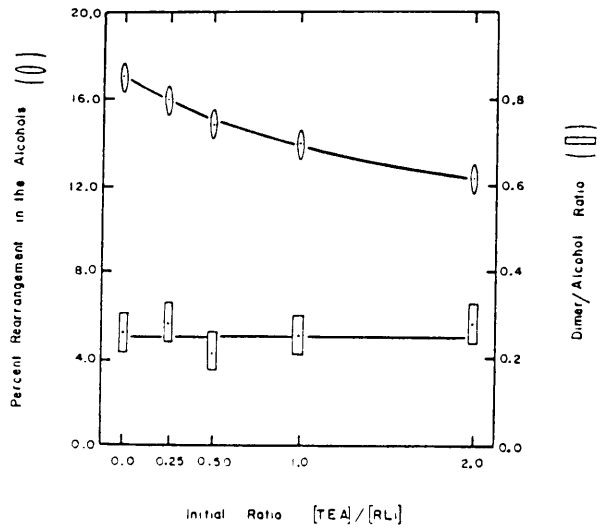

Figure 4. The influence of added triethylamine (TEA) on the products obtained on autoxidation of neophyllithium in *n*-pentane solution. The axes and initial concentrations are the same as those in Figure 3; the initial concentration of **1** was 0.05 *N* in each experiment.

product parameters relative to the initial ratio of neophyllithium to THF (Figure 3), triethylamine (Figure 4), and diethyl ether (Figure 5) show a qualitative correlation with the coordinating ability of the bases (THF ≫ triethylamine ≈ diethyl ether). Of particular interest is the clearly defined break in these product parameters at an approximate stoichiometry of 2 equiv of **1** to 1 equiv of THF (Figure 3). This break correlates with the previously determined stoichiometry of the complex between **1** and THF (Figure 1). When **1** is autoxidized in pure diethyl ether solution the formation of rearranged alcohol is completely suppressed. Thus the autoxidation of solvated **1** to alcohols apparently follows a much different pathway than does that of unsolvated **1**.

Increasing the rate of oxygen addition to a pure ether solution of **1** smoothly decreased the ratio of dimers to alcohols (Table II).[32] If the oxygen was added sufficiently rapidly that oxidation was complete in 1 min, essentially no dimeric products were formed. Thus, the reaction path leading to dimerization is completely suppressed if the availability of oxygen in ether solution is high. Aliquots removed during an autoxidation of **1** in pure ether solution at 10, 50, and 100% completion all had the same ratio of dimers to alcohols and contained no rearranged alcohol. Thus, as in pentane solution, alkoxide formed during the reaction had no apparent influence on the reaction products.

Lithium peroxide or sodium superoxide[33] added to pentane or diethyl ether solutions of **1** were apparently unreactive toward **1**. However, these results may not be mechanistically significant since the peroxide and superoxide salts appeared to be insoluble in the reaction solution.

Discussion

These studies permit two principal inferences concerning the mechanisms of autoxidation of neophyl-

(32) The peaks assumed to be compounds **10** and **11** in autoxidations run in ether-rich solutions were assigned only on the basis of retention times, and the yields reported in Table II for these compounds are thus uncertain. The apparent formation of rearranged dimers but not of rearranged alcohol is surprising.

(33) Sodium rather than lithium superoxide was used in these experiments since lithium superoxide is unstable thermally; see N.-G. Vannerberg, *Progr. Inorg. Chem.*, 4, 131 (1962).

Product, % (TEA)						Product, % (Et_2O)								
0.25	0.50	1.0	2.0	29	48	0.5	1.0	4.0	20	40	192[c]	192[c,d]	192[c,e]	192[c,f]
25.4	41.4	28.8	43.8	42.4	39.2	30.7	20.4	17.9	28.5	22.3	47.6	55.0	33.2	2
6.7	6.4	7.7	4.6	3.3	2.8	5.4	5.9	4.7	1.9	1.6	<0.1	<0.1	<0.1	<0.1
35.5	36.6	47.3	32.8	33.5	37.1	33.0	39.9	46.4	30.8	33.5	14.9	18.9	35.8	95
9.3	7.0	11.6	8.4	11.3	19.3	9.0	16.6	29.4	25.0	33.0	23.4	18.9	15.8	<0.2
2.2	1.5	1.9	1.8	1.2	2.0	2.2	2.2	2.4	3.6	4.2	3.5	2.2	3.0	<0.2
0.4	0.3	<0.2	0.3	<0.2	<0.2	0.3	<0.2	<0.2	<0.2	<0.2	<0.2	<0.2	<0.2	<0.2
79.5	93.2	97.3	91.7	91.7	100.4	80.6	85.0	100.8	88.2	94.6	89.4	95.0	87.7	97
13	12	7	11	5	5	12	6	4	6	6	6	5	8	
15.9	14.9	14.0	12.3	9.0	7.0	14.1	12.9	9.2	5.6	4.6	<0.7	<0.5	<0.3	<0.1
0.28	0.21	0.25	0.28	0.34	0.53	0.30	0.41	0.62	0.87	1.06	1.81	1.12	0.53	<0.1

effort was made to determine **2**, **3**, **4**, and **5** separately in these experiments. Cumyl alcohol (**6**) was present in trace amounts (<1%) in certain of these experiments, but was not analyzed quantitatively. [h] R refers to neophyl; R′ refers to benzyldimethylcarbinyl. [i] Identified by glpc retention time only in solutions containing THF and Et_2O.

lithium (**1**). First, slow autoxidation of **1** in hydrocarbon solutions proceeds to a large extent along pathways requiring a long-lived intermediate neophyl radical. The detection of a significant fraction (10–15%) of products containing the benzyldimethylcarbinyl moiety and the observation that the yields of these products increase on decreasing the oxygen addition rate (in pentane) and increasing the reaction temperature (in heptane) are both consistent with this contention. Thus, increasing the reaction temperature would be expected to increase the rate of the 1,2-phenyl migration relative to other reactions of the neophyl radical, while decreasing the oxygen addition rate would decrease the rate of the reaction of an intermediate neophyl radical with oxygen and increase its lifetime and probability of rearrangement. Second, the neophyl alcohol formed on autoxidation of **1** coordinated with donor ligands does *not* have free neophyl radical as its precursor. The substantial influence of small amounts of THF on the percentage of rearranged alcohol formed on autoxidation of **1** (Figure 3) and the general correlation between product distributions and the strength of coordination between **1** and the donor component of the solution indicate that the solvent effects that provide the basis for this assertion are not due simply to changes in bulk properties of the solvent, but rather to specific interactions between **1** and the donors. Further, since the solubility of oxygen in pentane and in the donor solvents examined is similar,[30] the lifetime of a neophyl radical and the probability of its rearrangement before trapping with O_2 should be essentially the same in hydrocarbon and donor solutions. Finally, ether solvents are not sufficiently active as hydrogen atom donors to suppress aryl migration in neophyl radicals generated in other reactions.[21,34] Thus, the decreased yield of benzyldimethylcarbinol observed when **1** is autoxidized in the presence of donor solvents is not due to rapid reaction of neophyl radicals with oxygen or solvent, but to a difference in the mechanisms of formation of alcohols from unsolvated and solvated **1**.

The role of the neophyl radical in the formation of dimers on autoxidation of solvated **1** is presently unclear, since rearranged dimers are apparently formed even in donor solvents, in which free neophyl radical can be excluded as a precursor of neophyl alcohol.

(34) C. Ruchardt and H. Trautwein, *Chem. Ber.*, **96**, 160 (1963); see also C. Ruchardt and H. Trautwein, *ibid.*, **95**, 1197 (1962).

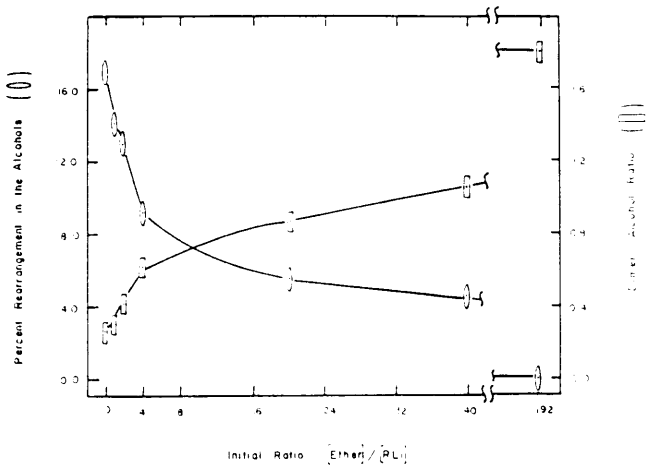

Figure 5. The influence of diethyl ether concentration on the products obtained on autoxidation of neophyllithium in *n*-pentane ether solutions. The axes have the same meaning as those in Figure 3. The initial concentration of **1** was 0.05 *N* in each experiment.

However, despite this uncertainty concerning the mechanism(s) of conversion of **1** to dimers, the arguments derived from the distributions of alcohols establish that at least two fundamentally different mechanisms exist for the autoxidation of this organolithium reagent.

Experimental Section

General Methods. All reactions involving organometallic compounds were carried out under atmospheres of prepurified or Grade A helium using standard techniques.[35] Dioxane was purified by distillation under nitrogen from a dark purple solution of sodium benzophenone dianion. Ether, tetrahydrofuran, and triethylamine were distilled from lithium aluminum hydride under a nitrogen atmosphere immediately before use. Hydrocarbon solvents were scrubbed with concentrated sulfuric acid to remove olefinic impurities and distilled from a suspension of sodium benzophenone ketyl under a nitrogen atmosphere immediately before use. Melting points were obtained using a Thomas-Hoover capillary melting point apparatus and are uncorrected. Boiling points are uncorrected. Nmr spectra were run as carbon tetrachloride solutions on a Varian A-60 spectrometer; chemical shifts are reported in parts per million downfield from tetramethylsilane and coupling constants in hertz. Infrared spectra were taken in sodium chloride cells using Perkin-Elmer Models 237, 237B, or 337 grating spectrometers. Mass spectra were determined on a Hitachi Perkin-Elmer Model RMU-6D mass spectrophotometer. Microanalyses were performed by Midwest Microlab, Inc., Indianapolis, Ind.

(35) D. F. Shriver, "The Manipulation of Air-Sensitive Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1969, Chapter 7.

Analytical glpc analyses were performed on F & M Model 810 instruments equipped with flame ionization detectors using response factors obtained with authentic samples. All components in the reaction mixtures could be separated using a silanized 6-ft 13% SE-52 on 80-100 mesh Chromosorb W column operating at 150° (for compounds **2**-**8**) or 230° (for compounds **9**-**11**). The monomeric hydrocarbons could be analyzed more accurately using an 8-ft 20% UC-W98 on 80-100 mesh Chromosorb W column at 110°. The yield of *tert*-butylbenzene formed in the oxidations was corrected for the amount of *tert*-butylbenzene present in the stock solution of **1**, as determined by 1,2-dibromoethane quench. Compounds were identified by collection from glpc and comparison of ir spectra (CCl_4) with those of authentic samples.

Concentrations of organolithium reagent solutions were determined by the Gilman double-titration method with 1,2-dibromoethane, using the procedure described previously.[21,36]

Neophyllithium (1), 2-methyl-1-phenyl-2-propane (4), 2-methyl-1-phenyl-1-propene (5), 2,5-dimethyl-2,5-diphenylhexane (9), 1,4-diphenyl-2,2,4-trimethylpentane (10), and 1,4-diphenyl-2,2,3,3-tetramethylbutane (11) were prepared as described previously.[21] ***tert*-Butylbenzene (2), isobutylbenzene (3), cumyl alcohol (6), and benzyldimethylcarbinol (7)** were commercial samples and were purified by distillation before use. **Bicumyl** was prepared by the method of Sayles and Kharasch.[37]

Neophyl alcohol (8) was prepared by the oxidation of neophylmagnesium chloride in ether at 0°.[38] Approximately 100 ml of a 2 *N* solution of neophyl Grignard reagent in ether was prepared from 33.0 g (0.20 mol) of neophyl chloride and 5.0 g (0.21 g-atom) of magnesium turnings. The Grignard reagent solution was cooled in an ice-water bath and stirred mechanically under a dry oxygen atmosphere for 1.5 hr. Ice and then saturated aqueous ammonium chloride solution were added to the reaction mixture with stirring. The ether and aqueous layers were separated, the aqueous layer was extracted twice with ether, and the combined ether layers were washed with brine, dried ($MgSO_4$), concentrated, and distilled using a short Vigreux column to yield 22.6 g (0.15 mol, 75%) of neophyl alcohol: bp 113-115° (14 mm), $n^{24}D$ 1.5249; lit.[38] bp 131° (30 mm), $n^{20}D$ 1.5261; lit.[38] bp 110-112° (12 mm), $n^{24}D$ 1.548; nmr (CCl_4) δ 7.25 (5 H, aryl H), 3.40 (2 H, s, CH_2), 1.25 (6 H, s, CH_3), and a broad peak for the alcohol proton; ir (CCl_4) 3600, 3400, 2970, 1604, 1500, 1450, 1390, 1370, 1280, 1025, 690 cm^{-1}.

Reaction of Neophyllithium with Lithium *tert*-Butyl Peroxide. A 1.5 *N* ether solution of methyllithium (0.35 ml, 0.52 mmol) was added over 5 min from a syringe to a stirred solution of 0.45 g (0.50 mmol) of *tert*-butyl hydroperoxide in 5 ml of ether at −78°. A 5-ml aliquot of a 0.10 *N* solution of **1** (0.50 mmol), containing *n*-pentadecane as an internal glpc standard, was added. The reaction was stirred at room temperature for 1 hr before hydrolysis. The yield of neophyl alcohol (glpc) was 90%. No 2-methyl-1-phenylpropan-2-ol was detected.

Extent of Aggregation of Neophyllithium in *n*-Pentane Solution. The apparent molecular weight of neophyllithium in *n*-pentane solution at room temperature was determined relative to 1,4-diphenyl-2,2,3,3-tetramethylbutane by isothermal distillation. In a typical experiment, one arm of a commercial isothermal distillation apparatus[39] was closed with a No-Air stopper. The other arm was attached to a vacuum-nitrogen manifold by a three-way stopcock. The remaining arm of the stopcock was sealed with a No-Air stopper. The apparatus was flamed-dried under vacuum, then evacuated, and filled with nitrogen a number of times. An aliquot of a 0.0107 *N* solution of 1,4-diphenyl-2,2,3,3-tetramethylbutane in *n*-pentane (0.0128 mmol) was transferred by forced siphon through a stainless steel cannula under a nitrogen atmosphere at −78° through the arm of the distillation apparatus capped with the No-Air stopper. The solution was allowed to warm to room temperature and its volume measured (1.20 ml). After freezing the solution with liquid nitrogen while under a nitrogen atmosphere, this arm was sealed under vacuum. The apparatus was allowed to warm to −78°, and an aliquot of a 0.10 *N* solution of neophyllithium in *n*-pentane (0.124 mmol of **1**) was added by stainless steel cannula under a nitrogen atmosphere to the other side of the apparatus. The apparatus was again allowed to warm to room temperature and the volume of the organometallic solution measured (1.24 ml). The two solutions were degassed by successive freeze-thaw cycles at liquid nitrogen temperature and the second arm was sealed under vacuum. The solutions were allowed to equilibrate at room temperature; equilibrium was reached within 3 days. The final concentration of **1** was calculated to be 0.07 *N*.

Extent of Aggregation of Neophyllithium in Diethyl Ether Solution. The apparent molecular weight of neophyllithium in diethyl ether solution was determined relative to *trans*-9-*tert*-butyl-10-methyl-9,10-dihydroanthracene at −20° in the manner described above for *n*-pentane. To one tube of the molecular weight apparatus were added 1.48 ml of a 0.0271 *N* diethyl ether solution of the standard (0.0401 mmol) and 1.55 ml of a 0.14 *N* diethyl ether solution of neophyllithium (0.217 mmol). The second tube contained 1.52 ml of the standard solution (0.0412 mmol) and 0.90 ml of the neophyllithium solution (0.126 mmol). In both cases equilibrium was attained at −20° within 15 hr. The final concentration of neophyllithium in the tube was 0.118 *N* and in tube two was 0.099 *N*.

Tube one was opened under a nitrogen atmosphere in the manner described in the neophyllithium preparation.[21] An excess of 1,2-dibromoethane was added to the neophyllithium solution. After mixing the two solutions in one side of the isothermal distillation apparatus, an aliquot of this mixture was analyzed by glpc for neophyl bromide and *trans*-9-*tert*-butyl-10-methyl-9,10-dihydroanthracene.

Comparison with a similar solution obtained from aliquots of the original neophyllithium and standard solutions indicated that 90% of the added neophyllithium was still present in the distillation apparatus.

Interaction of Neophyllithium in *n*-Pentane Solution with Donor Solvents. The extent of interaction between neophyllithium and donor solvents in *n*-pentane was determined by comparing the ratios of donor solvent to *n*-octane in the atmosphere and in solution.[26] The procedure used to examine the interaction between THF and neophyllithium is typical. A 100-ml round-bottomed flask containing a magnetic stirring bar and capped with a No-Air stopper was flamed-dried under a nitrogen stream, cooled, and rinsed with 5 ml of a 0.067 *N* solution of neophyllithium in *n*-pentane. The flask, containing a stirred solution of 200 μl of *n*-octane and 30 ml of a 0.067 *N* solution of neophyllithium (2.0 mmol) in *n*-pentane, was immersed in a room temperature water bath. To this solution was added 20 μl of THF (0.25 mmol) by microliter syringe. After allowing the THF to equilibrate between the vapor and liquid phases (*ca.* 1 hr) a 4- to 5-ml sample of the vapor over the solution was withdrawn using a 5-ml gas-tight syringe and analyzed for THF and *n*-octane by glpc, using an 8-ft 20% UC-W98 on 80-100 mesh Chromosorb W column at 90°. The gas-tight syringe was wrapped in a towel during the vapor transfer to avoid warming the syringe by hand contact, since such warming appeared to result in preferential loss of one of the components of the mixture. The vapor composition was usually determined twice. A 1-ml aliquot of the *solution* was then withdrawn by syringe, added to a nitrogen-filled tube sealed with a No-Air stopper, and protonolyzed with 20 μl of dodecan-1-ol. Dodecanol rather than water was used for protonolysis so that the composition of the solution would not be influenced by partitioning of THF into an aqueous layer. The ratio of THF to *n*-octane in the solution was then determined by glpc analysis of this solution. This procedure was repeated for additional aliquots of THF of 20, 50, and 100 μl. After addition and equilibration of the fourth aliquot of THF, the neophyllithium was protonolyzed with 0.67 ml of dodecan-1-ol (3.0 mmol). The results of these experiments are presented in Figure 1. The increase in the amount of THF present in the vapor phase after protonolysis clearly establishes that a complex is formed between neophyllithium and THF.

The association constants of *n*-butyllithium and neophyllithium in *n*-pentane solution with TEA and ether were determined using the same procedure. For comparison with Figure 1, the data on which the conclusions concerning the ability of diethyl ether to coordinate with *n*-butyllithium and **1** are based are summarized in Figure 6.

Oxidations of Neophyllithium (1). The reactions of **1** with oxygen were carried out in a modified 100-ml Kjeldahl flask (Figure 2). The beveled bottom of this flask ensured vigorous agitation throughout the volume of the solutions being oxidized (10 to 20 ml) using magnetic stirring. In typical experiments, the flask was flamed under vacuum and then filled with nitrogen and reevacuated a number of times before being charged with the neophyllithium solution

(36) H. Gilman, F. K. Cartledge, and S.-Y. Sim, *J. Organometal. Chem.*, 1, 8 (1963).

(37) D. C. Sayles and M. S. Kharasch, *J. Org. Chem.*, 26, 4210 (1961).

(38) (a) F. G. Whitmore, C. A. Weisgerber, and A. C. Shabica, Jr., *J. Amer. Chem. Soc.*, 65, 1469 (1943); (b) J. I. G. Cadogen and W. R. Foster, *J. Chem. Soc.*, 1958 (1960).

(39) Scientific Glass Apparatus Co., Inc., Catalog No. IM-8850. The two side arms measured a volume of 2.00 ml in 0.02-ml graduations.

containing *n*-pentadecane as an internal standard by forced siphon through a stainless steel cannula inserted through the side arm. Oxygen was supplied to the flask from a compressed gas cylinder through a capillary bleed fashioned of crimped 1/8-in. aluminum tubing fastened to a 12/5 ball joint with epoxy cement. Since the flow rate through this capillary was a function of the pressure differential across the capillary, it could be controlled accurately by regulating the pressure on the reducing valve at the oxygen tank.

Oxidations of the organometallic solutions were allowed to continue at a known oxygen addition rate until an excess of oxygen had been added to the reaction flask. After the oxidation reaction was complete, the reaction mixture was transferred by cannula to a dry centrifuge tube capped with a rubber septum and filled with nitrogen. The oxidation flask was rinsed with an equal volume of dry, oxygen-free solvent, the wash was added to the bulk of the reaction mixture in the centrifuge tube by transfer through the cannula, the combined solutions were hydrolyzed with 20–30 μl of water, and the hydrolyzed solutions were analyzed by glpc.

The joints on the oxidation apparatus were lubricated with Apiezon L grease. It was discovered that during the room-temperature oxidation reactions much of the grease was leached out of the joints by the solvent; however, Apiezon L is unreactive toward **1**. When Dow Corning high-vacuum grease was used in the joints, the dissolved grease reacted with **1** to form 2,4-dimethyl-4-phenyl-2-silapentan-2-ol.

The small amounts of THF, TEA, and ether used in the mixed solvent oxidation reactions were measured volumetrically using a microliter syringe. A 12-ml centrifuge tube which was capped with a No-Air stopper and which had been flame-dried under a nitrogen stream was charged with 10.0 ml of a 0.05 *N* solution of neophyllithium (0.50 mmol) in *n*-pentane. The donor solvents were added immediately before the solution was transferred to the oxidation apparatus.

The solutions of neophyllithium containing the lithium salt of neopentyl alcohol used in examining the influence of lithium alkoxides on the oxidation of **1** were prepared by allowing 10.0 ml of a 0.05 *N* solution of neophyllithium in *n*-pentane (0.50 mmol **1**) to react with 22.0 mg (0.25 mmol) of neopentyl alcohol in a dry 12-ml nitrogen-filled centrifuge tube which was capped with a No-Air stopper. These solutions were transferred to the oxidation apparatus, oxidized, hydrolyzed, and analyzed by glpc as described above.

Aliquots obtained from oxidation experiments carried to partial completion were transferred from the reaction flask by forced siphon under nitrogen through a stainless steel cannula into dry 12-ml nitrogen-filled centrifuge tubes, hydrolyzed, and analyzed.

Attempted Reactions of Neophyllithium with Sodium Superoxide and Lithium Peroxide. Weighed amounts of sodium superoxide (55 mg, 1.0 mmol) or lithium peroxide (46 mg, 1.0 mmol) were placed in dry 12-ml centrifuge tubes. The tubes were capped with No-Air stoppers and flushed with nitrogen. A solution (10 ml, 0.05 *N*) of neophyllithium in pentane (0.50 mmol) was added to the tubes at room temperature; the lithium salts were insoluble in this solvent, and no obvious reaction took place. Similarly, 5.0-ml aliquots of a 0.05 *N* solution of neophyllithium in ether (0.25 mmol) were added to tubes containing 28 mg (0.50 mmol) of sodium superoxide or 23 mg (0.50 mmol) of lithium peroxide. The lithium peroxide appeared to be insoluble, while the sodium superoxide appeared to be slightly soluble. The four heterogeneous reaction mixtures were stirred at room temperature for 4 hr. Glpc analysis of hydrolyzed aliquots showed that no reaction had occurred in any case.

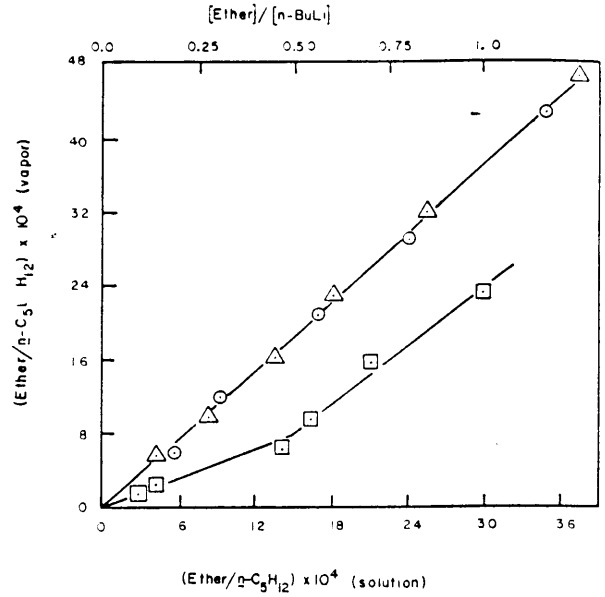

Figure 6. Vapor pressure–composition data used to examine the interaction between diethyl ether and neophyllithium (0.05 *N* in *n*-pentane, △) and *n*-butyllithium (0.10 *N* in *n*-pentane, ⊡). Data obtained in the absence of an organolithium reagent in pentane are indicated by ○. The axes are ratios of the areas due to diethyl ether and *n*-pentane in glpc traces of aliquots taken from the solution and from the vapor over the solution.

Reaction of the Lithium Salt of Neophyl Alcohol with Oxygen. Neophyl alcohol (1.543 g, 10.29 mmol) dissolved in *ca.* 100 ml of ether was allowed to react with 6.0 ml of 1.7 *N* ether solution of methyllithium (10.4 mmol), containing *n*-pentadecane as an internal glpc standard; the resulting lithium alkoxide was soluble at this concentration. A 10-ml aliquot of the solution was titrated to a phenolphthalein end point with 0.10 *N* hydrochloric acid. The total base concentration was 0.12 *N*. Oxygen was bubbled through the remainder of the solution at 0° for 6 hr, then hydrolyzed. Glpc analysis of aliquots taken before and after exposure to oxygen yielded the same ratio of neophyl alcohol to internal standard.

Reaction of *n*-Butyllithium with Oxygen. A 0.05 *N* ether solution of *n*-butyllithium containing *n*-nonane as a glpc internal standard was allowed to react with oxygen in the beveled-bottom oxidation apparatus at room temperature with an oxygen addition rate of 3.1 ml/hr. The two major reaction products were butan-1-ol (25%) and *n*-octane (15%).

Acknowledgment. We are indebted to Dr. Peter West (Dow Chemical Co.) for advice concerning the estimation of strength of coordination of Lewis bases to **1** using vapor-pressure measurements, and Dr. Jeanne Krieger for assistance in drawing the figures.