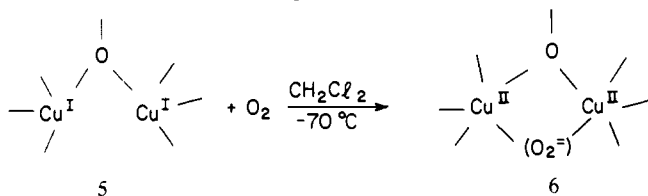bridging ligand is observed for a number of doubly bridged Cu(II) binuclear compounds of this same ligand.[6a,c,16]

When an orange (λ_{max} = 380 nm) dichloromethane solution of **5** is exposed to O_2 below -70 °C, an intense violet color develops due to the formation of the peroxide–Cu(II) complex, **6**. Ma-

nometric measurements at -78 °C indicate that 1 mol of dioxygen is taken up per mol of **5** (Cu:O_2 = 2:1). The visible absorption spectrum (Figure 2) of the violet solution exhibits a new strong transition at 505 nm (ϵ = 6300 M^{-1} cm^{-1}) associated with the formation of **6**. In addition, a band at 385 nm is observed along with an absorption in the d–d region near 610 nm. Confirming evidence for the formulation of **6** as a copper(II)–peroxide complex comes from resonance Raman spectroscopy. Here, a peak at 803 cm^{-1} is assigned to the O–O stretching vibration of a coordinated peroxide group, based on (a) the $^{18}O_2$ isotopic perturbation observed[17a] and (b) a comparison to the O–O stretch values observed for oxyhemocyanins, oxytyrosinase, and ionic peroxides.[17]

The visible absorption spectrum of **6** is significantly different from that of oxyhemocyanin,[1] suggesting that the mode of coordination of the peroxo group must be different. The present study demonstrates that a binuclear Cu(I) center can react with dioxygen to give a stable peroxide-binding Cu(II) compound in a synthetic system. To our knowledge, this is the first example of O_2 binding to Cu(I) where a distinct and strong visible absorption band (505 nm) is observed and where the oxidation state of the coordinated dioxygen ligand (as O_2^{2-}) is confirmed by vibrational spectroscopy.[17,19] At this point, we cannot distinguish between μ-1,1-, μ-1,2-, or terminally bound peroxide.[1-3,21] The Cu(I)···Cu(I) separation of 3.6–3.7 Å observed in **5** compares with that found in oxyhemocyanin,[1,2] suggesting that a μ-1,2-peroxo complex is possible. On the other hand, we have already characterized several phenoxo and X doubly bridged (X = OH,[6b,c] OMe,[6a] Cl,[16] μ-1, 1-N_3[16]) Cu(II) complexes containing **4** where Cu(II)···Cu(II) is ca. 3.1 Å;[6,16,22] thus μ-1,1-O_2^{2-} bridging cannot be ruled out.[23] Further studies of the physical and chemical characteristics of **6** are in progress.

Oxidation of Alcohols to Aldehydes with Oxygen and Cupric Ion, Mediated by Nitrosonium Ion

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Received February 15, 1984

Recent studies have demonstrated the ability of 2,2,6,6-tetramethylpiperidinyl-1-oxy (**1**, Tempo)[1] to mediate alcohol[2,3] and amine[4] oxidation by electrolysis, apparently via the nitrosonium ion **2**. Also under investigation are nonelectrochemical methods of nitroxyl-mediated oxidation. Here we report the room temperature oxidation of allylic and benzylic alcohols by *oxygen* using a catalyst mixture of cuprous chloride and nitroxyl **1**, as well as more general oxidations of primary alcohols, promoted by cupric chloride and mediated by the nitroxyl **1**.

A catalytic sequence for the oxidation by oxygen is proposed in eq 1–4, Scheme I. Cupric ion effects a one-electron oxidation of **1** to nitrosonium ion **2** (eq 1).[5,6] The alcohol is then oxidized by **2** (eq 2), generating the aldehyde and hydroxylamine **3**; rapid syn proportionation[3,4] of **3** with **2** regenerates **1** (eq 3). Finally, Cu(I) is regenerated by oxygen, in a process that consumes protons and gives Cu(II) and water (eq 4),[6] following a general method for recycling cupric ion.[7] The net reaction is alcohol oxidation by oxygen to afford aldehyde and water (eq 5). No net formation of acid is expected, and the usual requirement of added base in nitrosonium ion oxidations[3,4] might be avoided.

In the standard procedure, the alcohol (10 mmol), nitroxyl **1** or its 4-hydroxy analogue (1 mmol, 10 mol %),[8] and CuCl (1

(16) Karlin, K. D.; Hayes, J. C.; Hutchinson, J. P.; Zubieta, J. *J. Chem. Soc., Chem. Commun.* **1983**, 376–378.

(17) (a) Pate, J.; Solomon, E. I.; Cruse, R. W.; Karlin, K. D., to be published. (b) The peroxide stretch in oxyhemocyanins occur between 744 and 752 cm^{-1}, while that for oxytyrosinase (*Neurospora crassa*) occurs at 755 cm^{-1}.[1,18] ν_{O-O} for ionic peroxides and superoxide (O_2^-) occurs at ca. 800 and 1100 cm^{-1}, respectively.

(18) Eickman, N. C.; Solomon, E. I.; Larrabee, J. A.; Spiro, T. G.; Lerch, K. *J. Am. Chem. Soc.* **1978**, *100*, 6529–6531 and references therein.

(19) a number of Cu(I) complexes bind dioxygen reversibly or quasireversibly with the stoichiometry Cu:O_2 = 2:1. No vibrational data that confirm the formation of bound peroxide to Cu(II) have been reported.[20]

(20) (a) Simmons, M. G.; Merrill, C. L.; Wilson, L. J.; Bottomley, L. A.; Kadish, K. M. *J. Chem. Soc., Dalton Trans.* **1980**, 1827–1837. (b) Bulkowski, J. E.; Burk, P. L.; Ludmann, M.-F.; Osborn, J. A. *J. Chem. Soc., Chem. Commun.* **1977**, 498–499. (c) Agnus, Y.; Louis, R.; Weiss, R. *J. Am. Chem. Soc.* **1979**, *101*, 3381–3384. (d) Nishida, Y.; Takahashi, K.; Kuramoto, H.; Kida, S. *Inorg. Chim. Acta* **1981**, *54*, L103–L104. (e) Bulkowski, J. E.; Summers, W. E., III In ref 4, pp 445–457.

(21) Although it would seem unlikely in the present system, terminal binding of peroxide to only one of the two copper ions cannot be ruled out. Recent data indicate that peroxide in the binuclear iron center in hemerythrin is only bound to one iron atom. Elam, W. T.; Stern, E. A.; McMallum, J. D.; Sanders-Loehr, J. *J. Am. Chem. Soc.* **1983**, *105*, 1919–1923 and references therein.

(22) Karlin, K. D.; Hayes, J. C.; Zubieta J. In ref 4, pp 457–472.

(23) μ-1,1-Peroxo bridging is known to occur in cobalt complexes. Durand, R. R., Jr.; Bencosme, C. S.; Collman, J. P.; Anson, F. C. *J. Am. Chem. Soc.* **1983**, *105*, 2710–2718 and references therein.

(1) This reagent has been studied extensively by Golubev, Rozantsev, and co-workers, including formation of nitrosonium **2** and its reaction with organic functional groups. For leading references, see: Golubev, V. A.; Rozantsev, E. G.; Neiman, M. G. *Izv. Acad. Nauk SSSR* **1978**, 1874–1881.

(2) A mixture of *m*-chloroperoxybenzoic acid and **1** has been used to oxidize alcohols to aldehydes: (a) Cella, J. A.; Kelley, J. A.; Kenehan, E. F. *J. Org. Chem.* **1975**, *40*, 1860–1862. (b) Ganem, B. *Ibid.* **1975**, *40*, 1998–1999.

(3) Semmelhack, M. F.; Chou, C. S.; Cortés, D. A. *J. Am. Chem. Soc.* **1983**, *105*, 4492.

(4) Semmelhack, M. F.; Schmid, C. R. *J. Am. Chem. Soc.* **1983**, *105*, 6732.

(5) While a number of inorganic oxidants are known to convert **1** to **2**, this is the first report of Cu(II) providing this conversion. (a) With Sb(IV): Golubev, V. A.; Voronina, G. N. *Izv. Acad. Nauk SSSR* **1972**, 150. (b) With Sn(IV): Takaya, Y.; Matsubayashi, G.; Tanaka, T. *Inorg. Chem. Acta* **1972**, *6*, 339. (c) With Pd(II): Okunaka, M.; Matsubayashi, G.; Tanaka, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 907. (d) With Ti(IV) and Zr(IV): Golubev, V. A.; et al. *Bull. Acad. Sci.* **1977**, 1669.

(6) Electrochemical studies indicate that Cu(II) can indeed oxidize **1** to **2**. We find $E_{1/2}$ = +0.7 V (vs. Ag/Ag(I)) for the reversible CuCl/$CuCl_2$ couple (cyclic voltammetry at Pt) in dry acetonitrile containing 0.5 M $LiClO_4$. Under the same conditions, the redox couple **1/2** shows $E_{1/2}$ = +0.33 V (vs. Ag/Ag(I)).

(7) For example, a similar cycle is observed in the well-studied Wacker process: Szoni, G. *Adv. Chem. Ser.* **1968**, *70*, 53.

mmol, 10 mol %) are mixed with 25 mL of DMF and stirred at 25 °C. Oxygen is bubbled through the solution by use of a gas dispersion tube (50–60 mL/min). After the starting alcohol is consumed, the mixture is partitioned between 10% aqueous HCl and ether. From the ether solution, the pure aldehyde is isolated by chromatography (SiO$_2$) and short-path distillation. Although aliphatic alcohols do not give complete conversions under these conditions,[9] benzylic and allylic alcohols give aldehydes in high yield, with no sign of overoxidation (Table I). With the allylic alcohols in entries 10–12, no E/Z double-bond isomerization was detected. The usual selectivity[3] for primary over secondary alcohols is amplified; cyclohex-2-en-1-ol is inert over 18 h under these conditions (Table I entry 14). Electron-withdrawing groups on the arene ring in benzylic alcohols tend to retard the reaction (compare entries 6–8, Table I).

The useful limits and optimum reaction parameters were probed with *p*-methoxybenzyl alcohol (entries 1–6, Table I). The reaction is useful at −20 °C (but too slow at −60 °C), on larger scale (0.1 mol), at high concentration (1:1 v/v DMF/alcohol, 6.67 M), and with only 1 mol % of the catalysts. Most of the other alcohols tested failed to give complete conversion with less than 5–10 mol % catalyst. A variety of cupric salts with noncoordinating counterions (e.g., BF$_4$) were effective catalysts, but CuCl$_2$ and CuBr$_2$ failed to give efficient catalysis. At the same time, CuCl was found to be effective, suggesting a specific effect of chloride stoichiometry. Indeed, addition of an equimolar amount of NaCl to the "standard procedure" with CuCl led to strong inhibition and only 30–40% conversion of the alcohols.[10] Rigorous anhydrous conditions are not necessary; a medium of 5% aqueous DMF gives similar rates and yields.

Stoichiometric amounts of cupric ion can bring about oxidation of allylic, benzylic, *and* primary aliphatic alcohols using nitrosonium ion mediation. Under these conditions CuCl$_2$ is the reagent of choice, and a base is necessary to take up the HCl that is generated. The optimum conditions involve mixing the alcohol (50 mmol), nitroxyl **1** (10 mmol), CuCl$_2$ (110 mmol), and CaH$_2$ (150 mmol) in 100 mL of acetonitrile at 25 °C with overhead stirring. Freshly opened samples of CaH$_2$ (-40 mesh) consistently gave induction periods of 1–2 h. The entries in Table II are based on reactions with CaH$_2$ that had been allowed to age open to the atmosphere for 15 min and showed no induction period.[11] After reaction is complete, the solution is diluted with ether and filtered through a pad of Florsil. The filtrate is washed sequentially with NaI in 10% HCl (iodide anion reduces **1** and **2** to **3**, which is removed in the aqueous acid) and with aqueous sodium thiosulfate, and the aldehyde is isolated as usual. A series of successful examples is presented in Table II.

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(8) As described earlier,[4] the 4-hydroxy derivative **i** has significantly lower
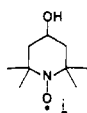
R_f on silica gel chromatography than typical aldehydes and ketones, facilitating removal of the residual reagent. It does not otherwise interfere, although the secondary hydroxyl group will be oxidized over extended periods under these conditions.

(9) The nitrosonium ion appears to decompose in the presence of aliphatic aldehydes and O$_2$; initial conversions are high, with rates comparable to allylic and benzylic alcohols, but the reactions slow dramatically at 30–40% conversion (using 10 mol % of **1**).

(10) A series of control experiments according to the standard procedure but leaving out each of the key reactants in turn (O$_2$, CuCl, **1**) demonstrated that each was necessary for efficient operation of the catalytic cycle.

(11) A series of experiments in which various components of the reaction mixture (CaH$_2$ powder, the suspension of CaH$_2$ in CH$_3$CN, and the suspension of CuCl$_2$ in acetonitrile) were allowed to age before the remaining components were added demonstrated that the induction period is due to the condition of the CaH$_2$. The basis for the induction period is not yet understood.

(12) A more complete study of intramolecular selectivity was carried out using the electrochemical system.[3]

Scheme I. Steps in the Catalytic Cycle of Oxidation of Oxygen
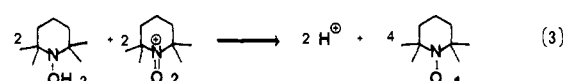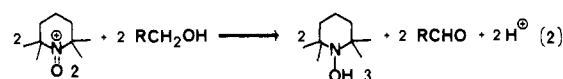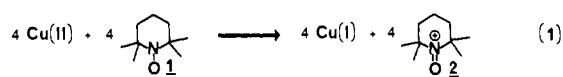
Table I. Conversion of Alcohols to Aldehydes with Oxygen[a]

entry	alcohol	aldehyde	time, h	yield[b]
1	*p*-MeOC$_6$H$_4$CH$_2$OH	*p*-MeOC$_6$H$_4$CHO	1.0	96%
2	*p*-MeOC$_6$H$_4$CH$_2$OH	*p*-MeOC$_6$H$_4$CHO	24.0[c,e]	97%
3	*p*-MeOC$_6$H$_4$CH$_2$OH	*p*-MeOC$_6$H$_4$CHO	1.0[e,f]	92%
4	*p*-MeOC$_6$H$_4$CH$_2$OH	*p*-MeOC$_6$H$_4$CHO	2.0[f,g]	91%
5	*p*-MeOC$_6$H$_4$CH$_2$OH	*p*-MeOC$_6$H$_4$CHO	6.0[h]	80%
6	*p*-MeOC$_6$H$_4$CH$_2$OH	*p*-MeOC$_6$H$_4$CHO	7.0[i]	25%[j]
7	C$_6$H$_5$CH$_2$OH	C$_6$H$_5$CHO	4.0[k]	94%[d]
8	*p*-NO$_2$C$_6$H$_5$CH$_2$OH	*p*-NO$_2$C$_6$H$_4$CHO	7.0	85%
9	piperonyl alcohol	piperonal	16.0[l,m]	85%
10	(*E*)-hex-2-en-1-ol	(*E*)-2-hexenal	1.75	100%[d]
11	geraniol	geranial	1.75	92%
12	cinammyl alcohol	cinammaldehyde	2.75	93%
13	myrtenol	myrtenal	2.0	92%
14	2-cyclohexenol	2-cyclohexenone	18.5[n]	0%

[a] Unless otherwise noted, according to the standard procedure: 10 mmol of alcohol, 1.0 mmol of CuCl, 1.0 mmol of **1**, 0.4 M in DMF (25 mL), at 25 °C. [b] Unless otherwise noted, the yields are based on distilled or chromatographed material. [c] Using 1 mol % of CuCl and of **1**. [d] Determined by GLPC analysis of the crude product. [e] At 1.0 M in DMF. [f] Using 100 mmol of alcohol, 10 mmol of CuCl, and 10 mmol of **1**. [g] At 6.67 M in alcohol in DMF. [h] At −20 °C. [i] At −60 °C. [j] 75% unreacted alcohol detected by NMR analysis on the crude product. [k] 5 mol % CuCl and **1**. [l] 2 mol % CuCl and **1**. [m] Using 25 mmol alcohol. [n] 100 mol % of CuCl and **1**.

Table II. Cupric Ion Oxidation of Alcohols[a]

entry	alcohol	product	time, h	yield
1	Ph(CH$_2$)$_2$CH$_2$OH	Ph(CH$_2$)$_2$CHO	4.5	86%
2	*p*-MeOC$_6$H$_4$CH$_2$OH	*p*-MeOC$_6$H$_4$CHO	3.0	90%
3	myrtenol	myrtenal	3.0	93%
4	1,8-dihydroxynonane	8-hydroxynonanal	10.0	55%[b]
5	(structure)	(structure)	17.0	74%[c]

[a] Standard procedure (see text) on 50-mmol scale. [b] 10-mmol scale. [c] The acid-sensitive product was isolated by filtration and concentration of the reaction mixture followed by chromatographic purification.

Secondary alcohols are oxidized very slowly even with excess nitroxyl **1** and copper. Under the conditions of Table II, 2-hexanol shows 21% conversion after 6 h, 25 °C, and 54% after 24 h. Somewhat more hindered, 5-decanol gives only 39% conversion in 75 h. This provides a useful selectivity: a mixture of 1-hexanol and cylohexanol showed 60% conversion of the primary alcohol after 2 h, with 0% conversion of cyclohexanol. Similarly, intramolecular selectivity is demonstrated with 1,8-nonanediol (Table II, entry 4). At >98% conversion, a 19:1 ratio of 8-hydroxy-

nonanal to 8-ketononanal is detected; the hydroxy aldehyde is obtained in 55% yield after purification.

Alkoxy Stabilization and Synthetic Utility of Tetrahedral Carbanions

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Received July 22, 1983

Heteroatom-substituted carbanions have been intensively studied in efforts to understand substituent effects on carbon acidity and to exploit the broad synthetic utility of these reactive species. Enhancement of the thermodynamic and kinetic acidity of carbon acids by many second-, third-, and fourth-row elements has been well established.[1] In contrast, although calculations suggest that oxygen substitution considerably increases carbanion stability,[2] experimental efforts have not yet provided unambiguous documentation of this effect.[1a,3] We report here a study supporting the considerable stabilizing influence of α-alkoxy groups upon lithium carbanions, as well as demonstration of the synthetic utility of some carbanions of this type.

A careful study of the tin–lithium exchange in eq 1 was undertaken
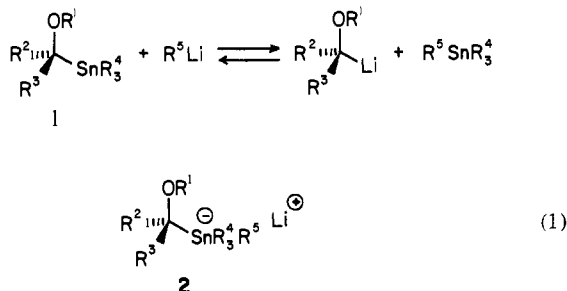
dertaken to ascertain the structural dependence of the position of this equilibrium.[4] Low-temperature ^{1}H NMR spectroscopy demonstrated that exchange took place to afford discreet organolithium species, with no evidence of a stannylate complex, 2, and was complete within 10 min at –60 °C in DME.[5,6] By

Table I. Reactions of α-Alkoxy Organolithium 1 with Various Electrophiles

	EtCHO	PhCHO	Me-CO-Me	H⁺(MeOH)	MeI	Me₂SO₄	Allyl-Cl	n-BuI
5ᵇ	73%	86%	70%	86%	8,69%	61%	5(R=H),60%	5(R=H),35% 8,61%
6ᵇ	82%	—	—	89%	—	90%	—	—
7ᶜ	89%ᶜ	91%ᶜ	62%	90%	65%	—	88%	92%

^{a} R = SnBu₃ + BuLi → R = Li. ^{b} ~2:1 mixture of isomers.

examining competitive exchange reactions of several α-alkoxy tri-n-butyl- and trimethylstannanes with n-BuLi and MeLi, the following order of relative stabilities was established (R′ = CH₂OMe):[6]
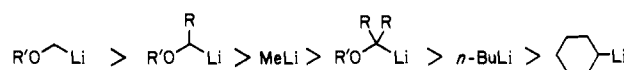
Since these competitive equilibration experiments completely favored a single organolithium species, as judged by ^{1}H NMR analysis, a minimum of 2 kcal/mol or 1.5 pK_a units separates each species in the above series. This demonstrates a substantial thermodynamic stabilizing influence of oxygen upon carbanionic centers which may be attributable to an inductive effect, an optimal orientation of the heteroatom lone pair, differences in the states of aggregation of the organolithium species, or a combination of these effects.[2]

These tin–lithium exchange processes are subject to kinetic factors in addition to the above thermodynamic considerations. The rate of exchange is strongly dependent upon the solvent employed (DME > THF > Et₂O) and the steric environment about the trialkylstannyl group [Me₃Sn >> (n-Bu)₃Sn >> (c-C₆H₁₁)₃Sn] (c-C₆H₁₁ = cyclohexyl). In the present study, dialkylalkoxymethyllithium species were conveniently generated only in DME. However, (phenylalkylalkoxymethyl)lithium species could be produced via tin–lithium exchange utilizing the trimethylstannyl moiety, rather than the tri-n-butylstannyl, in a variety of solvents (DME, THF, Et₂O). This contrasting behavior could be readily predicted through considerations of the thermodynamic stabilities of the relevant carbanions [e.g., 1 (R₂ = Me, R₃ = Ph > Me].

Considerable utility is conferred upon these (dialkylalkoxymethyl)lithium species by virtue of their stereospecific generation from the precursor stannane with retention of configuration *and* their stereospecific reaction with electrophiles with retention of configuration. This was demonstrated through a study of the α-alkoxy stannane species 3 and 4 derived from 4-*tert*-butylcyclohexanone. The ratio of axial to equatorial stannanes (3 and

(1) For reviews of heteroatom-substituted carbanions, see: (a) Krief, A. *Tetrahedron* 1980, *36*, 2531. (b) Beak, P.; Reitz, D. B. *Chem. Rev.* 1978, *78*, 275. (c) Ahlbrecht, H. *Chimia* 1977, *31*, 391. (d) Seebach, D.; Geiss, K.-H. In "New Applications of Organometallic Reagents in Organic Synthesis"; Seyferth, D., Ed.; Elsevier: Amsterdam, 1976, p 1.

(2) (a) Rondan, N. G.; Houk, K. N.; Beak, P.; Zajdel, W. J.; Chandrasekhar, J.; Schleyer P. v. R. *J. Org. Chem.* 1981, *46*, 4108. (b) Clark, T.; Schleyer, P. v. R.; Houk, K. N.; Rondan, N. G. *J. Chem. Soc., Chem. Commun.* 1981, 579. (c) Clark, T.; Korner, H.; Schleyer, P. v. R. *Tetrahedron Lett.* 1980, *21*, 743. (d) Lehn, J.-M.; Wipff, G. *J. Am. Chem. Soc.* 1976, *98*, 7498.

(3) (a) Cohen, T.; Matz, J. R. *J. Am. Chem. Soc.* 1980, *102*, 6900 and references therein. (b) Bordwell, F. G.; Van der Puy, M.; Vanier, N. R. *J. Org. Chem.* 1976, *41*. (c) Hunter, D. H.; Lin, Y.-t; McIntyre, A. L.; Shearing, D. J.; Zvagulis, M. *J. Am. Chem. Soc.* 1973, *95*, 8327. (d) Shatenshtein, A. I.; Gvozdeva, H. A. *Tetrahedron* 1969, *25*, 2749. (e) Slaugh, L. H.; Bergman, E. *J. Org. Chem.* 1961, *26*, 3158. (f) Dessy, R. E.; Kitching, W.; Psarras, T.; Salinger, R.; Chen, A.; Chivers, T. *J. Am. Chem. Soc.* 1966, *88*, 460.

(4) For recent utility of this exchange reaction, see: (a) McGarvey, G. J.; Kimura, M. *J. Org. Chem.* 1982, *47*, 5420. (b) Still, W. C.; Sreekumar, C. *J. Am. Chem. Soc.* 1980, *102*, 1201. (c) Still, W. C. *Ibid.* 1978, *100*, 1481. (d) For early work on this exchange process, see: Seyferth, D. *Ibid.* 1964, *86*, 883.

(5) Equilibration of the exchange reaction was judged complete when a stable ratio of integration values for the carbon–tin and carbon–lithium species were obtained. Integration values were reproducible to ±5% with a detection limit for the carbon–lithium species present (e.g., n-BuLi, MeLi) of at least 5% (of the theoretical amount of RLi introduced) at equilibrium. NMR data were confirmed by quantitative chromatographic and spectral analysis[7] of the products derived from protonation of the reaction mixture.

(6) The following tetraalkyl stannanes were synthesized[7] and analyzed for ligand exchange with methyllithium and n-butyllithium via low-temperature (–60 °C) NMR spectroscopy in deuterated solvents (THF, DME): Me₄Sn, n-BuSnMe₃, Me₃SnCH₂OMOM, Me₃SnCH(Me)OMOM, 1-Me₃Sn-(c-C₆H₁₁)-1-OMOM, 1-(n-Bu₃)Sn-1-(c-C₆H₁₁)-1-OMOM, n-Bu₃Sn(c-C₆H₁₁) (MOM = methoxymethyl).

(7) Satisfactory spectral and analytical data was obtained for all new compounds. Compounds 5 (R = H, Me), 6 (R = H, Me, EtCHOH), and 7 (R = H, Me, n-Bu, allyl) were confirmed by independent synthesis.