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**Reaction of *n*-Butyllithium and
2,2,6,6-Tetramethylpiperidine Nitroxyl¹**

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Stable nitroxyl radicals²⁻⁴ are widely used as radical scavengers⁴ and as probes for certain types of molecular motion.⁵ In the course of other problems that utilized ni-

Table I
Products from Reaction of *n*-Butyllithium and
2,2,6,6-Tetramethylpiperidine Nitroxyl (TEMPO)

Product	Yield, % ^a	
	Based on BuLi	Based on TEMPO
Butane	13	
Butene	4	
Octane	1	
Di- <i>n</i> -butyl ether	2	
<i>n</i> -Butyl alcohol	14	
TEMPOBu	65	46
TEMP		11
TEMPOH ^b		11
TEMPOCH ₃ ^c		33
Total	99	101

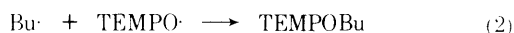
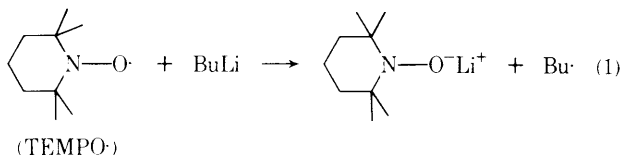
^a The reaction for which these products are reported consumed 1.27 mmol of *n*-butyllithium and 1.80 mmol of TEMPO. ^b TEMPOH was detected by GLC as the quantitative conversion of TEMPOH to TEMPO in the injection port of the GLC was demonstrated using authentic TEMPOH. ^c TEMPOCH₃ is formed from TEMPOLi⁺ by alkylation with dimethyl sulfate.

troxyl radicals in these applications, we required a procedure for destroying these radicals rapidly and quantitatively at low temperature in hydrocarbon solution. Here we report that the reaction of *n*-butyllithium with nitroxyl radicals is an effective method for accomplishing this objective, and describe the products of a representative reaction.

Results and Discussion

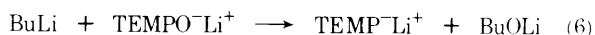
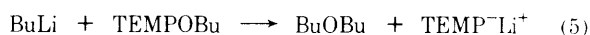
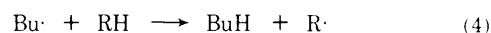
Addition of *n*-butyllithium (1.6 mmol, an excess) to a solution of 1.8 mmol of 2,2,6,6-tetramethylpiperidine nitroxyl^{2,3,6} in *n*-hexane solution at -70° resulted in rapid disappearance (<1 min) of the characteristic red color of the stable radical. The resulting mixture was treated with 1,2-dibromoethane in order to convert excess *n*-butyllithium to *n*-butyl bromide. An aliquot of this reaction mixture was hydrolyzed and analyzed by GLC. A second aliquot was first treated with dimethyl sulfate to O-methylate lithium 2,2,6,6-tetramethylpiperidine nitroxide and facilitate its analysis by GLC, then hydrolyzed and analyzed. Table I summarizes the observed yields of products. These yields are corrected for the quantities of butane and butenes present in the starting *n*-butyllithium solution, and for the presence of 0.33 mmol of *n*-butyl bromide—representing unreacted *n*-butyllithium—among the products. They therefore represent the products of a reaction that consumed 1.27 mmol of *n*-butyllithium and 1.80 mmol of the nitroxyl radical. For convenience, the starting nitroxyl radical and the products derived from it are abbreviated as derivatives of tetramethylpiperidine (TEMP): thus, the nitroxyl radical is abbreviated TEMPO·, *N*-*n*-butoxytetramethylpiperidine is abbreviated TEMPOBu, and similar abbreviations are used for related compounds.

A detailed examination of the mechanisms leading to those products has not been carried out. A plausible sequence leading to the major products starts with one-electron oxidation of *n*-butyllithium by TEMPO·,^{7,8} followed by coupling of a second equivalent of TEMPO· with the resulting *n*-butyl radical (eq 1 and 2). The extent of aggrega-



tion of the *n*-butyllithium may play a role in this reaction,⁹ but has not been explored. It is ignored in this formulation.

The variety of other products formed in the reaction clarifies the deviation of the stoichiometry of the reaction from the 2TEMPO:1BuLi expected on the basis of these two equations. Most of these products can be rationalized using straightforward reactions (eq 3–6).



Reactions 5 and 6 are similar to the well-established cleavage of the oxygen–oxygen bond of dialkyl peroxides and lithium hydroperoxides by organolithium reagents.^{9–11} Since these reactions appear to involve intermediate free alkyl radicals,¹¹ they may also contribute to other products formed. The observation among the products of a small quantity of a substance not alkylated by dimethyl sulfate and listed in Table I as TEMPOH is difficult to explain, and is probably an artifact. Independent experiments established that the conversion of authentic TEMPO[−]Li⁺ to TEMPOCH₃ by dimethyl sulfate was quantitative under the conditions employed in this assay. The presence of a derivative of TEMPO· that was not alkylated by dimethyl sulfate is compatible with its formulation as TEMPOH, but incompatible with the presence of a species having an acidic OH group in a solution containing butyllithium. It seems possible that TEMPO[−]Li⁺ present in this reaction mixture is less reactive than that in a solution containing only TEMPO[−]Li⁺ by virtue of its complexation with other species present in the mixture. In this event, the quantity of TEMPO[−]Li⁺ actually produced in the reaction should be considered to be the sum of the entries in Table I for TEMPOH and TEMPOCH₃.

The small quantities of butene and octane formed do not merit discussion, other than to note that the bimolecular reaction of butyl radicals would be expected to yield butene (by disproportionation) and octane (by coupling) in a ratio of approximately 1:7.¹² Thus, most of the butene and butane are formed by reactions other than bimolecular radical–radical disproportionation of *n*-butyl radicals. The coupling of TEMPO· and *n*-butyl radical generates little butane or butene (<5%).⁸ Hence the majority of the butane formed in the reaction of butyllithium and TEMPO· probably results from hydrogen abstraction from some other component of the reaction system, probably by *n*-butyl radicals. The major hydrogen donor has not been identified.

Attempts to reduce the importance of reaction 2, and thereby to increase the probability of reaction between butyllithium and butyl radicals, by adding TEMPO· very slowly to an excess of butyllithium were only partially successful. The yield of TEMPOBu was decreased from 46 to 25% under the best conditions examined, and the relative yield of butane was significantly increased. The product balance in these experiments was not, however, sufficiently high to justify development of this system as a method of generating alkyl radicals in the presence of alkyl lithium reagents.

In summary, the reaction of butyllithium with TEMPO· (and with other nitroxyl radicals examined) provides a rapid method of converting the radical to diamagnetic products.¹⁴ The reaction mechanism has not been established in any detail, but the reaction products are compatible with initial one-electron oxidation of the organolithium reagent by the nitroxyl radical.

Experimental Section

Organometallic reagents were manipulated using standard procedures.¹⁵ GLC analyses were carried out using an F & M Model 810 instrument and flame ionization detection, by unexceptional internal standard techniques. Butane and butene analyses utilized a 3-ft 3% Apiezon on alumina column; other analyses utilized an 8-ft 20% UC-W98 silicone rubber on Chromosorb P column. *n*-Hexane was purified by distillation under nitrogen from a suspension of sodium benzophenone ketyl. THF was distilled from LiAlH₄ and DME from disodium benzophenone dianion. TEMPO \cdot was prepared by oxidation of TEMP with hydrogen peroxide catalyzed by sodium phosphotungstate;⁶ it had mp 34–35° (lit.⁶ mp 39°). Reagent dimethyl sulfate was purified by washing with cold saturated sodium bicarbonate solution and drying over potassium carbonate.¹⁶ The dry solution was transferred to a Schlenk tube and traces of methanol were removed by a vacuum of 0.05 Torr. The dimethyl sulfate was stored in the Schlenk tube under prepurified nitrogen. It was reevacuated before use. Organolithium reagents were supplied by Foote Mineral Co., and were analyzed by the Gilman double titration method.¹⁷

***N*-Methoxy-2,2,6,6-tetramethylpiperidine (TEMPOCH₃).** DME (50 ml), 0.147 g (6.4 mg-atoms) of sodium metal, and 0.885 g (5.67 mmol) of freshly sublimed 2,2,6,6-tetramethylpiperidine nitroxyl were added to a flame-dried round-bottomed flask equipped with a condenser and a magnetic stirring bar and stoppered with a serum cap. The mixture was stirred under nitrogen at ambient temperature for 8 hr. Iodomethane (0.805 g, 5.67 mmol) was added to the resulting pale yellow solution of TEMPO \cdot -Na⁺, and the solution was stirred for an additional 4 hr under nitrogen. The reaction solution was saturated with sodium chloride, extracted with 50 ml of ether, and washed with distilled water and saturated sodium chloride solution. The ether was dried (MgSO₄) and concentrated to give a crude oil which was purified by column chromatography. The product was eluted from 6 g of silica gel G with 40 ml of cyclohexane followed by 40 ml of benzene, to give 0.4 g (41%) of *N*-methoxy-2,2,6,6-tetramethylpiperidine, having ir (CCl₄) 2980, 2930, 2810, 1475, 1385, 1355, 1060 cm⁻¹; NMR (CCl₄) δ 3.6 (s, 3 H, OCH₃), 1.0–1.5, multiplet (18 H); mass spectrum (70 eV) *m/e* (rel intensity) 171 (10.5), 156 (100), 88 (17), 69 (16), 55 (15), 41 (17).

***N*-Butoxy-2,2,6,6-tetramethylpiperidine (TEMPOBu).** The procedure for synthesizing TEMPOCH₃ was repeated using 1-iodobutane instead of 1-iodomethane, yielding 0.196 g (19%) of *N*-butoxy-2,2,6,6-tetramethylpiperidine, a colorless liquid, having ir (CCl₄) 2990, 2980, 2970, 2810, 1450, 1380, 1365, 1260, 1250, 1210, 1190, 1140, 1070, 1050 cm⁻¹. This ir spectrum was indistinguishable from that of TEMPOBu collected by GLC from a typical reaction of 2,2,6,6-tetramethylpiperidine and *n*-butyllithium. TEMPOBu had NMR (CCl₄) δ 3.6 (t, 2 H, *J* = 7 Hz, OCH₂-), 1.0–1.8 (m, 25 H).

Anal. Calcd for C₁₃H₂₇NO: C, 73.20; H, 12.74; N, 6.57. Found: C, 73.06; H, 12.62; N, 6.44.

Lithium 2,2,6,6-Tetramethylpiperidine Nitroxide. A solution of 0.03 g (0.192 mmol) of TEMPO \cdot in 3 ml of DME was titrated to a colorless end point with 0.47 *M* lithium naphthalenide in DME, giving lithium 2,2,6,6-tetramethylpiperidine nitroxide and naphthalene. Hydrolysis of this solution afforded *N*-hydroxy-2,2,6,6-tetramethylpiperidine. Treatment with dimethyl sulfate yielded TEMPOCH₃ in quantitative yield.

Reaction between *n*-Butyllithium and 2,2,6,6-Tetramethylpiperidine Nitroxyl. Typical Procedure. Freshly sublimed TEMPO \cdot (0.278 g, 1.8 mmol) and ca. 10 ml of *n*-hexane were added under nitrogen to a dry, stoppered, 40-ml centrifuge tube. *n*-Dodecane (104 mg) and *n*-pentane (28 mg) were added as internal GLC standards, and the solution was cooled to -78° in a Dry Ice-iso-propyl alcohol bath. One milliliter of 1.60 *M* *n*-butyllithium was

added to the mixture by syringe. When the reaction was complete, excess *n*-butyllithium was quenched with ca. 100 mg (0.535 mmol, 0.05 ml) of 1,2-dibromoethane. Five milliliters of the resulting solution was transferred to another dry centrifuge tube and hydrolyzed with 0.5 ml of distilled water. The remaining solution was treated with 0.2 ml (excess) of dimethyl sulfate, and shaken vigorously for 1 min. The products were analyzed by GLC. The hydrolyzed sample was used for butane, butene, and 2,2,6,6-tetramethylpiperidine analyses, the alkylated sample for all others. The results of this and similar reactions are summarized in Table I.

Registry No.—TEMPOCH₃, 34672-84-9; 2,2,6,6-tetramethylpiperidine nitroxyl (TEMPO), 2564-83-2; iodomethane, 74-88-4; TEMPOBu, 56514-19-3; 1-iodobutane, 542-69-8; *n*-butyllithium, 109-72-8.

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