

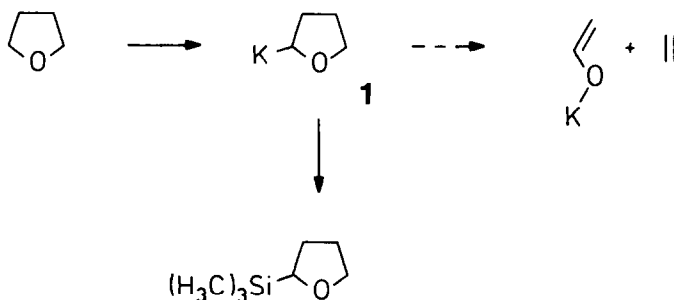
FACILE HYDROGEN/METAL EXCHANGE BETWEEN BUTYLPOTASSIUM AND SATURATED ETHERS

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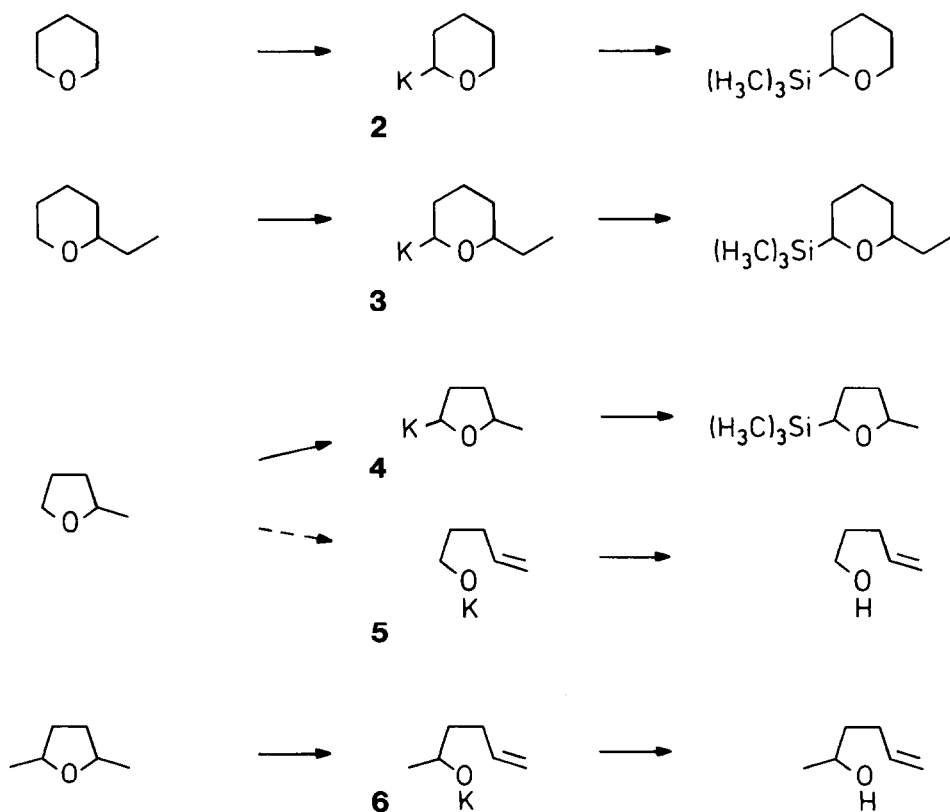
Summary : At temperatures between -100 and -40°C , lithium salt-free butylpotassium (prepared from dibutylmercury) readily metalates saturated ethers such as dimethyl ether or tetrahydrofuran.

In a systematic search for differences between pure organopotassium compounds and "LICKOR reagents" we have compared both with respect to their solubility and stability in ethers such as tetrahydrofuran (THF) ¹. The equimolar mixture of butyllithium and potassium *tert*-butoxide was found to survive when kept for hours in THF solution at -50°C . In contrast, as soon as butylpotassium prepared from dibutylmercury had dissolved in THF ² at -75°C it was consumed in a reaction generating 2-tetrahydrofuryl potassium (1) as the main product. When chlorotrimethylsilane was added 15 min later, the new potassium compound was trapped as 2-trimethylsilyl-tetrahydrofuran (76%) ^{3, 4}. Slowly at -75°C and rapidly at -50°C , 1 decomposed by fragmentation ⁵ to ethylene and the potassium enolate of acetaldehyde.

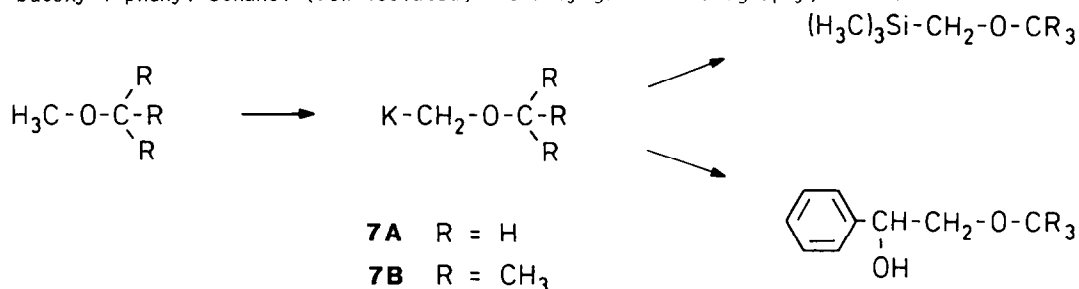


In contradiction to literature ⁶, butylpotassium proved to be entirely inert towards hexane, cyclopentane or other paraffins ^{7, 8}. Therefore, the high reactivity of THF must originate from a specific activating effect of the oxygen atom. Some indirect evidence seemed to argue in favor of a chain process involving butyl and 2-tetrahydrofuryl ⁹ radicals as alternating transient species. Such a mechanism would account for the unusually high reaction rate (estimated $E_a \leq 10$ kcal/mol) as for the inertness of "LICKOR reagents" under the same conditions (lithium compounds, particularly when aggregated, being efficient traps for free radicals ¹⁰).

An extension of our investigation to other substrates, however, led us to refute the radical hypothesis in favor of an ordinary four-center type metalation mechanism⁸ in which the oxygen atom provides neighboring-group assistance through complexation⁷ or, less probable, inductive effects¹¹. Tetrahydropyran was found to undergo again smooth metalation, giving the potassium compound **2** (68% isolated as the trimethylsilyl derivative³). As revealed by competition experiments, however, it reacted approximately 25 times slower than THF. Oxepane (hexamethylene oxide) reacted even more sluggishly and gave only a 27% yield of the corresponding trimethylsilyl-substituted product³. Ring strain is known to enhance CH-acidity but to impede homolytic scissions¹². On the other hand, alkyl branching should facilitate radical processes while it seriously hinders a concerted hydrogen/metal exchange. 2-Ethyl-tetrahydropyran was found to react exclusively at the unsubstituted α -methylene group (52% of **3** trapped as a trimethylsilyl derivative having the *cis*-configuration³). Besides predominant α -methylene metalation (21% of **4** trapped as a *cis/trans*-mixture³), 2-methyl-tetrahydrofuran is subject to concomitant β -elimination affording under ringopening 4-penten-1-ol (9% via alcoholate **5** and consecutive products¹³). Starting with *cis*- and *trans*-2,5-dimethyl-tetrahydrofuran, 5-hexen-2-ol (60% as the trimethylsilyl ether via alcoholate **6**) was identified as the exclusive product.



Dimethyl ether is metalated by butyl potassium with particular ease, the resulting methoxy-methylpotassium (7A) being perfectly stable below -60°C (27% trapped with chlorotrimethylsilane, 75% with benzaldehyde³). In a similar way, *tert*-butyl methyl ether was converted via the α -potassium compound (7B) into *tert*-butoxymethyl-trimethylsilane (43%) and 2-*tert*-butoxy-1-phenyl-ethanol (73% isolated; > 95% by gas chromatography)^{3, 14}.



Previously, a few α -lithio ethers such as methoxymethyl lithium or tetrahydropyranyl lithium have been described^{15, 16}. Their preparation, however, requires fairly laborious methods relying on halide¹⁵ or thioether¹⁶ cleavage with elementary metals or metal/metal exchange reactions¹⁷.

Working procedure : Dibutylmercury (0.79 g, 2.5 mmol) was added dropwise to a vigorously stirred suspension of potassium/sodium alloy (0.5 mL) in pentane (25 mL). After 30 min the solvent was stripped off and, at -75°C , the residue dissolved in precooled tetrahydropyran (10 mL). The mixture was kept 5 h at -45°C , then cooled to -75°C , treated with chlorotrimethylsilane (0.70 mL, 5.5 mmol), and allowed to reach slowly (1 h) 25°C . Again at -75°C , 10 mL pentane and 10 mL water were added. The organic layer was separated, washed and dried. The yield (based on dibutylmercury) was determined by gas chromatography (55 m Apiezon L, 100°C , octane as an internal standard after calibration). Then the product was isolated by distillation; bp. $86 - 88^{\circ}\text{C}/12 \text{ mmHg}$; 0,45 g. In other cases it was advantageous to use a 1 : 1 ether/pentane mixture rather than the neat liquid of the ether.

Acknowledgment. The work underlying this and the preceding communication was supported by the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung, Bern (grants no. 2.885.0-80 and 2.635.0-82).

References and notes

- [1] M. Schlosser and S. Strunk, preceding communication.
- [2] The same result was obtained in a THF/pentane (3 : 1) mixture at -100°C .
- [3] All new products were characterized by correct elemental analyses and appropriate spectroscopic data.

- [4] It was claimed, that 2-tetrahydrofuryl lithium was quenched with heavy water after 4 min exposure of tetrahydrofuran to butyllithium at +35°C (R. Bates, L. Kroposki and D. Potter, *J. Org. Chem.* 1972, 37, 560). Despite several attempts with a variety of electrophiles, however, we failed to intercept the postulated intermediate under the same or other reaction conditions.
- [5] (a) R.L. Letsinger, *Angew. Chem.* 1958, 70, 151, spec. page 154; (b) A. Maercker and W. Theysohn, *Justus Liebigs Ann. Chem.* 1971, 746, 70; (c) M. Jung and R. Blum, *Tetrahedron Lett.* 1976, 1096.
- [6] R.A. Finnegan, *Tetrahedron Lett.* 1963, 429.
- [7] J. Hartmann and M. Schlosser, *Helv. Chim. Acta* 1976, 59, 453.
- [8] See also : A.A. Morton and A.E. Brachman, *J. Am. Chem. Soc.* 1954, 76, 2973.
- [9] For organometallic reactions generating 2 see, e.g., : (a) V. Rautenstrauch and M. Geoffroy, *J. Am. Chem. Soc.* 1976, 98, 5035; (b) G. Mollé, P. Bauer and J.E. Dubois, *J. Org. Chem.* 1982, 47, 4120.
- [10] (a) K.S. Cheng, F. Bertini and J.K. Kochi, *J. Am. Chem. Soc.* 1973, 95, 1340; (b) The cleavage of diethyl ether by phenylsodium is substantially attenuated if as little as 5% of phenyllithium are added (G. Wittig, R. Ludwig and R. Polster, *Chem. Ber.* 1955, 88, 294); (c) When at -75°C butylpotassium is dissolved in tetrahydrofuran saturated with lithium *tert*-butoxide, it still attacks the solvent. In contrast, the presence of 1 equ. triphenylmethyl lithium drastically slows down the formation of 1.
- [11] S.D. Young, K.E. Coblens and B. Ganem, *Tetrahedron Lett.* 1981, 4887; but see also R.R. Fraser, M. Bresse and T.S. Mansour, *Chem. Commun.* 1983, 620.
- [12] M. Schlosser, *Struktur und Reaktivität polarer Organometalle*, Springer Verlag, Berlin, 1973, spec. page 67.
- [13] Roughly half of the pentenol underwent subsequent metalation at the allylic position. After quenching with chlorotrimethylsilane, 4-penten-1-ol (0.9%), (*Z*)-5-trimethylsilyl-3-penten-1-ol (1.1%) and the two corresponding trimethylsilyl esters (3.5% each) were obtained.
- [14] The latter compound was reported to form in 91% yield after metalation with *sec*-butyllithium in the presence of potassium *tert*-butoxide (E.J. Corey and T.M. Eckrich, *Tetrahedron Lett.* 1983, 3165). Depending on the conditions, this method, however, gave in our hands only yields ranging between 3% and 30% of adduct besides 4 other products (totaling 15 - 30%).
- [15] T. Cohen and J.R. Matz, *J. Am. Chem. Soc.* 1980, 102, 6900.
- [16] U. Schöllkopf, H. Küppers, H.J. Traeckner and W. Pitteroff, *Justus Liebigs Ann. Chem.* 1967, 704, 120.
- [17] (a) D.J. Peterson, *Organomet. Chem. Rev., Sect. A* 1972, 7, 295; (b) W.C. Still and A. Mitra, *J. Am. Chem. Soc.* 1978, 100, 1927; (c) W.C. Still and C. Sreekumar, *J. Am. Chem. Soc.* 1980, 102, 1201.

(Received in Germany 5 December 1983)