Pergamon

Tetrahedron Vol. 50, No. 20, pp. 5933-5944, 1994
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0040-4020/94 $6.00+0.00

0040-4020(94)E0283-Y

Mixed Tetramers of *sec*-Butyllithium and 3-Methoxypropyllithium; Degree of Intracluster Etheration and Reactivity of *sec*-Butyllithium towards Ethylene

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Key Words: Alkyllithiums; carbolithiation; Lewis base effects; NMR spectroscopy; aggregates.

Abstract: In benzene, neither *sec*-butyllithium (**1**) nor 3-methoxypropyllithium (**2**) react with ethylene, while in solutions containing **1** *plus* **2** 3-methylpentyllithium (**3**) is produced by ethylenation of **1**. Clusters $\mathbf{1}_n\mathbf{2}_{4-n}$ (n: 0 - 4) are indicated by NMR and $\mathbf{1}_2\mathbf{2}_2$ is deduced to be the most reactive species. At [**2**]:[**1**] = 2, the reaction order in **1** is 0.74, signifying reversible formation of a pre-reaction complex $\mathbf{1}_2\mathbf{2}_2$•ethylene.

The importance of organolithiums in synthesis can hardly be overemphasized.[1] It is a basic tenet of this chemistry that reactions are strongly accelerated by ether or tertiary amine solvents or additives. Representative examples are given in Table 1.[2-7] In addition, different modes of reaction of a substrate may differ in their sensitivity to ether or amine induced modulation of reactivity. By consequence, outcomes of reactions between the same or a similar set of reaction partners may be drastically different in different solvents *e.g.* Table 2.[8-12]

On addition of Lewis base (LB, ether, tertiary amine) or by use of a Lewis base solvent, mixtures of complexes $(RLi)_m \cdot (LB)_n$ (m,n: 1,3; 2,4; 4,1-4), their compositions depending on conditions,[13] are formed exothermically[14] and react much faster than the LB-free systems. While it is understandable intuitively that reactivity increases when LB complexation (often at *ca.* -80°C) converts tetramers into dimers and monomers (Table 1, entries 4 and 6, Table 2, entries 3 and 5) whose carbanions are both more accessible and less shielded by Li$^+$ than those of tetramers and hexamers,[15] a question looms with regard to LB-complexed tetramers. Why are they more reactive? Only vague suppositions of increased negative charge on carbon and weaker bonding between carbon and lithium, not specified whether pertaining to ground states or transition states, are found in the literature and in textbooks.[3, 12a, 16]

$$\overset{a}{C^{\gamma-}\cdots\cdots Li^{\gamma+}} \qquad \overset{b}{C^{\delta-}\cdots\cdots\cdots(Li\cdots\cdots LB)^{\delta+}}$$

Charges: δ > γ ; distances: b > a

Table 1. Lewis base effects in some reactions of σ-organolithiums.

Entry	Reaction	Lewis Base Solvent or Additive	Effect	Reference
1	PrI + *i*-BuLi → PrLi + *i*-BuI	Et_2O (-70 °C) pentane (-23 °C)	30 min[a] 30000 min	2
2	BuLi +1,1-diphenylethylene (benzene, 22 °C)	0.4% Et_2O	$k_{0.4\%\ Et_2O}:k = 136$	3
3	RLi + $CH_2{=}CH_2 \rightarrow RCH_2CH_2Li$ (R = *i*-Pr, *s*-Bu, *t*-Bu, pentane, -25 °C)	Et_2O (6 - 110 equiv.)	No reaction without Et_2O	4
4	*ortho*-Lithiation of anisole (*n*-BuLi, toluene-d_8, -64 °C)	TMEDA[b] (1 equiv.)	No reaction without TMEDA	5
5	$C_8H_{17}Li + H_2$ (decane, 29.5 °C)	TMEDA (1 equiv.)	$k_{TMEDA}:k = 7000$	6
6	*E*/*Z*-Isomerization of α-arylvinyllithiums (Et_2O, 27 °C)	THF	$k_{THF}:k = 1700$	7

[a] Time required for completion of reaction. [b] TMEDA = *N,N,N',N'*-tetramethylethylenediamine.

Table 2. Lewis base induced change in chemoselectivity.

Entry	Substrate	Reagent	Reaction mode	Reference
1	Benzyl chloride	EtLi/benzene	Wurtz coupling	8
2	Benzyl chloride	BuLi/Et_2O	Cl/Li-exchange	9
3	Benzyl chloride	BuLi/THF (-100 °C)	H/Li-exchange	9
4	Alkyl allyl ethers	BuLi/hexane (70 °C)	S_N2'-type coupling	10
5	Alkyl allyl ethers	*s*-BuLi/THF (-65 °C)	α-deprotonation	11

Conditions of entries 3 and 5 are frequently used in synthetically important deprotonations.[12]

Rapid interconversion of complexes and easy loss of LB [17] have so far prevented identification by NMR[18] and detailed study of the different members of the set $(RLi)_4{\cdot}(LB)_n$ (n: 1 - 4). As stable models of the complexes $(RLi)_m{\cdot}(LB)_n$ (m,n: 2,4; 4,4), we have prepared intramolecular analogs formed by alkyllithiums in which LB is part of the molecule.[19] X-ray structure data of tetrameric γ-methoxy- and γ-dimethylaminopropyllithium chelated intramolecularly by their own Lewis base groups were compared with those of crystalline $(EtLi)_4$ as Lewis base-free reference. The average distances of CH_2R to its three neighboring lithiums from which it has to separate upon reaction (2.257 Å, R = CH_2CH_2OMe, 2.270 Å, R = $CH_2CH_2NMe_2$, 2.281 Å, R = CH_3) do not reveal weakening of carbon lithium bonding in the Lewis base-containing clusters, as a matter of fact, their solid state structures are slightly more compact than that of ethyllithium. On this basis we proposed that coordination of Lewis base to lithium leaves the C_4Li_4-core of σ-organolithium tetramers basically unchanged.[20] Then, heats of complexation of Lewis base[14] must be caused mainly by the formation of coordinative bonds and enhanced reactivity of $(RLi)_4 \cdot (LB)_n$ as compared to $(RLi)_4$ can only be due to action of the aggregate-bonded Lewis base in transition states.[20] Transition states derive greater stabilization from aggregate-bonded Lewis base than do ground states! In what manner do Lewis bases operate in transition states of σ-organolithiums? Which of the complexes $(RLi)_4 \cdot (LB)_n$ (n: 1 - 4) is most reactive? These questions are the subject of the present paper.

Very little information is available regarding the reactivity of different complexes $(RLi)_4 \cdot (LB)_n$ (n: 1 - 4). In certain cases (*cf.* Fig. 1a,b), rates of reactions in hydrocarbon solutions increase approximately linearly with the molar ratio of added Lewis base and organolithium, $[LB]:[RLi]_f$ ($[RLi]_f$: formal organolithium concentration as obtained by titration with acid), until a plateau is reached at $[LB]:[RLi]_f \approx n:m$, suggesting that practically all lithium reagent has been converted into complex $(RLi)_m \cdot (LB)_n$ which is kinetically more active than the Lewis base-free reagent. From Figs. 1a and 1b $(BuLi)_4 \cdot 2Et_2O$ and $(BuLi)_4 \cdot 4MeOC_6H_4Me$ (see also ref. 5) may be inferred to be the kinetically active species, respectively. If equilibria $(RLi)_m + nLB \rightleftharpoons (RLi)_m \cdot (LB)_n$ are less favorable, the increase of $[(RLi)_m \cdot (LB)_n]$ with $[LB]:[RLi]_f$ is more sluggish and n:m cannot be derived from the graph. The system of Fig. 1c illustrates such a case.[23]

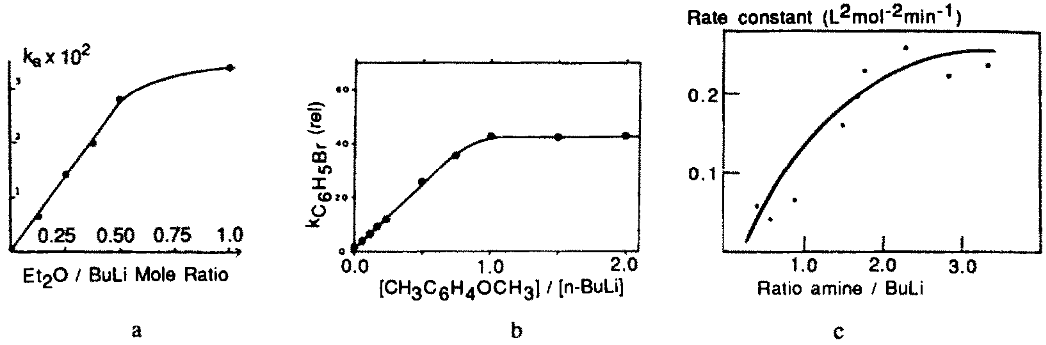


Figure 1. a) Dependence of the rate of Wurtz reaction between BuLi and octylbromide in hexane on the molar ratio Et_2O:BuLi.[21] (Reprinted with permission from *J. Am. Chem. Soc.* **85** (1963), 2171. Copyright 1963 American Chemical Society. b) Dependence of the relative rate of Br/Li-exchange of bromobenzene with BuLi in hexane on the mole ratio 4-methylanisole:BuLi.[22] (Reprinted with permission from *J. Am. Chem. Soc.* **104** (1982), 522. Copyright 1982 American Chemical Society. c) Dependence of the initial rate of polymerization of butadiene in hexane by BuLi on the molar ratio BuLi:TMEDA.[17a]

The rate law for the ethylenation of $(i\text{-}PrLi)_4 \cdot (Et_2O)_n$ and $(s\text{-}BuLi)_4 \cdot (Et_2O)_n$ in pentane with diethyl ether (Table 1, entry 3) is first order in ethylene and $[RLi]_f$, respectively, and second order in diethyl ether, indicating that the transition state contains ethylene, organolithium tetramer[24] and two ether molecules beyond the number contained in prevalent $(RLi)_4 \cdot (Et_2O)_n$[4] In the case of $(t\text{-}BuLi)_4 \cdot (THF)_n$, THF in excess of *ca.* 8 mol equiv. (2 M, Fig. 2) decreased the rate of ethylenation strongly, suggesting that higher etherates, *e.g.*

$(t\text{-BuLi})_4\cdot(\text{THF})_4$, are much less reactive than etherates containing fewer molecules of THF but having, instead, an empty coordination site on one or more of the lithiums for ethylene to be bonded in a prereaction complex.

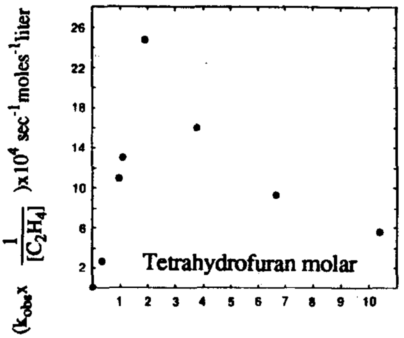


Figure 2. Dependence of the rate of ethylenation of *t*-butyllithium (0.242 M, pentane, -41°C) on the concentration of THF. (Reprinted with permission from *J. Am. Chem. Soc.* **91** (1969), 7425. [4] Copyright 1969 American Chemical Society).

Direct evidence that it is aggregate-bonded Lewis base (and not mere increase of polarity of the solvent) which causes the rate enhancements of Table 1 and Fig. 1a-c is provided by our findings with intramolecularly complexed alkyllithiums of proven structure: *In benzene* (20 °C) the (postulated) complex from tetrameric 3-lithio-1-methoxybutane and 1,1-diphenylethylene (DPE) goes to product fourty times faster than the complex from $(s\text{-BuLi})_4$ and DPE [25] and *in pentane* (20 °C) the tetramers 3-lithio-1-methoxybutane [26] and 3-lithio-1-dimethylaminobutane add to ethylene while $(s\text{-BuLi})_4$ is inert. [27] On first view, four methoxy (or dimethylamino) groups contained in a tetramer suffice to bring about the ethylenation of a secondary organolithium (Table 1, entry 3).

Hypothesizing about the mode of action of aggregate-bonded Lewis base in transition states we let us guide by our earlier observation that intramolecular Lewis base exchange is much easier in dimers $(\text{RLi})_2\cdot(\text{LB})_4$ than in tetramers $(\text{RLi})_4\cdot(\text{LB})_4$.[28] We proposed that this is due to compensation of most of the loss of Li···LB coordination energy incurred upon dissociation of one Li···LB bond, by tightening of the one remaining on lithium in dimers, which is absent in tetramers. The rate accelerations by aggregate-bonded Lewis base presented above may be explained similarly: breaking of Li···C (in dimers[15b] as well as in tetramers) could be facilitated by concomitant tightening of adjacent Li···LB. In a reasonable model of the transition state of addition to ethylene[27,29] (Fig. 3) only the methoxy groups 1 and 3 should operate in this way. The binding of methoxy group 4 is supposed to be essentially unchanged.

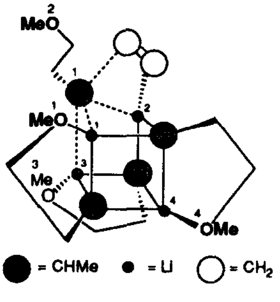


Figure 3. Proposed transition state of the addition to ethylene of tetrameric 3-lithio-1-methoxybutane.

Computer simulation of the dependence of the observed initial pseudo-first-order rate constants on the concentration of excess organolithium in the lithiations of *N,N*-dialkylbenzamides by (s-BuLi)$_4$ suggested that (s-BuLi)$_4$·(amide)$_3$ and (s-BuLi)$_4$·(amide)$_m$·(TMEDA)$_n$ (m+n=3) are more reactive than complexes (s-BuLi)$_4$·(amide)$_2$ and (s-BuLi)$_4$·amide·TMEDA, respectively.[23b] For easy reaction, presence on the substrate-tetramer complex of two assisting Lewis base molecules (which may be additional *N,N*-dialkylbenzamide substrate itself) seems required.

Our finding that addition to ethylene of 3-lithio-1-methoxybutane is promoted by the methoxy group of the reagent proper (the four methoxy groups present in its tetramer), prompted us to study the system [ethylene/(s-BuLi)$_4${≡ **1**$_4$}/(3-methoxypropyllithium)$_4${≡ **2**$_4$}/benzene]. In benzene, neither **1**$_4$ (due to the absence of a Lewis base) nor **2**$_4$ (primary alkyllithiums react only very sluggishly with ethylene) [30] *alone* added to ethylene. It was expected that in line with the well-known behaviour of σ-organolithiums [31] mixing of solutions of **1**$_4$ and **2**$_4$ would produce mixed tetramers **1**$_n$**2**$_{4-n}$ (n: 1 - 3). Reactivity towards ethylene of **1** under these conditions (maximally three methoxy groups *per* reactive tetramer) would provide evidence in support of our assumption that not all four Lewis base groups contained in tetrameric 3-lithio-1-methoxybutane and 3-lithio-1-dimethylaminobutane, respectively, are needed for activation, thus, lending support to our proposal of the transition state of Fig. 3.

EXPERIMENTAL

General

All manipulations involving the synthesis and sample preparation of organolithium compounds were carried out in evacuated and fully sealed glass apparatus. Solvents were dried on $LiAlH_4$ or sodium-potassium alloy and distilled from these agents before use. The ethene used was >99.7% pure.

***sec*-Butyllithium-*⁶Li* (1-*⁶Li*) and 1-lithio-3-methoxypropane-*⁶Li* (2-*⁶Li*)**

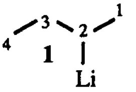
Di-*sec*-butyl mercury [32] dissolved in pentane was stirred at room temperature with an excess of thin cuttings of lithium-6 (96%). After 9 days the black slurry was filtered. NMR analysis of the colourless filtrate showed that **1**-^{6}*Li* had been formed and that no impurities were present. In the same way **2**-^{6}*Li* was prepared from bis(3-methoxypropyl) mercury [20]. The reaction product was purified by repeated crystallization from pentane until it was shown to be pure by NMR analysis.

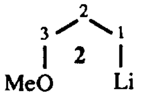
NMR experiments

NMR spectra were obtained with a Bruker MSL-400 spectrometer (^{1}H, 400.13 MHz; ^{13}C, 100.63 MHz).

Analysis of mixtures of clusters

NMR samples were prepared as follows: From a mixture of **1**-^{6}*Li* and **2**-^{6}*Li* in pentane the solvent was removed in high vacuum and the residue was dissolved in *cyclo*-C_5H_{10}/*cyclo*-C_6D_{12}, 92/8 mol-%. The resulting solution was divided among a ^{13}C-NMR tube and a ^{1}H-NMR tube. In the latter *cyclo*-C_5H_{10}/*cyclo*-C_6D_{12} was replaced by C_6D_6. In different mixtures the mole ratio **2**:**1** (R) was determined by ^{1}H-NMR measurements and found to be 0.32, 0.58, 1.07, 1.12, 1.61, 2.10, 2.16, 2.70, 2.75 and 4.90. ^{13}C-NMR spectra of these mixtures as well as of pure **1** and pure **2**, respectively, were recorded at -25 °C. Typical data (R = 1.07, see also Fig. 4) are given in Table 3.The signals of carbon atoms 1, 3 and 4 of **1** and 2 and 3 of **2**, recognizable in each type of cluster containing **1**(**2**), were integrated. Signals arising from **1**$_2$**2**$_2$ were used for normalizing. Averaging of the normalized signals of carbon atoms 1, 3 and 4 of **1** and 2 and 3 of **2** for every cluster and division by the number of units of **1**(**2**) *per* cluster gave the cluster percentages for different values of R as shown in Fig. 6.





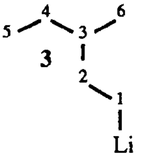


Table 3. ^{13}C-NMR signals of a mixture (R = 1.07) of **1** and **2** (*cyclo*-C_5H_{10}/*cyclo*-C_6D_{12}, 92/8 mol-%; -25 °C; δ, ppm).

Carbon atom (RLi)	$\mathbf{1}_4$	$\mathbf{1}_3\mathbf{2}$	$\mathbf{1}_2\mathbf{2}_2$	$(\mathbf{1})\mathbf{2}_3$	$\mathbf{2}_4$
1(**1**)	19.20	19.45	19.94	20.41	
2(**1**)^a	16.6	17.0	17.6	18.1	
3(**1**)	31.72	31.85	32.24^b	32.54	
			32.19^b		
4(**1**)	15.93	16.07^b	16.36^b	16.50	
		16.04^b	16.33^b		
1(**2**)^a		6.7	7.2	7.8	7.8
2(**2**)		30.29	30.40	30.53	30.72
3(**2**)		79.36	79.66	79.83	80.12
OMe(**2**)		58.63 - 58.72 (10 signals)^b			

^{a} Centers of septets are given (see Fig. 4). ^{b} Different signals for one type of cluster are ascribed to different "chelatomers" (see Fig. 5).

Kinetics

Initial rates of formation of 3-methylpentyllithium (**3**) [4] were determined for different R by following the reaction by ^{1}H-NMR [(C_6D_6, δ, ppm) -0.8 (2H), 0.98 (t, ^{3}J = 7.35 Hz, 3H), 1.04 (d, ^{3}J = 6.7 Hz, 3H), 1.24 (o, ^{3}J = 7.0 Hz, 1H), 1.28-1.34 (2H), 1.43-1.62 (2H)]. Reaction mixtures contained in sealed NMR tubes were prepared on a high vacuum line with break-seal connections in the following way: From a pentane solution containing **1** and **2** in known ratio the solvent was removed by evaporation. The residue was dissolved in 600 μl C_6D_6 and rinsed into an NMR tube. Ethylene was transferred into the NMR tube by connecting it to a 12 ml ampoule filled with ethylene at 0.46 bar (0.25 mmol; for the determination of the reaction order in $[\mathbf{1}]_f$ the pressure was 0.132 bar) and cooling it with liquid nitrogen during 5 hours, after which it was sealed-off, warmed to room temperature and transferred to the NMR spectrometer. ^{1}H-NMR spectra were recorded every 15 minutes during eight hours, and then every two hours during 58 hours. Each FID was accumulated in 64K data points, 96 scans during 15 minutes (sweep width 4762 Hz, acquisition time 6.88 s, pulse repetition time 8.9 s). Before Fourier transformation the FIDs were zerofilled to 128K and multiplied with an exponential apodization function (line broadening 0.25 Hz). The same phase and base line corrections were applied to all spectra. Integrals were calculated by the Bruker DISMSL software. After completion of the reaction the NMR tube was opened and the total base concentration determined by titration. In this way 16 experiments were carried out in which R varied from 0.3 to 9.6 and the average $[\mathbf{1}]_f$ was 0.1 M. The rate of formation of **3** was calculated from the increase of the integrals of the NMR signals of three extra protons ($C_4H_8 \rightarrow C_6H_{11}$) at 0.9 - 1.9 ppm. The time at which the sample had reached room temperature was taken as t = 0.

RESULTS AND DISCUSSION

As expected, mixing hydrocarbon solutions of **1** (tetramer *plus* a minor proportion of hexamer) [33] and $\mathbf{2}_4$ [20] in different mole ratios **2** : **1** (R), produces different mixtures of clusters $\mathbf{1}_n\mathbf{2}_{4-n}$ (n: 0-4) as evidenced by ^{13}C-NMR at -25 °C. Static C_4Li_4 skeletons were indicated by the septet nature of the proton decoupled signals of ^{13}C-2(**1**) and ^{13}C-1(**2**), respectively, obtained from solutions prepared from ^{6}Li labelled materials (see Fig.4) [34]. At room temperature, rapid intramolecular and intermolecular exchange processes among all species lead to broad singlets at 17.9 ppm and 7.6 ppm for ^{13}C-2(**1**) and ^{13}C-1(**2**), respectively.

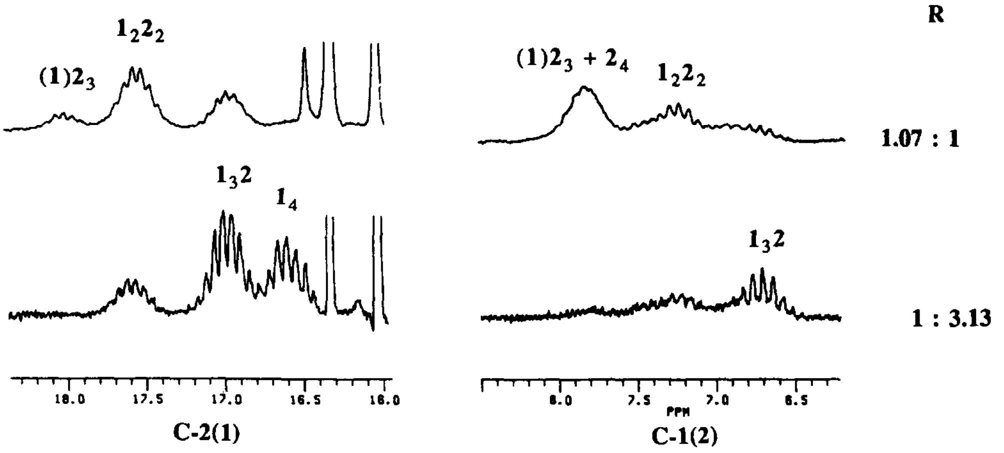


Figure 4. NMR signals (*cyclo*-C$_5$H$_{10}$/*cyclo*-C$_6$D$_{12}$, 92/8 mol-%; -25 °C) of ^{13}C-2(**1**) in clusters (**1**-^{6}*Li*)$_4$ - (**1**-^{6}*Li*)(**2**-^{6}*Li*)$_3$ and of ^{13}C-1(**2**) in clusters (**1**-^{6}*Li*)$_3$(**2**-^{6}*Li*) - (**2**-^{6}*Li*)$_4$.

Clusters $\mathbf{1}_2\mathbf{2}_2$, (**1**)$\mathbf{2}_3$, and $\mathbf{2}_4$[20] can form different types of "chelatomers" (see Fig. 5 and ref. 26b). In the case of $\mathbf{1}_2\mathbf{2}_2$, the two achiral types can occur as *d,l*- and *meso*-diastereomers, while for the chiral one four diastereomeric *d,l*-pairs are possible. Accordingly, under the conditions of Fig. 4 (slow exchange), ten peaks and several shoulders can be recognized for the methoxy carbon atoms and twin resonances are observed for ^{13}C-3(**1**) in $\mathbf{1}_2\mathbf{2}_2$ and for ^{13}C-4(**1**) in $\mathbf{1}_2\mathbf{2}_2$ and in $\mathbf{1}_3\mathbf{2}$. Assignment to specific species has not yet been possible.

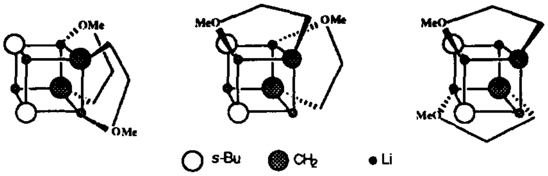


Figure 5. Types of chelatomers of $\mathbf{1}_2\mathbf{2}_2$. Analogous species are possible for (**1**)$\mathbf{2}_3$ and $\mathbf{2}_4$.

The distribution of clusters $\mathbf{1}_n\mathbf{2}_{4-n}$ (n: 0-4) for different values of R under the conditions of Fig. 4 is shown in Fig. 6 together with the statistical distribution. $\mathbf{1}_2\mathbf{2}_2$ is favored at the cost of the other clusters under all conditions. It is well-known for intermolecular systems that for successive additions of Lewis base to alkyllithium tetramers formation constants of complexes diminish and more so with increased branching at the α-carbon atoms.[4,17b,18a] The same is assumed to apply to our cases of intracluster Lewis base complexation. Clearly, steric factors and, perhaps, a saturation effect that is electronic in origin are involved.

In benzene solutions containing **2** ethylene added to **1** to form 3-methylpentyllithium (**3**)! The most salient conclusion from our studies therefore is, that less than four molecules of Lewis base *per* tetramer suffice for reactivity of **1** towards ethylene to arise. Also, since the indispensable methoxy groups are provided by **2**, some unknown *through-bond* interaction between oxygen and the negatively charged carbon atom in 3-lithio-1-methoxybutane can be excluded as a possible cause of the reactivity of the latter. It was hoped that study of the rate of ethylenation of **1** in systems with different cluster distribution would shed light on the relative reactivity of the various clusters (*i.e.* on the number of methoxy groups complexed to an alkyllithium tetramer that provides maximum assistance to reaction) and on the validity of our transition state proposal of Fig. 3.

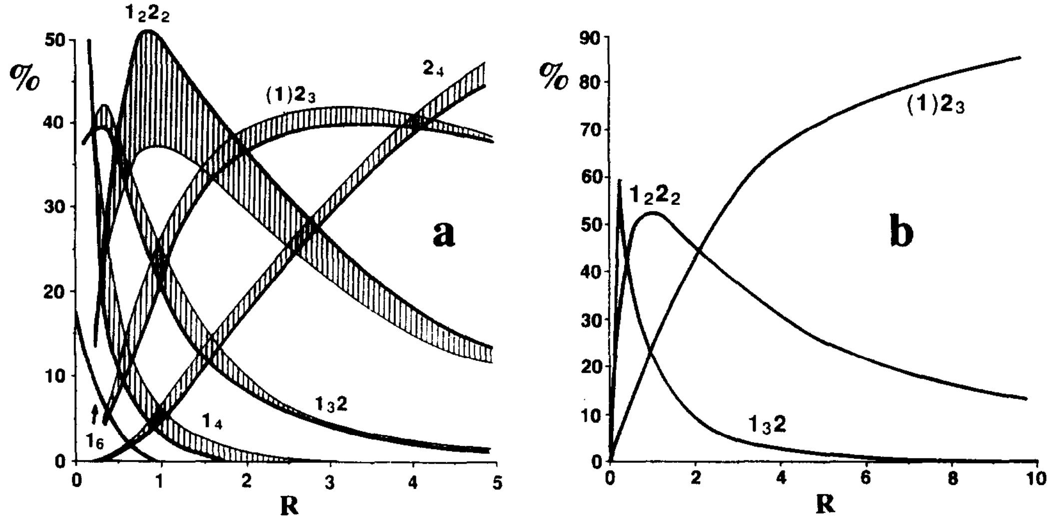


Figure 6. Distribution of clusters (%) for different values of R. Conditions of Fig. 4. (a) All clusters ($\mathbf{1}_6$ and $\mathbf{1}_n\mathbf{2}_{4-n}$, n=0-4), thick lines: experimental; thin lines: statistics of $\mathbf{1}_n\mathbf{2}_{4-n}$, n=0-4. (b) Experimental distribution of clusters containing both **1** and **2** ($\mathbf{1}_n\mathbf{2}_{4-n}$, n=1-3).

In order to exclude artefacts caused by contaminations as much as possible [35], measurements were carried out by NMR on samples contained in sealed NMR tubes and prepared on a high-vacuum line. Since clusters change by conversion of cluster-bonded **1** into cluster-bonded 3-methylpentyllithium (**3**), only *initial rates*, reflecting the properties of the system in its known starting composition were considered. At R=2, initial rates of addition in benzene-d_6 at 25 ± 1 °C, first-order in ethylene ($[C_2H_4]_{C_6D_6}$: 0.054 mol/L), were measured for $[\mathbf{1}]_f$ ranging from 0.086 to 0.950 mol/L. The slope of the plot of log ($\text{rate}_i/[\text{ethylene}]_i$) *vs.* $\log[\mathbf{1}]_{i,f}$ (Fig. 7, i: initial value) indicated the reaction order x in $[\mathbf{1}]_f$ to be 0.74. We assume this value of x to apply over the whole range of R.

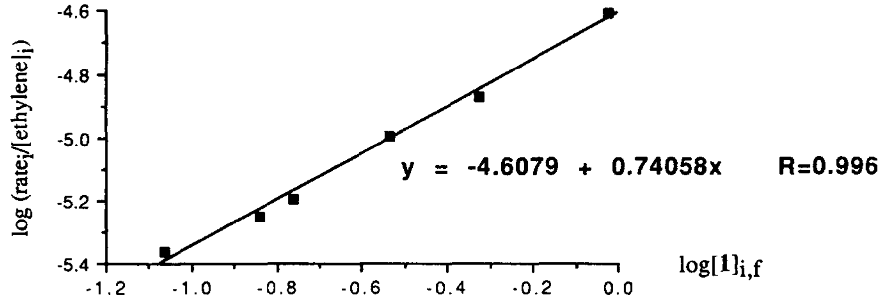


Figure 7. Determination of the reaction order x with respect to $[\mathbf{1}]_f$ (R=2; 25 ± 1 °C).

So far, two domains of organolithium reactivity have been recognized. In some reactions the reaction order x in $[\text{RLi}]_f$ has the value 1, concordant with the aggregates present under the conditions of reaction entering into the transition state either directly or in a complex with the substrate, formed in minute amount in a pre-equilibrium. On the other hand, many reactions have fractional values of x that are approximately the inverse of the degree of aggregation of the organolithium reagent.[36] It was inferred that in these cases a pre-equilibrium produces non-observable amounts of monomers that, as the actual reactive species, enter ***directly*** into transition states. However, Brown pointed out reactions that have fractional values of x while their rates are higher than expected on the basis of the energies estimated to be required for the break-down of $(RLi)_n$ (n = 4,6) into monomer. As the cause of fractional values of x he suggested that complexes between substrates and $(RLi)_n$ are present in non-negligible amounts, values of x signifying values of formation constants, K_c (for $(RLi)_4$, $[RLi]_f = 0.1$-1 M, [Substrate] = 0.002 M: $x \approx 0.1$, $K_c > 100$; $x \approx 1$, $K_c < 1$).[37] Complexes between substrates and organolithium reagents have been indicated in a number of cases[23b,35a,38] and magnitudes of formation constants have been estimated.[23b] While supported by calculations indicating the difficulty of breaking up $(MeLi)_4$ into monomer,[39] it is uncertain whether Brown's model holds when strong LB complexation of monomer and/or release of steric strain offsets the stabilization provided by multicenter Li-C bonding in the aggregates. In fact, ***the frequent coïncidence of*** x ***with*** 1/n ***and the lack of values in the range*** $1/n<x<1$, still appear to support the monomer hypothesis. The present value of 0.74 found for x in the ethylenation of **1** provides yet another one of these "missing cases"[25,40] incompatible with the monomer mechanism while indicating reversible prereaction complexation of substrate by the reactive cluster(s). For the archetypal ethylenation reaction (Table 1, entry 3) the value of x (= 1) does not distinguish between $(RLi)_4 \cdot nEt_2O$ entering into the transition state with ethylene directly or after reversible formation of an amount of complex that must be less than that generated in the present system.

For different values of R, we have determined initial rates of formation of **3**.[41] Division by the experimental values of $[\text{ethylene}]_i$ and $[\mathbf{1}]_i^{0.74}$ gave the rate constants (k_i, 25 ± 1 °C) for the ethylenation of **1** which are displayed in Fig. 8.

Apart from the crucial increase for $R = 0 \rightarrow R > 0$, variation of k_i with R is slight and does not suggest reaction of different species of greatly varying reactivity at different values of R. The rate profile of Fig. 8

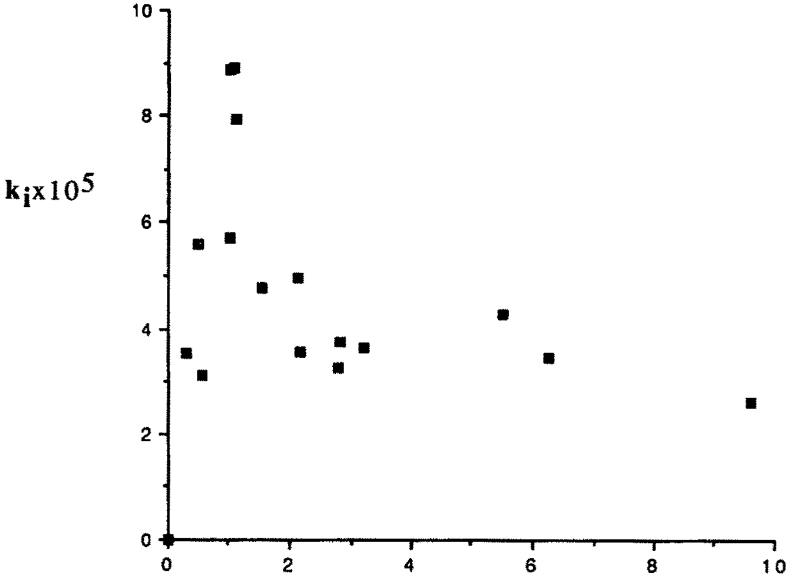


Figure 8. Rate constants (k_i, $L^{0.74}mol^{-0.74}sec^{-1}$, 25 ± 1 °C) for ethylenation of **1** at different R.

showing an accumulation of high values of k_i at R=1 and a slow decrease of k_i with increasing R towards values about one half of the maximum, is reminiscent of the THF effect shown in Fig. 2 and, most importantly, resembles the profile of the proportion of $\mathbf{1}_2\mathbf{2}_2$ in Fig. 6a,b (-25 °C). Disregarding the difference in temperature, one may conclude from this resemblance $\mathbf{1}_2\mathbf{2}_2$ to be the most reactive species in the ethylenation of **1**. If the mono-etherate $\mathbf{1}_3\mathbf{2}$ prevailing at $R < 1$ were more reactive than $\mathbf{1}_2\mathbf{2}_2$, a maximum of k_i would have been observed at $R = 0.33$. If the tris-etherated cluster $(\mathbf{1})\mathbf{2}_3$ prevailing at $R > 3$ were most reactive, a continuous increase of k_i would be observed in this range of R. The conjecture of $\mathbf{1}_2\mathbf{2}_2$ being more reactive than $\mathbf{1}_3\mathbf{2}$ is in line with our transition state proposal of Fig. 3 and with the suppositions discussed before, of two Lewis base molecules being required for efficient activation of C^- contained in a σ-organolithium tetramer. Possible causes for diminished reactivity of $(\mathbf{1})\mathbf{2}_3$ can only be guessed at. Is $(\mathbf{1})\mathbf{2}_3$ unable to pre-coordinate ethylene? For steric, for symbiotic[42] reasons? Is presence of a second coordinatively unsaturated lithium (*e.g.* as obtained by decoordination of MeO^4 in Fig. 3) necessary for sufficient electrophilic activation of ethylene? Future studies will address these questions as well as apply the present technique to probe the LB dependency of other important organolithium reactions (*cf.* Fig.1).

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(*Received* 25 *October* 1993)