Reaction of Organolithium Compounds with Alkali Metal Alkoxides – A Route to Superbases

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Organolithium compounds and lithium alkoxides form adducts, the reactivities of which are similar to those of the parent organolithium compounds. On the other hand, with heavy alkali metal alkoxides a metal interchange takes place, which gives rise to heavy alkali metal organic compounds. This is accompanied by a dramatic increase in the reactivity of the system, hence the name "Superbase" (SB) may be applied. This metal interchange is a general reaction and proceeds not only with organolithium compounds but also with lithium amides and lithium enolates of ketones and esters. SBs readily react with organic substrates to give heavy alkali metal derivatives of the substrate. Such reactions, followed by conversion with an electrophile, find wide application in organic synthesis. The properties of SBs may be further enhanced by using a greater than equimolar amount of a highly-branched heavy alkali metal alkoxide (R^2OM). In this review, the mechanism of SB reactions with substrates is discussed and the stoichiometric participation rather than catalytic effect of R^2OM is documented. Although various routes for the reaction of SBs with substrates may be envisaged, a heavy alkali metal organic compound is involved in all cases.

Introduction

Organolithium compounds react with alkali metal alkoxides in different ways depending on the metal of the alkoxide. Lithium alkoxides and organolithium compounds form adducts, the reactivities of which approach those of the parent organolithium compounds. On the other hand, heavy alkali metal alkoxides undergo a metal interchange with organolithium species, giving rise to heavy alkali metal organic compounds and lithium alkoxides. The reactivities of these systems are dramatically enhanced and this phenomenon warrants the name Superbase (SB). SBs are extremely strong bases; they readily react with many organic compounds and thus represent useful tools in organic synthesis.

The very first reference to the system prepared from butyllithium and sodium or potassium *tert*-butoxide can be found in a U.S. patent[1] [applied for on Nov. 14, 1963 by Wofford (Phillips Petroleum Co.)], where its use as a polymerization catalyst is described. A paper on this topic appeared much later.[2] The next account of this system appeared in a Czech patent[3] (applied for on Dec. 30, 1964, by Lochmann et al.), which was followed by a lecture[4] and a paper by the same authors[5] (submitted on Nov. 24, 1965). These communications and the following papers[6,7] described the metal interchange leading to the generation of heavy alkali metal organic compounds, as well as the formation of the latter through reaction of SBs with organic

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MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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substrates. Subsequently, the general nature of this metal interchange was established and more effective SBs were discovered.[7–11] Eventually, Schlosser submitted a paper (on Aug. 4, 1966) describing an increased reactivity of butyllithium (BuLi) in the presence of potassium *tert*-butoxide and explained this phenomenon in terms of solvation of the BuLi by the oxygen atom of the alkoxide, akin to the solvation of organometallics by ethers. Metallations of several substrates and their subsequent conversions into derivatives through in situ reactions with electrophiles were also described in this paper.[12] This author went on to investigate reactions of SBs with many organic substrates and contributed substantially to the use of SBs in organic synthesis; the relevant results have been summarized in two reviews.[13,14] The properties of SBs have also been investigated in other laboratories. Some salient accounts can be found in refs.[15–23]

The bulk of this review is focussed on the formation and properties of SBs based on results obtained by the author. As SBs find such widespread application in synthetic chemistry, a complete listing of their uses is beyond the scope of this survey (see other reports[13,14,24,25]). Some reactions with specific substrates are described here in greater detail merely in the context of elucidating the reaction mechanism. Throughout this paper, the term “organolithium compounds” is used to denote compounds having a carbon–lithium, a nitrogen–lithium, or an enolate group–lithium bond.

Interaction of Organolithium Compounds with Lithium Alkoxides

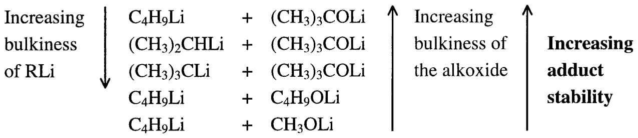
Preparation and Properties of $[R^1Li \cdot R^2OLi]_x$ Adducts

In mixtures of organolithium compounds and lithium alkoxides, adducts are formed according to Scheme 1.[26–29] This interaction is complex in nature, which stems from the ability of these compounds to form supermolecular aggregates.[30–32] The degree and strength of alkali metal alkoxide aggregation is controlled by the steric requirement of the alkoxy group and the properties of the metal.

$$1/x\,[R^1Li]_x + n\,1/y\,[R^2OLi]_y \rightleftharpoons 1/z\,[R^1Li \cdot n\,R^2OLi]_z$$

Scheme 1

In terms of increasing adduct stability, such systems may be ordered as shown in Scheme 2. Bulky organolithium compounds form adducts less readily than simple ones, whereas the opposite is true for the alkoxides. This is probably due to the fact that the stability of supermolecular aggregates of alkoxides decreases with increased branching, and that this no longer disfavours adduct formation. In accordance with these conclusions, the adduct composed of butyllithium (BuLi) and lithium *tert*-butoxide (*t*BuOLi) is easily formed, whereas lithium methoxide is unable to form such adducts.



Scheme 2

Structure of the $[C_4H_9Li \cdot (CH_3)_3COLi]_x$ Adduct

The structure of this adduct, which is isolable in crystalline form, was investigated by Boche et al. by means of X-ray diffraction analysis.[33] It was found to consist of tetrameric aggregates containing two kinds of Li atoms, some being bound to two C atoms and one O atom, the others to one C atom and two O atoms. The degree of aggregation of this adduct in benzene solution is also equal to four,[28,34] hence a solution structure similar to that in the crystalline state may be anticipated.

Reactivity of $[R^1Li \cdot R^2OLi]_x$ Adducts

The interaction of organolithium compounds with lithium alkoxides is also manifested in a change in the reactivity of the former,[35–38] although the effect is not so pronounced in this case. The addition of BuLi to 1,1-diphenylethene was chosen for a systematic investigation of the effect of lithium alkoxides on the reaction rate.[35] The ratios of the respective rate constants obtained in the absence and presence of various Li alkoxides at two different concentrations are given in Table 1. The effects of the lithium alkoxides on the rate of addition of BuLi are seen to be negligible, apart from in the case of lithium (–)-(1*R*)-menthoxide. At the lower concentration used, even this effect became very slight.

Table 1. Rate constants for the addition of butyllithium (BuLi) to 1,1-diphenylethene (DPE) in the presence of lithium alkoxides (ROLi)

R	ROLi[a] [10^{-2} mol/L]	BuLi [10^{-2} mol/L]	DPE [10^{-2} mol/L]	k_m/k[b]
(–)-(1*R*)-Menthyl	15.0	15.0	0.1010	4.65
(–)-(1*R*)-Menthyl	1.5	1.5	0.0101	1.20
tert-Butyl	15.0	15.0	0.1010	1.70
tert-Butyl	1.5	1.5	0.0101	0.93
Butyl	12.3[c]	15.0	0.1010	1.43
Butyl	1.1[c]	1.5	0.0101	0.82

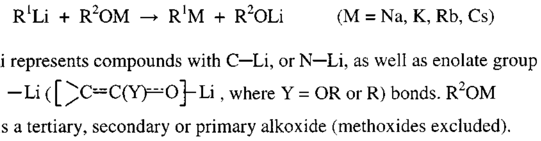
[a] In benzene at 29 °C. – [b] k_m and k are the rate constants for the addition of butyllithium to DPE in the presence and absence of ROLi, respectively. – [c] Saturated solution of lithium butoxide in the corresponding butyllithium solution.

Thus, in summary, it can be stated that lithium alkoxides influence the reactivity of BuLi only to a small extent.

Reaction of Organolithium Compounds with Heavy Alkali Metal Alkoxides – Formation of Superbases

Exchange of Li by Na, K, Rb, Cs

In continuation of the above investigation, it was found that heavy alkali metal alkoxides, in contrast to lithium alkoxides, increase the reactivity of organolithium compounds to a great extent, by a factor of more than 10^6. This is due to another reaction, which occurs in such systems after formation of an initial adduct (similar to the adducts with lithium alkoxides), namely a lithium–heavy alkali metal interchange as generalized in Scheme 3.[3–7,39–43] This interchange gives rise to organic compounds of heavy alkali metals and lithium alkoxides. It was first observed with organolithium compounds containing a C–Li bond, as that in BuLi.[3–6] Subsequently, it was also verified for compounds with an N–Li bond, as that in lithium diisopropylamide,[40] and finally it was found to occur with lithium enolates of esters[42] or ketones, such as lithiated pinacoline.[43] The structure of the starting heavy alkali metal alkoxide may also be varied, tertiary alkoxides being most suited for practical applications, while methoxides are unsuitable. Hence, the validity of this metal interchange scheme is quite general. The systems ($R^1Li + R^2OM$) are often called Superbases due to their increased reactivities.



$R^1Li + R^2OM \rightarrow R^1M + R^2OLi$ (M = Na, K, Rb, Cs)

R^1Li represents compounds with C–Li, or N–Li, as well as enolate group –Li ([>C=C(Y)=O]–Li, where Y = OR or R) bonds. R^2OM is a tertiary, secondary or primary alkoxide (methoxides excluded).

Scheme 3

Thus, the reactions according to Scheme 4 may proceed.

$C_4H_9Li + (CH_3)_2(C_2H_5)CONa$ (or K) $\rightarrow$ C_4H_9Na (or K) $+ (CH_3)_2(C_2H_5)COLi$

$(iso\text{-}C_3H_7)_2NLi + (CH_3)_3CONa$ (or K) $\rightarrow$ $(iso\text{-}C_3H_7)_2NNa$ (or K) $+ (CH_3)_3COLi$

$(CH_3)_2CLiCOOC_2H_5 + (CH_3)_3CONa$ (or K) $\rightarrow$ $(CH_3)_2CNa$(or K)$COOC_2H_5 + (CH_3)_3COLi$

Scheme 4

This metal interchange takes place not only in hydrocarbon media, from which the reaction product is precipitated, but also in media in which the product remains in solution, as has been verified either by EPR[16] or NMR[15,44] spectroscopy. These results indicate that separation of the reaction product is not the only driving force for the metal interchange.

An SB based on 2-ethylhexyllithium has recently been developed, which exhibits good solubility even in aliphatic hydrocarbons in the absence of any additive[41] (2-ethylhexylsodium is known to be soluble in hexane[45]). This modification is very convenient for reactions of SBs with organic substrates, particularly with those that are insoluble in hydrocarbons. Alternative solvent systems (e.g. with electron-donating solvents at low temperatures) are not compatible with all compounds.

Synthesis of Heavy Alkali Metal Organic Compounds Through Metal Interchange

Organic compounds of heavy alkali metals formed by metal interchange (Scheme 3) can in some cases be isolated in high yield and in a high state of purity,[5–7,39–43] making this a method of choice for their preparation. The procedure is extremely simple: hydrocarbon solutions of the organolithium compound and the heavy alkali metal alkoxide (both ca. 1 M) are mixed under stirring at room temperature; the insoluble product typically separates within a few minutes and can be collected by filtration. It should be noted that the purities of the starting compounds and solvents are of critical importance with regard to the quality of the product. Heavy alkali metal alkoxides soluble in hydrocarbons, such as potassium 2-methyl-2-butoxide (*tert*-pentoxide) (*t*PeOK) or menthoxide (rather than *t*BuOK) are best suited for the metal interchange and give rise to pure organopotassium compounds.

A number of pure heavy alkali metal organic compounds have been prepared through such metal interchange: compounds with a C–heavy alkali metal bond may be obtained from *n*-alkyl or aryllithium compounds in good yields (see Table 2). Their heavy alkali metal contents are close to the calculated values and the Li contents are generally less than 0.5%. For further details concerning this reaction, see refs.[47–53] Some organolithium compounds are barely soluble in aliphatic hydrocarbons, such as methyl- or phenyllithium. In these cases, the use of diethyl ether as a solvent or cosolvent has been proposed by Weiss.[54]

Several heavy alkali metal substituted amides have been prepared in benzene solution according to Scheme 3 (Table 3). Metal interchange with lithium amides that are well-soluble in benzene, e.g. lithium diisopropylamide, gives rise to heavy alkali metal amides of high purity in appreciable yields.[40]

Heavy alkali metal enolates of esters and ketones may also be prepared from the corresponding lithium enolates according to Scheme 3 (cf. Table 3 in ref.[7]). However, these compounds are more conveniently prepared by direct metallation of the parent carbonyl compounds with sodium or potassium hexamethyldisilazanes.[42,43]

Interaction of Organopotassium Compounds with Alkali Metal Alkoxides

The behaviour of organopotassium compounds towards alkali metal alkoxides seems to be very variable. Simple alkylpotassium compounds do not form adducts with potassium *tert*-pentoxide (*t*PeOK) or menthoxide, even in an excess of the alkoxide[55] (Scheme 5, Table 2), but do so with a three molar amount of lithium *tert*-pentoxide (*t*PeOLi), as is illustrated in the case of butylpotassium (formed by metal interchange)[56] (Scheme 6).

Table 2. Preparation of alkyl(aryl)sodium and potassium compounds by metal interchange

Reactants[a]			Isolated products				
R^1Li	R^2OM	$[R^2OM]/[R^1Li]$	R^1M	Yield	Metal content[b] [%]		
				%	M found	M calcd.	Li
C_4H_9Li	$(CH_3)_3CONa$	1.3	C_4H_9Na	83	28.02	28.70	0.10
$C_8H_{17}Li$	$(CH_3)_2(C_2H_5)CONa$	1.0	$C_8H_{17}Na$[c]	83	16.46	16.88	0.08
$C_{12}H_{25}Li$	$(CH_3)_3CONa$	1.0	$C_{12}H_{25}Na$	59	12.42	11.95	0.29
C_6H_5Li[d]	$(CH_3)_3CONa$	1.5	C_6H_5Na	80	21.5	23.0	0.50
C_4H_9Li	$(CH_3)_2(C_2H_5)COK$	1.0	C_4H_9K[c]	76	40.36	40.65	0.50
C_4H_9Li	$(CH_3)_2(C_2H_5)COK$	3	C_4H_9K[c]	92	41.02	40.65	0.12
$C_8H_{17}Li$	$(CH_3)_2(C_2H_5)COK$	1	$C_8H_{17}K$	88	25.15	25.67	0.26
$C_{12}H_{25}Li$	(–)-(1*R*)-menthoxide K	1.0	$C_{12}H_{25}K$	58	18.7	18.78	0.15

[a] In heptane or cyclohexane at 25 °C. – [b] Atomic absorption spectrometry. – [c] Impurities < 1%. [d] In the presence of diethyl ether (ref. [54]).

Table 3. Preparation of substituted sodium or potassium amides by metal interchange

R^1R^2NM	Yield[a]	Metal content[b] [%]			N content[c] [%]	
	[%]	M found	M calcd.	Li	found	calcd.
$(iso\text{-}C_3H_7)_2NNa$	68	18.80	18.66	0.15	11.26	11.37
$(iso\text{-}C_3H_7)(C_6H_{11})NNa$	78	14.78	17.08	0.07	8.21	8.58
$(C_6H_{11})_2NNa$	91	11.59	11.31	0.11	6.73	6.89
$(iso\text{-}C_3H_7)(C_6H_{11})NK$	59	22.26	21.80	0.25	7.76	7.81
$(C_6H_{11})_2NK$	74	17.01	17.82	0.17	6.21	6.38

[a] In benzene at 25 °C; $[R^2OM]/[LiNR^1R^3]$ = 1.0–1.3. – [b] Determined by atomic absorption spectrometry. – [c] According to Kjeldahl analysis.

$\text{BuLi} + (1\text{–}3)\ t\text{PeOK} \rightarrow t\text{PeOLi} + (0\text{–}2)\ t\text{PeOK} + \text{BuK}$
(no adducts formation)

Scheme 5

$\text{BuLi} + t\text{PeOK} + 2\ t\text{PeOLi} \rightarrow (\text{Bu}, t\text{PeO})(\text{Li, K})$ (mixed adduct)

Scheme 6

This mixed aggregate was isolated and was found to have an Li/K molar ratio of ca. 1.4 and a Bu/*t*PeO group ratio of ca. 1.2.

Benzyl- and phenylpotassium (formed by arene metallation by SB) behave in just the opposite manner: they do not react with *t*PeOLi (even in excess), but do form adducts with excess *t*PeOK[41,57] (Scheme 7).

$\text{BuLi} + t\text{PeOK} + \text{PhCH}_3 \rightarrow \text{BuH} + t\text{PeOLi} + \text{PhCH}_2\text{K}$

but: $\text{BuLi} + 3\ t\text{PeOK} + \text{PhCH}_3 \rightarrow \text{BuH} + t\text{PeOLi} + [\text{PhCH}_2\text{K} \cdot n\ t\text{PeOK}]$

$\text{PhK} + t\text{PeOK} \rightarrow [\text{PhK} \cdot n\ t\text{PeOK}]$

Scheme 7

The mixed benzylpotassium + *t*PeOK adduct was isolated as a microcrystalline solid; after hydrolysis a $PhCH_3$/*t*PeOH ratio of ca. 1.6 and an Li content of 0.4% were found.

Reaction of Superbases with Substrates

General Aspects and Synthesis of Heavy Alkali Metal Derivatives of the Substrates

It is well-known that heavy alkali metal organic compounds are much more reactive than the corresponding lithium derivatives. The formation of such a compound in the system organolithium compound + heavy alkali metal alkoxide is the predominant reason for the high reactivity of SBs towards organic substrates.[5,44,56]

These reactions may be very different in nature (Scheme 8). Some examples, not covering all the potential applications, are hydrogen–metal exchange (metallation), addition to multiple C=C or other bonds, Wurtz-type coupling with organic halides (even with non-activated halides such as BuBr), and the initiation of anionic polymerization.

$R^1Li + R^2OM + R^3H \rightarrow R^1H + R^2OLi + R^3M\ [pK(R^1H) > pK(R^3H)]$

$R^1Li + R^2OM + (C_6H_4)_2C{=}CH_2 \rightarrow (C_6H_4)_2CM\text{–}CH_2\text{–}R^1 + R^2OLi$

$R^1Li + R^2OM + R^3X \rightarrow R^1\text{–}R^3 + MX + R^2OLi$ + side-products (X = Br, I)

$R^1Li + R^2OM + n\ CH_2{=}C(CH_3)COOCH_3 \rightarrow R^1\text{–}[\text{–}CH_2\text{–}(CH_3)COOCH_3)\text{–}]_{n-1}\text{–}CH_2\text{–}(CH_3)COOCH_3)M + R^2OLi$ (M = Na, K, Rb, Cs)

Scheme 8

A common feature of all the reactions shown in Scheme 8 is that the resulting derivative of the substrate contains predominantly the heavy alkali metal.[5–7,41] This was confirmed by determining the individual alkali metals in the organometallic products isolated prior to protolysis. Hence, metal interchange must also be involved in reactions of SBs with organic substrates. These reactions can thus be used for the preparation of heavy alkali metal derivatives of the substrates. Some examples are shown in Table 4, where the isolated yields of the organometallic products are good, their heavy alkali metal contents are in good agreement with the calculated values, and the Li contents are below

Table 4. Reaction of organic compounds of lithium (R^1Li), heavy alkali metal alkoxides (R^2OM), and organic substrates

Reactants			Product	Yield	Metal content[a] [%]		
R^1Li	R^2OM	Organic substrate		[%]	M found	M calculated	Li
C_4H_9Li	$(CH_3)_3COK$	$C_6H_5CH_3$	$C_6H_5CH_2K$	93	28.35	30.02	0.40
C_4H_9Li	(-)(1*R*)-menthoxide K	C_6H_6	C_6H_5K	89	31.20	33.65	0.37
C_4H_9Li	(-)(1*R*)-menthoxide K	$C_6H_5CH(CH_3)_2$	$C_6H_5CK(CH_3)_2$[b]	92	22.30	24.70	0.44
C_4H_9Li	$(CH_3)_2(C_2H_5)ONa$	$Ph_2C{=}CH_2$	$Ph_2CNaC_5H_{11}$	86	7.90	8.83	0.08
$C_4H_9CH(C_2H_5)CH_2Li$	$CH_2(C_2H_5)COK$	$C_6H_5CH_3$	$C_6H_5CH_2K$	99	28.27	30.02	0.19
(iso-$C_3H_7)_2NLi$	$(CH_3)_3COK$	$C_6H_5CH_3$	$C_6H_5CH_2K$[c]	89	29.85	30.02	0.37
$(CH_3)_2(C{\dots}\underset{\substack{\mid\\ OCH_3}}{C}{\dots}O)Li$	$(CH_3)_3COK$	$CH_2{=}\underset{\substack{\mid\\ CH_3}}{C}{-}COOCH_3$	PMMA[d]				

[a] By atomic absorption spectrometry in the isolated organometallic product. – [b] Mixture of regioisomers. – [c] Nitrogen content 1.26%, i.e. contaminated with a small amount of potassium diisopropylamide. – [d] Poly(methyl methacrylate) obtained in a higher limiting conversion than in the absence of the alkoxide and with a microstructure corresponding to organopotassium initiators.

0.5%. For other examples of the preparation of heavy alkali metal organic compounds, see refs.[58,59] Conversely, there are also cases where the product composition does not match the calculated values and depends rather strongly on the reaction conditions, as will be shown below.

The substrate metallated with the SB may alternatively be reacted with an electrophile without isolation, and this is the way in which SBs are most often used in organic synthesis (see refs.[13,14,24,25]).

In principle, reactions of SBs with substrates can be carried out in one of two different ways. In Method A, the organolithium compound and heavy alkali metal alkoxide are mixed in an appropriate solvent prior to addition of the substrate. In Method B, one component of the SB is mixed with the substrate first, and only then is the other component of the SB added. In the latter case, the SB acts in statu nascendi[56,60] and shows slightly higher reaction rates; however, the conditions in the course of the reaction are neither constant nor well defined.

Typical procedures for the reaction of substrates with SBs are as follows: the substrate (in excess relative to R^1Li, if possible) is mixed with the SB components (according to Method A or B), the ratio R^2OM/R^1Li being 1.1–1.3 (for synthesis of the organometallic compound) or 2–3 (for use in organic synthesis; see below), in an appropriate solvent (typically an aliphatic hydrocarbon) at room temperature and the resulting mixture is stirred for 0.5–3 h under an inert gas. Potassium *tert*-pentoxide is preferred to *t*BuOK. Prolonged stirring and/or an increase in the temperature do not generally increase the yield but lead only to more side reactions. Ethereal solvents may be used at lower reaction temperatures and with substrates having a higher C–H acidity. Generally speaking, better yields of the desired metallated compounds are obtained with substrates having less sterically hindered and more acidic reaction sites and under conditions that favour the metallation (e.g. with an excess of the substrate in cases, where only monometalation is attempted).

Reactions of Superbases with Aromatic Hydrocarbons

The metallation of aromatic hydrocarbons has been studied in detail in order to elucidate the mechanism of SB reactions. This investigation involved the isolation of metallated substrates prior to their hydrolysis and analysis.

Metallation of toluene with the SB derived from 2-ethylhexyllithium (EtHexLi) and *t*PeOK was investigated first.[41] Table 5 highlights the key finding that under all conditions used for these experiments, relatively pure benzylpotassium with a low Li content was formed. The quality of the benzylpotassium was not affected even at ratios of *t*PeOK/EtHexLi below unity, e.g. at a ratio of 0.3. In this case, however, the yield of benzylpotassium was lower and corresponded exactly to the amount of potassium alkoxide present. This shows that potassium alkoxide actually participates in the metallation in a stoichiometric amount and is not merely a catalyst. As soon as all the potassium alkoxide is consumed, no further metallation takes place in spite of the presence of some remaining organolithium compound. Thus, metal interchange is substantial for reactions of SBs with organic substrates.

The reduced concentration of potassium alkoxide in an SB is also reflected in an extraordinarily decreased rate of metallation. Using equimolar amounts of the alkoxide and EtHexLi, the metallation of toluene is complete within ca. 10 min. However, with an SB containing only 0.3 equivalents of the alkoxide, the limiting yield of benzylpotassium was only obtained after more than 20 h.

The product of toluene metallation using an SB containing an excess of *t*PeOK was analyzed in a similar manner. With a small excess of this alkoxide, e.g. 1.3 molar, the quality of benzylpotassium formed remained virtually unchanged. On the other hand, with a large excess, e.g. 3

Table 5. Metallation of toluene with 2-ethylhexyllithium (EtHexLi) and potassium *tert*-pentoxide (*t*PeOK)

Reaction conditions[a]			Reaction product[b]					
[*t*PeOK]/[EtHexLi]	$[PhCH]_3$/[*t*PeOK]	Time [h]	Yield of solid[c] [%]	Metal content[d] [%]		[K]/[Li]	Content[e] [mol-%]	
				K	Li		$PhCH_3$	*t*PeOH
0.3	5	1	20	27.1	0.6	8.0	98	2.0
0.3	5	23	29	27.2	0.5	9.7	87	0.5
0.6	5	1	60	27.6	0.5	9.8	97	2.0
1.0	5	1	100	28.3	0.2	25.0	95	2.8
1.0	1	1	100	28.8	0.2	25.5	84	4.8
3.0	5	1	138[f]	28.6	0.4	12.7	70[f]	42[f]

[a] In heptane at 20 °C. – [b] Isolated as a solid before hydrolysis. – [c] Calculated as $PhCH_2K$, relative to EtHexLi. – [d] By atomic absorption spectrometry. – [e] By GLC after hydrolysis of the isolated product. – [f] Adduct of $PhCH_2K$ with *t*PeOK.

molar, an adduct of benzylpotassium with the excess of potassium alkoxide was isolated following toluene metallation. This excess of *t*PeOK in the SB causes an approximately 10-fold increase in the rate of toluene metallation in comparison with the SB composed of equimolar amounts of the components.

Further, the effect of lithium alkoxide concentration on the rate of toluene metallation with the SB prepared from BuLi and *t*PeOK was investigated.[56] The molar ratio of lithium *tert*-pentoxide (*t*PeOLi) to butylpotassium in the SB was varied in the range 7:1 to 0:1, either through the addition of an excess of the lithium alkoxide or by removing the lithium alkoxide from the SB reaction mixture by repeated washing prior to toluene addition. It would appear (Table 6) that the toluene metallation rate is influenced only slightly by the lithium alkoxide, and that the metallation rate in the presence of excess of the lithium alkoxide is decreased rather than increased. It should be stressed that the reactivity of neat butylpotassium, as obtained by complete removal of the *t*PeOLi after the metal interchange by washing, is of the same order of magnitude as that of the equimolar butylpotassium + *t*PeOLi mixture formed according to Scheme 3. Thus, in contrast to the potassium alkoxide, lithium alkoxide does not play a substantial role for the high reactivity of the SB.

Table 6. Metallation of toluene with Superbases prepared from butyllithium and alkali metal alkoxides followed by reaction with methyl iodide

Starting base system	molar ratio	Actual base system[a]	molar ratio	Method/ base form[b]	Conversion[c] [%]	$t_{1/2}$ [h]	Rate factor[d]	Product yield[e] [mol-%]		
								PhEt	xylenes	others[f]
BuLi		BuLi		A/sol.	0	$>>10^4$	$<<10^{-6}$	0	0	0
BuLi + *t*PeOLi	1:3	BuLi + *t*PeOLi	1:3	A/sol.	0	$>>10^4$	$<<10^{-6}$	0	0	0
BuLi + *t*PeOLi + *t*PeOK	1:6:1	BuK + *t*PeOLi	1:7	A/sol.	67	0.13	0.3	44	21	2
BuLi + *t*PeOLi + *t*PeOK	1:3:1	BuK + *t*PeOLi	1:4	A/sol.	67	0.072	0.5	46	21	0
BuLi + *t*PeOK	1:1	BuK + *t*PeOLi	1:1	A/insol.	73	0.036	1.0	43	18	12
BuLi + *t*PeOK	1:1	BuK[g]		A/insol.	71	0.042	0.9	54	8	9
BuLi + *t*PeOK	1:3	BuK + *t*PeOK + *t*PeOLi	1:2:1	A/insol.	96	0.005	7.2	86	2	8
BuLi + *t*PeOK	1:1	–		B/sol.	76	0.017	2.1	39	17	20
BuLi + *t* BuOLi + *t*PeOK	1:3:1	–		B/sol.	77	0.10	0.4	32	13	32

[a] After reaction according to Scheme 3. – [b] Method A: [BuLi + *t*PeOK] + toluene; Method B: [BuLi + toluene] + *t*PeOK; solution or insoluble; both in heptane at 20 °C. – [c] Toluene conversion after 30 min. – [d] $F = t_{1/2}$ (standard)/$t_{1/2}$. – [e] Reaction mixture quenched with methyl iodide 30 min. after toluene addition. – [f] 100 – (unchanged toluene + ethylbenzene + xylenes). – [g] *t*PeOLi removed before toluene addition by washing with heptane under strictly inert conditions.

Metallations of other aromatic hydrocarbons were investigated by employing the same procedure. Table 7 shows that the metallation of benzene is much more dependent on the reaction conditions than that of toluene.[57,61] In the case of benzene, the concentration of the substrate plays a most important role. Phenylpotassium was obtained in good yield and in a highly pure state at the highest benzene concentrations, e.g. if benzene was used as a solvent. With decreasing benzene concentration, the amounts of lithium and alkoxides in the product increased. These parameters could be somewhat improved by using a higher concentration of the potassium alkoxide; however, other conditions did not affect the product quality to any significant extent. Metallations of other aromatic hydrocarbons, such as cumene[62] or naphthalene,[55] with SBs were found to be even less straightforward (Table 8). Thus, optimal conditions for the metallation of aromatic hydrocarbons have to be assessed in each individual case.

A marked improvement in the product quality was observed when a small amount of diethyl ether was present during the metallation (Table 8).[55,57] In this way, the amounts of Li and other impurities present in the product could be halved or reduced even further.

The described dependence of the product composition on the substrate structure and reaction conditions may be re-

Table 7. Metallation of benzene with 2-ethylhexyllithium (EtHexLi) and potassium *tert*-pentoxide (*t*PeOK)

Reaction conditions[a]		Reaction product[b]			
[PhH]/[EtHexLi]	[*t*PeOK]/[EtHexLi]	Yield of solid[c] [mol-%]	[K]/[Li]	Content[d] [mol-%] PhH	*t*PeOH
31	1	97	12.3	93	3.4
5	1	98	5.9	86	5.5
1	1	90	2.4	82	11.3
1	1.3	91	6.6	77	10.4

[a] In heptane at 20 °C, 1 h. – [b] Isolated as a solid before hydrolysis. – [c] Calculated as PhK, relative to EtHexLi. – [d] After hydrolysis of the isolated product, determined by GLC.

Table 8. Metallation of aromatic hydrocarbons (ArH) with alkyllithium compounds (RLi) and potassium *tert*-pentoxide (*t*PeOK) and the influence of diethyl ether (Et_2O)

Reaction conditions[a]				Reaction product[b]	
ArH	RLi	[*t*PeOK]/[RLi]	[Et_2O]/[RLi]	Yield[c] [mol-%]	[K]/[Li]
Benzene	EtHexLi	1	0	90	2.4
Benzene	EtHexLi	1	6	70	8.3
Benzene	EtHexLi	1.3	0	91	6.6
Benzene	EtHexLi	1.3	6	82	16.3
Cumene	BuLi	1.1	0	75	4.1
Cumene	BuLi	1.1	6	43	30.5
Naphthalene	BuLi	1.1	0	71	1.9
Naphthalene	BuLi	1.1	6	75	3.0
Naphthalene	BuLi	1.1	15	85	3.1

[a] In heptane at 20 °C, [ArH]/[RLi] = 1. – [b] Isolated as a solid before hydrolysis. – [c] Calculated as ArK, related to RLi.

lated to the ability of organometallic compounds to form supermolecular aggregates. The course of metallation is controlled predominantly by kinetic effects. In those cases where the substrate is metallated slowly, either due to its structure or a low concentration, the concentration of the resulting organometallic product is also low. In this situation, other alkali metal compounds, such as alkoxides or Li compounds, are co-aggregated or co-precipitated with the product to a significant extent, yielding a low-purity product. Solvation of the organic alkali metal compounds with electron-donor solvents such as diethyl ether stabilizes the organometallics at lower degrees of aggregation and increases the metallation rate, which leads to higher product concentrations. Accordingly, the presence of diethyl ether during the metallation of aromatic hydrocarbons has been shown to have a favourable effect on the product purity.

Reactions of Superbases with Olefins

SBs can react with olefins in two different ways: by substitution of an olefinic hydrogen by the alkali metal (see for instance[21,22,25]) or by the addition of SB across the olefinic double bond.

Olefins with polarized double bonds add organometallics across this double bond, giving rise to new organometallic compounds. In some cases, addition of the new organometallic to the olefin may be repeated many times, ultimately leading to polymers (anionic polymerization).

Following reactions of 1,1-diphenylethene (1,1-DPE, anionic polymerization of which is difficult) with SBs prepared from BuLi and *t*PeOK or *t*PeONa, the organometallic products were isolated and analyzed.[55] The results indicated that addition of SB across the double bond was the major reaction rather than hydrogen–metal exchange. The reactivity of the 1,1-diphenylhexylpotassium formed in this reaction was so high that addition to another 1,1-DPE molecule was possible. Thus, reaction of a three-fold molar amount of 1,1-DPE relative to the SB resulted in the predominant formation of 1,1,3,3-tetraphenyloctylpotassium. The lithium content in all isolated products was $< 0.4\%$.

Another example of SB addition across an activated C=C double bond is seen in the anionic polymerization of methyl methacrylate, which is readily initiated by the SBs generated from a lithium ester enolate and sodium or potassium *tert*-butoxides.[7,63,64] The microstructure of the obtained poly(methyl methacrylate) revealed that metal interchange occurred even in this system and that the heavy alkali metal enolate was the active species in this polymerization.

Thus, lithium–potassium (sodium) interchange according to Scheme 3 takes place even in the case of additions of SBs to the C=C double bonds.

Reaction of Superbases with Organic Halides

Non-activated organic halides, such as butyl or octyl bromides, react with BuLi in hydrocarbons only to a negligible extent. If, however, a heavy alkali metal alkoxide is added to such a mixture, a fast or even vigorous reaction commences, in which products of C–C coupling are formed (e.g. reaction 2 in Scheme 9), or β-elimination of hydrogen halide (e.g. reaction 3 in Scheme 9) and halogen–metal exchange (e.g. reaction 4 in Scheme 9) take place.[65] Besides these main products, only lithium alkoxide and heavy alkali metal halide are detected in the mixtures prior to hydrolysis. Obviously, at some stage of the reaction the lithium–heavy alkali metal exchange must have occurred (e.g. reaction 1 in Scheme 9).

$$\begin{array}{llll} C_4H_9Li + tert\text{-}C_5H_{11}OK & \longrightarrow & C_4H_9K + tert\text{-}C_5H_{11}OLi & (1)\\ & \longrightarrow & R\text{-}C_6H_{13} + KBr & (2)\\ C_4H_9K + R\text{-}CH_2CH_2Br & \longrightarrow & R\text{-}CH{=}CH_2 + C_4H_{10} + KBr & (3)\\ & \longrightarrow & C_4H_9Br + R\text{-}CH_2CH_2K & (4)\end{array}$$

Scheme 9

Under favourable conditions, i.e. with primary or aromatic bromides or iodides, the reaction can be conducted in such a way that a high yield of the C–C coupling product is obtained, e.g. over 80%. Hence, the reaction between SBs and organic halides may be regarded as an improvement of the Wurtz hydrocarbon synthesis.

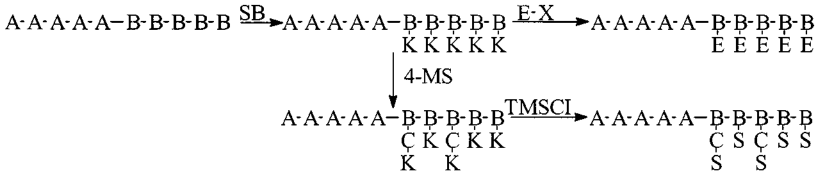
Use of Superbases in Polymer Chemistry

It emerged that SBs are also useful in polymer chemistry as initiators of anionic polymerization.[1,66–68] Another, even more promising use of SBs in polymer chemistry lies in the chemical modification of some polymers.

A suitable reagent for the metallation of some non-polar polymers was found about two decades ago, namely a mixture of BuLi and *N,N,N,N*-tetramethylethylenediamine (TMEDA).[69–71] SBs prepared from organolithium compounds and potassium alkoxides, however, seem to be superior to the TMEDA reagent because of higher reactivity, efficiency,[23,55] and regioselectivity.[72]

The procedure for multi-site functionalization of polymers using SBs involves two steps: (i) metallation of the polymer with the SB, which results in a multi-site potassium-metallated polymer, and (ii) in situ reaction of the metallated intermediate with an electrophile, giving rise to the multi-site functionalized polymer.[62] A similar procedure was suggested independently by Nemes.[73] Due to the high reactivity of the carbon–potassium bond in the metallated intermediate, the choice of electrophiles for step (ii) is wide and polymers with diverse functional groups are easily accessible. The procedure has been applied to various polymers, such as polystyrene,[62] polybutadiene,[74] poly(4-methylstyrene),[55] and polyether dendrimers.[75,76] In this way, polymers randomly substituted to various degrees with diverse functional groups are obtained in a simple one-pot process.

Non-polar copolymers, both random and block (e.g. A–B), can likewise be multi-site-functionalized employing a method similar to that described for homopolymers. If the difference in C–H acidities of various units (blocks) is sufficiently high ($pK_A - pK_B > 2$), it is possible to selectively metallate the more acidic units in the copolymer by appropriate choice of the SB.[72] For instance, the methyl groups in the block copolymer polystyrene-*block*-poly(4-methylstyrene) are selectively substituted, as illustrated in Scheme 10.



K = potassium; E–X = electrophile; E = e.g., $Si(CH_3)_3$, $C_{12}H_{25}$, CH_2OH, COOH, $COOCH_3$;
C = poly(4-methylstyrene); S = $Si(CH_3)_3$; 4-MS = 4-methylstyrene;
TMSCl = chlorotrimethylsilane

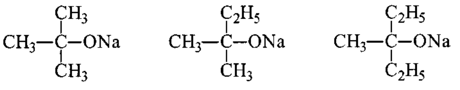
Scheme 10

The metallated (co)polymer intermediate is also effective as a multifunctional initiator of anionic polymerization, giving rise to grafted (co)polymers. In Scheme 10, this is shown for the case of grafting a block copolymer.[77]

By virtue of the great flexibility of the method, an appreciable number of novel random or block copolymers or diverse structures made up of selectively grafted (co)polymers can be prepared.

More Effective Modifications of Superbases (Second-Generation SBs)

The reactivity of an SB not only depends on the structure of the parent organolithium compound, it is also influenced by the alkoxide component. The effect of the structure and concentration of the heavy alkali metal alkoxide on SB properties has been investigated[8–11,56] using sodium alkoxides of structures I, II, and III (Scheme 11).



$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-ONa$ $CH_3-\overset{C_2H_5}{\underset{CH_3}{C}}-ONa$ $CH_3-\overset{C_2H_5}{\underset{C_2H_5}{C}}-ONa$

I II III

Scheme 11

In order to assess the SB reactivity, the time–conversion dependence in the reaction of modified SBs with organic halides was monitored. Some results are shown in Figure 1, in which the time–conversion curves for the reaction of octyl bromide with SBs of various compositions are plotted. It can clearly be seen that the reaction rate increases with the alkoxide concentration in the SB and with the degree of branching of the alkoxide.[9] The corresponding acceleration factors are summarized in Table 9. Rate accelerations caused by a similar modification of the SB could also be observed in metallations of aromatic hydrocarbons.

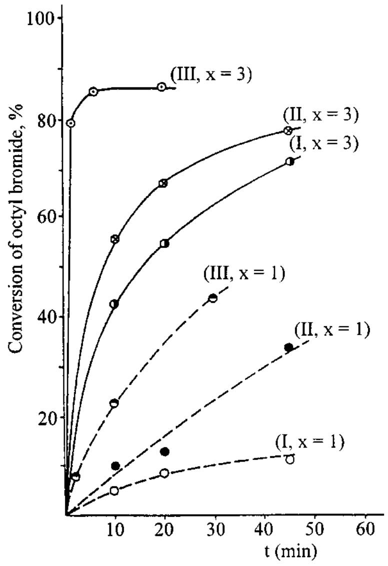


Figure 1. Conversion of octyl bromide in the reaction with various Superbases [$C_4H_9Li + x$ RONa] in heptane at –30 °C (by Br ion determination); R = *tert*-butyl (I), *tert*-pentyl (II), 3-methylpentan-3-yl (III) (see Scheme 11); x = 1 or 3

The effect of the alkoxide structure on SB properties is evidently associated with the degree of substitution on the alkoxide in the vicinity of the OM group. It was mentioned above that the strength of the alkoxide aggregation decreases with increasing substitution. The alkoxide autoaggregation competes with its other interactions and, there-

Table 9. Rates of reaction of octyl bromide with various Superbases [$C_4H_9Li + x$ RONa] and yields of dodecane (coupling product) in heptane at –30 °C

RONa R	[RONa]/ [C_4H_9Li] [x]	Reaction half-time [min]	Total acceleration factor	Yield of dodecane [%]
tert-butyl	1	> 1000	1	35
tert-pentyl	1	74	> 13	47
3-methylpentan-3-yl	1	40	> 25	55
tert-butyl	3	16	> 60	75
tert-pentyl	3	8	> 125	81
3-methylpentan-3-yl	3	0.8	> 1250	53[a]

[a] An appreciable amount of another reaction product was formed.

fore, these interactions can be expected to be favoured with more substituted alkoxides. The effects and structures of alkoxides I, II, and III (Scheme 11) are in accord with this statement. From a practical point of view, SBs prepared from *tert*-pentoxides appear to be much more suited for metallations than those prepared from *tert*-butoxides.

The structure and concentration of the heavy alkali metal alkoxide also affect the regioselectivity in reactions of SBs with substrates. For instance, in the reaction of an SB with octyl bromide, the yield of dodecane (the expected product of the C–C coupling) increased from 47 to 81% when the alkoxide to BuLi ratio was increased from 1 to 3 (Table 9).[9] Another striking example is the metallation of ethylbenzene (Figure 2).[11] Metallation of this substrate with various SBs followed by quenching with methyl iodide should give rise to cumene. In the reaction using the standard SB derived from BuLi and one equivalent of *t*BuOK, only 30% of cumene was obtained and the limiting conversion of ethylbenzene reached just 65% (curves 1a and 2a). On the other hand, use of a modified SB prepared from BuLi and three equivalents of potassium 3-methyl-3-pentoxide (a more branched alkoxide, akin to structure III in Scheme 11) (*t*MePeOK) under the same conditions resulted in 88% of cumene and a 100% conversion of ethylbenzene (curves 1b and 2b). Moreover, the metallation rate was about 10 times higher using the modified SB compared to that with the standard one.

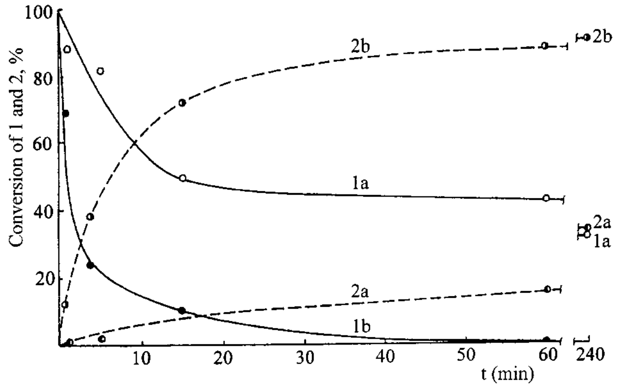


Figure 2. Metallation of ethylbenzene with various Superbases; $[BuLi]_0$ = 0.27 mol/L, heptane, 20 °C, metallation quenched with methyl iodide; curves: 1 (a,b) = ethylbenzene, 2 (a,b) = cumene; curves a: [ethylbenzene]/[BuLi]/[*t*BuOK] = 1:1:1; curves b: [ethylbenzene]/[BuLi]/[potassium 3-methyl-3-pentoxide] = 1:1:3

Consequently, the properties of the first-generation Superbases, prepared using one equivalent of heavy alkali metal *tert*-butoxide, have been considerably improved by using larger amounts of a more branched alkoxide of the same metal. Therefore, the latter can be designated as second-generation Superbases. They are more advantageous in organic and polymer chemistry in that they give higher yields of the desired products in a more straightforward process.

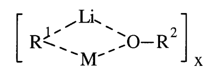
The origins of the novel properties of second-generation Superbases are probably complex. The described effect of heavy alkali metal alkoxides may be due to the formation of new SB supermolecular aggregate species possessing increased reactivities. More probably, however, the reasons may merely be physicochemical in origin, such as a change in the metal interchange equilibrium and/or rate, or a change in the solubilities or degrees of aggregation of the reaction components.

Reaction Mechanism

Mechanism of the Metal Interchange in the System $R^1Li + R^2OM$

Only limited information is available on the mechanism of the reaction between organolithium compounds and heavy alkali metal alkoxides. The situation is complicated by the autoaggregation of these compounds.

When organolithium compounds interact with heavy alkali metal alkoxides, an intermediate adduct is formed first, which is similar to the adducts of lithium alkoxides (see above) with the simplified structural units shown in Scheme 12. The adduct formation is obviously a dynamic equilibrium reaction.[28] An ab initio computational study of the model system $R^1Li + R^2OM$ (M = Na to Cs) showed that an adduct of the type depicted in Scheme 12 is the most stable in the system.[78] Further transformation of this adduct was not predicted in this study, obviously due to the simplified model structures and conditions (gas phase). Another computational study dealt with the system CH_3Li–CH_3OK, from which it was concluded that an intermediate 1:3 adduct was the most reactive.[79] The X-ray structure of a compound with intramolecular bridging similar to that in Scheme 12 has also been described.[80]



Scheme 12

In the next step, transformation of the [$R^1Li{\cdot}R^2OM$] intermediate according to Scheme 3 takes place. With the assumption that this intermediate has a structure similar to that of the BuLi + *t*BuOLi adduct,[33] the metal atoms bound to two oxygen atoms and one carbon atom could be lithium, while those bound to two carbon atoms and one oxygen atom could be the heavy alkali metal. If this were the case, splitting of the intermediate adduct to an organic heavy alkali metal compound and lithium alkoxide in the following reaction step may easily be envisaged.

The lithium–heavy alkali metal interchange proceeds in the direction opposite to the assumed one because it leads to a product containing a more electropositive heavy alkali metal bound to a less electronegative atom than the oxygen of the alkoxide, i.e. to a carbon or nitrogen atom, or to an enolate group. Therefore, the question of the driving force for this interchange is of great importance. The exchange process is certainly supported by a shift in the reaction equilibria due to the precipitation of the least soluble component in hydrocarbon solvents, which is most often the heavy alkali metal organic compound. However, the metal interchange also takes place in solution[15,16,44] and, therefore, some other effects must also be operative. The formation of an oxygen–lithium bond in the lithium alkoxide could be one of these effects. According to the HSAB principle, this alkoxide would seem to be thermodynamically more stable than the heavy alkali metal alkoxides. Moreover, lithium alkoxides appear as products in all kinds of metal interchange reactions, such as those reported above (Scheme 3). Another factor could be the different stabilities of supermolecular aggregates of various alkali metal alkoxides. The greater stability of lithium alkoxides compared with the corresponding heavy alkali metal alkoxides is reflected in the fact that various aprotic donor solvents have a less pronounced effect on the degree of aggregation of the former.[32]

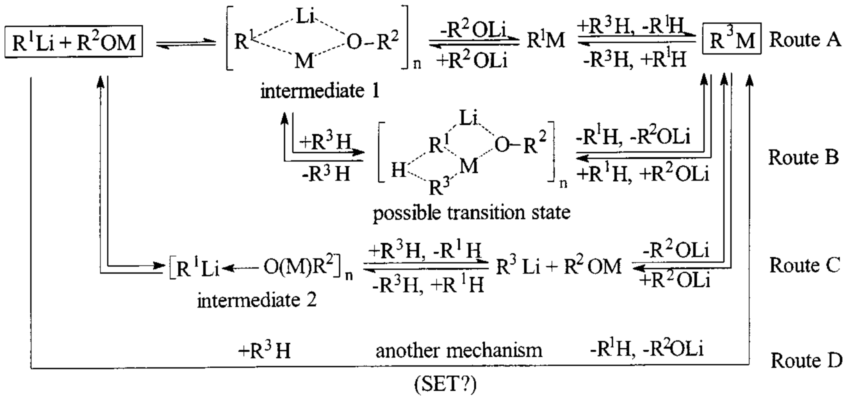
Mechanism of Reactions of Superbases with Organic Substrates

As mentioned above, two procedures can be used for the reaction of an organic substrate with an SB prepared from R^1Li and R^2OM. In Method A, the SB components are mixed first and only then is the substrate added. In this case, the heavy alkali metal organic compound is precipitated following metal interchange prior to addition of the substrate. There are then two possible modes of reaction of the substrate: (i) either the substrate is adsorbed onto the surface of the precipitate and the reaction takes place there, or (ii) the substrate reacts in solution with a very low concentration of the precipitated compound. In neither case can participation of alkali metal alkoxides present in the system be completely ruled out as, for instance, they may change the solubility or adsorption. Indeed, it follows from Table 6 that to some extent these alkoxides influence the behaviour of the organopotassium precipitate in the reaction with toluene: the reaction rate is increased in the presence of an excess of potassium alkoxide and decreased when the lithium alkoxide is in excess. Moreover, a change in the product distribution as a result of the presence of the alkoxides has also been observed,[56] in agreement with an earlier finding.[60] Nevertheless, in all these cases, the organopotassium compound in any form should remain the principal reagent (cf. below).

In the second commonly used procedure, Method B, the organic substrate is mixed with one component of the SB first and only then is the other SB component added. In this case, various routes can be suggested for the transition from the initial to the final stages, the structures of both of which are well established.

In the case of metallation of hydrocarbon R^3H, some of these pathways can be defined as shown in Scheme 13. According to Route A, the intermediate adduct 1 is first decomposed to the lithium alkoxide and the heavy alkali metal compound, which in a further step metallates the hydrocarbon R^3H to give a heavy alkali metal derivative. On the other hand, the intermediate adduct of type 1 (precursor of the C–heavy alkali metal compound) may also react directly with the substrate, yielding the heavy alkali metal derivative of the substrate through a transition state with a structure as that depicted in Scheme 13. This pathway is designated as Route B.

In the intermediate type 2, proposed in ref.,[12] activation of the organolithium compound is assumed to occur through solvation of the heavy alkali metal alkoxide, akin to that by electron-donor solvents (Route C). In this case, metallation should produce a lithium derivative of the substrate. In order to obtain the heavy alkali metal substituted substrate (as is isolated), an additional lithium–heavy alkali metal interchange must be assumed. The reason for this interchange is not clear within this hypothesis. Moreover, this idea does not explain why *t*BuOK increases the reactivity of BuLi through “solvation” to such an enormous extent (>> 10^6 times, ref.[56]), whereas *t*BuOLi is almost inactive in this respect (see above). It is questionable as to whether the difference in polarities of the O–Li and O–M bonds (M = Na, K, Rb, Cs) could cause such a change in the



Scheme 13

BuLi behaviour. Consequently, the mechanism of Route C is difficult to rationalize.

Finally, other mechanisms, e.g. those involving single-electron transfer (SET mechanism) cannot be ruled out either and are summarized in Route D.

The isolation of the heavy alkali metal derivative as the final product as well as the stoichiometric participation of the heavy alkali metal alkoxide in the reactions of SBs with organic substrates (see above) would seem to favour Routes A and B.

Structure of the "Active" Species in Reactions of Superbases

Let us summarize principal information on the R^1Li + R^2OM system: (i) After mixing of these components of the SB, metal interchange gives rise to the heavy alkali metal organic compound R^1M, which may be isolated in a pure state by washing. (ii) The organometallic products obtained from reactions of SBs with substrates isolated prior to hydrolysis contain predominantly the heavy alkali metal and only traces of lithium. This is found in reactions of SBs with substrates of different types, i.e. in metallations, in additions to double bonds, and in reactions with organic halides or polymers. (iii) Potassium alkoxide participates in reactions of SBs with substrates in a stoichiometric amount and does not merely act as a catalyst or as an activator of R^1Li. SBs having an R^2OM/R^1Li ratio below unity no longer metallate the substrate once all the R^2OM has been consumed, in spite of some unchanged R^1Li still being present. (iv) The reactivity of R^1Li + R^2OM mixtures is only slightly influenced by the concentration of the lithium alkoxide formed in the metal interchange. For instance, after complete removal of *t*PeOLi, BuK shows approximately the same reactivity as an equimolar mixture of the SB components. Mixtures of BuK with excess *t*PeOLi exhibit a decreased reactivity and, therefore, the formation of such an adduct cannot be responsible for the high SB reactivity. (v) The reactivities of SBs prepared from R^1Li and various R^2OM species increase with increasing concentration and bulkiness of R^2OM. (vi) A detailed NMR investigation of the system generated from triphenylmethyllithium and caesium 3-ethylhept-3-oxide in THF solution has shown that triphenylmethylcaesium and lithium 3-ethyl-3-heptoxide are formed through metal interchange and that they exist as separate species rather than as an adduct.[44]

Considering the points (i) to (vi), it can be concluded that in the reaction of a substrate with the R^1Li + R^2OM system, the metal interchange is the essential step and that the "active" species should be the heavy alkali metal organic compound or a derivative thereof.

When trying to decide which of the possible mechanisms proposed for the reactions of SBs with substrates is in fact correct, it should be borne in mind that the system involves a number of partial reactions, including coordination and aggregation equilibria. This makes the system very flexible. The rate and equilibrium constants may specifically depend on the properties of a given system, i.e. the structures of the reactants, the reaction conditions, and the reaction type. For instance, the extent of participation of Routes A and B in a reaction of an SB with a particular substrate depends primarily on the ratio of the rate constants for cleavage of the intermediate 1 according to Route A and those for direct metallation of the substrate by this intermediate. This ratio may be different in specific cases; thus, a substrate that is metallated more slowly would prefer Route A, while a more readily metallated substrate would be subject to a greater contribution from Route B.

Hence, it is questionable as to whether the reactions of SBs with substrates invariably proceed in exactly the same way. It could also be the case that one mechanism may predominate under certain conditions while another may become more important under other circumstances. Thus, any search for a "single universal active species" in SB reactions is irrelevant. Nevertheless, regardless of the actual path taken by the SB reactions with substrates, the metal interchange must take place at some stage in all cases and is an integral part of the reaction.

Acknowledgments

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