FACILE COUPLING OF ALKYL OR ARYL HALOGENIDES WITH ORGANOLITHIUM COMPOUNDS IN THE PRESENCE OF ALKOXIDES OF HEAVIER ALKALI METALS

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Nonactivated alkyl or aryl halogenides readily react with organolithium compounds in the presence of alkoxides of heavy alkaline metals. In the case of organic bromides and iodides, coupling products in the sense of the Wurtz reaction are mainly formed.

Organosodium or organopotassium compounds react with nonactivated organic halogenides much more quickly than the corresponding organolithium compounds[1], but they are much less accessible. Organolithium compounds react smoothly with alkoxides of heavy alkaline metals *via* the metal–metal exchange reaction, giving rise to an organic compound of a heavy alkaline metal[2-4]:

$$RLi + R'OM \rightarrow RM + R'OLi \quad (M = Na, K, Rb, Cs) . \qquad (A)$$

If reaction (A) is carried out in the presence of some suitable third compound, a compound of the latter with the heavy alkaline metal is formed[2-4], *e.g.*,

$$C_4H_9Li + (CH_3)_3COK + C_6H_5CH_3 \rightarrow$$
$$\rightarrow C_6H_5CH_2K + C_4H_{10} + (CH_3)_3COLi . \qquad (B)$$
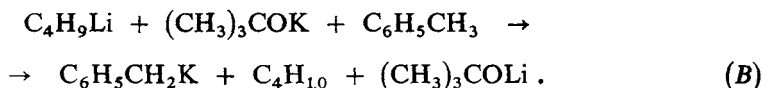
In a systematic investigation of the interaction between organolithium compound and alkaline alkoxides*, a similar exchange reaction (A) and a high reactivity towards the third compound were observed not only with alkyl- or aryllithium compounds (bond $\equiv C—Li$), but also with organolithium compounds of another type, *i.e.*, with lithium amides (bond $>N—Li$)[5] or lithium ketone and ester enolates

$$(bond >[C \doteq \overset{\overset{\textstyle Y}{|}}{C} \doteq O]^{(-)}Li^{(+)}, \text{ where } Y = R \text{ or } OR)^{6-7}.$$ In most cases mentioned above,

the corresponding organic compounds of heavy alkaline metals were isolated in high yields as the reaction products; the reaction is therefore suited for their preparation[2-8], *cf.* also[9]. An increased reactivity of organolithium compounds in the presence of tertiary potassium butoxide was later observed also by Schlosser[10], who however attributed this behaviour to the "solvation" of organolithium compounds with alkoxide $(R^{(-)}Li^{(+)} \leftarrow O^{(-)}(K^{(+)})C(CH_3)_3)$, similarly to, *e.g.*, the action of donor solvents like THF. This author and his colleagues successfully metallated a number of organic compounds by employing this procedure, but their conception can hardly explain the formation of organopotassium compounds as the final product $(cf.^{11})$.

It was suggested that the reaction of organolithium compounds with organic halogenides might be facilitated by using an exchange reaction with alkoxides of heavy alkaline metals (A). It was indeed observed that in a hexane solution containing an organolithium compound and a nonactivated organic halogenide, the addition of a heavy alkaline metal alkoxide brings about a vivid reaction, while the same mixture without alkoxide reacts only very slowly. A white precipitate appeared immediately in the reaction mixture; in the case of the reaction between equimolar amounts of butyllithium (BuLi), octyl bromide and potassium tert-pentoxide (t--PeOK), this precipitate was isolated in a 100% theor. yield and identified as an almost pure potassium bromide (metal content by means of AAS: K, found 31·81%, calc. 32·85%; Li, found 0·24%). In the IR spectrum of the mother liquor after isolation of the precipitate, only lithium tert-pentoxide (t-PeOLi) was observed, along with the organic products of the reaction. An explanation of the formation of KBr and t-PEOLi by means of a consecutive reaction of the primarily formed LiBr with t-PeOK is not plausible, because these compounds reacted with each other only very slowly under the given conditions. The conversion of t-PeOK to t-PeOLi by vigorous shaking with fine LiBr and steel beads in hexane did not even reach 10% after three hours (IR). Thus, these results do not confirm the role of a heavy alkaline metal alkoxide as an "activator" of the reaction of an organolithium compound, but rather indicate its direct participation in the described reaction with the organic halogenide.

After hydrolysis of the reaction mixture, the organic products of the reaction under investigation were determined by GLC (compared with authentic compounds, Table I). In most cases, the predominant components were coupling products of organometallic compound and organic halogenide (*e.g.*, reaction (D)), along with minor amounts of products arising by β-elimination of the halogenide (*e.g.*, reaction (E)), and as a consequence of the exchange reaction halogen–metal (*e.g.*, reaction (F)), as shown schematically for the reaction of n-octyl bromide:
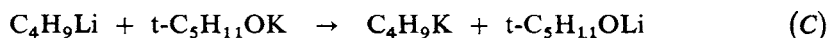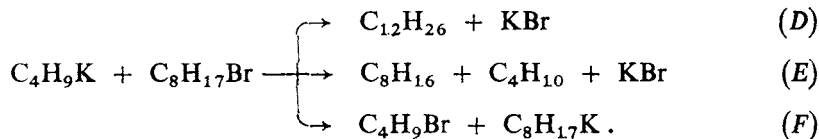
$$C_4H_9Li + t\text{-}C_5H_{11}OK \rightarrow C_4H_9K + t\text{-}C_5H_{11}OLi \qquad (C)$$

TABLE I

Results of the reaction RLi + R'OM + R"X → R—R" + R'OLi + MX + by-products (M = Na, K; X = halogen) at starting equimolar ratio of reaction components, in hexane at room temperature. Yield of R—R" (Y) related to RLi. Abbreviations: Bu butyl, t-Bu tert-butyl, t-Pe tert-pentyl, Oc octyl, EtHe 2-ethylhexyl, Ph phenyl, OcH octane, EtHeH 2-ethylhexane, DodeH dodecane, HxdeH hexadecane, OceH 1-octene, EtHeeH 2-ethyl-1-hexene, PhH benzene, BuPh butylbenzene, PhPh diphenyl, BB unresolved mixture of butane and butene, DiEtDodeH 5,8-diethyldodecane

RLi	R'OM	R"X	Y, mole %	Composition of reaction mixture, mole % (R'OM and MX excluded)					
BuLi	t-PeOK	BuCl	26.2	OcH 26.2	BuCl 3.3,	BB 70.5			
BuLi	t-PeOK	BuBr	79.8	OcH 79.8	BuBr —^{a},	BB 17.7			
BuLi	t-PeOK	BuI	80.6	OcH 73.6	BuI 0.6,	BB 25.8			
BuLi	t-PeOK	OcBr	62.1	HxdeH 7.1,	OcBr 2.1,	DodeH 54.3,	OceHe 7.8,	OcH 14.1,	BB 14.7
BuLi	t-PeONa	OcBr	61.3	HxdeH 5.8,	OcBr 3.1,	DodeH 54.1,	OceHe 5.8,	OcH 14.1,	BB 17.0
BuLi	t-BuONa	OcBr	61.3	HxdeH 4.4,	OcBr 3.9,	DodeH 54.0,	OceHe 5.2,	OcH 14.1,	BB 18.5
BuLi^b	t-PeOK^b	OcBr^b	77.3	HxdeH 13.0,	OcBr 26.7,	DodeH 25.5,	OceHe 2.8,	OcH 6.4,	BB 35.5
BuLi^c	t-PeOK^c	OcBr^c	61.4	HxdeH 4.1,	OcBr 46.0,	DoDeH 29.2,	OceHe 4.4,	OcH 7.5,	BB 8.8
BuLi	t-PeOK	OcBr	56.3^d	HxdeH 6.8,	OcBr 2.2,	DodeH 47.1,	OceHe 10.1,	OcH 15.8,	BB 18.0
BuLi	t-PeOK	OcBr	39.7^e	HxdeH 9.4,	OcBr 0.5,	DodeH 39.7,	OceHe —^{a},	OcH —^{a},	BB 20.9
BuLi	t-PeOK	PhBr	63.1	PhPh 1.3,	PhBr 0,	BuPh 54.0,	PhH 22.2,	OcH 5.8,	BB 16.7
EtHeLi	t-PeOK	EtHeBr	86.4	DiEtDodeH 76.7,	EtHeBr 0.8,	EtHeeH^f 7.9,	EtHeH 14.6,	OcH 5.8	

^{a} Undetermined. The other values in this experiment are related to the starting amount of BuLi. ^{b,c} [BuLi] : [t-PeOK] : [OcBr] = ^{b} 1 : 0.5 : 1, ^{c} 1 : 1 : 2. ^{d} Reaction temperature −45 to −50°C. ^{e} In THF at −40 to −45°C. ^{f} Probably.

$$\text{C}_4\text{H}_9\text{K} + \text{C}_8\text{H}_{17}\text{Br} \longrightarrow \begin{cases} \longrightarrow \text{C}_{12}\text{H}_{26} + \text{KBr} & (D) \\ \longrightarrow \text{C}_8\text{H}_{16} + \text{C}_4\text{H}_{10} + \text{KBr} & (E) \\ \longrightarrow \text{C}_4\text{H}_9\text{Br} + \text{C}_8\text{H}_{17}\text{K}. & (F) \end{cases}$$

The products of reaction (F) may react further in the sense of reactions (D) and (E) (cf. the formation of hexadecane; Table I). The exchange metal–metal reaction (e.g. (C)) is involved in the reaction with halogenide in some way. In addition, trace quantities of unidentified compounds are also formed.

The heavy alkaline metal alkoxide plays a decisive role in the reaction of the organometallic compound with the organic halogenide. Conversion of the halogenide is proportional to the amount of alkoxide added. At the equimolar ratio of all three reaction components the conversion of bromides or iodides is higher than 96% theor. On the contrary, at BuLi : t-PeOK : octyl bromide = 1 : 0·5 : 1 the conversion of bromide was only 59% theor. With potassium alkoxides added, the rate of the reaction of organometallic compound and halogenide is much higher than that observed with sodium alkoxides. A lower temperature during the addition of potassium alkoxides $(-45°\text{C}$ instead of $20°\text{C})$ had only a weak effect on the composition of organic reaction products, but the yield of coupling was negatively affected, if hexane was replaced with THF at $-45°$ (Table I).

The extent of β-elimination can be easily compared using the reaction between BuLi and various butyl halogenides (analogy to reaction (E)). For instance, Table I shows that in the reaction of butyl chloride the products of β-elimination predominate and coupling occurs only to some 26% theor. On the other hand, with butyl bromide or iodide the coupling yield is about 80% theor., while the β-elimination is represented only little. Hence, it can be inferred that bromides and iodides are better suited for the coupling with the organometallic compound than chlorides.

The coupling of organic nonactivated halogenides with organolithium compounds in the presence of a heavy alkaline metal alkoxide described in this study is a simple and rapid method for the preparation of hydrocarbons and some of their derivatives. The yields of coupling products are relatively high (60—86% theor.), but not higher than those obtained in the known coupling of halogenides with organocuprates[12]. The new reaction proceeds under much more favourable conditions and therefore may be employed also on a larger than laboratory scale. Thus, only one equivalent of the expensive organolithium compound is consumed in the reaction, in the contradistinction to two or more equivalents in the case of cuprates; also, cheaper and safer aliphatic hydrocarbons can be used as the medium instead of THF or aromatic solvents; and, lastly, the reaction proceeds at room temperature and does not require cooling to low temperatures.

EXPERIMENTAL

All operations with organic compounds of alkali metals were performed in an atmosphere of purified argon. Reagents and solvents were rectified and dried before use. Alkali alkoxides were prepared by a reaction of the alcohol with the alkali metal (molar ratio 1 : 1·3) in THF, isolation as crystals and final drying at 60°C *in vacuo*. For analyses of the reaction mixture a GLC apparatus Perkin–Elmer F 30 (columns packed with 10% GEXE-60 on Chromosorb) and decane as the internal standard were used.

Procedure: To a solution of organolithium compound and organic bromide or iodide in an aliphatic hydrocarbon ($c \sim 1$ mol/l, molar ratio 1 : 1), a solution of the same molar amount of t-PeOK in the same solvent ($c \sim 1$ mol/l) is added with continuous stirring. The same, or somewhat poorer yields of coupling are obtained, if a solution of sodium tert-butoxide in cyclohexane is used ($c \sim 0\cdot8$ mol/l), or in the case of reverse mixing procedure, where a solution of organolithium compound is added dropwise to a suspension of potassium tert-butoxide in hydrocarbon and organic halogenide. The reaction temperature is maintained by cooling within $15-35°C$. After the dropwise addition has been completed (mostly within 10 min), the mixture is stirred at room temperature one hour (with sodium alkoxides three hours), then hydrolyzed with a small excess of water and analyzed.

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