METALLATION OF BENZENE WITH THE SYSTEM ORGANOLITHIUM COMPOUND–POTASSIUM TERT-PENTOXIDE*

Lubomír LOCHMANN

Institute of Macromolecular Chemistry,
Czechoslovak Academy of Sciences, 162 06 Prague

By acting with the system organolithium compound and potassium tert-pentoxide on benzene, phenylpotassium is obtained as the main product, the purity of which is considerably dependent on reaction conditions. The relatively purest phenylpotassium (molar ratio K/Li > 12) can be obtained at a high benzene concentration in the reaction mixture and/or in the presence of diethyl ether. This dependence makes the metallation of benzene differ from a similar metallation of toluene, and it is therefore not possible to suggest general optimal conditions for such a metallation of different substrates yet.

In the reaction of organolithium compounds with heavier alkali metal alkoxides lithium is exchanged for a heavier alkali metal, thus giving rise to an organic compound of a heavier alkali metal and lithium alkoxide[2-5]. If the reaction is carried out in the presence of a third component possessing a suitable reactivity, a derivative of this component substituted with the heavier alkali metal is obtained. This fact has been demonstrated both by an analysis of the isolated products[2-5] and on the basis of characteristic properties of heavier alkali metal compounds using NMR spectroscopy[6] and EPR spectroscopy[7]. The lithium–heavier alkali metal exchange proceeds not only in the case of organolithium compounds with the C—Li bond, but also with compounds having the N—Li bond (substituted lithium amides)[8] or lithium enolates of ketones[9] and esters[10] (*cf.* the review[11]). Recently, the reaction between this system and toluene has been investigated[1]. In this reaction benzylpotassium is formed in a good yield and purity under different conditions used; potassium alkoxide participates in the reaction in a stoichiometric amount. A similar reaction with benzene was not so unambiguous, however, and has therefore been studied in greater detail. Metallation of benzene with a mixture of butyllithium and potassium (−) (1R)-menthoxide or text-butoxide has been performed earlier[5,12].

EXPERIMENTAL

Chemicals

2-Ethylhexyllithium (EtHexLi) and potassium tert-pentoxide (t-PeOK) were prepared and hexane was purified as in ref.[1]. Benzene and diethyl ether were rectified with lithium aluminium hydride, diethyl ether was additionally dried with sodium benzophenone ketyl. All operations with organic compounds of alkali metals were carried out in the atmosphere of purified argon. Butyllithium was prepared form Li and butylchloride in hexane.

Metallation Procedures

Butyllithium or EtHexLi (as 0·8 molar solutions in hexane) (0·015 mol), t-PeOK (as a molar solution in hexane) and benzene were mixed with stirring in chosen amounts during 5 min at 25°C. After stirring for the given time, the precipitate formed was isolated by centrifuging and analyzed. Ways of mixing used: *a*) to a mixture of RLi and benzene the solution of t-PeOK was added dropwise; *b*) to a mixture of EtHexLi and t-PeOK solutions after 15 min at 25°C benzene was added dropwise; *c*) to a mixture of t-PeOK solution and benzene EtHexLi solution was added dropwise; *d*) to a mixture of EtHexLi solution, benzene, and diethyl ether at 0 ± 5°C t-PeOK solution was added dropwise.

Analysis of Isolated Precipitates

Alkali metals were determined by atomic absorption spectrometry. GLC analyses were performed on a Perkin–Elmer 8310 apparatus in columns (length 2 m, i.d. 1·8 mm) packed with 15% Apiezon L on Chromosorb W-HP 80—100 mesh (GLC of the hydrolyzed products) or in columns (length 1·8 m, i.d. 2 mm) packed with 10% of 1,8-bis-(2,4-dinitrophenylcarbonyloxy)--3,6-dioxaoctane on Chromosorb W 80—100 mesh (GLC of the products derivatized with methyl iodide). Decane was used as internal standard and octane as solvent in both cases. *Hydrolysis*: A sample of the precipitate was suspended in five volumes of octane, the internal standard was added, a five-molar amount of water was also added under cooling to −30°C and the mixture was warmed to room temperature with shaking. *Reaction of the precipitate with methyl iodide*: Similar to hydrolysis, but methyl iodide was used in a three-molar amount.

Interaction of Phenylpotassium with Alkali Alkoxides

(i) Phenylpotassium (0·765 g, 0·0066 mol) was shaken with 20 ml of hexane solution of t-PeOK (0·020 mol) and three steel beads at room temperature for 6 h. Yield of the precipitate after repeated washing with hexane (6 times) was 1·27 g. Metal content: 32·64% K, 0·093% Li (the starting PhK contained 1·90% Li). Products of hydrolysis: 22 mole % PhH, 60·2 mole % t-PeOH. (ii) Phenylpotassium (0·61 g, 0·0053 mol) was shaken with 16 ml of hexane solution of lithium tert-butoxide (0·016 mol) under otherwise the same conditions as sub (i). Yield of the precipitate was 0·57 g. Metal content: 30·00% K, 1·24% Li (the starting PhK contained 0·44% Li). Products of hydrolysis: 75 mole % PhH, 1·5 mole % tert-butylalcohol, 3 mole % t-PeOH (as in the starting PhK).

RESULTS AND DISCUSSION

In the reaction of organolithium compounds (RLi) and potassium tert-pentoxide with benzene in a hydrocarbon medium, phenylpotassium was formed as the main

product according to the scheme

$$C_6H_6 + RLi + CH_3CH_2C(CH_3)_2OK = C_6H_5K + RH +$$
$$+ CH_3CH_2C(CH_3)_2OLi \qquad (A)$$
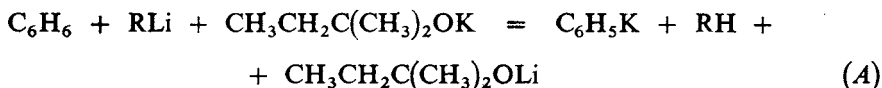
and was isolated from the reaction mixture as an insoluble precipitate. The organo-lithium compounds used were butyllithium (BuLi, $R = CH_3CH_2CH_2CH_2$) and 2-ethylhexyllithium (EtHexLi, $R = CH_3CH_2CH_2CH_2CH(C_2H_5)CH_2$). The latter organolithium compound forms a homogeneous metallation mixture with potassium tert-pentoxide (t-PeOK) in aliphatic hydrocarbons, thus ruling out the possibility of contamination of phenylpotassium (PhK) with an organopotassium compound RK (ref.[1]). The content of the individual alkali metals and compounds arising after the reaction with water or methyl iodide were determined in the isolated precipitate. The results are summarized in Table I.

The content of PhK and other compounds in the isolated precipitate depended considerably on the rection conditions used. The benzene concentration in the reaction mixture influenced the purity of PhK formed in the reaction very much. At the highest benzene concentration, *i.e.* in the reaction of benzene solution of both remaining reactants (molar ratio EtHexLi : t-PeOK : benzene = 1 : 1 : 31) the product contained a low amount of impurities, and the content of lithium compounds was also low (molar ratio K/Li = 12). On the contrary, at the equimolar ratio of all three reactants the content of impurities and lithium compounds in the product increased (molar ratio K/Li < 3). As expected, these products contained a major amount of di- and trimetallated benzenes (about 10 mole %) and, quite unexpectedly this time, a major amount of alkoxides (10—16 mole %), lithium compounds and some other compounds, such as metallated diphenyl.

The composition of the reaction product of equimolar amounts of reactants in heptane did not change essentially, if some conditions were changed, such as the reaction time (0·05—24 h) or the procedure used in mixing the reactants (*cf.* procedures *a*), *b*), *c*)), or if the temperature was maintained at 55°C during the reaction. Purity of the isolated PhK became somewhat improved, however, after the t-PeOK concentration in the mixture had been raised. As follows from Table I, these relations were valid for both EtHexLi and BuLi, but the differences observed in the latter case were smaller. After some products had reacted with methyl iodide, GLC revealed also a minor quantity of benzene (below 12 mole %), the origin of which could not be fully elucidated.

A distinct improvement in the quality of isolated PhK was achieved after diethyl ether had been added to the reaction mixture (Table II). In these experiments the reaction temperature was maintained at $0 \pm 5°C$, in order to inhibit the reaction (if any) between organic compounds of alkali metals and ether. In this way, relatively

TABLE I

Metallation of benzene (PhH) with the system organolithium compound (RLi)–potassium tert-pentoxide (t-PeOK) according to the reaction (A) (procedure a), 25°C, heptane; yield of precipitate as phenyl potassium (PhK) related to RLi). Analysis of reaction products and of products (mole %) of their hydrolysis or reaction with methyl iodide. Abbreviations: DiPh diphenyl, To toluen, Xy xylene, t-PeOH tert-pentylalcohol

PhH	RLi	t-PeOK	t	Yield	Metal content, wt.%		$\frac{[K]}{[Li]}$	Hydrolysis of PhK			Reaction of PhK with CH$_3$I			
			h	%	K	Li		PhK	t-PeOK	DiPh	PhH	To	m,p-Xy	o-Xy
mol l^{-1}														
						RLi = 2-ethylhexyllithium								
10·3	0·335	0·335	1	97	30·60	0·44	12·34	93	3·4	0·4	12	70	0	0
1·76	0·352	0·352	1	98	29·34	0·88	5·93	86	5·5	—	8	65	7	0
1·69	0·338	0·338	1^a	100	27·87	0·88	5·63	90	6·0	0·4	6	85	2	0
0·343	0·350	0·350	1	90	28·05	2·11	2·36	82	11·3	1·1	4	57	13	1
0·363	0·370	0·370	24	96	25·92	1·91	2·41	71	11·7	—	6	64	11	1
0·363	0·370	0·370	0·05	76	27·20	1·83	2·64	72	11·0	—	10	53	9	1
0·363	0·370	0·370	1^b	93	25·86	2·24	2·05.	66	14·2	—	0	45	8	1
0·363	0·370	0·370	1^c	101	26·44	1·90	2·47	67	16·6	—	0	48	9	0·5
0·326	0·433	0·331	1	91	31·55	0·85	6·60	77	10·4	—	9	48	11	3
						RLi = butyllithium								
10·3	0·336	0·336	1	98	28·0	0·89	5·59	96	3·0	0·5	12	69	0·5	0
2·15	0·430	0·430	1	93	28·3	0·97	5·18	93	6·5	—	5	75	3	1
0·497	0·508	0·508	1	84	30·06	1·22	4·37	81	10·4	—	5	48	9	1
0·497	0·508	0·508	0·05	74	33·73	1·13	5·30	74	10·5	—	10	44	11	2

^{a} Reaction at 55°C. ^{b} Procedure b). ^{c} Procedure c).

TABLE II

Metallation of benzene (PhH) by means of the system 2-ethylhexyllithium (RLi)–potassium tert-pentoxide (t-PeOK) in the presence of diethyl ether (Et$_2$O) (procedure d), heptane, 1 h, -5 to 5°C; yield of precipitate as phenylpotassium (PhK) related to RLi). Analysis of reaction products and of products (mole %) of their hydrolysis or reaction with methyl iodide. Abbreviations cf. Table I

PhH	RLi	t-PeOK	Et$_2$O	Yield %	Metal content, wt. %		$\dfrac{[K]}{[Li]}$	Hydrolysis of PhK			Reaction of PhK with CH$_3$I			
					K	Li		PhH	t-PeOH	DiPh	PhH	To	m,p-Xy	o-Xy
	mol l^{-1}													
1·56	0·312	0·312	0·954	93	29·98	0·74	7·19	87	6·1	0·15	8	72	1	0
0·343	0·350	0·350	1·07	76	30·09	1·09	4·90	81	5·7	0·32	6	69	3·7	0·7
0·309	0·315	0·315	1·93	70	30·46	0·65	8·32	80	4·5	traces	5	62	2·4	0·6
0·349	0·356	0·451	1·09	82	31·07	0·34	16·26	76	8·2	traces	5	63	3·6	0

pure PhK could be obtained even at the equimolar ratio of the reactants. With increasing ether concentration in the mixture its effect became more pronounced, and the content of such impurities as lithium compounds, tert-pentyl alcohol, diphenyl, and also the content of polymetallated benzene derivatives was smaller. Modification of the reaction (A) by adding diethyl ether is advantageous mainly for preparative purposes, and its usefulness will be investigated further.

The interaction between PhK, on the one hand, and potassium or lithium alkoxides, on the other, was also investigated. PhK readily formed a nonstoichiometric adduct (mixed aggregate) with t-PeOK, similarly to the behaviour of benzylpotassium[1]. Thus, e.g., after the reaction of PhK with a three-molar quantity of t-PeOK in heptane, an adduct having the composition $(C_6H_5K . 2\cdot74\, t\text{-}C_5H_{11}OK)_x$ was isolated. On the contrary, in a similar reaction of lithium tert-butoxide no interaction could be detected to any important extent $(cf.$ the yield of this product and the content of tert-butyl alcohol in it).

The change of the quality of the metallation product of benzene with reaction conditions is obviously related to the ability of organic compounds of alkali metals to form stable supermolecular aggregates. Such aggregation has been observed with many types of organolithium compounds[13,14]. Both the equilibrium constants and the rate of aggregation are high, so that immediately after these compounds had been formed almost complete aggregation took place. These aggregates are less reactive than the parent monomeric species.

In the metallations at low benzene concentration it may be assumed that the concentration of forming PhK is also lower, so that other alkali metal compounds, such as alkoxides and lithium compounds present in the mixture, become more incorporated during its aggregation and precipitation. The formation of mixed PhK–t-PeOK aggregates proceeds smoothly, and although lithium alkoxides in their aggregated form react only little with PhK $(cf.$ Experimental), such reaction cannot nevertheless be ruled out for the less aggregated lithium alkoxides *in statu nascendi*. Moreover, the possible formation of an adduct between PhK and t-PeOK consumes the free t-PeOK from the reaction mixture and thus limits the formation of PhK still more. On the contrary, solvation of organic compounds of alkali metals with electron-donor compounds (e.g., diethyl ether) raises the rate of their reactions and stabilizes these compounds at the lower degree of aggregation. In agreement with these known facts, the addition of diethyl ether in the metallation of benzene by means of the RLi and t-PeOK system has a favourable effect on the purity of the product (Table II). Similarly, the products obtained in the exchange reaction between PhLi and sodium tert-butoxide or potassium $(-)(1R)$-menthoxide in the presence of diethyl ether were purer[15] than those obtained in the pure hydrocarbon medium[16].

The GLC analysis of isolated precipitates after hydrolysis revealed the presence of trace quantities of higher-boiling compounds, such as diphenyl. The latter could arise by a similar mechanism as described by Schleyer[17] for isopropylbenzene, *i.e.*,

by the dimerization of intermediately formed radical anions (*cf.* parallel values of contents of dimetallated benzenes and diphenyl in products summarized in Tables I and II).

The composition of products in the investigated metallation of benzene depends much more on the reaction conditions used than in the similar case of toluene[1]. Therefore, the optimal conditions needed for the metallation of various substrates with the system RLi–heavier alkali metal alkoxide may differ from each other. Hence, rules generally valid for an advantageous metallation may be derived only after the reactions of a major number of substrates have been checked.

The author is indebted to Mrs H. Jakubův and Mrs E. Plachetková for technical assistance.

REFERENCES

1. Lochmann L., Trekoval J.: J. Organomet. Chem. *326*, 1 (1987).
2. Lochmann L., Pospíšil J., Lím D.: Tetrahedron Lett. *1966*, 257.
3. Lochmann L., Pospíšil J., Lím D.: Czech. 132254, applied 30. 12. 1964, Chem. Abstr. *73*, 25642f (1970).
4. Báča J., Lochmann L., Jůzl K., Čoupek J., Lím D.: *IUPAC Symposium on Macromolecules, Prague 1965*, Preprint P 508; J. Polym. Sci., C No. *16*, 3865, (1968).
5. Lochmann L., Lím D.: J. Organomet. Chem. *28*, 153 (1971).
6. Boche G., Etzrodt H.: Tetrahedron Lett. *24*, 5477 (1983).
7. Wilhelm D., Clark T., Schleyer P.v.R.: J. Organomet. Chem. *273*, C 1 (1984).
8. Lochmann L., Trekoval J.: J. Organomet. Chem. *179*, 123 (1979).
9. Lochmann L., De R. L., Trekoval J.: J. Organomet. Chem. *156*, 307 (1978).
10. Lochmann L., Trekoval J.: J. Organomet. Chem. *99*, 329 (1975).
11. Lochmann L., Trekoval J.: Collect. Czech. Chem. Commun., in press.
12. Schlosser M.: J. Organomet. Chem. *8*, 9 (1967).
13. Setzer W. N., Schleyer P.v.R.: Adv. Organomet. Chem. *24*, 353 (1985).
14. McGarrity J. F., Ogle C. A.: J. Am. Chem. Soc. *107*, 1805 (1985).
15. Thirase G., Weiss E.: J. Organomet. Chem. *81*, C 1 (1974).
16. Lochmann L.: Unpublished results.
17. Wilhelm D., Clark T., Schleyer P.v.R.: J. Chem. Soc., Chem. Commun. *1983*, 211

Translated by L. Kopecká.