Hydrocarbon-Soluble Organoalkali-Metal Reagents. Preparation of Aryl Derivatives[1]

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Unsolvated arylalkali-metal reagents ArM (M = Li, Na, K) are solubilized in benzene or toluene by magnesium 2-ethoxyethoxide. The soluble complexes appear to have definite and reproducible compositions as characterized by the M/Mg ratio. this ratio was found to be (Ar = Ph) 4:1 for M = Li, 2:1 for M = Na, and 1:1 for M = K. Additional analytical data showed that phenylsodium and phenylpotassium form the soluble complexes $[Na_2Mg(Ph)_2(OCH_2CH_2OEt)_2]_n$ and $[KMg(Ph)(OCH_2CH_2OEt)_2]_n$, respectively. The chemical behavior of the latter species is reminiscent of the relevant arylalkali-metal reagents; i.e., they are powerful metalating agents. Solutions of the above complexes have a long shelf life at temperatures 20 °C or lower. Thus, sodiation and kaliation of organic compounds under homogeneous conditions now are possible.

Organic derivatives of the heavier alkali metals, as compared to their lithium counterparts, have found rather limited synthetic application.[2] The main reason for this is certainly their intractable nature.[3] Thus, organosodium and organopotassium reagents are completely insoluble in solvents in which they can survive long enough in order to be useful as "self" reagents. The problem was only partly solved by the use of sodium and potassium alkoxides for the "instant" generation of butylsodium and butylpotassium, as exemplified in eq 1.[4] The availability of

$$\mathrm{BuLi} + t\text{-}\mathrm{BuOK} \rightarrow \mathrm{BuK} + t\text{-}\mathrm{BuOLi} \qquad (1)$$

hydrocarbon-soluble organosodium reagents is desirable for several reasons. Most importantly, sodium metal is cheaper than lithium. Furthermore, organosodium and organopotassium reagents might present certain advantages over butyllithium as metalating agents. They do not require a Lewis base as a catalyst in order to effect the more difficult metalations as do the alkyllithium.[5] In addition, one could reasonably expect that in metalation, orientation and specificity will vary with the metal in RM, and therefore, the hydrocarbon-soluble organosodium reagents could be an alternative to organolithiums as metalating agents.[6] Lastly, the availability of hydrocarbon-soluble organosodium and organopotassium reagents will permit the systematic study of metalation under homogeneous conditions, under which one can reasonably expect that more reliable results will be obtained. Indeed, earlier studies of metalations under heterogeneous conditions by organosodium and organopotassium reagents showed that results such as yields, selectivities, and even reactivities often varied markedly from one experimenter to another.[7] In this paper we report on our study of the interaction between arylalkali-metal reagents and certain magnesium alkoxides. This interaction leads to the formation of hydrocarbon-soluble species with organoalkali-metal-like reactivity.

Table I. Solubilizing Unsolvated Arylalkali-Metal Reagents in Benzene (Toluene) by Magnesium 2-Ethoxyethoxide

entry	ArM	source of Ar	method[a]	ratio of M/Mg	concn[b]
1	PhLi	Ph_2Hg	A	4:1	
2	PhLi	Ph_2Hg	B	3:1	
3	PhLi	PhBr	B	3:1	1.3
4	2-thienyllithium	thiophene	B	3:1	1.7
5	PhNa	PhCl	A	2:1	1.4
6	PhNa	PhCl	B	2:1	
7	PhNa	Ph_2Hg	A	2:1	
8	PhK	Ph_2Hg	A	1:1 (1.6:1)[c]	0.77
9	PhK	Ph_2Hg	B	1:1	

[a] Method A: ArM prepared in the presence of $Mg(OCH_2CH_2OEt)_2$. Method B: adding alkoxide to preformed ArM. [b] In moles per liter of ArM; the indicated concentration is the highest observed and not the highest possible (solubility). [c] The ratio in parentheses was obtained by employing a 5-day reaction time. The ratio 1:1 is readily reproduced.

The Arylalkali Metal–Magnesium Alkoxide System. In Scheme I are given some of the possible modes of interaction between an arylalkali-metal reagent and a magnesium alkoxide. One possibility is metal–metal interchange (eq i), which leads to the formation of an alkali-metal alkoxide and to an arylmagnesium alkoxide. Another possible mode of interaction could be complex formation between the interacting species (eq ii), and a third possibility could be a mixed mode involving initially a metal–metal interchange step followed by complex formation among the species shown on both sides of eq i. Our study showed that arylalkali metals and magnesium alkoxides react according to eq ii.

Scheme I

$$\mathrm{ArM} + \mathrm{Mg(OR)_2} \rightarrow \mathrm{MOR} + \mathrm{ArMgOR} \qquad \text{(i)}$$

$$n\mathrm{ArM} + m\mathrm{Mg(OR)_2} \rightarrow \mathrm{(ArM)}_n\mathrm{(Mg(OR)_2)}_m \qquad \text{(ii)}$$

Various alkoxides of magnesium such as $Mg(O\text{-}n\text{-}Bu)_2$, $Mg(OCH_2CH_2OCH_3)_2$, and $Mg(OCH_2CH_2OEt)_2$ were found to form more or less hydrocarbon-soluble complexes with *unsolvated* organoalkali-metal reagents. Far better solubility was observed with magnesium 2-ethoxyethoxide (1), and therefore, only the preparation of these species will be described. For example, when 1 was added to a large excess of phenylsodium suspended in benzene, we obtained a benzene-soluble complex. Analogous soluble complexes were formed by the phenyl derivatives of lith-

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[1] Screttas, C. G. U.S. Patent 3932545, 1976; *Chem. Abstr.* **1976**, *85*, 33177.

[2] For a recent review see: Kaiser, E. M. *J. Organomet. Chem.* **1982**, *227*, 135.

[3] Coates, G. E.; Green, M. L. H.; Wade, K. "Organometallic Compounds", 3rd ed.; Methuen: London Vol. 1, p 42.

[4] Screttas, C. G. Ph.D. Thesis, The University of Tennessee, 1966, p 106. Lochmann, L.; Pospišil, J.; Lim, D. *Tetrahedron Lett.* **1966**, *257*. Schlosser, M. *J. Organomet. Chem.* **1967**, *8*, 9.

[5] Screttas, C. G.; Eastham, J. F. *J. Am. Chem. Soc.* **1965**, *87*, 3276; **1966**, *88*, 5668.

[6] For a recent example of metal-dependent orientation in metalation see: Schlosser, M.; Schneider, P. *Helv. Chim. Acta* **1980**, *63*, 2404.

[7] Benkeser, R. A.; Trevillyan, A. E.; Hooz, J. *J. Am. Chem. Soc.* **1962**, *84*, 4971. Benkeser, R. A.; Foster, D. J.; Sauve, D. M. *Chem. Rev.* **1957**, *57*, 867.

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ium and potassium. These complexes can be prepared either by adding 1 to an excess of the arylalkali-metal reagent or by preparing the organometallic reagent in situ, i.e., in the presence of 1. The soluble species were characterized by determining the M/Mg ratio in solution. Unsolvated phenyllithium, like the other phenylalkali metals, is entirely insoluble in benzene or toluene. With 1, PhLi formed two different soluble complexes distinguished by the relative Li/Mg ratios and 3:1 and 4:1; see Table I. The larger ratio was obtained by generating PhLi in the presence of 1 by the reaction of Ph_2Hg with lithium metal. This reaction is very sluggish and requires reaction times on the order of 1 week at room temperature. It seems, therefore, that the prolonged contact of PhLi with the magnesium alkoxide is responsible for the production of the soluble complex with a maximum Li/Mg ratio of 4:1. Similarly, unsolvated 2-thienyllithium is insoluble in toluene, but it becomes soluble in the presence of 1, and the soluble complex has a Li/Mg ratio of 3:1. Phenylsodium and 1 form a soluble complex in benzene with a Na/Mg ratio of 2:1, regardless of the mode of preparation. It is quite impressive that analyses of the Na/Mg ratio of the complex from over two-dozen batches gave identical results; i.e., Na/Mg = 2:1. Phenylpotassium and 1 form a benzene-soluble complex with a K/Mg ratio of 1:1. This result was very readily reproducible. Only on stirring a large excess of PhK with 1 for several days did it become possible to obtain a soluble complex with a K/Mg ratio of 1.6. It appears that there is a trend in the composition of the soluble complexes in the series PhM (M = Li, Na, K), namely, the M/Mg ratio decreases as the ionization potential of the M atom decreases or as the ionic radius of M^+ increases.

The composition of the soluble complexes was investigated further by determining the number of available Ph groups in solution. This was done by carrying out double titrations using, in the case of the PhNa–1 complex, ethylene bromide[8] and, in the case of the PhK–1 complex, benzyl chloride. Thus, we concluded that the number of available Ph groups in solution is equal to the number of alkali-metal atoms. This result was substantiated by quantitative proton NMR spectroscopy. Therefore, the soluble species derived from PhNa and PhK should be $[Na_2Mg(Ph)_2(OCH_2CH_2OEt)_2]_n$ and $[KMg(Ph)(OCH_2CH_2OEt)_2]_n$, respectively.

The structure of the latter species was studied briefly by proton and carbon-13 NMR spectroscopy. In Figure 1a is shown the ^1H NMR spectrum of the PhNa–1 complex. From the intergrated spectrum the $(Ph)/(OCH_2CH_2OEt)$ ratio was estimated to be 1.9, close to the calculated one of 1.8, on the basis of the titration results. For comparison purposes is also given the spectrum of 1 (Figure 1b). We notice that the signals due to both uncomplexed and complexed (with PhNa) magnesium 2-ethoxyethoxide are diffuse. The spectral appearence, however, differs markedly. Upon complexation the Mg–O–CH_2 protons remained unperturbed. The band due to the CH_2–O–CH_2 protons was shifted upfield by 0.31 ppm, as was the CH_3 proton signal, which became more shielded by 0.27 ppm. In the respective carbon-13 NMR spectra (Figure 2) and on the basis of our assignment, the C(1) carbon appears to have undergone the largest deshielding by 3.24 ppm whereas the C(2) signal remained almost unperturbed. a downfield shift of 0.92 ppm was exhibited by C(3) and a smaller upfield shift (0.2 ppm) by C(4). The aromatic carbon bearing the metal is found at 141.76 ppm.

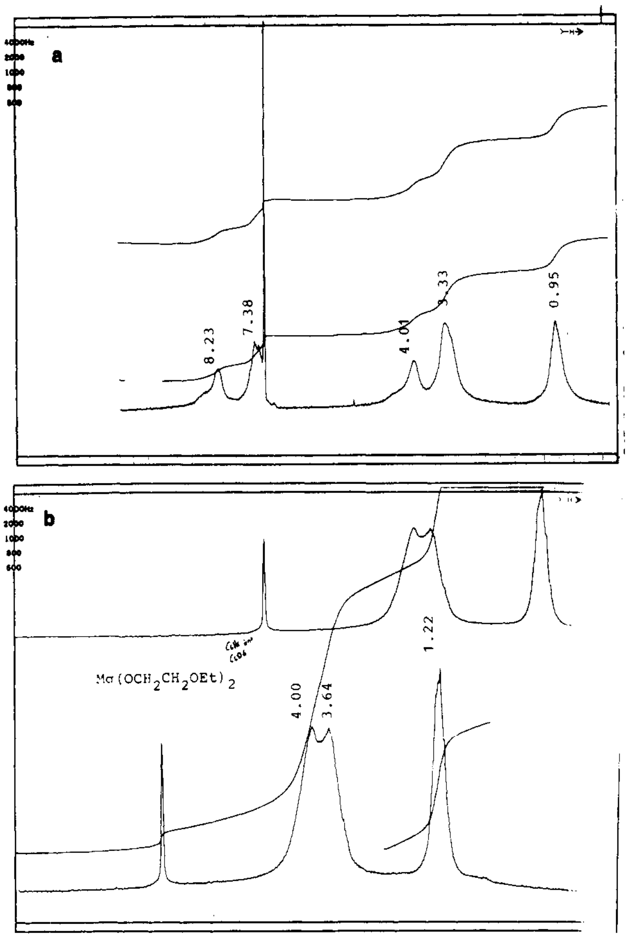

Figure 1. The 80-MHz ^1H NMR spectrum of (a) $[Na_2Mg(Ph)_2(OCH_2CH_2OEt)_2]_n$ and (b) $Mg(OCH_2CH_2OEt)_2$ (solvent C_6D_6).

Analogous proton (Figure 3) and Carbon-13 (Figure 4) spectra were exhibited by the PhK–1 complex. The integrated proton spectrum confirmed the titration result; i.e., the $(Ph)/(OCH_2CH_2OEt)$ ratio is 1:2. Again, the resonance bands are diffuse just as in the case of the PhNa–1 complex. Here, the largest change in the chemical shifts of the alkoxy protons upon complexation was exhibited by the Mg–O–CH_2 proton signal, which was shifted to a lower field by 0.23 ppm. The CH_2–O–CH_2 protons were shifted to a higher field by 0.20 ppm, and the CH_3 band became more shielded by 0.09 ppm. In the respective carbon-13 spectrum, C(1) and C(3) appear more deshielded by 4.39 and 1.42 ppm, respectively, whereas C(2) was shifted to a higher field by 0.43 ppm and C(4) remained almost unperturbed. This information probably indicates that coordination takes place through both the magnesium atom as well as through the ether linkage. The lack of fine structure in the proton bands could also mean that the soluble species are higher aggregates of the "unit structure" indicated by the analysis. In such a case these complexes could bear some analogy to the $Mg_4Hg_2[Si(CH_3)_2Ph]_6(OCH_2CH_2OMe)_6(CH_3OCH_2CH_2OCH_3)_2$ complex.[9] In any case the structure of the soluble species should be considered unknown.

The soluble complexes exhibit normal organometallic reactivity toward carbon dioxide and benzophenone. The expected acid and carbinol were formed in 90%, or better, yields. The PhNa and PhK complexes behave as effective metalating agents, reminiscent of organoalkali-metal

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(8) Gilman, H.; Cartledge, F. K.; Sim, S.-Y. *J. Organomet. Chem.* **1963**, *1*, 8.

(9) Sadurski, E. A.; Ilsley, W. H.; Thomas, R. D.; Glick, M. D.; Oliver, J. P. *J. Am. Chem. Soc.* **1978**, *100*, 7761.

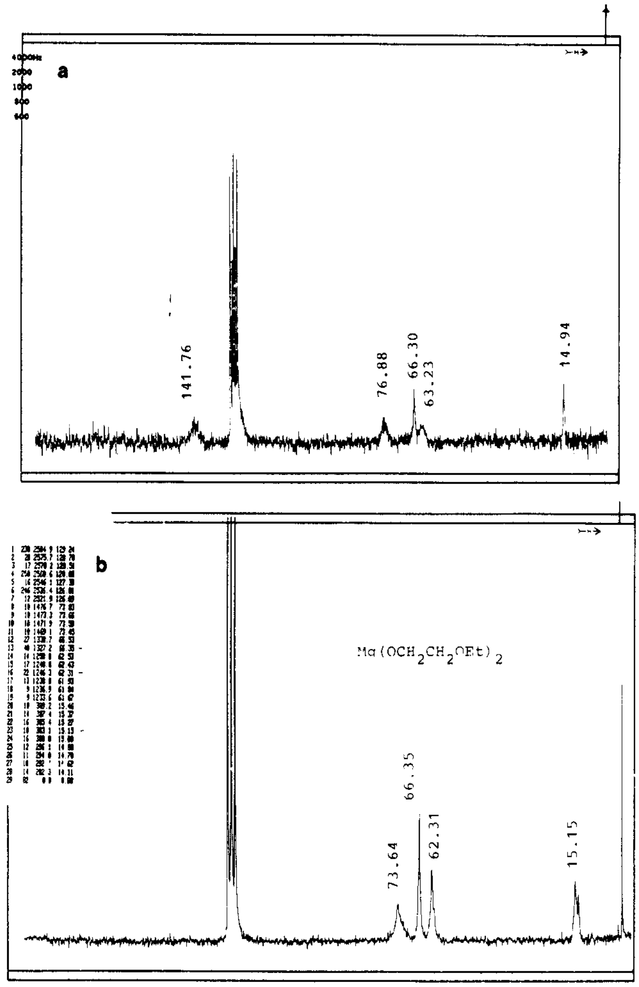

Figure 2. The ^{13}C NMR spectra of (a) $[Na_2Mg(Ph)_2(OCH_2CH_2OEt)_2]_n$ and (b) $Mg(OCH_2CH_2OEt)_2$ (solvent C_6D_6).

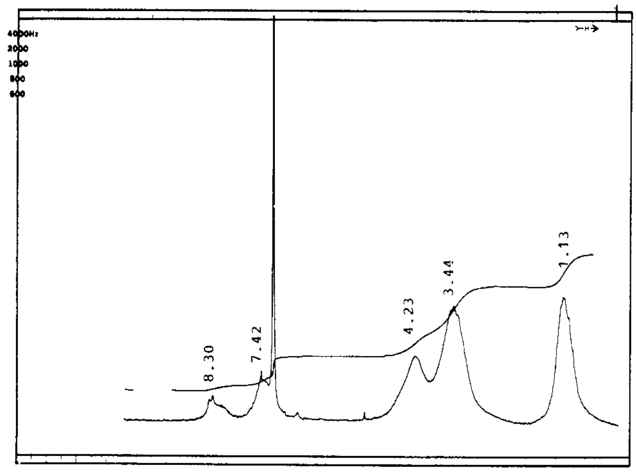

Figure 3. The ^1H NMR spectrum of $[KMg(Ph)(OCH_2CH_2OEt)_2]_n$ in C_6D_6.

reagents.[7] For example, the PhK-1 complex metalated toluene rapidly. Also, the PhNa complex was found to metalate toluene slowly at room temperature and to dimetalate dibenzofuran[10] more rapidly. The analogy between these soluble complexes and the respective insoluble organoalkali-metal reagents applies to both reactivity and specificity. For example, the PhNa complex metalated thioanisole on the methyl group, just as RNa reagents do under heterogeneous conditions[7,11] (eq 2) along with some demethylation.

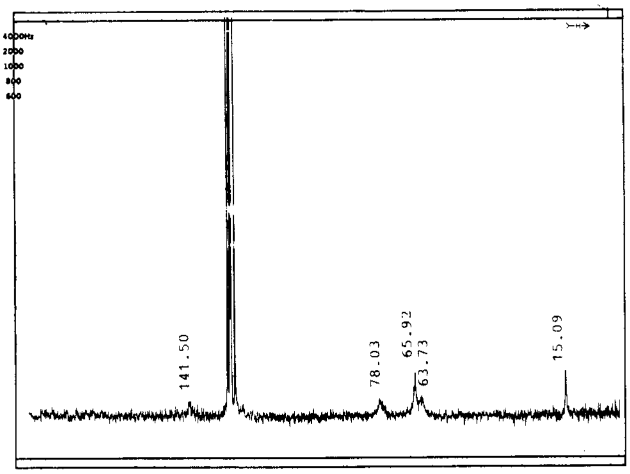

Figure 4. The ^{13}C NMR spectrum of $[KMg(Ph)(OCH_2CH_2OEt)_2]_n$ in C_6D_6.

$$\text{PhNa complex} + PhSCH_3 \rightarrow PhSCH_2Na + PhSNa \quad (2)$$

Solutions of the complexes in benzene appear to be stable for a long time. For example, a solution of the PhNa-1 complex did not lose any of its activity during a 1-month period at 13–22 °C. At higher temperatures crystalline precipitates are formed. The transformation that leads to the formation of the insoluble species appears to be rather rapid at temperature above 50 °C.

It is felt that the availability of the soluble complexes with organosodium- and organopotassium-like reactivity as shelf reagents will enable one to study metalations by these reagents under *homogeneous* conditions and to asses their synthetic potential. Such investigations are in progress.

Experimental Section

Proton and carbon-13 NMR spectra were recorded with a Varian FT 80A NMR spectrometer. Samples of organometallic compounds for NMR analysis were prepared in Schlenk tubes to which an NMR tube was fused. The Schlenk tube was flamed under vacuum, then cooled under an atmosphere of argon before charging the reactants and the solvent benzene-d_6, and finally sealed under vacuum with a hand torch. Phenyllithium, prepared from lithium and bromobenzene in diethyl ether, was desolvated by heating at 40–60 °C in vacuo, ca 0.06 mbar, for 8 h. The same conditions were used in the preparation of unsolvated 2-thienyllithium, which was obtained by metalating thiophene with *n*-butyllithium in Et_2O. Diphenylmercury was prepared according to the literature.[12] 2-Ethoxyethanol was purchased from Merck and was dried over 4A molecular sieves for several days before use. Benzene and toluene solvents were dried over 4A molecular sieves, degassed under vacuum and saturated with argon shortly before use.

Product Analysis. The compositions of the soluble complexes were determined by standard acid titration of a hydrolyzed 1.00-mL aliquot after centrifugation. This gave the total alkalinity. In the same or another aliquot magnesium was determined by EDTA titration.[13] The difference between total alkalinity and the alkalinity due to magnesium is the concentration of ArM in solution. This was confirmed by double titration, using ethylene bromide for the PhNa complex and benzyl chloride for the PhK complex. Thus, the nonactive alkalinity was found to be within 5%, or better, equal to that corresponding to the magnesium

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[10] Gilman, H.; Moore, F. W.; Baine, O. *J. Am. Chem. Soc.* **1941**, *63*, 2479.

[11] Gilman, H.; Bebb, F. J. *J. Am. Chem. Soc.* **1949**, *71*, 4062.

[12] Weygand/Gilgetag "Preparative Organic Chemistry"; Hilgetag, G., Martini, A., Ed.; Wiley: New York, 1972; p 773.

[13] "Vogels Textbook of Quantitative Inorganic Analysis", 4th ed.; Revised by Bessett, J., Denney, R. C., Jeffery, G. H., Mendham, J.; Longman Group: London, 1978; p 325.

content. It should be stressed that the successful application of double titration requires long contact times between the complex and the ethylene bromide or benzyl chloride, i.e., on the order of 1 h.

Magnesium 2-Ethoxyethoxide (1).[14] 2-Ethoxyethanol (300 mL), magnesium powder (12.3 g), and 3.3 g of $HgCl_2$ were stirred (Hershberg stirrer) under an atmosphere of argon. A rapid evolution of hydrogen and heat begun after the mixture was stirred rapidly for a few minutes. The reaction was controlled by cooling with a water bath. When the metal had dissolved, more magnesium was added twice in 6.3-g portions and stirring was continued while the mixture was heated to 50–70 °C for about 24 h. The unreacted metal was filtered under an atmosphere of argon, and the filtrate was evaporated to dryness in vacuo. Desolvation of the alkoxide was complete after the mixture was heated at 70–95 °C for 24 h at ca. 0.06 mbar. Anal. Calcd for $C_8H_{18}O_4Mg$: Mg, 12; equiv wt (standard acid titration), 101.22. Found: Mg, 11.84; equiv wt, 101.2.

Phenylsodium–1 Soluble Complex (Method A). Sodium metal (13.5 g, 0.587 mol) was stirred and heated in 100 mL of refluxing methylcyclohexane and 1.0 g of palmitic acid under a 40-mmHg positive pressure of argon, until it melted. The stirring rate was increased, and 1.0 mL of 1,2-dichloroethylene was added at once to the stirred metal. After the mixture was stirred at the maximum rate for a few minutes, heating was discontinued and methylcyclohexane was removed from the resulting sodium dispersion by vacuum evaporation. The reaction system was refilled with argon. Dry benzene (75 mL) was added to the dispersion, followed by 22.5 g (0.11 mol) of 1. Chlorobenzene (29.5 g, 0.26 mol) in 75 mL of benzene was added at ca. 35 °C (about 3 h). An aliquot of the reaction mixture was withdrawn and centrifuged under argon. The supernatant liquid was titrated for total alkalinity by standard acid to pH 7. It was found to be 2.4 N. Magnesium was determined in the same aliquot, and it was found to be 0.60 M. These results indicate a Na/Mg ratio of 2.0:1.0.

Phenylsodium–1 Soluble Complex (Method B). To a suspension of phenylsodium, prepared from 13.5 g of sodium metal, dispersed as described in the previous paragraph, 30 g of chlorobenzene in 70 mL of benzene at 34–38 °C, was added 20.5 g of 1. The resulting mixture was stirred for 0.25 h, and then a 20-mL aliquot was withdrawn and centrifuged under argon. Titration of the supernatant liquid indicated a total alkalinity of 2.9 N and a magnesium concentration of 0.707 M. These correspond to a Na/Mg ratio of 2.1:1.0.

Phenylpotassium–1 Soluble Complex. Diphenylmercury (5.4 g, 15 mmol), potassium metal (1.3 g, ca. 33 mol), 1 (2.1 g, 10.37 mmol), and benzene (20 mL) were stirred under argon for 14 h at room temperature. Within a few hours after the stirring was discontinued, a clear supernatant layer formed from which a 1.00-mL aliquot was withdrawn and titrated: total alkalinity, 1.34 N; magnesium content, 0.42 M; K/Mg ratio = 1.19:1.0. More alkoxide (1.0 g) was added, followed by 10 mL of benzene. The resulting mixture was stirred for 0.5 h and then was allowed to stand. Titration of the supernatant liquid indicated the following: total alkalinity, 1.37 N; magnesium content, 0.445 M; K/Mg ratio = 1.08:1.0.

Phenylpotassium–1 Soluble Complex (Prolonged Reaction Time). Diphenylmercury (7.2 g, 20 mmol), potassium metal (1.8 g, 46 mol), and benzene (40 mL) were stirred under argon overnight. Alkoxide 1 (7.0 g, ca. 35 mmol) was added to the PhK suspension, and the mixture was stirred for 2 h. Titration of a centrifuged aliquot indicated a K/Mg ratio of 0.8:1.0. After 11 mL was withdrawn from the supernatant liquid, more Ph_2Hg (1.8 g, 5 mmol) was added as well as 1.0 g of potassium metal, and the resulting mixture was stirred for 5 days. A new titration of the supernatant liquid indicated the following: total alkalinity, 1.74 N; magnesium content, 0.485 M; K/Mg ratio = 1.6:1.0.

Carbonation of the Phenylsodium–1 Complex. Eighteen milliliters of a solution of the title compound in benzene that contained 20 mmol of PhNa equivalent was injected into a slurry of crushed dry ice and ether. Due to the presence of magnesium ions some carboxylic acid precipitated on adding water to the carbonation mixture. The three phases were separated by centrifugation. The water layer was washed once with toluene and twice with hexane and acidified with 20% H_2SO_4. The precipitate was washed with hexane and air-dried. On acidification, the precipitate gave crystalline acid. The combined acidified mixtures were extracted with 4 × 75 mL of ether. The combined ether extracts were dried over $MgSO_4$. Evaporation of ether, after the drying agent was removed, gave 2.3 g (94%) of almost pure benzoic acid, mp 116–118 °C (lit.[15] mp 122 °C).

Reaction of the Phenylsodium–1 Complex with Benzophenone. To a solution of 3.0 g (16 mmol) of benzophenone in 10 mL of dry benzene was added 20 mL of a solution of the title complex, containing 11.8 mmol of PhNa equivalent. After being stirred for ca. 10 min, the reaction mixture was subjected to steam distillation. The nonvolatile product was taken up in toluene. The toluene solution was dried over $MgSO_4$ and evaporated to constant weight to yield 3.0 g (98%) of triphenylcarbinol, which after one recrystallization from hexane melted at 158–160 °C (lit.[16] mp 164–165 °C).

Metalation of Dibenzofuran by the Phenylsodium–1 Complex. Dibenzofuran (2.5 g, 14.9 mmol) was stirred for 21 h at room temperature with 20 mL of a solution of the PhNa complex, containing ca. 23.5 mmol of PhNa equivalent. The mixture was carbonated, and the carbonation mixture was worked up as described in the carbonation of the PhNa–1 complex itself (see relevant paragraph above). The yield of acid (vacuum dried) was 2.95 g. A portion of this product was esterified with diazomethane and analyzed by NMR, i.e., by comparing aromatic with aliphatic protons. It was found to be a mixture of dicarboxylic acid(s) (ca. 75 %) and monocarboxylic acid(s) (25%). Thus, the metalation yield is estimated to be 89%. The carbonation product on recrystallization from glacial acetic acid afforded a product, which did not melt up to 290 °C. Literature[17] melting point for the highest melting isomer of the monocarboxylic acids, i.e., dibenzofuran-2-carboxylic acid, was 271–272 °C.

Metalation of Thioanisole by the Phenylsodium–1 Complex. Twenty milliliters of a solution of the title complex containing ca. 20 mmol of PhNa equivalent was added to 5 mL of thioanisole. The resulting mixture was stirred at 64 °C for 24 h. Carbonation afforded an acidic product with a thiophenol odor. This material was heated at 40 °C under vacuum until the thiophenol odor disappeared. It weighed 1.1 g (32%) and melted at 59–60 °C, after one crystallization from hexane (lit.[18] mp for $PhSCH_2CO_2H$ 61–62 °C).

Acknowledgment. We thank Mrs. M. Voyadji and M. Kyttari for technical assistance.

Registry No. 1, 46142-17-0; $HgCl_2$, 7487-94-7; $PhSCH_2CO_2H$, 103-04-8; PhLi, 591-51-5; $[Na_2Mg(Ph)_2(OCH_2CH_2OEt)_2]_n$, 89597-13-7; $[KMg(Ph)(OCH_2CH_2OEt)_2]_n$, 89597-15-9; 2-ethoxyethanol, 110-80-5; phenylsodium, 1623-99-0; chlorobenzene, 108-90-7; phenylpotassium, 3605-36-5; diphenylmercury, 587-85-9; benzoic acid, 65-85-0; benzophenone, 119-61-9; triphenylcarbinol, 76-84-6; dibenzofuran, 132-64-9; dibenzofuran-2-carboxylic acid, 22439-48-1; thioanisole, 100-68-5; 2-thienyllithium, 2786-07-4.

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[14] For a general reference see: Bradley, D. C.; Mehrotra, R. C.; Gaur, D. P. "Metal Alkoxides"; Wiley: London, 1978.

[15] "Dictionary of Organic Compounds"; Eyre and Spottiswood: London, 1965; Vol. 1, p 344.

[16] Reference 15; Vol. 5, p 3200.

[17] Reference 15; Vol. 2, p 894.

[18] Reference 15; Vol. 4, p 2703.