Metal Alkoxide Modified Organometallic Reagents. Preparation and Stability of Organolithium Reagents in Tetrahydrofuran in the Presence of Magnesium 2-Ethoxyethoxide

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The metalating ability of alkyllithium reagents and their tendency to cleave THF are greatly diminished in the presence of magnesium 2-ethoxyethoxide, 1. Advantage may be taken of this to generate organolithium reagents in THF in the presence of 1 under conditions not normally favorable to their stability. Thus, by reaction with metallic lithium in the presence of 1 in THF, the compounds RX (R = *n*-Bu, *s*-Bu, *t*-Bu, cyclohexyl, menthyl, *p*-methoxyphenyl, *o*-(methoxymethyl)phenyl; X = Cl, Br) have been converted to the corresponding organometallic reagents. In the absence of 1 the alkyllithium reagents formed react with the solvent, resulting in reduced yields and often alternative products. In the case of the preparation of the arylmetal reagents the presence of 1 suppresses either subsequent orthometalation (R = *p*-methoxyphenyl) or Wittig rearrangement (R = *o*-(methoxymethyl)phenyl) to give a clean replacement of halogen by the metal. The presence of THF is also tolerated in the preparation of these two arylmetal reagents by halogen–metal exchange using *n*-butyllithium in the presence of 1 whereas if 1 is absent little or none of the desired product is obtained.

Introduction

Basic ethereal solvents such as tetrahydrofuran have many desirable properties as organometallic reaction media. They promote, for example, the preparation and reactivity of organometallic reagents and may additionally influence the outcome of a reaction.[1] A drawback to the use of organolithium reagents in tetrahydrofuran (THF), however, is their limited stability due to cleavage of the solvent.[2,3] The half-life of a reagent, RLi, depends on the nature of R and decreases in the order R = aryl > primary alkyl > secondary alkyl > tertiary alkyl.[2] Thus, when THF is required as a solvent, organolithium reagents are usually generated in situ and preferably used at low temperatures.

As part of recent work of ours on the solubilization of organoalkali reagents in hydrocarbon media by magnesium 2-ethoxyethoxide, we noticed that the metalating ability of these reagents was somewhat attenuated.[4] Since the cleavage of THF by organolithiums is widely believed to proceed by way of an initial metalation of the ether,[3] we considered that this might be partially or wholely suppressed in the presence of the magnesium alkoxide, thus permitting the storage of the reagents for a longer period.

The study of metal alkoxide/organometal systems is of interest also because they are formed during many reactions of organometallic reagents with substrates containing carbonyl or hydroxy groups. They may also be present if the substrate contains a readily cleavable group or an ether group that is susceptible to Wittig rearrangement. As mentioned previously, reaction with an ethereal solvent is a further source of alkoxide, and, although this may be slow in comparison with other reactions, the fact that the solvent is usually present in a large excess will ensure that appreciable amounts of alkoxide will be present. Lastly, traces of oxygen will react with most organometallic reagents to give the corresponding alkoxides.

The presence of alkoxide affects both the structure and the reactivity of the organometallic reagents. Brown et al., on the basis of spectroscopic and cryoscopic measurements, concluded that the ethyllithium hexamer in cyclohexane is not disrupted by addition of LiOEt, which initially corrdinates to two vacant sites on the cluster.[5] In diethyl ether, however, LiOEt appears to displace EtLi from the tetramer, $(EtLi)_4$, to give $Et_3Li_4(OEt)$.[6] More recently, McGarrity and Ogle have provided evidence that tetranuclear *n*-butyllithium/lithium *n*-butoxide clusters can be formed in THF by the successive replacement of BuLi in $(n\text{-BuLi})_4$ by *n*-BuOLi.[7] It was also demonstrated that these mixed aggregates have a greater reactivity than $(n\text{-BuLi})_4$ itself in the reaction with benzaldehyde, and that $Li_4(n\text{-Bu})_2(\text{OBu-}n)_2$, for example, had a reactivity comparable to that of the dimer, $(n\text{-BuLi})_2$, which in turn was about 10 times more reactive than the tetramer.[8] An analogous rate enhancement of the reaction of organolithium reagents with esters in the presence of LiOEt has been observed by Smith and co-workers,[9] and Baryshnikov et al. have reported the increased reactivity of *n*-BuLi with THF in the presence of LiOBu-*t*.[10] In numerous other studies on the reactions of organolithium reagents, however, there appears to have been little consideration of the effect of the metal alkoxides.[11]

Metal alkoxide/organometal systems in which the two metals are different have also been studied. Of these, perhaps the most widely known are the so-called LICKOR reagents where the metal alkoxide is commonly KOBu-*t* or an analogous tertiary alkoxide and the organometal is an organolithium reagent.[12–15] These are very powerful metalating reagents, and it has been suggested that the active organometallic reagent is essentially the corresponding organopotassium, which can be isolated under suitable conditions.[14] Schlosser, however, has shown that,

(1) See, for example: Eisch, J. J. *Organometallic Syntheses*; Academic Press: New York, 1981. "Comprehensive Organic Chemistry; Barton, D., Ollis, W. D., Eds.; Pergamon Press: Oxford, 1979.
(2) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon Press: Oxford, 1974. Wakefield, B. J. In *Comprehensive Organic Chemistry*; Barton, D., Ollis, W. D., Eds.; Pergamon Press: Oxford, 1979; Vol. 3, p 943ff.
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(7) McGarrity, J. F.; Ogle, C. A. *J. Am. Chem. Soc.* **1985**, *107*, 1805.
(8) McGarrity, J. F.; Ogle, C. A.; Brich, Z.; Loosli, H. R. *J. Am. Chem. Soc.* **1985**, *107*, 1810.
(9) Al-Aseer, M. A.; Allison, B. D.; Smith, S. G. *J. Org. Chem.* **1985**, *50*, 2715.
(10) Baryshnikov, Yu. N.; Kaloshina, N. N.; Vesnovskaya, G. I. *J. Gen. Chem. USSR* **1977**, *47*, 2535.
(11) See ref 9 and Al-Aseer, M. A.; Smith, S. G. *J. Org. Chem.* **1984**, *49*, 2608 for discussions of the mechanism of the reaction of organolithium reagents with carbonyl compounds and for further references.
(12) Lochmann, L.; Pospisil, J.; Lim, D. *Tetrahedron Lett.* **1966**, 257.
(13) Schlosser, M. *J. Organomet. Chem.* **1967**, *8*, 9.
(14) Lochmann, L.; Trekoval, J. *J. Organomet. Chem.* **1987**, *326*, 1.
(15) Schlosser, M.; Strunk, S. *Tetrahydron Lett.* **1984**, *25*, 741.

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Table I. Hydrogen–Metal Exchange Reactions Using *n*-Butyllithium[a]

entry	substrate	mmol of $Mg(OR)_2$[b]	solvent[c]	product	yield, %
1	Ph_2CH_2	0	A	Ph_2CHCO_2H	28
2	Ph_2CH_2	10	B	Ph_2CHCO_2H	trace
3	Ph_2CH_2	0	C	Ph_2CHCO_2H	63
4	Ph_2CH_2	10	C	Ph_2CHCO_2H	9
5	anisole	0	A	o-$C_6H_4(OMe)CO_2H$	60
6	anisole	10	B	o-$C_6H_4(OMe)CO_2H$	3.5
7	anisole	0	C	o-$C_6H_4(OMe)CO_2H$	81
8	anisole	10	C	o-$C_6H_4(OMe)CO_2H$	20
9	thiophene	0	A	2-thienoic acid	80
10	thiophene	10	B	2-thienoic acid	57
11	thiophene	0	C	2-thienoic acid	71[d]
12	thiophene	10	C	2-thienoic acid	71

[a] See Experimental Section for details. In all cases 20 mmol each of substrate and *n*-butyllithium were used. Temperature 0–25 °C; time 20 h. [b] R = $EtOCH_2CH_2$. [c] A = 30 mL of MCH/2 mL of THF; B = 30 mL of MCH/10 mL of THF; C = 11 mL of MCH/10 mL of THF. [d] Approximately 4% of 2,5-thiophenedicarboxylic acid was also isolated.

when freshly prepared, these reagents are superior to organopotassiums themselves,[15] and it is quite possible that again the alkoxide enhances the reactivity by the initial formation of mixed clusters. Other mixed metal alkoxide/organometal systems that have received attention include $LiOR'/R_2Mg$ for the alkylation–oxidation of aldehydes,[16] $Mg(OR')_2/RLi$ and $Mg(OR')_2/R_2Mg$ for the alkylation–oxidation of formamides,[17] CuOBu-*t*/RLi,[18] Ti(OPr-*i*)$_4$/RLi, and Ti(OPr-*i*)$_4$/RMgX,[19] $Y(OR')_3$/RLi and $Sm(OR')_3$/RLi,[20] and Hf(OPr-*i*)$_4$/RLi.[21] Each of these systems has certain advantages in terms of reactivity and selectivity, and it can be anticipated that, given the wide range of metal alkoxides already known,[22] this class of reagents may find considerable application in organic synthesis.

The present paper describes the preparation of organolithium reagents in THF in the presence and in the absence of magnesium 2-ethoxyethoxide by well-established routes:

$$R'H + RLi \xrightarrow{THF} R'Li + RH \quad (1)$$

$$R'X + 2Li \xrightarrow{THF} R'Li + LiX \quad (2)$$

$$ArBr + RLi \xrightarrow{THF} ArLi + RBr \quad (3)$$

Results and Discussion

(a) Hydrogen–Metal Exchange. In order to demonstrate the effect of $Mg(OCH_2CH_2OEt)_2$, **1**, on the metalating ability of *n*-BuLi in THF, a number of representative reactions were carried out with diphenylmethane, anisole, and thiophene. Reactions with or without added alkoxide were carried out in parallel, and the organometallic product obtained was identified by carboxylation. From the results presented in Table I, it can be seen that in the presence of the alkoxide the extent of metalation is reduced, with the yield being determined by the solvent composition and the nature of the substrate. Thus, for diphenylmethane, metalation is almost completely suppressed in the presence of alkoxide when only a small amount of THF (sufficient to solvate 1 and *n*-BuLi) is present (entries 1 and 2), and even when the THF/methylcyclohexane, MCH, ratio was increased only 9% of diphenylacetic acid was obtained compared with 63% of diphenylacetic acid without added alkoxide (entries 3 and 4). In analogous reactions with anisole, slightly more metalation was observed in the presence of alkoxide but, again, these were much lower than those obtained in its absence (entries 5–8). In the case of thiophene substantial amounts of metalation were noted both with or without added alkoxide (entries 9–12). We are therefore able to obtain some idea as to the range of substrates that are not susceptible to metalation—or rather that display low rates of metalation—using the alkoxide/organolithium system under our conditions.[23]

Table II. Reactions of Organic Halides with Lithium Metal in THF[a]

entry	RX	mmol of $Mg(OR)_2$[b]	product	yield, %
1	*n*-BuCl	0	*n*-$BuCO_2H$	45
2	*n*-BuCl	10	*n*-$BuCO_2H$	71
3	*s*-BuCl	0	*s*-$BuCH_2CH_2CO_2H$	54[c]
4	*s*-BuCl	10	*s*-$BuCO_2H$	58
5	*t*-BuCl	0	*t*-$BuCH_2CH_2CO_2H$	trace
6	*t*-BuCl	10	*t*-$BuCO_2H$	30[d]
7	c-$C_6H_{11}Cl$	0	c-$C_6H_{11}CH_2CH_2CO_2H$	60[c]
8	c-$C_6H_{11}Cl$	10	c-$C_6H_{11}CO_2H$	68
6	menthyl chloride	0	menthanecarboxylic acid	43
10	*p*-$MeOC_6H_4Br$	0	mixture of at least three acids	
11	*p*-$MeOC_6H_4Br$	10	*p*-$MeOC_6H_4CO_2H$	59
12	*o*-$MeOCH_2C_6H_4Cl$	0	*o*-$MeOCH_2C_6H_4CO_2H$	6
13	*o*-$MeOCH_2C_6H_4Cl$	10	*o*-$MeOCH_2C_6H_4CO_2H$	71

[a] See Experimental Section for details. In all cases 20 mmol of halide and 40 mmol of Li were used. Temperature 0 °C; time 140 min. [b] R = $EtOCH_2CH_2$. [c] Based on half the amount of organic halide taken (see text). [d] See text and Experimental Section for details of improved procedures.

(b) Halogen–Metal Exchange Using Lithium Metal. The instability of organolithium reagents in ethereal solvents is considered, as stated above, to be due to an initial metalation of the solvent followed by decomposition.[2,3] In the case of THF, ethene and the enolate of acetaldehyde are produced (eq 4 and 5). On the basis of the metalation

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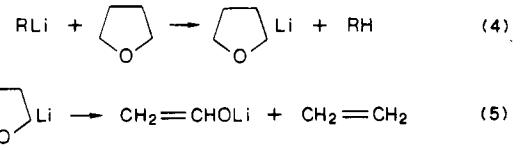
(17) Screttas, C. G.; Steele, B. R. *J. Org. Chem.* **1988**, *53*, 5151.
(18) Posner, G. H.; Whitten, C. E.; Sterling, J. J. *J. Am. Chem. Soc.* **1973**, *95*, 7788.
(19) Yamamoto, Y.; Maruyama, K.; Komatsu, T.; Ito, W. *J. Org. Chem.* **1986**, *51*, 886. Reetz, M. T.; Wenderöth, B. *Tetrahedron Lett.* **1982**, *23*, 5259.
(20) Mukerji, I.; Wayda, A.; Dabbagh, G.; Bertz, S. H. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 760.
(21) Kauffmann, T.; Pahde, C.; Wingbermühle, D. *Tetrahedron Lett.* **1985**, *26*, 4059.
(22) Bradley, D. C.; Mehrotra, R. C.; Gaur, D. P. *Metal Alkoxides*; Academic Press: London, 1979.

(23) The pK_a's for diphenylmethane, anisole, and thiophene in THF have been determined to be 35.9, 38.4, and 33.0, respectively. Fraser, R. R.; Bresse, M.; Mansour, T. S. *J. Chem. Soc., Chem. Commun.* **1983**, 620. Fraser, R. R.; Mansour, T. S.; Savard, S. *Can. J. Chem.* **1985**, *63*, 3505. The apparently readier metalation of anisole compared to diphenylmethane may reflect kinetic rather than thermodynamic acidity: cf., Cram, D. J. *Fundamentals of Carbanion Chemistry*; Academic Press: New York, 1965; Chapter 1.



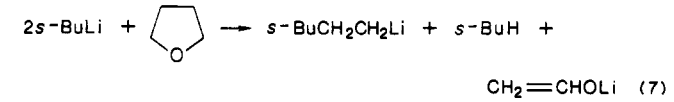
(4)

(5)

experiments reported in section a, it was reasonable to expect that reaction 4 would be suppressed in the presence of 1, and we have thus carried out the preparation of some simple organolithium reagents in THF by reaction 2 both in the presence and in the absence of 1. The results are presented in Table II, with the yields given for the products obtained after carbonation. It is evident that in the presence of the alkoxide the yields are increased, sometimes dramatically so, and that also the expected product is always obtained. Thus for *n*-BuCl yields of 71 and 45% of pentanoic acid were obtained with and without alkoxide respectively. For *s*-BuCl the expected 2-methylbutanoic acid was obtained, in 58% yield, only when alkoxide was present. In the absence of alkoxide 4-methylhexanoic acid was obtained, presumably by the reaction of the initially formed *s*-BuLi with ethene formed by reactions 4 and 5[24] (eq 6) and subsequent carbonation of the organolithium.

$$s\text{-BuLi} + CH_2{=}CH_2 \rightarrow s\text{-BuCH}_2\text{CH}_2\text{Li} \qquad (6)$$

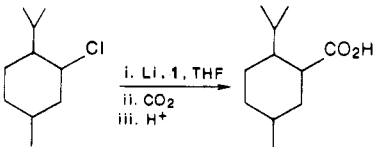
In this case the yield given reflects the overall stoichiometry of reaction 7.



(7)

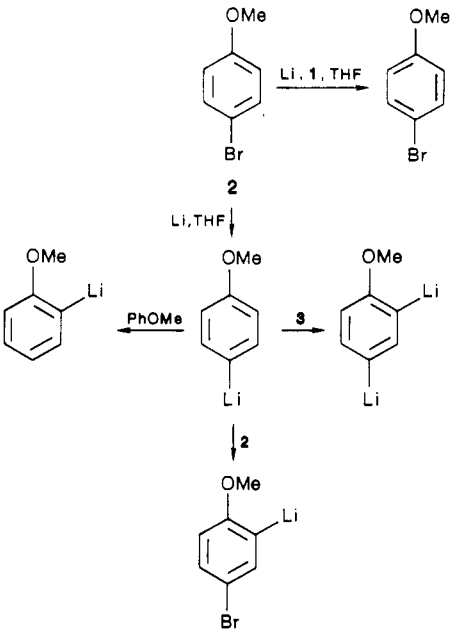
With *t*-BuLi a similar result was obtained. The results for the three isomeric butyllithiums follow the trend in stability mentioned in the introduction. It should be noted, however, that the reactions in this series and those described below were, except where stated otherwise, carried out with the alkoxide as an initial suspension in THF, in which it dissolves only very slowly in the cold. Subsequently, however, the formation of the *tert*-butyl organometallic reagent was examined by using a preformed solution of the alkoxide, and in this way the yield of 2,2-dimethylpropanoic acid increased to 57%. A further increase in yield to 66% was achieved by the use of lithium dispersion. Clearly the use of a solution of the alkoxide enables the more rapid formation of the alkoxide/organometallic aggregate, thus inhibiting metalation by "free" *t*-BuLi.

Alicyclic halides gave similar results to those for *sec*-butyl chloride. Thus, in the presence of alkoxide, chlorocyclohexane reacted with lithium to give, after carbonation, a 68% yield of the corresponding acid, whereas in the absence of alkoxide 3-cyclohexylpropanoic acid was produced. Likewise, menthylcarboxylic acid was prepared from menthyl chloride:

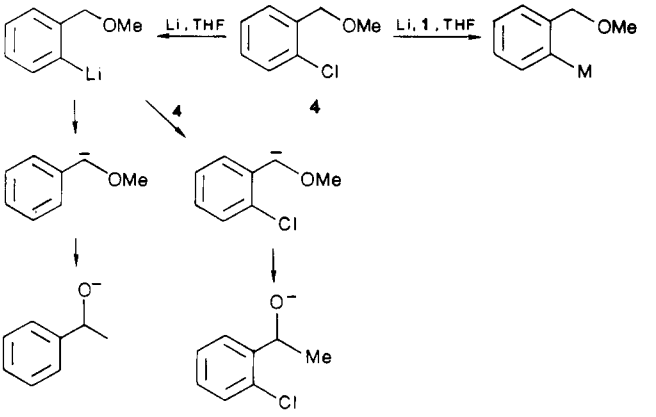


It is appropriate to mention at this point that these reagents may be applied to synthetically more useful reactions. The *tert*-butyl and cyclohexyl reagents, for example, reacted with benzaldehyde to give 64% and 50%, respectively (based on the benzaldehyde used), of the corresponding carbinols. Their reaction with tertiary formamides has been reported elsewhere.[17]

Scheme I



Scheme II



The reaction of aromatic halides with lithium in THF can pose special problems. One of these is the presence of ortho-directing metalating groups.[25] While these can be extremely useful in organic synthesis, they can on occasions cause undesirable side reactions. An example is provided by the reaction of *p*-bromoanisole with lithium in THF (entry 9). Carbonation produced a mixture of at least three acids (as judged by ^{13}C NMR). The initially formed (*p*-methoxyphenyl)lithium orthometalates *p*-bromoanisole to give anisole and (*o*-methoxy-*p*-bromophenyl)lithium. The anisole may also be metalated ortho to the methoxy group, and there is also the possibility of obtaining dimetalated products (Scheme I). In the presence of 1 only *p*-methoxybenzoic acid was produced after carbonation (entry 10).

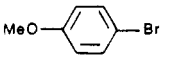
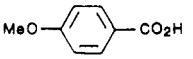
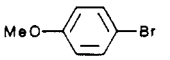
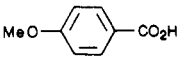
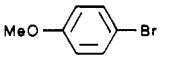
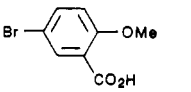
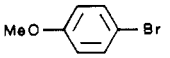
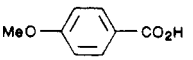
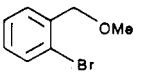
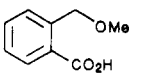
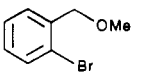
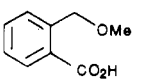
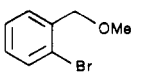
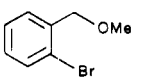
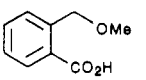
The Wittig rearrangement, which proceeds by way of an initial metalation,[26] can also be suppressed in the presence of the alkoxide. Thus reaction of *o*-chlorobenzyl methyl ether with lithium metal alone in THF gave, after carbonation, not more than 6% of *o*-(methoxymethyl)-

(24) Bartlett, P. D.; Friedman, S.; Stiles, M. *J. Am. Chem. Soc.* **1953**, *75*, 1771. Spialter, L.; Harris, C. W. *J. Org. Chem.* **1966**, *31*, 4263.

(25) For recent reviews, see: Narasimhan, N. S.; Mali, R. S. *Synthesis* **1983**, 958. Beak, P.; Snieckus, V. *Acc. Chem. Res.* **1982**, *15*, 306. Gschwend, H. W.; Rodriguez, H. R *Org. React.* **1979**, *26*, 1.

(26) Schöllkopf, U. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 763.

Table III. Reaction of Aryl Bromides with *n*-Butylithium[a]

entry	substrate	mmol of $Mg(OR)_2$[b]	solvent[c]	product	yield, %
1		0	A		70
2		10	A		40
3		0	B		8
4		10	C		50
5		0	A		49
6		10	A		38
7		0	B	not characterized	trace
8		10	C		47

[a] See Experimental Section for details. Temperature 0–25 °C; time 20 h. [b] R = $EtOCH_2CH_2$. [c] A = 2 mL of MCH; B = 20 mL of MCH/2 mL of THF; C = 20 mL of MCH/4 mL of THF.

benzoic acid. In the presence of 1 the same acid was obtained pure in 71% yield (entries 12, 13). The alkoxide inhibits the metalation at the benzylic position by the initially formed aryllithium, and so the Wittig rearrangement does not occur (Scheme II).

(c) Halogen–Metal Exchange Using *n*-Butyllithium. This method of preparation of organolithiums can also be applied in the presence of magnesium 2-ethoxyethoxide. Examples of this reaction (eq 3) are given in Table III for *p*-bromoanisole and *o*-bromobenzyl methyl ether. In hydrocarbon solvent with *n*-BuLi by itself, reasonable yields of aryllithium—again as estimated from the yield of carbonation product—are obtained. In this case no complications are observed primarily due to the fact that the aryllithium is insoluble in the solvent and also because no strong Lewis base is present. In the presence of 1 in the same solvent the yields are somewhat lower. When THF is present, however, we observe that with *n*-BuLi alone virtually no aryllithium is produced. In the case of *p*-bromoanisole a small amount of orthometalated product was formed—the major part of the organolithium presumably reacting with THF. For *o*-bromobenzyl methyl ether only a trace of the corresponding acid was obtained, owing to subsequent Wittig rearrangement of the initially formed organolithium as described previously. In the presence of 1 the expected products are formed in moderate yields.

Experimental Section

All reactions were carried out under an atmosphere of argon. Solvents were dried, degassed, and argon-saturated before use. Organic halides were obtained from commercial sources except for *o*-chlorobenzyl methyl ether and *o*-bromobenzyl methyl ether, which were prepared by standard methods.[27,28] NMR spectra were recorded on a Varian FT80 spectrometer in $CDCl_3$ and are reported in ppm from Me_4Si. Melting points are uncorrected.

Magnesium 2-ethoxyethoxide was prepared as described elsewhere.[4]

(a) Metalations with *n*-Butyllithium (Table I, Entries 1–12). (1) Without $Mg(OCH_2CH_2OEt)_2$. In a flask was placed 11 mL of 1.8 M *n*-BuLi in methylcyclohexane (MCH) (20 mmol). After the mixture was cooled in ice, additional MCH was added in the case of entries 1, 5, and 9 as indicated. The substrate (20 mmol) and the indicated amount of THF were added. The reaction mixture was allowed to warm up slowly to room temperature overnight. It was then poured with a current of argon onto crushed dry ice in ether. When the carboxylation mixture had reached room temperature, water was added, and the solvents and other volatile materials were removed on a rotary evaporator. The residue was treated with 20% H_2SO_4 to generate the free acid, which was extracted with 4 × 50 mL of Et_2O (entries 1, 3, 5, and 7) or CH_2Cl_2 (entries 9 and 11). The organic extracts were combined and reduced to a small volume on a rotary evaporator and then stirred overnight with excess concentrated Na_2CO_3 solution. This mixture was then extracted twice with 50 mL of toluene and twice with 50 mL of hexane. The aqueous layer was acidified with 20% H_2SO_4 and extracted with 3 × 50 mL of Et_2O or CH_2Cl_2 as above. The combined organic extracts were dried over anhydrous $MgSO_4$. After filtration, the solution was reduced to a small volume on a rotary evaporator and then left to evaporate overnight at room temperature in a preweighed beaker. The identity, purify, and composition of the products were determined by ^1H NMR analysis by comparison with spectra of authentic materials.[29] The results are presented in Table I.

(2) With $Mg(OCH_2CH_2OEt)_2$. To 2 g (10 mmol) of $Mg(OCH_2CH_2OEt)_2$ was added 11 mL of 1.8 M *n*-BuLi in MCH (20

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mmol). Additional MCH was added as appropriate (entries 2, 6, and 10), and the mixture was stirred until a clear solution was obtained. The solution was then cooled in ice; 20 mmol of substrate followed by the indicated amount of THF was added, and the reaction mixture was allowed to warm slowly to room temperature overnight. Subsequent treatment was as described in (1) above.

(b) Reaction of Organic Halides with Lithium Metal (Table II). General Procedure for Entries 1–11. Lithium metal (0.29 g, 41 mmol), beaten into a sheet and cut into small pieces, and, for entries 2, 4, 6, 8, 10, and 11, 2 g (10 mmol) of $Mg(OCH_2CH_2OEt)_2$ was covered with THF (4 mL) and cooled in ice. A solution of 20 mmol of the halide in 12 mL of THF was added with vigorous stirring over 20 min. After the addition, stirring was continued for 2 h in the ice bath. The reaction mixture was then carbonated and worked up as described above. CH_2Cl_2 was used to extract the acids except for *p*-methoxybenzoic acid for which Et_2O was employed. The products were characterized by comparison of their ^1H NMR spectra with those of authentic materials.[29] The results are presented in Table II.

***o*-(Methoxymethyl)benzoic Acid (Entries 12 and 13).** The above procedure was followed except that the volumes of THF were both 10 mL instead of 4 and 12 mL. ^1H NMR data: δ 2.85 (s, 3 H), 4.26 (s, 2 H), 6.60–7.50 (m, 4 H), 10.38 (br s, 1 H); mp 93–4 °C (lit.[30] mp 94–5 °C).

2,2-Dimethylpropanoic Acid (Improved Procedures). (a) To 7.5 mL of 1.4 M $Mg(OCH_2CH_2OEt)_2$ in THF (10 mmol) was added 0.29 g (41 mmol) of Li pieces. After the mixture was cooled in ice, a solution of *t*-BuCl (1.9 g, 20 mmol), in 12 mL of THF was added over 30 min with vigorous stirring. Stirring was continued for 2 h, and then the reaction mixture was carbonated and worked up in the usual way to give 2,2-dimethylpropanoic acid, 1.2 g, 57%.

(b) To 8 mL of 1.4 M $Mg(OCH_2CH_2OEt)_2$ in THF was added 1.6 g of ca. 30% lithium dispersion in mineral oil. A purple suspension formed (presumably due to metal–metal exchange). The subsequent procedure was as given in (a), yield 1.35 g, 66%.

(c) Reaction of Organic Bromides with *n*-Butyllithium (Table III). (1) Without $Mg(OCH_2CH_2OEt)_2$. To 11 mL of 1.8 M *n*-BuLi in MCH (20 mmol) and 10 mL MCH cooled in ice was added 20 mmol of aryl bromide. THF (2 mL) was added for entries 3 and 7. The reaction mixture was allowed to warm to room temperature overnight, poured onto crushed dry ice in Et_2O, and worked up in the usual way.

(2). With $Mg(OCH_2CH_2OEt)_2$. To 2 g (10 mmol) of $Mg(OCH_2CH_2OEt)_2$ were added 10 mL of MCH and 12 mL of 1.8 M *n*-BuLi in MCH (20 mmol), and the mixture was stirred until a clear solution was obtained. The solution was cooled in ice, and the aryl bromide (20 mmol) was added. THF (4 mL) was added for entries 4 and 8. The reaction mixture was allowed to warm to room temperature overnight, poured onto crushed dry ice in Et_2O, and worked up in the usual way.

The results are given in Table III. The products were characterized by comparison of their ^1H NMR spectra with those of authentic compounds.[29]

Phenylcyclohexylcarbinol. To 2 g (10 mmol) of $Mg(OCH_2CH_2OEt)_2$ covered with 4 mL of THF was added 0.3 g (43 mmol) of Li pieces. After the mixture was cooled in ice, a solution of 2.4 g (20 mmol) of chlorocyclohexane in 12 mL of THF was added with vigorous stirring over 20 min. Stirring was continued for a further 2 h at the bath temperature. Unused Li was removed, and PhCHO (2.1 mL, 20 mmol) was added over 10 min. Stirring was continued for 1 h at room temperature. The reaction mixture was hydrolyzed with cold, dilute H_2SO_4 and extracted with 3 × 50 mL of CH_2Cl_2. The extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated on a rotary evaporator. Vacuum distillation gave 1.9 g (50%) of the alcohol (bp 94 °C/4 mm, mp 46–8 °C, lit.[31] mp 50 °C).

2,2-Dimethyl-1-phenylpropan-1-ol. Li metal (0.6 g, 87 mmol) was beaten into a sheet, cut into small pieces, and placed in a flask; 15 mL of 1.4 M $Mg(OCH_2CH_2OEt)_2$ in THF was added. After the mixture was cooled to 0 °C, a solution of *t*-BuCl (3.8 g, 40 mmol) in 24 mL of THF was added with vigorous stirring over ca. 40 min. Stirring was continued for a further 2 h with ice cooling. Unused Li was removed, and PhCHO (3.1 g, 30 mmol) was added over 10 min. Stirring was continued for 1 h at room temperature. Workup as for phenylcyclohexylcarbinol gave 3.1 g (64% based on PhCHO used) of the product (bp 74–5 °C/1 mm, lit.[32] bp 110–111 °C/15 mm).

Registry No. Ph_2CH_2, 101-81-5; $Mg(O(CH_2)_2OEt)_2$, 14064-03-0; Ph_2CHCO_2H, 117-34-0; *o*-$C_6H_4(OMe)CO_2H$, 579-75-9; BuCl, 109-69-3; *s*-BuCl, 78-86-4; *t*-BuCl, 507-20-0; *p*-$MeOC_6H_4Br$, 104-92-7; *o*-$MeOCH_2C_6H_4Cl$, 59579-08-7; $BuCO_2H$, 109-52-4; *s*-$Bu(CH_2)_2CO_2H$, 1561-11-1; *s*-$BuCO_2H$, 116-53-0; *t*-$BuCO_2H$, 75-98-9; *c*-$C_6H_{11}(CH_2)_2CO_2H$, 701-97-3; *c*-$C_6H_{11}CO_2H$, 98-89-5; *p*-$MeOC_6H_4CO_2H$, 100-09-4; *o*-$MeOCH_2C_6H_4CO_2H$, 88550-19-0; *o*-$MeOCH_2C_6H_4Br$, 52711-30-5; $C_6H_{11}Cl$, 542-18-7; anisole, 100-66-3; thiophene, 110-02-1; 2-thienoic acid, 527-72-0; 2,5-thiophenedicarboxylic acid, 4282-31-9; menthyl chloride, 16052-42-9; methanecarboxylic acid, 65-85-0; phenylcyclohexylcarbinol, 945-49-3; benzaldehyde, 100-52-7; 2,2-dimethyl-1-phenylpropan-1-ol, 3835-64-1.

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