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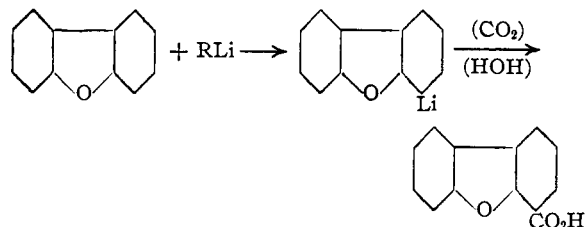
Secondary and Tertiary Alkyl lithium Compounds and Some Interconversion Reactions with Them<sup>1</sup>

BY HENRY GILMAN, FRED W. MOORE AND OGDEN BAINE

Primary alkyl lithium compounds are readily prepared in diethyl ether by conventional procedures.<sup>2</sup> It was generally believed that secondary alkyl lithium compounds could not be prepared directly in diethyl ether until isopropyl lithium was made in a 20% yield.<sup>3</sup> We are now reporting the preparation of this RLi compound in low boiling petroleum ether in 75% yield. Furthermore, *t*-butyllithium can be prepared in the same solvent. In the preparation of these and other alkyl lithium compounds in petroleum ether, the RCl compounds are distinctly superior to the RBr compounds (see Experimental).

The availability of a series of normal and branched alkyl lithium compounds provides an essential means for formulating generalizations on the types of RLi compounds to effect some preferential reactions. For our immediate purposes we were interested in learning whether it was possible to get predominantly one of the three following types of interconversion reactions where all appeared possible: hydrogen-metal (metalation), halogen-metal, and metal-metal.

**Metalation.**—The relative effectiveness of the alkyl lithium compounds in metalation was established by comparative studies with dibenzofuran.



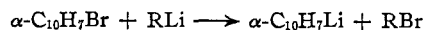
In diethyl ether, *n*-butyllithium is most effective and methyllithium is least effective. *n*-Butyllithium is more effective in di-*n*-butyl ether than in diethyl ether.<sup>4</sup> In petroleum ether, the second-

ary RLi compounds, like isopropyl lithium and *s*-butyllithium, are decidedly more effective than the corresponding normal RLi compounds; and *t*-butyllithium is the best of all isomeric butyllithium compounds. Isobutyllithium, like *n*-butyllithium, is a relatively very weak metalating agent in petroleum ether.

Benzene, toluene and related aromatic hydrocarbons cannot generally be used as solvents, not only because they markedly reduce the rates of most RLi reactions, but more particularly because they undergo metalation. Actually, in some experiments using toluene as solvent, *s*-butyllithium metalated the toluene laterally to give (subsequent to carbonation) an 8% yield of phenylacetic acid. This suggests that *t*-butyllithium may possibly provide an effective means for the preparation of benzyl lithium, which is one of the very few RLi compounds now inaccessible by direct synthesis.

An examination of some organosodium compounds like *p*-tolylsodium and benzylsodium has shown that these compounds di-metalate dibenzofuran in relatively high yields. Although benzylpotassium is more reactive than benzylsodium in most reactions, it did not metalate dibenzofuran under corresponding conditions.

**Halogen-Metal Interconversion.**—It was shown previously<sup>5</sup> that in the X-M interconversion reaction



the order of decreasing effectiveness of some RLi compounds in diethyl ether was: *n*-C<sub>3</sub>H<sub>7</sub>Li, C<sub>2</sub>H<sub>5</sub>Li, *n*-C<sub>4</sub>H<sub>9</sub>Li, C<sub>6</sub>H<sub>5</sub>Li, CH<sub>3</sub>Li. We now find that in petroleum ether the order of decreasing effectiveness of some RLi compounds is: *s*-C<sub>4</sub>H<sub>9</sub>Li, *i*-C<sub>3</sub>H<sub>7</sub>Li, *t*-C<sub>4</sub>H<sub>9</sub>Li, *n*-C<sub>4</sub>H<sub>9</sub>Li = *i*-C<sub>4</sub>H<sub>9</sub>Li, *n*-C<sub>3</sub>H<sub>7</sub>Li. Incidentally, there appears to be no advantage to the use of higher alkyl lithium compounds, for *n*-amyllithium in diethyl ether is less effective than *n*-butyllithium. *n*-Butylsodium can be used in the X-M reaction with  $\alpha$ -bromonaphthalene, but it is less satisfactory than *n*-butyllithium.

It will be noted that whereas in petroleum ether

(5) Gilman and Moore, *ibid.*, **62**, 1843 (1940).

(1) This study was made partly with the aid of a grant from the American Philosophical Society to one of us (O. B.). Paper XLI in the series: "Relative reactivities of organometallic compounds"; the preceding paper is Gilman and Yale, *THIS JOURNAL*, **63**, in press (1941).

(2) Gilman, Langham and Moore, *ibid.*, **62**, 2327 (1940). For pertinent citations see ref. 15 of this earlier paper.

(3) Gilman, Zoellner, Selby and Boatner, *Rec. trav. chim.*, **54**, 584 (1935).

(4) This is in agreement with earlier results on the metalation of dibenzothiophene: Gilman and Bebb, *THIS JOURNAL*, **61**, 109 (1939).

*t*-butyllithium is more effective than *s*-butyllithium as a metalating agent, the order is reversed in the X-M reaction. This may be due to a greater coupling<sup>5</sup> tendency of the *t*-butyl halide which is a product of the initial X-M reaction. However, *s*-butyllithium apparently adds more rapidly than *t*-butyllithium to 1,1-diphenylethylene.

An application of the different rates of metalation and halogen-metal interconversion reactions where a metal-metal interconversion reaction is also possible is described in the following paper.<sup>6</sup>

### Experimental

**Preparation of Alkylolithium Compounds in Petroleum Ether.**—The conventional apparatus described recently<sup>2,7</sup> was used in the several preparations. After adding 50 ml. of dry, "unsaturate-free" petroleum ether (b. p. 28–38°) to the flask, slightly more than 0.7 g. (0.1 g. atom) of lithium is rasped directly into the flask, through a paper cone or funnel, in an emerging stream of nitrogen. Then to the rapidly stirred and gently refluxed solvent is added dropwise 0.05 mole of the RX compound in 50 ml. of the petroleum ether. Reaction sets in soon, as is evidenced by the increased rate of refluxing and the appearance of the lithium particles, which soon become somewhat blue in color and no longer float on the surface. The halide is added over a one-hour period. When addition is completed, refluxing and stirring are continued until there is no visible evidence of reaction. If there is no bubbling around the lithium particles, when the external heat is removed and stirring is stopped, the reaction is substantially complete. The subsequent operations of settling, filtering and analysis by titration have been described.<sup>2</sup> The residue from the reaction may be disposed of by adding it, in small portions, to a large volume of water in a well-ventilated hood.

Methylolithium cannot be prepared satisfactorily in this manner because of its insolubility in the petroleum ether specified. Ethyllithium appears to be of limited solubility, also. The aryllithium compounds, when formed in this solvent by interconversion reactions, are soluble in moderate concentrations. Studies are now in progress on the possible direct preparation of these compounds in this and related solvents.

The yields of alkylolithium compounds prepared in accordance with the general procedure described above are given in Table I.

The yields given in Table I are not only comparable to, but also lower than, those obtained with somewhat slower addition of the RX solution. For example, the yield of *n*-butyllithium from *n*-butyl chloride is sometimes slightly in excess of 91%. An especially pure *t*-butyl chloride is recommended for the preparation of *t*-butyl-

(6) Gilman, Moore and Jones, *THIS JOURNAL*, **63**, 2482 (1941); see, also, Wittig and Fuhrmann, *Ber.*, **73**, 1197 (1940).

(7) See Adams, Wolff, Cain and Clark, *THIS JOURNAL*, **62**, 1772 (1940), for another useful apparatus.

TABLE I  
YIELDS OF SOME ALKYLITHIUM COMPOUNDS PREPARED  
IN PETROLEUM ETHER

RX compound	yield % RLi	RX compound	yield % RLi
C <sub>2</sub> H <sub>5</sub> Br	50	<i>n</i> -C <sub>4</sub> H <sub>9</sub> Cl	85
<i>n</i> -C <sub>3</sub> H <sub>7</sub> Br	60	<i>i</i> -C <sub>4</sub> H <sub>9</sub> Cl	85
<i>n</i> -C <sub>3</sub> H <sub>7</sub> Cl	85	<i>s</i> -C <sub>4</sub> H <sub>9</sub> Cl	85
<i>i</i> -C <sub>3</sub> H <sub>7</sub> Br	15	<i>t</i> -C <sub>4</sub> H <sub>9</sub> Cl	50
<i>i</i> -C <sub>3</sub> H <sub>7</sub> Cl	75	<i>n</i> -C <sub>5</sub> H <sub>11</sub> Cl	85
<i>n</i> -C <sub>4</sub> H <sub>9</sub> Br	70		

lithium, and even with purified chloride the yields of this RLi compound are erratic. On the basis of more than 60 preparations of *t*-butyllithium, the yield ranges between 50 to 60% in two out of five experiments; between 30 to 40% in two out of five experiments; and between 0 to 5% in one out of five experiments. It is rather probable that additional experiments in various laboratories will remove the particular difficulties, as was the case with the preparation of *t*-butylmagnesium chloride.<sup>8</sup> Some special advantages to the use of petroleum ether as a solvent have already been mentioned.<sup>2</sup>

Studies by Mr. Haubein have shown that secondary and tertiary alkylolithium compounds cleave diethyl ether rather rapidly. Methylolithium is exceptional with all RLi compounds in this respect, for it does not cleave diethyl ether after a refluxing period of eleven days. Partly because of this and partly because of the greater solubility of some —OLi compounds over —OMgX compounds, methylolithium enjoys certain advantages over methylmagnesium halides in the Zerewitinoff analysis.<sup>9</sup>

**Metalation of Dibenzofuran.**—All RLi compounds listed in Table II were prepared in petroleum ether. In those reactions carried out in diethyl ether, all but 5 ml. of the petroleum ether was removed by distillation and diethyl ether was then added. Equivalent quantities of dibenzofuran were used. When refluxing is started, the solution is usually of a clear, light-yellow color, and this gradually changes to a deep orange as refluxing is continued. Carbonation was effected in the usual manner.

Some other experiments were carried out in diethyl ether under conditions not strictly comparable with those given in Table II. The first number represents the hours of refluxing; and

(8) Gilman and Zoellner, *ibid.*, **50**, 425 (1928). See, particularly, the extensive and elegant studies by Whitmore and co-workers on *t*-alkylmagnesium halides described in *THIS JOURNAL*.

(9) Studies by R. Christian.

TABLE II

RLi	Medium	Reflux time, hours	% yield 4-dibenzofurancarboxylic acid
<i>n</i> -C <sub>4</sub> H <sub>9</sub> Li	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O	4	55, 56
<i>n</i> -C <sub>4</sub> H <sub>9</sub> Li	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O	12	56.7
<i>i</i> -C <sub>4</sub> H <sub>9</sub> Li	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O	4	46, 52
<i>i</i> -C <sub>4</sub> H <sub>9</sub> Li	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O	12	53
<i>s</i> -C <sub>4</sub> H <sub>9</sub> Li	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O	4	11, 12.7
<i>s</i> -C <sub>4</sub> H <sub>9</sub> Li	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O	12	11.6
<i>i</i> -C <sub>3</sub> H <sub>7</sub> Li	Pet. ether	24	22.5
<i>n</i> -C <sub>4</sub> H <sub>9</sub> Li	Pet. ether	24	1.2, 1.3
<i>i</i> -C <sub>4</sub> H <sub>9</sub> Li	Pet. ether	24	1, 1.2
<i>s</i> -C <sub>4</sub> H <sub>9</sub> Li	Pet. ether	24	22.6, 30.8, 24, 23
<i>t</i> -C <sub>4</sub> H <sub>9</sub> Li	Pet. ether	24	32, 34, 31, 32
<i>n</i> -C <sub>4</sub> H <sub>9</sub> Li	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> O	6	43.6
<i>n</i> -C <sub>4</sub> H <sub>9</sub> Li	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> O	24	76

the second number, the per cent. of acid obtained subsequent to carbonation: CH<sub>3</sub>Li (6) (3.1); C<sub>2</sub>H<sub>5</sub>Li (6) (47.5); *n*-C<sub>4</sub>H<sub>9</sub>Li (6) (51.4), (12) (49.2), (24) (59); *n*-C<sub>6</sub>H<sub>11</sub>Li (6) (45); C<sub>6</sub>H<sub>5</sub>Li (6) (31.3). Under corresponding conditions, *n*-butyllithium metalated dibenzothiophene (after refluxing for twelve hours) to give a 61.5% yield of 4-dibenzothiophenecarboxylic acid.

Table III contains the results on the metalation of dibenzofuran by some organosodium compounds. The product in these cases was 4,6-dibenzofurandicarboxylic acid.

TABLE III

RNa	Medium	Reflux time, hours	% yield 4,6-dibenzofurandicarboxylic acid
<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Na	C <sub>6</sub> H <sub>6</sub>	14	60, 61
<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Na	C <sub>7</sub> H <sub>8</sub>	12	73
<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Na	C <sub>7</sub> H <sub>8</sub>	24	88, 86
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Na	C <sub>7</sub> H <sub>8</sub>	12	70, 80
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Na	C <sub>7</sub> H <sub>8</sub>	24	70, 71

Benzylpotassium (prepared in accordance with some recent directions<sup>10</sup>) did not metalate dibenzofuran after refluxing for forty-eight hours in toluene. That the benzylpotassium was actually present in these reactions is evident from the fact that the yields of phenylacetic acid were in the range of 70–80%.

**Halogen-Metal Interconversion with  $\alpha$ -Bromonaphthalene.**—Equivalent quantities of  $\alpha$ -bromonaphthalene and RLi compound were allowed to react at room temperature in petroleum ether (b. p. 28–38°) for varying times, and then carbonated. The numbers given in Table IV are the per cent. yields of  $\alpha$ -naphthoic acid.

(10) Gilman, Pacevitz and Baine, THIS JOURNAL, 62, 1514 (1940).

TABLE IV

Time, hours	<i>n</i> -C <sub>4</sub> H <sub>9</sub> Li	<i>i</i> -C <sub>4</sub> H <sub>9</sub> Li	<i>n</i> -C <sub>6</sub> H <sub>13</sub> Li	<i>i</i> -C <sub>6</sub> H <sub>13</sub> Li	<i>s</i> -C <sub>4</sub> H <sub>9</sub> Li	<i>t</i> -C <sub>4</sub> H <sub>9</sub> Li
0.25			10	12	77	26
.50	11	71	17	16	81	32
1	18	78	27	24	80	34
2	21	47	40	35	63	30

Separate experiments were carried out on the interconversion reaction of *n*-amyllithium with  $\alpha$ -bromonaphthalene to determine whether an odd numbered normal RLi compound was more effective than the preceding even numbered normal RLi compound. Ziegler and co-workers<sup>11</sup> observed that *n*-propyllithium added to 1,1-diphenylethylene more rapidly than either ethyl- or *n*-butyllithium; and we noted that *n*-propyllithium was more effective than ethyl- or *n*-butyllithium in a halogen-metal interconversion reaction. The yields of  $\alpha$ -naphthoic acid, in diethyl ether and at room temperature, were 58, 59, 58, 47 and 36%, respectively, after the following number of minutes: 0.5, 1, 5, 10 and 30. Since the yields with *n*-butyllithium<sup>5</sup> under the same conditions were 84, 78, 73, 68 and 65%, respectively, *n*-amyllithium appears to be less reactive than *n*-butyllithium in this reaction.

In another series of experiments,  $\alpha$ -bromonaphthalene was allowed to react with *n*-butylsodium (prepared from di-*n*-butylmercury) in petroleum ether (b. p. 28–38°) at 25°. The yields of  $\alpha$ -naphthoic acid were 17, 20, 28 and 28%, respectively, after the following numbers of minutes: 2, 4, 8 and 16.

**Addition of Alkyl Lithium Compounds to 1,1-Diphenylethylene.**—The approximate extent of addition of some RLi compounds to 1,1-diphenylethylene at room temperature was measured by carbonating the reaction product and weighing the solid acid or mixtures of acids. The numbers in Table V indicate the per cent. yields of unpurified acids.

TABLE V

Time, hours	<i>n</i> -C <sub>4</sub> H <sub>9</sub> Li	<i>i</i> -C <sub>4</sub> H <sub>9</sub> Li	<i>s</i> -C <sub>4</sub> H <sub>9</sub> Li	<i>t</i> -C <sub>4</sub> H <sub>9</sub> Li
(benzene-petroleum ether)				
8	12	13	82	
48	35	37	82	
(petroleum ether)				
8			13	7
48			90	18

(11) Ziegler, Crössmann, Kleiner and Schäfer, Ann., 473, 1 (1929).

### Summary

Hitherto inaccessible secondary and tertiary alkyl-lithium compounds can now be obtained by direct reaction of alkyl chlorides and lithium in low-boiling petroleum ether.

The relative effectiveness of a series of alkyl-lithium compounds for metalation and for halogen-metal interconversion reactions in different solvents has been examined.

AMES, IOWA  
MEMPHIS, TENNESSEE

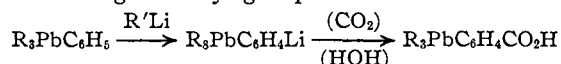
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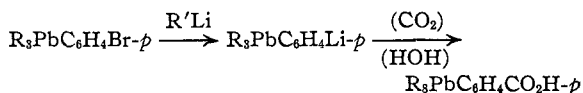
## Preferential Cleavage of Radicals in Some Organometallic Compounds<sup>1</sup>

BY HENRY GILMAN, FRED W. MOORE AND R. G. JONES

The primary objective in this study was the introduction of water-solubilizing groups into some relatively unreactive organometallic compounds. Two ways suggested themselves. The first was a nuclear metalation, followed by carbonation, as a means of inserting the water-solubilizing carboxyl group.



Second, halogen-metal interconversion reactions were examined.



Both reactions were unsatisfactory because metal-metal interconversions took place more rapidly than either metalation or halogen-metal interconversion.

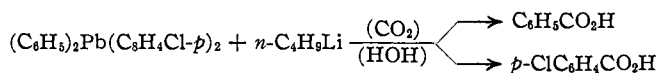
From earlier work it was to be expected that the speed of a halogen-metal interconversion reaction would be greatest if iodine were the nuclear halogen and that this speed would be further enhanced by having the iodine ortho to an activating alkoxy group. A compound like *bis*-(3-iodo-4-methoxyphenyl)mercury,  $(CH_3O \text{---} \text{C}_6\text{H}_3\text{---} I)_2Hg$ , gave promise

of satisfying the essential conditions. The compound was synthesized by reactions described in the experimental part and, when treated with *n*-butyllithium followed by carbonation, actually yielded an organomercury compound containing a carboxyl group. However, even in this case and with only a two-minute period of reaction, the metal-metal interconversion was appreciable. This general approach may prove more satisfac-

(1) Paper XLII in the series: "Relative reactivities of organometallic compounds"; the preceding paper is Gilman, Moore and Baine, *THIS JOURNAL*, **63**, 2479 (1941).

tory with RM compounds that undergo the M-M interconversion less readily such as those of germanium, but it now appears that the reaction is of little promise because M-M interconversions proceed much more rapidly than metalation and appreciably faster than X-M interconversions.

**Preferential Cleavage of Radicals.**—As an outgrowth of the afore-mentioned objective, a study was made of the rates of M-M interconversion of some symmetrical and unsymmetrical organometallic compounds of lead, tin and mercury. An illustrative reaction with an unsymmetrical compound is



Using one-half an equivalent of *n*-butyllithium it was observed that the acids formed on carbonation of the reaction mixture consisted of a mixture of 98% *p*-chlorobenzoic acid and 2% benzoic acid. That is, the *p*-chlorophenyl radical was cleaved much more rapidly than the phenyl radical.

As was the case in a recently reported study on organobismuth compounds,<sup>2</sup> the series formulated by placing the organic radicals in the order of decreasing ease of cleavage from organolead compounds by means of *n*-butyllithium does not agree with similar series based upon cleavage of RM compounds with other cleaving agents. Furthermore, there were sufficient variations in the bismuth, tin, lead and mercury series, using the same cleaving agent (*n*-butyllithium), to emphasize the importance not only of the radicals and the cleaving agent, but, also, of the central metallic element.

(2) Gilman and Yale, *ibid.*, **63**, in press (1941).