Synthetic Aspects of Tertiary Diamine Organolithium Complexes

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The metalations of benzene, toluene, propene, and 1-butene with butyllithium–TMEDA complexes were studied. Factors controlling the metalation rate are discussed including temperature, structure of butyllithium isomer, amount of TMEDA, and solvent. Optimum conditions are described for the formation of TMEDA complexes of benzyl-, phenyl-, allyl-, and crotyllithium and benzyllithium · triethylenediamine (TED). Synthetic uses of these complexes demonstrate that they react in the same way as other organolithium compounds. Ring-isomer formation during metalation of toluene using n-*butyllithium–TMEDA complexes is also examined. The conditions for the lithiation of TMEDA and other tertiary diamines and monoamines (including trimethylamine) are given. The reaction of lithiated TMEDA with 1-bromobutane produced* N-n-*pentyl-N,N',N'-trimethylenediamine in 40% yield.*

The literature describing tertiary diamine organolithium compounds has grown tremendously since the initial announcements of these versatile reagents (1, 2). Much of this literature has centered on polymerization or polymer studies using these complexes as catalysts. The synthetic potential of these complexes and their preparations have been discussed, but there has been no intensive study to determine the optimum conditions for their preparation for synthetic applications (1–6). Synthetic applications usually require an isolation step or some procedure to ensure purity of the complex. Even investigations of the general utility and conditions for use of these complexes are not extensive. The most significant factor in their reactivity from a synthetic point of view is the ability of these complexes to metalate or replace certain activated hydrogens in hydrocarbons with the lithium cation (7, 8). The new aromatic,

benzylic, or allylic organolithium tertiary diamine complex is then reactive enough to react selectively with a variety of reagents:
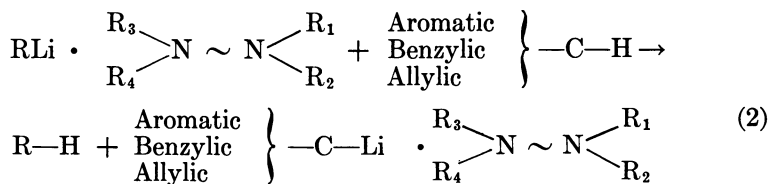
$$>N \sim N <\cdot R\text{Li} + R'\text{H} \rightarrow R\text{H} + >N \sim N <\cdot R'\text{Li} \qquad (1)$$

The results reported here describe an investigation of the optimum conditions of preparation of the tertiary diamine phenyllithium, benzyllithium, allyllithium, and lithiated TMEDA complexes. These reagents were allowed to react with some common reagents to help delineate the synthetic usefulness of the complexes.
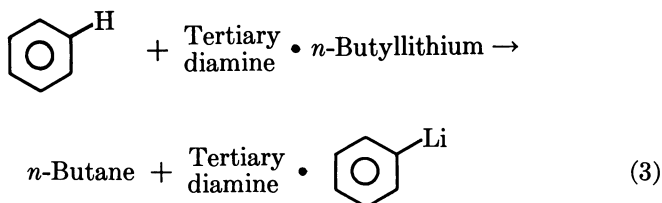
The accompanying papers in this volume, the literature cited in them, and this paper discuss reasons for the enhanced reactivity of these complexes. Mechanistic discussion has been left to a minimum in this paper to emphasize preparative and synthetic aspects. (A useful analogy as to what these complexes can do or how they will react is to consider their behavior to be similar to hydrocarbon soluble alkylsodium compounds if they were to exist.)

Results and Discussion

Reactivity of Various Tertiary Diamines in the Preparation of Tertiary Diamine Organolithium Complexes by Metalation. Previous work has shown that the reactivity and the rate of metalation for Reaction 2 of the tertiary diamine organolithium complexes is a function of the tertiary diamine in the complex (1, 9). In the specific case of the metala-

$$
\text{RLi} \cdot \begin{array}{c} R_3 \\ R_4 \end{array}\!\!>\!\!N \sim N\!\!<\!\!\begin{array}{c} R_1 \\ R_2 \end{array} + \left. \begin{array}{c} \text{Aromatic} \\ \text{Benzylic} \\ \text{Allylic} \end{array} \right\} \!-\!C\!-\!H \rightarrow
$$

$$
\text{R}\!-\!\text{H} + \left. \begin{array}{c} \text{Aromatic} \\ \text{Benzylic} \\ \text{Allylic} \end{array} \right\} \!-\!C\!-\!\text{Li} \quad \cdot \begin{array}{c} R_3 \\ R_4 \end{array}\!\!>\!\!N \sim N\!\!<\!\!\begin{array}{c} R_1 \\ R_2 \end{array} \qquad (2)
$$

tion of benzene as shown in Reaction 3, a tertiary diamine was added to *n*-butyllithium in benzene at room temperature in a 1:1 molar ratio. After the initial temperature rise, the heated solution began evolving *n*-butane at 45°-50°C (*n*-butane is very soluble in benzene, and usually

$$
\text{C}_6\text{H}_5\text{H} + \begin{array}{c} \text{Tertiary} \\ \text{diamine} \end{array} \cdot n\text{-Butyllithium} \rightarrow
$$

$$
n\text{-Butane} + \begin{array}{c} \text{Tertiary} \\ \text{diamine} \end{array} \cdot \text{C}_6\text{H}_5\text{Li} \qquad (3)
$$

no gas evolution occurs unless the temperature is raised). The rate of gas evolution was quite sensitive to the structure of the tertiary diamine. The order of reactivity observed using this procedure was N,N,N',N'-tetramethylethylenediamine (TMEDA) $>$ N,N,N',N'-tetramethyl-1,3-butanediamine $>$ N,N,N',N'-tetramethyl-1,3-propanediamine $>$ triethylenediamine (TED or DABCO) and 2-methyltriethylenediamine $>$ $N,N,-N',N'$-tetramethyl-1,4-butanediamine. The tertiary diamines, N,N,N',N'-tetramethylmethylenediamine and N,N'-dimethyl-1,4-piperazine, caused little or no gas evolution indicating essentially no metalation in the hour in which the other tertiary diamine complexes reacted.

The order of reactivity agrees with previous studies—TMEDA being by far the most reactive of the readily available tertiary diamines. [Sparteine appears to be the most activating of the tertiary diamines investigated (*1, 10*)]. Recent reports by Langer and others indicate that increased activation is expected from the methyl tertiary polyamines containing more than two basic nitrogens, all separated by two carbons (*11*). Preparative and synthetic work centered on TMEDA and TED (DABCO) because of their economic practicality.

Optimum Conditions for Preparing Phenyllithium from Benzene. The optimum procedure for metalation of an aromatic compound in high yield was to use the aromatic compound itself as the solvent. The alkyllithium compound used mainly in this study was *n*-butyllithium because it was convenient and economical.

The following general procedure was used to determine the completion of reaction. The calculated amount of TMEDA was added to the solution of *n*-butyllithium in benzene over one to two minutes. The stirred solution (under argon) was kept at the desired temperature; aliquots of this reacting solution and the final solution were then taken, allowed to react with trimethylsilyl chloride, and analyzed by GLC. These results may indicate the mechanism of the metalation reaction in addition to determining optimum metalation conditions for benzene. The results are listed in Table I.

A number of conclusions can be drawn. The effect of excess tertiary diamine above a 1-mole equivalent is not as significant for rapid metalation as is the initial amount of TMEDA. Practical metalation could only be obtained with a 1:1 molar ratio at 40°C and a 2:1 ratio at 60°C; the 4:1 ratio required reflux. Side reactions appeared to cause a problem only with the 4:1 ratio at the higher temperatures. Benzene as the solvent accelerated the reaction sixfold over hexane with 10% mole excess as the solvent. Some of this acceleration may be solvent effect. The use of *sec*-butyllithium increased the metalation rate eight times.

As expected, the metalation rate increased with temperature. The rate was relatively rapid over the initial 60% and then slowed dramati-

Table I.   Study of the Metalation Rate of Benzene
by Butyllithium and TMEDA

Run	Molar Ratio BuLi: TMEDA	T, °C	Elapsed Time, hrs	% Reaction[b]	% Yield	Comments
1	1:1[a]	22	1.0	34		
			2.5	60		
			7.8	79		
			21.8	100[c]	101	Almost gel initially, then became fluid. Some product ppt at end; sol. in benzene
2	2:1[a]	22	5.0	13		
			30.0	38		
			70.5	53	(100)[d]	
3	1:2[a]	22	1.0	32		
			2.0	50		
			4.5	82		
			20.0	100[c]	—	
4	1:1[a]	40	0.5	67		
			1.0	91		
			3.0	100[c]	97	Some product pptd; dissolved in added benzene, almost gel initially but became fluid rapidly; some product pptd, sol. in TMEDA.
5	2:1[a]	40	1.0	37		
			3.8	57		
			21.0	85	—	
6	4:1[a]	40	18.3	65	—	
7	1:1[a]	60	15 min	95		
			34 min	100[c]	100	Some product pptd; dissolved in added benzene.
8	2:1[a]	60	0.5	71		
			2.0	92		
			4.5	99	—	Some product pptd; dissolved in added benzene.
9	4:1[a]	60	2.0	60	—	Some product pptd; dissolved in added benzene.

Table 1.   Continued

Run	Molar Ratio BuLi: TMEDA	T, °C	Elapsed Time, hrs	% Reac- tion[b]	% Yield	Comments
10	2:1[a]	60 (reflux)	0	—		
		76	12 min	—		
		81	24 min	95.0		
		82	39 min	99.1		
		82	44 min	100[c]	—	Haze, insol. in added benzene.
11	4:1[a]	68 (reflux)	0	—		
		81	38 min	99.5	93	Considerable prod- uct pptd; sol. in benzene.
12	1:1[e]	66	3.0	98.5		
			3.9	100.0[c]	92	Some product pptd.
13	2:1[e]	66	5.3	86	—	
14	4:1[e]	66	2.8	42	—	
15	1:1[f]	79	38 min	97.5		
			105 min	100.0[c]	84	
16	1:1[g]	67	32 min	99		
			35 min	100[c]	79	Considerable haze.

[a] Conditions unless otherwise noted: TMEDA added over 1 min to organolithium solution at temp. Used 24% *n*-butyllithium in benzene.

[b] Represents percent of butyllithium reacted. Assumed only metalation of benzene occurring.

[c] These numbers were very close to the exact time the reaction finished because gas evolution was observed up to the end of the reaction. A trace of butyllithium generally remained at this point (<0.1%).

[d] Complete accountability of butyllithium (phenyllithium plus butyllithium).

[e] Used 15.2% *n*-butyllithium in hexane and added 10% excess benzene over stoichiometric.

[f] Used 14.6% *n*-butyllithium in cyclohexane with 10% excess benzene.

[g] Used 11.9% *sec*-butyllithium in hexane with 10% excess benzene.

cally. (This complex type of behavior would be expected from previous mechanistic studies of organolithium reactions.) The metalation rate of aromatics by organolithium–tertiary diamine complexes is, therefore, a function of organolithium concentration, organolithium structure, concentration of aromatic, temperature of metalation, and amount and structure of tertiary diamine. Although none of these factors is surpising, they all must be kept in mind in optimizing a particular metalation using organolithium–tertiary diamine complexes.

In cases where the amount of TMEDA is to be minimized, the 2:1 ratio can be prepared at 60°C for five hours, but the reaction would have to be run slightly more dilute to maintain complete solubility. Another factor when preparing phenyllithium–TMEDA complexes with ratios

greater than 1:1 is that these solutions tend to supersaturate and continue to throw down precipitate for hours—even days—after the reaction has been completed.

The metalation rate of TMEDA is much slower than that of benzene, and the phenyl anion is more stable than is the metalated TMEDA anion so that no interference by the TMEDA metalation was observed.

The 4:1 ratios were unsatisfactory; the excessive amount of precipitate that formed was insoluble in benzene. (This ratio might be satisfactory if the phenyllithium that formed reacted *in situ* but a somewhat lower yield would result.

Laboratory quantities of the dark, red-brown solutions although highly reactive, were not pyrophoric when in air. More dilute solutions of the complexes were bright yellow. When phenyllithium–TMEDA solutions of higher ratios were prepared, the precipitated complexes were also bright yellow. The odor of phenol was noticed after hydrolysis of the air-oxidized complexes.

Work with TED (triethylenedimaine) showed that reasonable metalation rates were obtained only at ratios of 1:1 in benzene. The reaction required 2.5 hours in refluxing benzene for completion. The bright yellow, crystalline product had a modest solubility in benzene and precipitated from solution. The solid complex may be pyrophoric in large amounts. The solubilities of various organolithium–tertiary diamine complexes are listed in Table II.

Table II.   Solubility of Organolithium–Tertiary Diamine Complexes

Organolithium[a]	Tertiary Diamine	Ratio RLi: Diamine	Solvent	RLi, wt % of Solution
Phenyllithium	TMEDA	1:1	benzene	19
		2:3	hexane	8
		4:1[b]	benzene	7.9
Benzyllithium		2:1	toluene	36
		2:1	cyclohexane	Two liquid layers formed
		3:1	toluene	4.5, top layer (two layers)
	TED	1:1	hexane	0.13
Allyllithium	TMEDA		THF	10.7
			1,2-dimethoxyethane	Reacts
			hexane	0.3
			diethyl ether	3.5
			cyclohexane	0.4
		2:1	diethyl ether	1.2
Crotyllithium		1:1	hexane	11

[a] All solubilities at room temperature (22°C); analysis using Gilman double titration (17).
[b] Slurry present—only solution in equilibrium was analyzed.

Table III. Stability of Organolithum–TMEDA Complexes

Organolithium Compound	Ratio RLi: Diamine	T, °C	Conc wt %	Solvent	% Lost of Contained Active Material/ Day[a]
Phenyllithium	1:1	35	15	benzene	0.67
Benzyllithium	1:1	35	14	toluene	0.31
	3:2	35	22		0.30
	2:1	30	38 (sat.)		0.046
	2:1	30	9		0.046
Lithiated N,N,N',N'-tetramethylethylenediamine	—	35	19	hexane	0.52

[a] Analysis of solutions using Gilman double titration with a time period of about three weeks (*17*)

Table III lists the decomposition rates of several organolithium–TMEDA complexes. The stability of the complexes is relatively good, but the presence of excess TMEDA above 1-mole equivalent significantly decreases stability. Solutions of the phenyllithium–TMEDA complex should be stored below 10°C for long shelf life.

It might be expected that in the presence of TMEDA or other tertiary diamines anomalous reaction products might be obtained with organolithium compounds such as benzyllithium. A number of reports in the literature disclose instances of the expected reaction products from reactions such as carbonation to the carboxylic acid and addition to benzophenone (*1, 3, 4, 12*). The phenyllithium–TMEDA (1:1) complex in benzene was allowed to react with benzophenone to give a 95% yield of triphenylcarbinol and with cyclohexanone to yield 59% of the 1-phenylcyclohexanol. The reaction with excess trimethylsilyl chloride is apparently quantitative. The main consideration in using these complexes is to use low temperatures for reaction and aqueous washes of ammonium chloride solution in the work-up to remove all of the tertiary diamine (the odor can be detected in low concentrations.)

Optimum Conditions for Preparing Benzyllithium from Toluene. Both the TMEDA and TED complexes of benzyllithium were investigated. Toluene metalation proceeds much faster than does benzene metalation under similar conditions. The benzyllithium complexes were more soluble in hydrocarbon solvents than were the corresponding phenyllithium complexes. This method of preparation of benzyllithium is the most convenient of the few literature procedures available. Other procedures described are the cleavage of benzyl methyl ether with lithium

metal, the exchange of benzyltin compounds with an organolithium compound, and the dibenzylmercury reaction with lithium metal (*13, 15, 46*). The direct reaction of benzyl chloride and lithium metal in ether leads only to the coupling product.

Only a brief study was made of the metalation rate of toluene by *n*-butyllithium because the reaction proceeded readily with TMEDA under most conditions. The runs listed in Table IV indicate just how much faster toluene metalation proceeded compared with benzene metalation. This rate was about 6.5 times faster with hexane as the solvent and at least 10 times faster when the corresponding aromatics (toluene and benzene) were used as the solvents.

The crystalline yellow 1:1 benzyllithium–TMEDA complex has a lower solubility in toluene than does the (benzyllithium)$_2$–TMEDA complex which tends to form oils. Because of its higher solubility and to eliminate as much of the tertiary diamine as possible, the 2:1 complex was used for synthetic evaluations. It is probably the optimum ratio to use in this benzyllithium system. Solutions of up to 38 wt % benzyllithium in toluene or about 59 wt % of the (benzyllithium)$_2$–TMEDA complex have been prepared. At ratios of 4:1 or more in toluene, a dark-red tar or oil also separated from the solution. With hexane as the solvent, yellow crystals of the 1:1 benzyllithium–TMEDA complex precipitated; at a ratio of 2:1 or more, a dark-red oil separated instead.

Because toluene metalation is very fast, the best preparative procedure is to slowly add TMEDA to *n*-butyllithium in toluene at about 60°C because of the need to drive off butane as it forms and prevent its build-up in the reaction solution. The reaction is quite exothermic because of the initial solvation of TMEDA. In small-scale preparations (200-ml or less) this precaution is not necessary. An added benefit of adding the TMEDA at a steady rate to the warm solution is that the reaction rate is almost instantly controllable and readily followed by observing the rate of gas evolution. Concentrations of *n*-butyllithium in toluene to about 26 wt % could be used without having to add additional toluene to ensure product solubility.

The yield for the 26-mole Run 10, Table IV, was determined by GLC (using the trimethylsilyl derivative) and by the Gilman double titration technique, both of which gave 100% yield (*17*). The product solution was clear, dark red–brown, and had good thermal stability. The concentrated solutions were highly reactive to air but did not ignite. (The solution should be stored cool or frozen when stored for longer than four months.)

The possibility of using the solid, golden yellow complex benzyllithium–TED (1:1) as an alternative for some special applications prompted a study of the best conditions for its preparation. The benzyl-

Table IV. Toluene Metalation by *n*-Butyllithium–Tertiary Diamine Complexes

Run	Molar Ratio *n*-BuLi: Diamine	*T*, °C	Elapsed Time, min	% Reaction	% Yield	Comments
1	1:1[a] TMEDA	52	3	100[b]	98	Too fast to measure accurately
2	2:1[a] TMEDA	77	16	100[b]	100	
3	4:1[a] TMEDA	77	36	99[b]		
			45	100	96	Two layers formed; bottom was a red oil. Added TMEDA caused one phase to form
4	1:1[c] TMEDA	66	36	100[b]	100	Entire solution solidified to yellow crystals on cooling, holding the hexane
5	1:1[c] TED	68	135[b]	—	90	Isolated by filtration; bright yellow crystals
6	1:1[c] TED	68	135[b]	—	96	Isolated by evaporating solvent; bright yellow crystals
7	8:1[e] TMEDA	89	75	(100)[d]	—	Red-black tar
8	3:1[e] TMEDA	70	10	—	—	Two layers
9	1:1[f] TMEDA	70	120 (slow addition)	—	100	
10	2:1[g] TMEDA	60–65	60	—	100 (titration and glc)	Complete solution; large-scale run

[a] 14% *n*-butyllithium in toluene used for these runs.
[b] Evolution of gas ceased at this point, and trimethylsilyl derivative was made. Yields were based on GLC analysis.
[c] 15.2% *n*-butyllithium in hexane used with 10% excess toluene added.
[d] The reaction was run until gas evolution ceased. The product was too intractable to dissolve readily in solvents for analysis.
[e] 19.5% *n*-butyllithium in toluene used.
[f] 26.4% *n*-butyllithium in toluene used.
[g] 22.0% *n*-butyllithium in toluene used.

lithium–TED (1:1) is fairly soluble in toluene, but it has only a slight solubility in hexane. Therefore, the solvent of choice was an aliphatic hydrocarbon such as hexane. The metalation rate of toluene by *n*-butyllithium in hexane with TED was about a fourth of what it was with TMEDA, but it still proceeded at a convenient rate at 68°C. Greater than 1:1 ratios (less TED) seriously slowed the metalation reaction so that only the 1:1 ratio with TED is considered practical.

The optimum procedure for preparing the butyllithium–TED (1:1) complex was to add the TED solid directly to 15-20% *n*-butyllithium in hexane at 40°–50°C. (When the TED was added near room temperature, a gel stage formed.) The exotherm from the solution was moderate, and the temperature was allowed to rise to reflux. Only a 20% excess of toluene was added because large excesses solubilized the product. The yield of the dried, yellow crystals was from 82 to 90%. When the hexane solution was evaporated without filtration to dryness, a yield of 96% was obtained. No side products were observed. The crystals were very sensitive to air; they charred and smoked, but no flame was observed in laboratory quantities. The crystals were stable for at least five years at room temperature when protected from air and moisture. The TED could not be sublimed away (only 0.2% weight loss) from the 1:1 complex crystals at 0.14 torr before decomposition occurred at 125°C.

Isomer Formation during Metalation of Toluene Using *n*-Butyllithium and TMEDA. There have been several reports describing *o*-, *m*-, and *p*-tolyllithium from isomer formation stemming from ring metalation of toluene in addition to the normal benzyl metalation using *n*-butyllithium–TMEDA (*1, 16, 18, 19*). These previous works found about 10% ring metalation of which meta metalation comprised about 60% of the total. Analysis of the crystalline benzyllithium–TED complex showed no ring metalation isomers present.

Table V summarizes the results of both this investigation and those reported in the literature. The amount of ring metalation and relative ratios of isomers vary somewhat according to the procedure used and on standing. This is evidently a case of kinetic control *vs.* thermodynamic control, as pointed out by Broaddus (*18*). Therefore the procedure for metalation affected the initial amount of ring-isomer formation directly as expected in a kinetically controlled reaction that involves temperature of metalation, amount of TMEDA, and subsequent treatment or storage of the product solution. A recent report discusses a similar system of anion equilibration between *m*- and *p*-xylyllithium with TMEDA, and anion equilibration between the meta and benzyl positions of ethylbenzene using TMEDA or *N,N,N',N',N''*-pentamethyldiethylenetriamine (PMDET) (*20*).

Ring-isomer formation during metalation was analyzed by GLC using the dimethyl sulfate derivative, which produced a mixture of xylenes and ethylbenzene in this system. (Dimethyl sulfate is a better reagent for organolithium derivative formation than is trimethylsilyl chloride or carbon dioxide.)

The toluene-metalation system in this study differs from that of Broaddus in that pure toluene was used as the solvent; a RLi to TMEDA ratio of two was used. Analyses were usually run after complete reaction of the *n*-butyllithium unless otherwise noted. Higher reaction temperatures were used, and the final concentration of benzyllithium in solution was higher.

The results reported by others as well as our own indicate that the main contaminating ring isomer is meta, the more acidic (reactive) position compared with the ortho or para positions when only electronic or resonance effects are considered. In addition, the statistical factor of two meta-hydrogens probably also contributes to the predominance of *m*-tolyllithium formation compared with formation of the para isomer. The combined meta and para isomer content is reported because of the difficulty in obtaining good separation of the xylene mixture formed by derivatization.

One of the specific effects influencing total ring-isomer content was the ratio of RLi to TMEDA. In Run 2, a ratio of 0.5 (large excess TMEDA) was used, and the total amount of ring isomer initially formed and present after one hour was small (less than 2.1%). When the amount of TMEDA was decreased to a RLi-to-TMEDA ratio of two, the amount of ring isomer present when the reaction was completed was 11.5%, agreeing with the work of previous workers. In Run 6, enough TMEDA was added to an already formed benzyllithium-in-toluene solution with a RLi:TMED ratio of two to change the ratio to 0.5. The amount of meta ring isomer decreased from 6.3 to 5.2% in about 15 minutes at 30°C. The effect of the large TMEDA excess was more pronounced when it was present during metalation, although still effective after the fact.

A number of experiments were carried out to determine the effect of temperature and time on the ring-isomer content of the (benzyllithium)$_2$ · TMEDA in toluene solutions. In all cases—0°C, room temperature, or 60°C—the amount of ring isomer decreased with time with the ortho isomer disappearing far more rapidly than the meta or para ring isomers. This change is caused either by equilibration of the tolyllithium isomers to the more thermodynamically stable benzyllithium, or by a more rapid decomposition reaction of these ring isomers with TMEDA. The measured stability of these solutions indicate that selective decomposition is not a good explanation. (Run 6, after being heated at

Table V.   Isomer Content of

Run	Mole Ratio RLi: TMEDA	Addition		Heating		Elapsed Time at Temp. after Prep
		T °C	Time min	T °C	Time min	
1(a)	2	60	20	70	10	1 hr
						2.5 days
						60 days
						90 days
2	0.5	60	20	70	10	1 hr
3	2	40	60	—	—	—
4	2	65	60	—	—	—
5	2	40	15	70	40	—
6	2	40	60	—	—	—
	2			70	15	—
				60	30	
				60	90	
				60	390	
7	2	55	90	70	20	180(0°) days
8(d)	1	30	20	69	15	1 hr
						60 days
						90 days
9(e, d, f)	1	30		—	—	15 min
						2 hrs
10(d, g)	1	25		—	—	5 hrs

a TMEDA was added to 25% n-butyllithium in toluene while stirring at designated temp. The RLi compounds reacted with dimethyl sulfate to produce ethylbenzene and xylenes.

b Total resolution of m- and p-xylenes was not accomplished; thus the meta and para isomers are reported together.

Table VI.   Reactions of (Benzyllithium)$_2$

Run	Reactant	T, °C	Time, min
1	Trimethylsilyl chloride	−5	45
2	1-Bromobutane	−20	90
3	Benzonitrile	−5	45
4	Ethyl acetate	5-10	60
5	Ethyl benzoate	5-10	60
6	Cyclopentanone	−40	30
7	Cyclohexanone	−5	60
8	2-Butanone	−15	60
9	Diisopropyl ketone	−5	60
10	Benzaldehyde	−35	20
11	Benzophenone	−15	20

a Yield based on recrystallized or distilled product unless otherwise noted; *see*

Benzyllithium–TMEDA Complexes

Ring-isomers			Comments
$\%(m+p)$[b]	$\%o$	% Benzyl	
8.5	3.0	88.5	
5.9	1.4	92.7	
1.6	—	98.4	
0.3	—	99.7	
1.1	—	98.9	
8.5	1.0	90.5	Addition of RLi to TMEDA (inverse)
9.1	1.6	89.3	
7.3	—	92.7	
6.5	9.1	84.4	Incomplete reaction at this point
6.6	5.0	88.4	Complete reaction
6.1	3.6	90.3	
6.3	0.9	92.8	Add TMEDA to produce 1:2 ratio at this point to give 5.2% *meta* and 94.8% benzyl.
3.8	—	96.2	Yield at this point is 98%
0.8	—	99.2	26-mole scale
6.3	1.0	92.7	
2.1	—	97.9	
—	—	100.0	
9	3	89.0	Incomplete reaction at this point
6	2	92.0	
7.6	1.8	90.6	

[c] No isomer is reported when less than 0.1%
[d] 15% *n*-butyllithium in hexane used in this run; hexane was solvent.
[e] Broaddus (*18*) used carbon dioxide for derivatization.
[f] Hexane-toluene mixture was the solvent for this run.
[g] Chalk and Hoogeboom (*16*) used trimethylsilyl chloride for derivatization.

–TMEDA in Toluene

		Product	
Product		% Yield	bp or mp, °C[a]
benzyltrimethylsilane		81	59-62 (5 mm)
n-amylbenzene		84	71-74 (5 mm)
benzylphenyl ketone		16	(Crude)
1,1-dibenzylethanol		43	122-125 (0.4 mm)
1,2,3-triphenyl-2-propanol		22	(Crude)
1-benzylcyclopentanol		35	55
1-benzylcyclohexanol		59	54
2-benzyl-2-butanol		53	92-94 (0.5 mm)
3-benzyl-2,4-dimethyl-3-pentanol		82	96-99 (0.1 mm)
1,2-diphenylethanol		55	64
1,1,2-triphenylethanol		92	86

experimental for literature physical constants and references.

60°C for 6.5 hours, still showed at least 98% yield, while ring-isomer content decreased to 2.8% with no ortho or para isomer.)

The equilibration of the ring anions to the benzyl anion is the probable explanation, especially considering the recent work of Gau and our observation of an equilibration between *m*-xylene and toluene in the presence of (benzyllithium)$_2$ · TMEDA (20). (In fact, this type of system might be the basis of another route for a hydrocarbon acidity scale.) The more rapid disappearance of the ortho isomer, compared with the meta, may be the result of a possible intramolecular route for conversion to the benzyl anion. The meta and para isomers probably change to the benzyl anion by an intermolecular route that would be slower and agree with what was observed. Although complete resolution by GLC of the para and meta isomers was not done in this study, the para disappeared faster than the meta, but much slower than the ortho. In other time studies on the disappearance of the meta isomer at room temperature, about half the initial amount of this isomer was gone in three days and all of it in two to three months.

Aging these benzyllithium solutions to remove the ring-isomer content is not practical in most cases, and use of large amounts of TMEDA to promote conversion can also cause problems later in synthetic use. Since heating the toluene product solution did not cause serious decomposition at 60°C, this could provide a solution to the problem for most

Table VII. Reactions

Run	Reactant	Solvent	T, °C	Time, min
1	1-Bromobutane	Et$_2$O	35	60
2	Bromobenzene	Et$_2$O	35	60
3	Iodobenzene	Et$_2$O	20	60
4	Benzonitrile	THF	−10	60
			25	60
5	Ethyl acetate	Et$_2$O	35	45
6	Ethyl benzoate	THF	0	60
7	Methyl vinyl ketone	THF	−10	60
8	Crotonaldehyde	Et$_2$O	0	60
9	2-Butanone	Et$_2$O	0	60
10	Cyclopentanone	THF	−10	60
11	Cyclohexanol	THF	0	60
12	Diisopropyl ketone	Et$_2$O	−10	30
13	Benzaldehyde	THF	0	60
14	Benzophenone	Et$_2$O	−10	120
15	Indanone	THF	−10	60
16	Fluorenone	Et$_2$O	35	60
17	Lithium benzoate	THF	65	45

[a] Yield based on recrystallized or distilled product unless otherwise noted. *See*

applications. The solid benzyllithium–TED complex may also be an alternative.

Synthetic Application of (Benzyllithium)$_2$–TMEDA and Benzyllithium–TED. All the synthetic application studies were run with an aged (benzyllithium)$_2$–TMEDA toluene solution that had 0.8% of the total organolithium compounds present as the tolyllithium isomers (only meta present) or with benzyllithium–TED crystalline complex free of ring isomers.

A number of standard organolithium reactions were examined using the two benzyllithium complexes. The conditions used for the various runs listed in Tables VI and VII were selected by experience to give good yields but were not optimized. (Because of the high reactivity of organolithium reagents in general, all variables of a given reaction affect the yield. In other words there is always a set of optimum conditions that may vary markedly from one reacting compound to another even though the same organolithium compound is used.)

Reaction conditions are given in the experimental section. Yields vary considerably, but most of the normal organolithium reactions occur in satisfactory-to-good yields. When readily enolizable protons are present, lower yields might be expected and were found—as with cyclopentanone. Buhler, in a recent optimization study, found the yield of the tertiary alcohols from cyclopentanone, cyclohexanone, and benzo-

of Benzyllithium–TED

		Product	
Product		% Yield[a]	bp or mp, °C
n-amylbenzene		80	62 (0.5 mm)
2-benzylbiphenyl		32	50
2-benzylbiphenyl		20	49
benzylphenyl ketone		59	54
1,1-dibenzylethanol		25	Crude oil
1,2,3-triphenyl-2-propanol		66	83
1,2,3-triphenyl-2-propanol		0	Condensation products
1,2,3-triphenyl-2-propanol		0	Condensation products
2-benzyl-2-pentanol		65	67 (0.3 mm)
1-benzylcyclopentanol		72	56
1-benzylcyclohexanol		55	54
3-benzyl-2,4-dimethyl-3-pentanol		60	110 (1 mm)
1,2-diphenylethanol		81	65
1,1,2-triphenylethanol		99	87
1-benzyl-1-indanol		20	141
9-benzyl-9-fluorenol		83 (crude)	126
benzylphenyl ketone		44	53

experimental for literature references for physical constants when available.

phenone to be 75, 89, and 73%, respectively (21). The corresponding yields using the tertiary diamine benzyllithium complexes were both higher and lower than those results. Lower reaction temperatures and slower addition rates and perhaps a cosolvent should increase yields in most cases. The workup of the products was normal, but several washes of the product in organic solution with aqueous ammonium chloride or dilute hydrochloric acid were required to ensure complete removal of the tertiary diamine.

The solutions of (benzyllithium)$_2$–TMEDA were much more convenient to use than the solid, relatively insoluble benzyllithium–TED complex. The reaction yields vary between these two complexes. Whether this is a function of the different solvent systems used for each, lack of optimization, or the actual tertiary diamine present was not examined, however.

These results show that the organolithium complexes are synthetically useful and are similar in their reaction products to the usual organolithium compounds.

Optimum Conditions for Preparation of Allyllithium and Crotyllithium from Olefins. Like benzyllithium, allyllithium is also difficult to prepare directly from lithium metal and allyl chloride because of the excessive coupling that occurs.

$$2CH_2 = CHCH_2Cl + 2Li \rightarrow CH_2 = CHCH_2CH_2CH = CH_2 + 2LiCl \quad (4)$$

Some success has been reported with Reaction 4 using low temperatures (22). We have obtained up to 61% with the procedure cited in Ref. 22 with some difficulty. A number of other routes have been found for preparing allyllithium, including the cleavage of allyl ethers with lithium metal, exchange of alkyllithium compounds with allyltin compounds, and

Table VIII.   Preparation of Allyllithium– and

Run	Product	Olefin	Time min	Solvent	RLi
1	Allyllithium	propene	30	cyclohexane	sec-BuLi
2			30	cyclohexane	sec-BuLi
3			150	hexane	n-BuLi
4			90	hexane	sec-BuLi
5			30	hexane	sec-BuLi
6			30	hexane	sec-BuLi
7	Crotyllithium	1-butene	90	cyclohexane	sec-BuLi
8		trans-2-butene	90	cyclohexane	sec-BuLi

[a] Yield of allyllithium–TMEDA complex based on isolated solid.
[b] GLC analysis of dimethyl sulfate derivative formed at 20° and 55° C gave 29.0

the reaction of diallylmercury with lithium metal (*22–27*). The metalation of propene with *n*- or *sec*-butyllithium–TMEDA complexes is one of the most convenient routes to allyllithium as shown in Table VIII.

$$CH_2 = CHCH_3 + C_4H_9Li \cdot TMEDA \rightarrow$$
$$CH_2 = CHCH_2Li \cdot TMEDA + C_4H_{10} \tag{5}$$
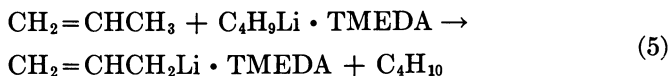
The metalation proceeded faster for Reaction 5 than toluene metalation, but it was hard to get the excess concentration necessary for rapid reaction. An aliphatic solvent was necessary for the reaction since all other solvents produced side reactions regardless of whether an aromatic or an ether was used. Propene in 50% excess was added to *n*-butyllithium in hexane containing a 1:1 mole ratio of TMEDA at 0°C. A larger excess of propene may produce oligomers. This solution was warmed to 30°C in a pressure apparatus. After three hours the yellow slurry was filtered to give a 65% yield of allyllithium–TMEDA; from 10 to 20% of the product remained in the filtrate. The solid, yellow-orange complex was not pyrophoric in air, although it was instantly reactive. When higher temperatures (about 50°C) were used and the propene added at atmospheric pressure, the competing metalation of TMEDA occurred, and only a trace of allyllithium formed. The lithiated TMEDA evidently did not metalate propene at a significant rate (if at all) under these conditions.

The metalation proceeded so readily with *sec*-butyllithium that the reaction was run to completion at −5° to 5°C in 0.5 hour. (*tert*-Butyllithium was usually slower in metalation reactions and led to more side reactions than did *sec*-butyllithium in these systems.) About 81% of the yellow–orange product precipitated from solution. The metalation reac-

Crotyllithium–TMEDA Complexes

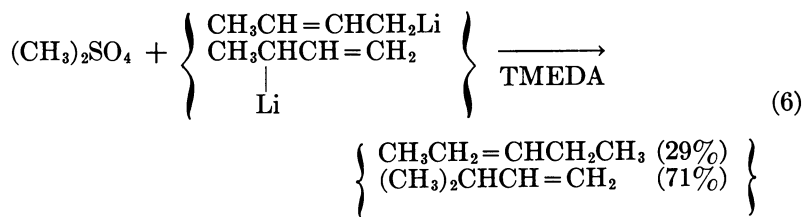| Ratio RLi: TMEDA	T °C	% Yield
1:2	2	81
1:2	−5–5	two liquid layers
1:1	30 (15 psi)	64
1:1	−5–0	77
4:1	−7–4	gel formation
1:1	−5–5	79
1:1	0–5	92[b,c]
1:1	0–10	55[c]

± 1%, and 29.5 ± 1% terminal lithium, respectively.
 [c] Yield calculated by base titration of solution.

tion with a 2:1 ratio produced two liquid layers without any precipitate. When a 4:1 ratio of sec-butyllithium to TMEDA was used, a gel and a solid slurry that did not break up on heating were obtained.

The optimum procedure, therefore, was to add TMEDA to sec-butyllithium in an aliphatic solvent such as hexane at −5°C. About 50% excess of propene was then added quickly at 0 to 5°C. The solution was stirred at that temperature for 30 min and then warmed quickly to 45°C to let any sec-butyllithium left react. The solution was then cooled to 10°C and filtered. The slurry itself can be used without isolation.

The corresponding metalation of 1-butene or trans-2-butene was slightly more rapid than that of propene and gave a solution of crotyl-lithium–TMEDA. The crotyllithium–TMEDA compound was quite soluble in aliphatic hydrocarbons, giving dark, yellow-red solutions. (These crotyllithium solutions slowly deposited yellow crystals on stand-ing, so they should be used soon after preparation.) The metalation proceeded faster with 1-butene than with trans-2-butene, which may explain the lower yield obtained with the latter. A synthetic study of the crotyllithium was not made because its reactions gave at least two prod-ucts, as expected from literature reports on other crotyl anions.

Reaction with dimethyl sulfate produced only 29% trans-2-pentene and 71% 2-methyl-2-butene. In other words about 29% of the lithium reacted from the C-1 position of the crotyl group with only trans con-figuration and 71% from the internal C-3 position. Essentially the same positional ratio was obtained at 20° as at 55°C.

$$(CH_3)_2SO_4 + \begin{Bmatrix} CH_3CH=CHCH_2Li \\ CH_3CHCH=CH_2 \\ \quad | \\ \quad Li \end{Bmatrix} \xrightarrow[\text{TMEDA}]{} \tag{6}$$

$$\begin{Bmatrix} CH_3CH_2=CHCH_2CH_3 \quad (29\%) \\ (CH_3)_2CHCH=CH_2 \quad (71\%) \end{Bmatrix}$$

Table IX.   Reaction of Allyllithium–TMEDA

Compound	Reagent	T °C	Solvent	Time min
Allyllithium·TMEDA	Benzophenone	20	Et₂O	75
	Cyclohexanone	20	Et₂O	45
Crotyllithium· TMEDA	Acetone	−20	Cyclohexane	20

(ª) See experimental for literature physical constants and references.

The reaction with acetone gave a similar result. Table IX lists the results from several reactions of reagents with allyllithium–TMEDA and crotyl-lithium–TMEDA.

Lithiated Tertiary Amines and Diamines and Their Reactions. The formation of lithiated TMEDA by organolithium reagents, especially *n*-butyllithium, was first described in 1965 by Langer (*2*).

$$n\text{-}C_4H_9Li + (CH_3)N(CH_2)_2N(CH_3)_2 \rightarrow$$

$$(CH_3)_2N(CH_2)_2N(CH_3)CH_2Li + C_4H_{10} \qquad (7)$$

$$I$$
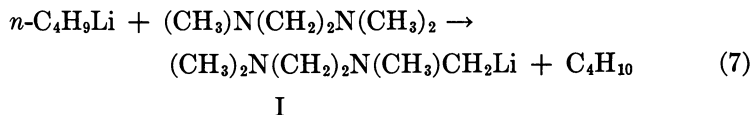
Since then, further work by Langer and his co-workers has shown that this is a general reaction with the higher homologs of TMEDA (*5, 8*). Preparation of these lithiated tertiary diamines and a number of synthetic reactions are given in those references. As further background to the possible reactions that may occur with other tertiary amines and diamines, the work of Lepley and co-workers with *n*-butyllithium and aromatic tertiary amines should also be examined (*29–33*).

One problem in working with the lithiated tertiary diamines is that they will undergo further decomposition when overheated or on standing. For example lithiated TMEDA yields lithium dimethylamide, dimethyl-vinylamine, and lithium acetylide (*1, 2, 5, 34*). Lithiated TMEDA (I) in hexane decomposes at a rate of 0.52% of the initially contained material per day at 35°C. Therefore solutions of the lithiated tertiary diamines and amines should be stored at 10°C or lower for long periods of storage.

The preparation of monolithiated *N,N,N′,N′*-tetramethylethylenedi-amine (I) was studied under several sets of conditions to optimize its preparation. The lithiation of other tertiary monoamines and diamines was also examined.

TMEDA was added in 1:1 mole ratios to hydrocarbon solutions of the alkyllithium compound. The solutions were kept at a given temperature until gas evolution ceased. The dark, orange-brown solutions were analyzed using the Gilman procedure when complete reaction of the

and Crotyllithium–TMEDA

| Product	Product [a]	
	mp or bp, °C	% Yield
1,1-diphenyl-3-buten-1-ol	125 (0.6 mm)	91
1-allylcyclohexanol	64 (7.5 mm)	52
2,3-dimethyl-4-penten-2-ol, and *trans*-2-methyl-4-hexen-2-ol	65–71 (120 mm)	11

starting alkyllithium was observed (*17*). This analysis for the carbon-bound lithium gave reproducible, consistent results for the lithiated tertiary diamines.

However inconsistencies were found in this procedure with solutions of lithiated tertiary monoamines so that only total base titrations were used for their analysis. In most cases a small amount of the decomposition product was filtered from the product solution. The solid on hydrolysis produced dimethylamine and acetylene (*34*). Product solutions up to 30 wt % in hexane were readily produced without solubility problems. No lithiation of TMEDA on the methylene carbons was observed. This was determined by preparation of the dimethylsulfate derivative of the lithiated TMEDA and examining for *N,N,N′,N′*-tetramethyl-1,2-propanediamine in the presence of the product, *N*-ethyl-*N,N′,N′*-trimethyl-1,2-ethanediamine.

Although *n*-butyllithium lithiated the TMEDA efficiently at a convenient rate, *sec*-butyllithium worked even more smoothly. Surprisingly *tert*-butyllithium was quite poor, although some of the problem was caused by the low-boiling solvent, pentane. For instance *tert*-butyllithium in refluxing pentane took 14 hours to completely react with TMEDA.

A summary of the lithiation of tertiary amines and diamines is given in Table X. The actual total base minus the base stemming from carbon-bound lithium present divided by the amount of carbon-bound lithium present was used to obtain the ratio of tertiary nitrogen to carbon-bound lithium reported in the table. Agreement between Runs 1 through 11 was surprisingly good. Yields for the same runs were also quite good— 90 to 100%—with both *n*- or *sec*-butyllithium. *sec*-Butyllithium was preferred because of the milder conditions involved. The conditions become especially important when lithiation of potentially more sensitive (yet more unreactive) tertiary amines or diamines is attempted. Runs 9 through 15 show some interesting but unexploited metalation results. The lithiation rate for the reactions in Table X was observed by gas evolution, and the solutions were analyzed when the gas evolution ceased.

Reaction occurred in only a few hours with *sec*-butyllithium and trimethylamine, but the yields seemed to be lower than those obtained with TMEDA.

$$(CH_3)_3N + sec\text{-}C_4H_9Li \rightarrow (CH_3)_2NCH_2Li + n\text{-}C_4H_{10} \qquad (8)$$
$$II$$
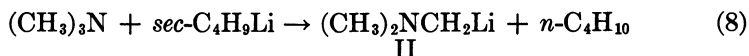
This may be because II has less thermal stability than does the lithiated TMEDA (I). The lithiation of trimethylamine has also been reported under slightly different conditions by Peterson (*35*). Analysis of

these tertiary monoamines in Runs 14 to 19 were inconsistent using the Gilman double titration with benzyl chloride, and only total-base titration was used for assay of the solution. It was assumed that all decomposition products, including LiH and lithium dimethylamide, were insoluble. The lithiation of the tertiary monoamines was performed in all cases with a mole ratio of alkyllithium to tertiary monoamine of 1:2 to keep the RLi:tertiary nitrogen ratio the same as that used with the tertiary diamines. In those cases noted in Table X, the total base in solution was measured and divided by three to estimate yield. (Analysis for the unreacted starting alkyllithium was not affected in these solutions.)

In Runs 10 and 12 the precipitate was very heavy and the total soluble base was quite low. In those two instances the product was apparently insoluble or the lithiated tertiary amine structure too unstable and decomposition resulted.

Each lithiated tertiary amine or diamine will have optimum conditions for preparation to ensure complete reaction with minimum decomposition. These optimum conditions may be determined by observing the rate of gas evolution as a function of tertiary amine or diamine ratio and temperature together with analysis of the final solution or slurry.

Only a few reactions were tried with the lithiated tertiary amines and diamines; these are reported in Table XI. The yields for the coupling of organic halides with lithiated TMEDA were reasonable for a non-optimized reaction. Changes in a few conditions were made to see whether some obvious improvements could be made. In general the yields ranged from 30 to almost 50%. Alkyl bromides gave the best yields in this coupling reaction. The reaction of lithiated TMEDA (I) with a reactive ketone and an aldehyde again gave low yields. Less-reactive reagent molecules should give higher yields. The lithiated trimethylamine (II) produced a good yield of the amine alcohol with benzaldehyde, although low yields were obtained in coupling with 1-iodopropane and 1-bromooctane.

Another possible problem is in the work-up of these compounds since the products are very soluble in water and organics. Only further study can determine whether the products from the reactions of these lithiated tertiary amine and diamine compounds will give high-enough product yields to permit these novel organolithium compounds to become dependable reagents for the chemist.

Experimental

All reagents were reagent-grade chemicals. Hydrocarbon solvents were dried over sodium wire. TMEDA was dried over sodium wire and then distilled under reduced pressure. TED was tried under vacuum to the point of sublimation. Liquid tertiary amines and diamines were

Table X.   Preparation of Lithiated

Run	Amine	T °C	Time hr	RLi[a]
1	TMEDA	55	1.0	sec-BuLi
2 [d]		49	1.0	sec-BuLi
3		47	1.25	sec-BuLi
4 [e]		55	1.0	sec-BuLi
5		60	2.5	n-BuLi
6		64	3.5	n-BuLi
7 [f]		36	14.0	tert-BuLi
8 [d]		45	0.75	cyclopentyl Li
9	N,N,N'N'-Teramethyl-1,3-butanediamine	55	0.75	sec-BuLi
10	N,N'-Dimethyl-1,4-piperazine	65	1.0	sec-BuLi
11	Triethylenediamine (TED)	65	1.0	sec-BuLi
12	N,N,N',N',-Tetramethyl-methylenediamine	63	1.5	sec-BuLi
13	N-Methylpyrrolidine[g]	55	0.5	sec-BuLi
14	N-Methylpiperidine[g]	55	1.5	sec-BuLi
15	Triethylamine[g]	65	1.0	sec-BuLi
16	Trimethylamine[g]	80[h]	5.25	n-BuLi
17		70[h]	5.5	n-BuLi
18		60[h]	3.0	sec-BuLi
19		60[h]	6.5	sec-BuLi

[a] Hexane is solvent unless otherwise stated.
[b] Analysis done using total base and Gilman benzyl chloride coupling [(17)].
[c] Analysis of gas from hydrolysis of yellow ppt. showed dimethylamine and acetylene present.
[d] Solvent is cyclohexane.
[e] RLi:tertiary diamine ratio is 1:2.

all distilled before use and protected from air. All lithium compounds were from Foote Mineral Co. Elemental analyses were performed by Micro-Analysis, Inc., of Wilmington, Del. All reactions were run under argon, and air-sensitive materials were also handled under argon. GLC analyses were performed on a Varian-Aerograph 90P3 Chromatograph with a thermal conductivity detector. The column used for trimethylsilyl derivatives was 5-ft, SE-30/Chromasorb W.

Tertiary Amines and Diamines

Wt % Product Conc. in Sol.	Product Sol. Anal. tert- N/RLi[b]	% Yield	Comments
19.0	2.06	94	Slight ppt., no RLi left by GLC[c]
18.5	2.06	95	Heated slightly beyond point when gas evolution ceased.
17.9	2.19	94	2% RLi left
—	—	—	5% RLi left after 60 min at 55°C; considerable ppt
24.0	2.26	90	5% RLi left
27.3	1.95	100	Heated slightly beyond point when gas evolution ceased
22.0	1.86	96	Trace RLi left, lot of ppt
30.0	1.96	100	3% RLi left, no ppt., only haze
21.4	1.86	95	No RLi left, some ppt. also formed
—	—	—	No RLi left, heavy ppt.; double titration showed no product
12.3	2.20	68	No RLi left, heavy ppt.; analysis on slurry.
—	—	—	No RLi left, heavy ppt.; double titration showed no product
7.6	3.1 (theory 3.0)	57	No RLi left; heavy ppt
14.3	—	90[i]	Only trace RLi left, mod. ppt.; double titration showed low yield.
14.4	—	98[i]	Trace RLi left, mod. ppt.; low low yield by titration
8.9	—	67[i]	No RLi left
—	—	—	5% RLi left
6.6	—	60[i]	No RLi left
—	—	—	8% RLi left

[f] Solvent is pentane.
[g] RLi:tertiary amine ratio is 1:2.
[h] Pressure reactor used.
[i] Gilman double titration does not give good results with this amine; yield based on total base in solution.

n-Butyllithium in Benzene (or Toluene). A 12-liter flask equipped with stirrer, pressure-equalizing dropping funnel, reflux condenser, and thermometer was flushed thoroughly with argon. (Nitrogen must not be used because it will react with lithium metal powder.) The flask was charged with 573 grams of 1% Na-Li powder and 6,650 ml of benzene. The reaction was first initiated with 100 ml of 1-chlorobutane while stirring. The temperature was maintained at 35°–37°C and the remainder

Table XI.   Reactions of Lithiated

Run	Lithiated Compound[a]	Reagent	Addition T, °C	Total Time, min
1	TMEDA	1-iodobutane	−5	30
2		1-bromobutane	0	30
3			10	75
4		1-chlorobutane	68	90
5		1-bromobutane	0	30
6		2-bromobutane	−10	30
7		iodobenzene	10	75
8		1-bromooctane	20	30
9			−20	30
10			−10	30
11		bromocyclohexane	−5	30
12		cyclopentanone	5	50
13		valeraldehyde	−10	30
14	Trimethylamine	1-iodopropane	−10	30
15		1-bromooctane	−20	30
16		valeraldehyde	−10	30
17		benzaldehyde	−10	60

[a] Reagent added as a molar equiv. based on the lithiated TMEDA or trimethylamine present; solvent was hexane in all cases.

of the 3,310 grams of 1-chlorobutane was added over 3.5-hrs. The slurry was stirred 2 hr more before filtration. The yellow filtrate analyzed to be 26.99% n-butyllithium. The Gilman correction was 0.28% (17). The yield was 83% with no wash on the filter cake. (Actual yield estimated to be about 90%.)

Lithiation of Benzene by n-Butyllithium–TMEDA. A 500-ml flask equipped with stirrer, reflux condenser, and thermometer was purged with argon and then charged with the required amount of 24.4% n-butyllithium in benzene (120 to 200 ml). The stirred solution was heated to the desired temperature and the heat removed. Purified TMEDA was then added in the proper molar ratio (30 to 50 ml) using a large syringe over 0.5 to 1.0 min while cooling with a heptane-dry ice bath to maintain proper temperature. (Do not use rapid addition for preparations larger

TMEDA and Trimethylamine

RLi Used for Lithiation of tert-Amine	Product	% Yield	°C, bp[b]
sec-BuLi	N-n-pentyl-N,N',N'-trimethyl-1,2-ethanediamine	40	182
		49	182
		33	61 (4.5 mm)
		18	
n-BuLi		44	
sec-BuLi	N-(2-methylbutyl)-N,N',N'-trimethyl-1,2-ethanediamine	33	52 (2.9 mm)
	N-benzyl-N,N',N'-trimethyl-1,2-ethanediamine	30	69 (0.3 mm)
	N-n-nonyl-N,N',N'-trimethyl-1,2-ethanediamine	40	85 (0.5 mm)
		37	
n-BuLi		30	
	N-(cyclohexylmethyl)-N,N',N'-trimethyl-1,2-ethanediamine	18	69 (0.5 mm)
sec-BuLi	N-(hydroxycyclopentylmethyl)-N,N',N'-trimethyl-1,2-ethanediamine	28	81 (1.5 mm)
n-BuLi	N-(2-hydroxyhexyl)-N,N',N'-trimethyl-1,2-ethanediamine	39	84 (0.7 mm)
	N,N,N-n-butyldimethylamine	32	92
sec-BuLi	N,N,N-n-nonyltrimethylamine	12	52 (2.9 mm)
n-BuLi	condensation product	—	—
	N,N,N-(1-hydroxyl-1-phenylethyl) dimethylamine	49	72 (0.25 mm)

[b] *See* experimental for literature references and physical constants when available.

than 250 ml—it is too vigorous.) The evolution of gas was observed as it passed out of the system through an oil bubbler. Periodically a 2-ml sample of the solution was withdrawn and injected into a serum bottle containing 2 ml of trimethysilyl chloride and 10 ml of diethyl ether. This derivative solution was hydrolyzed, washed, and dried over anhydrous sodium sulfate. The ether layer was analyzed by GLC, and the amounts of n-butyltrimethylsilane and phenyltrimethylsilane were determined.

% Unreacted n-butyllithium

$$= \frac{(Area)_{TMS\ butyl}}{\frac{Mw_{TMS\ butyl}}{Mw_{TMS\ phenyl}}(Area)_{TMS\ phenyl} + (Area)_{TMS\ butyl}}$$

When all of the gas had evolved, the heat was removed, the solution weighed, and a sample allowed to react with trimethylsilyl chloride and analyzed by GLC.

$$\% \text{ Yield} = \frac{(\text{Area}) \text{ TMS butyl}}{(\text{moles BuLi}) (130) (\text{area}) \text{ benzene}}$$

$$[(\text{Initial wt benzene present}) - (\text{moles BuLi})78]$$

Recommended Preparation of Phenyllithium–TMEDA in Benzene. A 5-liter flask fitted with a thermometer, stirrer, reflux condenser, and pressure-equalizing dropping funnel was flushed with argon and charged with 878 grams (13.65 moles) of n-butyllithium (27.1%) in benzene and 2,560 ml of benzene. (It is not necessary to use n-butyllithium at this concentration because the 1:1 complex is not soluble in benzene beyond about 19% phenyllithium at room temperature. The extra benzene need not be added when an *in situ* reaction is planned.) The slow addition of 1,960-ml (13.0 moles) of TMEDA was begun. The temperature was allowed to rise to 50°C with about one-third of the TMEDA added. The gas evolution was vigorous at this point, and the rest of the TMEDA was added over 1.5 hrs as butane evolution gradually slowed. (Good cooling in the condenser was necessary to prevent the carryover of benzene with the butane.) The solution was then heated cautiously to 79°C then cooled quickly under argon. Yield was 100%—6,100 grams of an 18.89% phenyllithium solution. Phenyllithium:TMEDA mole ratio was 1.04 by Gilman double titration (*17*).

Thermal Stability of Organolithium–TMEDA Complexes. About 400 ml of the organolithium–TMEDA complex was placed in a bottle and then analyzed using the Gilman double titration (*17*). The bottle was placed in a circulating constant-temperature oil bath at the desired temperature (usually 35°C) and left for 30 days. The solution was reanalyzed.

% Decomposition of active material/day

$$= \frac{(\text{Net contained}) \text{ initial} - (\text{Net contained}) \text{ final}}{(\text{Net contained}) \text{ initial} (30 \text{ days})}$$

Preparation of (Benzyllithium)$_2$–TMEDA in Toluene. A 12-liter flask equipped with pressure-equalizing dropping funnel, stirrer, reflux condenser, and thermometer was purged with argon and charged with 7,096 grams of 22.8% n-butyllithium in toluene. The system was sealed from the air by an oil bubbler under slight positive argon pressure. About 30% of 1,470 grams of TMEDA (1% excess) was added over 40 min to bring the reaction to 56°C with vigorous gas evolution. The complete addition took 95 min. The flask was heated to 70°C and then cooled to room temperature. The clear, deep red-orange solution weighed 7,100 grams; it was analyzed as 36.0 wt % benzyllithium by Gilman double titration with 101% yield. Analysis by GLC using trimethylsilyl chloride derivative and mesitylene as an internal standard gave 35.5% concentration and a yield of 100%.

Ring-Isomer Content in Benzyllithium–TMEDA Complexes. Only solutions of benzyllithium–TMEDA complexes with little or no butyllithium were analyzed. A 2-ml aliquot of the solution in a syringe was injected into a small bottle containing 10 ml of ether and 3 ml of dimethyl sulfate under argon. The reaction was vigorous. After 20 min the solution was washed with water, dried over anhydrous Na_2SO_4, and analyzed by GLC using a 10-ft, 10% Triton-S305/Chromasorb W at 90°C. (Only partial resolution of meta and para isomers was obtained, although it could have been observed whether a relatively small amount of para isomer was present.) The percent of ring isomer was calculated from the total amount of ring isomer plus the ethylbenzene present.

Preparation of Benzyllithium–TED Solid Complex. A 500-ml flask equipped with a stirrer, thermometer, and reflux condenser after purging with argon was charged with 184 grams 15.2% n-butyllithium in hexane, and 47.9 grams TED (2% deficiency) was added. The solution was then heated after adding 48.2 grams of toluene (12% excess). The solution was refluxed 3.25 hrs. It was then cooled to 10°C, stirred for 1 hr, and filtered under argon. The yellow crystals were dried for 6 hrs (1 mm) at room temperature. The yield was 89% or 80.6 grams of solid complex.

Preparation of Allyllithium–TMEDA Solid Complex. A 1-liter flask equipped with a gas inlet tube, stirrer, and thermometer was purged with nitrogen and charged with 437 grams of 10.0% sec-butyllithium in hexane. The solution was cooled to −5°C, and 77.7 grams of TMEDA were added with cooling to maintain −5°C. About 43.0 grams (50% excess) of propene were dissolved in the solution in 30 min. The solution was then added to a 1-liter heavy-wall pressure bottle, sealed, and heated to 45°C with mechanical shaking (a Parr low-pressure reactor). The solution was then cooled to 10°C and filtered. The yellow-orange precipitate was rinsed with pentane and blown dry with argon. The yield was 90 grams of the solid complex desired or 80%. (Pressure is optional in final warm-up.)

Preparation of Crotyllithium–TMEDA. A 500-ml flask equipped with a stirrer, thermometer, condenser, and gas-inlet tube was purged with argon and charged with 191 grams of 12.2% sec-butyllithium in cyclohexane. The solution was cooled to −5°C, and 41.4 grams (2% deficiency) of TMEDA was added while cooling to maintain −5°C. To this solution 30.6 grams (50% excess) of 1-butene was added at 0°C in 20 min. The solution was allowed to warm to 25°C over 30 min, heated to 40°C quickly, and then cooled to room temperature. The dark, red-orange solution titrated as 3.39N base or 1.13M with a volume of 297 ml, corresponding to a yield of 92%. GLC analysis of the trimethylsilyl derivative of this solution gave the composition of the solution as 29.5 ± 1% 1-lithio-2-butene (terminal) and 70.5 ± 1% 2-lithio-3-butene (internal) at 55°C. Analysis of the solution at 20°C gave 29.0% terminal.

Preparation of Lithiated *N,N,N′,N′*-Tetramethylethylenediamine. A 500-ml flask equipped as above was charged with 157 grams of 11.4% sec-butyllithium in cyclohexane. The solution was cooled to 0°C and 32.5 grams of TMEDA was added while stirring with further cooling to maintain 0°C. The solution was heated to 49°C for 1 hr (when gas evolution completely stopped), then cooled to room temperature. The dark, brown-red solution was almost clear and weighed 175 grams. GLC

analysis of the trimethylsilyl derivative showed no *sec*-butyllithium remaining. Analysis of the solution by Gilman double titration gave a net product concentration of 18.5% with the mole ratio of total base to carbon-bound lithium of 2.06. The yield based on this titration was 95%.

Preparation of Lithiated Trimethylamine. After purging a 500-ml heavy-wall bottle with argon, it was charged with 175 grams (0.325 mole) of 11.9% *sec*-butyllithium in cyclohexane. This solution was cooled under argon to −10°C, and 38.4 grams (0.65 mole) of trimethylamine was dissolved in the solution with cooling to maintain −10°C. The bottle was sealed off, placed in a Parr laboratory pressure reactor, and heated to 60°C for 3 hrs with shaking. The clear, dark, brown-yellow solution was cooled to ambient temperature and analyzed. The solution weighed 190 grams, and contained no *sec*-butyllithium by GLC analysis of the trimethylsilyl chloride derivative. Total base analysis of the filtered solution was 19.2% indicating a product concentration of at least 6.6% for a 60% yield.

Preparation of Other Lithiated Tertiary Amines and Diamines. The procedure followed for these compounds was the same as that used for the lithiated TMEDA described above.

Synthetic Reactions of Organolithium-Tertiary Diamine Complexs. When (benzyllithium)$_2$–TMEDA, phenyllithium–TMEDA, crotyllithium–TMEDA and lithiated TMEDA or trimethylamine solutions were used, from 0.4 to 0.5 mole of the organolithium complex in the hydrocarbon solvent was added to a 500-ml flask under argon and cooled to the appropriate temperature. In the cases of benzyllithium–TED and allyllithium–TMEDA the solid complexes were added as a solvent. A molar equivalent of the particular reactant was added *via* a pressure-equalizing dropping funnel over a given interval with stirring at a constant temperature. (About 10% excess of the organolithium compound was used.) At a selected time the solution was hydrolyzed with excess water. The organic layer was separated from the aqueous layer, washed two or three times with 10% aqueous ammonium chloride, and dried over anhydrous Na$_2$SO$_4$. The solvent was removed by distillation at reduced pressures. The crude product was purified by recrystallization or distillation. In all cases the infrared spectra were compared with knowns or were examined to ascertain their agreement with the assigned structures. The physical constants were also compared with literature values when possible. Analyses were made in cases where doubt existed concerning the structure because starting materials having similar structures may have been contaminants; the results were in agreement.

PHENYLLITHIUM–TMEDA IN BENZENE. *Benzophenone*. Added benzophenone dissolved in benzene at 5°C over 1 hr; let warm 1 hr; hydrolyzed, used extra benzene during work-up; recrystallized from 1:1 methanol-ethanol; mp 161°C (lit. mp 162.5°C); 95%, triphenylcarbinol (*36*).

Cyclohexanone. Added cyclohexanone dissolved in THF at 0°C in 1 hr; let warm 1 hr; hydrolyzed; recrystallized from heptane; mp 60°C (lit. mp 61°C); 59%, 1-phenylcyclohexanol (*37*).

(BENZYLLITHIUM)$_2$–TMEDA IN TOLUENE. *Trimethylsilyl chloride*. Added trimethylsilyl chloride dissolved in ether at −5°C over 1 hr; let

warm 0.5 hr; hydrolyzed; distilled product; bp 59°–62°C (5 mm) (lit. bp 184°–5°C); 81%, benzyltrimethylsilane (*38*).

1-Bromobutane. Addition at −20°C over 1 hr; let warm 0.5 hr; hydrolyzed; distilled product; bp 61°–64° (0.5 mm) (lit. bp 81°C (202 mm)); 84%, *n*-amylbenzene (*36*).

Benzonitrile. Added benzonitrile at −5°C over 1 hr; let warm 1.5 hrs; used 20% HCl for hydrolysis; recrystallized from ethanol; mp 53°–54°C (lit. mp 60°C); 16% crude, benzylphenyl ketone (*36*).

Ethyl acetate. Added 0.5-mole equivalents ethyl acetate at 0°C over 1 hr; let warm 0.5 hr; hydrolyzed; distilled; bp 122°–125°C (0.4 mm) [lit. bp 122°C (0.4 mm)]; 43%, dibenzylethanol (*39*).

Ethyl benzoate. Added 0.5-mole equivalents of ethyl benzoate at 5°C over 1 hr; let warm 0.5 hr; hydrolyzed, recrystallized from heptane; mp 55°–79°C (crude) (lit. mp 86°C); 22%, 1,2,3-triphenyl-2-propanol (*40*).

Cyclopentanone. Added cyclopentanone at −40°C over 6 min; let warm to 0°C; hydrolyzed; distilled, recrystallized from heptane; mp 55°C (lit. mp 59°C); 35%, 1-benzylcyclopentanol (*37*).

Cyclohexanone. Added cyclohexanone at −5°C over 1 hr; let warm for 1 hr; hydrolyzed; recrystallized from heptane; mp 55°C (lit. mp 61°C); 59%, 1-benzylcyclohexanol (*37*).

2-Butanone. Added 2-butanone at −15°C over 1 hr; let warm for 0.5 hr; hydrolyzed; distilled; bp 92°–94°C (0.5 mm) [lit. bp 110°–112°C (4 mm)]; 53%, 2-benzyl-2-butanol (*41*).

Diisopropyl ketone. Added diisopropyl ketone at −5°C over 1 hr; let warm 0.5 hr; hydrolyzed; distilled; bp 96°C (0.1 mm) [lit. bp 99°C (1 mm)]; 82%, 3-benzyl-2,4-dimethyl-3-pentanol (*42*).

Benzaldehyde. Added benzaldehyde at −35°C over 20 min; hydrolyzed; distilled; bp 62°C (0.5 mm) [lit. bp 81°C (10 mm)]; 80% *n*-amylbenzene (*36*).

Benzophenone. Added benzophenone dissolved in toluene at −15°C over 18 min; let warm over 50 min; hydrolyzed; recrystallized from ethanol; mp 86°C (lit. mp 89°C); 92%, 1,1,2-triphenylethanol (*36*).

BENZYLLITHIUM–TED. *1-Bromobutane.* Added 1-bromobutane to complex dissolved in ether at reflux over 1 hr; refluxed overnight; hydrolyzed; distilled; bp 62°C (0.5 mm) (lit. bp 81°C); 80%, *n*-amylbenzene (*36*).

Bromobenzene. Added mole equivalents bromobenzene to complex dissolved in diethyl ether at reflux over 65 min; stand overnight; hydrolyzed; recrystallized from methanol; mp 50°C (lit. mp 56°C); 32%, 2-benzylbiphenyl (*44*).

Iodobenzene. Same procedure as for bromobenzene; mp 49°C (lit. mp 56°C); 20%, 2-benzylbiphenyl (*43*).

Benzonitrile. Added benzonitrile to complex dissolved in THF at −10°C over 1 hr, stirred at −10°C for 0.5 hr; let warm for 1 hr; hydrolyzed normally, but added 20% HCl to crude solid product in isolation to complete hydrolysis of imine; recrystallization from ethanol; mp 53°C (lit. mp 60°C); 59%, benzylphenyl ketone (*36*).

Ethyl acetate. Added 0.5-mole equivalent ethyl acetate to the complex dissolved in diethyl ether at 35°C over 45 min; let warm overnight; hydrolyzed; oil residue isolated after removal of volatiles; infrared indi-

cated that the tertiary alcohol was present but impure; 25% crude; 1,1-dibenzylethanol (*39*).

Ethyl benzoate. Added 0.5-mole equivalent ethyl benzoate to complex dissolved in THF at 0°C over 0.5 hr; let warm over 1.5 hr; hydrolyzed; recrystallized from ethanol; mp 83°C (lit. mp 86°C); 66%, 1,2,3-triphenyl-2-propanol (*39*).

Methyl vinyl ketone. Added methylvinyl ketone to complex dissolved in THF at −10°C over 50 min; let warm over 1 hr; hydrolyzed; distilled; pot temperature maintained below 75°C, yet apparent decomposition or rearrangement occurred; pot residue had a bp > 78°C (0.2 mm); infrared indicated considerable hydroxyl and carbonyl groups present in pot residue.

Crotonaldehyde. Added crotonaldehyde to complex dissolved in diethyl ether at 0°C over 20 min; let warm over 1 hr; hydrolyzed; no product, only polymer isolated.

2-Butanone. Added 2-butanone to complex dissolved in diethyl ether at 0°C over 40 min; let warm over 1 hr; hydrolyzed; distilled; bp 67°C (0.3 mm) [lit. bp 110°–112°C (14 mm)]; 65%, 2-benzyl-2-butanol (*41*).

Cyclopentanone. Added cyclopentanone to complex dissolved in THF at −10°C over 1 hr; let warm over 1 hr; hydrolyzed; recrystallized from heptane; mp 56°C (lit. mp 59°C); 1-benzylcyclopentanol (*37*).

Cyclohexanone. Added cyclohexanone to complex dissolved in diethyl ether at −10°C over 1 hr; let warm overnight; hydrolyzed; recrystallized from heptane; mp 55°C (lit. mp 61°C); 45%, 1-benzyl-cyclohexanol (*37*).

Diisopropyl ketone. Added diisopropyl ketone to complex dissolved in diethyl ether at −10°C in 5 min; let warm to 10°C over 18 min; hydrolyzed; distilled; bp 110°C (1 mm) [lit. bp 99°C (1 mm)]; 60%, 3-benzyl-2,4-dimethyl-3-pentanol (*42*).

Benzaldehyde. Added benzaldehyde to complex dissolved in THF at 0°C over 1 hr; let warm over 2 hrs; hydrolyzed; recrystallized from ethanol; mp 65°C (lit. mp 67°C); 81%, 1,2-diphenylethanol (*36*).

Benzophenone. Added benzophenone dissolved in diethyl ether to complex dissolved in diethyl ether at −10°C over 0.5 hr; stirred 0.5 hr more at −10°C, then let warm overnight; hydrolyzed; recrystallized from methanol; mp 87°C (lit. mp 89°C); 99%, 1,1,2-triphenylethanol (*36*).

Indanone. Added indanone dissolved in THF to complex dissolved in THF at −10°C for 45 min; let warm over 1.5 hrs; hydrolyzed; distilled and recrystallized from ethanol; mp 141°C (lit. mp 155°C); 20%, 1-benzyl-1-indanol (*44*).

Fluorenone. Added fluorenone dissolved in diethyl ether to complex dissolved in diethyl ether at 35°C over 25 min; hydrolyzed; recrystallized from cyclohexane; mp 133°–136°C (lit. mp 143°C); 83%, 9-benzyl-9-fluorenol (*45*).

Lithium benzoate. Added lithium benzoate to complex dissolved in THF at 35°C, heated to reflux for 25 min, cooled, stirred 1 hr before hydrolysis; hydrolyzed; recrystallized from ethanol; mp 56°C (lit mp 60°C); 44%, benzylphenyl ketone (*36*).

ALLYLLITHIUM–TMEDA. *Benzophenone.* Added benzophenone dissolved in diethyl ether to slurry of the complex in diethyl ether at 20°C

over 0.5 hr; stirred 1 hr; hydrolyzed; distilled bp 128°C (0.6 mm) [lit. bp 135°C (0.5 mm)]; 91%, 1,1-diphenyl-3-buten-1-ol (*46*).

Cyclohexanone. Added cyclohexanone to slurry of the complex in diethyl ether at 20°C over 20 min; stirred 20 min; hydrolyzed; distilled; bp 64°–68°C (8 mm [lit. bp 81°C (15 mm)]; 52%, 1-allylcyclohexanol (*47*).

CROTYLLITHIUM–TMEDA IN HEXANE. Added acetone to complex in solution at −20°C over 0.5 hr; let warm over 40 min; hydrolyzed; distilled; bp 65°–71°C (120 mm) [lit. bp 133°–135°C (760 mm); 142°C. (760 mm)]; 11%, 2,3-dimethyl-4-penten-2-ol and *trans*-2-methyl-4-hexen-2-ol; infrared indicated no cis olefin bonds (*48*).

LITHIATED *N,N,N′,N′*-TETRAMETHYLETHYLENEDIAMINE (I) IN HEXANE. These reactions were acidified after hydrolysis and the organic layer discarded. The aqueous layer was made basic with NaOH solution and extracted with ether. The ether layer was distilled after drying over anhydrous Na_2SO_4.

1-Bromobutane. Added one-mole equivalent TMEDA to 12% *sec*-butyllithium in hexane and heated at 55°C for 1 hr, cooled to 0°C and added 0.95-mole equivalent of 1-bromobutane over 0.5 hr; let warm to 20°C; hydrolyzed; distilled; bp 182°C (760 mm) [lit. bp 183°C (760 mm)]; 49%, *N-n*-pentyl-*N,N′,N′*-trimethylethyl-1,2-ethanediamine (*49*). Analytically calculates for $C_{10}H_{24}N_2$: C, 69.75; H, 13.95; N, 16.29. Found: C, 69.75; H, 13.89; N, 16.49.

2-Bromobutane. Added 1-mole equivalent TMEDA to 11.4% *sec*-butyllithium in hexane at 0°C, heated to 50°C for 1 hr and then cooled to 0°C; added 1-mole equivalent 2-bromobutane over 20 min; let warm over 0.5 hr; worked up; hydrolyzed; distilled; bp 52°C (2.9 mm); 33%, *N*-(2-methylbutyl)-*N,N′,N′*-trimethyl-1,2-ethanediamine.

Iodobenzene. Added 1-mole equivalent TMEDA to 12% *sec*-butyllithium in hexane at 0°C, heated at 55°C for 1.5 hrs; cooled to 0°C and added 1-mole equivalent iodobenzene over 15 min; stirred 1 hr at 20°C; hydrolyzed; distilled, bp 69°C (0.3 mm) [lit. bp 116°–119°C (10 mm)]; 30%, *N*-benzyl-*N,N′,N′*-trimethyl-1,2-ethanediamine (*49*). Analytically calculated for $C_{12}H_{20}N_2$: C, 75.00; H, 10.42; N, 14.58. Found: C, 75.01; H, 10.32; N, 14.41.

1-Bromooctane. Added 1-mole equivalent TMEDA to 13% *sec*-butyllithium in hexane at 0°C, heated at 50°C for 1.25 hrs, cooled to 20°C; added 1-mole equivalent 1-bromooctane over 0.5 hr, stirred 0.5 hr more; hydrolyzed; distilled; bp 85°C (0.5 mm) [lit. by 135°–139°C (11 mm)]; 40%, *N-n*-nonyl-*N,N′,N′*-trimethyl-1,2-ethanediamine (*50*).

Bromocyclohexane. Added 1-mole equivalent TMEDA to 15.5% *n*-butyllithium in hexane at 0°C, heated to reflux 3.75 hrs and cooled to 0°C; added 1-mole equivalent bromocyclohexane over 20 min at 0°C; warmed slowly over 0.5 hr; hydrolyzed; distilled; bp 69°C (0.5 mm); 18%, *N*-(cyclohexylmethyl)-*N,N′,N′*-trimethyl-1,2-ethanediamine.

Cyclopentanone. Added 1-mole equivalent TMEDA to 11.9% *sec*-butyllithium at 0°C, heated to 50°C for 1.25 hrs, cooled to 0°C and added 1-mole equivalent cyclopentanone over 20 min; stirred 20 min at 20°C; hydrolyzed; distilled; bp 81°C (1.5 mm); 28%, *N*-(1-hydroxycyclopentylmethyl)-*N,N′,N′*-trimethyl-1,2-ethanediamine.

Valeraldehyde. Added 1-mole equivalent TMEDA to 15.5% *n*-butyl-lithium in hexane at 0°C, heated at reflux 3.75 hrs, cooled to −10°C, and added 1-mole equivalent valeraldehyde over 20 min; let warm over 0.5 hr; hydrolyzed; distilled; bp 84°C (0.7 mm); 39%, *N*-(2-hydroxyl-hexyl)-*N,N′,N′*-trimethyl-1,2-ethanediamine.

LITHIATED TRIMETHYLAMINE (II) IN HEXANE. Lithiation of trimeth-ylamine was done in a pressure reactor during the heating step for actual lithiation of the tertiary amine.

1-Iodopropane. Added 2 mole equivalents trimethylamine to 15.1% *n*-butyllithium in hexane at 0°C; solution heated at 70°C for 5 hrs and cooled to −10°C; 0.85-mole equivalent 1-iodopropane added over 20 min; warmed over 0.5 hr; hydrolyzed; distilled; bp 92°C (760 mm) [lit. bp 95°C (760 mm)]; 32%, *N,N,N-n*-butyldimethylamine (*51*).

1-Bromooctane. Added 2-mole equivalents trimethylamine to 13.2% *sec*-butyllithium in hexane, heated to 60°C for 3 hrs, cooled to −10°C, and added 1-mole equivalent 1-bromooctane over 20 min; let warm to 20°C; hydrolyzed; distilled; bp 52°C (2.9 mm) [lit. bp 209°C (741 mm)]; 33%, *N,N,N*-dimethylnonylamine (*52*).

Benzaldehyde. Added 2 mole equivalents trimethylamine to 11.9% *sec*-butyllithium in cyclohexane at −10°C, heated to 50°C for 6 hrs, cooled to −10°C; added 0.85-mole equivalent benzaldehyde over 0.5 hr; let warm over 0.5 hr; hydrolyzed; distilled; bp 72°C (0.25 mm) [lit. bp 170°C (760 mm)]; 49%, (1-hydroxy-1-phenylethyl)dimethylamine (*53*).

Acknowledgment

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