fonamide bis(methylimine). The yield of hydrogen was 101%; the yield of product was 78%. The boiling point and infrared spectrum of the product were identical with those of the compound prepared from N,N-dimethylmethanesulfenamide and methylchloramine (above).

Acknowledgments. The author wishes to acknowledge the capable assistance of Mr. A. L. Voegele in the execution of most of the laboratory work. Dr. Roger Reaville performed the low-temperature nmr studies.

Polylithiation. II.[1] Polylithiation of Toluene and the Formation of Poly(trimethylsilyl)toluenes

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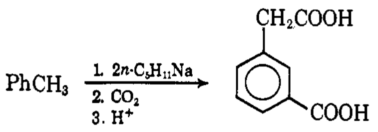
Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. *Received October 14, 1967*

Abstract: Toluene undergoes polylithiation by excess *n*-butyllithium in the presence of N,N,N′,N′-tetramethylethylenediamine. Derivatization of the reaction mixture with trimethylchlorosilane yields α,α,p-tris(trimethylsilyl)toluene as the major product along with mono- and bis(trimethylsilyl)toluenes. α,p- and α,o-dilithiotoluene and α,α,p-trilithiotoluene appear to be the principal polylithiated species produced from toluene. Lithiation experiments were also carried out on benzyltrimethylsilane, *o*-, *m*-, and *p*-trimethylsilyltoluenes, benzyllithium, and *o*-, *m*-, and *p*-lithiotoluenes, producing a series of new bis- and tris(trimethylsilyl)toluenes.

Toluene is known to react with alkylsodium and alkylpotassium compounds to give benzylsodium and benzylpotassium. The dimetallation of toluene by excess *n*-amylsodium has been studied by Morton, who found that homoisophthalic acid was produced when disodiotoluene was derivatized with carbon dioxide.[2]

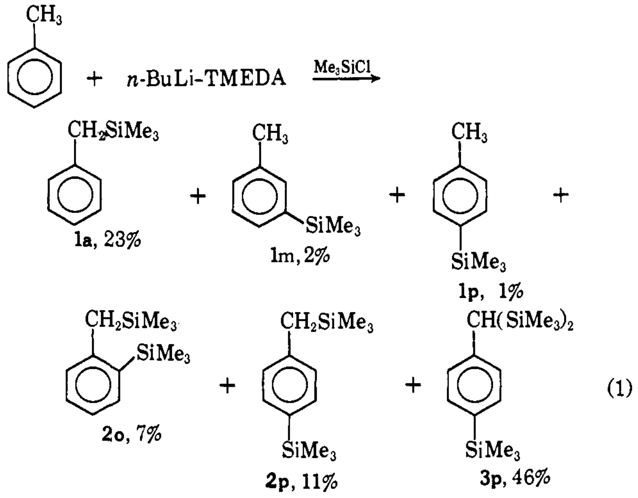


(1)

Metallation of toluene with alkyllithium compounds was generally unsuccessful until the discovery that tertiary amines activate alkyllithium compounds in metallation reactions.[3] Using either diazabicyclo[2.2.2]octane (DABCO) or N,N,N′,N′-tetramethylethylenediamine (TMEDA), Eberhardt and Butte found that toluene undergoes quantitative metallation to benzyllithium with *n*-butyllithium.[4]

In connection with our studies of polylithiation,[1] we have investigated the reaction of toluene with excess *n*-butyllithium in the presence of TMEDA. The addition of toluene to an excess of *n*-BuLi–TMEDA in hexane results in a bright orange solution which gradually turns deep red, separates into two liquid layers, and finally solidifies into a red precipitate and a colorless solution. The lithiated toluene mixture was studied by derivatizing with trimethylchlorosilane and with deuterium oxide. The results indicate that up to three atoms of hydrogen on the toluene nucleus can be replaced by lithium.

Derivatization with Trimethylchlorosilane. Treatment of the lithiated toluene with Me$_3$SiCl produced a mixture of mono-, di-, and trisilylated products, as shown in eq 1. The per cent yields given are only illustrative; although the ratios **1a**:**1m**:**1p** and **2o**:**2p** remain essentially constant, the total amounts of mono-, di-, and trisilylated products varied with conditions of the metallation reaction. However, reactions under a wide variety of conditions gave *only the isomers shown* and no others.



(1)

The amount of TMEDA used in the reaction was varied over a factor of 200 to establish the optimum N:Li ratio (Table I). Even at very low TMEDA concentration (N:Li = 1:10) a substantial amount of trisubstituted product was produced. However, the highest yield of polymetallated products was obtained with N:Li = 1:2, and this ratio was used in all subsequent experiments.

The influence of the *n*-butyllithium:toluene ratio on the yield of mono-, di-, and trisubstituted products was also studied. The results are given in Table II. Even with equimolar amounts of *n*-butyllithium and

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[1] R. West, P. A. Carney, and I. C. Mineo, *J. Am. Chem. Soc.*, **87**, 3788 (1965), will be taken as the first paper in this series.

[2] A. A. Morton, E. L. Little, and W. O. Strong, *ibid.*, **65**, 1339 (1943).

[3] H. Gilman, *Org. Reactions*, **8**, 258 (1957).

[4] G. G. Eberhardt and W. A. Butte, *J. Org. Chem.*, **29**, 2928 (1964). The tetra- and pentalithiation of toluene by ethyllithium at 100° has also been reported.[5] However, our attempts to repeat this experiment gave no polylithiation and only a low yield of benzyllithium.

[5] T. V. Talalaeva and K. A. Kocheshkov, *Dokl. Akad. Nauk SSSR*, **77**, 621 (1951).

Table I. Lithiation of Toluene. The Ratio of TMEDA to *n*-Butyllithium

[*n*-BuLi, *M*]	[TMEDA], *M*	N:Li	[$C_6H_5CH_3$], *M*	Time, hr	Yield, %		
					1a, m, p	**2o, p**	**3p**
0.16	0.16	2:1	0.036	24	33	Trace	None
0.16	0.08	1:1	0.036	24	25	16	14
0.16	0.04	1:2	0.036	22	10	16	54
0.16	0.028	1:3	0.036	29	16	25	33
0.16	0.008	1:10	0.036	30	Trace	10	22

Table II. Lithiation of Toluene. Yields of Trimethylsilyltoluenes with Various Amounts of *n*-Butyllithium

n-BuLi:toluene	Yield,[a] %	Yield, %		
		1a,m,p	**2o,p**	**3p**
5:1[b]	80	10	16	54
3:1[b]	90	12	36	42
2:1[b]	77	39	23	14
1:1[c]	40	23	8	9

[a] Based on toluene recovered. [b] 24-hr intermittent reflux (6 hr total reflux). [c] 48 hr, room temperature.

toluene, substantial amounts of di- and trisilylated products were obtained, indicating that di- and trilithiation compete favorably with monolithiation.

The polylithiation reaction was also studied as a function of time. Up to 4 hr after mixing, some of the *n*-BuLi–TMEDA complex remained as an insoluble crystalline material suspended in the reaction mixture. This gradually disappeared and the reaction mixture became homogeneous after about 6 hr. A small amount of an insoluble oil began to separate from the solution after 18 hr, and a larger amount of oil, containing most of the active lithium, was observed after 44 hr. Finally, after 100 hr all of the lithium-containing material had precipitated as a red solid. The results upon quenching with Me_3SiCl after various time intervals are given in Table III. There is very little dependence of the product distribution on the homogeneity of the reaction mixture.[6] At very long reaction times the yields decline, probably because the lithiated toluenes slowly metallate TMEDA. From Table III it is again apparent that di- and trilithiation are at least as rapid as monolithiation, for even when only 20% of the toluene had reacted, the trisilyl compound **3p** made up 25% of the products.

Table III.[a] Lithiation of Toluene. Yields as a Function of Time

Time, hr	% reacn	Yield, %		
		1a,m,p	**2o,p**	**3p**
2	20	9.6 (48)[b]	5.6 (28)	5.0 (25)
4	40	16 (41)	9.6 (24)	16 (41)
7.5	..	.. (33)	.. (35)	.. (33)
13	..	.. (32)	.. (27)	.. (42)
20	60	15 (25)	10 (17)	35 (58)
44	91	26 (29)	19 (21)	46 (51)
100	69	24 (35)	13 (19)	32 (46)

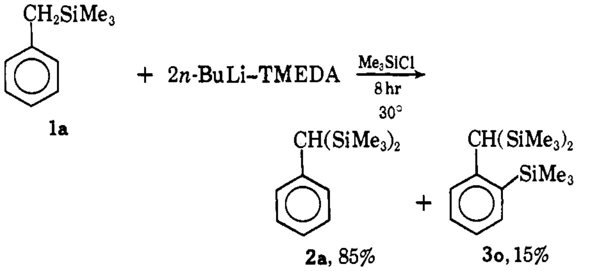
[a] All reactions were carried out at room temperature with 3*n*-BuLi–TMEDA per toluene. [b] Percentages in parentheses are normalized to 100%.

The four isomers of trimethylsilyltoluene and α,*p*-bis(trimethylsilyl)toluene had been prepared previously, but none of the other bis- or tris(trimethylsilyl)toluenes were known. In order to identify the isomers resulting from the metallation reaction, each isomer was synthesized independently. The known compounds *o*-, *m*-, and *p*-trimethylsilyltoluene (**1o**, **1m**, and **1p**) were prepared from the corresponding bromotoluenes, by reaction with lithium metal followed by coupling with trimethylchlorosilane.

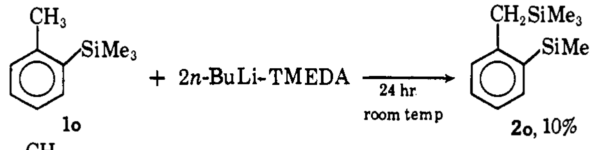
$$C_7H_7Br \xrightarrow{Li} C_7H_7Li \xrightarrow{Me_3SiCl} C_7H_7SiMe_3 \qquad (2)$$

Benzyltrimethylsilane (**1a**) was also synthesized from benzyllithium and trimethylchlorosilane.

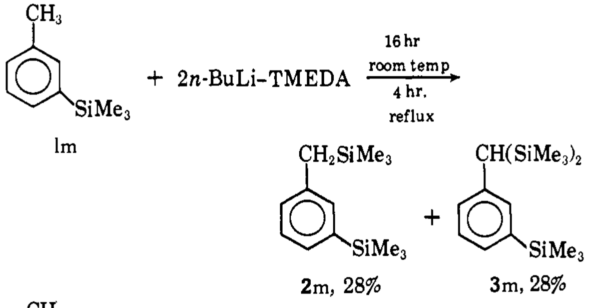
All of the four monotrimethylsilyl isomers were metallated with *n*-butyllithium TMEDA, and then treated with trimethylchlorosilane, to produce the bis- and tristrimethylsilyl isomers shown in eq 3–6. The



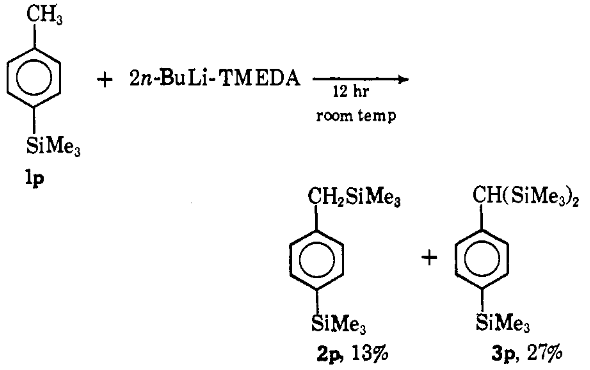
(3)



(4)



(5)



(6)

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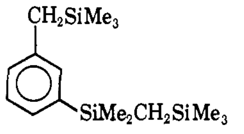
[6] In earlier studies involving sodium and potassium compounds, differences in results have frequently been attributed to surface and steric effects when insoluble reactants are present. *Cf.* A. A. Morton and C. E. Claff, *J. Am. Chem. Soc.*, **76**, 4935 (1954); D. Bryce-Smith and E. E. Turner, *J. Chem. Soc.*, 861 (1953).

new compounds **2a**, **2o**, **2m**, **3o**, **3m**, and **3p** were all separated by preparative gas chromatography and characterized by analysis and nmr spectroscopy (Table IV). The syntheses provide unambiguous identification of compounds **2o**, **2p**, and **3p** obtained from lithiation of toluene. In no case was any ring metallation found when the ring was already substituted with a trimethylsilyl group. In only one instance was there any evidence of other products than those outlined above. In the reaction of *m*-trimethylsilyltoluene (eq 4) there was isolated approximately 30% of a compound in which one of the hydrogens on the trimethylsilyl group was metallated and derivatized to give

Table IV. Proton Nmr Data for Trimethylsilyltoluenes[a]

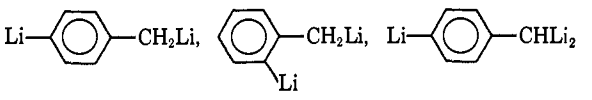
Compd	Ar–C–Si-$(CH_3)_3$	Ar–Si$(CH_3)_3$	Benzyl	Phenyl
1a	10.03 (9)		7.96 (2)	2.97 (5)
1m		9.75 (9)	7.70 (3)	2.88 (4)
1p		9.76 (9)	7.68 (3)	2.70, 2.87 (4)[b]
1o		9.70 (9)	7.60 (3)	2.91 (4)
2o	10.00 (9)	9.72 (9)	7.77 (2)	2.90 (4)
2p	10.00 (9)	9.77 (9)	7.98 (2)	3.12, 2.74 (4)[b]
2a	10.00 (18)		8.62 (1)	3.10 (5)
2m	10.03 (9)	9.78 (9)	7.98 (2)	3.03 (4)
3p	9.97 (18)	9.75 (9)	8.56 (1)	3.12, 2.73 (4)[b]
3o	9.98 (18)	9.70 (9)	8.13 (1)	2.97 (4)
3m	9.98 (18)	9.77 (9)	8.56 (1)	3.05 (4)

[a] In τ values. [b] J_{H-H} = 8.0 cps for **1p**, **2p**, and **3p**.



Discussion

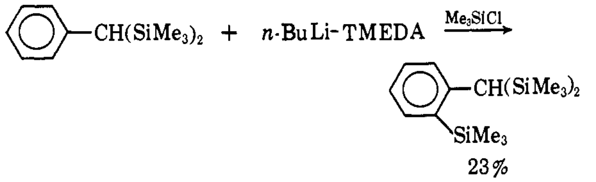
In interpreting the results of the derivatization experiments described above, it is important to know whether the trimethylsilyl derivatives accurately reflect the positions of lithiation of the toluene, or whether some of the products arise from lithiation during derivatization. It was easy to show that up to 3 equiv of *n*-butyllithium were consumed in reaction with toluene, producing 3 mol of butane. However, this finding does not necessarily indicate that toluene becomes trilithiated, for some metallation of TMEDA may also take place. However, for a variety of reasons we believe that the trimethylsilyl derivatives do indicate the actual positions of lithiation of the toluene, and that the major intermediates are benzyllithium and



The replacement of more than one hydrogen on a carbon atom by lithium finds precedent in recent reports of the formation of $MesCOCHLi_2$ and $PhCLi_2CN$,[7] as well as our own work on C_3Li_4.[1]

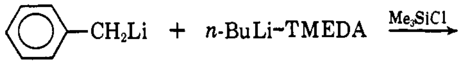
Bey and Weyenberg[8] have studied the rate of lithiation of protons by *n*-BuLi compared with the rate of coupling of *n*-BuLi to trimethylchlorosilane. Only highly acidic protons are metallated at a rate competitive with the rapid coupling reaction. The moderately acidic proton in triphenylmethane is not acidic enough for such competitive lithiation to take place.[8] It is probable that all of the protons in the toluene system are even less acidic than the proton of triphenylmethane, and so should be lithiated even more slowly.

Moreover, the products actually obtained in the trimethylsilylation of lithiated toluene are not those which would be expected if extensive metallation took place during derivatization. Suppose, for instance, that benzyllithium were the major lithiated species present. It could couple to form benzyltrimethylsilane, which could subsequently be further metallated and silylated. But the results of eq 2 show that lithiation and silylation of benzyltrimethylsilane gives only **2a** and **3o**, neither of which are obtained from toluene. Similarly α,α-bis(trimethylsilyl)toluene cannot be an intermediate, for lithiation and trimethylsilylation of this compound gives only the *ortho* isomer **3o** (eq 7), whereas the *para* isomer, **3p**, is the only one obtained from toluene. All of these results indicate that no significant amount of lithiation is taking place during derivatization, and that the positions of the trimethylsilyl groups in the final products accurately reflect the position of lithium atoms in the metallated toluene.



(7)

Benzyllithium appears to be the main precursor for the polylithiated toluenes, as was shown by the following experiments. An authentic sample of benzyllithium, prepared from dibenzylmercury and lithium, was treated with excess *n*-BuLi–TMEDA and later with trimethylchlorosilane. Exactly the same di- and trisubstituted products as obtained from toluene were produced (eq 8). On the other hand, *o*-, *m*-, and *p*-lithiotoluenes, prepared from the corresponding bromotoluenes and lithium metal, reacted only very slowly with *n*-BuLi–TMEDA to give very small amounts of di- and trisubstituted compounds after derivatization. Thus, it is unlikely that these lithio compounds are intermediates in the toluene reaction.



1a + **2o** + **2p** + **3p** (8)

Another possibility which was investigated is that the polylithiotoluenes form by disproportionation of benzyllithium. Authentic benzyllithium was refluxed with hexane and TMEDA for 18 hr, and then derivatized with trimethylchlorosilane. No product other than benzyltrimethylsilane was obtained, indicating that disproportionation of benzyllithium does not take place under the conditions of the experiment.

In the light of all the above results, the reaction pathway shown in eq 9 can account for the formation of all of the observed products.

In the reaction sequence shown in (9), it is supposed that only two intermediate species undergo further metallation: benzyllithium and α,α-dilithiotoluene.

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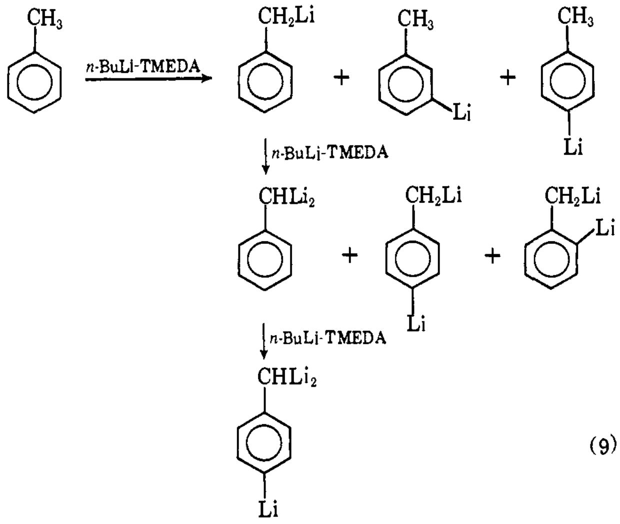
[7] E. M. Kaiser and C. R. Hauser, *J. Am. Chem. Soc.*, **88**, 2348 (1966).

[8] A. E. Bey and D. R. Weyenberg, *J. Org. Chem.*, **31**, 2036 (1966).

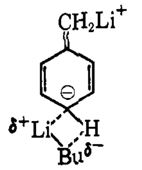


(9)

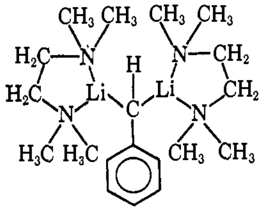
This assumption is consistent with our experimental finding that benzyllithium is lithiated rapidly, whereas ring-lithiated toluenes are lithiated only very slowly. In order to account for the lack of any α,α-bis(trimethylsilyl)toluene in the products, it is further supposed that the α,α-dilithio compound undergoes rapid and specific lithiation in the *para* position. With these assumptions, the reaction sequence 9 accounts for the remarkably specific pattern of products formed in the reaction.

Mechanism of Polylithiation. Although the major monosubstituted product is benzyltrimethylsilane, about 3% of *m*- and *p*-trimethylsilyltoluenes are found, arising from ring-lithiated toluenes. This agrees with the findings of Chalk and Hoogeboom,[9] who found about 9% ring-lithiated toluenes, predominantly *meta*, in the metallation of toluene with less than 1 equiv of *n*-BuLi.[9] The finding of a substantial amount of *meta* isomer is consistent with the current view of metallation as a nucleophilic attack on hydrogen by the alkyl anion.[6,10,11] If the inductive effect of the alkyl group directs the orientation of lithiation, as proposed by Benkeser, *et al.*,[12] the *meta* isomer is expected to predominate.

Further lithiation of benzyllithium appears to follow an entirely different mechanism. Only *ortho* and *para* substitution takes place on the ring. The results contrast with those of Morton, who found exclusive *meta* disubstitution for the dimetallation of toluene with amylsodium.[2] In order to account for the disubstituted isomers which are found, it is suggested that the high negative charge present in the benzyllithium causes a change in mechanism for a nucleophilic attack on hydrogen to an electrophilic attack on carbon by the positive lithium.[13] It is probable that the difference in mechanism is one of degree of participation of the lithium only, because the attack of the positive lithium will cause the C–H bond to be weakened and therefore more reactive to the alkyl anion as in the following diagram.

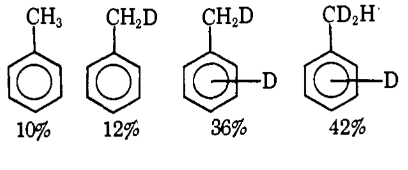


The single trisubstituted isomer **3p** must arise from a very facile lithiation of the α,α-dilithiotoluene, because bis(trimethylsilyl)phenylmethane (**2a**) is never present in a large enough concentration in the products to allow for its characterization. The high charge density on the *para* carbon atom would account for such a fast reaction if the metallation takes place *via* electrophilic attack. *ortho* trisubstitution is probably precluded by the steric effect of the two bulky TMEDA molecules coordinated to the lithium atoms in the methyl group.



Derivatization with D$_2$O. Mass spectrographic and nmr analysis of a mixture of deuterated toluenes obtained by quenching the lithiated intermediates with D$_2$O gave results generally consistent with those reported above for trimethylchlorosilane.

The nmr spectrum of the product mixture after D$_2$O quenching consisted of two broad resonances at τ 2.88 and 7.75, corresponding to the phenyl and methyl protons, respectively. On four independent samples the ratio of methyl to phenyl protons was determined to be 2.6:1, 2.6:1, 2.7:1, and 2.7:1 by integration of the peak areas. These ratios do not, of course, define a unique isomer composition. However, one can calculate an expected ratio for methyl to phenyl protons by taking the product distribution found when the lithiated intermediates, prepared under identical conditions, were derivatized with trimethylchlorosilane, assuming that a deuterium atom has replaced each trimethylsilyl group. Such a calculation was done for the following mixture



(Table II, line 2). The ratio of methyl to phenyl hydrogens thus calculated is 2.8:1, in close agreement with the experimental values of 2.6:1 and 2.7:1.

The mass spectrum of the deuterated mixture showed that the highest mass present was 95, corresponding to the replacement of three protons by deuterium. The following peak heights and mass percentages were determined from a typical spectrum: [mass, height (cm)] 91, 1.2, 5%; 92, 4.1, 16%; 93, 10.9, 43%; 94, 7.0, 28%; 95, 2.0, 8%. Under the conditions of

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[9] A. J. Chalk and T. J. Hoogeboom, Abstracts of Papers, 3rd International Symposium on Organometallic Chemistry, Munich, Germany, Sept 1967, p 68.

[10] D. Bryce-Smith, *J. Chem. Soc.*, 1079 (1954).

[11] G. E. Hall, R. Piccolini, and J. D. Roberts, *J. Am. Chem. Soc.*, 77, 4540 (1955).

[12] R. A. Benkeser, A. E. Trevillyan, and J. Hooz, *ibid.*, 84, 4971 (1962).

[13] This mechanism is the same as that suggested much earlier by Morton for all metallation reactions: A. A. Morton, *J. Am. Chem. Soc.*, 69, 969 (1947).

ionization used, toluene itself was shown to give peaks at 91 $(M - 1)^+$ and 92 (parent peak) in 60:40 intensity ratio. The above data for the deuterated toluenes was analyzed assuming that the deuterated compounds give the same $(M - 1)^+ : M^+$ ratio, and that loss of deuterium or protium is equally probable. The calculated amounts of toluene-d_1, -d_2, and -d_3 under these assumptions are 16, 41, and 38%, in fairly good agreement with the results from trimethylchlorosilane derivatization.

The mixture of deuterated toluenes was oxidized to a mixture of deuterated benzoic acids, and the nmr and mass spectra were recorded. In the case of the nmr, the ratio of phenyl protons to acid proton was in good agreement with the expected value if only one deuterium were present in the ring for any of the isomers. However, this ratio was too insensitive to a change in product ratio to merit much consideration.

The mass spectrum showed a major mass peak at 123, corresponding to one hydrogen replaced by deuterium. However, a peak was also found at mass 124, with intensity such that 12% of the benzoic acid should have contained two deuterium atoms on the ring. The small inconsistency with the results from trimethylchlorosilane derivatization could be explained by slight deuterium–protium exchange during derivatization.

Experimental Section

All reactions were carried out in an atmosphere of dry nitrogen. All reactants were added by syringe to apparatus which had been flamed and cooled under a nitrogen stream. Analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Nmr spectra were recorded on a Varian A-60 or A-60A spectrometer, using TMS as an internal standard in CCl_4 solution. Gas chromatographic separations were made on a Varian/Aerograph chromatograph using columns packed either with SE-30 or QF-1 silicone on Chromosorb W. The thermal conductivity correction factors of each isomer were determined with pure samples. Analytical results are estimated to be good within about ±5%.

I. Reaction of Trimethylsilyltoluenes with Excess *n*-BuLi–TMEDA. A. Preparation of Monosubstituted Toluenes. The monosubstituted trimethylsilyltoluenes, **1m**, **1p**, and **1o** were prepared by treating the corresponding bromides with Li metal and derivatizing with trimethylchlorosilane. Benzyltrimethylsilane (**1a**) was prepared by the method of Wittig, Meyer, and Lange[14] from dibenzylmercury and lithium metal, followed by trimethylchlorosilane: **1a**, n^{23}_{D} 1.4909 (lit.[15] n^{25}_{D} 1.4910); **1m**, n^{23}_{D} 1.4912 (lit.[16] n^{25}_{D} 1.4902) (*Anal.* Calcd for $C_{10}H_{16}Si$: C, 73.10; H, 9.80; Si, 17.10. Found: C, 73.48; H, 9.70; Si, 17.10); **1p**, n^{23}_{D} 1.4897 (lit.[16] n^{25}_{D} 1.4892) (*Anal.* Found: C, 73.20; H, 9.90; Si, 16.96); **1o**, n^{23}_{D} 1.5014 (lit.[16] n^{25}_{D} 1.5005) (*Anal.* Found: C, 73.07; H, 9.82; Si, 16.94).

B. Reactions with Excess *n*-BuLi–TMEDA. For each of the four isomers prepared above, 1.6 g (0.01 mol) of trimethylsilyltoluene was added to 12.5 ml (0.02 mol) of 1.6 *M* *n*-BuLi and 0.7 ml (5 mmol) of TMEDA. The conditions of the reactions and yields of products are summarized in eq 3–6 in the text. In each case, after the designated reaction time, 3.3 g (0.03 mol) of trimethylchlorosilane was added, and the mixture was stirred at room temperature until the Gilman test 1 was negative. The resultant mixture was filtered and the filtrate washed with sodium bicarbonate solution and with dilute aqueous HCl to remove the excess chlorosilane and amine. The dried hexane solution was distilled to remove the solvent and *n*-butyltrimethylsilane. The products were isolated by preparative gas chromatography and characterized: **2o**, n^{23}_{D} 1.5003 (*Anal.* Calcd for $C_{13}H_{24}Si_2$: C, 66.02; H, 10.23; Si, 23.75. Found: C, 65.90; H, 9.90; Si, 24.13); **2m**, n^{23}_{D} 1.4866 (*Anal.* Found: C, 65.94; H, 10.21; Si, 23.54); **2p**, n^{23}_{D} 1.4912 (lit.[16] n^{25}_{D} 1.4915) (*Anal.* Found: C, 65.95; H, 10.35; Si, 23.49); **2a** (*Anal.* Found: C, 66.34; H, 10.26; Si, 23.64); **3o**, mp 43.5–44.5° (*Anal.* Calcd for $C_{16}H_{32}Si_3$: C, 62.22; H, 10.47; Si, 27.31. Found: C, 61.28; H, 10.27; Si, 27.07); **3m**, n^{23}_{D} 1.4935 (*Anal.* Found: C, 62.19; H, 10.43; Si, 27.35); **3p**, n^{23}_{D} 1.4984 (*Anal.* Found: C, 62.23; H, 10.41; Si. 27.32).

Several generalizations can be drawn from the nmr peak positions for the various isomers, which are listed in Table IV. Aryltrimethylsilane protons give a resonance at τ 9.7–9.8, and so are easily distinguishable from benzyltrimethylsilane protons, which have τ 9.9–10.1. Also benzylic protons in benzyltrimethylsilanes appear at τ 7.6–8.0, whereas if two trimethylsilyl groups are present on the same carbon the benzyl resonance appears at τ 8.1–8.7. *ortho*-, *meta*-, and *para*-substituted compounds were classifiable by the pattern of their phenyl resonances, the *para* compounds giving a clean quartet as expected.

II. Lithiation of Toluene. A. Derivatization with Trimethylchlorosilane. In a typical reaction, 2.8 ml (0.20 mol) of TMEDA was added to a stirred solution of 50 ml (0.08 mol) of 1.6 *M* *n*-BuLi in hexane. After 15 min, 2.9 ml (0.027 mol) of toluene was added, and the yellow solution was stirred at room temperature for 44 hr. The resulting, bright-red, two-phase mixture was cooled to 0°, and 13 ml (0.12 mol) of trimethylchlorosilane was added as quickly as possible. Stirring was continued until the solution was pale yellow and the precipitate white. The product mixture was worked up as previously described in section B above.

The following product ratios were determined by glpc of the residue: toluene 11%; **1a**, 23%; **1m** and **p**, 3%; **2o**, 7%; **2p**, 11%; and **3p**, 46%.

From a similar reaction (larger scale) a mixture of products was fractionally distilled, and the isomers **1a**, **1m**, **1p**, **2o**, **2p**, and **3p** were collected by preparative gas chromatography and compared with those described in I.

B. Derivatization with D_2O. The above procedure was repeated up to the point of derivatization except that the mixture was refluxed intermittently over a period of 24 hr to remove the butane formed. The reaction mixture was cooled to 0°, and 2.2 g (0.12 mol) of D_2O was added slowly by syringe. The resulting mixture was filtered, and the deuterated toluene was isolated by fractional distillation on a spinning-band column. Nmr and mass spectral data were obtained on the mixture of deuterated toluenes.

A small sample of the toluene mixture was oxidized with basic potassium permanganate[17] to give a mixture of deuterated benzoic acids which were analyzed by nmr and mass spectroscopy.

III. Preparation and Reactions of Benzyllithium. A solution of benzyllithium in ether was prepared by the method of Wittig, Meyer, and Lange[14] from 3.1 g (8.0 mmol) of dibenzylmercury and 0.6 g (0.08 g-atom) of lithium.

A. Reaction with TMEDA and Hexane. The solution of benzyllithium was added by syringe to 10 ml of dry hexane containing 0.3 ml (2.0 mol) of TMEDA, and the ether was removed by distillation. The resulting dark brown solution was refluxed for 16 hr. At the end of the reflux period, there was present a significant quantity of metallic grey precipitate (mercury) indicating that all of the dibenzylmercury had not reacted to form benzyllithium. Trimethylchlorosilane, 2 ml (0.02 mol), was added, and the mixture was stirred at room temperature for 1 hr.

The product mixture was filtered, washed with sodium bicarbonate solution and with dilute HCl, and distilled to remove the solvent. Fractional distillation of the residue yielded 2.0 g of benzyltrimethylsilane (**1a**), 76%, and 0.3 g of a white, crystalline material, mp 50.5–51.5°, identified as *sym*-diphenylethane (lit.[18] mp 52°), 21%. No other products were present by glpc analysis.

B. Reaction with Excess *n*-BuLi–TMEDA. A solution of benzyllithium was transferred by syringe to a solution of 0.6 ml (4 mmol) of TMEDA in 10 ml of dry hexane. The ether was removed by distillation and 10 ml (0.016 mol) of 1.6 *M* *n*-BuLi in hexane was added. The reaction mixture was refluxed for 16 hr, resulting in an orange solution and dark brown precipitate. Trimethylchlorosilane, 3.3 g (0.03 mol), was added, and the mixture stirred at room temperature for 1 hr.

The product mixture was worked up as previously described. Glpc analysis of the residue after removal of the solvent showed **1a**, 50%; **2o**, 12%; **2p**, 17%; and **3p**, 20%.

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IV. Reactions of *o*-, *m*-, and *p*-Lithiotoluenes with Excess *n*-BuLi–TMEDA. Solutions of *o*-, *m*-, and *p*-lithiotoluene were prepared by reacting 2.7 g (0.016 mol) of the appropriate bromotoluene with 0.3 g (0.04 g-atom) of lithium in 10 ml of dry ether. The solution of the lithiotoluene was transferred to 0.12 ml (8 mmol) of TMEDA in 10 ml of dry hexane. The ether was removed by distillation and 20 ml (0.032 mol) of 1.6 *M* *n*-BuLi in hexane was added. The resulting solution was refluxed for 16 hr. The dark colored solution and precipitate were quenched with 6.5 g (0.06 mol) of trimethylchlorosilane. The product mixture were worked up in the manner previously described.

A. ***p*-Lithiotoluene.** Glpc analysis of the residue showed **1p**, 82%; **2p**, 15%; and **3p**, 3%.

B. ***m*-Lithiotoluene.** Glpc analysis of the residue showed **1m**, 48%; **2m**, 28%; and **3m**, 24%.

C. ***o*-Lithiotoluene.** Glpc analysis of the residue showed **1o**, 90%; **2o**, 10%.

In a similar experiment, the *o*- and *p*-lithiotoluenes were allowed to react with excess *n*-BuLi–TMEDA at room temperature for 24 hr. No polysubstituted products could be detected by glpc after derivatization with trimethylchlorosilane.

V. Reaction of Bis(trimethylsilyl)phenylmethane (2a) with *n*-BuLi–TMEDA. Compound **2a**, 2.5 g (0.01 mol), was added to a mixture of 2.5 ml (0.02 mol) of 1.6 *M* solution of *n*-BuLi and 0.7 ml (5 mmol) of TMEDA. After 24 hr at room temperature, the yellow solution was quenched with 3.3 g (0.03 mol) of trimethylchlorosilane. The product mixture was worked up as described above to give 75% starting material **2a** and 23% compound **3o**. No other products were observable by glpc.

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Purine Nucleosides. XX. The Synthesis of 7-β-D-Ribofuranosylpurines from Imidazole Nucleoside Derivatives[1]

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Abstract: A general route for the preparation of 7-glycosylpurines has been accomplished utilizing imidazole nucleosides. The utility of this synthetic route is demonstrated by the preparation of several 6- and 2,6-disubstituted 7-(β-D-ribofuranosyl)purines. The synthesis of the requisite imidazole nucleosides, ring closure procedures, assignment of anomeric configuration, and proof of the site of glycosidation of these β anomers is presented. A new and convenient preparation of 4-amino-5-carboxamido-1-(β-D-ribofuranosyl)imidazole (XV, iso-AICAR) has been accomplished *via* the fusion procedure. The synthesis of the β anomers of a number of 7-ribosylpurines, related to purine nucleosides isolated from naturally occurring vitamin B_{12} analogs which are obtained from certain microbiological sources, has now been achieved.

The first purine nucleoside isolated from a naturally occurring analog of vitamin B_{12} (pseudovitamin B_{12}) created considerable interest when it was characterized[2] as a 7-ribosylpurine.[3] This was the first example of a naturally occurring purine nucleoside which possessed the glycosyl moiety at any position other than N-9. A number of additional purines and purine ribosides were subsequently isolated from other naturally occurring analogs of vitamin B_{12} and characterized or presumed to be either 7-ribosylpurines or degradation products derived from 7-ribosylpurines.[4] This, of course, prompted active investigations in search of a general route for the synthetic preparation of 7-glycosylpurines. However, the laboratory synthesis of these compounds has been hindered by the inability[5] to develop a facile method for directing the carbohydrate moiety to N-7 rather than N-9 in the glycosidation of a preformed purine. The usual site of glycosidation in unsubstituted purines (no substituent on a ring nitrogen) has been shown[6] to occur primarily at N-9 with the only major exceptions being 7-glycosyltheophyllines[6,7] which possess a methyl group at N-1 and N-3. Other 7-glycosylpurines have recently been prepared[8,9] by using the directive influence,[10] probably steric, exerted by various 3-substituted purines. This approach possesses some inherent disadvantages,[2,10b] *viz.*, the initial preparation of appropriate 3-substituted purines and the numerous problems associated with the subsequent removal of the blocking groups at N-3. However, this latter approach has been the preferred method in view of the finding[11] that a number of reported 7-glycosylpurines were in actuality 3-glycosylpurines. This suggested that N-3 of a preformed purine should be blocked to ensure glycosidation at N-7. These difficulties were strong

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