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NOTE

Ring metalation of toluene by butyllithium in the presence of *N,N,N',N'*-tetramethylethylenediamine*

The use of chelating tertiary diamines for increasing the reactivity of lithium alkyls, and in particular, the effect of *N,N,N',N'*-tetramethylethylenediamine (TMEDA) on n-butyllithium has recently received much attention[1-5]. Thus, it has been reported that benzene is converted to phenyllithium in thirty minutes at 80° [1] while benzyllithium is produced "quantitatively" from toluene within minutes at room temperature[4]. Reactions of this type have thus been recommended as preparative methods[4b].

Eberhardt and Butte, however, have suggested earlier that in the case of the alkylbenzenes, metalation may occur on the ring in addition to the position on the side chain. They obtained some evidence in support of metalation meta to the alkyl group, but were unable to detect *ortho* and *para* metalation. Thus, before such reactions are used preparatively, some investigation into the extent of such ring metalation seemed in order.

Should ring metalation occur, it would also allow a comparison with the metalation of alkylbenzenes by sodium—and potassium—alkyls where a kinetically controlled sequence of ring metalation followed by isomerization to the α position has been found[6,7]. No such case of isomerization of lithium alkyls has previously been recorded[8].

We have, therefore, examined the reactions of the TMEDA–butyllithium complex with benzene and toluene, following the reactions by quenching with dimethyl sulfate or trimethylchlorosilane and examining the products by GLC. The quenching reaction in the case of toluene was carried out both by addition to, and addition of, the quenching reagent in order to see whether the mode of addition, as well as the nature of the reagent, affected the reaction products. Some "abnormal" reactions of benzyl anions (reactions at a ring position) have been found using trimethylchlorosilane[9].

We can confirm the reported reactivity of TMEDA–butyllithium toward benzene. Thus, in hexane, TMEDA–butyllithium (1.16 *M*) reacted with benzene (1.16 *M*) to give 50 % metalation after 300 minutes at 25°, while in benzene, a 0.17 *M* solution of the butyllithium complex was 98 % converted to phenyllithium after one hour, and quantitatively after twenty hours.

A similar reactivity of the complex was found towards toluene. However, significant quantities of the ring-metalated isomers were found on derivatization (Table 1). The four possible isomers were found in constant proportions, independent of the extent of reaction, and the nature of, or the mode of addition of, the quenching reagent.

Analysis of the resulting silanes produced the data shown in Table 1.

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TABLE 1

ISOMER FORMATION FROM TOLYLLITHIUM AND TRIMETHYLCHLOROSILANE

Time (min)	Benzyltrimethylsilane		*m*-Tolyltrimethylsilane		*p*-Tolyltrimethylsilane		*o*-Tolyltrimethylsilane	
	(Mmoles)	(%)^a	(Mmoles)	(%)	(Mmoles)	(%)	(Mmoles)	(%)
0.5	0.86	90.8	0.051	5.34	0.017	1.82	0.020	2.06
1.0	1.66	90.7	0.098	5.34	0.035	1.93	0.038	2.05
2.5	4.09	90.2	0.259	5.71	0.090	1.98	0.093	2.06
5.0	7.18	89.9	0.473	5.92	0.176	2.20	0.160	2.00
10.0	9.95	90.2	0.654	5.92	0.218	1.98	0.212	1.92
300.0	11.21	90.6	0.704	5.69	0.240	1.94	0.216	1.75

^{a} The percent figures are the isomer distributions within the respective samples.

In a similar experiment, but using dimethyl sulfate as the quenching reagent, the distribution of isomers shown in Table 2 was found.

The results, therefore, indicate that a considerable proportion of ring-lithiated products are found when TMEDA–butyllithium is used to prepare benzyllithium, and that these proportions do not decrease with time as in the case of similar sodium and potassium metalations. This suggests that either there is a rapid equilibration among the isomeric lithium species to give the proportions found in Tables 1 and 2 or that no isomerization occurs and the proportions depend on kinetic factors. In order to distinguish between these possibilities, attempts were made to synthesize the various isomers from the bromo-substituted toluenes using an equivalent of TMEDA in toluene and lithium metal. The authors are not aware of any literature preparation along these lines, but the preparation of Grignard reagents from aryl halides has recently been reported using an equivalent of a tertiary amine in benzene solution in place of ether solvents[10].

Reaction was obvious from the immediate formation of a yellow color which, however, rapidly deepened to a dark brown. The reactions were quenched with trimethylchlorosilane and the products examined by GLC. These preparations were generally unsatisfactory, resulting in the formation of products apparently higher in molecular weight than those expected. Only in the case of *o*-bromotoluene was a tolyltrimethylsilane identified and this gave solely the *o*-derivative (comparison

TABLE 2

ISOMER FORMATION FROM TOLYLLITHIUM AND DIMETHYL SULFATE

Time (min)	Ethylbenzene (%)	*m*-Xylene (%)	*p*-Xylene (%)	*o*-Xylene (%)
0.5	88.4	6.17	3.08	2.32
1.0	90.4	5.24	2.42	2.02
2.5	89.9	5.58	2.55	1.95
5.0	90.4	5.19	2.47	1.98
10.0	89.9	5.43	2.57	2.09
180.0	89.8	5.59	2.60	2.02

with authentic samples prepared by conventional Grignard techniques). It therefore seems unlikely that the constant proportions of isomers given in Tables 1 and 2 reflect a rapid equilibration.

Experimental

Starting materials

Toluene. Purified by preparative GLC (F & M Prepmaster 775) and shown to be free from ethylbenzene and the isomeric xylenes by GLC (Perkin–Elmer 226). Dried over molecular sieves (1 week) and purged with a stream of nitrogen for 20 min.

N,N,N′,N′-Tetramethylethylenediamine (TMEDA) and trimethylchlorosilane. Dried over calcium hydride and distilled under vacuum.

n-Butyllithium. A 1.622 *M* solution in hexane from Foote Mineral Company was analyzed by direct titration with 0.1 *N* HCl after hydrolysis[11].

Benzyltrimethylsilane and tolyltrimethylsilanes. Made by conventional Grignard techniques[12,13] and purified by preparative GLC. The resulting compounds gave refractive indices in reasonable agreement with literature values (Table 3).

TABLE 3

REFRACTIVE INDICES AND NMR DATA ON SILANES

Trimethylsilane	n_D^{25}		τ-Value for
	Lit.[12,13]	Found	$Si(CH_3)_3$[a]
Benzyl	1.4909	1.4912	10.02
o-Tolyl	1.5005	1.5026	9.70
m-Tolyl	1.4902	1.4908	9.77
p-Tolyl	1.4892	1.4899	9.78

[a] 10% in CCl_4, tetramethylsilane internal standard

Toluene metalation

17.0 ml (163 mmoles) of toluene was reacted with 10 ml n-butyllithium in hexane in the presence of 2.50 ml (16.55 mmoles) of TMEDA and 0.172 g dodecane (internal standard) at 25° under nitrogen. Aliquots (1 ml) were injected at suitable time intervals into vials containing 0.3 ml (2.4 mmole, about a five fold excess) of trimethylchlorosilane. The solutions were then filtered from lithium chloride and analyzed by GLC using a Perkin–Elmer 226 equipped with flame-ionization detector.

A 150′ × 10 mil di-isodecyl phthalate (DIDP) capillary column was used in series with a 150′ × 10 mil di(3,3,5-trimethylcyclohexyl) phthalate capillary column. Comparison of the results with a calibrated mixture of trimethylsilanes and dodecane in toluene allowed the determination of the absolute quantities of each isomer shown in Table 1. A similar experiment, using dimethylsulfate in place of trimethylchlorosilane gave the results of Table 2. In this case, no internal standard was used so that only the isomer distribution is recorded. However, using the excess toluene as an approximate standard, the same conversions with time were found as those in Table 1 within experimental error.

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