References and Notes

(1) This work was presented in preliminary form to the 10th Middle Atlantic Regional Meeting of the American Chemical Society on February 23, 1976 at Philadelphia.
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(9) Several examples of the reduction of selenocyanates to selenols using hypophosphorous acid, have been recorded: (a) E. Sekido, Q. Fernando, and H. Freiser, *Anal. Chem.*, **36**, 1768 (1964); (b) M. V. Lakshmikantham, M. P. Cava, and A. F. Garito, *J. Chem. Soc., Chem. Commun.*, 383 (1975).
(10) Tetraphenylarsonium bromide (mp 275–276 °C) was obtained by recrystallization of commercial tetraphenylarsonium chloride (mp 255–256 °C) thrice from 48% hydrobromic acid. For a general procedure to interconvert arsonium salts, see S. Andreades and E. W. Zahnow, *J. Am. Chem. Soc.*, **91**, 4181 (1969).

Metalation Reactions. 19. Selectivity in the Metalation of Polymethylbenzenes

J. Klein* and A. Medlik-Balan

Contribution from the Department of Organic Chemistry, The Hebrew University, Jerusalem, Israel.

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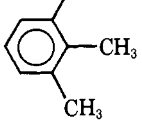
Abstract: The metalation of 1,2,3- and 1,2,4-trimethyl- and 1,2,4,5-tetramethylbenzene with butyllithium-TMEDA gave bis-1,2- and -1,3-lithiomethyl compounds and that of 1,2,3,5-tetramethylbenzene led to bis-1,2- and -1,3-lithiomethyl and to tris-1,3,5-lithiomethyl derivatives. No bis-1,4-lithiomethyl compounds were obtained with this reagent. The last compounds were formed using butyllithium-potassium *tert*-butoxide as metalating agent. With this reagent also tetrametalation of 1,2,3,5-tetramethylbenzene was observed. The lithium compounds were characterized by their ^{1}H NMR spectra and by their reaction with trimethylchlorosilane. Their reaction with borane led to benzylic alcohols. The directive effects of methyl and lithiomethyl groups and their possible reasons are discussed.

We have found recently[1] that *o*- and *m*-xylene and mesitylene can be di- and trilithiated with butyllithium-TMEDA at room temperature to bis- and tris(lithiomethyl)benzene, respectively. However *p*-xylene gave under similar conditions a product that was dilithiated at the same benzylic carbon. It was concluded[1] that metalation with butyllithium was favored to proceed in such a manner that charge alternation was maintained in the delocalized carbanion.

The selectivity of dimetalation of polymethylbenzenes can be studied only when more than two methyl substituents are located on the ring. However, the only trimethylbenzene studied previously was mesitylene, in which all the methyls are equivalent by its symmetry and cannot be distinguished in the metalation. Other tri- and tetramethylbenzenes have therefore been submitted to the metalation with butyllithium.

The treatment of 1,2,3-trimethylbenzene (I) with butyllithium in hexane in the presence of tetramethylethylenediamine (TMEDA) gave (Table I) a 2:1 mixture of 2,3- (II) and 2,6-dimethylbenzyllithium (III) and one dilithium derivative exclusively, the bis(1,2-lithiomethyl)-3-methylbenzene (IVa).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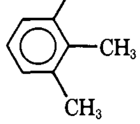
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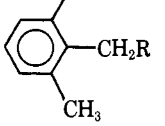
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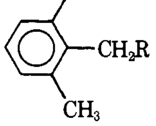

IV

a, R = Li c, R = K
b, R = $Si(CH_3)_3$ d, R = $OCOCH_3$

The composition of the products of metalation was determined by treatment of the reaction mixture with trimethylchlorosilane and isolation of the corresponding trimethylsilyl derivatives IIb–IVb. The disilyl derivative was separated and characterized by its ^{1}H NMR spectrum (Table II). The ratio of the monosilyl compounds IIb and IIIb has been determined by the ^{1}H NMR of their mixture, the symmetrical IIIb being easily distinguished from IIb. IIIb was characterized by a singlet at 2.21 ppm (6 H) corresponding to the two equivalent methyls and by a singlet at 2.11 ppm of the methylene (2 H) α to the trimethylsilyl group. IIb was characterized by a singlet at 2.24 ppm (3 H) corresponding to one benzylic methyl and a singlet at 2.11 ppm ascribed to the other benzylic methyl and the methylene α to the trimethylsilyl group. The assignment of the signals was verified when samples of different isomeric ratios were compared. The reduction of the amount of IIb was accompanied by the lowering of the signal height at 2.11 ppm and in samples where IIIb was the major product, the spectrum was composed of a sharp singlet at 2.21 and a lower singlet at 2.11 ppm.

The lithium derivatives IIa–IVa have been identified in the hexane solution by their ^{1}H NMR spectrum and particularly in the aromatic region. After short metalation times, the protons para to the lithiomethyl groups were found at 5.5–5.73 ppm and the ortho-meta protons at 6.07–6.43 ppm. The signals of IIIa were particularly clear in THF solution, where the para proton appeared as a triplet at 5.53 and the meta protons as a doublet at 6.18 ppm. Longer metalation intervals in hexane-TMEDA led to IVa, which exhibited a multiplet of the two protons para to the lithiomethyl groups at 5.43–5.53 and one proton para to the methyl as a doublet of doublets at 6.06 ppm.

Metalation of I was also carried out with various amounts of butyllithium and potassium *tert*-butoxide according to the procedure of Schlosser.[2] The reaction mixture was treated with trimethylchlorosilane and the composition of the silylated products determined. A ratio of IIb and IIIb was obtained (Table I) after short metalation times that was similar to that

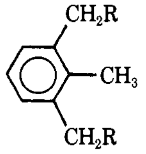
Table I

Substrate	Metalating agent[a] (mol[b])	Duration of metalation (h)	Products[c] (%)
I	BuLi (1); TMEDA (1)	6	I (22.5); IIb (30); IIIb (16); IVb (31)
I	BuLi (4); TMEDA (4)	24	IIb (4.5); IIIB (2.5); IVb (93)
I	BuLi (1); *t*-BuOK (1)	2	IIb (49.2); IIIb (32.8); IVb (10.5); Vb (7.5)
I	BuLi (2); *t*-BuOK (2)	16	IIb (14.5); IIIb (18); IVb (24.7); Vb (28); VIb (14.5)
I	BuLi (3); *t*-BuOK (3)	24	IIb + IIIb (12.6); IVb (14); Vb (29); VIb (44.5)
I[d]	BuLi (4)	48	IIb (45); IIIb (55)
I[d,e]	BuLi (4)	48	IId (48); IIIc (52)
I[e]	BuLi (1); *t*-BuOK (1)	2	IId (49); IIId (27); IVd (11.9); Vd (12.3)
I[e]	BuLi (2); *t*-BuOK (2)	16	IId (7.4); IIId (6.4); IVd (34.4); Vd (51.6)
I[e]	BuLi (1); TMEDA (1)	8	I (27); II (51); III (22)
VII	BuLi (1); TMEDA (1)	6	VII (22.8); VIIIb + IXb + Xb (68); XIb (2.2); XIIb (7.3)
VII	BuLi (4); TMEDA (4)	24	VIIIb + IXb + Xb (37); XIb (23); XIIb (40)
VII	BuLi (1); *t*-BuOK (1)	2	VII (10.5); VIIIb + IXb + Xb (73); XIb (2.5); XIIb (14)
VII	BuLi (2); *t*-BuOK (2)	16	VIIIb + IXb + Xb (12.3); XIb (13.8); XIIb (60); XIIIb (13.8)
VII	BuLi (3); *t*-BuOK (3)	24	XIb (9.5); XIIb (48); XIIIb (42.5)
VII[d,e]	BuLi (4)	48	VIIId (21.2); IXd (60); Xd (18.5)
VII[e]	BuLi (1); *t*-BuOK (1)	2	VIIId (24); IXd (36); X (17); XId (4.2); XIId (19)
VII[e]	BuLi (2); *t*-BuOK (2)	16	VIIId + IXd (9.1); Xd (3.1); XId (13.9); XIId (73.8)
VII[e]	BuLi (1); TMEDA (1)	8	VIId (30); VIIId (16.5); IXd (29.5); Xd (24)
XIV	BuLi (6); TMEDA (4)	48	monosilyl (12.1); XVb (27.2); XVIb (24.2); XVIIb (36.1)
XIV	BuLi (6); *t*-BuOK (6)	24	XVb (2.5); XVIb (13); XVIIb (41.5); XVIIIb (30)
XX	BuLi (6); TMEDA (6)	48	XXIb (23); XXIIb (23); XXIIIb (54)
XXIV	BuLi (2.5); *t*-BuOK (2.5)	8	XXV (21.5); XXVIb (12.5); XXVII (43.5); XXVIII (20)
XXIX	BuLi (31); *t*-BuOK (3)	24	XXXb (14.5); XXXIb (85.5)

[a] The reaction was performed in hexane at room temperature. [b] Moles relative to the substrate. [c] After treatment with trimethylchlorosilane. [d] Metalation in THF. [e] With treatment of the metalation product with borane (instead of trimethylchlorosilane) and subsequent oxidation and acetylation.

obtained with butyllithium-TMEDA. However, this ratio changed with time and amount of the metalating agent, whereas in the metalation with butyllithium-TMEDA it was constant. It seems that the intermediate potassium derivative IIc reacts faster than IIIc with butylpotassium. Another possibility is the occurrence of transmetalation in potassium derivatives.

The metalation with butyllithium and potassium *tert*-butoxide yielded in addition to IVc the second possible dimetalated product Vc, as evidenced by the formation of Vb on treatment with trimethylchlorosilane. Moreover, the trimetalated product VIc was obtained that subsequently yielded VIb. The ratio between IVc and Vc changes with reaction conditions. Possible explanations are either faster metalation of IVc than that of Vc or equilibration by transmetalation.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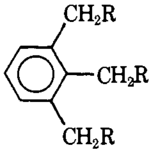
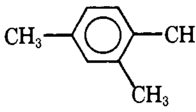

VI

Metalation with butyllithium in THF without added catalyst was also carried out. Only monometalation products IIa and IIIa were obtained in a 45:55 ratio. Since the separation of the monosilyl derivatives IIb and IIIb have proved difficult, the treatment of the metalation mixture with borane and subsequent oxidation[3] was performed. The obtained alcohols were transformed into acetates IId–Vd, separated, and characterized (Table II). The ratio of the acetates obtained confirmed the ratio determined by ^1H NMR of the lithium or silyl derivatives. The structure of the acetates was determined by ^1H NMR and the identity of the various protons established by the position of their signals in the presence of Eu(fod)$_3$ shift reagent. The two ortho protons of the symmetrical Vd appeared as a doublet at low field 9.1 ppm and the one meta proton as a triplet at 7.42 ppm. The protons of the methylene and of the acetyl groups appeared also at lower field (at 10.4 and 6.6 ppm, respectively) relative to the spectrum in the absence of the shift reagent.

The addition of the shift reagent to IVd removed the accidental equivalence of the two methylene and acetate groups, respectively. Only one aromatic proton was shifted significantly in the presence of this reagent to lower field 8.9 ppm. The remaining two aromatic protons appeared at 7.5 ppm, the two methylene groups at 12.7 and 11.4 ppm and the acetyl methyl groups at 5.25 and 5.5 ppm.

The selectivity of the metalation of 1,2,4-trimethylbenzene (VII) with butyllithium-TMEDA was less pronounced than that of I. Treatment of the metalation mixture with trimethylchlorosilane gave a mixture of the three monosilyl derivatives VIIIb, IXb, and Xb that could not be separated, and the two disilyl compounds XIb and XIIb (Table I). The ratio of IXa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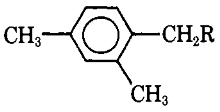
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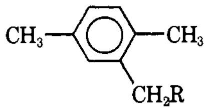
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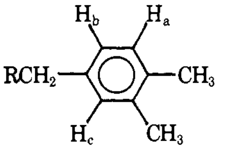
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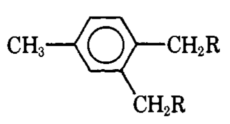
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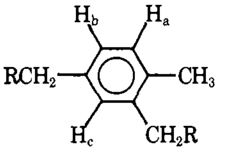
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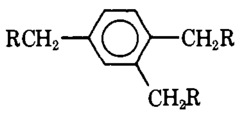

XIII

Table II

Compd	Chemical shift δ of the protons (ppm)			
	Aromatic	Ar-CH_2-R Ar-CH-R_2	ArCH_3	Ar-C-R
IIb	6.82 (m) 3	2.11 (s) 2	2.24 (s) 3; 2.11 (s) 3	−0.01 (s) 9
IIIb	6.87 (s) 3	2.11 (s) 2	2.21 (s) 6	0.02 (s) 9
IId[a]	6.89 (s) 3014.4 (s) 2	2.14 (s) 3; 2.20 (s) 3	1.99 (s) 1	
IIId[a]	6.93 (s) 3	4.53 (s) 2	2.33 (s) 6	1.46 (s) 1
IVb	6.8 (s) 3	2.05 (s); 2.1 (s) 2	2.25 (s) 3	0.0 (s) 9; 0.02 (s) 9
Vb	6.69 (m) 3	2.08 (s) 4	2.08 (s) 3	−0.01 (s) 9
VIb	6.66 (m) 3	2.0 (s) 6		0.0 (s) 18; 0.02 (s) 9
IVd	7.18 (m) 3	5.0 (s) 4	2.28 (s) 3	2.0 (s) 6
Vd	7.16 (s) 3	5.18 (s) 4	2.4 (s) 3	1.98 (s) 6
IXb	6.9 (d) 1; 6.7 (m) 2	2.0 (s) 2	2.23 (s) 3; 2.13 (s) 3	0.0 (s) 9
IXd	6.89 (s) 2; 6.96 (s) 1	4.89 (s) 2	2.23 (s) 6	1.96 (s) 3
Xd	6.96 (s) 3	4.89 (s) 2	2.17 (s) 6	1.99 (s) 3
VIIId	6.89 (s) 3	4.89 (s) 2	2.17 (s) 6	1.99 3
XIb	6.73 (m) 3	1.95 (s) 4	2.25 (s) 3	−0.016 (s) 18
XId	7.13 (m) 3	5.06 (s) 4	2.36 (s) 3	2.0 (s) 6
XIIb	6.88 (d) 1; 6.55 (m) 2	1.97 (s) 2; 2.03 (s) 2	2.16 (s) 3	0.017 (s) 18
XIId	7.16 (s) 2; 7.29 (s) 1	5.06 (s) 2; 4.99 (s) 2	2.36 (s) 3	2.0 (s) 6
XIIIb	6.75 (d) 1; 6.55 (m) 2	1.88 (s) 6		0.0 (s) 27
XVb	6.59 (br s); 6.53 (br s) 1	2.01 (s) 2; 1.98 (s) 2	2.16 (s) 3; 2.17 (s) 3	−0.01 (s) 9; −0.04 (s) 9
XVIb	6.47 (m) 2	1.98 (s) 2; 2.08 (s) 2	2.08 (s) 3; 2.21 (s) 3	−0.01 (s) 9
XVIIb	6.33 (s) 2	1.91 (s) 2; 2.05 (s) 4	2.02 (s) 3	−0.01 (s) 27
XVIIIb	6.38 (s) 2	1.96 (s) 2; 2.08 (s) 4 2.02 (s) 2		−0.01 (s) 36
XXIb	6.61 (s) 1; 6.74 (s) 1	1.99 (s) 2	2.15 (s) 9	−0.01 (s) 9
XXIIb	6.63 (s) 2	1.95 (s) 4	2.18 (s) 6	−0.01 (s) 18
XXIIIb	6.56 (s) 1; 6.82 (s) 1	2.0 (s) 4	2.15 (s) 4	−0.01 (s) 18
XXVb	6.56 (d) 2; 6.73 (d) 2	1.98 (s) 2	2.25 (s) 3	0.02 (s) 9
XXVIb	6.60 (d) 2; 6.78 (d) 2	1.36 (s) 1	2.23 (s) 3	0.0 (s) 18
XXVIIb	6.81 (s) 4	2.01 (s) 4		−0.03 (s) 18
XXVIIIb	6.82 (s) 4	1.45 (s) 1; 2.03 (s) 2		0.02 (s) 27

[a] R = OH.

to the other two monolithiated products VIIIa and Xa was determined by ^{1}H NMR directly after short metalation times on the metalated mixture. A high field aromatic proton signal appeared at 5.6 ppm as a doublet, and this was assigned[1] to the proton para to the lithiomethyl group in IXa. The other two isomers do not have such a para proton and their aromatic protons appeared together with the other aromatic protons of IXa at 6.14–6.5 ppm. The ratio 1:4.5 of the two groups of signals permitted the determination that the amount of IXa in the mixture of the three monolithiated derivatives is more than 50%. Longer metalation intervals permitted the observation by ^{1}H NMR of the dilithium derivative XIIa, which showed the protons ortho-para to the two lithiomethyl groups as a doublet at 5.0 ppm and the ortho-ortho proton as a broad singlet at 5.5 ppm. The ortho protons, including those of XIa, showed up at 6–6.3 ppm. The ratio of the three products of monometalation with butyllithium-TMEDA was determined by their reaction with borane and subsequent oxidation and acetylation. The three acetates VIIId, IXd, and Xd have been obtained in a 24:41:34 ratio.

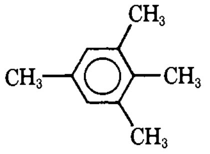
Metalation of VII in THF gave a solution of isomeric lithium derivatives which exhibited the para proton of IXa at 5.44 ppm (d) and its remaining protons at 6.1–6.37 ppm (m). The two other isomers showed signals at 5.74–5.94 ppm. Treatment of the metalation mixture with borane and subsequent oxidation and acetylation yielded the three monoacetates VIIId, IXd, and Xd in a 21:60:19 ratio. These were separated and identified by ^{1}H NMR.

Somewhat different results were obtained on metalation of VII with butyllithium-potassium *tert*-butoxide. Treatment of this reaction mixture with trimethylchlorosilane led to a mixture of the monosilyl VIIIb, IXb, and Xb, and the disilyl derivatives XIb and XIIb. The last compounds have been obtained in a 1:5 ratio. The trisilyl compound XIIIb was also obtained in the presence of a larger amount of the metalating agent. The ratio of the monopotassium intermediates VIIIc, IXc, and Xc was determined by treatment of the metalation mixtures with borane and subsequent oxidation and acetylation. In this mixture, IXd is still the most abundant of all isomers, but its percentage is lower than in the product of metalation with butyllithium in THF. The structure of IXd was proven by comparison with a sample synthesized in an unequivocal manner in the following way: 2,5-dimethylbenzyl chloride was converted into its Grignard reagent, then treated with borane, oxidized to the corresponding benzyl alcohol, and acetylated.

The structure of the isomers IIId and Xd was not clear from their ^{1}H NMR spectra (Table II). However, addition of Eu(fod)$_3$ shift reagent to samples of these compounds permitted the identification of the isomers by the characteristic shift to low field of the aromatic protons ortho to the acetoxy group. In Xd two aromatic protons H_b and H_c were shifted to low field (9.6 ppm) and appeared as a superposition of a doublet and a singlet. The third aromatic proton appeared as a doublet at 7.3 ppm. The isomer VIIId exhibited a shift to low field of one aromatic proton only that appeared as a doublet at 8.4 ppm, showing the presence of an ortho proton. In IXd only one proton was shifted to low field 8.1 ppm in the presence of the shift reagent, but this proton appeared as a singlet.

The two diacetates XId and XIId were also distinguished by their ^{1}H NMR spectrum in the presence of the same shift reagent. Two aromatic protons were shifted in both to low field and one of them appeared as a singlet at 8.9 and 12.9 ppm, respectively. The other appeared a doublet at 9.0 and 8.9 ppm, respectively. However, in XIId the singlet corresponding to H_c proximate to two acetoxy groups was shifted much more than the other proton in XIId and more than each of the shifted protons in XId. The third aromatic proton in both isomers appeared as a doublet at 7.5 and 7.6 ppm, respectively. The difference in the chemical shift of the two acetyl protons and the two methylene groups was also larger in XIId than in XId in the presence of the shift reagent, as expected for the different complexation with a hindered and an unhindered acetoxymethylene group, respectively.

The possibility of tetrametalation at benzylic positions was explored in 1,2,3,5-tetramethylbenzene (XIV). Metalation of this compound with an excess of butyllithium-TMEDA in hexane gave in addition to the monolithium the dilithium XVa and XVIa and the trilithium derivative XVIIa, since subsequent treatment with trimethylchlorosilane gave a mixture of monosilyl derivative that was not separated, two disilyl derivatives XVb and XVIb, and a trisilyl compound XVIIb. Structure XVII was assigned to the trisilyl derivative for two reasons. First, none of the 1,2,3- and 1,2,4-trimethyl- nor 1,2,3,4- nor 1,2,4,5-tetramethylbenzene were trilithiated under similar conditions, but mesitylene[1] was converted to the symmetrical tris(lithiomethyl)benzene. The preference for meta di- and trilithiation was attributed by us to electronic factors. The ^1H NMR spectrum of XVIIb (Table II) supports this assignment, since it exhibits the symmetry of this compound and shows an upfield shift for the methyl group that is apparently induced by two neighboring silyl groups. The methyl in the isomeric symmetric XIXb is too far from the silyl groups to be affected by them.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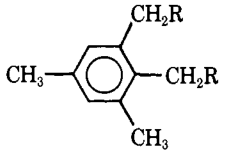
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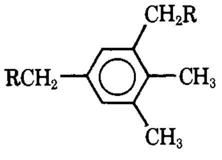
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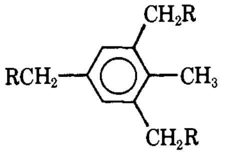
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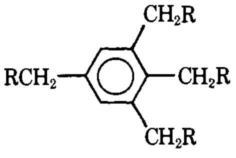
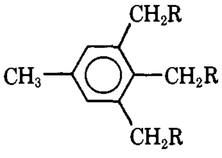
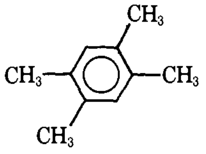
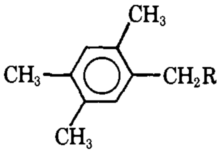

XVIII


XIX

Tetrametalation of XIV was achieved with butyllithium-potassium *tert*-butoxide. Treatment of this metalation mixture with trimethylchlorosilane (Table I) gave XVb, XVIb, XVIIb, and the tetrasilyl derivative XVIIIb, identified by its elemental analysis, ^1H NMR spectrum, and the molecular ion in its mass spectrum. Two additional products were obtained in this reaction in a total yield of 13% that are apparently additional disilyl and trisilyl derivatives.

Metalation of durene with butyllithium-TMEDA was much slower than that of the other studied compounds. This reaction yielded the mono XXIa and the two dilithio derivatives XXIIa and XXIIIa, which were characterized by conversion to the corresponding silyl compounds XXIb, XXIIb, and XXIIIb, respectively. The two isomers XXIIb and XXIIIb were distinguished by the equivalence of the two aromatic protons in XXIIb, whereas these two protons in XXIIIb exhibited different chemical shifts.


XX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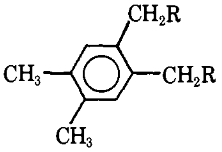
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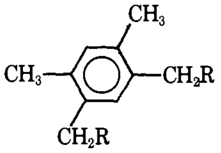
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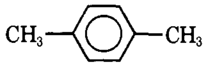
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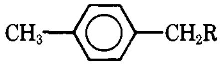
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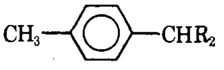
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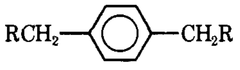
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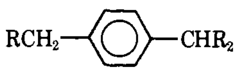
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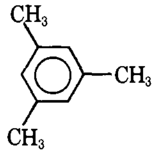
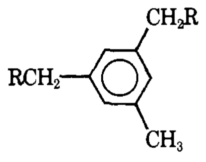
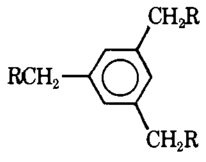

XXIX


XXX


XXXI

The successful metalation of two para methyls in VII and XIV with butyllithium-potassium *tert*-butoxide led us to reexamine the metalation of *p*-xylene, which was found by us[1] to give with butyllithium-TMEDA the *gem*-dilithio derivative XXVIa as the only product of dimetalation. Indeed the bis(potassiomethyl)benzene XXVIIa was obtained now on metalation of *p*-xylene with butyllithium-potassium *tert*-butoxide as shown by its conversion to disilyl derivative XXVIIb. Moreover, the di- and tripotassium XXVIc and XXVIIIc, respectively, have been obtained also, which gave the corresponding silyl derivatives XXVIb and XXVIIIb.

Similarly mesitylene also gave with this reagent the di- and tripotassio XXXc and XXXIc, and subsequently the disilyl XXXb and trisilyl derivatives, respectively.

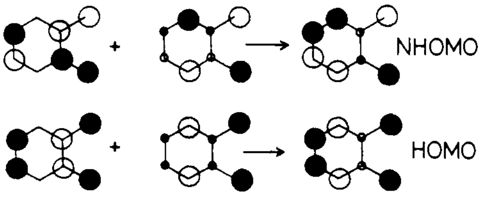
Discussion

A selectivity pattern emerges from the metalation studied here and previously. Several rules can be formulated: (A) No measurable ring metalation was observed. (B) Benzylic monometalation at the position ortho or meta to a methyl group is favored over that to a para methyl. (C) No dimetalation by proton abstraction from a methyl para to the benzylic methylene anionic group occurred by the action of butyllithium-TMEDA. However, such para dimetalation took place with butylpotassium. (D) Butyllithium in THF does not perform dimetalation. (E) Trilithiation by butyllithium-TMEDA took place only when the three metalated methyl groups were in the 1,3,5-positions on the ring. (F) Tetrametalation at all four methyl groups of a tetramethylbenzene was achieved with butylpotassium under mild conditions.

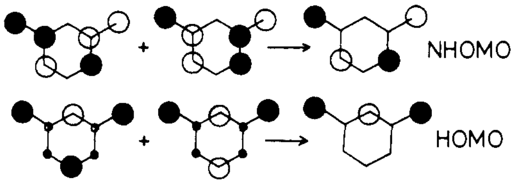
The reluctance of butyllithium to perform dimetalation at two methyls para to each other can be explained by the instability of the dilithiated compounds, in which there is no charge alternation.[1,4] A series of compounds was shown by us[1,4,5-9] to prefer a second lithiation to occur in such a manner as to introduce the new negative charge on the same set of atoms as the first charge. This is not possible in the para metalation, but takes place in the metalation of two meta methyls. Abstraction of a proton by butylpotassium is much faster and, the transition state being more like the mono than the dianion, para dimetalation is not prohibited. This stringent requirement for charge alternation in the dilithio compounds, except the case of the ortho dimethylbenzenes (see below), seems to be in contradiction with the larger covalent character of the carbon-lithium relative to the carbon-potassium bond, which reduces in the first case to a greater extent the amount of charge on the carbons, thus leading to less charge-charge repulsion. It is possible that the reason for this preferential formation of the dilithium derivative with charge alternation in the molecule consists in the stabilization of benzyllithium compounds and some other derivatives of delocalized carbanions by lithium bridging[10] between the benzylic and the ortho ring carbon. Such a bridging is favored only when there is charge alternation and negative charge is available at the positions ortho to the benzylic methylene groups. Lithium bridging was found by calculation[11] to be a stabilizing factor in another dilithium compound, a sesquiacetylene derivative which is formed by proton abstraction from a propargylic position in an acetylene in such a manner that the second negative charge is also introduced on the same set of starred atoms leading to charge alternation. This occurs in preference to an abstraction of an alternative proton at the other propargylic position that would have led to the extension of the resonating system and simultaneously spreading the charge more uniformly over the whole delocalized system.

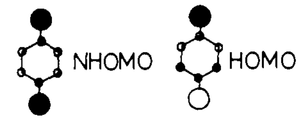
It remains to be explained the easy metalation of two methyls ortho to each other on the aromatic ring. The two filled p_z orbitals of the two methylene groups may interact with each other through space[12,13] or through the connecting bonds.[14] Hoffmann explained the larger stability of the *cis*-methylallyl anion[12] relative to its trans isomer by orbital occupancy, which lowered the energy of the symmetrical orbitals and led to an attractive, through space interaction between the p orbitals of the methyl and terminal methylene. Epiotis[16,17] applied his approach to steric attractions to explain the longer stability of ethylene with two substituents containing lone pair electrons in 1,1 or cis-1,2 positions relative to those with these substituents in the trans-1,2 positions. The attractive in-phase long range interaction between the lone pairs in cis-1,2 positions were considered[16,17] to be related to aromatic stabilization.

Similar concepts might be applied to the *o*-xylylene dianion. CNDO[18] calculations have shown that the antisymmetric combination of the lone pair orbitals interact stronger with a vacant than a filled orbital of benzene to give a molecular orbital next to the highest occupied one (NHOMO), thus giving away charge to this ring. The symmetrical combination of the lone pairs interacts stronger with a filled orbital of benzene, giving the HOMO and one lower lying orbital. The withdrawal of charge from the antisymmetric combination of the lone pairs should lead to a net attractive interaction between these pairs and stabilization. Indeed, a positive Mulliken overlap population was found between the two p_z orbitals of the methylene groups. However, this overlap is small and the total Mulliken population overlap is negative. Kollman[19] has ascribed the diminution of the angle between the two fluorines in a similar system, the 1,1-difluoroethylene, not to an attractive interaction between the two fluorines, since no positive overlap was found between them, but to a change in the character of the C-F bonds. This analysis of the F-C-F bond shrinkage was refuted by Epiotis,[20] who has analyzed in great detail all the interactions and found that this shrinkage is due to the relief of long range antibonding interactions and to a two-electron $n_S \cdots \pi^*$ stabilizing interaction. This last interaction leads to a F···F negative overlap population. However, this antibonding situation is overcompensated by bonding situations. Stabilization of olefins containing neighboring cis or geminal groups cannot be ascribed to an increase of electronegativity only, since our results show that a *decrease* of electronegativity (on going from a methyl group to a methylene anion group) stabilizes a neighboring ortho relative to a remote para arrangement of such groups.



The correlation between charge withdrawal from the antisymmetric combination of the two lone pairs and stabilization by cyclic "aromatic" delocalization due to a positive overlap of these pairs does not apply in the case of *m*-xylylene dianion. The dianion is the most stable of all the three isomers. It has also, like the ortho isomer, a stronger interaction between the antisymmetric combination of lone pairs and a vacant orbital than with a filled benzene orbital. Although more charge remains in the symmetric combination of the lone pairs, overlap between them is not meaningful, due to their distance.





The relation between in-phase interaction and stability might therefore have additional reasons than simple overlap, since there is no doubt that many compounds including allylic anions[21-24] having an additional substituent with a lone pair are more stable in the cis than in the trans configuration. It is also of interest that the *p*-xylylene dianion, the least stable of the three isomers, exhibits a larger interaction between the symmetric combination of lone pairs and a vacant orbital than with a filled benzene orbital, so that the NHOMO contains the combination shown below. The separation between the HOMO and NHOMO increases in the order meta < ortho < para xylylene dianions. These levels are in the meta isomer almost degenerate. The order of stability of the xylylene dianions can be compared with that of olefins with two substituents containing lone pairs. The sequence for olefins containing two allylic methylenes carrying negative charges was found experimentally[1,4,5] to be: Y (geminal) > U (cis) > extended (trans). The same sequence was observed now for the xylylene dianions, i.e., Y (meta) > U (ortho) > extended (para). The meta isomer has to be considered a Y form, and its stability is found also in the parent trianion of XXXI (of 1,3,5-trimethylenebenzene) derived by abstraction of a proton from each of the methyl groups of mesitylene. The CNDO calculations[18] have found the *m*-xylylene dianion to be more stable than its ortho isomer, but the para dianion was slightly more stable than the ortho isomer. Moreover the stability of the dilithium derivatives of these dianions was according to these calculations in the order: ortho > meta > para. It seems that the CNDO method used does not lead to accurate results in this series. However, the extended Hückel[26] calculations and "ω-β" method[27] gave results in agreement with experimental results. The stability of the xylylene dianions by these calculations was found to be in the sequence meta > ortho > para. The ortho and meta dilithium derivatives of these compounds were also found by the extended Hückel method to have comparable energies, which were lower than that of their para isomer. The failure of the CNDO calculations to give the right sequence of stabilities for these dilithium derivatives is probably due to the excessively large stabilizing interaction found in these calculations when two neighboring lithium atoms are present in the molecule, as in the ortho isomer. Despite the expected difficulties in the X^+Y^- bonding calculations by CNDO, this method was used previously successfully to calculate monoanions and their lithium derivatives.[28] The CNDO calculations of the lithium derivatives[1] reflected the acidities of the compound more faithfully than that of the anions.[1]

The larger stability of the *o*-xylylene dianion relative to its para isomer supports the concept of Epiotis[16,17] on the stabilization by lone pair attractive interactions, since a larger stabilization of the para isomer is expected due to electrostatic interactions. Some stabilization of the ortho isomer may be due to chelation and bridging of the two methylenes by lithium atoms, but its preferential formation in solvents of different polarity and coordinating ability and also when potassium is the counterion seems to support the inherently larger stability of the *o*- relative to the *p*-xylylene dianion. A different analysis of the stabilization of U relative to extended forms was given recently by Bingham,[29] where stabilization by isolation of charges by bending of the system was stressed.

However, the even larger stability of the *m*-xylylene dianion points to an additional effect that determines the sequence of stabilities, since direct interaction between the two methylenes by overlap should be almost nil due to their distance, and no stabilization by angle shrinking is expected. We attribute this stabilization to the formations of a system with charge alternation, all the charges being delocalized on the same set of starred atoms. In this way, each carbon of this starred set is isolated from other atoms of this set by an uncharged (or with a slight opposite charge[1,4,25]) atom.

We would like to comment on the use of the concept "aromaticity" in a large number of recent publications, including ours[5] to explain stabilization of Y or U forms containing $(4n + 2)$ electrons. There is no doubt, that electronic interactions stabilize these forms, but the question arises whether every kind of stabilization containing the "magic" number of electrons is aromaticity. First, we would like to point out that the trianion of 1,3,5-trimethylenebenzene[1] contains 12 π electrons and is stabilized equally well as the meta and more than the *o*-xylylene dianion. Secondly, it was always understood that aromatic stabilization is due to cyclic delocalization. It now seems that, although lone pair interactions in 1,1- and 1,2-substituted olefins lead to stabilization of the system, this is not due to a direct positive overlap and cyclic delocalization of these pairs, but rather its indirect interactions involving other orbitals. This effect is best illustrated in the *m*-xylylene dianion. It seems to us that, if some original meaning of the initial concept of aromaticity is to be left, it should apply to systems with direct cyclic delocalization. The 1,1- and the 1,2-substituted olefins and similarly the 1,2- and 1,3-substituted benzenes should not be included into the group of aromatic compounds,[1,4,25] although the underlying stabilizing factors might be similar to those in the aromatic compounds with cyclic delocalization.

The potassium cation in a benzylpotassium can apparently also function slightly as a part of a chelating system to facilitate metalation at an ortho methyl. The potassium derivatives undergo, in contrast to the lithium compounds, transmetalation so that the *m*-xylylene dianion derivative is formed preferentially after longer reaction periods. The proportions of VIIIc formed at the beginning of the reaction are too high to allow for the proportion of the dipotassium derivative XIIc without assuming transmetalation. The potassium derivative of the *m*-xylylene dianion XIIc is favored over the ortho isomer XIc by a factor of 5:1, whereas for the lithium derivatives XIIa and XIa, where chelating is a stabilizing factor, this proportion is less than 2:1. In the lithiation of I only the dilithium derivative IVa was formed and none of Va, perhaps due to better chelation because of the steric compression introduced by an additional ortho methyl.

A clear-cut example for the preferential dilithiation of two meta methyls vs. ortho ones is supplied by the metalation of 1,2,4,5-tetramethylbenzene. Only one monolithiated compound is formed in this case and this compound can yield either ortho or meta methyl metalation. Each of these methyls is deactivated in a similar manner by a para methyl. The attack by butyllithium of a methyl meta to the benzylic methylene to yield XXIIa is favored by a factor larger than 2 relative to the ortho one leading to XXIa.

The rate of monometalation of a benzylic methyl located ortho is larger than that para to another methyl. CNDO/2[18] calculations were performed to find out whether overlap between the p_z orbitals of the neighboring methylene and methyl group,[30] similar to that found by Epiotis for olefins, is responsible for the stabilization of the first anion. No positive overlap population between the two ortho exocyclic carbons was found in these calculations. It was found, however, that the lithium cation is energetically more stable when bridging the benzylic and the ortho ring carbon linked to the methyl than to the other carbon. This effect is in agreement with gas-phase acidity[31] and basicity[32] measurements and also with MO calculations,[33,34] showing that alkyls stabilize proximate positive and negative charges. However, lithium cation stabilization by the ortho methyl cannot be the only factor determining the larger rate of metalation of a methyl ortho than para to another methyl, since a similar observation was made on the rate of hydrogen-deuterium exchange in Me_2SO[35] and cyclohexylamine.[35] The concepts of Hoffmann[12] and Epiotis[30] might therefore explain at least partly this preferential reaction. However, another factor advanced by Streitwieser,[37-39] an entropy factor, cannot be dismissed. Entropy consideration permit also an understanding of the unusually high reactivity in the metalation of the methyl at the 2-position of 1,2,3-trimethylbenzene. This methyl is the most hindered one in rotation and the loss of entropy on converting into a conjugate methylene is less than for the other methyls. It is metalated despite the hindered approach to it that is larger than to the other methyls. The ratio IIb/IIIb is 45:55 in THF. The expected ratios of IIb/IIIb on statistical considerations and without taking into account the larger steric hindrance for the approach to the 2-methyl is 2:1. The entropy effect accelerates therefore the metalation at this methyl by a factor larger than 2 relative to the other methyls. The order in the rate of monometalation[1] *m*- > *o*- > *p*-xylenes parallels the rate of hydrogen-deuterium exchange in cyclohexylamine.[36] The differences in the rate are small as in the exchange in cyclohexylamine.[36] The large differences in exchange rate in Me_2SO[35] were ascribed to internal return[35,37,40,41] in this solvent. This is now confirmed by our results, since metalation by butyllithium yielding butane and benzyllithium is not prone to internal return due to the very large difference in acidities between butane and toluene. The diffusion of butane away from benzyllithium should be very fast.

The tetrametalation of a tetramethylbenzene with butylpotassium by abstraction of a proton from each methyl is of great interest. It is known that potassium, unlike sodium, but

Table III

	Analysis				
	Calcd, %		Found, %		
	C	H	C	H	IR absorption spectra, cm^{-1}
IIb + IIIb	75.0	10.4	75.8	10.4	690, 720, 1250, 1470, 1580
IVb	68.18	10.6	68.1	10.4	690, 720, 845, 1150, 1250, 1455, 1580
Vb	68.18	10.6	68.21	10.6	690, 730, 770, 845, 1250, 1460, 1570
VIb	64.2	10.7	65.1	10.79	690, 730, 765, 845, 925, 1060, 1155, 1250, 1450, 1580
IId	74.1	6.7	74.84	7.0	725, 780, 965, 1030, 1240, 1385, 1475, 1740
IIId	74.1	6.7	74.5	7.8	775, 960, 1020, 1240, 1380, 1475, 1590, 1740
IVd	66.1	6.7	65.88	6.88	800, 1035, 1240, 1380, 1740
Vd	66.1	6.7	66.25	6.87	790, 1030, 1230 1740
VIIIb + IXb + Xb	75.0	10.4	75.34	10.40	700, 850, 1170, 1250, 1500, 1610
XIb					690, 850, 1250, 1500, 1610
XIIb	68.18	10.6	68.38	10.75	690, 850, 1300, 1500, 1610
XIIIb	64.2	10.7	64.41	10.70	690, 850, 1250, 1490, 1610
VIIId + IXd	74.15	7.87	74.1	7.67	820, 965, 1030, 1230, 1380, 1740
XIId	66.1	6.7	65.82	6.86	
XVb	69.	10.79	69.45	11.42	690, 850, 1250
XVIb	69.	10.79	70.66	11.20	690, 850, 1170, 1250
XVIIb	65.14	10.86	65.14	10.82	690, 840, 875, 1160, 1250, 1420, 1470, 1570, 1610 (M + 350)
XVIIIb	62.5	10.9	62.1	10.79	690, 840, 875, 950, 980, 1170, 1250, 1430, 1470, 1570, 1610 (M + 422)
XXIIb	69.	10.79	70.28	11.03	700, 850, 1250, 1500
XXIIIb	69.	10.79	71.17	11.10	695, 850, 1250, 1500
XXVIIb	67.2	10.4	66.91	10.42	695, 845, 1070, 1160, 1220, 1250, 1420, 1500

like lithium compounds, prefers allylic to vinylic metalation.[42] The charge in a benzylic potassium derivative is largely delocalized into the ring[43] and is expected to impede or even prevent further metalation. It appears, however, that the concentration of the negative charge in the aromatic ring does not interfere with repeated benzylic metalation at the other methyls. Still further metalation seems possible. The kind of interaction of the potassium cation with benzylic anions seems to be of great interest.

Experimental Section

^1H NMR spectra were recorded in CCl_4 on a Varian T60 apparatus using Me_4Si as an internal standard. The ^1H NMR spectra of the products of metalation were taken directly on solutions obtained in reactions performed in NMR tubes under various conditions similar to those indicated in Table I. Gas chromatographic separations were performed on a Varian Aerograph A-90-P-3, IR spectra were recorded on a Perkin-Elmer 337 spectrometer. Analyses were performed by Mrs. Goldstein of the Microanalytical Laboratory of the Hebrew University. The analyses and absorption spectra of the products are recorded in Table III. All the polymethylbenzenes used were commercial samples (Aldrich).

Calculations. CNDO/2 calculations were performed by a modified version of the program written by Clark and Ragle.[44] Standard bond length were used: C-H, 1.094; C-C in ring, 1.39; $C-CH_3$, 1.54; C-Li, 2.2 Å.

Metalation with butyllithium in the presence of TMEDA was performed by a standard procedure, an example of which will be given for metalation of 1,2,3-trimethylbenzene. To 33 ml of butyllithium (1.5 M) in hexane (0.05 equiv), kept in an ice bath, 6.8 ml (0.05 mol) of TMEDA was added dropwise. To this mixture 1 g of 1,2,3-trimethylbenzene was added. The ice bath was removed and the mixture was left at room temperature for the period indicated in Table I, then cooled again in an ice bath and a 5 M excess (65 ml) of trimethylchlorosilane was rapidly added to the solution. The reaction mixture was left overnight, then filtered. The filtrate was washed with aqueous bicarbonate, aqueous 5% hydrochloric acid, and again with aqueous bicarbonate. The solvent was evaporated and the products in the residue were separated by GLC on a 2 m × ¼ in. column of 15% SE-30 on Chromosorb W at 150–190 °C. Yields were evaluated by referring to a standard and were in the range of 85–90%.

Metalation with Butyllithium–Potassium *tert*-Butoxide. 2.8 g of potassium *tert*-butoxide (twice sublimed) was added to a 150-ml reaction flask under an argon atmosphere, followed by 10 ml of dry hexane. The mixture was cooled in an ice bath and 17 ml of butyllithium 1.5 M in hexane (0.025 equiv) was added followed by 1 g of 1,2,3-trimethylbenzene. The reaction mixture was left at room temperature for the period indicated in Table I. A brown-red mass was formed that was filtered on a sintered glass filter under an argon atmosphere and washed with hexane (it is very pyrophoric in air). The brown powder was cooled in an acetone–dry ice bath and dry THF was added followed by 5 g of trimethylchlorosilane. The reaction mixture was left overnight, then water was added, the organic phase separated, and the aqueous layer extracted with ether. Isolation and identification of products was performed as described above. Reaction with trimethylchlorosilane was carried out also directly in the hexane medium and the same reaction products were obtained. The procedure in hexane was used in general.

Reaction with Borane. Metalation was carried out as described above, using 1 g of 1,2,3-trimethylbenzene (0.083 mol), 0.93 g of potassium *tert*-butoxide, and 5.5 ml of butyllithium (1.5 M) in hexane. The reaction mixture was cooled in an ice bath and 8.5 ml of a solution of 2 M borane in THF was added. (Hydroboration was performed also by filtering the reaction mixture and adding dry THF as described above.) The reaction mixture was stirred for 2 h, the excess of diborane decomposed by slow addition of 15 ml of water, and the product oxidized by 10 ml of 3 N NaOH and dropwise addition of 15 ml of 30% hydrogen peroxide with subsequent stirring for 2 h. The organic phase was separated and the aqueous layer was extracted with two 30-ml portions of ether. After evaporation of the solvent, the residue was distilled at 120–130 °C (25 mm), yield 0.9 g (80%). The products were separated at 140 °C by GLC on a 2 m × ¼ in. column of 15% SE-30 on Chromosorb W, mesh size 60/80.

Acetylation was carried out by adding 1 ml of pyridine and 1 ml of acetic anhydride to 0.5 g of the alcohol. The mixture was left overnight, then poured on ice and the product extracted with ether. The ether solution was washed several times with aqueous sodium bicarbonate and after evaporation of the solvent, the products in the residue were separated at 150 °C by GLC on a 2 m × ¼ in. column of 15% DEGS on Chromosorb W.

Metalation in THF. Hexane was evaporated in vacuum from 22 ml of a solution of butyllithium in hexane (1.5 M). The residue was cooled in an acetone–dry ice bath, argon admitted, and 20 ml of dry THF was added. The temperature was brought to 0 °C by changing the dry ice–acetone bath to an ice bath and 1 g of 1,2,3-trimethylbenzene was added. The reaction mixture was left at 0 °C for 48 h. The reaction with trimethylchlorosilane or borane was carried out as described before.

^1H NMR spectra in the presence of Eu(fod)$_3$ were recorded by adding small portions of this shift reagent to CCl_4 solutions of the samples in NMR tubes until well resolved spectra were obtained and further addition had no significant influence on the spectra. (Excess must be avoided, since considerable broadening is obtained.)

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Kinetics and Mechanism of Lithium Aluminum Hydride and Lithium Alkoxyaluminohydride Reductions of Ketones in Diethyl Ether

Karl E. Wiegers[1] and Stanley G. Smith*

Contribution from the Roger Adams Laboratory, School of Chemical Sciences, University of Illinois, Urbana, Illinois 61801.

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Abstract: The kinetics of reaction of the ketones 2,4,6-trimethylbenzophenone, 2,2′-diethylbenzophenone, and 2,2′-dimethylbenzophenone with excess lithium aluminum hydride and lithium *tert*-butoxyaluminohydrides were studied by stopped-flow UV spectroscopy in diethyl ether solution at 25.0 °C. Under these conditions, the reductions are first order in ketone, but the kinetic orders in stoichiometric lithium aluminum hydride range from 0.5 to 0.6, indicating participation by both monomeric and dimeric lithium aluminum hydride. Kinetic isotope effects measured for reductions using $LiAlD_4$ in ether correspond to k_H/k_D values of 1.3–1.4. The rates of reduction by $LiAlH_4$ of substituted 2,4,6-trimethylbenzophenones were correlated with σ constants and yielded a value for ρ of +1.95. The kinetics of ketone reductions with lithium *tert*-butoxyaluminohydrides are consistent with disproportionation of the alkoxide species.

Since the initial discovery of lithium aluminum hydride in 1947,[2] thousands of applications of this powerful reducing agent have been reported.[3] The formulation of detailed mechanisms for the reduction of ketones by lithium aluminum hydride and its alkoxy derivatives[4] in ether solvents has been impeded by the paucity of kinetic data for these very fast reactions and by a lack of information regarding the structure and composition of these reagents in solution.

Recently Ashby and co-workers[5,6] reported association data for several complex metal hydrides and their alkoxy derivatives in diethyl ether and tetrahydrofuran (THF). Between 0.1 and 0.45 m, the association i value for $LiAlH_4$ in ether varies from 1.75 to 2.2,[5,7] but $LiAlH_4$ exists as ion pairs or triple ions in THF.[6] Unfortunately, no association measurements were carried out on the alkoxy derivatives of $LiAlH_4$ in ether.

Since the original preparation of lithium tri-*tert*-butoxy-