Tetrahedron Letters No. 40, pp 3843 - 3846.
© Pergamon Press Ltd. 1979. Printed in Great Britain.

0040-4039/79/1001-3843$02.00/0

SIDE AND CONSECUTIVE REACTIONS IN METALLATION OF ALKYL PHENYL ETHERS:

I. THE REACTION OF PHENETOLE WITH ETHYLLITHIUM

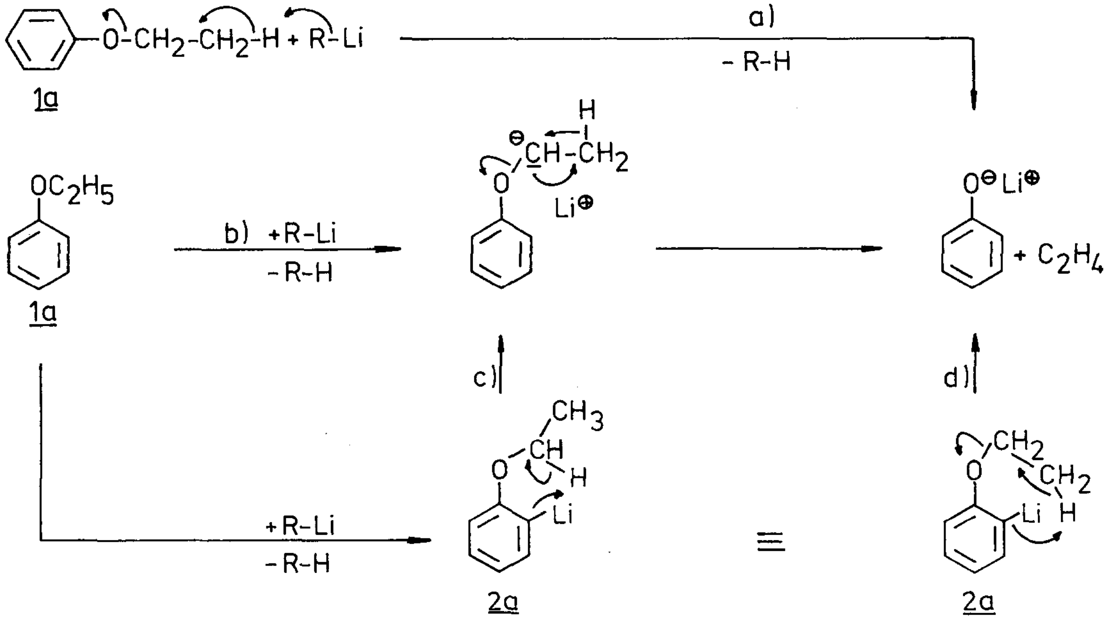
Adalbert Maercker[+] and Rainer W. Stumpe
Gesamthochschule Siegen, Organische Chemie, D-5900 Siegen 21, West Germany

Summary: Two different mechanisms become operative in the cleavage of phenetole by ethyllithium. Furthermore the metallated species adds to ethene or undergoes a condensation reaction to yield a biphenyl derivative.

It is known for a long time that phenetole (1a) can be cleaved by sodium-organic compounds with the formation of ethene and sodium phenoxide.[1)] Six different mechanisms may theoretically become operative, each of them leading to the same reaction products:

a) attack of a ß-hydrogen atom by the base (ß-elimination),
b) attack of an α-hydrogen atom by the base (α-elimination),
c) α-elimination following ortho-metallation (o'α-elimination),
d) ß-elimination following ortho-metallation (o'ß-elimination).

Mechanisms c) and d) not only may occur by an intramolecular but also by an intermolecular process.

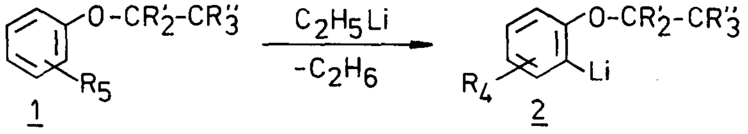


By deuteration of the α-positions Letsinger2) has shown already 20 years ago that with 1b the α-elimination - favoured by Ziegler3) - does not take place. In order to gain more insight into this type of ether cleavage reactions we synthesized the deuterated phenetoles 1c and 1d and treated them without further solvents with $[D_5]$-ethyllithium. Ethyllithium was chosen because this in contrast to the more usual n-butyllithium can be prepared crystalline and free of solvent.4)

Starting with 1c and $[D_5]$-ethyllithium, Letsinger's2) results could be confirmed. The main reaction, however, besides β-elimination being ortho-metallation. $[D_6]$-ethane besides $[D_5]$-ethane and 1,1-$[D_2]$-ethene could be detected by mass spectrometry.

Most interestingly the corresponding β-deuterated species 1d shows a quite different behaviour. Here neither $[D_6]$-ethane nor 1,1-$[D_2]$ethene were present in the gas phase of the reaction mixture. The exclusive formation of $[D_5]$-ethane and $[D_3]$-ethene shows that besides ortho-metallation - which again represents the main reaction path - here only α-elimination becomes operative. Obviously the deuterium isotope effect in these reactions is larger than the difference in activation energy for the α- and β-elimination respectively. The same is true also for the cleavage of dialkyl ethers.5) Increasing substitution of the β-position, however, more and more leads to retardation of the rate of cleavage. Thus it is reasonable to assume that for 1a β-elimination represents the favoured way of cleavage.

	R	R'	R''
a	H	H	H
b	H	D	H
c	D	D	H
d	H	H	D
e	H	D	D

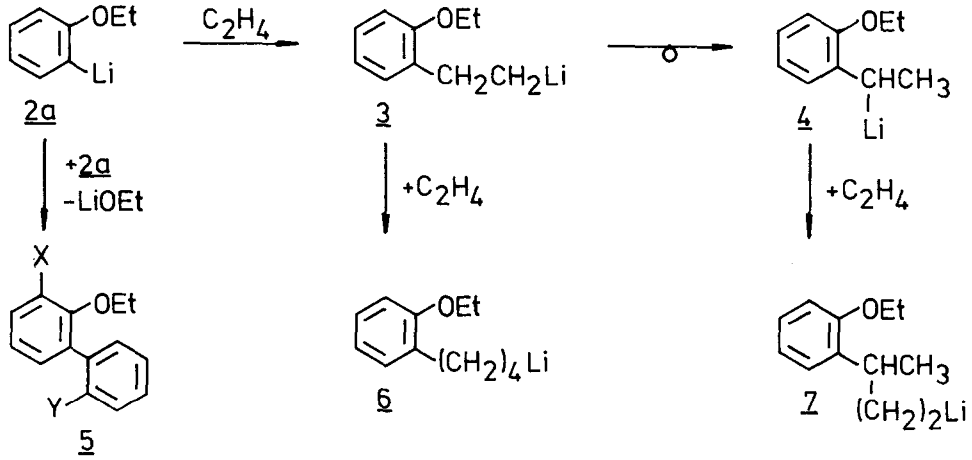


The metallation product of 1a with ethyllithium in THF - in contrast to the literature6) - was found to be exclusively the ortho derivative 2a. Not even a trace of the meta or para derivative could be detected upon treatment with gaseous formaldehyde, solid carbon dioxide or deuterium oxide after various periods of time (2 hours up to several months). 2a is rather stable even in THF as the solvent. Only in the presence of 1e a transmetallation reaction occured, degenerated of course with 1a.

$$\underline{2a} + \underline{1e} \rightleftharpoons \underline{2e} + \underline{1a}$$

The transmetallation is followed by a very slow decomposition of 1a yielding ethene and lithium phenoxide. This ether cleavage reaction corresponds to an intermolecular o'ß-elimination reaction whereby one molecule of 1a is recovered in each step.

Another source for 1a and ethene involves the protophilic attack of the solvent THF by 2a. The hereby formed ethene together with that originating from the cleavage of 1a is partly inserted into the lithium carbon bond of still unchanged 2a. The primarily formed lithium compound 3, however, is rather reactive. Rearrangement to the more stable benzyllithium derivative 4 is catalysed by 1a. Those 1,2 proton shifts obviously cannot take place by an intramolecular process.[7] Higher homologs 6 of the unbranched alkyllithium compound 3 therefore could be found starting from crystalline 2a, when the concentration of 1a in the reaction mixture remains low. The same is true even in the presence of 1a with the corresponding deuterated compound 3, which is formed from $[D_4]$-ethene by working in $[D_8]$-THF. In this case the retardation of the intermolecular 1,2 deuteron shift is due to the deuterium isotope effect.



	X	Y
a	H	H
b	H	Li
c	Li	H

The most interesting reaction of 2a without any doubt is the condensation of two molecules with the formation of a biphenyl derivative 5a. Lithium alkoxide thereby can be split off by an intermolecular as well as by an intramolecular process. The reaction mechanism was found to be strongly dependent on the solvent. In pure THF there is no reason to assume a benzyne intermediate.[8]

A dimer is rather suggested as an intermediate in this condensation reaction, yielding 5a by splitting off lithium ethoxide in an intermolecular process. We could also show that there is no reaction between 2a and 1a itself with the immediate formation of 5a. The first product rather is 5b, a compound which could not have been formed by metallation of 5a, because metallation yields only the additionally found lithium compound 5c.

While in etheral solvents all attempts to trap a benzyne intermediate were unsuccessful,[9] we succeeded in doing so by adding 2 moles N,N,N',N'-tetramethyl ethenediamine (TMEDA) as a strongly complexing agent to a slurry of 2a in benzene. By performing the reaction in the presence of anthracene, triptycene could be isolated by column chromatography. We believe that TMEDA by strongly solvating the lithium cation leads to ionization of the lithium carbon bond with the formation of a solvent separated ion pair followed by splitting off lithium ethoxide intramolecularly yielding benzyne. The benzyne mechanism was also discussed by Glaze[10] for the photolysis of 2-methoxyphenyllithium in diethyl ether. More experiments with 1-[^{13}C]-phenetole are under investigation in order to prove the mechanism of this condensation reaction.

REFERENCES AND NOTES

1) A.A. MORTON and A.E. BRACHMAN, J. Amer. Chem. Soc., 76, 2973 (1954).
2) R.L. LETSINGER and D.F. POLLART, J. Amer. Chem. Soc., 78, 6079 (1956).
3) K. ZIEGLER and H.-G. GELLERT, Liebigs Ann. Chem., 567, 185 (1950).
4) T.V. TALALAEVA and K.A. KOCHESHKOV, J. Gen. Chem. USSR (engl. Transl.), 23, 399 (1953), [Chem. Abstr., 49: 3001b (1955)].
5) A. MAERCKER and W. DEMUTH, Liebigs Ann. Chem., 1977, 1909.
6) D.A. SHIRLEY, J.R. JOHNSON, Jr. and J.P. HENDRIX, J. Organometal. Chem., 11, 209 (1968).
7) A. MAERCKER and J. TROESCH, J. Organometal. Chem., 102, C1 (1975).
8) There are no products arrising from the cleavage of THF by benzyne. Cf. R.S. PAL and M.M. BOKADIA, Pol. J. Chem., 52, 1473 (1978), [Chem. Abstr., 90: 21866k (1979)].
9) G. SCHALLER, Diss., Univ. Erlangen-Nürnberg, West Germany, 1975.
10) W.H. GLAZE and A.C. RANADE, J. Org. Chem., 36, 3331 (1971).

(Received in Germany 17 July 1979)