Tetrahedron Letters, Vol.22, No.44, pp 4355 - 4358, 1981
Printed in Great Britain
0040-4039/81/444355-04$02.00/0

EPR EVIDENCE FOR A SINGLE ELECTRON TRANSFER MECHANISM IN REACTIONS OF AROMATIC KETONES WITH LITHIUM AMIDES

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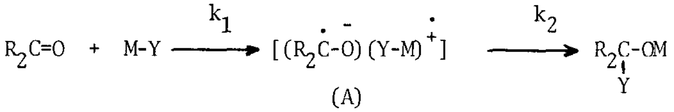
SUMMARY: Direct spectroscopic evidence (EPR) supporting a single electron transfer mechanism in the reaction of lithium amides with aromatic ketones is presented.

We have recently provided convincing evidence in support of a single electron transfer (SET) mechanism in reactions of sterically hindered aromatic ketones with reagents of main group elements (metal alkyls and metal hydrides) (eq. 1) by providing direct spectroscopic evidence (EPR and UV/visible) as well as indirect evidence (product formation studies).[1-6] By using a sterically



$$R_2C{=}O \;+\; M\text{-}Y \xrightarrow{k_1} \underset{(A)}{[(R_2\overset{\cdot}{C}\text{-}\overset{-}{O})(Y\text{-}\overset{\cdot}{M})^{+}]} \xrightarrow{k_2} R_2\underset{Y}{C}\text{-}OM \qquad (1)$$

(Where Y = H or R)

hindered ketone, such as dimesityl ketone, we have been able to detect the radical intermediate (A) by EPR spectroscopy since k_2 should be rate determining when coupling of sterically hindered radicals are involved.[5,6] However, when benzophenone was employed, no stable intermediate was detected. Since k_2 is dependent on the steric requirement of both the ketone and the reagent (M-Y), we decided to study the reactions of benzophenone with more sterically hindered reagents such as lithium amides.

We have recently reported that lithium amides react with polynuclear hydrocarbons and alkyl halides via a SET mechanism.[7] In addition, there are two reports in the literature concerning reactions of lithium di-isopropylamide with benzophenone.[8,9] One report described the mechanism of this reaction to be of a polar nature involving reduction of benzophenone to behzhydrol via a six-center transition state[8] and the second report described the formation of benzhydrol and tetraphenylethylene oxide (no quantitative results) when the reaction was carried out in 20% HMPA/THF (60°C, 24 Hr).[9] Formation of tetraphenylethylene oxide was suggested to proceed via a SET mechanism. It is important to note that no such product could be observed when this reaction was carried out at lower temperature. Furthermore, in reactions of Grignard reagents with benzophenone, we have shown that although the pinacol product $Ph_2C(OH)C(OH)Ph_2$, (precursor of tetraphenylethylene oxide) is an indirect indication of an electron transfer process, it certainly does not provide information about the degree to which electron transfer takes place in the main product forming step. This is because of the fact that the pinacol is merely a minor by-product which can be formed not only as a result of ketyl escape from the solvent cage containing the radical anion-cation intermediate, but also as the result of an independent secondary process. Here we wish to report spectroscopic information concenring the reactions of benzophenone and dimesityl ketone with various lithium amides e.g., lithium di-isopropylamide, lithium di-n-butylamide and lithium diphenylamide, which clearly demonstrates the involvement of a single electron transfer mechanism in these reactions as the major reaction pathway.

When aromatic ketones (benzophenone or dimesityl ketone) were allowed to react with lithium amides (LiNR$_2$ where R = Pr^i, Bu^n and Ph) in THF, blue colored solutions formed which were found to be paramagnetic in nature, exhibiting strong EPR signals. The concentration of the radica intermediate increased with time and eventually reached a maximum concentration. In the reaction of a particular ketone, the rate of electron transfer and the amount of radical intermediate (-35% were observed to be dependent on the nature of the amide reagent. It was found that lithium diispropylamide transfers an electron at a much faster rate than either lithium di-n-butylamide or lithium diphenylamide on reaction with the same ketone. In the reaction of benzophenone with those amide reagents which contain β-hydrogens (such as LiNPr$^i_2$ and LiNBu$^n_2$), the intensity of the EPR signal decreased as the product (Ph$_2$CHOH) formed. However, in the reaction of those same amides with dimesityl ketone, once the maximum EPR signal was observed, no decrease in the EPR signal with time was observed and indeed no reaction product was found on hydrolysis.

In a typical experiment, when lithium di-isopropylamide was allowed to react with a benzophenone solution in THF at 0^{o}C, a deep blue color developed within a few minutes. This solution showed a complex EPR spectrum which consisted of several well-defined lines (Fig. 1). The intensit of the signal increased rapidly with time and after 8 hours the estimated concentration of the radical intermediate was calculated to be ≈35%. Reduction product (Ph$_2$CHOH) was formed slowly throughout the course of the reaction. Complete conversion of benzophenone to benzhydrol was ob-

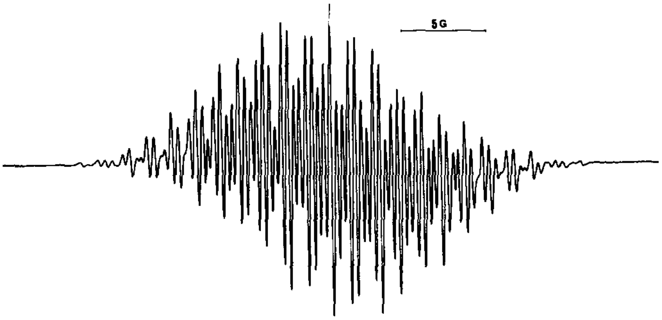
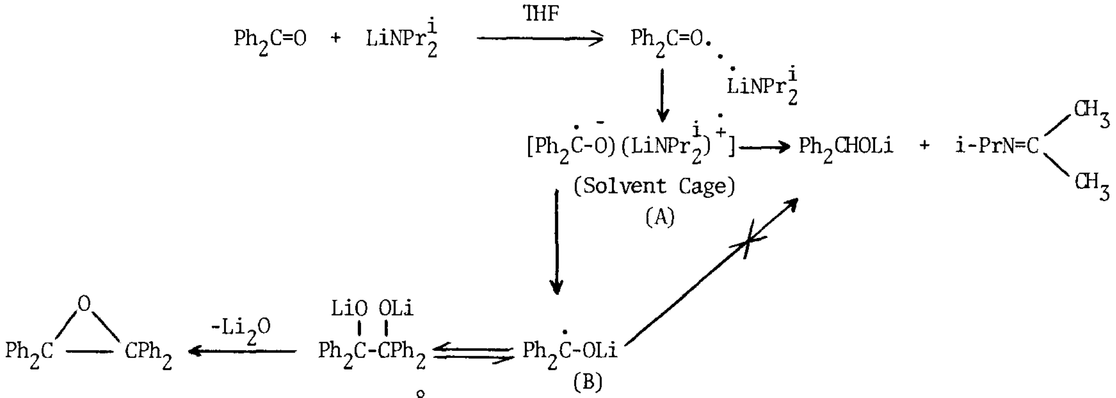


Figure 1: EPR spectrum of the intermediate formed in the reaction of lithium di-ispropylamide and benzophenone in THF at 8^{o}C.

served after 4 days at which time the EPR signal completely disappeared, thus indicating that product formation was proceeding directly from the radical intermediate. Several similar experiments were carried out at temperatures ranging from 0°C to R.T. (24°C) and in every case no other product (e.g., tetraphenylethylene oxide) was observed. The reduction product formed in this reaction is probably the consequence of β-hydrogen atom abstraction from the amide radical cation by the radical anion, (Scheme 1).

SCHEME 1



It was previously shown[8] that the hydrogen involved in reducing benzophenone by LDA is the α-hydrogen of the isopropyl group and the by-product of the reduction is N-isopropyl acetone imine. It also appears that the formation of tetraphenylethylene oxide observed by Scott, et. al., in reactions at highter temperatures is probably the result of a minor side reaction, i.e., the disproportionation of the radical intermediate (A). At lower temperature, this disproportionation does not take place and the reaction proceeds via a β-hydrogen atom transfer step to give exclusively the reduction product. Since lithium benzophenone ketyl is stable in THF and in the presence of the reagents it is unlikely that reduction product is formed as a result of hydrogen atom transfer by (B).

Acknowledgements:

We grately acknowledge support of this work by the National Science Foundation (Grant No. CHE 78-00757).

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(Received in USA 6 June 1981)