Tetrahedron Letters No.48, pp. 6075-6080, 1966. Pergamon Press Ltd.
Printed in Great Britain.

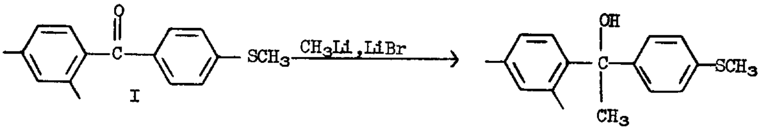
KINETICS OF THE ADDITION OF LITHIUM REAGENTS TO KETONES (1)

Stanley G. Smith (2)

W. A. Noyes Chemical Laboratory
University of Illinois, Urbana, Illinois, 61803

(Received 23 September 1966)

Since lithium reagents and Grignard reagents are of considerable interest, (3) it is desirable to have quantitative measures of their relative reactivity in typical systems. In this paper, the kinetics of the addition of the lithium reagent prepared from methyl bromide and lithium (4) in diethyl ether to 2,4-dimethyl-4'-methylmercaptobenzophenone (I) are presented. These data may be compared with those reported earlier for the reaction of the corresponding Grignard reagent. (5)



The kinetics were measured spectroscopically by following the change in absorbance of the ketone using a stopped flow technique (6) with lithium reagent concentrations from 0.014 to 0.15 M and ketone concentrations in the range of 1 to 3 x 10^{-3} M at 25.0° in diethyl ether. The data, presented as pseudo-first order rate constants for the disappearance of the ketone, are summarized in Table I. These rate constants correspond to reaction half-lives of 0.02 to 0.05 seconds. Under similar conditions, we previously (5) found a pseudo-first order rate constant for the addition of e.g. 0.11 M methylmagnesium bromide to ketone I of 4.6×10^{-3} sec.$^{-1}$, making the lithium reagent ca. 7,000 times more reactive than the Grignard reagent in this reaction, at these concentrations.

TABLE I

Summary of Rate Constants for the Reaction of Methyllithium with Ketone I in Diethyl Ether at 25.0°.

10^2 MeLi, M	10^3 Ketone I, M	k_1, sec.$^{-1}$	$k_1/(\text{MeLi})^{1/4}$
1.39	1.1	13.2	(38)
1.86	1.1	17.9	48
3.22	1.1	24.2	57
3.35	1.2	22.0	51
5.0	2.0	26.0	55
5.5	1.2	27.4	57
6.4	1.2	28.9	57
7.7	1.2	29.3	56
10.1	3.2	30.8	55
10.3	1.2	30.7	54
11.8	2.0	32.2	55
14.8	3.2	34.2	55
		Av.	55 ± 2

A plot, fig. 1, of k_1 vs. the concentration of methyl lithium displays downward curvature. Such non-linearity of the pseudo-first order rate constant in concentration of methyllithium would result if under these conditions the lithium reagent were substantially associated and in rapid equilibrium with more reactive dissociated forms as has been suggested for other reactions involving alkyl lithiums (7). For example, a rate constant, Table I, of 55 $M^{-0.25}$ sec.$^{-1}$ representing a tetrameric reagent (8) in equilibrium with a reactive monomer adequately describes the data now available. Apparent low reaction orders can also arise from a mechanism involving complex formation between the reactants (9). Thus, a mechanism similar to that suggested for the addition of Grignard reagents to ketones (5) is also compatible with the kinetic data. However in marked contrast to the Grignard reagent where a complex displays a unique absorbance in the UV, the spectrum of the ketone in the presence of 0.1 M methyllithium is essentially the same as that of the ketone in ether from 300 to 400 mμ (10). Further experiments are in progress.

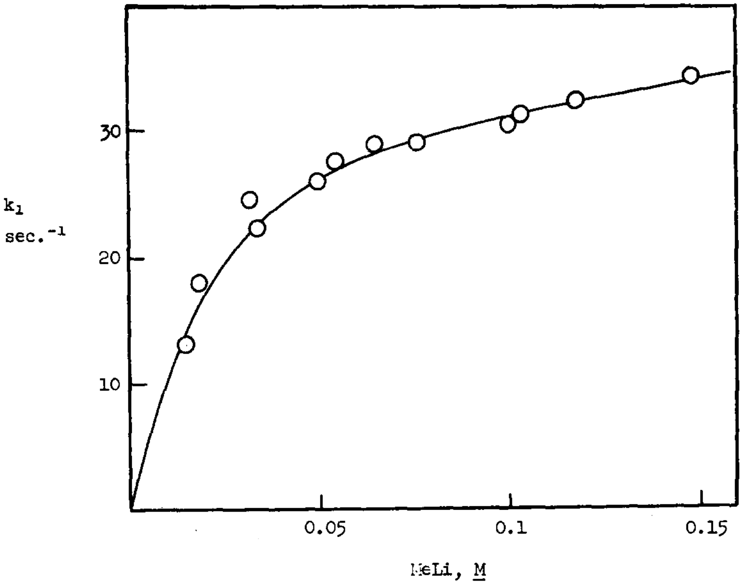


Fig. 1 - Plot of observed first-order rate constant for the reaction of ketone I with an excess of methyllithium in ether at 25.0° *vs.* The concentration of the methyllithium.

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