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KINETIC STUDIES ON THE METALLATION OF LOW ACIDITY ACETYLENIC HYDROCARBONS BY THE UV METHOD

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Summary

1-Phenyl-1-butyne and 1-phenyl-1-propyne have been metallated at the propargylic position with an excess of n-butyllithium in diethyl ether at 25°C. The formation of mono- and di-lithio derivatives has been followed by the UV-Visible method and the pseudo-first order rate coefficients for consecutive irreversible reactions have been calculated. Monolithio derivatives have been prepared by metallation with methyllithium in ether/tetrahydrofuran. The pseudo-first order rate constant of the metallation of the previously prepared monoanion of 1-phenyl-1-butyne to its dianion has been calculated, and found to be about ten times smaller than that obtained from the consecutive reactions.

Introduction

Metallation of acetylenic compounds has been studied extensively. Recently, the reaction has been extended to hydrocarbons of relatively low acidity by employing appropriate solvents and catalysts [1]. Lithiation [2] is particularly useful because of the commercial availability of organolithium reagents and the relative safety in their handling. Only a few kinetic studies have been carried out on lithiation, and these refer mainly to acidic hydrocarbons such as fluorene [3], triphenylmethane [4] and phenylacetylene [5].

In the past few years, it has been demonstrated that acetylenic compounds undergo easy metallation at the propargylic position [1a,6]. The rates of metallation of alkylarylacetylenes were studied by following the formation of the corresponding silylated products [7], employing relatively high concentrations of both substrate and metalating agent.

It is known that organolithium reagents are generally associated [4a,8], and the degree of association depends on various factors, e.g., solvent, concentration and temperature [1d]. Consequently, one would expect changes in the mechanism of the metallation process on varying one or more of the above parameters. We now report some kinetic studies by the UV method of the metallation of acetylenic hydrocarbons with alkyllithium reagents.

Results

1-Phenyl-1-butyne (I) and 1-phenyl-1-propyne (IV) have been metallated with an excess of n-butyllithium (BuLi) in anhydrous diethyl ether at room temperature.

$$\underset{\text{(I)}}{C_6H_5C{\equiv}CCH_2CH_3} \xrightarrow{k_1} \underset{\text{(II)}}{[C_6H_5C{\equiv}CCHCH_3]Li} \xrightarrow{k_2} \underset{\text{(III)}}{[C_6H_5C{\equiv}CCCH_3]Li_2}$$

$$\underset{\text{(IV)}}{C_6H_5C{\equiv}CCH_3} \xrightarrow{k_1'} \underset{\text{(V)}}{[C_6H_5C{\equiv}CCH_2]Li} \xrightarrow{k_2'} \underset{\text{(VI)}}{[C_6H_5C{\equiv}CCH]Li_2}$$

The formation of the anions can be observed in dilute solutions by their UV spectra. Compounds I and IV were added (in separate experiments) directly to a solution of an excess of BuLi in ether in the absorption cell of a UV spectrophotometer, and the spectra of the solutions were recorded at appropriate intervals, with an ethereal solution of BuLi of the same concentration as a reference. Immediately after mixing the components, a strong absorption peak at 362 nm was formed at a region in which the starting materials did not absorb. The absorption peak, which is attributed to monoanion II or V, was gradually shifted to higher wavelengths, until it reached a new maximum at 382 nm, corresponding to the dianion (III or VI). The transformation of the mono- into the dilithium derivative is accompanied in both metallations of I and IV by a bathochromic shift of about 20 nm.

The attempts to measure the rates of the metallation by the UV method gave results which are not always easy to interpret. First, organolithiums are highly sensitive towards atmospheric contaminants, especially water and oxygen. Therefore, basic impurities may be expected to be present to some degree in all samples of these reactions, even though precautions were taken to exclude con-

TABLE 1

UV ABSORPTION DATA FOR LITHIO-DERIVATIVES

Compound [a]	λ_{max} (nm) (ϵ) [b]
II	362(1440)
III	382(10,000)
V	362(645)
VI	382(24,200)

[a] For preparation and measurement conditions see the experimental section. [b] In diethyl ether. [II] = 45×10^{-5} *M*, [III] = 9.15×10^{-5} *M*, [V] = 7.85×10^{-5} *M*, [VI] = 3.59×10^{-5} *M*.

TABLE 2

PSEUDO-FIRST ORDER RATE CONSTANTS DATA FROM METALLATION WITH AN EXCESS OF n-BUTYLLITHIUM IN DIETHYL ETHER AT 25°C

Reaction	k (min^{-1})[a]
I → II	0.013
II → III	0.023
IIa → III	0.0027
IV → V	0.110
V → VI	0.573

[a] All correlation coefficients were higher than 0.98. Initial concentrations: [BuLi] = 3.2×10^{-2} *M*, [I] = 9.15×10^{-5} *M*, [IIa] = 34×10^{-5} *M*, [IV] = 3.59×10^{-5} *M*.

taminants during the preparation and subsequent handling. Second, the absorption band of the mono- and dilithio derivatives of the studied acetylenes overlap closely (Table 1). Moreover, the large molar extinction of the dilithio derivative means that its presence in even small concentrations makes the measurement of the rate of the first step of metallation very difficult. The use of several calculation programs [9] for two consecutive first order reactions permits the interpretation of the results of several sets of k_1 and k_2, and k'_1 and k'_2. In spite of these difficulties, many of the results obtained are in good agreement with each other, and indicate that dimetallation is faster than monometallation (Table 2).

The order with respect to BuLi in diethyl ether is found to be 0.5 in the concentration range of 0.032 *M* to 0.32 *M*, and unity with respect to compound I ([I] = 3×10^{-5} to 14.5×10^{-4} *M*).

Obviously, the close overlap between the absorption bands of II and III and between V and VI, plus the observation that the molar extinctions of each dilithio derivative is of a different order of magnitude from that of its corresponding monolithio derivative, may introduce some errors in the calculation of the rate constants. Therefore, derivative II was prepared independently and then further metallated to form III. According to a known procedure [1b,10], I was metallated with an excess of methyllithium (MeLi) in anhydrous diethyl ether/tetrahydrofuran (64 : 36, respectively) and a monolithio derivative, which will be assigned IIa, was formed. The order with respect to MeLi was 0.37 (in the contration range of 0.055 to 1.09 *M*), and unity with respect to substrate I. Then IIa was treated with BuLi in ether to form the dilithio derivative, III:

$$\text{IIa} \xrightarrow{k_{2a}} \text{III}$$

The reaction was again found to be a first order one with respect to the substrate. However, in contrast with the other results, the order with respect to BuLi was also unity. The pseudo-first order rate constant, k_{2a}, was measured by the same technique, and found to be about ten times smaller than the corresponding k_2 (Table 2).

Discussion

There could be some doubt whether the bathochromic shift on dianion formation reflects a real difference between the absorption of the mono- and di-anions. Shifts of similar magnitude have been found previously on changing the temperature [11], the counterion [11—13], or the solvent [14], or by specific solvation [15] and formation of various solvated species [12]. The solvation and dissociation of the mono- and dilithium derivatives may be different. However, the constancy of the shift in the studied compounds and in other different enyne systems with no phenyl group [16] in which the charge dispersal and solvation are probably different, seems to indicate that there is a difference between the spectra of the mono- and dianions. This conclusion is in agreement with the known spectrum of PhLi [17], in which a bathochromic shift relative to benzene was found for the $\pi \rightarrow \pi^*$ transition.

Metallations with BuLi were generally found to be of fractional order with respect to the organometallic reagent, e.g. 1/6 in benzene solution [3a], 0.5 in THF [3c], 0.25 in THF [4c]. Additions to activated double bonds have also orders in BuLi of 0.4 in THF [18a], 0.3 in ether [18b], and 0.5 in THF [3c,19]. First order reactions in BuLi were also found in additions to ethylene [20] or metallation of indene [21]. Reaction orders for MeLi are also generally fractional, e.g., 0.27 for addition to a double bond in THF [18a], and 0.25 for metallation of triphenylmethane in THF [4c]. It is assumed that the alkyllithium reagents which generally exists as hexameric aggregates in hydrocarbon solutions and tetrameric ones in ethers undergo dissociation to monomers in a preequilibrium reaction (eq. 1) and that the reaction of the monomers with the substrate

$$(\mathrm{RLi})_n \rightleftharpoons n(\mathrm{RLi}) \qquad (1)$$

$$\mathrm{RLi} + \mathrm{S} \rightarrow \mathrm{product} \qquad (2)$$

(S) is a rate-determining step (eq. 2). This explains the 1/6 order in butyllithium in benzene and the 0.25 order in butyl- or methyllithium in ethers. The half order in butyllithium in THF was explained [3c,19] by the assumption that in this solvent a butyllithium dimer is the species that is present. Others, however, assume the presence of tetramers in this solvent [4c,18a].

The order of 0.5 for butyllithium in the metallations of I and IV in ether, in which this reagent exists in tetrameric form [3a,22], requires either that the active species is the dimer [2] and not the monomer or that a more complex

$$(\mathrm{RLi})_4 \rightleftharpoons 2(\mathrm{RLi})_2 \qquad (3)$$

$$(\mathrm{RLi})_2 + \mathrm{I}\ (\text{or IV}) \rightarrow \mathrm{II}\ (\text{or V}) \qquad (4)$$

reaction occurs (eq. 3, 4). The last possibility would accommodate other orders such as 0.4; 0.5; 0.3 or 0.37, as found in the metallation of I with MeLi. These may be artifacts due to inaccurate measurements, or to mixed reactions, in which monomer, dimer, and tetramer react, each with its specific rate constant. A more involved mechanism consists of additional equilibria between organolithium compound (again, as monomer or its various aggregates) and the substrate, in the case the acetylene.

The interpretation of the second step of metallation of the mono- to the dilithio derivative is even more complicated, because of a lack of information on the structure of the monolithiated intermediate. This may be present in solution as a monomer (e.g., benzyllithium is monomeric in THF and phenyllithium is dimeric in ether [8b]), as a dimer, or in the form of various aggregates with itself or with the metallating agent. The difference in the rate constant for dimetallation of I by direct reaction with butyllithium from that when the monolithiated compound was prepared with methyllithium (k_2 and k_{2a}, respectively) may be ascribed to complexes with different metallating reagents, or with lithium bromide, or again to a different solvation by the small amount of THF present in the IIa solution. The order of unity with respect to butyllithium may be due either to a direct proton abstraction

$$C_6H_5C{\equiv}CCHLiCH_3{\cdot}MeLi + (BuLi)_4 \rightarrow C_6H_5C{\equiv}CCLi_2CH_3 \tag{5}$$

(eq. 5) or to a rate-determining (r.d.) displacement of methyllithium by butyllithium in the complex, followed by an intramolecular proton abstraction by BuLi (eq. 6).

$$\begin{tikzcd} \underset{(IIa)}{C_6H_5C{\equiv}CCHLiCH_3 \cdot MeLi} + (BuLi)_4 \arrow[r] & C_6H_5C{\equiv}CCHLiCH_3 \cdot BuLi \arrow[d, "r.d."] \\ & C_6H_5C{\equiv}CCLi_2CH_3 \end{tikzcd} \tag{6}$$

Experimental

Reagents

Tetrahydrofuran was first dried over calcium hydride and immediately before use was distilled under argon from lithium benzophenone ketyl. Diethyl ether was distilled from lithium aluminium tetrahydride and stored over strips of sodium metal. Pure 1-phenyl-1-butyne and 1-phenyl-1-propyne were purchased from Farchan Research Laboratories and used without purification. Methyllithium was prepared in diethyl ether at ~1.2 M concentration from methyl bromide and excess lithium metal. n-Butyllithium in hexane was purchased from Foote Mineral Co. Preparation of this reagent in diethyl ether was carried out by a vacuum technique with which the hexane was distilled off and anhydrous diethyl ether, of about the same volume as the distillate, was added to the oily butyllithium. The total alkalinity, of both methyl- and butyl-lithium, was measured by double titration with 0.10 M HCl and 0.10 M NaOH using phenolphthalein as indicator.

Kinetic measurements

A large excess of the metallating reagent over substrate was always employed. The pseudo-first order rate coefficients were obtained by measuring D_t, the absorbance of the reaction solution at time t, and D_∞, the maximum absorbance at a given concentration. Most reactions were run at least in duplicate, the reproducibility being ±3%. The reactions were followed by measuring the rate of increase of the monoanion spectrum at 362 nm and of the dianion spectrum at 382 nm, employing a UV-Visible spectrophotometer. All spectra were recorded at 25°C after injecting the appropriate amount of substrate to the measuring cell containing the metallating agent under an inert atmosphere. A cell containing the appropriate alkyl lithium and concentration was used as the reference.

Concentrations

For studying the reaction orders with respect to BuLi and MeLi, concentrations of 0.016 to 0.32 *M* and 0.055 to 1.09 *M*, respectively, were used. For measuring λ_{max} and ϵ of the monolithio derivatives, II and V, their preparation was accomplished by employing [MeLi] = 0.218 *M* in diethyl ether/THF mixture (64 : 36 by volume, respectively) and 5×10^{-3} *M* of both I and IV. The exact concentrations of II and V in the metallation mixtures were determined by quenching with trimethylchlorosilane. An aliquot from each of the metallation mixtures was diluted with a known volume of ether and the spectrum was recorded. (The exact concentrations are written underneath Table 1). This procedure was repeated at least three times to diminish possible errors. Since substrate IV could undergo trimetallation in excess of BuLi, the dilithio derivative VI was prepared separately by metallation with two mol of BuLi and then diluting an aliquot with ether and recording the spectrum for measuring the molar extinction (Table 1).

For the metallation of IIa to III, substrate I (5×10^{-3} *M*) was metallated with MeLi (0.218 *M*) to form IIa. Then, in separate experiments, aliquots of 0.06—0.20 ml were introduced into the measurement cell which contained n-BuLi (0.032—0.32 *M*) in diethyl ether. The spectra of the monoanion were recorded at various times.

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