

**Figure 2.** Spectra of alamethicin in methanol- $d_4$ : (a) one-dimensional spectrum, (b) two-dimensional absorption mode homonuclear cross-polarization spectrum, and (c)–(e) cross section taken parallel to the  $F_1$  axis at the  $H(C_\alpha)$  chemical shifts of Leu 12, Pro 14, and Pro 2, respectively. These positions are indicated by arrows in the 2D spectrum. A complete assignment of the spectral region shown is available in a supplementary table.

agree with spectral assignments made by Davis and Gisin<sup>13</sup> and Banerjee et al.<sup>14</sup> A large number of relay connectivities are observed for this mixing time; for example, the  $H(C_\alpha)$ –Me connectivities for Val 9, Val 15, and Leu 12 are readily identified. Cross sections parallel to the  $F_1$  axis, taken at the  $H(C_\alpha)$  chemical shifts of Pro 14 and Pro 2 (Figure 2d,e) clearly show the connectivity to the  $C_\beta$  protons and relay to the  $C_\gamma$  and  $C_\delta$  protons. A similar section taken at  $H(C_\alpha)$  of Leu 12 (Figure 2c) shows the connectivity to the inequivalent  $C_\beta$  protons at 1.95 and (previously misassigned) 1.58 ppm and relay to the  $C_\gamma$  (1.92 ppm) and  $C_\delta$  protons (0.91 and 0.94 ppm). Some other new assignments are also found and are available in a supplementary table.

The experiment described in this paper relies on the same principles as heteronuclear cross-polarization experiments<sup>1–4</sup> and

is also closely related to the TOCSY experiment<sup>10</sup> and to experiments concerning the disappearance of  $J$  modulation in the presence of very rapid pulsing.<sup>15–17</sup>

Clearly, the method described in this paper is extremely powerful for the analysis of complicated coupling networks. Preliminary experiments on a number of proteins have shown that the method is particularly suitable for determination of connectivity in poorly resolved systems. As will be demonstrated elsewhere, effective suppression of the water resonance is also feasible with this technique. The experimental scheme of our new technique shows a close resemblance to an experiment proposed recently for the measurement of transverse NOE.<sup>18</sup> However, for the short mixing times used in the new experiment cross peaks due to NOE are often very weak and will also have opposite sign relative to diagonal and Hartmann–Hahn cross peaks.<sup>19</sup>

**Acknowledgment.** We are indebted to Rolf Tschudin for continuous technical support.

**Registry No.** Alamethicin, 27061-78-5.

**Supplementary Material Available:** Table of high-field  $^1H$  NMR assignments of alamethicin (1 page). Ordering information is given on any current masthead page.

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### Transition Structures for Additions of LiH and MeLi to Ethylene and Acetylene

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Received January 15, 1985

The additions of alkyllithium compounds to double and triple bonds and the reverse processes, such as  $\beta$ -hydride eliminations from alkyllithiums to give alkenes, are synthetically useful reactions.<sup>2</sup> Such additions to cyclic olefins proceed with syn stereochemistry.<sup>3</sup> Eliminations can be catalyzed by hydride acceptors at low temperatures,<sup>4</sup> and have therefore been proposed to be stepwise reactions involving intermediate  $\beta$ -lithiocarbenium ions.<sup>5</sup> However, concerted mechanisms for LiH eliminations from alkyllithiums are indicated by recent experiments.<sup>6</sup> This prompted us to extend our work on LiH and  $CH_3Li$  additions to carbonyl compounds<sup>7</sup> to the corresponding reactions involving carbon-carbon multiple bonds.

The geometries of the species shown in Figure 1 were optimized with the 3-21G basis set<sup>8</sup> using the GAUSSIAN 80 and 82 series of

(1) (a) University of Pittsburgh. (b) Universität Erlangen-Nürnberg.  
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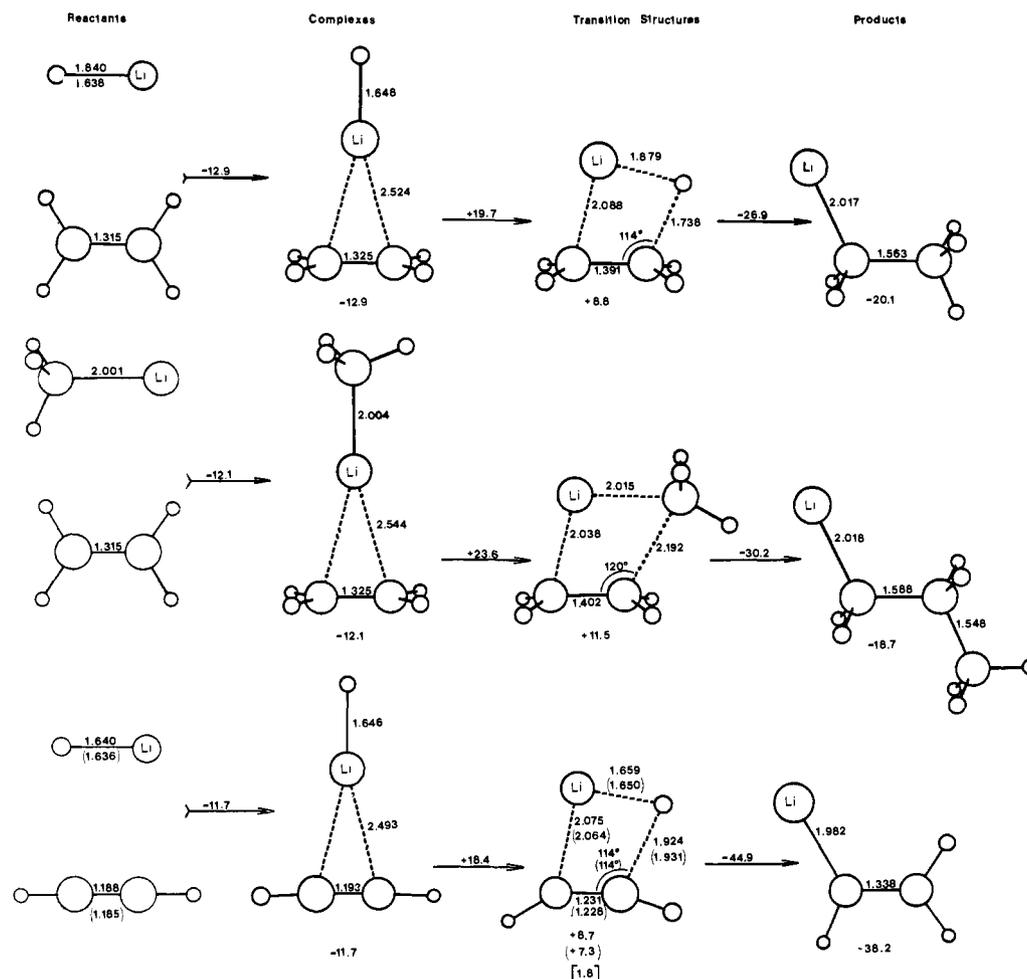


Figure 1. 3-21G (6-31G\*) geometries for reactions of LiH with ethylene, MeLi with ethylene, and LiH with acetylene. Energies shown under the structures are relative to isolated reactants. The [MP2/6-31G\*\*//6-31G\*] energy of the LiH + acetylene transition structure is given in brackets.

programs.<sup>9,10</sup> Transition structures were characterized as stationary points with one imaginary frequency. The transition structure for the reaction of LiH with acetylene was also located with the more extensive 6-31G\* basis set.<sup>11</sup> The 3-21G transition structures for the additions of H<sup>-</sup> and CH<sub>3</sub><sup>-</sup> to ethylene and of H<sup>-</sup> to acetylene are shown for comparison in Figure 2.<sup>12</sup>

The geometry and energy of the transition structure studied with two basis sets changes very little upon improvement of the basis set (see Figure 1). While electron correlation is relatively unimportant for relative energies of stable ionic species,<sup>13</sup> single-point MP2/6-31G\* calculations on 6-31G\* geometries on the

LiH + acetylene reaction indicate that the activation energy is significantly lowered by inclusion of correlation energy corrections.

Monomeric LiH and MeLi form relatively stable complexes with  $\pi$  bonded molecules.<sup>14</sup> In solution, where lithium compounds are aggregated and solvated,<sup>2a,15</sup> an analogous complex could be formed by displacement of a solvent molecule. Before correlation energy corrections, the conversion of the complexes to addition products requires activation energies of 18–24 kcal/mol. The transition structures for LiH addition to both ethylene and acetylene are about 7 kcal/mol above the reactants;<sup>16</sup> this value is 12 kcal/mol for the MeLi addition.

The calculated activation energy for  $\beta$ -hydride elimination from ethyllithium is 27 kcal/mol, which compares favorably with the experimental activation energy of  $30.3 \pm 0.3$  kcal/mol measured from associated (probably hexameric) octyllithium.<sup>6</sup> The calculated activation energy for MeLi elimination from propyllithium is 3 kcal/mol higher than for LiH elimination from ethyllithium. This is consistent with the experimental observation that LiH elimination is faster than RLi elimination.<sup>2</sup>

Activation energies for hydride addition to ethylene and acetylene have been estimated at 16 kcal/mol.<sup>11</sup> The presence of Li<sup>+</sup> lowers the activation energy relative to isolated reactants by at least 10 kcal/mol. This can be attributed to the electrostatic stabilization of the developing carbanion by Li<sup>+</sup>. The position of Li<sup>+</sup> in the complexes and transition structures is very similar,

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(10) Complete geometries and energies are available as supplementary material.

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(12) The 3-21G activation energies are -4.9, -1.3, and -2.1 kcal/mol, respectively, since an electrostatically stabilized ion-molecule complex of reactants is formed in these reactions. 4-31G transition structures for the addition of H<sup>-</sup> to ethylene and acetylene (Strozier, R. W.; Caramella, P.; Houk, K. N. *J. Am. Chem. Soc.* **1979**, *101*, 1340) and a DZ + diffuse basis transition structure for H<sup>-</sup> plus acetylene (Dykstra, C. E.; Arduengo, A. J.; Fukunaga, T. *J. Am. Chem. Soc.* **1978**, *100*, 6007) have been reported previously. Experimental activation energies of about 16 kcal/mol are estimated for H<sup>-</sup> additions in these references.

(13) E.g.: Kos, A. J.; Jemmis, E. D.; Schleyer, P. v. R.; Gleiter, R.; Fischbach, U.; Pople, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 4996.

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(16) LiH does not add to unsaturated hydrocarbons under normal conditions because it is an insoluble crystalline aggregate.

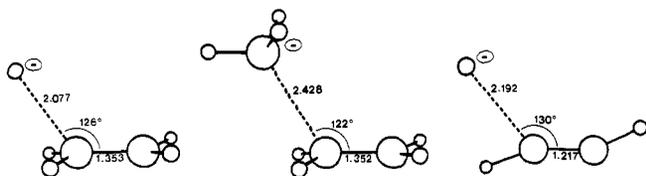


Figure 2. 3-21G geometries of transition structures for reactions of hydride with ethylene, methyl anion with ethylene, and hydride with acetylene.

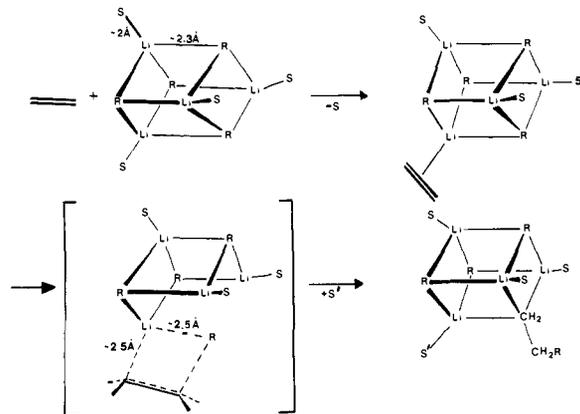


Figure 3. Possible mechanism for the addition of an alkyllithium tetramer to ethylene.

with some lateral displacement and a significant decrease of the  $C^{\delta-}-Li^+$  distance.<sup>17</sup>

The angle of attack of  $H^-$  or  $Me^-$  on ethylene or acetylene is significantly larger than tetrahedral,<sup>18</sup> even though little CC bonding has developed in the transition structures. The presence of the  $Li^+$  counterion decreases this angle slightly, as compared to isolated anion additions.

Activation energies and transition structures for additions to formaldehyde are not influenced significantly by dimerization of  $LiH$  or  $MeLi$ ,<sup>7</sup> perhaps because the aggregation of organolithium compounds arises primarily from electrostatic effects.<sup>19</sup> A conceivable mechanism of addition of a solvated lithium tetramer to ethylene is shown in Figure 3. Displacement of solvent and coordination of ethylene should be slightly exothermic, since initial solvation energies of alkyllithium tetramers with THF are typically 7–8 kcal/mol, and 2–6 kcal/mol with ether.<sup>20</sup> Since the lone pair of the methyl anion is pointed toward the center of the lithium tetrahedron, two of the methyl–lithium bonds must be lengthened in order to allow rotation of the lone-pair to interact with the ethylene terminus. The activating effect of Lewis basic solvents upon the addition reaction<sup>2a</sup> may be due to greater ease of lengthening of these bonds when lithium is additionally coordinated in the transition state.

**Acknowledgment.** We are grateful to the National Science Foundation, the Deutsche Forschungsgemeinschaft, and the Fonds der Chemischen Industrie for financial support of this research and to the Alexander von Humboldt Foundation for a U.S. Senior Scientist Award to K.N.H.

**Registry No.**  $LiH$ , 7580-67-8;  $CH_3Li$ , 917-54-4; ethylene, 74-85-1; acetylene, 74-86-2.

**Supplementary Material Available:** Listings of geometries and energies (4 pages). Ordering information is given on any current masthead page.

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## Multiple Substitutions in Radical-Chain Chlorinations. A New Cage Effect

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It is widely agreed that radical-chain  $Cl_2$  chlorinations of aliphatic systems in noncomplexing solvents or in gas phase are slower when electronegative substituents are present;<sup>1a</sup> For example, alkyl chlorides react less rapidly than the corresponding alkanes. Thus, the behavior we report here appears to be anomalous: In  $CCl_4$  or  $CFCl_3$  solvents, photochlorinations with low conversions of cyclohexane, isobutane, neopentane, or 2,3-dimethylbutane, with careful exclusion of  $O_2$ , result in formation of unexpectedly large proportions of multiply chlorinated products, resulting from further chlorination of the monochloro products. Although this is an effect which gives the appearance that the chloro derivatives are more reactive than the alkane, the dependence on alkane concentration leads us to a novel proposal, a type of elementary process which appears to have been unrecognized heretofore.

For example 1000  $\mu\text{mol}$  of purified cyclohexane (purity 99.99%; 0.10 M) with 309  $\mu\text{mol}$  of  $Cl_2$  in  $CCl_4$  (10 mL) shows no product formation in the dark, but on brief exposure to a tungsten lamp results in formation of 74  $\mu\text{mol}$  of cyclohexyl chloride, 67  $\mu\text{mol}$  of dichlorides, and 39  $\mu\text{mol}$  of a mixture of trichlorides; these are produced in the presence of more than 800  $\mu\text{mol}$  of unreacted cyclohexane. The composition of these multiply halogenated products is readily recognizable with GC-mass spectrum analysis. Thus, cyclohexyl chloride appears to be far more reactive than cyclohexane. The more usual behavior, cyclohexane more reactive than cyclohexyl chloride, is observed in chlorination of undiluted cyclohexane (18.5 mmol; no added solvent) with 483  $\mu\text{mol}$  of  $Cl_2$ , resulting in formation of 460  $\mu\text{mol}$  of cyclohexyl chloride and 15  $\mu\text{mol}$  of dichlorides (no trichlorides).

With low conversion conditions we report here that the amount of polychlorinated product relative to the total amount of chlorinated product increases with decreasing concentration of cyclohexane. This can be seen in Table I. In the first four reactions, each starting with 10 mol %  $Cl_2$  with respect to cyclohexane, the percentage of polychlorinated product increases from 6% in the photochlorination of neat cyclohexane to 56% in the reaction carried out with 0.030 M cyclohexane in  $CCl_4$ . The same increases in the percentage of polychlorinated product were observed in the reactions that initially contained 30 mol %  $Cl_2$ . Despite the 3-fold greater conversion of the cyclohexane, there is only a slightly increased percentage of polychlorinated product. This effect is independent of the  $Cl_2$  concentration and is attributable to the change of cyclohexane concentration and to the percentage of its conversion. For example, a reaction of 0.020 M cyclohexane in  $CCl_4$  in the presence of 0.031 M  $Cl_2$ , stopped early by quenching with corn oil, resulted in  $\sim 20\%$  loss of the original 200  $\mu\text{mol}$  of cyclohexane and production of 12.4  $\mu\text{mol}$  of cyclohexyl chloride, 16.0  $\mu\text{mol}$  of dichlorides, and 11.0  $\mu\text{mol}$  of a mixture of trichlorides, 68% polychlorinated product. A reaction identical except for 0.006 M  $Cl_2$  resulted in an identical product composition. Thus, the percentage of polychlorination is independent of  $[Cl_2]$  and dependent on  $[C_6H_{12}]$ .

An analogous result is obtained with low conversion photochlorinations of 2,3-dimethylbutane (DMB). In pure DMB the two isomeric  $C_6H_{13}Cl$ 's are produced in  $\sim 100\%$  yield; with 0.10 M DMB in  $CFCl_3$  (10 mL), 102  $\mu\text{mol}$  of  $Cl_2$  produces 41  $\mu\text{mol}$  of monochlorides and 24  $\mu\text{mol}$  of dichlorides. This result is independent of either the presence of HCl produced in the reaction, or its presence initially at 0.5 M, or of scavenging of HCl by anhydrous  $K_2CO_3$ .

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