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Kinetic Study of a Lanthanide Catalyzed Mukaiyama Addition Reaction

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ABSTRACT.-The reaction of benzaldehyde with the trimethylsilyl enolate of methyl isobutyrate catalyzed by Cp"2YbCl is first order in the enolate and first order in the Lewis acid-base complex of the Yb compound with the aldehyde. Trimethylsilyl chloride needs to be present but does not appear in the rate expression. A mechanism is proposed.

Bis(1,3-bis(trimethylsilyl)cyclopentadienyl)ytterbium(III) chloride, Cp"2YbCl, 1, has been shown [1] to be an effective catalyst for the Mukaiyama-type reaction [2] of aldehydes with the silyl enolates of esters. Unlike the typical Lewis acids used for such Mukaiyama reactions, such as titanium tetrachloride, which must be used in stoichiometric amounts, 1 is a catalyst that is effective in 1 mole percent quantities. The significant stereochemical specificity shown by 1 suggests that it may become a useful reagent for organic synthesis. Accordingly, we present here a kinetic study of this reaction as an aid to determining the reaction mechanism. The reaction studied is shown in the following equation:

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Kinetic Runs: Appropriate amounts of the trimethylsilyl enol ether of methyl isobutyrate, 2, benzaldehyde, the catalyst 1 and trimethyl-silyl chloride were loaded in an NMR tube and dissolved in 0.6 mL of CD$_2$Cl$_2$. The initial time was recorded on mixing. The $^1$H NMR spectra were run on UC Berkeley FT-NMR 200 and 250 MHz instruments equipped with superconducting magnets, deuterium lock system and Nicolet software. Temperature was monitored by a Doric Trendicator 410A. The temperature in all runs varied from 19.8-23.0 °C but within a run the variation was 0.2 °C. The reactions were monitored by the integrated proton peaks of the methyl and methoxy groups of 2 and 3. Pseudo-first order rate constants were determined from the change in the ratio of 2/(2+3). Second order rate constants were obtained by dividing by the concentrations of 1. Results are summarized in Table I.

Table I. Kinetic results

<table>
<thead>
<tr>
<th>Run</th>
<th>2 M</th>
<th>PhCHO, M</th>
<th>1, M</th>
<th>TMSCI, M</th>
<th>$10^3k_1$, s$^{-1}$</th>
<th>$k_2$, s$^{-1}$M$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.40</td>
<td>0.44</td>
<td>0.023</td>
<td>0.47</td>
<td>4.1</td>
<td>0.18</td>
</tr>
<tr>
<td>2</td>
<td>0.41</td>
<td>0.44</td>
<td>0.046</td>
<td>0.42</td>
<td>7.9</td>
<td>0.17</td>
</tr>
<tr>
<td>3</td>
<td>0.39</td>
<td>0.87</td>
<td>0.083</td>
<td>0.53</td>
<td>16.5</td>
<td>0.20</td>
</tr>
<tr>
<td>4</td>
<td>0.39</td>
<td>0.46</td>
<td>0.020</td>
<td>0</td>
<td>a</td>
<td>a</td>
</tr>
<tr>
<td>5</td>
<td>0.40</td>
<td>0.43</td>
<td>0.045</td>
<td>0.59</td>
<td>7.1</td>
<td>0.16</td>
</tr>
<tr>
<td>6</td>
<td>0.94$^b$</td>
<td>1.07</td>
<td>0.058</td>
<td>1.38</td>
<td>4.8</td>
<td>0.08</td>
</tr>
<tr>
<td>7</td>
<td>0.41</td>
<td>0.48</td>
<td>0.035</td>
<td>0.41$^c$</td>
<td>4.9</td>
<td>0.14</td>
</tr>
</tbody>
</table>

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$^a$Rate is slower but kinetic behavior was poor.
$^b$Silyl enol ether = Z-1-t-butyldimethylsilyloxy-1-ethoxy-1-propene
$^c$TMSCI was replaced by t-BuMe$_2$SiCl.

First order kinetics in the concentration of 2 was found. Runs 1-3 show that the reaction is pseudo-first order in the catalyst concentration. The concentration of the aldehyde is not important since it complexes with the aldehyde. This complexation was shown by the color change on adding aldehyde to the catalyst and by the following NMR experiment. A mixture of 1 mole of p-tolualdehyde and 0.1 mole of 1 in toluene-d$_8$ showed broadened resonances for the aromatic and
aldehyde protons indicative of fast exchange with the paramagnetic species. On cooling to -40 °C, the peaks, including the aldehyde proton at 10 ppm, narrowed as the slow exchange limit was approached. Thus, the exchange of free and coordinated aldehyde is rapid at room temperature. That complexation is complete was shown by infrared spectroscopy. A sample of 1 molar equivalent each of benzaldehyde and 1 in CH2Cl2 showed a strong absorption at 1660 cm⁻¹ for the coordinated aldehyde but none at 1720 cm⁻¹ for free benzaldehyde.

In the absence of added trimethylsilyl chloride, reaction is slow and erratic. In runs 1, 2, 3 and 5 the molar equivalents of TMSCl vary from 1.0 to 1.5 without a significant effect on the rate constant. Thus, so long as some added TMSCl is present it has no effect on the rate. Use of the more hindered t-butyldimethylsilyl chloride (run 7) has little effect on the rate. When the hindered silyl group is put on the enol ether (run 6) it does have a small but significant rate-retarding effect. Finally, in the absence of aldehyde, silyl exchange of this silyl enol ether with TMSCl does not occur.

The kinetic results are consistent with a mechanism in which the rate determining step involves reaction of the silyl enolate with the aldehyde-coordinated ytterbium complex to give an intermediate ytterbium-complexed aldol product, 4, with loss of TMSCl. The intermediate 4 reacts rapidly with the external TMSCl to give the silylated product 3 liberating the catalyst which then rapidly coordinates with aldehyde to start the process anew. This mechanism is shown in the Scheme, with a model for the transition state that is also consistent with the stereochemical results. The dotted lines in this transition state represent bonding interactions that may well be essentially ionic. This transition state is based on the Chan, et al [3] modification of the familiar Zimmerman-Traxler cyclic model [4]. The direct involvement of the silyl group at the transition state is consistent with the retarding effect of a t-butyl group on silicon.

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SCHEME

OR

\[ \text{O}_\text{SiMe}_3 + \text{Cp''}_2 \text{YbCl}_\text{OCHPh} \]

\[ \text{Cp''} \text{YbCl} + \text{Cp''}_2 \text{YbCl} \]

REFERENCES
