Thermally Initiated $S_{RN1}$ Reactions of Ketone Enolates with Iodobenzene in Dimethyl Sulfoxide. Relative Reactivities of Enolate Ions with Phenyl Radical

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Received May 18, 1984

The enolate ions of acetone, pinacolone, cyclohexanone, 2-butanone, and 3-pentanone react smoothly in the dark with iodobenzene in Me$_2$SO to give high yields of substitution product. Phenylacetone enolate reacts very slowly, and 2-acyclocyclohexanone enolate fails to react. The relative reactivities of these enolate ions as determined from competition experiments in which pairs of enolates are allowed to react with PhI in Me$_2$SO are pinacolone 1.00, acetone 1.09, cyclohexanone 0.67, 2-butanone 1.10 (total reactivity), 3-pentanone 1.40, and phenylacetone 0.39. The data show that there is less than a 4-fold difference in reactivity among the enolates nucleophiles despite a basicity difference of nearly 10$^3$. These reactivities are interpreted as measurements of the relative rates of reaction of the enolates with phenyl radical. The results are consistent with the notion that the reaction of enolate ions (and other nucleophiles) with phenyl radical occurs at or near the encounter controlled limit.

Recently Scamehorn and Bunnett have described a remarkable reaction between pinacolone enolate ion and iodobenzene in Me$_2$SO.2 This aromatic nucleophilic substitution reaction, which proceeds rapidly in the dark, has been shown to have the characteristics of a free radical chain reaction, and is thought to occur by the $S_{RN1}$ mechanism3 (eq 1). The reaction is stimulated by light, inhibited by radical scavengers, and follows a complex kinetic rate equation. All of these effects, as well as many others, are readily accommodated by the radical chain mechanism of Scheme I (plus various termination steps) but not by other mechanisms for aromatic nucleophilic substitution. In Scheme I, initiation occurs by electron transfer to iodobenzene producing a radical anion. In the dark reactions which are the subject of this report, this is a thermal process and most likely involves electron transfer from the enolate ion.45

Scheme I

\[ \text{PhI} + e^- \rightarrow [\text{PhI}]^- \]  
\[ [\text{PhI}]^- \rightarrow \text{Ph}^- + \text{I}^- \]  
\[ \text{Ph}^- + \text{R}^- \rightarrow [\text{PhR}]^- \]  
\[ [\text{PhR}]^- \rightarrow [\text{PhI}]^- + \text{PhR} \]

We have found that other ketone enolate ions also undergo this dark reaction in Me$_2$SO. The reactions of several ketone enolates with iodobenzene were studied, and the relative reactivities of various enolate ions with iodobenzene were measured, both individually and in competition reactions with iodobenzene. These reactions are particularly well suited to reactivity studies of this kind. They do not depend on photostimulation, and they do not require liquid ammonia, the solvent used for most $S_{RN1}$

| Table 1. Dark Reactions of Ketone Enolate Ions (0.40 M) with Iodobenzene (0.10 M) in Me$_2$SO at 25 °C for 60 Min |
|-------------|-----|-----|
| ketone       | I-  | PhR |
| acetone      | 55  | 50  |
| pinacolone   | 65  | 60  |
| cyclohexanone| 95  | 70$^a$ |
| 2-butanone   | 80  | 70$^a$ |
| 3-pentanone  | 75  | 70  |
| phenylacetone| <1  | <1$^a$ |
| 2-acyclocyclohexanone | 0  |

$^a$ Iodide determinations by titration; substitution product yields (PhR) determined by GLC; average of 2-4 experiments and rounded to nearest 5%. Benzene, 25%, also found. $^b$ Two enolates form; the ratio of 3-phenyl/1-phenyl products is 2.8. $^c$ Yields of PhR ranged from trace (ca. 0.2%) to 1.2%.

Results and Discussion

The results of the dark reactions of several enolate ions with iodobenzene in Me$_2$SO are summarized in Table I. In all cases, potassium enolates were generated by interaction of potassium tert-butoxide with the corresponding ketone. In Me$_2$SO, potassium tert-butoxide is a considerably stronger base than any of the enolates studied, and conversion of the ketones to enolate ions is complete under the conditions utilized. The reactions summarized in Table I were conducted under identical conditions for 1 h. The results represent a measure of the reactivity of the enolate ions reacting individually. The data show that all of the enolates react at about the same rate except the more weakly basic ones, phenylacetone and 2-acyclocyclohexanone. Phenylacetone enolate (ketone pKa (Me$_2$SO) 19.8) reacts at least 50 times slower with iodobenzene than does the pinacolone counterpart. 2-Acylocyclohexanone enolate (ketone pKa (DMF) 14.1) failed to react. 2-Butanone reacts with potassium tert-butoxide to give anions which form 3-phenyl- and 1-phenyl-2-butanone in a 2.8:1 ratio. This is not far from the 3-phenyl/1-phenyl ratio of 2.2 reported by Rossi and Bunnett$^5$ for the photostimulated reaction in liquid am-

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(1) Presented in part at the 16th Great Lakes Regional ACS Meeting, Illinois State University, June, 1982. Abstract 211.
that the product distribution is determined in eq (6). The analysis entails the assumption that the complex kinetics are characteristic of these SRN1 dark reactions in Me$_2$SO, and are not due to impurities generated during the reaction by trace amounts of oxygen. Thus, attempts to scale up these reactions for preparative purposes are often unsuccessful. Higher concentrations of iodobenzene produce little increase in rate, and lower percent conversions result.

We were concerned that the complex kinetic behavior might be due to small amounts of oxygen. Indeed, since oxygen is known to stimulate the reaction of pinacolone enolate and iodobenzene, this might be the reason that the reactions occur at all in the dark. A procedure was devised in which the reactants were subjected to several freeze–pump–thaw cycles with carefully deoxygenated nitrogen. Absolutely no change was observed in the shape of concentration vs. time plots from similar reactions in Me$_2$SO at 35 °C of 1.9 × 10$^{-4}$ M$^{-1}$ s$^{-1}$, a value near the encounter controlled limit. The results thus show that the ability of carbanions (within a similar reactivity range) to react efficiently in competition reactions suggests that the propagation steps occur readily, but that pinacolone enolate reacts much more slowly with phenyl radicals than does acetone enolate. This narrow range of nucleophile reactivity is in keeping with suggestions that these reactions of nucleophiles with phenyl radicals are very fast and occur at nearly encounter controlled rates. Very recently, Bunnett and Herr reported an absolute rate constant for the reaction of pinacolone enolate with phenyl radical in Me$_2$SO at 35 °C of 3.2 times faster with 2-quinolyl radical than does acetone enolate. This narrow range of nucleophile reactivity is in keeping with suggestions that these reactions of nucleophiles with phenyl radicals are very fast and occur at nearly encounter controlled rates. Very recently, Bunnett and Herr reported an absolute rate constant for the reaction of pinacolone enolate with phenyl radical in Me$_2$SO at 35 °C of 2.6 times faster with 2-quinolyl radical than does acetone enolate. This narrow range of nucleophile reactivity is in keeping with suggestions that these reactions of nucleophiles with phenyl radicals are very fast and occur at nearly encounter controlled rates. Very recently, Bunnett and Herr reported an absolute rate constant for the reaction of pinacolone enolate with phenyl radical in Me$_2$SO at 35 °C of 2.6 times faster with 2-quinolyl radical than does acetone enolate.

Experimental Section

Materials. The Me$_2$SO was purified by drying for two days over molecular sieves followed by vacuum distillation through a Vigreux column (<45 °C). After a second distillation from calcium hydride and sodium amide, the Me$_2$SO was stored under N$_2$ in a foil wrapped flask and transferred by syringe to preclude contact with oxygen. Potassium tert-butoxide was freshly sublimed and stored in a quartz ampule. Sodium amide was sublimed under vacuum through a cold finger. Potassium tert-butoxide was freshly sublimed and stored in a quartz ampule. Potassium tert-butoxide was freshly sublimed and stored in a quartz ampule.

Table II. Relative Reactivities of Enolate Ions with Iodobenzene in Me$_2$SO (25 °C) from Competition Experiments

<table>
<thead>
<tr>
<th>Enolate</th>
<th>relative rate$^a$</th>
<th>pKa (Me$_2$SO)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>pinacolone</td>
<td>1.00</td>
<td>27.7</td>
</tr>
<tr>
<td>acetone</td>
<td>1.09</td>
<td>26.5</td>
</tr>
<tr>
<td>cyclohexanone</td>
<td>0.67</td>
<td>26.4</td>
</tr>
<tr>
<td>2-butane</td>
<td>1.0</td>
<td>26.5</td>
</tr>
<tr>
<td>3-pentanone</td>
<td>1.40</td>
<td>27.1</td>
</tr>
<tr>
<td>phenylacetone</td>
<td>0.39</td>
<td>19.8</td>
</tr>
</tbody>
</table>

$^a$Average of 2 or more experiments: ratios reproducible within ±5%.

Individual vs. Competition Reactivities. It is noteworthy that phenylacetone enolate is at least 50 times more reactive than pinacolone enolate when measured individually, but only 2.6 times less reactive in the competition reactions, i.e., phenylacetone reacts more rapidly in the presence of pinacolone enolate than in its absence.

These results are readily accommodated by the SRN1 mechanism. Measured individually, the reaction rates reflect not only the rates of the propagation steps but also the rates of the initiation and termination steps. The ready reactivity of phenylacetone enolate in competition reactions suggests that the propagation steps occur readily, but that phenylacetone enolate acts sluggishly to initiate the radical chain. In the competition experiment, the radical chain is initiated by the more reactive pinacolone enolate, and once initiated, both nucleophiles may react with the phenyl radicals produced.

The observation that phenylacetone enolate reacts with phenyl radicals only 2.6 times more slowly than does pinacolone enolate despite a difference in basicity of nearly 10$^8$ is consistent with another recent study of nucleophile reactivity in aromatic SRN1 reactions by Bunnett and Galli. They found only a 6-fold difference in reactivity among several phosphorus nucleophiles and pinacolone enolate. Similarly, the enolate from 2,4-dimethyl-3-pentanone has been found to react 3.2 times faster with 2-quinolyl radical than does acetone enolate. This narrow range of nucleophile reactivity is in keeping with suggestions that these reactions of nucleophiles with phenyl radicals are very fast and occur at nearly encounter controlled rates. Very recently, Bunnett and Herr reported an absolute rate constant for the reaction of pinacolone enolate with phenyl radical in Me$_2$SO at 35 °C of 2.6 times faster with 2-quinolyl radical than does acetone enolate. This narrow range of nucleophile reactivity is in keeping with suggestions that these reactions of nucleophiles with phenyl radicals are very fast and occur at nearly encounter controlled rates. Very recently, Bunnett and Herr reported an absolute rate constant for the reaction of pinacolone enolate with phenyl radical in Me$_2$SO at 35 °C of 2.6 times faster with 2-quinolyl radical than does acetone enolate.

The results are consistent with the notion that nucleophile basicity is an important factor in reactivity by electron-transfer pathways. Bordwell and Clemmensen have shown that the ability of carbanions (within a structural family) to transfer an electron is directly related to their basicity. If initiation of these reactions occurs by transfer of an electron from the nucleophile to iodobenzene, as seems likely, then the more weakly basic enolates (phenylacetone and acetylcyclohexanone) would be expected to be poorer in initiation as is observed.

(10) The possibility that pinacolone enolate reacts more slowly is ruled out because the extent of reaction in the competition experiment (61%) is virtually identical with that of pinacolone reacting alone (65%) under the same conditions.


just prior to use, quickly weighed, and transferred directly to the nitrogen flushed reaction flask. Iodobenzene was distilled, and the colorless liquid stored in a foil wrapped brown bottle. The ketones were dried over molecular sieves and distilled through a Vigreux column. A sizeable forerun was discarded, and the main fraction distilled again. Purity was checked by GLC. The nitrogen was purified by passage through two Altech Oxytraps connected in series. The second trap was an indicating type.

GLC Analysis. GLC analysis of products was carried out on either a Varian 3750 or a Varian 400D flame-ionization instrument. A 1/4 in. × 6 ft. Carbowax 20M on Chromosorb WHP or a 1/4 in. × 4 ft. 5% OV-101 column was used. Yields of products were determined by use of internal standards. In all cases, the area ratios were corrected for molar response determined from standard solutions of the products and the internal standard. Preparative GLC was carried out on an Aerograph A-90P instrument using a 1/4 in. × 6 ft. SE-30 column.

Reaction of Iodobenzene and Ketone Enolate in MeSO4. General Procedure. MeSO4 (25 mL) was transferred by syringe into a N2-purged 100-mL 3-neck flask fitted with two stoppers and a closed-end 12-mm tube with a 60° bend. The flask and tube were wrapped with black opaque tape. Freshly sublimed potassium tert-butoxide (1.22 g, 0.010 mol) was added, and the tube was charged with 1.00 g (0.010 mol) of pinacolone and 0.51 g (0.0025 mol) of iodobenzene. Stirring was employed to dissolve the base, and the tube containing the ketone and PhI was cooled with a dry ice-acetone bath. The system was evacuated and filled with nitrogen. This procedure was repeated 3-8 times. After the freeze-pump-thaw cycles were complete, the reactants were added to the flask by rotation of the bent tube. The solution was stirred and the flask placed in a 25 °C temperature bath. After 1 h, 6 N sulfuric acid (1.85 mL) was added. The solution was diluted with 50 mL of water and extracted 3X with ether. The combined ether extract was washed with water (3X) and dried (MgSO4), and an internal standard (phenylacetone) added for GLC analysis. In one experiment, both ketones and the iodobenzene were added together. The results were the same as when the ketones were added separately.

Kinetic experiments were carried out as above except that aliquots were removed by syringe under a positive pressure of nitrogen, quenched with acid, and titrated for iodide ion.

Oxygen sensitivity was probed by injecting oxygen gas by syringe into the purged vessel, stirring for 15-20 min, and then adding reactants as described. Experiments with atmospheres containing 5, 10, 50, 100, and 1000 ppm oxygen were carried out as above. At these concentrations, there was little if any effect on the amount of reaction during 60 min.

Calculation of Relative Reactivities. The relative reactivities (Table II) from competition experiments were calculated from the equation \( k_R / k_H = 1N [R_2R_2] / [R_1R_1] = 1N [R_2R_2] / [R_1R_1] \) where \( R_1 \) and \( R_2 \) are the initial and final enolate ion concentrations, respectively.

Reaction Products. The products from these reactions have been previously reported from similar photochemical processes in MeSO4 or NH4. Samples of 2-phenylcyclohexanone, 3-phenyl-2-butanone, and 2-phenyl-3-pentanone used for GLC analysis were prepared by standard literature methods.

Acknowledgment. This research was supported by Research Corporation, an equipment grant from the National Science Foundation, and Ripon College faculty development funds.

Reduction and Thermal Rearrangement of 9-Methylene-10-ethyl-10-phenyl-9,10-dihydroanthracene

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Received June 15, 1984

The thermolysis of 9-methylene-10-ethyl-10-phenyl-9,10-dihydroanthracene (2) results in a 1,5-ethyl rearrangement to yield 9-propyl-10-phenylanthracene. The rearrangement is shown to occur by an intermolecular radical process. Thermolysis of 2 in thiphene suppressed the rearrangement reaction and yielded instead the reduced product, a mixture of cis- and trans-9-methylene-10-ethyl-10-phenyl-9,10-dihydroanthracene (8). This unexpected result is discussed. The addition of hydrogen and tri-n-butyltin hydride to 2 is shown to be stereo-selective whereas the addition of thiphene is not. The geometric relationships of various substrates at C-9 and C-10 in 9,9,10-trisubstituted-9,10-dihydroanthracenes have been established.

The semibenzene rearrangement refers to the thermal rearrangement of cross conjugated methylenecyclohexadienes such as 1 to give aromatic compounds. This type of rearrangement was first reported by Auwers at the