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Thermally Initiated $S_{RN}1$ Reactions of Ketone Enolates with Iodobenzene in Dimethyl Sulfoxide. Relative Reactivities of Enolate Ions with Phenyl Radical[1]

Richard G. Scamehorn,* Jerry M. Hardacre, Jeanne M. Lukanich, and Lee R. Sharpe

Department of Chemistry, Ripon College, Ripon, Wisconsin 54971

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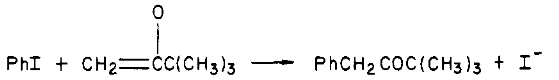
The enolate ions of acetone, pinacolone, cyclohexanone, 2-butanone, and 3-pentanone react smoothly in the dark with iodobenzene in Me_2SO to give high yields of substitution product. Phenylacetone enolate reacts very slowly, and 2-acetylcyclohexanone enolate fails to react. The relative reactivities of these enolate ions as determined from competition experiments in which pairs of enolates are allowed to react with PhI in Me_2SO 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 enolate nucleophiles despite a basicity difference of nearly 10^8. 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_2SO.[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 $S_{RN}1$ mechanism[3] (eq 1). The reaction is stimulated by light,



$$\mathrm{PhI} + \mathrm{CH_2{=}\overset{\overset{\large O}{\|}}{C}C(CH_3)_3} \longrightarrow \mathrm{PhCH_2COC(CH_3)_3} + \mathrm{I^-} \qquad (1)$$

inhibited by radical scavangers, 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.[4,5]

Scheme I

$$\mathrm{PhI} + e^- \rightarrow [\mathrm{PhI}]^{-\cdot} \qquad (2)$$

$$[\mathrm{PhI}]^{-\cdot} \rightarrow \mathrm{Ph}\cdot + \mathrm{I}^- \qquad (3)$$

$$\mathrm{Ph}\cdot + \mathrm{R}^- \rightarrow [\mathrm{PhR}]^{-\cdot} \qquad (4)$$

$$[\mathrm{PhR}]^{-\cdot} \rightarrow [\mathrm{PhI}]^{-\cdot} + \mathrm{PhR} \qquad (5)$$

We have found that other ketone enolate ions also undergo this dark reaction in Me_2SO. 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 $S_{RN}1$ reactions. Reproducible conditions, including concentration, are therefore somewhat easier to attain.

Table I. Dark Reactions of Ketone Enolate Ions (0.40 M) with Iodobenzene (0.10 M) in Me_2SO at 25 °C for 60 Min

	product yields, %[a]	
ketone	I^-	PhR
acetone	55	50
pinacolone	65	60
cyclohexanone	95	75[b]
2-butanone	80	70[c]
3-pentanone	75	70
phenylacetone	<1	<1[d]
2-acetylcyclohexanone		0

[a] Iodide determinations by titration; substitution product yields (PhR) determined by GLC; average of 2–4 experiments and rounded to nearest 5%. [b] Benzene, 25%, also found. [c] Two enolates form; the ratio of 3-phenyl/1-phenyl products is 2.8. [d] 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_2SO are summarized in Table I. In all cases, potassium enolates were generated by interaction of potassium *tert*-butoxide with the corresponding ketone. In Me_2SO, potassium *tert*-butoxide is a considerably stronger base than any of the enolates studied,[6] 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-acetylcyclohexanone. Phenylacetone enolate (ketone p*K*a (Me_2SO) 19.8) reacts at least 50 times slower with iodobenzene than does the pinacolone counterpart. 2-Acetylcyclohexanone enolate (ketone p*K*a (DMF) 14.1)[7] 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[8] 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.

[2] Scamehorn, R. G.; Bunnett, J. F. *J. Org. Chem.* **1977**, *42*, 1449.

[3] Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.

[4] Swartz, J. E.; Bunnett, J. F. *J. Org. Chem.* **1979**, *44*, 340.

[5] Fox, M. A.; Younathan, J.; Fryxell, G. E. *J. Org. Chem.* **1983**, *48*, 3109.

[6] The p*K*a of *tert*-butyl alcohol in Me_2SO is ca. 32. Olmstead, W. N.; Margdin, Z.; Bordwell, F. G. *J. Org. Chem.* **1980**, *45*, 3295.

[7] Yokoi, H.; Kishi, T. *Chem. Lett.* **1973**, *7*, 749.

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Table II. Relative Reactivities of Enolate Ions with Iodobenzene in Me_2SO (25 °C) from Competition Experiments

ketone	relative rate[a]	p*K*a (Me_2SO)[b]
pinacolone	1.00	27.7
acetone	1.09	26.5
cyclohexanone	0.67	26.4
2-butanone	1.10[c]	
3-pentanone	1.40[d]	27.1
phenylacetone	0.39	19.8

[a] Average of 2 or more experiments; ratios reproducible within ±5%. [b] Reference 17. [c] Total reactivity. [d] One experiment.

monia and is similar to results obtained from S_N2 reactions of enolates with alkyl halides, which often give the more substituted product in greater amount.[9]

It was previously reported that the dark reaction of pinacolone enolate and iodobenzene follows a complex kinetic rate equation.[2] We have observed similar behavior with the enolates in this study. The release of iodide ion is initially very fast, but the rate decreases dramatically as the reaction progresses toward completion. Furthermore, the processes are nearly zero order in iodobenzene. 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,[2] 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 which oxygen exclusion was less rigorous. In fact, the percent reaction increased from 45% (conditions of Table 1) using tank nitrogen without purification and without the pumping cycles, to 67% with the above method. We conclude that the complex kinetics are characteristic of these $S_{RN}1$ dark reactions in Me_2SO, and are not due to impurities generated during the reaction by trace amounts of oxygen.

Several experiments were done in which oxygen was added to the atmosphere in the system. There was little or no effect on the extent of reaction after 1 h with oxygen concentrations ranging from 5 to 1000 ppm, indicating insensitivity to low concentrations of oxygen.

Competition Experiments. Table II summarizes the results of experiments in which equimolar amounts of two enolate nucleophiles (0.20 M) were allowed to react competitively with iodobenzene (0.05 M). The relative reactivities were determined from the amounts of substitution products (eq 6). The analysis entails the assumption

$$R_1^- + R_2^- + PhI \rightarrow PhR_1 + PhR_2 + I^- \qquad (6)$$

that the product distribution is determined in eq 4 (Scheme I), and that it is essentially irreversible, and that eq 5 inevitably and rapidly follows.

The results clearly show that in competition reactions all of the ketone enolates react at nearly the same rate. There is less than a 4-fold difference in reactivity among all of the enolate ions. Examination of Scheme I indicates that the findings are a measure of the relative rates of reaction of the enolate ions with phenyl radical (eq 7).

$$R_1^- + R_2^- + Ph\cdot \rightarrow [R_1Ph]^{-\cdot} + [R_2Ph]^{-\cdot} \qquad (7)$$

Individual vs. Competition Reactivities. It is noteworthy that phenylacetone enolate is at least 50 times less 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.[10]

These results are readily accommodated by the $S_{RN}1$ 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 $S_{RN}1$ reactions by Bunnett and Galli.[11] 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.[12] 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.[4] Very recently, Bunnett and Herr reported an absolute rate constant for the reaction of pinacolone enolate with phenyl radical in Me_2SO at 35 °C of 1.9×10^8 M^{-1} s^{-1}, a value at or near the encounter controlled limit.[13]

The results are consistent with the notion that nucleophile basicity is an important factor in reactivity by electron-transfer pathways.[14,15] Bordwell and Clemmens have shown that the ability of carbanions (within a structural family) to transfer an electron is directly related to their basicity.[14] 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.

Experimental Section

Materials. The Me_2SO 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_2SO was stored under N_2 in a foil wrapped flask and transferred by syringe to preclude contact with oxygen.[16] Potassium *tert*-butoxide was freshly sublimed

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(8) Rossi, R. A.; Bunnett, J. F. *J. Org. Chem.* **1973**, *38*, 3020.

(9) (a) House, H. O.; Trost, B. M. *J. Org. Chem.* **1965**, *30*, 1341, 2502. (b) House, H. O. "Modern Synthetic Reactions", 2nd ed.; Benjamin: Menlow Park, CA, 1972; p 546.

(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.

(11) Bunnett, J. F.; Galli, C. *J. Am. Chem. Soc.* **1981**, *103*, 7140.

(12) (a) Hay, J. V.; Wolf, J. F. *J. Am. Chem. Soc.* **1975**, *97*, 3702. (b) Komin, A. P.; Wolf, J. F. *J. Org. Chem.* **1977**, *42*, 2481.

(13) Herr, D. J. C. Ph.D. Thesis, University of California, Santa Cruz, 1984.

(14) Bordwell, F. G.; Clemmens, A. H. *J. Org. Chem.* **1982**, *47*, 2510; *J. Org. Chem.* **1981**, *46*, 1035.

(15) Tolbert, L. M.; Siddiqui, S. *Tetrahedron* **1982**, *38*, 1079.

(16) Ritchie, C. D.; Skinner, G. A.; Badding, V. G. *J. Am. Chem. Soc.* **1967**, *89*, 2069.

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 3760 or a Varian 400D flame-ionization instrument. A $^1/_8$ in. × 6 ft 5% Carbowax 20M on Chromsorb WHP or a $^1/_8$ 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 Me_2SO. General Procedure. Me_2SO (25 mL) was transferred by syringe into a N_2-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 3× with ether. The combined ether extract was washed with water (3×) and dried ($MgSO_4$), and an internal standard (phenylacetone) added for GLC analysis. The aqueous layers were combined and an eliquot was used for iodide analysis. For each ketone studied, the product from at least one reaction was isolated by preparative GLC or by column chromatography on silica gel, and the IR and NMR spectra were compared with those of authentic compounds. Four identical experiments carried out as above with iodobenzene and pinacolone gave yields (I^-) of 67.2%, 60.0%, 66.5%, and 68.1%.

Competition Experiments. Typical Procedure. The competition experiments were carried out as described above except that equimolar amounts of two ketones were used; these were added by syringe and allowed to stir for several minutes prior to addition of the iodobenzene. In a typical experiment, acetone (0.29 g, 5.0 mmol) and pinacolone (0.50 g, 5.0 mmol) were added by syringe to 1.22 g (10.0 mmol) of potassium *tert*-butoxide in 25 mL of Me_2SO. After the pump cycles, iodobenzene (0.50 g, 2.5 mmol) was added. The organic products were analyzed by GLC. 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 $k_{R_1}/k_{R_2} = \ln [(R_1)_0/(R_1)_t]/\ln [(R_2)_0/(R_2)_t]$ where R_0 and R_t are the initial and final enolate ion concentrations, respectively.[18]

Reaction Products. The products from these reactions have been previously reported from similar photochemical processes in Me_2SO[19] or NH_3.[20] Samples of 2-phenylcyclohexanone,[21] 3-phenyl-2-butonone,[22] and 2-phenyl-3-pentanone[23] used for GLC analysis were prepared by standard literature methods.

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[17] (a) Matthews, W. S.; Bares, J. E.; Bartmess, J. E.; Bordwell, F. G.; Cornforth, F. J.; Drucker, G. E.; Margolin, Z.; McCallum, R. J.; McCollum, G. J.; Vanier, N. R. *J. Am. Chem. Soc.* **1975**, *97*, 7006. (b) Bordwell, F. G., private communication.

[18] Bunnett, J. F. In "Investigation of Rates and Mechanisms of Reactions", 3rd ed.; Lewis, E. S., Ed.; Wiley-Interscience: New York, 1974; Part I, p 159.

[19] Scamehorn, R. G.; Bunnett, J. F. *J. Org. Chem.* **1977**, *42*, 1457.

[20] Bunnett, J. F.; Sundberg, J. E. *Chem. Pharm. Bull.* **1975**, *23*, 2620; *J Org. Chem.* **1976**, *42*, 1702.

[21] Newman, M. S.; Farbman, M. O. *J. Am. Chem. Soc.* **1944**, *66*, 1550.

[22] Sheirz, E. R. *Chem. Abstr.* **1954**, *48*, 1438.

[23] Leake, W. W.; Levine, R. *Chem. Ind. (London)* **1955**, 1160.

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

H. M. Walborsky* and T. J. Bohnert

Department of Chemistry, Florida State University, Tallahassee, Florida 32306

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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 thiophenol surpressed the rearrangement reaction and yielded instead the reduced product, a mixture of *cis*- and *trans*-9-methyl-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 stereoselective whereas the addition of thiophenol is not. The geometric relationships of various substituents 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