J. Am. Chem. Soc. **1998,** *120,* 10801−10806

Aggregation and Reactivity of the Cesium Enolate of *p*-Phenylisobutyrophenone in Tetrahydrofuran[1]

Andrew Streitwieser,* James A. Krom, Kathleen V. Kilway, and Alessandro Abbotto

Contribution from the Department of Chemistry, University of California, Berkeley, California 94720-1460

Received April 27, 1998

Abstract: Reinvestigation of the cesium enolate (CsPhIBP) of 1-biphenylyl-2-methylpropanone (*p*-phenylisobutyrophenone, PhIBP) in tetrahydrofuran (THF) solution at 25.0 °C shows that its UV−visible spectrum changes with concentration with $\lambda_{\max}$ moving to longer wavelengths in more dilute solution. Analysis of the spectral data over a wide concentration range by singular value determination (SVD) combined with the p*K* measurements indicates a mixture of monomer (M), dimer (D), and tetramer (T) with equilibrium constants of $K_{1,2} = D/M^2 = 2.89 \times 10^4\ M^{-1}$ and $K_{1,4} = T/M^4 = 7.78 \times 10^{12}\ M^{-3}$. The p*K* of the monomer is 25.08. The data are also compared with the corresponding data obtained for the lithium ion pair system reported in the following paper. We find that the cesium ion pair is more highly aggregated and much more basic than the lithium ion pair. The average aggregation number of CsPhIBP at 10^{-3} M is 3.2, substantially greater than the value of 2.2 reported previously; the revision arises from our taking into account the concentration-dependent extinction coefficient and absorption band shape of CsPhIBP. The revised value also requires that a correction be applied to our previously reported kinetics of the reaction of CsPhIBP with methyl tosylate (MeOTs); the data indicate that the CsPhIBP ion pair monomer reacts, instead of the free enolate ion that we reported previously. Similarly, alkylation by *p-tert*-butylbenzyl chloride (BnCl) occurs dominantly via the monomer. More limited studies at −20 °C indicate greater aggregation at the lower temperature. Alkylation reactions with MeOTs and BnCl again occur predominantly with the monomer. The reaction products at room temperature are those of C-alkylation with BnCl and equal amounts of C- and O-alkylation with MeOTs.

Introduction

Alkali metal enolates and related compounds have assumed a singular importance in organic chemistry since the development of methodologies that allow their quantitative formation in nonpolar solvents, as is indicated by an extensive literature.[2] Although Zook was apparently the first to recognize that simple enolates are aggregated in nonpolar solvents,[3−6] his pioneering work was not followed up until the extensive NMR studies of Jackman on the aggregation of simple enolates and the consequences for reactivity.[7] The aggregation of enolates and other organoalkali compounds is now recognized as a general phenomenon, and much of the recent attention has focused on the possibility that aggregation is important in controlling reaction stereochemistry.[8−10]

We have recently shown that the UV spectra of alkali enolates in THF frequently vary with concentration indicating that different aggregates have significantly different spectra.[11] This method combined with the effect of a concentration-dependent aggregation equilibrium on another equilibrium ("coupled equilibrium"), which we have taken usually as a proton-transfer equilibrium to a suitable indicator ("ion pair acidity"), provides an important tool for determining the stoichiometry and equilibrium constants for aggregation.[12−14] We previously communicated cesium ion pair acidity studies of 1-biphenylyl-2-methylpropanone (*p*-phenylisobutyrophenone, PhIBP) and kinetics of reaction of its cesium enolate (CsPhIBP) with methyl tosylate (MeOTs),[15] before we recognized the effect of these spectral changes with concentration. Reevaluation of those results changes profoundly the conclusion that free ions are dominant in the alkylation reactions of cesium enolates in THF. We show in the present paper that ion pair monomers are actually the dominant species in such reactions.

Results and Discussion

All of the experiments were performed at 25.0 °C with THF as the solvent except where indicated. Additional studies at −20 °C are discussed separately.

CsPhIBP Absorption Spectra. Although the biphenylyl chromophore proved suitable for the UV−visible absorption

---

[1] Carbon Acidity. 101.

[2] For some recent reviews, see: Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1624−1654. Heathcock, C. H. In *Comprehensive Synthetic Chemistry*; Trost, B., Ed.; Pergamon Press: New York, 1991; pp 181−238. Jackman, L. M.; Bortiatynski, J. *Adv. Carbanion Chem.* **1992**, *1*, 45−87.

[3] Zook, H. D.; Rellahan, W. L. *J. Am. Chem. Soc.* **1957**, *79*, 881−6.

[4] Zook, H. D.; Gumby, W. L. *J. Am. Chem. Soc.* **1960**, *82*, 1386−9.

[5] Zook, H. D.; Russo, T. J.; Ferrand, E. F.; Stotz, D. S. *J. Org. Chem.* **1968**, *33*, 2222−8.

[6] Zook, H. D.; Russo, T. J. *J. Am. Chem. Soc.* **1960**, *82*, 1258−9.

[7] Reviewed in: Jackman, L. M.; Lange, B. C. *Tetrahedron* **1977**, *33*, 2737−69.

[8] Williard, P. G.; Salvino, J. M. *Tetrahedron Lett.* **1985**, *26*, 3931−4.

[9] Wei, Y.; Bakthavatchalam, R. *Tetrahedron* **1993**, *49*, 2373−2390.

[10] Juaristi, E.; Beck, A. K.; Hansen, J.; Matt, T.; Mukhopadhyay, T.; Simson, M.; Seebach, D. *Synthesis* **1993**, 1271−90.

[11] Ciula, J. C.; Streitwieser, A. *J. Org. Chem.* **1992**, *57*, 431−432; correction p 6686.

[12] Abbotto, A.; Streitwieser, A. *J. Am. Chem. Soc.* **1995**, *117*, 6358−9.

[13] Abu-Hasanayn, F.; Stratakis, M.; Streitwieser, A. *J. Org. Chem.* **1995**, *60*, 4688−9.

[14] Abu-Hasanayn, F.; Streitwieser, A. *J. Am. Chem. Soc.* **1996**, *118*, 3186−7.

[15] Krom, J. A.; Streitwieser, A. *J. Am. Chem. Soc.* **1992**, *114*, 8747−8.

10.1021/ja981437y CCC: $15.00

spectroscopy used in the ion pair acidity equilibria, the spectra exhibited strong overlap of the absorption bands of PhIBP (which absorbs at wavelengths less than 380 nm) and its cesium ion pair. Thus, only half of the absorption band of CsPhIBP (380 nm and longer) could be used to avoid interference from PhIBP. The data treatment was further complicated by the concentration dependence of its extinction coefficient and shape (Figure S1, Supporting Information). From the extinction coefficient determinations, the working curve shown in Figure S2 (Supporting Information) was constructed to compute unknown concentrations from absorbance readings at 380 nm. The plot is distinctly nonlinear and does not quite obey Beer's law.

To further characterize the spectroscopic data the method of singular value decomposition (SVD) was used, a linear algebraic method[16] that we have applied previously in other studies of aggregation.[17] The method has been widely used in spectroscopic studies.[18] An initial series of 36 spectra of varying CsPhIBP concentration (2.2×10^{-5} to 4.3×10^{-3} M) in the wavelength region 380−600 nm was obtained and the absorbance data were digitized at 0.5 nm intervals. SVD gave two linearly independent "basis spectra" with singular values of 207 and 4.0 that adequately describe the observed spectra. The other 34 basis spectra, with singular values of 0.26 and lower, clearly describe only the spectrometer noise.

The SVD analysis would therefore suggest the presence of two aggregate species. We calculated equilibrium constants for all possible binary systems from monomer/dimer through heptamer/octamer using the SVD output according to our published method,[17] but we were unable to obtain satisfactory agreement with the acidity results (vide infra). A reexamination of the spectrum of CsPhIBP at still more dilute concentrations suggested the presence of a third component, yet SVD persisted in indicating the presence of only two. We suspected that we were being misled by SVD, probably because of limitations caused by instrument noise, and that there are actually three important aggregate species in this system. Our analysis using the SVD output[17] uses linear algebra and it is generally impossible to model a three-component system with two basis spectra; thus, we abandoned the attempt to define the system by SVD alone. At the two concentration extremes, λ_{max} changed little with further concentration change, suggesting that these extremes represent almost pure monomer (M) and tetramer (T) with dimer (D) contributing importantly only to the spectra at intermediate concentrations. Fitting the spectra with this assumption gave a first approximation to the spectra and concentrations of the three components. This fitting was then refined by using the proton-transfer equilibria. This analysis of the spectra, in contrast to our previous analysis,[17] is not completely independent of the acidity data; nevertheless, the final results are internally consistent and strongly suggest that SVD failed to detect three components because their spectra are linearly dependent (within instrument error) over the restricted wavelength range of this study.

Cesium Ion Pair Acidity. The ion pair acidity is defined by eq 1 relative to an appropriate indicator in the proton-transfer equilibrium 2. The indicator ion pair scale for cesium salts in THF was published earlier.[19]

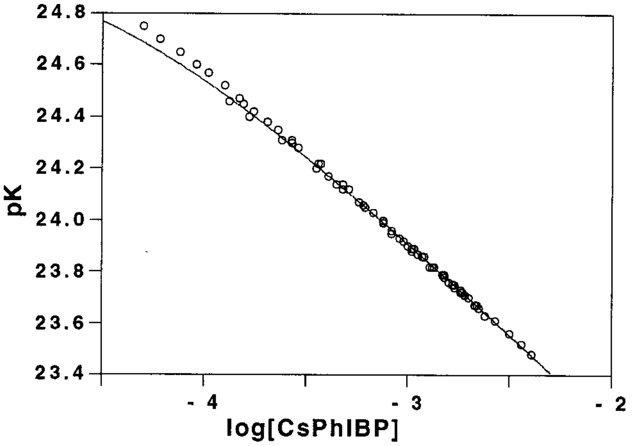


Figure 3. p*K* of CsPhIBP as a function of formal concentration. The open circles are experimental data. The points are calculated with $K_{1,2} = 2.89 \times 10^4$ M^{-1}, $K_{1,4} = 7.78 \times 10^{12}$ M^{-3}. pK_a = 25.08.

$$pK(\mathrm{RH}) - pK(\text{Ind-H}) = -\log K \tag{1}$$

$$\mathrm{RH} + \mathrm{Ind}^- \mathrm{Cs}^+ \rightleftarrows \mathrm{R}^-\mathrm{Cs}^+ + \text{Ind-H} \tag{2}$$

The cesium ion pair acidity of PhIBP was measured (68 determinations) against the indicator 9-*tert*-butylfluorene (tBuFL), which has a cesium ion pair p*K* of 24.39 at 25 °C.[19] It was found that the observed acidity varies between about 23.5 and 25.0, depending on the concentration of CsPhIBP (Figure 3), showing that aggregation of CsPhIBP is important. Equilibrium 2 is defined for the monomer; any aggregation reduces the concentration of the monomer below the formal concentration of the substrate and reduces the apparent p*K* of the substrate. It is this combination of the proton-transfer equilibrium with the aggregation equilibrium that we refer to as *coupled equilibria*.

We had shown previously[20] that the slope of such a plot at any point gives the average aggregation number $\bar{n}_{agg}$ according to eq 3:

$$\text{slope} = \frac{1}{n_{agg}} - 1 \tag{3}$$

Fitting a line through a few points at the highest concentration gives $\bar{n}_{agg} = 3.2$, but the curvature of the plot shows that the average aggregation number depends on the concentration. The measured acidity does not correlate with the concentration of the tBuFL ion pair showing that it does not form mixed aggregates with CsPhIBP. Alternatively, from the aggregation equilibrium constants the concentration of monomer can be calculated at any formal concentration of CsPhIBP and the apparent p*K* can be computed. In practice, these data were combined with the spectral data in the following analysis. Assuming a monomer/dimer/tetramer system, the total formal enolate concentration (symbolized as {CsPhIBP}) is given by eq 4:

$$\{\mathrm{CsPhIBP}\} = [\mathrm{M}] + 2[\mathrm{D}] + 4[\mathrm{T}] \tag{4}$$

Substituting for the equilibrium constants for formation of the dimer ($K_{1,2}$) and the tetramer ($K_{1,4}$) from the monomer gives eq 5:

---

[16] Press, W. H.; Flannery, B. P.; Teukolsky, S. A.; Vetterling, W. T. *Numerical Recipes (Fortran Version)*; University Press: Cambridge, 1989.

[17] Krom, J. A.; Petty, J. T.; Streitwieser, A. *J. Am. Chem. Soc.* **1993**, *115*, 8024−8030.

[18] Malinowsky, E. R. *Factor Analysis in Chemistry*; Wiley: New York, 1991.

[19] Streitwieser, A.; Ciula, J. C.; Krom, J. A.; Thiele, G. *J. Org. Chem.* **1991**, *56*, 1074−6.

[20] Kaufman, M. J.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 6092−7.

$$\{\mathrm{CsPhIBP}\} = [\mathrm{M}] + 2K_{1,2}[\mathrm{M}]^2 + 4K_{1,4}[\mathrm{M}]^4 \qquad (5)$$

The observed acidity of the ketone is related to its true acidity K_a (i.e., ion pair equilibrium with respect to monomeric enolate) by eq 6:

$$K_{\mathrm{obs}} = K_a\{\mathrm{CsPhIBP}\}/[\mathrm{M}] \qquad (6)$$

From a series of observed acidity measurements at varying concentration eqs 5 and 6 were used to compute K_a, $K_{1,2}$, and $K_{1,4}$ by a series of successive iterations. An initial guess for K_a, $K_{1,2}$, and $K_{1,4}$ was used to solve for the monomer concentration for each experiment from eq 5, and the (unweighted) sum of the squares of the deviations from the observed acidities was calculated by using eq 6. The parameters were adjusted, and the procedure was repeated until the sum of the squares was minimized. We found $K_a = 0.206$ (pK = 25.08), $K_{1,2} = 2.89 \times 10^4$ M^{-1}, and $K_{1,4} = 7.78 \times 10^{12}$ M^{-3}. From these results, the corresponding equilibrium constant for dimerization of the dimer to tetramer, $K_{2,4}$, was 0.93×10^4 M^{-1}; that is, the tendency of the dimer to dimerize to tetramer is only slightly less than dimerization of the monomer. The pK is probably reliable to ±0.1 units. The probable errors in $K_{1,2}$ and $K_{1,4}$ are more difficult to judge because of the complexity of their derivations; however, although three significant figures are given for consistency, these numbers might not be reliable past a single figure.

For each acidity run, the spectrum of the enolate was obtained by our usual method of using the SVD basis and the spectrum of the indicator to model the spectrum of the equilibrium mixture. From the concentrations of the aggregates, determined by the above analysis, and the observed absorbance A of the enolate, we calculated the extinction coefficients ϵ of the putative aggregates at each wavelength by a linear least-squares fit to eq 7.

$$A = \epsilon_1[\mathrm{M}] + \epsilon_2[\mathrm{D}] + \epsilon_4[\mathrm{T}] \qquad (7)$$

The resulting spectra show a blue shift with increasing degree of aggregation, as would be expected. Furthermore, these hypothetical spectra are *linearly dependent* to an extraordinary degree of precision over the wavelength range of these experiments, and we confirmed that each can be described by an appropriate linear combination of the original 2-dimensional SVD basis. Thus, our entire set of data is internally consistent with the plausible assumption of a monomer/dimer/tetramer enolate system, but is inconsistent with any reasonable two-component hypothesis. Finally, this analysis suggests that SVD failed to indicate three significant components because of a fortuitous linear dependence among the absorption spectra of the aggregates over the wavelength range of the investigation. We suspect that this complication would have been avoided had we been able to use the entire absorption spectrum of the enolate.

The resulting spectra are shown in Figure 4. As indicated in this figure, the noise in the resulting components makes it impossible to determine accurately each of the $\lambda_{\max}$; nevertheless, it is clear that these wavelengths are in the order λ(M) > λ(D) > λ(T). This is the order expected from a simple electrostatic argument. The transition dipole is expected to be oriented away from the enolate oxygen toward the π-system. Accordingly, such an electron density shift to the excited state would be more difficult in an aggregate where the enolate oxygen is close to more cations.

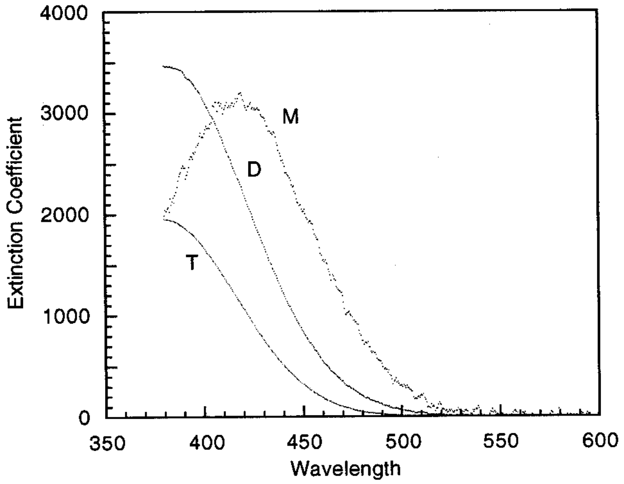


Figure 4. Spectra of tetramer, dimer, and monomer of CsPhIBP from the SVD and pK analysis.

The cesium ion pair pK scale compares numerically very well with ionic pK values in DMSO; that is, the effect of structure on the DMSO pK values is similar to that for the cesium ion pairs in THF, at least for highly delocalized carbanions.[19] The more localized charge in enolate ions might be expected to show somewhat greater electrostatic attraction to a cation, and this is just what is found in the present example. Bordwell[21] reports a pK of 26.25 for isobutyrophenone. A *p*-phenyl substituent is only slightly electron-withdrawing; σ_p is 0.01.[22] Thus, the DMSO pK of *p*-phenylisobutyrophenone is expected to be close to 26.2, or 1.1 units higher than the cesium ion pair pK in THF. This difference indicates only a slightly increased attraction of cesium cation to the enolate ion, relative to highly delocalized indicator anions, undoubtedly because the cesium cation is rather large, the largest alkali cation. The difference with the much smaller lithium cation is striking. The ion pair pK of the LiPhIBP monomer is 15.88.[12,23] Both enolates are contact ion pairs, but the lithium pK is referred to solvent-separated indicators whose dissociation constants are about 10^2-10^3 greater than that of the cesium indicators, which are contact ion pairs.[24] Since the ionic pK values must be the same,[24] the relative acidity differences, K_a, can be related to the corresponding dissociation constants, K_d, by eq 8.

$$\frac{K_a(\mathrm{CsEn})}{K_a(\mathrm{LiEn})} = \frac{K_d(\mathrm{CsIn})}{K_d(\mathrm{LiIn})} \cdot \frac{K_d(\mathrm{LiEn})}{K_d(\mathrm{CsEn})} \qquad (8)$$

The experimental results show that the dissociation constant of the cesium enolate to the ions is about 10^6 greater than that of the lithium enolate.

Alkylation Reactions. It has been suggested that enolate aggregates in THF participate in reactions[25] and some alkylation experiments have been interpreted in terms of reaction of enolate aggregates.[7] We recently reported that for the lithium enolate of *p*-phenylsulfonylisobutyrophenone the monomer is orders of magnitude more reactive than the dimer in an alkylation reaction in THF.[13] We reported previously that the alkylation of

---

[21] Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456−63.

[22] Charton, M. *Prog. Phys. Org. Chem.* **1981**, *13*, 191.

[23] Abbotto, A.; Leung, S. S.-W.; Streitwieser, A.; Kilway, K. V. *J. Am. Chem. Soc.* **1998**, *120*, xxxx.

[24] Kaufman, M. J.; Gronert, S.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 2829−35.

[25] Seebach, D.; Amstutz, R.; Dunitz, J. D. *Helv. Chim. Acta* **1981**, *64*, 2622−6.

CsPhIBP by methyl tosylate involves the free enolate ion in THF, but this result is now shown to be in error.

The observation that the spectra of CsPhIBP vary with concentration and the application of SVD and p*K* results in substantial improvement over our previously reported preliminary average aggregation number of 2.2 for this system.[15] The previous results are erroneous as a direct consequence of our inability at that time to account for concentration-dependent absorption band shapes. Additionally, we failed to detect the varying extinction coefficient because the measurements were not carried out at the more dilute concentrations achieved in the present studies. We also reported initial rates of reaction of CsPhIBP with methyl tosylate (MeOTs) monitored by the absorbance change at 380 nm; we have carried out a correction of the original data that takes into account the variable extinction coefficient (Table S1, Supporting Information). A least-squares fit of the data to the rate law in eq 9 gives $k = (6.5 \pm 0.8) \times 10^{-3}$ M^{-1} s^{-1}, $x = 0.27 \pm 0.06$ (Figure S5, Supporting Information).

$$\text{rate} = k\{\text{CsPhIBP}\}[\text{MeOTs}] \tag{9}$$

Thus, the reaction is 0.27 order in CsPhIBP. The average aggregation number of CsPhIBP over the concentration range of the kinetics experiments is essentially constant with a value $\bar{n}_{\text{agg}} = 3.2$. The average aggregation number $\bar{n}_{\text{r}}$ of the reactive intermediate is computed from the equatio, $x = \bar{n}_{\text{r}}/\bar{n}_{\text{agg}}$; thus, $\bar{n}_{\text{r}} = 0.86 \pm 0.19$, indicating that it is the monomeric CsPhIBP ion pair that reacts with MeOTs. Alternatively, the initial rate divided by [MeOTs] can be compared directly to the concentration of monomeric CsPhIBP as in Figure S6 (Supporting Information). The result is a rate constant of 14.5 ± 2.4 M^{-1} s^{-1}. The precision of the kinetic data is limited by the experimental difficulties; thus, although it is clear that the bulk of the alkylation reaction occurs through monomer we cannot exclude some small fraction of reaction via higher aggregates. Note that this is a substantially different conclusion than we reached before;[15] the discrepancy follows directly from our earlier inaccurate determination of $\bar{n}_{\text{agg}}$ (vide supra).

Alkylation rates were also measured for *p-tert*-butylbenzyl chloride, BnCl. A plot of log(rate/[BnCl]) vs log{CsPhIBP} is linear with a slope of 0.31 ± 0.03 and with better precision than the MeOTs kinetics (data are in Table S2 and Figure S7, Supporting Information). A direct comparison of the rate vs the concentration of monomer (Figure 8) gives a linear relationship with $k_2 = 3.20 \pm 0.05$ M^{-1} s^{-1}. Any significant contribution by higher aggregates in the rate would show up as an upward curvature in this plot but no such curvature is evident. Thus, alkylation by monomer dominates even under conditions where dimer and tetramer dominate the aggregation equilibrium. The generalization that alkylation reactions of cesium and lithium enolates in THF involve dominantly the monomer even in the presence of large excesses of aggregates has now been established in our laboratory with several enolates. One example is the cesium enolate of 2-(*p*-biphenylyl)cyclohexanone in which it was also shown that the alkylation rates are little affected by added cesium tetraphenylborate.[26] This result proves that free ions play no significant role in THF.

The system is that of a classic Curtin–Hammett type[27] as shown in Scheme 1. The combination of rate constants and equilibrium constants determines the flux of reaction through different reactants.

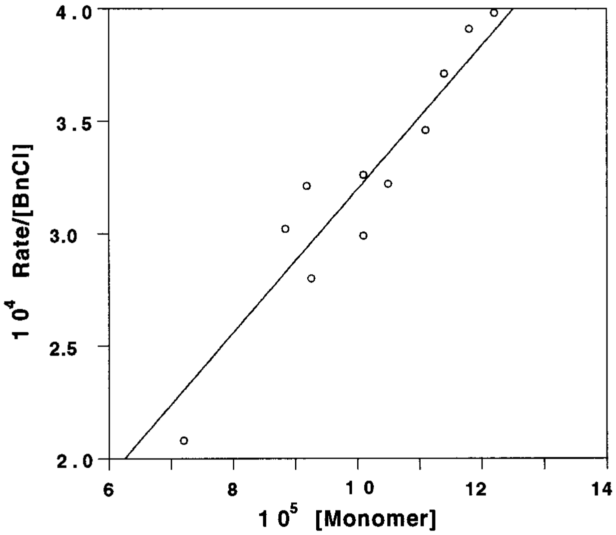


Figure 8. Initial rate of *p-tert*-butylbenzyl chloride, BnCl, as a function of monomer concentration at 25 °C. The slope of the line shown is the second-order rate constant, 3.20 ± 0.05 M^{-1} s^{-1}.

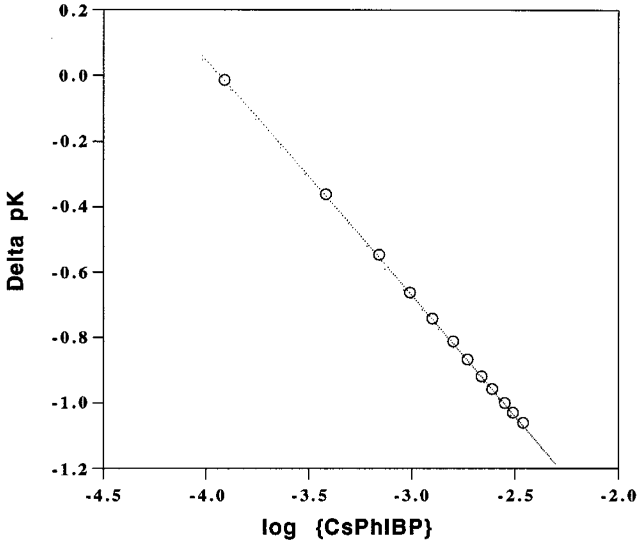
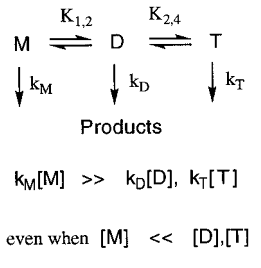


Figure 9. p*K* difference relative to tBuFL at −20 °C. Open circles are the experimental points whose best least squares linear fit is −2.853 − 0.7276 log{CsPhIBP}, $R^2 = 0.999$. The locus of points is the calculated fit for a M, D, T equilibrium with $K_{1,2} = K_{2,4} = 1.16 \times 10^5$ M^{-1}.

Scheme 1. A Curtin–Hammett System Applied to Enolate Aggregates



Studies at −20 °C. Equilibrium studies were also carried out with tBuFL at −20 °C but not as extensively as above. The experimental Δp*K* values vary linearly with log{CsPhIBP} with a slope corresponding to an aggregation number, $\bar{n}_{\text{agg}}$, of 3.67 (Figure 9). The data are insufficient to do a complete analysis, but an approximate analysis was carried out in the following way. It was shown above that $K_{2,4}$ for dimerization of the dimer

---

(26) Wang, D. Z. Results to be published.

(27) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83–134.

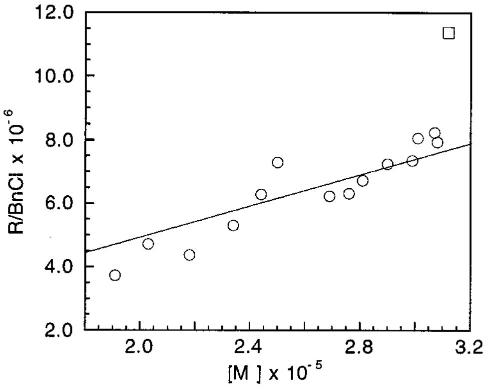


Figure 10. Initial rate of *p-tert*-butylbenzyl chloride, BnCl, as a function of monomer concentration at −20 °C with $K_{1,2} = K_{2,4} = 1.16 \times 10^5$ M^{-1}. The line shown has been forced through the origin and has a slope of 0.247 ± 0.006 (the square point is not included in the calculated fit).

is only somewhat smaller than $K_{1,2}$ for dimerization of the monomer at 25 °C. If we assume that $K_{2,4} = K_{1,2} = K$ at −20 °C, K can be derived from $\bar{n}_{agg}$ from the dependence of $\bar{n}_{agg}$ on [M], [D], and [T] by using eq 10 (derived in Appendix A, Supporting Information).

$$\bar{n} = \frac{[M] + 4[D] + 16[T]}{[M] + 2[D] + 4[T]} \tag{10}$$

A point in the median range in Figure 9 corresponds to $K = 1.16 \times 10^5$ M^{-1}. This value was used to calculate the locus of points also shown in Figure 9 that fit excellently the experimental results. The points have a barely detectable curvature. The values of $K_{1,2}$ of 2.89×10^4 M^{-1} at 25 °C and 1.16×10^5 M^{-1} at −20 °C give $\Delta H° = -4.6$ kcal mol^{-1} and $\Delta S° = 4.9$ eu. These thermodynamic properties have high probable errors although the results are quite internally consistent. The positive entropy change for a dimerization reaction, for example, implies that even the large cesium cation loses substantial solvation in forming the dimer.

Rate measurements were also carried out at −20 °C. The data for the reaction of CsPhIBP with *p-tert*-butylbenzyl chloride at −20 °C are given in Table S4 (Supporting Information). Figure 10 shows a plot of the initial rate divided by the BnCl concentration compared to the monomer concentration calculated from the Δp*K* results at −20 °C, namely $K_{1,2} = K_{2,4} = 1.16 \times 10^5$ M^{-1}. The plot gives a second-order rate constant, $k_2 = 0.247 \pm 0.006$ M^{-1} s^{-1}. Together with the rate constant at 25 °C, the corresponding $\Delta H^‡$ is 7.9 kcal mol^{-1}, a low value for a displacement reaction, and $\Delta S^‡ = -30$ eu, a reasonable value for a second-order reaction.

A similar treatment with methyl tosylate at −20 °C gives results with more scatter, Figure S11 and Table S5 (Supporting Information). The derived second-order rate constant with monomer is 0.463 ± 0.027 M^{-1} s^{-1}. Together with the rate constant at 25 °C, $\Delta H^‡ = 10.9$ kcal mol^{-1} and $\Delta S^‡ = -17$ eu. It is interesting that methyl tosylate reacts faster than *p-tert*-butylbenzyl chloride at both temperatures despite a higher activation energy. The more positive $\Delta S^‡$ for the methyl tosylate reaction suggests that the coordination of the cesium cation with the tosylate group in the transition structure is accompanied by greater loss of solvation than with the alkyl chloride. The difference is so large that the larger error in the tosylate runs probably would not change the qualitative result; that is, the qualitative result follows from the higher reactivity of MeOTs at both temperatures but the rate difference is less at the lower temperature.

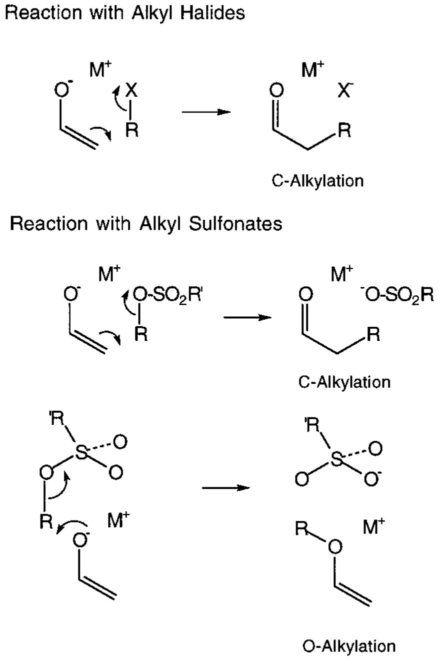


Figure 12. Six-membered-ring transition structures rationalize C- and O-alkylation.

A pronounced difference between the MeOTs and BnCl reactions is also found in the reaction products. The benzylic chloride gave only 3% O-alkylation even under a variety of concentrations (Table S6, Supporting Information), whereas MeOTs gave almost equal amounts of C- and O-alkylations; the C/O alkylation ratio is 1.2 as reported previously.[15] A similar pattern was found three decades ago by Zook.[5] Brändström suggested in 1953 that reactions of metal enolates in nonpolar solvents proceed via six-membered-ring transition structures.[28] His proposal was formulated in terms of ionic and covalent bonding, but the concepts apply just as well to ion pair displacement reactions with essentially complete ionic bonding. The importance of such ring structures in ion pair displacement reactions has been shown by ab initio calculations.[29] Imposition of a six-membered-ring transition structure favors C-alkylation for an alkyl halide, but ring structures can be written for both C- and O-alkylation for sulfonates as shown in Figure 12.

Conclusion

The cesium enolate of *p*-phenylisobutyrophenone exists in THF solution as a mixture of monomer, dimer, and tetramer. At a formal concentration of 0.1 M enolate, 0.3% is present as monomer and about 1% is as dimer; the remainder of almost 99% is present in the tetramer. Even under such conditions where the ion pair monomer is a minor constituent, it is the dominant reactant in alkylation displacement reactions.

Experimental Section

PhIBP was prepared according to the procedure of Long and Henze;[30] the isolated material was purified by multiple recrystallizations from ethanol followed by sublimation under high vacuum. The spectrophotometry apparatus, preparation of the materials, SVD techniques, and the methods for measuring ion pair acidity have been detailed previously.[17] The extinction coefficient for the cesium ion pair of

---

(28) Brändström, A. *Arkiv Kemi* **1953**, *6*, 155−194.

(29) Choy, G. S.-C.; Abu-Hasanayn, F.; Leung, S. S.-W. Results to be published.

(30) Long, L. M.; Henze, H. R. *J. Am. Chem. Soc.* **1941**, *63*, 1939.

PhIBP was obtained by titrating to end point a solution of PhIBP with diphenylmethylcesium in THF.

Kinetic Studies. Methyl tosylate was obtained from Aldrich and distilled under vacuum prior to use. The kinetic experiments were performed in the glovebox with use of the same apparatus as for acidity studies. In a typical run, a quantity of PhIBP (about 5 mg) was dissolved in a known quantity of THF. Diphenylmethylcesium was added until the desired concentration of enolate was obtained as determined by the UV−visible absorption spectrum. The spectrum was monitored at 25.0 °C for several minutes to verify the stability of the enolate solution. A known quantity of methyl tosylate was added to the enolate solution as an oil, the reactor was shaken vigorously, and the reactor was placed in the thermostated cell holder of the spectrophotometer. The decrease in the absorbance was monitored at the absorbance maximum at 10 s intervals, beginning at 20 s after the addition, for a total reaction time of 70 s; the data point at zero time was included with these points in the analysis. In most cases, a first-order equation gave a satisfactory fit to the curve; in the faster reactions, an exponential function was used. The initial rates were then obtained from the derivative of the curve at time zero. The kinetic analysis results are summarized in Tables S1, S2, S4, and S5 (Supporting Information). Each entry is a separate kinetic experiment in which the initial rate was determined from the first 5−10% reaction. The change in absorbance with time was converted to the rate of reaction of CsPhIBP by using the calibration curve in Figure S2 (Supporting Information). For convenience, this curve was converted to an empirical correlation between absorbance and concentration and only data were used that were within the range of the measured calibration curve.

Product Studies. Product analysis for *p*-*tert*-butylbenzyl chloride was determined at 20 °C; the cell was allowed to sit in the block for 5 min before any spectra were taken. After the reaction was completed, the cell was taken out of the box, and the solution was transferred to a Schlenk flask. The THF was evaporated for 2 h to give a white residue. This solid was dissolved in $CDCl_3$ and filtered through a Celite plug, then an NMR spectrum was taken. The C/O ratio did not change with the length of evaporation. The C/O ratio for the alkylation of the CsPhIBP with BnCl was determined by using ^{1}H NMR (Bruker, 300 MHz). The ratios were determined by using integration of the benzylic protons, and whenever possible the ratio of the vinylic methyls of the O-alkylated product was compared with the methylene of the C-alkylated product. The delays for the NMR experiments were longer than the experimentally calculated T_1 values (0.60 s, CH_2 and 0.93 s, CH_3).

1-(4-Biphenylyl)-2-methyl-2-(*p*-*tert*-butylbenzyl)-1-propanone. PhIBP (0.1 g, 0.046 mmol) and biphenylyldiphenylmethane (BDPM; 4 mg, 0.013 mmol) were placed in a screw-top vial, and 3 mL of dry, degassed THF was added. Aliquots of DPMCs (0.1 M) were added until PhIBP was completely deprotonated as indicated by the purple color of the end point indicator (BDPM, $pK_a = 30.07$, $\lambda_{max} = 568$, $\epsilon = 44500$). An aliquot of 4-*tert*-butylbenzyl chloride (0.1 mmol) was added to the vial and the mixture was allowed to react until completion as seen by the disappearance of color and formation of CsCl. The solution was removed from the glovebox, transferred to a Schlenk flask, and evaporated for a period of 10 h. The resulting solid was dissolved in methylene chloride, filtered through a Celite plug, and chromatographed on a preparatory plate with hexanes as the eluent. The third isolated band yielded the C-alkylated product: mp 100.5−101.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66−7.04 (m, 13 H), 3.09 (s, 2 H), 1.35 (s, 6 H), 1.30 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.7, 149.2, 143.5, 140.0, 137.9, 134.7, 130.1, 128.9, 128.4, 127.9, 127.1, 126.6, 126.4, 48.8, 45.9, 34.4, 31.4, 26.2. Anal. Calcd for $C_{27}H_{30}O$: C, 87.52; H, 8.16. Found: C, 87.39; H, 8.27.

The second isolated band resulting from the above chromatography yielded a small amount of a film that could be further characterized as the O-alkylated product, 1-(4-biphenylyl)-1-(p-*tert*-butylbenzoxy)-2-methyl-1-propene, only by NMR: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65−7.28 (m, 13 H), 4.46 (s, 2 H), 1.84 (s, 3 H), 1.73 (s, 3 H), 1.32 (s, 9 H).

Acknowledgment. This research was supported in part by grants from the National Institutes or Health and the National Science Foundation.

Supporting Information Available: Tables of kinetic results and ion pair acidity equilibria (Tables S1−S5) and C/O-alkylation (Table S6), Figures S1, S2, S5−S7, S11, and derivation of eq 10 (13 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

JA981437Y