

## Cesium Ion Pair Acidities of some *N,N*-Dialkylacetamides and Aggregation of Their Cesium Enolates in Tetrahydrofuran

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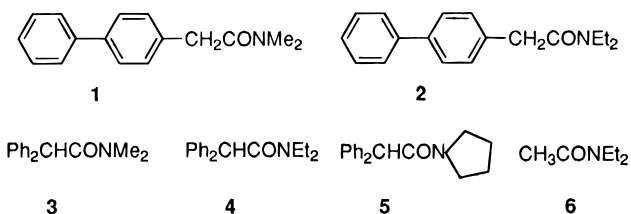
Cesium ion pair acidities are reported of some *N,N*-dialkylacetamides at 25 °C in tetrahydrofuran. The cesium enolates of  $\alpha$ -arylacetamides are essentially monomeric at concentrations of about  $10^{-4}$  M, but small amounts of dimers are present for the enolates of *N,N*-dimethyl- and *N,N*-diethyl(4-biphenyl)acetamide ( $K_{\text{dimer}}$  is approximately  $400 \text{ M}^{-1}$ ). The cesium enolate of *N,N*-dimethyl-diphenylacetamide forms small amounts of dimers, but the dimerization constant of  $<100 \text{ M}^{-1}$  is near the limit of detection of our methods. The enolate of *N,N*-diethylacetamide has an average aggregation number of 3.3, consistent with a mixture of dimers and tetramers. The cesium ion pair p*K*s of the  $\alpha$ -arylacetamides are about 25–26, and that of *N,N*-diethylacetamide is greater than 33.7. The acidity data are in good agreement with measurements that have been reported in the literature for similar systems.

The paucity of systematic studies of amide enolates stands in contrast to the vast literature concerning ketone enolates. The disparity is attributable to the ubiquity of ketone enolates in synthetic chemistry. Simple alkylation and addition reactions of amide enolates have been known for some time,<sup>1–5</sup> but were not used extensively until asymmetric syntheses were demonstrated.<sup>6–9</sup> Recent studies have focused on their reactivities in Michael additions.<sup>10–14</sup>

It has become recognized that alkali metal enolates,<sup>15–19</sup> phenolates,<sup>20–24</sup> and similar compounds<sup>25,26</sup> generally aggregate in nonpolar solvents; dimeric, tetrameric, and hexameric species are especially common. Papers of Arnett and co-workers<sup>17</sup> and of Jackman and co-workers<sup>22</sup> give comprehensive citations to this literature. Consid-

eration of aggregation effects is important in interpreting reactivity, and of special interest is the possibility that aggregates play an important role in stereoselective reactions.<sup>15,27,28</sup> We report here a study of the cesium ion pair acidities of several *N,N*-dialkylamides and the aggregation of their cesium enolates in tetrahydrofuran (THF); the results provide a comparison to related ketones.<sup>18</sup> In the only other study of aggregation of amide enolates to our knowledge, the lithium salt of *N,N*-dimethylcycloheptatrienecarboxamide was found to be partially aggregated in melting THF.<sup>29</sup>

The present study includes the compounds **1–6** and their cesium salts (Cs-**1**–Cs-**6**).



### Results

**Cesium Ion Pair Absorption Spectra.** The cesium ion pairs of the compounds selected for study, with the exception of the cesium salt of **6** (Cs-**6**), absorb in the visible or near-UV. It was for this reason that the biphenyl compounds **1** and **2** were chosen for study; the absorbance of phenyl derivatives is too far in the UV to be useful. The absorption spectra were found to be slightly concentration dependent. For each ion pair, a series of 13–15 absorption spectra at varying concentrations was acquired and processed by the singular value decomposition (SVD) method.<sup>30,31</sup> The total concentration ranges for the SVD experiments were  $(0.4\text{--}4.0) \times 10^{-4}$

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- (1) Carbon Acidity, 94.
- (2) Needles, H. L.; Whitfield, R. E. *J. Org. Chem.* **1966**, *31*, 989.
- (3) Gassman, P. G.; Fox, B. L. *J. Org. Chem.* **1966**, *31*, 982.
- (4) Woodbury, R. P.; Rathke, M. W. *J. Org. Chem.* **1977**, *42*, 1688.
- (5) Woodbury, R. P.; Rathke, M. W. *J. Org. Chem.* **1978**, *43*, 881, 1947.
- (6) Evans, D. A.; Takacs, J. M. *Tetrahedron Lett.* **1980**, *21*, 4233.
- (7) Evans, D. A.; McGee, L. R. *Tetrahedron Lett.* **1980**, *21*, 3975.
- (8) Evans, D. A.; Nelson, J. V.; Taber, T. R. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Wilen, S. H., Eds.; Wiley: New York, 1982; Vol. 13.
- (9) Sauriol-Lord, F.; Grindley, T. B. *J. Org. Chem.* **1981**, *46*, 2831.
- (10) Stefanovsky, Y.; Gospodova, T.; Viteva, L. *Tetrahedron* **1986**, *42*, 5355.
- (11) Oare, D. A.; Henderson, M. A.; Sanner, M. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 132.
- (12) Viteva, L.; Stefanovsky, Y. *Tetrahedron Lett.* **1990**, *31*, 5649.
- (13) Viteva, L.; Gospodova, T. S.; Stefanovsky, Y. N. *Tetrahedron* **1994**, *50*, 7193.
- (14) Nomura, M.; Kanemasa, S. *Tetrahedron Lett.* **1994**, *35*, 143.
- (15) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1988**, *21*, 456.
- (16) Jackman, L. M.; Lange, B. C. *Tetrahedron* **1977**, *33*, 2737.
- (17) Palmer, C. A.; Ogle, C. A.; Arnett, E. M. *J. Am. Chem. Soc.* **1992**, *114*, 5619.
- (18) Ciulla, J. C.; Streitwieser, A. *J. Org. Chem.* **1992**, *57*, 431.
- (19) Abbotto, A.; Streitwieser, A. *J. Am. Chem. Soc.* **1995**, *117*, 6358.
- (20) Jackman, L. M.; Çizmeciyen, D.; Williard, P. G.; Nichols, M. A. *J. Am. Chem. Soc.* **1993**, *115*, 6262.
- (21) Jackman, L. M.; Rakiewicz, E. F.; Benesi, A. J. *J. Am. Chem. Soc.* **1991**, *113*, 4101.
- (22) Jackman, L. M.; Petrei, M. M.; Smith, B. D. *J. Am. Chem. Soc.* **1991**, *113*, 3451.
- (23) Jackman, L. M.; Rakiewicz, E. F. *J. Am. Chem. Soc.* **1991**, *113*, 1202.
- (24) Jackman, L. M.; Chen, X. *J. Am. Chem. Soc.* **1992**, *114*, 403.
- (25) Arnett, E. M.; Moe, K. D. *J. Am. Chem. Soc.* **1991**, *113*, 7288.
- (26) Carlier, P. R.; Lucht, B. L.; Collum, D. B. *J. Am. Chem. Soc.* **1994**, *116*, 11602.

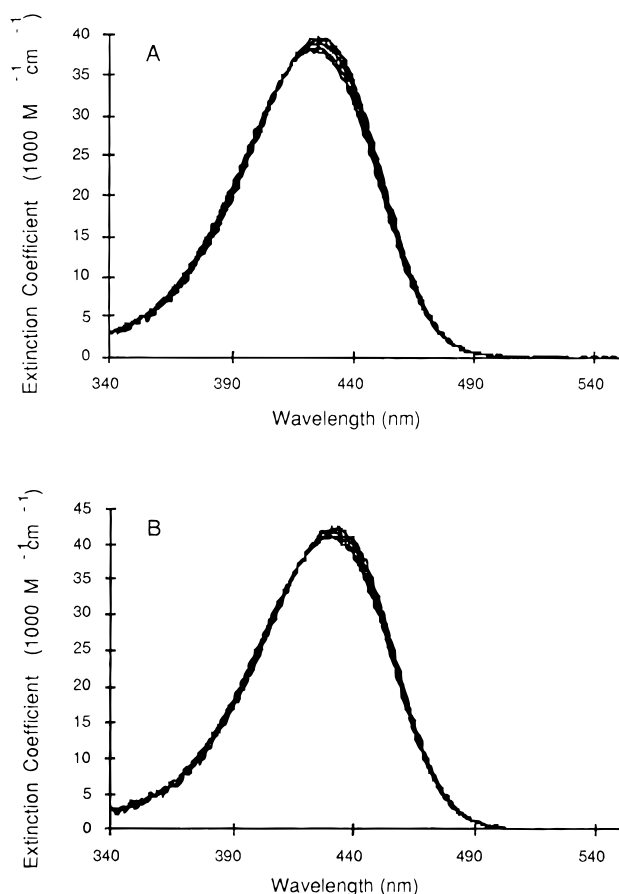
(27) Seebach, D. In *The Robert A. Welch Foundation Conferences on Chemical Research XXVII. Stereospecificity in Chemistry and Biochemistry*; Houston, TX, 1983; p 93.

(28) Carlier, P. R.; Lo, K. M. *J. Org. Chem.* **1994**, *59*, 4053.

(29) Bauer, W.; Seebach, D. *Helv. Chim. Acta* **1984**, *67*, 1972.

(30) Golub, G. H.; Reinsch, C. In *Linear Algebra*; Wilkinson, J. H., Reinsch, C., Eds.; Springer-Verlag: Heidelberg, 1971. Press, W. H.; Flannery, B. P.; Teukolsky, S. A.; Vetterling, W. T. *Numerical Recipes (Fortran Version)*; University Press: Cambridge, 1989.

(31) Malinowsky, E. R. *Factor Analysis in Chemistry*; Wiley: New York, 1991.



**Figure 1.** Concentration dependence of the UV-visible absorption spectra of the cesium enolates of **1** (A) and **2** (B). The isosbestic points are at 412 nm (A) and 416 nm (B).

**Table 1. Spectroscopic Data for the Cesium Enolates of the Aryl-Substituted Amides**

compound <sup>a</sup>	$\lambda_{\max}$ (nm)	$\epsilon$ ( $M^{-1} \text{ cm}^{-1}$ )	$S_1^b$	$S_2^b$
<b>1</b> , BiphCH <sub>2</sub> CONMe <sub>2</sub>	412 <sup>c</sup>	35,600 <sup>c</sup>	352.7	5.5
<b>2</b> , BiphCH <sub>2</sub> CONEt <sub>2</sub>	416 <sup>c</sup>	36,600 <sup>c</sup>	351.9	4.4
<b>3</b> , Ph <sub>2</sub> CHCONMe <sub>2</sub>	392	19,400	344.7	2.2
<b>4</b> , Ph <sub>2</sub> CHCONEt <sub>2</sub>	398	18,700	396.9	1.6
<b>5</b> , Ph <sub>2</sub> CHCONC <sub>4</sub> H <sub>8</sub>	388	19,000	356.8	2.0

<sup>a</sup> Spectroscopic data for the cesium enolate of the indicated amide. <sup>b</sup>  $S_1$  and  $S_2$  are the first and second singular values from the SVD procedure. <sup>c</sup> Data are for the isosbestic point (see text).

M for the biphenylacetamides and  $(0.3\text{--}7.0) \times 10^{-4}$  M for the diphenylacetamides. The SVD results show that the spectra of each ion pair are the sums of two components having different concentration dependence. Furthermore, extinction coefficient measurements of Cs-**1** and Cs-**2** at varying concentrations revealed isosbestic points at 412 and 416 nm, respectively (Figure 1). We could not locate clear isosbestic points in the absorption spectra of the diphenylacetamide enolates, but the concentration dependencies of these spectra are probably smaller than the experimental error in our extinction coefficient measurements. (See the Experimental Section for details.) The spectroscopic data are collected in Table 1.

**Cesium Ion Pair Acidity.** The acidities of the aryl-substituted acetamide derivatives were measured against the indicator 9-*tert*-butylfluorene (*t*BuFl), which has a pK of 24.39 on the cesium ion pair acidity scale in THF.<sup>32</sup> The existence of suitable absorption spectra for the ion pairs of these compounds allows the use of the double

indicator method of acidity determination, in which the concentrations of the ion pairs are determined by linear least-squares best fitting of the spectra of the separate species to the spectrum of the equilibrium mixture.<sup>33</sup>

The acidity of **6** was determined against diphenylmethane ( $\text{p}K_{\text{Cs}} = 33.25$ ),<sup>32</sup> but the lack of a suitable enolate absorption necessitated the use of the less precise single indicator method.<sup>34,35</sup> The observed acidities at 25 °C are presented in Figure 2.

## Discussion

We first consider the possibility that the cesium amide enolates investigated here are significantly aggregated to ion pair dimers or higher aggregates. It has been shown that aggregation of the ion pair of interest causes the apparent acidity of its conjugate acid to increase as the formal concentration of the ion pair is increased.<sup>35</sup> This behavior arises because the ion pair acidity is defined relative to monomeric species, and aggregation is essentially a side reaction that consumes the monomer. Thus, the apparent acidity, which we determine by measuring the formal (total) concentration, increases because aggregation is favored by increasing concentration. Concentration-dependent aggregation equilibria sometimes can also be detected by UV-visible absorption spectroscopy. Since higher order aggregates generally absorb at shorter wavelengths than lower order aggregates, the absorption bands of the solutions exhibit a blue shift as the concentration is increased. Usually the shift is rather small, so we analyze the spectroscopic data by singular value decomposition (SVD), which is sensitive to systematic changes in the shapes of the absorption bands. Detailed discussions of SVD<sup>29,30</sup> and its application to spectroscopy<sup>31</sup> can be found elsewhere.

The SVD results show that the UV-visible absorption spectra of each of the ion pairs investigated here (except Cs-**6**, which was not examined spectroscopically because of the lack of a suitable chromophore) consist of two components, which suggests the presence of two distinct chemical species in equilibrium. The actual spectra of these species are not provided by the SVD treatment. Nevertheless, we have shown that such spectra can be constructed from the SVD output with the assumption of a particular aggregation model.<sup>33</sup> For example, if we assume that an ion pair system consists of an equilibrium between monomer and dimer, then the hypothetical monomer and dimer spectra can be constructed, and the equilibrium constant can be calculated with the aid of the experimentally measured extinction coefficient. Our experience has shown that many aggregation models will be consistent with the spectroscopic data, but in general only one will also be consistent with the acidity data;<sup>33</sup> this combination is an example of coupled equilibria.

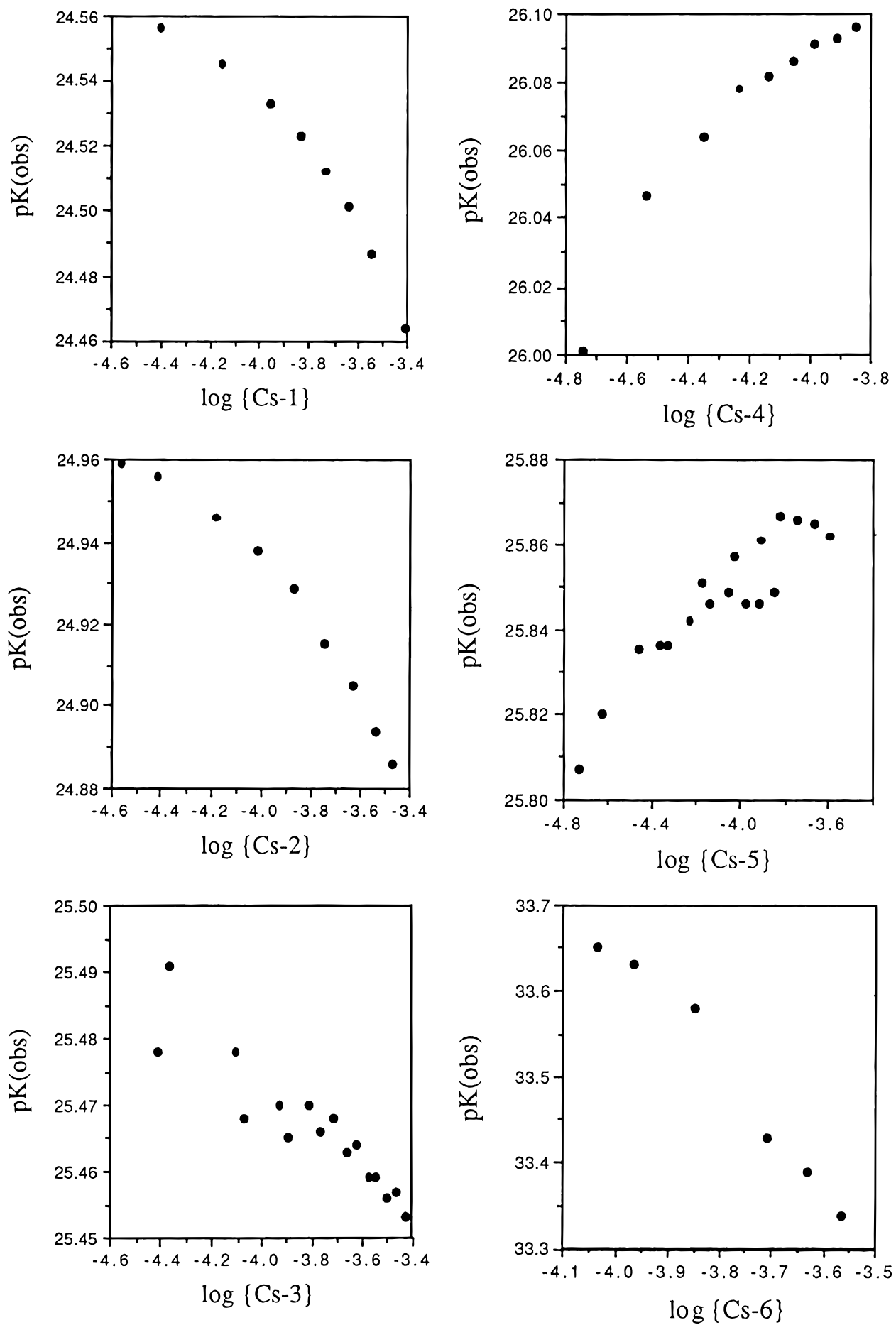
The spectra of Cs-**1** and Cs-**2** clearly show concentration-dependent behavior. When extinction coefficient measurements are made, the normalized spectra show isosbestic points (Figure 1) as well as blue shifts with increasing concentration. These observations are evidence of simple equilibria between two aggregated spe-

(32) Streitwieser, A.; Ciula, J. C.; Krom, J. A.; Thiele, G. J. *Org. Chem.* **1991**, *56*, 1074.

(33) Krom, J. A.; Petty, J. T.; Streitwieser, A. *J. Am. Chem. Soc.* **1993**, *115*, 8024.

(34) Streitwieser, A., Jr.; Reuben, D. M. E. *J. Am. Chem. Soc.* **1971**, *93*, 1794.

(35) Kaufman, M. J.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 6092.



**Figure 2.** Concentration dependence of the observed cesium ion pair acidities of the amides.

**Table 2. Hypothetical Aggregation Constants Calculated from Spectroscopic and Acidity Data**

enolate	$pK_{Cs}^a$	assumed equilibrium <sup>b</sup>	calcd aggregation constant	
			from spectroscopy	from acidity
Cs-1	24.87	M/Di	470 M <sup>-1</sup>	470 M <sup>-1</sup>
		M/Tr	3.0 × 10 <sup>6</sup> M <sup>-2</sup>	5.5 × 10 <sup>5</sup> M <sup>-2</sup>
		M/Te	1.4 × 10 <sup>10</sup> M <sup>-3</sup>	9.4 × 10 <sup>8</sup> M <sup>-3</sup>
Cs-2	25.26	M/Di	440 M <sup>-1</sup>	350 M <sup>-1</sup>
		M/Tr	3.2 × 10 <sup>6</sup> M <sup>-2</sup>	4.9 × 10 <sup>5</sup> M <sup>-2</sup>
		M/Te	1.6 × 10 <sup>10</sup> M <sup>-3</sup>	9.6 × 10 <sup>8</sup> M <sup>-3</sup>
Cs-3	25.48	M/Di	120 M <sup>-1</sup>	87 M <sup>-1</sup>
		M/Tr	6.8 × 10 <sup>5</sup> M <sup>-2</sup>	1.1 × 10 <sup>5</sup> M <sup>-2</sup>
		M/Te	2.0 × 10 <sup>9</sup> M <sup>-3</sup>	2.0 × 10 <sup>8</sup> M <sup>-3</sup>
Cs-4	26.09	M/Di	83 M <sup>-1</sup>	<i>c</i>
		M/Tr	4.4 × 10 <sup>5</sup> M <sup>-2</sup>	
		M/Te	1.0 × 10 <sup>9</sup> M <sup>-3</sup>	
Cs-5	25.85	M/Di	69 M <sup>-1</sup>	<i>c</i>
		M/Tr	6.6 × 10 <sup>5</sup> M <sup>-2</sup>	
		M/Te	2.1 × 10 <sup>9</sup> M <sup>-3</sup>	

<sup>a</sup> True cesium ion pair acidity of the conjugate acid with respect to the monomeric ion pair. The  $pK$ s are statistically corrected per acidic hydrogen. <sup>b</sup> M/Di, monomer–dimer; M/Tr, monomer–trimer; M/Te, monomer–tetramer. <sup>c</sup> The acidity data are not consistent with aggregation hypotheses. See text for discussion.

cies. The shifts in the spectra of the 2,2-diphenylacetamide enolates are not obvious, and the SVD output indicates that they are only slightly greater than the noise of the instrument. Although the spectroscopic shifts of these ion pairs are consistent with aggregation, the experimental results are not compelling. Additionally, we shall see below that the spectra of the structurally related **4** and **5** enolates change under the conditions of the acidity experiments.

The acidity data, discussed below, clearly indicate that the aryl-substituted ion pairs are mainly monomeric at the concentrations in these experiments (about 10<sup>-4</sup> M). In the analyses of the spectra, therefore, we only considered aggregation models that include the monomer. Hypothetical spectra of the aggregates were constructed from the SVD output according to monomer/dimer, monomer/trimer, and monomer/tetramer aggregation models, as mentioned above; data for the hypothetical spectra and equilibrium constants are presented in Table 2. The hypothetical aggregation constants for the diphenylacetamide enolates are prone to error because we were not able to find isosbestic points in their absorption spectra; thus, we have simply used the extinction coefficient at the  $\lambda_{max}$  in the calculations.

We now turn to the discussion of the acidity experiments. Inspection of Figure 2F shows that the acidity of **6** depends on the formal ion pair concentration; the quantitative treatment by the usual method<sup>35</sup> gives an average aggregation number of 3.3 for the cesium enolate of **6** (Cs-**6**). Note that this method gives only average values, so the value of 3.3 does not necessarily indicate a trimer. Comparison with literature data for similar compounds suggests that Cs-**6** is probably a mixture of dimers and tetramers. Trimeric species are known, however, for some alkali amides in the absence of donating ligands, both in solution and in crystal structures.<sup>36,37</sup>

The acidities of the aryl-substituted acetamides are nearly independent of concentration, showing that the cesium enolates of these compounds are essentially

monomeric at concentrations of about 10<sup>-4</sup> M. The acidities of **1** and **2** increase slightly with increasing ion pair concentration (Figures 2A and 2B), consistent with enolate aggregation. The acidity of **3** also increases, but the acidity change over the entire concentration range is about the same magnitude as the experimental error (Figure 2C). Hypothetical aggregation equilibrium constants were calculated from the acidity data according to a published procedure;<sup>33</sup> the results are collected in Table 2. Comparison with the aggregation constants calculated from the spectroscopic data shows best agreement for the monomer/dimer model in each case, but the discrepancies between the two analyses are rather large for Cs-**2** and Cs-**3**. We conclude that the cesium enolates of the biphenyl-substituted acetamides are slightly aggregated, probably to ion pair dimers; the data for the enolate of **3** are consistent with aggregation, but the putative dimerization constant is barely significant when compared to experimental error. The higher tendency of the enolates from the monosubstituted acetamide **1** to aggregate when compared to the disubstituted isomer **3** is probably associated with steric effects.

The apparent decreases in the acidities of **4** and **5** (Figures 2D and 2E) are not consistent with aggregation and are probably artifacts caused by anomalies in the spectra of their enolates; the shapes of the absorption bands of the enolates alone or in the presence of their conjugate acids are slightly different than in the acidity experiments, i.e., in the presence of the *t*-BuFl cesium ion pair. Consequently, small errors in the concentration determinations are caused by the inability to precisely model the equilibrium spectra from the spectra of the separate components. The errors are relatively larger at the lower concentrations, and we assume that the measurements at higher concentrations are more accurate. We considered the possibility that the spectroscopic anomalies in the equilibrium measurements are caused by mixed aggregate formation between the enolate and the indicator ion pair, but the spectrum of the indicator ion pair is unchanged in the acidity experiment. Although we have no explanation for the anomalies in their spectra, these enolates seem to be essentially monomeric.

As expected from previous studies of similar systems,<sup>38</sup> an aryl substituent on the acetamide enolate stabilizes it with respect to aggregation by delocalizing the charge. The slightly greater tendency of the biphenylacetamide enolates to aggregate when compared with their diphenyl isomers is perhaps due to subtle steric effects. Another possible explanation is that a small population of the biphenylacetamide enolates adopts the *E* configuration, which would be expected from steric considerations to dimerize more readily; of course, a similar configuration is not available to the diphenyl systems. NMR spectroscopic studies suggest that the enolate of *N,N*-dimethylphenylacetamide assumes only the *Z* configuration in DMSO solution,<sup>39,40</sup> but this free enolate ion is not aggregated under these conditions. Under our conditions, the *E* isomer could be stabilized by aggregation. We note that small amounts of *E* configured amide enolates have been observed in certain cases.<sup>41</sup> In a

(38) Kaufman, M. J.; Gronert, S.; Bors, D. A.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 602.

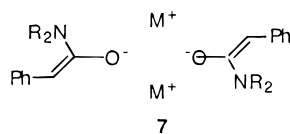
(39) Bobylev, V. A.; Petrov, M. L.; Komarov, V. Y.; Vasil'ev, V. V.; Ionin, B. I. *Zh. Org. Khim.* **1983**, *19*, 20.

(40) Bradamante, S.; Pagani, G. A. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1035.

(36) Mootz, D.; Zinnius, A.; Böttcher, B. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 378.

(37) Lucht, B. L.; Collum, D. B. *J. Am. Chem. Soc.* **1994**, *116*, 7949.

reasonable structure for the dimer, such as **7**, the *E* phenyl group is far from the coordination center.



We were surprised to find that the amide enolates examined in this study seem to be less aggregated than ketone enolates of similar structure.<sup>18</sup> For example, the cesium enolates of 1,3-di(4-biphenyl)acetone and 1,1,3,3-tetraphenylacetone have dimerization constants of 595 and 570 M<sup>-1</sup>, respectively. On the basis of electronic and steric considerations, the cesium enolates of  $\alpha,\alpha$ -diphenylacetophenone and of **3** offer the best comparison; the ketone enolate has a dimerization constant of 2310 M<sup>-1</sup>, but the dimerization constant of the amide enolate is <100 M<sup>-1</sup>. We have no satisfactory explanation for these observations.

Ion pair aggregation causes the apparent *pK* to decrease from the true value defined relative to monomeric species. Thus, the true cesium ion pair *pK* of *N,N*-diethylacetamide is greater than 33.7, consistent with Bordwell's estimate of 34–35 for the *pK* of *N,N*-dimethylacetamide in DMSO.<sup>42</sup> For further comparison, Fraser and co-workers determined the *pK* of *N*-methylpyrrolidone in THF with lithium counterion to be less than 33.8 on their acidity scale.<sup>43</sup> After adjusting their scale so that the *pK* of triphenylmethane coincides with its value on our lithium ion-pair acidity scale,<sup>44,45</sup> we find that *N*-methylpyrrolidone would have a *pK* of less than 30.2 on our lithium scale. This is in rough accord with our measurement of the cesium ion pair acidity of *N,N*-diethylacetamide because, for contact ion paired species, lithium *pK* values are generally lower by 3–7 *pK* units when compared with their cesium *pK* values.<sup>35,38</sup> Thus, it seems safe to conclude that simple *N,N*-dialkylamides have effective *pK*s of about 35 and 30 in THF on the cesium and lithium scales, respectively, but we reemphasize that the acidities will be concentration-dependent because of ion pair aggregation.

The cesium ion pair *pK* of **1** (24.87) compares favorably with the ionic *pK* of *N,N*-dimethylphenylacetamide in DMSO<sup>42</sup> (*pK* = 26.9 when statistically corrected per hydrogen), with some of the difference being due to the extra acidifying effect of biphenyl compared with phenyl.

The aryl-substituted acetamides have similar acidities, as might have been anticipated from acidity measurements of the aryl-substituted acetones.<sup>18</sup> In that study, however, it was found that diphenyl substitution is more acidifying than biphenyl (1,3-di(4-biphenyl)acetone, *pK*<sub>Cs</sub> = 17.10; 1,1,3,3-tetraphenylacetone, *pK*<sub>Cs</sub> = 16.57), just the opposite of the findings for the acetamides. In fact, diphenyl is usually more acidifying than either monophenyl or biphenyl, but exceptions occur when the steric congestion in the anion is great enough that the aryl substituents are forced out of planarity to the extent

that an extra aryl substituent is actually destabilizing. For example, Bordwell found that  $\alpha,\alpha$ -diphenylacetophenone is less acidic than  $\alpha$ -phenylacetophenone.<sup>46</sup> Since the steric environment in the acetophenones is similar to the acetamides studied here, we assume that a similar mechanism operates. Further evidence is provided by altering the substitution at nitrogen. For the biphenylacetamides, replacement of dimethylamino by diethylamino is deacidifying by 0.4 *pK* unit in the biphenylacetamides and 0.6 *pK* unit in the diphenylacetamides. Although the difference of 0.2 *pK* unit is small, it is probably genuine since locking the ethyl groups into a pyrrolidino ring (**5**) is acidifying by just that amount.

## Conclusion

Cesium ion pair acidity and UV–visible spectroscopic studies have established that the cesium enolates of *N,N*-dialkyl(4-biphenyl)acetamides aggregate in THF solution, forming small amounts of dimeric species at concentrations of about 10<sup>-4</sup> M. Similar studies of cesium enolates of *N,N*-dialkyldiphenylacetamides show that their dimerization constants must be less than about 100 M<sup>-1</sup>. The greater tendencies of the biphenylacetamide enolates to aggregate is probably due to lower steric demand when compared with their diphenyl isomers, possibly because they have a less sterically demanding *E*-configuration available. The cesium enolate of *N,N*-diethylacetamide is rather highly aggregated, probably forming a mixture of dimers and tetramers. For reasons that are not clear, the aryl amide enolates are less aggregated than structurally related ketone enolates.

The cesium ion pair acidities of the arylacetamides are similar, with *pK*<sub>Cs</sub> values of about 25–26 at 25 °C. *N,N*-Diethylacetamide has a *pK*<sub>Cs</sub> of greater than 33.7. The acidities determined here are in good agreement with Bordwell's measurements in DMSO<sup>42</sup> and Fraser's measurement of *N*-methylpyrrolidone with lithium counterion in THF.<sup>43</sup> The data suggest that the effective C–H acidities of simple amides are about 35 on the cesium ion pair scale and about 30 on the lithium ion pair scale.

## Experimental Section

With the exception of **1**, all of the amides are known compounds. They were prepared by the reaction of the corresponding acyl chloride with an excess of the amine. The solid amides were purified by recrystallization from ethanol or diethyl ether, and *N,N*-diethylacetamide was purified by distillation through a spinning-band fractionating column. *N,N*-Diethyl-2-(4-biphenyl)acetamide is an oil and was purified by column chromatography over silica gel. The purification of THF was accomplished by described procedures, and our methods of acidity determination, which make use of an inert atmosphere glovebox and fiber-optic UV–visible spectrophotometer, have been published.<sup>33</sup>

***N,N*-Dimethyl-2-(4-biphenyl)acetamide (1).** The commercial reagents were used without purification. A solution of 3.5 g (16 mmol) of biphenylacetic acid (Aldrich) in 25 mL of thionyl chloride (Aldrich) was gently warmed under a drying tube until the effervescence of HCl was evident (about 60 °C). The reaction mixture was stirred for an additional 2 h, and a solution of dimethylamine in diethyl ether was prepared by extracting a 40% aqueous solution of the amine with diethyl ether. The reaction mixture was allowed to cool, and the thionyl chloride was removed by distillation under reduced pressure. The crude acyl chloride was dissolved in diethyl

(41) Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.

(42) Bordwell, F. G.; Fried, H. E. *J. Org. Chem.* **1981**, *46*, 4327.

(43) Fraser, R. R.; Bresse, M.; Mansour, T. S. *J. Chem. Soc., Chem. Commun.* **1983**, 620.

(44) Gronert, S.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 7016.

(45) Kaufman, M. J.; Gronert, S.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 2829.

(46) Bordwell, F. G.; Bares, J. E.; Bartmess, J. E.; McCollum, G. J.; Van Der Puy, M.; Vanier, N. R.; Matthews, W. S. *J. Org. Chem.* **1977**, *42*, 321.

ether and carefully added to the vigorously agitated ethereal dimethylamine solution. The mixture was filtered, and the solids were washed with two portions of ether. The combined ethereal extracts were dried over  $\text{MgSO}_4$ , and the solvent was removed by rotary evaporation. The crude solid (3.4 g) was recrystallized twice from diethyl ether to give pure amide: mp 88–89 °C;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  3.01 (s, 3 H), 3.10 (s, 3 H), 3.76 (s, 2 H), 7.3–7.7 (m, 9 H). Anal. Calcd for  $\text{C}_{16}\text{H}_{17}\text{NO}$ : C, 80.30; H, 7.16; N, 5.85. Found: C, 80.34; H, 7.37; N, 6.09.

**Extinction Coefficient Measurements.** A solution of known concentration of the amide in THF was prepared in a UV cuvette, and a tiny amount (about 50  $\mu\text{g}$ ) of 9-phenylthioxanthene (PSX) was added as an end point indicator. (Diphen-

ylmethyl)cesium was added to the cell until the red-brown color of cesiated PSX persisted, and the spectrum was obtained. The solution was successively diluted with known amounts of THF, and the spectrum was obtained after each dilution. The color of the cesiated PSX persisted throughout the experiment. The spectrum of the end point indicator was subtracted from each spectrum, and the extinction coefficient at each concentration was calculated in a straightforward manner.

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