





Figure 3. Correlation between  $\epsilon$  and IP.

is developed. With both  $X = NH_3^+$  and  $O^-$ , all energy levels are markedly perturbed.

The photoelectron spectra of many of these compounds have been examined and the ionization potentials determined.<sup>8</sup> It was previously found that the calculated molecular orbital energies for a series of alkenes were linearly related to the vertical ionization potentials, provided that a nonzero intercept was allowed.<sup>9</sup> The same is true in this case, and the correlation holds for both s- and p-type orbitals (Figure 3). The relation between the quantities is given by

$$-IP = 0.83\epsilon - 1.5$$

This is essentially the same as that found for the alkenes.

The separation of the charge shifts into the  $\sigma$  and  $\pi$  components and the extension of these calculations to ethyl derivatives will be presented at a later time.

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# Photoselected Fluorescence Detected Circular Dichroism

Sir:

We report the first quantitative measurement of photoselected fluorescence detected circular dichroism (FDCD). In this measurement the optical activity of a chromophore is obtained by measuring the difference in fluorescence intensity for left and right circularly polarized excitation under conditions where rotation before emission is negligible. It was first pointed out by Ehrenberg and Steinberg that for these conditions the FDCD spectrum is not predicted by the simple theory of Turner et al.<sup>1-3</sup> Tinoco et al. subsequently developed a theory for this photoselected case.<sup>4</sup> According to this theory, the FDCD spectrum of the unoriented molecule can be obtained if a particular polarization of the fluorescence is detected. We have measured the FDCD spectrum of 10-dcamphorsulfonic acid (CSA) and of morphine in glycerol and find reasonable agreement with this theory.

When the detector is perpendicular to the exciting light, and a linear polarizer is placed in front of it, the following expression can be derived for the measured FDCD signal when fluorophore rotation is negligible:<sup>1,2,4</sup>

$$\theta_{\rm F}^{\circ} = -14.32 \times \left[ \frac{8R(1+\cos^2\phi) + (8R_{33}/3)(2-3\cos^2\phi)}{D(4-\cos^2\phi) - (D_{33}/3)(2-3\cos^2\phi)} - 2R_1 \right]$$
(1)

 $\phi$  is the angle that the detected polarization makes with the axis perpendicular to the excitation beam (i.e., when the polarizer is perpendicular to the excitation beam,  $\phi = 0^{\circ}$ ), R and D are the average rotational and dipole strengths, respectively, and  $R_{33}$  and  $D_{33}$  are the rotational and dipole strengths along the direction of the emission transition moment. The quantity  $R_1$ is given by

$$R_1 = \frac{\Delta A}{2A} - \frac{2.303\Delta A \times 10^{-A}}{2(1 - 10^{-A})}$$
(2)

where A is the absorbance of the sample and  $\Delta A$  is the absorbance for left circularly polarized light minus that for right circularly polarized light. Equation 1 predicts that the FDCD spectrum can be a function of polarizer angle and that  $\theta_{\rm F}^{\circ}$  =  $-14.32(4R/D - 2R_1)$  when  $\phi = 35.25^{\circ}$ . The values of 4R/Dand  $R_1$  can be obtained by measuring the circular dichroism (CD) and absorption spectra of the sample if only one species is present. Thus, comparison of the FDCD spectrum predicted

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Figure 1. Photoselected FDCD spectra of 0.43 M 10-d-camphorsulfonic acid in glycerol:  $(--) \phi = 0^{\circ}; (---) \phi = 35^{\circ}; (---) \phi = 90^{\circ}; (x)$  spectrum predicted from CD and absorption spectra. Base line solution was  $1.0 \times 10^{-4}$  M DL-tryptophan in water. Filter was Corning 4-72 and cell path length was 1 mm.

from eq 1 with the experimental spectrum provides a convenient test for the theory.

The apparatus is a modified version of the previously described instrument.<sup>1,5</sup> A linear polarizer on a rotatable mount is placed between the cell and the photomultiplier. Initial experiments on optically inactive, fluorescent dyes dissolved in glycerol gave large artifactual ellipticities in the measurement for  $\phi = 0^{\circ}$ . These appear to be due to imperfect circularly polarized light. The circular polarization has been improved by mounting the Pockel's cell modulator on a kinematic mount for precise alignment and replacing the original switching voltage on the cell with an accurate high voltage square wave. This has reduced the artifact from  $\sim$ 200 mdeg to  $\sim$ 50 mdeg for  $\phi = 0^{\circ}$ . The artifact is negligible for  $\phi = 90^{\circ}$ . The instrument is calibrated with CSA in water as described previously.5 The glycerol is certified Spectroanalyzed grade from Fisher and is redistilled to remove interfering fluorescence impurities.

The fluorescence of CSA in glycerol is highly polarized as indicated by a linear depolarization ratio,  $(F_{\parallel} - F_{\perp})/(F_{\parallel} + F_{\perp})$ , of 0.5 at the long wavelength edge of the excitation spectrum.<sup>6</sup> Thus photoselection effects will be present. The FDCD spectra of CSA in glycerol for  $\phi = 0$ , 35, and 90° are shown in Figure 1. The maximum ellipticity is on the order of 800 mdeg, so that artifactual contributions are negligible. The spectra shown in Figure 1 are dependent on  $\phi$ . This is not true for CSA dissolved in water where the depolarization ratio is only 0.02. According to eq 1, the CD and absorption spectra of CSA can be used to predict the FDCD spectrum for  $\phi =$ 35.25°. Points calculated from eq 1 are shown in Figure 1. These points agree with the spectrum measured for 35° within experimental error. Thus there is good agreement between experiment and theory.

One of the major potential applications of FDCD is to study local conformations in macromolecules. In some cases, this will involve the photoselected case. The above results demonstrate that it is possible to obtain quantitative information by choosing the polarization of the detected fluorescence. However, measurements on phenylalanine tRNA and human serum albumin indicate that typical signals will be on the order of 50



Figure 2. Photoselected FDCD spectra of  $4.05 \times 10^{-3}$  M morphine in 90% glycerol-10% water (v/v), 0.1 M H<sub>2</sub>SO<sub>4</sub>: (--)  $\phi = 0^{\circ}$ ; (--)  $\phi = 35^{\circ}$ ; (--)  $\phi = 90^{\circ}$ ; (x) spectrum predicted from CD and absorption spectra. Filter was Wratten 18-A and cell path length was 1 mm.

mdeg.<sup>7,8</sup> Thus artifacts can be a serious problem. Measurements on optically inactive, fluorescent dyes dissolved in glycerol indicate that the artifacts are similar ( $\pm 15$  mdeg) for concentrated (absorbance >5) and dilute solutions. This is reasonable, if the artifact arises from imperfect circularly polarized light that changes between the left and right cycles. In contrast, eq 1 predicts that the FDCD signal at high concentrations approaches zero for  $\phi = 35.25^{\circ}$ . It also indicates that, for any  $\phi$ , the difference between the FDCD measured for a concentrated and dilute sample containing one species is given by twice the second term of eq 2. The different response of artifact and signal to concentration can be used to further reduce and correct for the artifact. This method has been tested by measuring the FDCD of morphine in glycerol.

The depolarization ratio of morphine in 90% glycerol is 0.3 in the long-wavelength band, so that photoselection effects are present. A concentrated solution of  $8 \times 10^{-2}$  M was used as the base line. This corresponds to an absorbance of 11.2 at the 286-nm maximum. The Pockel's cell orientation was adjusted to give a minimum difference between the base lines at  $\phi = 35^{\circ}$ for the concentrated sample and for sodium fluorescein in water. Then the spectrum of a  $4 \times 10^{-3}$  M sample was recorded. The differences of spectra measured for concentrated and dilute morphine are shown in Figure 2, along with the result predicted from the CD and absorption spectra of the dilute sample. The 0 and 90° spectra are essentially coincident and agree well with the result predicted. This does not mean that the artifact has been completely eliminated, however. The 35° measurement gives a 270-290-nm band with an average ellipticity of 25 mdeg, rather than the expected 9 mdeg. Thus the absolute error in the measurement is roughly  $\pm 15$ mdeg.

The importance of this work is that it provides the first experimental verification that photoselected FDCD can be studied by choosing the polarization of the detected fluorescence. Artifacts have been reduced to a level of ~15 mdeg. Preliminary results on human serum albumin indicate that this . is sufficient to determine 4R/D for its single fluorescent tryptophan to  $\pm 30\%$ .<sup>9</sup> Other proteins should give similar results. Since many conformational arguments require only the sign of the optical activity, this should provide much useful information.

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## Benzylic Organolithium Carbanion Reactivity. 3. Kinetic Studies with Neopentyl Halides and Benzyl Fluoride

### Sir:

Benzylic organolithium reagents couple rapidly with benzylic chlorides and more slowly with benzylic fluorides to give phenylated ethanes in 91-97% yields.<sup>1</sup> In coupling reaction competition experiments at 25 °C, mixtures of Ph<sub>2</sub>CHF and PhCH<sub>2</sub>F showed a normal steric hindrance to displacement effect. A kinetic investigation of the coupling reactions of triphenylmethyllithium (1) and diphenylmethyllithium (4) with benzyl fluoride and neopentyl halides was begun in order to establish the rate law for the process. These halides were chosen because they are structurally incapable of undergoing elimination of HX and for their convenient rates. Now we can report that the coupling reactions of 1 and 4 with neopentyl iodide (2a) and neopentyl bromide (2b), as well as with benzyl fluoride, follow second-order rate laws and exhibit steric and halogen kinetic effects characteristic of conventional  $S_N 2$ processes.

Neopentyl iodide reacts with 0.1-0.32 M tetrahydrofuran (THF) solutions of trityllithium to give 3,3-dimethyl-1,1,1-triphenylbutane<sup>2</sup> (3) in 85-95% yields in preparative as well as in kinetic runs (eq 1). Benzhydryllithium (4) couples simi-

Ph<sub>3</sub>CLi + XCH<sub>2</sub>C(CH<sub>3</sub>)<sub>3</sub> 
$$\longrightarrow$$
 Ph<sub>3</sub>CCH<sub>2</sub>(CH<sub>3</sub>)<sub>3</sub> (1)  
1 3  
2a, X = I  
b, X = Br  
c, X = Cl (no reaction)

larly with 2a or 2b to give 3,3-dimethyl-1,1-diphenylbutane<sup>3</sup> (5) (eq 2) in high yields. Both of these reactions exhibit second-order kinetics overall with first-order dependence on both the organolithium and the alkyl halide. This was demonstrated

Ph<sub>2</sub>CHLi + 2 
$$\xrightarrow{25 \circ C}$$
 Ph<sub>2</sub>CHCH<sub>2</sub>(CH<sub>3</sub>)<sub>3</sub> (2)  
4 (a or b) 5

by observing the pseudo-first-order decay of 1 and 4 in the presence of excess of either reactant.

In kinetics runs where the concentrations of RLi and R'X are comparable and range from 0.08 to 0.29 M, second-order rate constants were secured for eq 1 and 2 from plots that are linear to 80% conversion or better by least-squares analysis. For each kinetic run, the rates of disappearance of 1 or 4 and **2a** or **2b** were measured and are represented as  $k_{\rm RLi}$  and  $k_{\rm R'X}$ for comparison with the rate of formation of the hydrocarbon coupling product  $(k_{\rm hc})$ .<sup>4</sup> The purpose of this approach is to monitor side reactions of RLi with the solvent and alternative reaction paths such as carbenoid formation. For the reaction of **1** with **2a** at 25.0 °C, the k values  $(\times 10^{-3} \text{ L mol}^{-1} \text{ s}^{-1})$  are as follows:  $k_{\rm RLi} = 3.3 \pm 0.13$ ;  $k_{\rm R'X} = 3.2 \pm 0.10$ ; and  $k_{\rm hc} = 2.7 \pm 0.25$ . Thus formation of (CH<sub>3</sub>)<sub>3</sub>CCHLiX is not as significant for reaction of **1** with **2a** at 25 °C as it is at 40 °C where reactant disappearance rates are almost twice as great as the coupling product formation rate.

Furthermore, in the coupling reaction of 0.03 M 1 with 0.03 M benzyl fluoride, (6) to give 64-74% yields of *unsym*-tetraphenylethane (7), formation of PhCHLiF is  $\frac{1}{4}$  to  $\frac{1}{3}$  as fast as coupling, as shown by the isolation of *trans*-stilbene.<sup>5</sup> The rate of formation of 7 ( $k_{hc} = 0.074 \pm 0.03 \text{ M}^{-1} \text{ s}^{-1}$  at 0 °C) is substantially higher than we indicated earlier.<sup>7</sup>

The rate constants  $k_{\rm hc}$  for the coupling reaction of 1 and 2a at 0, 25, and 40 °C give a good Arrhenius plot with  $\Delta H = 15.5$  kcal/mol and  $\Delta S = -23.1$  cal/(mol deg). These results show that the sterically hindered ion-pair nucleophile (1) reacts at a substantial rate with neopentyl halides 2a and 2b by a process whose energy parameters compare favorably with those expected for a polar process.<sup>8</sup> In contrast 1 reacts with triphenylmethyl chloride by an electron-transfer process.<sup>1b</sup>

Analysis of the rate constants in Table I for diphenylmethyllithium coupling reactions with alkyl halides shows that neopentyl iodide couples with diphenylmethyllithium 6.5 times faster than neopentyl bromide. A recent literature value for the same element effect rate ratio for the reactions of 4 with isopropyl iodide and bromide is 25.8 (uncorrected for the elimination reaction).<sup>9</sup> Thus the reactivity ratio obtained here agrees quite well with that found for well-recognized  $S_N 2$  reactions, rather than with values reported for radical-anion rate ratios.<sup>9b</sup> In addition, an alkyl group steric effect of  $10^{-6}$  is found for the rate difference between neopentyl bromide and *n*-hexyl bromide.

That 1 and 4 react by a normal  $S_N^2$  mechanism with 2a and 2b is supported by the inversion of configuration of chiral  $\alpha$ -phenylethyl chloride during coupling with diphenylmethyllithium<sup>10</sup> together with the known inversion of configuration in chiral neopentyl-*1-d* tosylates and halides during displacements with a variety of nucleophiles.<sup>11</sup>

Neopentyl iodide reacts with Ph<sub>2</sub>CHLi to produce a bimolecular coupling product 8.5 times faster than Ph<sub>3</sub>CLi. At first sight this result seems lower than expected in that Ph<sub>2</sub>CHLi is 100 times stronger as a base than Ph<sub>3</sub>CLi ( $pK_a =$ 33.5 for Ph<sub>2</sub>CH<sub>2</sub> vs. 31.5 for Ph<sub>3</sub>CH).<sup>12</sup> However, trityllithium in THF exists 100% as solvent-separated ion pairs,<sup>13</sup> while

Table I. Rate Constants for the Reaction of Diphenylmethyllithium with Alkyl Halides

no. of runs	R-X (concn, M)	[Ph <sub>2</sub> CHLi], M	k, L mol <sup>-1</sup> s <sup>-1</sup> at 25 °C		
			k <sub>RLi</sub>	k <sub>R'X</sub>	k <sub>hc</sub>
1 2	$neo-C_5H_{11}-I(0.094)$	0.084	$2.82 \times 10^{-2}$ 3.63 × 10^{-3}	$3.68 \times 10^{-3}$	$2.33 \times 10^{-2}$ $3.55 \times 10^{-3}$
ref 9	$n-C_6H_{13}-Cl$	0.107	$1.0 \times 10^{1}$ 2.7 × 103	5.00 7 10	5.557710
ref 9	$i-C_3H_7-Br$		$1.9 \times 10^{2}$		
ref 9	<i>i</i> -C <sub>3</sub> H <sub>7</sub> -I		$4.9 \times 10^{3}$		