

**Table II.** Times  $t$  for 50% Change of Surface Pressure during Irradiation of Monolayers at Constant Surface Area  $A$ 

compound	$A$ , nm <sup>2</sup> /molecule	$T$ , °C	$t$ , s
1-diazo-2-oxopentadecane	0.40	6.6	3
1-diazo-2-oxopentadecane	0.18	6.6	33
1-diazo-2-oxononadecane	0.18	29.0	23
1-diazo-2-oxoheneicosane	0.19	29.2	17
dioctadecyl 2-diazopropanedioate	0.38	31.2	28
<i>cis</i> -1-diazo-2-oxo-10-nonadecene	0.42	11.6	9
azido ketone <b>1</b>	0.19	6.6	4
azido ketone <b>1</b>	0.19	21.2	3
diazo ketone <b>2</b>	0.28	37.6	1
diazo ketone <b>2</b>	0.21	37.6	21

nm<sup>2</sup>/molecule. This probably arises because the expanded phase disappears before the photoreaction is complete, rather than actually representing the influence of chain packing on the rate of the photoreaction.

Table II lists values of the irradiation times corresponding to 50% change in the surface pressure for monolayers of the various surface-active compounds. All of the photoreactions are rapid, proceeding to completion in under 90 s. High extinction coefficients at the exciting wavelength are necessary for rapid reaction. This is illustrated by studies of the photochemistry of the compound octadecanoyl azide in monolayers.<sup>16</sup> Because the aliphatic azido ketone has an extinction coefficient of only 300 M<sup>-1</sup> cm<sup>-1</sup> at 254 nm, its photoreactions were much slower, with typical half-reaction times of 20 min. As shown by the results for the long-chain azido ketone **1** in Table II, the rate of the photoreaction is only slightly affected by temperature. Several of the compounds showed very large changes in surface pressure on irradiation. For example, the surface pressure of monolayers of **1** jumps from 8 to 34 mN m<sup>-1</sup>, an increase of over 300%, on irradiation at surface areas just above the collapse area of the starting compound.

## Conclusions

The small size and comparatively simple photochemistry of the diazo ketone, diazo ester, and azide chromophores make long-chain compounds containing such hydrophilic groups well-suited for study in monolayers. Although the photoreactions are straightforward, the changes in head-group polarity produced by elimination of nitrogen and addition of water cause a wide variety of pronounced alterations in the behavior of these monolayers. Irradiation of monolayers of some compounds, such as 1-diazo-2-oxoheneicosane and dioctadecyl 2-diazopropanedioate, leads only to changes in monolayer compressibility and collapse pressure, without changing the monolayer structure. More pronounced changes are shown by monolayers of 1-diazo-2-oxononadecane and the aromatic diazo ketone **2**, which undergo phase transitions on irradiation. By irradiating monolayers of *cis*-1-diazo-2-oxo-10-nonadecane at high applied pressure, it is possible to push the monolayer off the water surface. Finally, irradiation of 1-diazo-2-oxopentadecane monolayers on an alkaline subphase leads to disappearance of the monolayers because the photolysis products are water soluble.

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**Registry No.** **1**, 90670-26-1; **2**, 90670-25-0; **3** (R = heptadecyl), 75240-80-1; 1-diazo-2-oxononadecane, 79196-27-3; 1-diazo-2-oxopentadecane, 90670-23-8; 1-diazo-2-oxoheneicosane, 80797-59-7; 1-diazo-2-oxononacosane, 90670-24-9; dioctadecyl 2-diazopropanedioate, 90670-27-2; *cis*-1-diazo-2-oxo-10-nonadecene, 90670-28-3; nonadecanoic acid, 646-30-0; 2-hydroxypropanedioic acid dioctadecyl ester, 90670-29-4; octadecanoyl chloride, 112-76-5; 4-(octadecyloxy)benzoyl chloride, 56800-40-9; dioctadecyl propanedioate, 16832-80-7; 4-octadecyloxybenzoic acid, 15872-50-1.

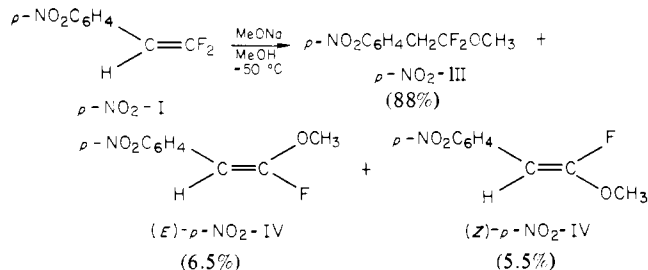
## Proton-Transfer Reactions. 5.<sup>1</sup> An Observed Primary Kinetic Isotope Effect That Increases with Increasing Temperature

Heinz F. Koch\* and Andrew S. Koch

Contribution from the Department of Chemistry, Ithaca College, Ithaca, New York 14850. Received July 1, 1983

**Abstract:** Reactions of XC<sub>6</sub>H<sub>4</sub>CH=CF<sub>2</sub> (I) with methanolic sodium methoxide result in formation of carbanions, (XC<sub>6</sub>H<sub>4</sub>CHCF<sub>2</sub>OMe)<sup>-</sup> (II), that partition to yield XC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CF<sub>2</sub>OMe (III) and XC<sub>6</sub>H<sub>4</sub>CH=CFOMe (IV). Product ratios for reactions in pure MeOD and MeOH are used to calculate the primary kinetic isotope effect (PKIE) associated with proton transfer from methanol to neutralize the carbanions. Compounds studied and their relative rates at 25 °C are *m*-CF<sub>3</sub>-I (1.0), *m*-NO<sub>2</sub>-I (7.7), *p*-CN-I (50), and *p*-NO<sub>2</sub>-I (240). The calculated PKIE,  $k^H/k^D$ , for the neutralization reaction are as follows: *m*-CF<sub>3</sub>-I, 1.28 (0 °C) and 1.40 (+50 °C); *m*-NO<sub>2</sub>-I, 1.20 (-50 °C), 1.29 (0 °C), and 1.39 (+50 °C); *p*-CN-I, 1.33 (-70 °C), 1.36 (-50 °C), 1.69 (0 °C), and 2.11 (+50 °C); *p*-NO<sub>2</sub>-I, 11.3 (-70 °C), 9.62 (-50 °C), 7.12 (0 °C), and 6.44 (+25 °C). The increase of PKIE with increasing temperature is discussed in terms of a multistep mechanism.

We recently reported significant differences for localized and delocalized carbanions that are neutralized by a competition between proton transfer from methanol,  $k_{add}^H$ , or by ejection of fluoride,  $k_{elim}^F$ .<sup>2</sup> For example, *p*-nitro- $\beta,\beta$ -difluorostyrene, *p*-NO<sub>2</sub>-I, reacts with methanolic sodium methoxide at -50 °C to yield 88% of a saturated ether, *p*-NO<sub>2</sub>-III, and 12% of the isomeric vinyl ethers, (*E*)- and (*Z*)-*p*-NO<sub>2</sub>-IV.



(1) Part 4: Koch, H. F.; Dahlberg, D. B.; Lodder, G.; Root, K. S.; Touchette, N. A.; Solsky, R. L.; Zuck, R. M.; Wagner, L. J.; Koch, N. H.; Kuzemko, M. A. *J. Am. Chem. Soc.* **1983**, *105*, 2394-2398.

(2) Koch, H. F.; Koch, J. G.; Koch, N. H.; Koch, A. J. *J. Am. Chem. Soc.* **1983**, *105*, 2388-2393.

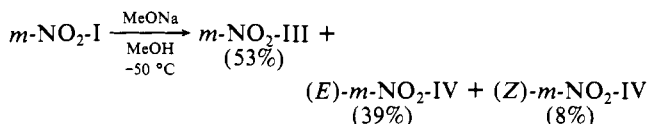
On the other hand, *m*-nitro- $\beta,\beta$ -difluorostyrene, *m*-NO<sub>2</sub>-I, reacts

Table I. Primary Kinetic Isotope Effects (PKIE) for Reaction of  $(XC_6H_4CHCF_2OMe)^-$  with Methanol

X	PKIE						$\Delta E_a^{D-H}$ , kcal mol <sup>-1</sup>	$A^H/A^D$
	-70 °C	-50 °C	-25 °C	0 °C	+25 °C	+50 °C		
<i>m</i> -CF <sub>3</sub> <sup>a</sup>				1.28 (1.22)	1.34 (1.25)	1.40 (1.28)	-0.31 ± 0.01 (-0.17 ± 0.01)	2.2 (1.7)
<i>m</i> -NO <sub>2</sub>		1.20	1.24	1.29	1.35	1.39	-0.22 ± 0.02	2.0
<i>p</i> -CN	1.33	1.36	1.53	1.69	2.04	2.11	-0.56 ± 0.05	5.1
<i>p</i> -NO <sub>2</sub>	11.3	9.62	8.14	7.12	6.44		+0.72 ± 0.01	1.9

<sup>a</sup>Results in parentheses were obtained by mass spectrometry on *m*-CF<sub>3</sub>C<sub>6</sub>H<sub>4</sub>CH<sup>H</sup>CF<sub>2</sub>OMe obtained when reaction was carried out in 50:50 mixture of MeOH:MeOD.

to give 53% saturated ether, *m*-NO<sub>2</sub>-III, and 47% of the two vinyl ethers, (*E*)- and (*Z*)-*m*-NO<sub>2</sub>-IV. Note that reaction of the *p*-nitro

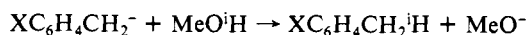
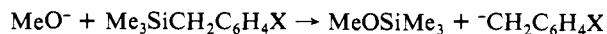


compound yields almost equal amounts of the isomeric vinyl ethers, whereas *m*-nitrostyrene favors formation of the *E* isomer over (*Z*)-*m*-NO<sub>2</sub>-IV by about 5:1. The temperature dependence of the competing product-forming reactions also differs for the two compounds. Saturated ether formation decreases with increasing temperature for *p*-nitro, 88% at -50 °C to 50% at +25 °C, while the reverse occurs for *m*-nitro, 53% at -50 °C and 59% at +25 °C. Finally the moderate primary kinetic isotope effect (PKIE) for proton transfer from oxygen to carbon decreases with increasing temperature for the formation of *p*-NO<sub>2</sub>-III,  $k^H/k^D = 11.3$  (-70 °C) to 6.44 (+25 °C); however, the near-unity PKIE observed for the formation of *m*-NO<sub>2</sub>-III results in a small increase with increasing temperature,  $k^H/k^D = 1.20$  (-50 °C) to 1.39 (+50 °C).

We attribute differences in the product-forming reactions to the formation of a more stable  $\pi$ -delocalized anion, *p*-NO<sub>2</sub>-II-F, from the reaction of *p*-NO<sub>2</sub>-I, than the intermediate, *m*-NO<sub>2</sub>-II-F, generated from the reaction of methoxide and *m*-NO<sub>2</sub>-I. With charge localized on the benzylic carbon of *m*-NO<sub>2</sub>-II-F, the first fluorine to rotate into a position periplanar to the lone pair electrons will be ejected. With less negative charge in the benzylic position of *p*-NO<sub>2</sub>-II, the rate of fluoride ejection is decreased. This allows for a free rotation about the >C-CF<sub>2</sub>OMe bond and results in the formation of almost equal amounts of (*E*)- and (*Z*)-*p*-NO<sub>2</sub>-IV.

Proton transfer from methanol to the negative carbon occurs from the hydrogen-bonded carbanion, II-H, Scheme I. The rate-limiting step for the neutralization of *m*-NO<sub>2</sub>-II-F is the formation of *m*-NO<sub>2</sub>-II-H,  $k_1$ .<sup>3</sup> We estimate  $k_2 \gg k_{-1}$  by 10<sup>3</sup> or more, and therefore the low-energy step for *m*-NO<sub>2</sub>-II-H is the proton-transfer reaction,  $k_2$ . Since the PKIE associated with  $k_1$  is small, Scheme I could account for the low  $k^H/k^D$  observed for the formation of *m*-NO<sub>2</sub>-III. Since the neutralization of *p*-NO<sub>2</sub>-II-F via proton transfer has a moderate PKIE, the rate-limiting step appears to be the proton-transfer step,  $k_2$ .

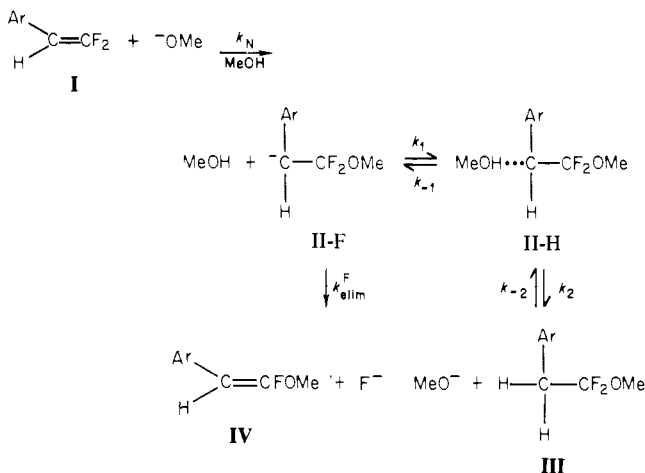
Large differences in the PKIE have been reported for the neutralization of benzyl anions generated by a reaction of methoxide with benzyltrimethylsilanes in mixtures of MeOH and MeOD:<sup>4</sup>



(<sup>H</sup>H = isotopic hydrogen)

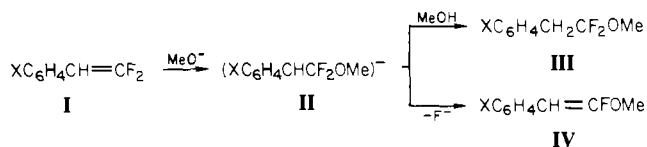
Values of  $k^H/k^D = 1.2$ –1.3 at 25 °C were calculated for the neutralization of a number of substituted benzyl anions, with (*p*-NCC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>)<sup>-</sup> giving a slightly larger value (2.0), and [*p*-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>]<sup>-</sup> resulting in a  $k^H/k^D = 10$  at 25 °C. This sug-

## Scheme I



gested to us that we do a more detailed measurement of the temperature dependence of the PKIE associated with the reactions of I and include *m*-CF<sub>3</sub>-I and *p*-CN-I in the study.

Difluorostyrenes have an advantage over the silanes in that the intermediate carbanion, II, can partition between the ejection of  $\beta$ -fluoride and the protonation reaction:



We used gas chromatography to analyze the product distributions of reactions run in pure MeOD and MeOH. Although the rate-limiting step is the reaction of methoxide and I (Scheme I), product distributions are controlled by subsequent reactions. Since reaction of IV with fluoride to regenerate II-F does not occur under our reaction conditions and  $k_N \gg k_2$  by at least 10<sup>3</sup>,<sup>3</sup> relative amounts of III and IV are formed according to the values of  $k_{\text{elim}}^{\text{F}}$  and

$$k_{\text{add}} = k_1 k_2 / (k_{-1} + k_2) \quad (1)$$

The PKIE can be calculated by assuming  $(k_{\text{elim}}^{\text{F}})^{\text{MeOH}} \approx (k_{\text{elim}}^{\text{F}})^{\text{MeOD}}$ :

$$\frac{k^H}{k^D} = \frac{(\% \text{ III} / \% \text{ IV})^{\text{MeOH}}}{(\% \text{ III} / \% \text{ IV})^{\text{MeOD}}} \quad (2)$$

This turned out to be a reasonable assumption since the fractionation factor for fluoride in H<sub>2</sub>O/D<sub>2</sub>O has been reported as unity.<sup>5,6</sup> Results are tabulated in Table I.

Since  $k_2 \gg k_{-1}$  for the *m*-nitro and *m*-(trifluoromethyl) compounds, eq 1 can be simplified:

$$k_{\text{add}} = k_1 \quad (3)$$

The observed PKIE therefore measures  $k_1^H/k_1^D$ . A model for

(3) Koch, H. F.; Koch, J. G.; Donovan, D. B.; Toezko, A. G.; Kielbania, A. J., Jr. *J. Am. Chem. Soc.* **1981**, *103*, 5417–5423.

(4) Macciantelli, D.; Seconi, G.; Eaborn, C. *J. Chem. Soc., Perkin Trans. 2* **1978**, 834–838.

(5) Albery, W. J. In "Proton-Transfer Reactions"; Caldin, E. F., Gold, V., Eds.; Chapman and Hall: London, 1975, p 283.

(6) We thank Jerry Kresge for pointing out this reference.

**Table II.** Formation of  $\text{XC}_6\text{H}_4\text{C}^i\text{HHC}_2\text{F}_2\text{OCH}_3$  (%)<sup>a</sup> from Reaction of  $\text{XC}_6\text{H}_4\text{CH}=\text{CF}_2$  with  $\sim 0.3$  N MeONa in MeOH

temp, °C	X = <i>p</i> -NO <sub>2</sub>		X = <i>p</i> -CN		X = <i>m</i> -NO <sub>2</sub>	
	MeOH <sup>b</sup>	MeOD <sup>b</sup>	MeOH	MeOD	MeOH <sup>b</sup>	MeOD <sup>b</sup>
-70	94.1 ± 0.4	58.6 ± 0.6	87.5 ± 0.4 <sup>d</sup>	83.4 ± 0.3 <sup>d</sup>		
			87.2 ± 0.4	83.9 ± 0.2		
			86.9 ± 0.8	83.7 ± 0.2		
-50	88.1 ± 0.2	43.8 ± 0.3	86.0 ± 0.3 <sup>d</sup>	82.1 ± 0.1 <sup>d</sup>	52.6 ± 0.4	48.0 ± 0.1
			86.2 ± 0.4	82.2 ± 0.3		
			86.4 ± 0.1	82.0 ± 0.3		
-25	78.3 ± 0.6	30.7 ± 0.4	85.3 ± 0.2 <sup>d</sup>	79.0 ± 0.2 <sup>d</sup>	55.7 ± 0.1	50.4 ± 0.3
			85.2 ± 0.2	79.1 ± 0.2		
			85.2 ± 0.1	79.3 ± 0.2		
0	65.3 ± 1.3	20.9 ± 0.3	81.5 ± 0.6 <sup>c</sup>	72.2 ± 0.6 <sup>c</sup>	58.4 ± 0.2	52.1 ± 0.2
			81.9 ± 0.6 <sup>c</sup>	73.0 ± 0.4 <sup>c</sup>		
			82.9 ± 0.2 <sup>b</sup>	74.5 ± 0.2 <sup>b</sup>		
+25	49.9 ± 0.6	13.2 ± 0.2	79.2 ± 0.3 <sup>c</sup>	65.0 ± 0.4 <sup>c</sup>	59.4 ± 0.2	52.0 ± 0.2
			78.4 ± 0.4 <sup>c</sup>	65.3 ± 0.6 <sup>c</sup>		
			79.7 ± 0.2 <sup>b</sup>	65.4 ± 0.2 <sup>b</sup>		
+50			73.5 ± 0.2 <sup>c</sup>	57.7 ± 0.2 <sup>c</sup>	59.5 ± 0.2	51.0 ± 0.1
			74.0 ± 0.3 <sup>c</sup>	57.0 ± 0.2 <sup>c</sup>		
			75.0 ± 0.2 <sup>b</sup>	58.6 ± 0.2 <sup>b</sup>		

<sup>a</sup> Calculated from uncorrected gas chromatographic analysis by using a Varian VISTA CDS 401 with an automatic sampler. Between 8 and 15 injections were made for each data point to obtain %  $\text{XC}_6\text{H}_4\text{CH}_2\text{CF}_2\text{OCH}_3$  reported. <sup>b</sup> Single runs for ca.  $10t_{1/2}$ . <sup>c</sup> Two samples taken at ca.  $1t_{1/2}$  and  $2t_{1/2}$ . <sup>d</sup> Three samples taken at ca.  $1t_{1/2}$ ,  $2t_{1/2}$  and  $10t_{1/2}$ .

this low PKIE could come from the work of Gold and Grist<sup>7</sup> on possible origins of the kinetic solvent isotope effect (KSIE) for methanol on the reactions of methoxide ion. They conclude that the KSIE are due to a multiple solvated methoxide ion which has a deuterium fractionation factor of 0.74. If the fractionation factor for  $\text{>C}^-\cdots^i\text{HOMe}$  is similar to that for methoxide, then PKIE values of 1.2–1.5 associated with the neutralization reactions could be reasonable. It is not known if this effect increases slightly with increasing temperature.

Although the measured isotope effect for reaction of *p*-NO<sub>2</sub>-I to form *p*-NO<sub>2</sub>-III decreases with increasing temperature, the  $A^{\text{H}}/A^{\text{D}} = 1.9$  suggests anomalous Arrhenius behavior for the PKIE. This type of behavior can arise when neither  $k_1$  or  $k_2$ , eq 1, is clearly rate limiting.<sup>8</sup> With assumed values for  $k_2^{\text{H}}/k_2^{\text{D}} = 12$  and  $k_1^{\text{H}}/k_1^{\text{D}} = k_{-1}^{\text{H}}/k_{-1}^{\text{D}} = 1.35$ , the  $(k^{\text{H}}/k^{\text{D}})_{\text{obsd}} = 6.44$  at 25 °C for the formation of *p*-NO<sub>2</sub>-III can be rationalized when  $k_{-1}^{\text{D}} = 8.1k_2^{\text{D}}$ ,<sup>9</sup> and the experimental value for the formation of *p*-CN-III, 2.04 at 25 °C, can arise if  $k_{-1}^{\text{D}} = 0.62k_2^{\text{D}}$ . The reported PKIE for the neutralization of *p*-nitrobenzyl anion,  $(k^{\text{H}}/k^{\text{D}})_{\text{obsd}} = 10$ , would result from  $k_{-1}^{\text{D}} = 39k_2^{\text{D}}$ . The difference in  $k_{-1}^{\text{D}}/k_2^{\text{D}}$  for  $(p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}_2)^-$  compared to *p*-NO<sub>2</sub>-II-H is reasonable and in the correct direction when one considers that  $-\text{CF}_2\text{OMe}$  should stabilize *p*-NO<sub>2</sub>-II-H more than it would the  $\pi$ -delocalized *p*-NO<sub>2</sub>-II-F.

A frequent interpretation of observed PKIE that gradually increase within a series of compounds is to correlate the value of  $k^{\text{H}}/k^{\text{D}}$  with a  $\text{p}K_{\text{a}}$  difference between the acid and conjugate acid of the base involved in the proton-transfer reaction.<sup>10</sup> Eaborn et al.<sup>4</sup> attempted such an analysis for the isotope effects measured from the neutralization of benzyl anions generated by reaction of various benzyltrimethylsilanes with methanolic methoxide. After studying more systems,<sup>11</sup> they noted a breakdown of this analysis and suggested that differences between delocalization by conjugation and delocalization that occurs via  $\sigma$  bonds must be taken into account.<sup>11b</sup> We concur with this and further suggest that benzyl anion is more stable as a hydrogen-bonded localized

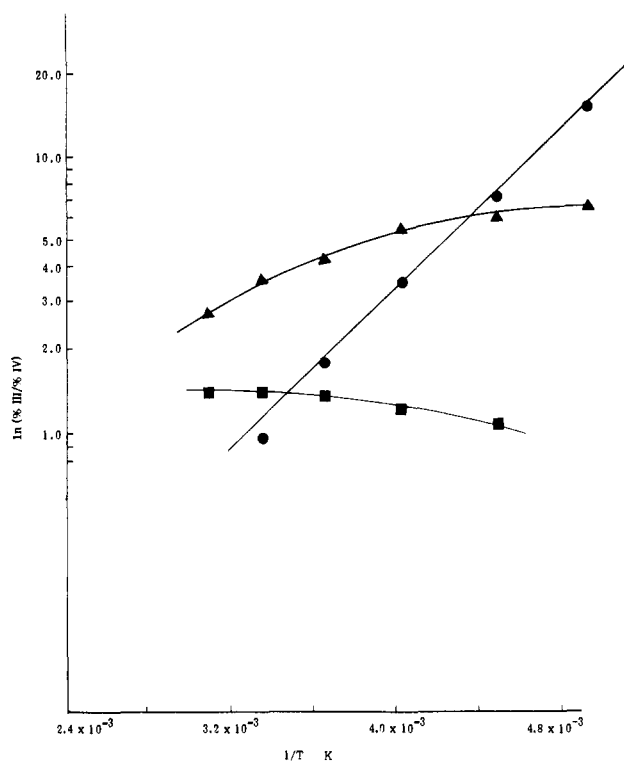
(7) Gold, V.; Grist, S. *J. Chem. Soc. B* **1971**, 2282–2285.

(8) Koch, H. F.; Dahlberg, D. B. *J. Am. Chem. Soc.* **1980**, *102*, 6102–6107.

(9) If  $k_1^{\text{H}} = 1.35k_1^{\text{D}}$ ,  $k_{-1}^{\text{H}} = 1.35k_{-1}^{\text{D}}$ ,  $k_2^{\text{H}} = 12k_2^{\text{D}}$ , and  $k_{-1}^{\text{D}} = 8.1k_2^{\text{D}}$ , then  $k_{-1}^{\text{H}} = 10.9k_2^{\text{D}}$ . The expected PKIE,  $(k^{\text{H}}/k^{\text{D}})_{\text{obsd}}$ , can be calculated from a revision of eq 1,  $(k_1^{\text{H}}/k_1^{\text{D}})[(k_2^{\text{D}}/(8.1k_2^{\text{D}} + k_2^{\text{D}}))/(12k_2^{\text{D}}/(10.9k_2^{\text{D}} + 12k_2^{\text{D}}))]$ .

(10) More O'Ferrall (More O'Ferrall, R. A. In ref 5, pp 223–226) has an excellent discussion, with references to original literature, regarding this approach.

(11) (a) Seconi, G.; Eaborn, C.; Fischer, A. *J. Organomet. Chem.* **1979**, *177*, 129–135. (b) Seconi, G.; Eaborn, C.; Stamper, J. G. *Ibid.* **1981**, 153–168.



**Figure 1.** Plot of  $\ln(\% \text{III}/\% \text{IV})$  vs.  $1/T$  for the partitioning of carbanions,  $(\text{XC}_6\text{H}_4\text{CHCF}_2\text{OMe})^-$  to form  $\text{XC}_6\text{H}_4\text{CH}_2\text{CF}_2\text{OMe}$  (III) and  $\text{XC}_6\text{H}_4\text{CH}=\text{CFOMe}$  (IV). The circles are for the reaction of methanolic sodium methoxide with *p*-NO<sub>2</sub>-I, the triangles for *p*-CN-I, and the squares for *m*-NO<sub>2</sub>-I.

carbanion than as a  $\pi$ -delocalized anion.<sup>12</sup>

Finally, comment should be made regarding the temperature dependence of  $k_{\text{add}}^{\text{H}}/k_{\text{elim}}^{\text{F}}$  for reactions of the substituted  $\beta,\beta$ -difluorostyrenes with methanolic methoxide and the anomalous PKIE data associated with the formation of *p*-CN-III. The percent saturated ethers obtained from reactions of *p*-NO<sub>2</sub>-I, *p*-CN-I, and *m*-NO<sub>2</sub>-I are recorded in Table II, and plots of  $\ln(\% \text{III}/\% \text{IV})$  vs.  $1/T$  for reactions in MeOH are shown in Figure 1. The product distribution ratios for *p*-NO<sub>2</sub>-I give a linear correlation between  $-70$  and  $0$  °C. The  $25$  °C point is ca. 15% below the line, and this could arise from a competing meth-

(12) Koch, H. F. *Acc. Chem. Res.* **1984**, *17*, 137–144.

oxide-promoted dehydrofluorination of *p*-NO<sub>2</sub>-III to yield *p*-NO<sub>2</sub>-IV. Dehydrofluorination reactions usually have a greater activation energy than the corresponding alkene reaction. The partial loss of *p*-NO<sub>2</sub>-III would therefore be significant only for the 25 °C point. The PKIE associated with this elimination is near unity,<sup>1,3</sup> and the same deviation is observed for reaction in MeOD. Both *p*-CN-I and *m*-NO<sub>2</sub>-I result in curved plots. There is a similar curvature associated with reactions run in MeOD, and this results in linear plots for ln(*k*<sup>H</sup>/*k*<sup>D</sup>) vs. 1/*T*, when *k*<sup>H</sup>/*k*<sup>D</sup> is calculated with eq 2.

Scheme I is similar to ones proposed for methoxide-catalyzed proton exchange with methanol when reaction is accompanied by internal return, *k*<sub>2</sub> > *k*<sub>-1</sub>.<sup>13</sup> The solvent, MeOD, would exchange with MeOH in a diffusion-controlled step from II-F, and the kinetic expression for this exchange reaction is

$$k_{\text{exch}}^{\text{H}} = k_{-2}^{\text{H}}k_{-1}^{\text{H}}/(k_2^{\text{H}} + k_{-1}^{\text{H}}) \quad (4)$$

We have published the effect that internal return has on the Arrhenius behavior of PKIE.<sup>8</sup> These calculations predict *A*<sup>H</sup>/*A*<sup>D</sup> values greater than unity, equal to unity, and less than unity as well as the possibility of negative values for Δ*E*<sub>a</sub><sup>D-H</sup>. Since the PKIE reported in this study are the reverse process of exchange reactions, the experimental results found in Table I are consistent with a reaction occurring via Scheme I. We have not obtained enough experimental data to perform meaningful model calculations for these systems, and we are continuing work along these lines.

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## Experimental Section

**Materials.** Synthesis of the substituted β,β-difluorostyrenes has been reported previously.<sup>2</sup> Methanolic sodium methoxide solutions were made from a reaction of sodium with methanol. Small chunks of freshly cut sodium were washed with MeOH prior to placing them into MeOH which was used for the reaction. Methanol-*O-d* was purchased from Aldrich and used without further purification.

**Product Studies.** A 25-mL Erlenmeyer flask was charged with 15 mL of methanolic sodium methoxide (ca. 0.3 N), fitted with a well-rolled cork, and placed into a constant-temperature bath. When temperature had been reached (10-15 min), 25 μL of compound and 25 μL of standard were added. Studies with *p*-NO<sub>2</sub>-I and *m*-NO<sub>2</sub>-I were carried out for approximately 10 half-lives, at which point 3 5-mL aliquots were transferred to a 125-mL separatory funnel (Teflon stopcock) containing ca. 100 mL of dilute HCl and 1.6 mL of CCl<sub>4</sub>. The separatory funnel was shaken vigorously for about a minute, and after layer separation, the CCl<sub>4</sub> was drawn off into an autosampler vial. Each sample was analyzed at least five times with a Varian VISTA CDS 401 equipped with an autosampler, TCD detectors, and a 2 × 1/8 in., 10% OV 101 on 100/120 Supelcon AW DMCS column. The *p*-CN-I studies at -70, -50, and -25 °C were carried out by sealing the flask with a septum and taking aliquots at 1, 2, and 10 half-lives, while runs at 0, 25, and 50 °C used two separate runs at each temperature. One run was sampled at 1 and 2 half-lives, while the other was allowed to react for 10 half-lives.

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**Registry No.** I (X = *m*-CF<sub>3</sub>), 90605-29-1; I (X = *m*-NO<sub>2</sub>), 84750-94-7; I (X = *p*-CN), 38936-00-4; I (X = *p*-NO<sub>2</sub>), 1742-99-0; MeOH, 67-56-1; D<sub>2</sub>, 7782-39-0.

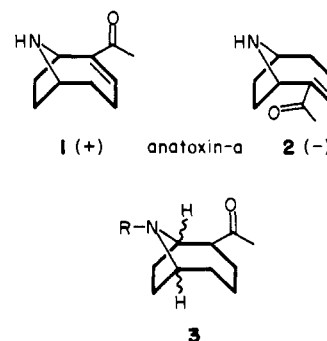
## Chiroselective Syntheses of (+)- and (-)-Anatoxin *a*

John S. Petersen, Gregor Fels,<sup>1</sup> and Henry Rapoport\*

Contribution from the Department of Chemistry, University of California, Berkeley, California 94720. Received January 13, 1984. Revised Manuscript Received March 6, 1984

**Abstract:** (+)- and (-)-anatoxin *a* of high optical purity have been synthesized directly from D- and L-glutamic acid, respectively. Initial carbon-carbon bond formation proceeding from the pyroglutamate via sulfide contraction and transfer of the amino acid chirality by catalytic hydrogenation are central to the synthesis. Cyclization to the bicyclic system was effected by nucleophilic attack on the iminium ion, generated by decarbonylation of the α-amino acid. The dihydroanatoxin thus formed, whose α and β diastereomers were both characterized, was ultimately converted to the enone by dehydrogenation with palladium acetate.

The study of neurotoxins has contributed significantly to the understanding of neuronal processes.<sup>2</sup> Among these toxins, anatoxin *a*, a potent nerve-depolarizing agent, has been the subject of considerable study despite the difficulties of obtaining this natural product.<sup>3</sup> Also, comparison of the activity of the natural (+)-anatoxin (**1**) with racemic anatoxin has left some ambiguity



(1) Fellow of the Deutsche Forschungsgemeinschaft. Present address: Max Planck Institut für Ernährungsphysiologie, Dortmund.

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as to the action of (-)-anatoxin (**2**), which would be difficult to clarify without a source of (-)-anatoxin.<sup>3a,d</sup> Consequently we have developed improved and chiroselective alternatives to our earlier synthetic efforts<sup>4</sup> that now make available both enantiomers of