Since many aliphatic trichloromethyl compounds and their derivatives are now readily available by telomerization reaction of olefins with carbon tetrachloride or chloroform, the electrochemical reduction described above opens a route to the simple preparation of α,ω-bifunctional aliphatic compounds.

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Optical Rotatory Properties of Diketopiperazines

Sir:

We wish to present results from optical rotatory dispersion (ORD) and spectral studies on two diketopiperazines, a hitherto uninvestigated class of compounds. These diketopiperazines are the simplest and most rigid among cyclic polypeptides and thus would be expected to display: (a) the $n-\pi^*$ Cotton effect of the peptide band arising from local rigidity,[1] and (b) aspects of "exciton" interactions among peptide chromophores, a familiar phenomenon in the α-helix.[2]

The ORD studies on L-alanyl-L-alanyldiketopiperazine (LALADKP) and L-alanyl-L-seryldiketopiperazine (LALSDKP) (Cyclo Chemical Corp., Los Angeles, Calif.) were done using a Cary Model 60 spectropolarimeter. In the concentration range (10^{-4} to 2×10^{-3} *M*) of measurements, the samples showed no concentration dependence of ultraviolet absorption or rotation. However, infrared measurements on LALADKP in dioxane revealed triplet amide I bands, implying association of the compounds in dioxane, and probably also in acetonitrile, in which the rotatory dispersion is very similar. However, competitive hydrogen bonding should prevent any DKP association in ethanol and water solutions.[3]

The ultraviolet spectra of LALADKP and LALSDKP were measured in solvents of different polarities. From both theory[4] and analogous experiments on a lactam,[1] we had hoped to observe the $n-\pi^*$ peptide band. However, this was not observed, and the failure may be due to smaller oscillator strength for this band compared to the lactam, or to masking by the very broad $\pi-\pi^*$ band centered below 1950 A.

The ORD of the two diketopiperazines in various solvents are shown in Figures 1 and 2. In the solvents studied, both DKP's exhibit a negative Cotton effect around 2300 A, which shows a long-wave shift with decreasing solvent dielectric constant. The exceptional result in acetonitrile may well be due to association. The general solvent dependence and location of this Cotton effect lead us to conclude that this is due to the $n-\pi^*$ transition of the peptide chromophore. Further, LALADKP displays another minimum around 2050 A in the hydroxylic solvents, preceding a much larger maximum below 1950 A. It appears most consistent to interpret the dispersions in Figure 2 as the result of three Cotton effects, a negative one around 2200 A, another negative one around 2000 A, and a large positive one below 1950 A. The locations, signs, and relative magnitudes of the latter two Cotton effects strongly suggest their origin to be due to exciton split $\pi-\pi^*$ transition of the peptide, analogous to the α-helix.[5] It should be pointed out that the data of LALSDKP are consistent with two Cotton effects; it is very likely, however, that the trough around 2050 A in Figure 1 is here masked by the large negative $n-\pi^*$ Cotton effect and the much larger positive one below 1950 A. In general, the rotations of LALSDKP are larger than those of LALADKP, presumably because the latter is more symmetric than the former.

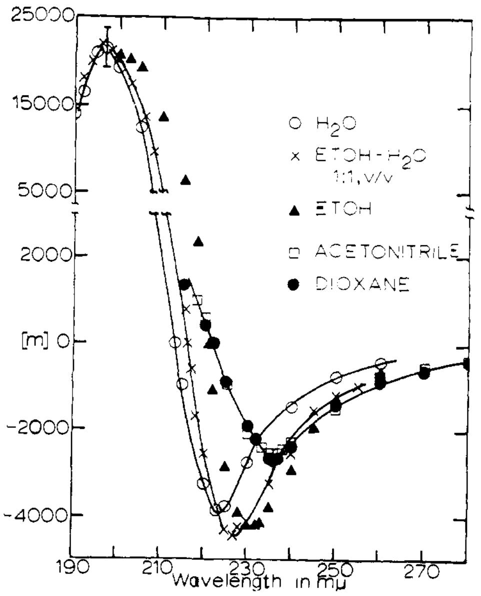

Figure 1. ORD of L-alanyl-L-seryldiketopiperazine at room temperature. The mean residue rotation, [*m*], = 0.79[α]. No refractive index corrections have been made.

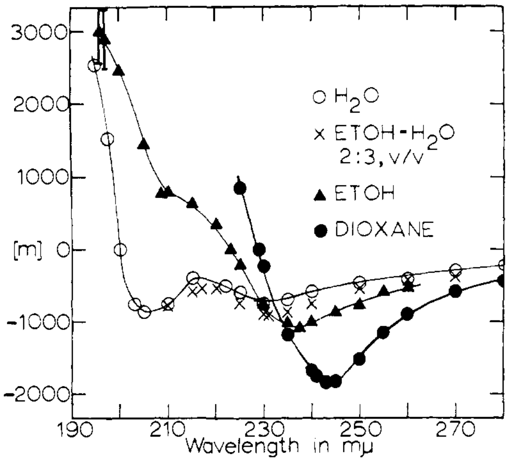

Figure 2. ORD of L-alanyl-L-alanyldiketopiperazine at room temperature. [*m*] = 0.71[α]. No refractive index corrections have been made.

The six-membered dipeptide ring of these diketopiperazines is very nearly coplanar,[6] permitting one to inspect each peptide group independently. Application of the quadrant rule[1,7] predicts: (a) a negative

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(1) B. J. Litman and J. A. Schellman, *J. Phys. Chem.*, **69**, 978 (1965).
(2) G. Holzwarth and P. Doty, *J. Am. Chem. Soc.*, **87**, 218 (1965).
(3) J. S. Franzen and R. E. Stephens, *Biochemistry*, **2**, 1321 (1963).
(4) N. S. Bayliss, *J. Chem. Phys.*, **18**, 292 (1950); *J. Phys. Chem.*, **58**, 1002 (1954).
(5) Drs. F. A. Bovey and F. P. Hood of the Bell Telephone Laboratories have observed a negative $n-\pi^*$ Cotton effect and also a pronounced exciton splitting in L-prolyl-L-prolyldiketopiperazine. We thank them for a preprint of their forthcoming paper.
(6) R. B. Corey, *J. Am. Chem. Soc.*, **60**, 1598 (1938).

n-π^* Cotton effect in these diketopiperazines, which is realized, and (b) that the absolute magnitude of this Cotton effect increases with decreasing solvent dielectric constant. The latter prediction is not well realized. The discrepancy here may be possibly due to (i) association in dioxane and acetonitrile solutions, and (ii) small but finite mixing of the n-π^* and π-π^* transitions because of deviations from planarity of the ring. However, it is worth noting that since the potential terms that generate the n-π^* Cotton effect are of the quadrupole type,[7] this partial rotation would show a sharper dependence on the distance of the perturbing group than on the solvent dielectric constant.

The results reported here suggest that neither the n-π^* Cotton effect nor the exciton split of the degenerate π-π^* transition of the peptide chromophore is unique to the α-helix, but can be achieved in cases where the proper molecular rigidity,[1] orientation of the vicinal groups, and also proper geometric disposition of identical peptide chromophores[8,9] are realized. Thus, the negative Cotton effect at 2250 A that Ruttenberg, *et al.*,[10] have observed in cyclic tyrocidine B and gramicidin S-A might be due to the activation of the Cotton effect of the n-π^* transition by molecular rigidity imposed by cyclization.

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(7) J. A. Schellman and P. Oriel, *J. Chem. Phys.*, 37, 2114 (1962).

(8) W. Moffitt, *ibid.*, 25, 467 (1956).

(9) W. Kauzmann, *Ann. Rev. Phys. Chem.*, 8, 413 (1957).

(10) M. A. Ruttenberg, T. P. King, and L. C. Craig, *J. Am. Chem. Soc.*, 87, 4196 (1965).

(11) Fellow of the Jane Coffin Childs Memorial Fund for Medical Research. This investigation has been aided by grants from the Jane Coffin Childs Memorial Fund for Medical Research and U. S. Public Health Service Grant No. GM 10900.

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The Chromium(II)-Catalyzed Aquation of the Iodopentaaquochromium(III) Ion[1]

Sir:

Most studies of Cr^{2+}-CrX^{2+} ($X^- = F^-, Cl^-, Br^-, N_3^-, -NCS^-, -SCN^-$) exchange reactions are directed toward the elucidation of the role of the bridging ligand X^- in the electron-transfer process.[2-6] Such studies are usually conducted at high acid and low chromium(II) concentrations. Under these conditions, with the exception of the chromium(II)-catalyzed isomerization of $CrSCN^{2+}$, no net reaction is detected, and the rates of exchange are independent of $[H^+]$ in the concentration range studied.[3] A path inverse in $[H^+]$ is featured in the Cr^{2+}-$CrSCN^{2+}$ reaction,[6] but this path does *not* result in loss of thiocyanate from the coordination sphere of chromium(III).

In contrast with these observations, we have found that chromium(II) catalyzes the aquation of halogenopentaaquochromium(III) complexes *via* a path inversely proportional to $[H^+]$.

$$CrX^{2+} + Cr^{2+} = Cr^{3+} + X^- + Cr^{2+} \quad (X^- = Cl^-, Br^-, I^-) \quad (1)$$

By using low $[H^+]$ and high $[Cr^{2+}]$, the reactions represented by eq 1 can be detected readily. The catalytic effect of chromium(II) is quite striking in the case of CrI^{2+},[7,8] and consequently we chose this system to provide a clear illustration of the lability of acidopentaaquochromium(III) complexes in the presence of chromium(II). In addition, kinetic studies of the CrI^{2+}-Cr^{2+} reaction are of special significance in view of the current interest in the reactions of CrI^{2+}.[9-13]

The disappearance of CrI^{2+} was followed spectrophotometrically at 475 or 306 mμ. Two sources of CrI^{2+} were used. In the majority of the experiments, CrI^{2+} was generated *in situ* by the reaction of *excess* chromium(II) with iodine[9,14] (which in turn was generated by the reaction of iodate with a sight excess of iodide). Following the rapid Cr^{2+}-I_2 reaction[15] ($k > 10^3\ M^{-1}\ sec^{-1}$), the slower chromium(II)-catalyzed aquation of CrI^{2+} was observed. Some experiments were carried out with CrI^{2+} prepared by the Cr^{2+}-I_2 reaction and purified by ion-exchange chromatography.[11] The kinetic measurements, summarized in Table I, were treated on the basis of the rate law

$$\frac{-d \ln [CrI^{2+}]}{dt} = k' = k_1 + \frac{k_2}{[H^+]} + \frac{k_3[Cr^{2+}]}{[H^+]} \quad (2)$$

Values of the rate coefficient k_3 (*cf.* column 3 of Table I) were calculated from the observed pseudo-first-order rate coefficients k' using the known[11] values of k_1 and k_2 (the rate coefficients for spontaneous aquation of CrI^{2+} *via* $[H^+]$-independent and $1/[H^+]$-dependent paths, respectively). Under the experimental conditions used, the contribution of the spontaneous aquation (k_1 and k_2 paths) of CrI^{2+} to its over-all disappearance was less than 10% in all experiments. Although the values of k_3 scatter considerably, they remain reasonably constant when $[Cr^{2+}]$, $[H^+]$, and $[CrI^{2+}]$ are varied by factors of $\sim$10, $\sim$10, and $\sim$60, respectively, and we conclude that eq 2 provides an adequate description of the kinetics of the CrI^{2+}-Cr^{2+} system. It must be noted, however, that our data do not rule out an additional path of the form $k_4[CrI^{2+}] \cdot [Cr^{2+}]$. The present results indicate that $0 \leqslant k_4 < 1 \times 10^{-2}\ M^{-1}\ sec^{-1}$. Experiments in progress at higher

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(1) This work was supported by Grant GP-2001 from the National Science Foundation.

(2) H. Taube and E. L. King, *J. Am. Chem. Soc.*, **76**, 4053 (1954).

(3) D. L. Ball and E. L. King, *ibid.*, **80**, 1091 (1958).

(4) R. Snellgrove and E. L. King, *Inorg. Chem.*, **3**, 288 (1964).

(5) A. Haim and N. Sutin, *J. Am. Chem. Soc.*, **87**, 4210 (1965).

(6) A. Haim and N. Sutin, *ibid.*, **88**, 434 (1966).

(7) At 0.200 *M* hydrogen ion concentration and 25° the half-life for aquation of CrI^{2+}, calculated from the values given by Swaddle and King,[11] is 2.71×10^3 sec. When $[H^+] = [Cr^{2+}] = 0.200\ M$, the half-life (25°) for disappearance of CrI^{2+} calculated from the present data is 32 sec.

(8) It is conceivable that chromium(II) is the catalytic impurity suggested by Swaddle and King[11] to explain the higher rates of aquation of CrI^{2+} observed by Espenson.[9] For example, the half-life for disappearance of CrI^{2+} at $[H^+] = 0.200\ M$ and 25° measured by Espenson[9] is 2.41×10^3 sec, to be compared with the calculated[7] value of 2.71×10^3 sec. If the difference between these values is ascribed to the catalytic effect of chromium(II), the necessary concentration of the catalyst is $3.0 \times 10^{-4}\ M$. This value may be sufficiently small to be attributed to slight stoichiometric inequalities in the Cr^{2+}-I_2 reaction used to generate CrI^{2+}.[9]

(9) J. H. Espenson, *Inorg. Chem.*, 3, 968 (1964).

(10) J. H. Espenson, *ibid.*, **4**, 1834 (1965).

(11) T. W. Swaddle and E. L. King, *ibid.*, **4**, 532 (1965).

(12) M. Ardon, *ibid.*, **4**, 372 (1965).

(13) P. Moore, F. Basolo, and R. G. Pearson, *ibid.*, **5**, 223 (1966).

(14) H. Taube and H. Myers, *J. Am. Chem. Soc.*, **76**, 2103 (1954).

(15) The reaction of $\sim 1 \times 10^{-4}\ M\ I_2$ with $\sim 5 \times 10^{-5}\ M\ Cr^{2+}$ (25°, $[H^+] = 1.0\ M$) is complete within 20 sec.