search Fund, administered by the American Chemical Society, for generous financial support.

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(1) J. L. Boston, D. W. A. Sharp, and G. Wilkinson, *J. Chem. Soc.*, 3488 (1962); R. S. Dickson and G. Wilkinson, *Chem. Ind. (London)*, 1432 (1963).

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(3) M. A. Ogliaruso, M. G. Romanelli, and E. I. Becker, *Chem. Rev.*, **65**, 261 (1965).

(4) The notable ability of **1** as charge-transfer acceptor was studied by Dickson and Wilkinson (ref 2).

(5) This carbonyl band has satellites at 1808 and 1851 cm^{-1}, and several of the other adducts have a single close-lying satellite band. In all of the bridge carbonyl-containing products in the table, however, the major band in this region appears at or very close to 1825 cm^{-1}.

(6) J. Sauer, *Angew. Chem., Int. Ed. Engl.*, **6**, 16 (1967).

(7) Another electron-deficient diene, hexachlorocyclopentadiene, violates not only the Alder endo rule but the cis rule as well in many of its Diels-Alder reactions. V. Mark, *J. Org. Chem.*, **39**, 3179, 3181 (1974).

(8) While the cis rule is consistently upheld, the question of endo vs. exo addition has not yet been answered. The usefulness of NMR shift reagents in this connection is sharply limited by the fact that the electron-deficient bridge carbonyl shows no tendency to complex with, for example, $Eu(fod)_3$. See Z. W. Wolkowski, C. Beautè, and R. Jantzen, *J. Chem. Soc., Chem. Commun.*, 619 (1972).

(9) Methyl-substituted benzenes form highly colored complexes[2] and then react further with dienone **1** at elevated temperatures in a manner to be described elsewhere. This reaction is not, however, Diels-Alder addition.

(10) E. W. Garbisch, Jr., and R. F. Sprecher, *J. Am. Chem. Soc.*, **91**, 6785 (1969); **88**, 3433, 3434 (1966).

(11) Using the Hückel parameters $\alpha_O = \alpha + \beta$ and $\beta_{C=O} = \beta_{C=C}$, one finds the LUMO at $\alpha + 0.19\beta$ and the HOMO at $\alpha + 0.62\beta$ for cyclopentadienone itself.

(12) This orientational preference emerges from a full HMO treatment of transition state interactions, but it is traceable principally to lower LUMO coefficients at the diene termini in the dienone than in the diene. See M. J. S. Dewar, "The Molecular Orbital Theory of Organic Chemistry", McGraw-Mill, New York, N.Y., 1969, Chapter 6.

(13) C. H. De Puy, M. Isaks, K. L. Eilers, and G. F. Morris, *J. Org. Chem.*, **29**, 3503 (1964).

(14) Owing to its great volatility, the dienone is also valuable as a trapping reagent in gas phase experiments. As an example, tetrafluorocyclobutadiene has been intercepted in the vapor phase with this compound. M. J. Gerace, unpublished results; see also M. J. Gerace, D. M. Lemal, and H. Ertl, *J. Am. Chem. Soc.*, preceding paper in this issue.

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Competitive Intramolecular Displacement of the Neutral Amide Group. Rearrangement and Dehydration Reactions of Asparagine and Glutamine

Sir:

The rearrangement and dehydration of N-blocked asparagine and, to a lesser extent, glutamine derivatives have been reported to give either nitriles or imides.[1] We now report the first observation of both products from a single derivative in a reaction which apparently involves competitive O and N displacement by an amide under neutral conditions.

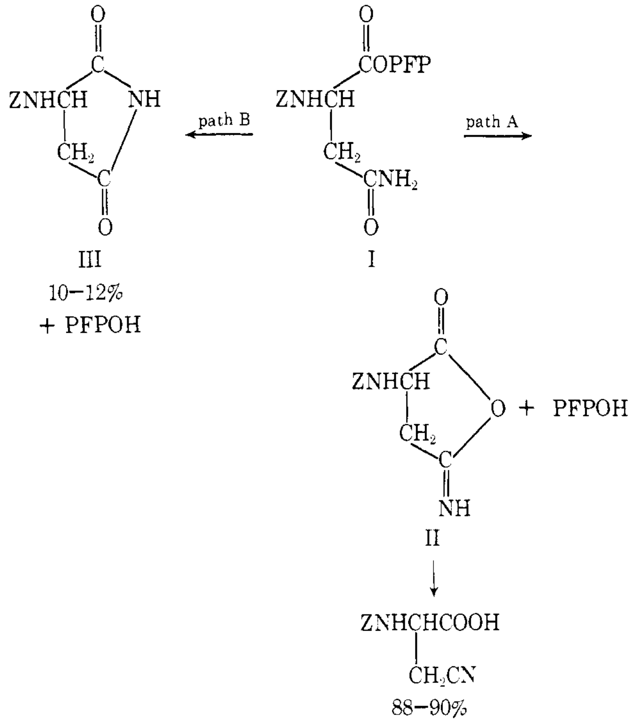
We recently described the decomposition of the pentafluorophenyl ester of *N*-benzyloxycarbonyl-L-asparagine (I) (Z-Asn-OPFP).[2] A kinetic study of this reaction and the reaction of related active esters was undertaken, and products have been identified. Rate constants were obtained for the rearrangement of the esters (Table I) as 0.1 *M* solutions in DMF (treated with Amberlyst-15) by spectrophotometric determination of the liberated phenols.

Table I. The Rearrangement of Z-Asn and Z-Gln Active Esters in DMF at 25°

Compound	k, sec^{-1}	$t/2$
Z-Asn-OPFP	9.9×10^{-5}	117 min
Z-Asn-OPCP	5.2×10^{-5}	222 min
Z-Asn-ONP	8.9×10^{-6}	1296 min
Z-Gln-OPFP		100 hr

Isolation of the products of Z-Asn-OPFP by silica gel column chromatography, using the solvent system of ref 3, revealed that two simultaneous reactions were contributing to the overall first-order reaction observed; the first being nucleophilic attack by oxygen (path A, Scheme I) giving eventually the optically active β-cyanoalanine derivative, II,[3] and the second involving attack by nitrogen (path B) to yield the optically active succinimide derivative III.[4] As the specific rotations of all products and starting materials were known, the reaction could also be monitored by polarimetry and gave results in agreement with those of Scheme I. In the case of other active esters of Z-Asn, indicated in Table I, roughly the same ratio of these products could be detected on elevated temperature.

Scheme I. The competitive intramolecular displacement by the amide group of Z-Asn-OPFP in DMF at 25°



Several conclusions may be drawn from this observed reaction. (1) The rearrangement does not compete with acylations during peptide synthesis since the half-life of the coupling reaction of I with proline-*tert*-butyl ester is about 2 min under these conditions. (2) The rearrangement is strongly temperature dependent; the ester I can be prepared in pure form only at 0°, a temperature at which kinetic studies showed the rearrangement to be slow. (3) The reaction also shows strong solvent dependence: no reaction was observed in dioxane or ethyl acetate. In the case of Gln active esters generally the imide formation is favored, accelerated by protic solvents. Thus Z-Gln-OPFP is stable in DMF, but the addition of 10% water produces the corresponding glutarimide derivative in 41% yield. In another example, recrystallization of crude Z-Gln-OSu from ethyl acetate produces pure active ester with good yield, while recrystallization from isopropyl alcohol causes the formation of the imide.[1h] Similarly, isopropyl alcohol favors the imide formation of Z-Asn-OSu. In pyridine, the nitrile is formed exclusively.

These observations are in agreement with those of Meyers[1i] and Dewey[1j] and should be considered when asparagine and glutamine-derived active esters are used in peptide synthesis.

References and Notes

(1) For a general discussion see J. A. Shafer in "The Chemistry of Amides", J. Zabicky, Ed., Interscience, New York, N.Y., 1970, p 704. Specific examples of nitrile formation are (a) C. Ressler and H. Ratzkin, *J. Org. Chem.*, **26**, 3356 (1961); (b) B. Liberek, *Chem. Ind.* (*London*), 987 (1961); (c) D. V. Kashelikar and C. Ressler, *J. Am. Chem. Soc.*, **86**, 2467 (1964); (d) R. P. Paul and A. S. Kende, *ibid.*, **86**, 741, 4162 (1964); (e) C. Ressler, G. R. Nagarajan, M. Kirisawa, and D. V. Kashelikar, *J. Org. Chem.*, **36**, 3960 (1971); and of imide formation are (f) E. Sondheimer and R. W. Holley, *J. Am. Chem. Soc.*, **76**, 2467 (1954); (g) *ibid.*, **79**, 3767 (1957); (h) H. Zahn and E. Th. J. Fölsche, *Chem. Ber.*, **102**, 2158 (1969); (i) C. Meyers, R. T. Havran, I. L. Schwarz, and R. Walter, *Chem. Ind.* (*London*), 126 (1969); (j) R. S. Dewey, H. Barkemeyer, and R. Hirschmann, *ibid.*, 1632 (1969).

(2) L. Kisfaludy, M. Löw, O. Nyéki, T. Szirtes, and I. Schön, *Justus Liebigs Ann. Chem.*, 1421 (1973).

(3) Z-Ala(CN)-OH: mp 128–129°; $[\alpha]^{25}\text{D}$ −43.2 (±0.4) (*c* 1, DMF) R_f = 0.2 in ethyl acetate (90):pyridine (5.4):acetic acid (1.6):water (3).

(4) Z-ASu: mp 69–74°; $[\alpha]^{25}\text{D}$ −35.7 (±0.4) (*c* 1, 95% EtOH), R_f = 0.7 in the solvent system of ref 3.

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Raman Circular Intensity Differential Spectroscopy. The Spectra of (−)-α-Pinene and (+)-α-Phenylethylamine

Sir:

The feasibility of using Raman spectroscopy to investigate the chirality of dissymmetric compounds was first discussed in a series of theoretical papers[1,2] by Barron and Buckingham. The method, which must be seen in the more general framework of optically active scattering,[3] is highly attractive as it allows the use of vibrational optical activity for configurational assignments.

The appropriate measure of the effect is the circular intensity differential (CID) Δ, defined as[1]

$$\Delta_{\|,\perp} = \frac{(I_{\mathrm{r}}^{\|,\perp} - I_{\mathrm{l}}^{\|,\perp})}{(I_{\mathrm{r}}^{\|,\perp} + I_{\mathrm{l}}^{\|,\perp})}$$

$I_{\mathrm{r}}^{\|,\perp}$ and $I_{\mathrm{l}}^{\|,\perp}$ are the intensities of the scattered light 90° to the incident right (r) and left (l) circularly polarized light, with an analyzer oriented parallel ($\|$) and perpendicular ($\perp$) to the scattering plane, respectively.

Experimental verification of the effect has proved difficult, and first reports[5,6] were based on artifacts. The CID's subsequently reported by Barron, Bogaard, and Buckingham[4,7,8] for a few Raman bands are confirmed as genuine by our observations. In addition, we also present the first measurement of complete difference spectra in parallel polarization, namely for the two compounds (−)-α-pinene and *d*-(+)-α-phenylethylamine. Based on these spectra a sector rule is presented for a methyl group in a chiral environment. This is the first example of future sector rules in vibrational optical activity[2] which will emerge for various largely localized group frequencies.

Our instrumentation is shown schematically in Figure 1. The polarization of the laser beam was varied between right and left circular with square wave modulation. Synchronous single photon counting was used to avoid drift problems.[9] $(I_{\mathrm{r}}^{\|} - I_{\mathrm{l}}^{\|})$ and $(I_{\mathrm{r}}^{\|} + I_{\mathrm{l}}^{\|})$ were measured at each wavenumber increment and processed on line[10] by an IBM 1800 computer. The digital data were filtered with a 15 point (14 cm^{-1} interval) cubic smoothing function. The slit width was 8 cm^{-1}. We were successful in using the microcapillary sample handling technique[11] for R-CID. The microcapillary technique has been shown to have a high accuracy for the measurement of depolarization ratios.[12] In addition, we have also constructed a capillary cell with a flat, strain-free bottom end which has allowed us to precisely monitor the circular polarization of the laser beam after passing through the cell. Pilot measurements using internal nonoptically active standards in an optically active sample have also been performed to assure the validity of our results. The optical purity of the compounds measured was checked prior to the measurements on a Cary 60, and the compounds were stable under our measuring conditions. Typical sample sizes ranged from 50 to 200 μg.

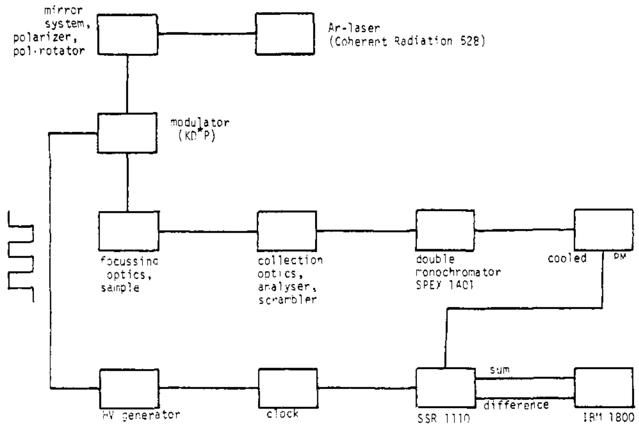

Figure 1. Experimental block diagram.

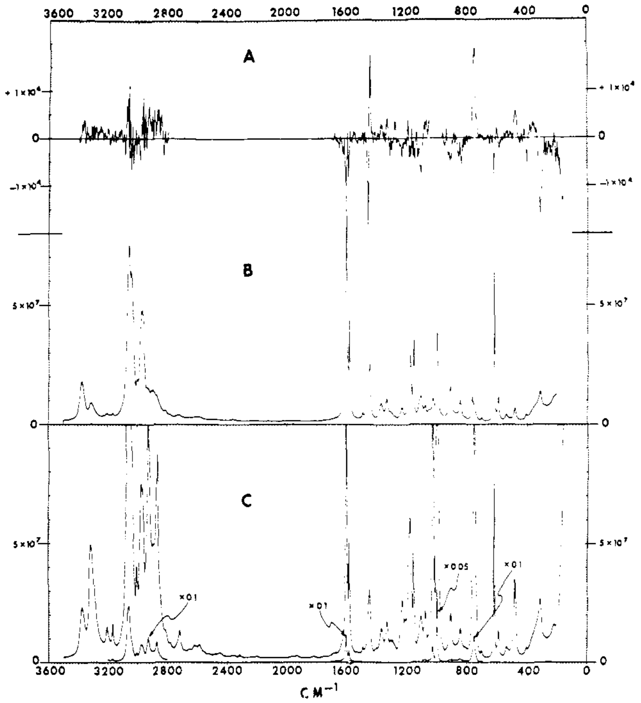

Figure 2. Difference and sum spectra for *d*-(+)-α-phenylethylamine in photon counts: (A) $(I_{\mathrm{r}}^{\|} - I_{\mathrm{l}}^{\|})$, (B) $(I_{\mathrm{r}}^{\|} + I_{\mathrm{l}}^{\|})$, (C) $(I_{\mathrm{r}}^{\perp} + I_{\mathrm{l}}^{\perp})$. $(I_{\mathrm{r}}^{\|} - I_{\mathrm{l}}^{\|})$ for the polarized line at 1002 cm^{-1} is omitted and, the peak at 755 cm^{-1} is doubtful. See error discussion.

Sum $(I_{\mathrm{r}}^{\|} + I_{\mathrm{l}}^{\|})$ and difference $(I_{\mathrm{r}}^{\|} - I_{\mathrm{l}}^{\|})$ spectra for the two compounds are given in Figures 2 and 3, and CID's in Table I. The accuracy of the data, and the possibility of observing an artifact, depend on the count rate and on the degree of polarization of a band. Bands with $\zeta > 0.15$ appear