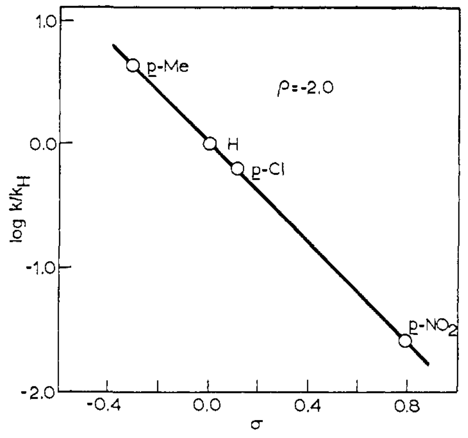

Figure 1. Plot of the logarithm of the relative rate of the cerium(IV) oxidation of 2-aryl-1-phenylethanols *vs.* σ^+ of the substituent of the 2-phenyl ring.

In Table I are presented the relative rates of cerium(IV) oxidation for four alcohols. Figure 1, which is a plot of the log of these rates against σ^+,[8] clearly shows that an excellent Hammett relationship with $\rho = -2.0$ exists for this reaction. Most radical reactions correlate better with σ^+ than with σ and give ρ's in the range of -0.69 to -1.46.[6,9] The relatively large negative ρ of -2.0 for the cerium(IV) oxidative cleavage of 2-aryl-1-phenylethanols indicates that a fair amount of positive charge is developed on the β carbon in the transition state that leads to cleavage. Nevertheless, a ρ of -2.0 is closer to those reported for radical reactions than the -5.0 range reported for cationic processes.[10]

Table I. Relative Rates of Cerium(IV) Oxidation of 2-Aryl-1-phenylethanols, $C_6H_5CHOHCH_2C_6H_5Z$, in 75% Aqueous Acetonitrile

Z	k_{rel}^a
p-CH_3	4.2 ± 0.4
H	(1.00)
p-Cl	0.63 ± 0.05
p-NO_2	0.027 ± 0.010

[a] Based on at least three runs. See ref 5 for method of analysis.

Competition experiments with 2-(*p*-methoxyphenyl)-, 2-(*m*-methoxyphenyl)-, and the 2-(*p*-acetamidophenyl)-1-phenylethanols were also carried out, but it was found that all of these alcohols were oxidized at least 100–1000 times faster than 2-(*p*-methylphenyl)-1-phenylethanol. Since the σ^+ for *m*-methoxy is close to that of hydrogen and *p*-chloro,[8] it is concluded that methoxy and acetamido substituents so activate the aromatic ring that a different mechanism must operate. A good possibility is the initial oxidation of the substituted benzene ring to a radical cation.[11]

Oxidative cleavages of alcohols by oxidants such as chromic acid and lead(IV) in addition to cerium(IV) have been reported.[12] A major question is whether these cleavages are one- or two-electron oxidations. For example, two-thirds of the products from the oxidation of secondary alcohols by chromic acid are cleavage products which are thought to result from a two-electron oxidation by chromium(V) or a one-electron oxidation by chromium(IV).[12a–d,g] Although cleavage by chromium(V) has been the favored mechanism,[12a–d] Roček and Radkowsky[12g] have recently presented firm evidence that the cleavage of cyclobutanol is a one-electron oxidation by chromium(IV) and suggest that all cleavages by chromic acid are one-electron oxidations by chromium(IV). The relative rate of oxidative cleavage of 2-aryl-1-phenylethanols that possess well-behaved substituents by oxidants other than cerium(IV) should provide a means of characterizing these cleavages as one- or two-electron processes. A one-electron oxidative cleavage should give a ρ of -2, but a two-electron process should give a more negative ρ. Experiments designed to establish this postulate and investigate other aspects of the cerium(IV) oxidation of 1,2-diarylethanols are in progress.

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(8) Values of σ^+ were obtained from H. C. Brown and Y. Okamota, *J. Am. Chem. Soc.*, 80, 4979 (1958).

(9) (a) P. D. Bartlett, *ibid.*, 82, 1756 (1960); (b) R. L. Huang and K. H. Lee, *J. Chem. Soc., C*, 935 (1966).

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(13) National Aeronautics and Space Administration Trainee, 1967–1968.

Paul M. Nave,[13] Walter S. Trahanovsky
Department of Chemistry
Iowa State University of Science and Technology
Ames, Iowa 50010

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Optical Properties of the *cis*-Vinyl Amide Chromophore

Sir:

Recent studies in these laboratories, concerned with the spectroscopic properties of tautomeric equilibria, have revealed a conjugated chromophoric system of unusual properties. We wish to report optical rotatory dispersion (ORD) and circular dichroic (CD) studies of Schiff base derivatives of 1-(*o*-hydroxylaryl)-butane-1,3-diones, **1** and **2**.[1,2] Large molecular rotations are observed for these derivatives, which may approach values comparable to the classic inherently dissymmetric chromophores.[3] For instance, **2b** exhibits $[\Phi]_D$ 4.3° × 10^3 (Table I) while hexahelicene[4]

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(1) Satisfactory elemental analyses and pmr, ultraviolet, and infrared spectral properties suitable for the assigned structures were obtained for all compounds. Ultraviolet spectra were taken on a Cary Model 14 UV-VIS spectrometer; ORD and CD curves were obtained on a Cary Model 60 spectropolarimeter equipped with a Cary Model 6001 CD accessory. Rotations at 589 mμ were determined on a Perkin-Elmer Model 141 automatic polarimeter. Compound **1a** has been previously characterized.[2]

(2) G. O. Dudek and E. P. Dudek, *Tetrahedron*, **23**, 3245 (1967).

(3) K. Mislow in "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," G. Snatzke, Ed., Heyden and Sons, Ltd., London, 1967, Chapter 10.

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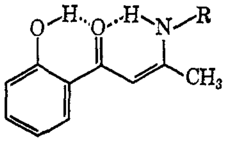
Table I. Optical Properties of Schiff-Base Derivatives Containing the Conjugated *cis*-Vinyl Amide Chromophore

			ORD			
Compd[a]	Configuration of amine	$[\Phi]_D$, deg[b]	1st extremum $[\Phi]$, deg (mμ)	$[\Phi] = 0$ mμ	2nd extremum $[\Phi]$, deg (mμ)	CD $[\theta]$, deg (mμ)
1a	*R*(+)	−2600	−45,600 (379)	357	+55,600 (330)	−57,300 (355)
b	*R*(+)	−3310	−51,980 (380)	358	+64,150 (325)	−76,600 (355)
c	*S*(+)	+223				+7,700 (358)
2a	*R*(+)	−3740	−31,000 (400)	377	+43,400 (350)	−55,400 (386) −56,700 (370)
b	*R*(+)	−4260	−48,000 (400)	375	+46,100 (348)	−64,000 (385) −68,000 (370)
c	*S*(+)	+291				
d	*S*(L)	+549	+12,200 (398)	372	−11,150 (340)	+7,240 (384) +8,600 (368)

[a] All rotations reported were determined in methanol solution. [b] Symbols listed in Chapter 2 of ref 5.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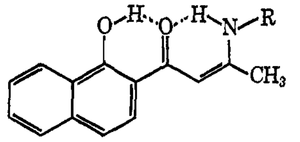
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a, R = $CH(CH_3)C_6H_5$
b, R = $CH(CH_3)C_{10}H_7$
c, R = $CH(CH_3)C_2H_5$
d, R = $CH(CONH_2)CH_2CH(CH_3)_2$

exceeds this by less than a factor of three, $[\Phi]_D$ 12.1° $\times 10^3$.

Analogous to the dimedone–amine condensation products,[5] these conjugated vinyl amides (**1** and **2**) possess optical properties which include, in addition to the very intense specific rotations and ellipticities, extraordinary amplitudes associated with the Cotton effect and sensitivity of the ORD curves to the nature of the substituents at the asymmetric center. The electronic transition (Figure 1) associated with this Cotton effect, in the case of the α-phenylethylamine derivatives, is shifted to longer wavelength by 83 mμ (**1a**) to 95 mμ (**2a**) compared with the corresponding dimedone derivative.[5] The extinction coefficients for these absorptions are large (ϵ 3–4 $\times 10^4$). Nevertheless, the very large rotations permit the ready observation of the ORD and CD curves. The molecular amplitudes for these derivatives, containing the conjugated *cis*-vinyl amide system, are larger than that for comparable dimedone derivatives, such as that of the (*S*)-α-phenylethylamine for which $a = -620°$, while for **1a** $a = -1020°$. The appreciable increase in specific rotations observed at the sodium D line is due to this bathochromatic shift and enhancement of rotations.

Pmr studies[1,2] indicate that these derivatives exist as the enamine tautomer but differ from the dimedone amine derivatives in that the vinyl amide group is in the chelated *cis* form, whereas in the latter it must be *trans*. The *cis* conformation is indicated by the low-field N–H pmr signal at 11–12 ppm. This resonance, due to strong intramolecular hydrogen bonding, is insensitive to concentration and solvent effects. Concomitantly, the strongly associated hydroxyl group (δ_{OH} 13–15 ppm) maintains near-planarity of the aromatic group with the carbonyl.

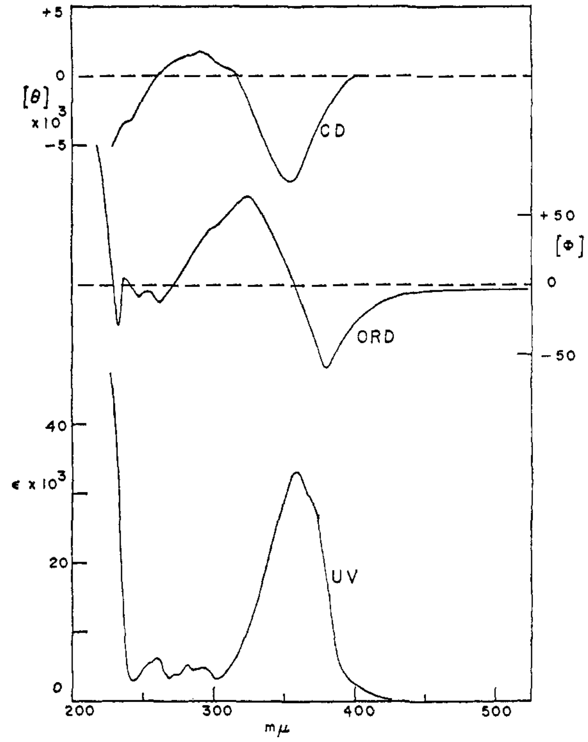

Figure 1. Spectra (methanol solution) of (*R*)-(+)-*o*-hydroxy-(α-[1-naphthyl]ethylamino)crotonophenone.

One would be hesitant to suggest an inherently dissymmetric chromophore to this system held together by internal hydrogen bonds. With these compounds, however, the hydrogen bonds are extremely strong and may so perturb the sp^2-hybridized oxygen that the electronic distribution is no longer symmetrical, thus enhancing the effect of the asymmetric amine. In addition, the chromophore and the asymmetric amine are in better juxtaposition in the *cis vs.* a *trans* form, possibly increasing the magnitude of the Cotton effect.

When the asymmetric center does not bear an aromatic substituent, the amplitudes and specific rotations decrease by an order of magnitude, increasing the difficulty of observing the Cotton effect in the presence of such a strongly absorbing chromophore (**1c**, **2c**). Crabbe, *et al.*,[6] noted this effect in the dimedone condensation products and attributed it to homoconjugation of the aromatic group with the vinyl amide system. The nearly identical electronic absorption spectra of

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(5) P. Crabbe, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1965, pp 309–312.

(6) E. Santos, J. Padilla, and P. Crabbe, *Can. J. Chem.*, **45**, 2275 (1967).

the alkyl amide derivatives **1c** and **2c** with those of aryl alkylamine derivatives **1a,b** and **2a,b** offer little evidence to support such a hypothesis.

The sign of the Cotton effect for the *cis*-vinyl amide derivatives is opposite to that of the dimedone derivatives of the same optically active amines. This was intimated in the work of Potapov[7] with optically active amine Schiff base derivatives of 1-arylpropane-1,3-dione. In that case, both *cis* and *trans* forms were isolated and found to exhibit specific rotations of differing sign between 400 and 500 mμ. In solution, mutarotation was observed resulting in an equilibrium of *cis* and *trans* forms. Earlier studies by Dudek and Volpp[8] have pointed out the importance of the terminal methyl group in this system in stabilizing the *cis*-vinyl amide form. With compounds **1** and **2** (**a**–**d**) no evidence was obtained for the presence of the *trans*-vinyl amide isomer in solution.

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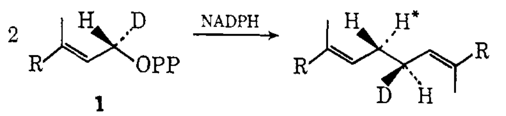
(7) V. M. Potapov, *Tetrahedron*, 23, 4357 (1967).
(8) G. O. Dudek and G. P. Volpp, *J. Am. Chem. Soc.*, **85**, 2697 (1963).

Robert A. Coburn, Gerald Dudek
Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138
Received June 10, 1968

An *in Vitro* Model for the Enzymatic Coupling of Farnesol

Sir:

The enzymatic coupling of farnesol pyrophosphate to yield the hydrocarbon squalene has received considerable study,[1] resulting in a detailed description of the stereochemical relationships of the starting material and product, as expressed by the conversion **1** to **2** (R =



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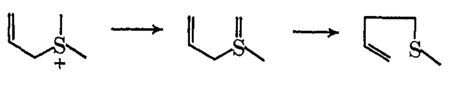
2

geranyl-CH$_2$–). Thus a hydrogen atom is lost from the terminus of one unit, being replaced stereospecifically by hydrogen from the dihydronicotinamide coenzyme, while the other unit undergoes an inversion of configuration at C-1 during the coupling process. Three mechanisms have been considered for this process,[1,2] but the published experimental work does not yet allow an unequivocal decision to be made concerning the mechanism, one group favoring a pathway involving a sulfur ylide[3] and another investigator providing evidence for a cyclopropane-containing intermediate.[4] More recently it has been suggested that the formation of phytoene, the precursor of the carotenoids, proceeds by a coupling mechanism similar to that operative in the squalene case.[5]

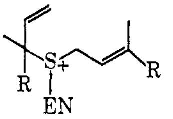
We[6] and others[7,8] have independently observed a very facile rearrangement of sulfonium ylides, which may be expressed by structures **3**–**5**. This reaction involves



3 **4** **5**

a concerted rearrangement of six electrons and is apparently driven by the formal valence change of sulfur from four to two. Such processes have been described in many places in the earlier literature[6] and proceed in a wide variety of molecular environments, even allowing substitution of heteroatoms into the cyclic array of ylide **4**. The recognition and facility of this process induced us to test whether it would be a chemically feasible method of coupling two farnesol-like molecules, and we report here the successful conclusion of these experiments.

On the assumption that the enzymatic coupling process involved a thiol we deduced that the linking of two farnesyl pyrophosphates to such a function might occur in the unsymmetrical sense, exemplified by salt **6** (R = geranyl-CH$_2$–). Therefore we prepared sulfide **7**[9]



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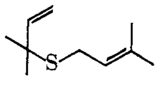

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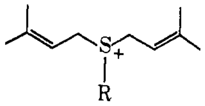

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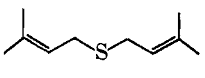
and carried out alkylations of this species. Our usual procedure[6] (triethyloxonium fluoroborate in dichloromethane), however, led exclusively to the rearranged salt **8** (R = C_2H_5),[6] and so we investigated this reaction by nmr. From $-30°$ to room temperature sulfide **7** is readily isomerized to its symmetrical isomer **9**[6] by both Lewis acids (boron trifluoride ether) and protonic acids (trifluoroacetic acid), and this isomerization is faster than the alkylation, hence the production of **8**.

However, by using the less hindered reagent, trimethyloxonium fluoroborate in nitromethane,[10] alkylation was rapid at $-20°$ and led to the required salt **10** (nmr (deuteriochloroform, $-20°$),[11] δ 1.73–1.86 (12 H, 4-CH_3), 2.69 (3 H, -SCH_3), 3.68–4.15 (2 H, multiplet, S–CH_2–), 5.38 (1 H, triplet, olefinic, J = 8 cps), 5.83 (2 H, vinyl, multiplet), 6.15 (1 H, quartet, vinyl, J_1 = 10, J_2 = 15 cps)) recovered by precipitation with pre-



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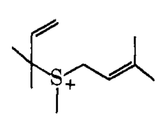

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cooled ether. This compound was reasonably stable up to 5° but at +15° was gradually isomerized into **8** (R = CH_3), however at a rate much slower than the

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(1) J. W. Cornforth, R. H. Cornforth, C. Donninger, and G. Popjak, *Proc. Roy. Soc.* (London), **B163**, 492, 1966; J. W. Cornforth and G. Ryback, *Ann. Rept. Progr. Chem.*, **62**, 428 (1965); R. B. Clayton, *Quart. Rev.* (London), **19**, 168 (1965); I. D. Frantz and G. J. Schroepfer, *Ann. Rev. Biochem.*, **36**, 691 (1967).
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(4) H. C. Rilling, *J. Biol. Chem.*, **241**, 3233 (1966).
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(6) J. E. Baldwin, R. E. Hackler, and D. P. Kelly, *Chem. Commun.*, 537, 538 (1968).
(7) R. B. Bates and D. Feld, *Tetrahedron Letters*, 417 (1968).
(8) G. M. Blackburn, W. D. Ollis, J. D. Plackett, C. Smith, and I. O. Sutherland, *Chem. Commun.*, 186 (1968).
(9) C. G. Moore and B. R. Trego, *Tetrahedron*, **18**, 205 (1962).
(10) This homogeneous system was first brought to our notice by Dr. R. A. Olofson.
(11) All chemical shift data are expressed relative to tetramethylsilane, and spectra were obtained at room temperature and 60 Mc, unless otherwise stated.