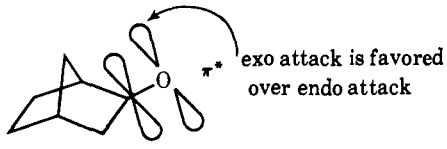
singlet ketone possessing the characteristics of the simple model, mentioned above, for an n,π^* state. There are, of course, two choices for attack on the faces of the carbonyl group by *t*-DCE. On the basis of *ground-state* nucleophilic additions to the carbonyl group,[5] exo attack by *t*-DCE should be favored for **1**, while endo attack by *t*-DCE should be favored for **6**; however, endo attack for **6** should occur at a slower rate than unhindered exo attack. Similar reasoning leads to the conclusion that "steric approach" controls the reactivity of molecules **1**–**10** toward nucleophilic attack by *t*-DCE on the excited carbonyl group, and the reactivity pattern **1** > **2** > **3** ~ **4** > **5** ~ **6** ~ **7** ~ **8** > **9** corresponds well to the expected accessibility of the faces of the excited carbonyl group's half-filled π^* orbital to *t*-DCE (Scheme I). The close agreement between

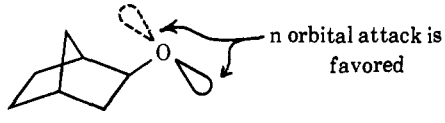
Scheme I. Quenching of Alkanone Fluorescence by 1,2-Dicyanoethylene



the $k_q^f\tau_f$ values for **1** and **10** provides strong support for the preference of exo over endo attack for *t*-DCE on alkanone singlets.

In striking contrast to the correlation of the fluorescence quenching of **1**–**10** by *t*-DCE with the ground-state model for nucleophilic attack on the π face of the carbonyl group,[5] the quenching of the fluorescence of **1**–**10** by *c*-DEE displays a totally different response to ketone structure. It appears that quenching by *c*-DEE is most efficient when interaction from the sides of the carbonyl function are sterically accessible (Scheme II).

Scheme II. Quenching of Alkanone Fluorescence by 1,2-Diethoxyethylene



Thus, the reactivity pattern **1** ~ **6** ~ **10** > **3** > **2** ~ **4** ~ **8** > **5** ~ **7** > **9** nicely parallels the expected accessibility of the excited carbonyl's n orbital to *c*-DEE and electrophilic attack. The slightly higher $k_q^f\tau_f$ value for **3** over **2** may reflect a difference in lifetimes or result from puckering of the excited carbonyl[6] in a fashion so as to favor quenching of **3** over **2** by *c*-DEE.

Since preliminary measurements of the quantum yields for oxetane formation for **1**, **4**, and **8** (0.12, 0.048, and 0.032, respectively)[7] parallel the quenching reactivity of *t*-DCE toward these ketones, we feel that the quenching mechanism is intimately connected to oxetane formation. Further studies are presently in progress to substantiate this proposal.

In summary, quantitative study of the variation of fluorescence quenching reactivities of *t*-DCE and *c*-DEE as a function of ketone structure has provided compelling evidence for the occurrence of two distinct quenching mechanisms. In one case the electron-poor ethylene *t*-DCE interacts with the nucleophilic faces of the excited carbonyl group and in the other case the electron-rich ethylene *c*-DEE interacts with the electrophilic (half-filled) n orbital of the excited carbonyl group.

(5) For example, see H. C. Brown and J. Muzzio, *J. Amer. Chem. Soc.*, **88**, 2811 (1966), and references therein. See also E. L. Eliel and Y. Senda, *Tetrahedron*, **26**, 2411 (1970).

(6) Cases of both photochemical and spectroscopic results which can be interpreted in terms of a nonplanar n,π^* carbonyl function are known: O. Jeger and K. Schaffner, *Pure Appl. Chem.*, **21**, 247 (1970); C. A. Emeis and L. J. Oosterhoff, *Chem. Phys. Lett.*, **1**, 129 (1967); W. D. Chandler and L. Goodman, *J. Mol. Spectrosc.*, **35**, 232 (1970).

(7) Quantum yields for oxetane formation were determined for acetonitrile solutions of ketone (0.5 *M*) and *t*-DCE (0.1 *M*) employing benzophenone–benzhydrol actinometry.

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Tris[3-(*tert*-butylhydroxymethylene)-*d*-camphorato]europium(III). A Reagent for Determining Enantiomeric Purity[1]

Sir:

Examination of the ^{1}H nmr spectra of polar chiral substances in solutions of optically active alcohols or amines has proved a valuable method for the direct determination of enantiomeric purity.[2,3] However, the magnitude of the chemical-shift difference between corresponding protons of enantiomers obtained using this technique is normally small,[2] and restricts its utility in applications involving complex spectra. We wish to report the observation of relatively large frequency differences between corresponding resonances of enantiomeric amines dissolved in achiral solvents containing tris[3-(*tert*-butylhydroxymethylene)-*d*-camphorato]europium(III) (**2**). These observations indicate that **2** and related compounds should provide the basis for a useful method for determining the enantiomeric purity of certain compounds for which procedures based on diastereomeric interaction between solute and solvent fail.

Compound **2** was prepared by conversion of *d*-camphor to *tert*-butylhydroxymethylene-*d*-camphor (**1**),[4] followed by reaction of the latter compound with europium(III) trichloride in the presence of base.[5] The properties of **2** resemble those of tris(dipivaloylmethido)europium(III), except that **2** is appreciably the more soluble in nonpolar solvents. The nmr spectrum of **2** is localized between +2 and −1 ppm from TMS.

Figure 1 illustrates the influence of **2** on the spectrum of a representative chiral amine, α-phenylethylamine (**3**). The large downfield shift of the resonances of **3** from their positions in the absence of **2** is the expected result of pseudocontact interaction between the eu-

(1) Supported by the National Institutes of Health, Grant No. GM 16020.

(2) W. H. Pirkle and S. D. Beare, *J. Amer. Chem. Soc.*, **91**, 5150 (1969), and references therein.

(3) M. Raban and K. Mislow, *Top. Stereochem.*, **2**, 199 (1967).

(4) The procedure followed was modeled on that of B. O. Linn and C. R. Hauser, *J. Amer. Chem. Soc.*, **78**, 6066 (1956). Compound **1** had bp 87–95° (0.05 mm). *Anal.* Calcd for $C_{12}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 76.11; H, 10.28.

(5) K. J. Eisentraut and R. E. Sievers, *ibid.*, **87**, 5254 (1965). The work-up described by these authors was modified by omission of the sublimation step, and purification of the crude product by extraction into absolute ethanol, filtration, precipitation by addition of water, and dehydration under vacuum: mp 131–134°. *Anal.* Calcd for $C_{36}H_{69}O_6Eu$: C, 62.99; H, 8.11. Found: C, 62.71; H, 8.19.

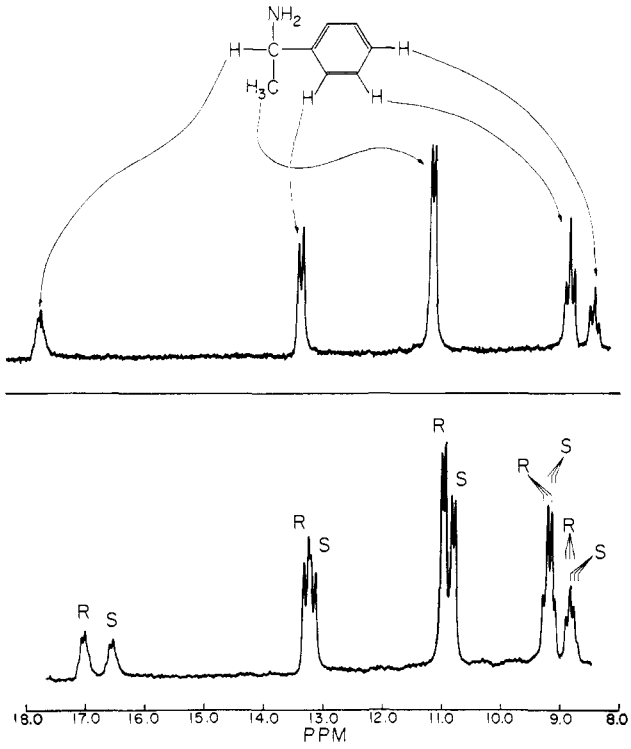
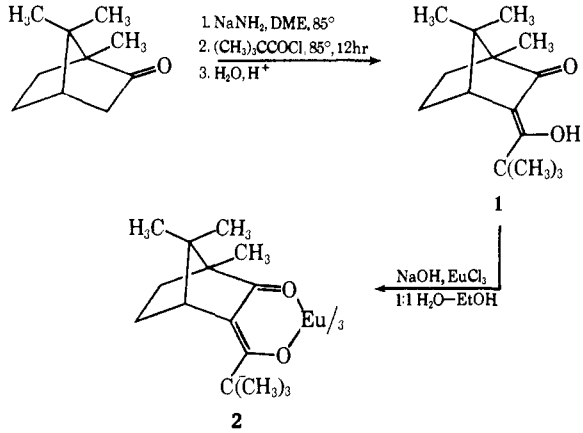


Figure 1. Spectra of solutions prepared from (*S*)-α-phenylethylamine (10 μl) (upper), and a mixture of (*R*)- and (*S*)-α-phenylethylamine (7 and 5 μl, respectively), in 0.3 ml of a carbon tetrachloride solution of **2** (~0.15 *M*). The chemical-shift scale applies only to the spectrum of the mixture; that of the pure *S* enantiometer was displaced slightly to lower field due to differences in concentrations of the samples.

ropium(III) ion and a rapidly exchanging mixture of coordinated and free amine.[6] More noteworthy in



these spectra are the frequency *differences* in the resonance of corresponding protons of (*R*)- and (*S*)-**3**, ranging from ~0.5 ppm for the C*H*NH$_2$ proton to ~0.07 ppm for the para hydrogen of the aromatic ring. These separations depend on the concentration of **2**: the difference between the C*H*NH$_2$ resonances of ~0.3 *M* solutions of **3** is too small to be observable when [**2**] = 0.015 *M*, reaches a maximum of 0.55 ppm for [**2**] = 0.14 *M*, and decreases to 0.4 ppm at [**2**] = 0.50 *M*.

(6) The potential of lanthanide ions as nmr shift reagents in organic structural analysis was first demonstrated by C. C. Hinckley, *J. Amer. Chem. Soc.*, 91, 5160 (1969); *J. Org. Chem.*, 35, 2834 (1970). See also J. K. M. Sanders and D. H. Williams, *Chem. Commun.*, 422 (1970); J. Briggs, *et al.*, *ibid.*, 749 (1970).

These frequency shifts probably reflect differences in the stability constants for the diasteriomeric complexes formed between (*R*)-**3** or (*S*)-**3** and **2**, since an alternative explanation for their origin, involving unequal magnitudes for the pseudocontact shifts within diastereomeric amine–europium complexes of *equal* stability, cannot easily be used to rationalize the fact that *all* of the protons of (*R*)-**3** resonate at lower field than their counterparts in (*S*)-**3**. The frequency shifts between the C*H*NH$_2$ resonances of (*R*)- and (*S*)-**3** in the presence of the praseodymium analog of **2** reached 0.67 ppm; however, the resolution obtained in the presence of this reagent was appreciably lower than that in solutions of **2**.

Other enantiomeric amines exhibit useful spectral differences in the presence of **2**. Thus, for example, the C*H*NH$_2$ resonances of (*R*)- and (*S*)-amphetamine were separated by 0.7 ppm when their pseudocontact shifts reached ~17 ppm from TMS, and the C*H*$_2$-CHNH$_2$ resonances of (*R*)- and (*S*)-2-aminobutane were separated by 1.4 ppm at shifts of ~12 ppm from TMS. On the other hand, shifts between corresponding resonances of less strongly basic enantiomeric substances were generally too small to be useful, although these resonances were still subject to appreciable pseudocontact shifts. Thus, while the C*H*OH resonances of (*R*)- and (*S*)-2,2,6,6-tetramethyl-4-heptyn-3-ol differed by 0.1 ppm at shifts of ~6.9 ppm from TMS ([**2**] ~ 0.3 *M*), distinguishable shift differences were not observed for resonances of 2-octanol, α-phenylethanol, cyclohexylmethylcarbinol, or benzylmethyl sulfoxide.

The use of **2** to determine enantiomeric purities of amines is complementary to techniques employing optically active solvents. The potential of **2** rests in the large shifts observed between resonances of enantiomers in its presence, and in the spectral simplification common to shift reagents;[6] however, these advantages are gained at the expense of a loss in spectral resolution.

Further study of the application of reagents resembling **2** to the direct determination of enantiomeric purity will be described later.

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Reaction of the Active Site of Papain with a "Reporter" Group Labeled Phenacyl Halide

Sir:

Despite the recent advances made in the investigation of the cysteine proteinases, the chemistry of the most thoroughly studied enzyme in this group, papain, remains far less developed than that of chymotrypsin, the best understood of the serine proteinases.[1,2] Although the primary amino acid sequence[3] and the three-dimensional structure[4] of papain are now known and

(1) M. L. Bender and F. J. Kézdy, *Annu. Rev. Biochem.*, 34, 49 (1965).
(2) D. M. Blow and T. A. Steitz, *ibid.*, 39, 716 (1970).
(3) R. E. J. Mitchel, I. M. Chaiken, and E. L. Smith, *J. Biol. Chem.*, 245, 3485 (1970).
(4) J. Drenth, J. N. Jansonius, R. Koekoek, H. M. Swen, and B. G. Wolthers, *Nature (London)*, 218, 929 (1968).