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

Sir:

Examination of the <sup>1</sup>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.<sup>2,3</sup> However, the magnitude of the chemical-shift difference between corresponding protons of enantiomers obtained using this technique is normally small,<sup>2</sup> 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 enantio-

meric 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**),<sup>4</sup> followed by reaction of the latter compound with europium(III) trichloride in the presence of base.<sup>5</sup> The properties of **2** resemble those of tris(dipivaloylmethido)europium(III), except that **2** is appreciably 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,  $\alpha$ -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-

(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<sub>12</sub>H<sub>22</sub>O<sub>2</sub>: 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<sub>12</sub>H<sub>18</sub>O<sub>2</sub>Eu: C, 62.99; H, 8.11. Found: C, 62.71; H, 8.19.

(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).

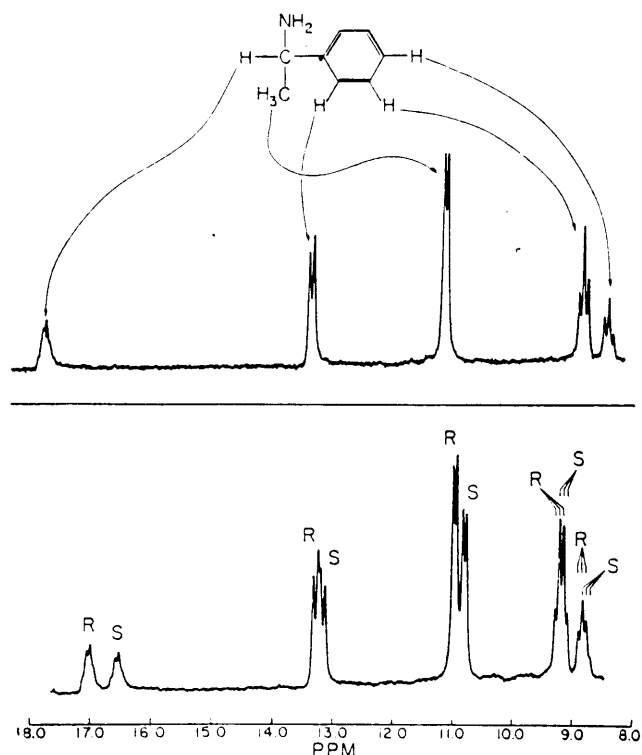
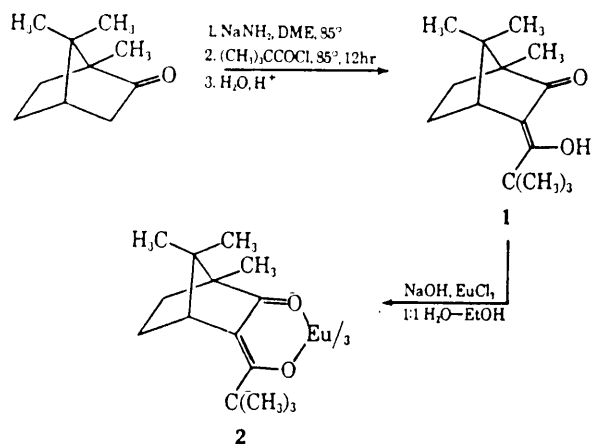


Figure 1. Spectra of solutions prepared from (*S*)- $\alpha$ -phenylethylamine (10  $\mu$ l) (upper), and a mixture of (*R*)- and (*S*)- $\alpha$ -phenylethylamine (7 and 5  $\mu$ l, respectively), in 0.3 ml of a carbon tetrachloride solution of **2** ( $\sim 0.15$  M). The chemical-shift scale applies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

europium(III) ion and a rapidly exchanging mixture of coordinated and free amine.<sup>6</sup> More noteworthy in



(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 spectra are the frequency *differences* in the resonance of corresponding protons of (*R*)- and (*S*)-**3**, ranging from  $\sim 0.5$  ppm for the  $CHNH_2$  proton to  $\sim 0.07$  ppm for the para hydrogen of the aromatic ring. These separations depend on the concentration of **2**: the difference between the  $CHNH_2$  resonances of  $\sim 0.3$  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. These frequency shifts probably reflect differences in the stability constants for the diastereomeric 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  $CHNH_2$  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  $CHNH_2$  resonances of (*R*)- and (*S*)-amphetamine were separated by 0.7 ppm when their pseudocontact shifts reached  $\sim 17$  ppm from TMS, and the  $CH_2$ - $CHNH_2$  resonances of (*R*)- and (*S*)-2-aminobutane were separated by 1.4 ppm at shifts of  $\sim 12$  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  $CHOH$  resonances of (*R*)- and (*S*)-2,2,6,6-tetramethyl-4-heptyn-3-ol differed by 0.1 ppm at shifts of  $\sim 6.9$  ppm from TMS ( $[2] \sim 0.3$  M), distinguishable shift differences were not observed for resonances of 2-octanol,  $\alpha$ -phenylethanol, cyclohexylmethylcarbinol, or benzylmethylsulfoxide.

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;<sup>6</sup> 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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