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Use of Tris(dipivalomethanato)praseodymium(III) for the Determination of the Chirality of Simple Amines and Cyclic 1,2-Amino Alcohols[1]

Sir:

Our interest in biologically important simple amines and 1,2-amino alcohols has prompted us to seek a rapid, convenient micromethod for determining the absolute stereochemistry of these compounds. A recent report has shown that the chirality of cyclic α-glycols can be established from the induced Cotton effects (CE) observed in the circular dichroism (CD) spectra of a mixture of the α-glycol and tris(dipivalomethanato)praseodymium(III) [Pr(DPM)$_3$] in carbon tetrachloride.[2,3] Since the sign of the CD at *ca.* 310 nm was a measure of the chirality of the α-glycols, the extension of this method to 1,2-amino alcohols was proposed.[2] In this communication we report our observations on the CD spectra of Pr(DPM)$_3$ complexes with simple amines and the extension of the α-glycol method to cyclic 1,2-amino hydroxy compounds with known chirality and fixed conformation.

Although steroidal monoalcohols showed no CE when combined with Pr(DPM)$_3$,[2] the isolation of crystalline lanthanide adducts such as Ho(DPM)$_3$(4-picoline)$_2$[4] led us to expect that Cotton effects may be observed with Pr(DPM)$_3$ and optically active amines. Sanders and Williams had also shown that Eu(DPM)$_3$ coordinates more strongly with many amines than with alcohols.[5] The effects of Pr(DPM)$_3$ on the CD spectra of some optically active simple amines are summarized in Table I. In every case a first Cotton effect was observed at *ca.* 315 nm and a second effect of opposite sign and similar magnitude was observed at *ca.* 290 nm.[6] The value of [θ] increased rapidly as the ratio of Pr(DPM)$_3$ to **1** increased to 0.5 and was relatively insensitive to further increases in Pr(DPM)$_3$ concentration. This is consistent with the results of Reuben's work with β-picoline where he found that association of the type Pr(DPM)$_3$(amine)$_2$ was dominant over a large range of reagent to substrate ratios.[7] The Pr(DPM)$_3$-(amine)$_2$ adducts listed in Table I show an induced CE that can be correlated with the Cahn, Ingold, and Prelog *R* and *S* designations of absolute configuration.[8] In this study, amines of the *S* configuration have a first CE of one sign (positive) while those of the *R* configuration have the opposite sign (negative). This observation is probably fortuitous and is not related directly to the configuration based on the *R,S* system. The observed correlation with the Cahn, Ingold, and Prelog designation of absolute configuration is more likely due to the circumstance that in all the cases studied the substituents (other than nitrogen) on the asymmetric center followed a decreasing size sequence which is the same as the Cahn, Ingold, and Prelog sequence rule order. These observations suggest the possibility of using Pr(DPM)$_3$ for determining the stereochemistry of amines.[9] However, in order to establish the usefulness of this method, it will be necessary to study additional amines possessing various types of substituents.

Table I. CD Data for Optically Active Amine–Pr(DPM)$_3$ Complexes in Carbon Tetrachloride[a]

No.	Entry[b]	10^3M	10^3[Pr(DPM)$_3$], M	$[\theta] \times 10^{-2}$ (nm)[c-e]
1	(*R*)-α-Methylphenethylamine	1.1	0.60	−31 (313)
2	(*S*)-α-Methylphenethylamine	1.1	0.60	+32 (313)
3	(*R*)-α-Methylbenzylamine	1.2	0.60	−26 (313)
4	(*S*)-α-Methylbenzylamine	1.1	0.63	+22 (313)
5	(*R*)-α-(1-Naphthyl)ethylamine	1.2	0.56	−23 (313)
6	(*S*)-α-(1-Naphthyl)ethylamine	1.0	0.52	+24 (313)
7	Dehydroabietylamine	0.73	1.05	−3.6 (310)
		2.3		+0.18 (310)[f]
8	(*R*)-*N*-Methyl-α-methylphenethylamine [deoxy-(+)-ephedrine]	1.0	0.62	−20 (311)
9	(17*R*)-17α-Amino-5α-androstan-3β-ol	1.0	1.0	−32 (318)

[a] CD measurements were made at room temperature using a Durrum-Jasco Model J-20 recording spectropolarimeter. The solution of the compound studied and Pr(DPM)$_3$ were prepared in CCl_4 which had been distilled from P_2O_5 and stored over molecular sieve. The CD curves were recorded within a few hours after preparation. [b] Compounds **1–7** were obtained from Aldrich Chemical Co. and used without further purification. Compound **8** was prepared as described by K. W. Rosenmund and E. Karg, *Ber.*, **75**, 1850 (1942), substituting 10% Pd/C. Compound **9** was prepared as described by M. Davis, E. W. Parnell, and D. Warburton, *J. Chem. Soc. C*, 1688 (1966). [c] Only the high wavelength CE is given. [d] The CD curves of the amines in the absence of Pr(DPM)$_3$ showed no or only negligible CE when carried out under similar conditions. [e] Unless the liquid amine was weighed directly into solvent, a five–ten fold reduction of [θ] was sometimes observed. This was attributed to carbonate formation. [f] This is [θ] for **7** at 310 nm in the absence of Pr(DPM)$_3$ but is not the λ_{max} for **7**.

The results obtained in Table II show that the method for determining the chirality of cyclic α-glycols can be extended to cyclic β-amino alcohols. The chirality of the β-amino alcohols is defined, as for the α-glycols,[2] as being negative or positive, respectively, when the Newman projection represents an anticlockwise (left handedness) or clockwise (right handedness) rotation from the forward hetero atom to the rearward hetero atom as illustrated for **11**.

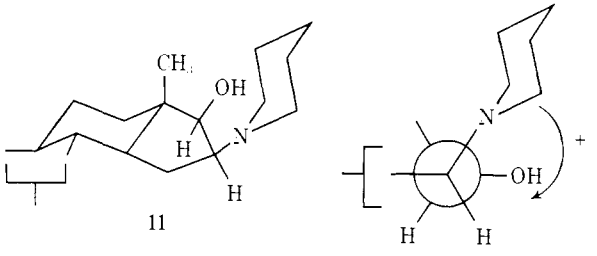
As entries **10**, **11**, **13**, and **15** indicate, the sign of the first CE is the same as the predicted chirality. Al-

(1) This work was carried out under Contract No. PH-43-65-1057 with the Pharmacology–Toxicology Program, National Institute of General Medical Sciences, National Institutes of Health.
(2) K. Nakanishi and J. Dillon, *J. Amer. Chem. Soc.*, **93**, 4058 (1971).
(3) N. Harado and K. Nakanishi, *Accounts Chem. Res.*, **5**, 257 (1972).
(4) W. DeW. Horrocks, Jr., J. P. Sipe, III, and J. R. Luber, *J. Amer. Chem. Soc.*, **93**, 5258 (1971).
(5) J. K. M. Sanders and D. H. Williams, *J. Amer. Chem. Soc.*, **93**, 641 (1971).
(6) The α-glycols showed similar CD curves, although the observed [θ] values were generally somewhat larger than those for the amines.[2]
(7) J. Reuben, *J. Amer. Chem. Soc.*, **95**, 3534 (1973).
(8) R. S. Cahn, C. Ingold, and V. Prelog, *Angew. Chem., Int. Ed. Engl.*, **5**, 385 (1966).
(9) Entry **7** is of particular interest because the amino group is not at the asymmetric center but separated from it by a methylene group, suggesting the possibility of using Pr(DPM)$_3$ adducts with amines to determine the stereochemistry of more remote asymmetric centers.

Table II. CD Data for Cyclic 1,2-Amino Alcohol–Pr(DPM)$_3$ Mixtures in Carbon Tetrachloride[a]

No.	Entry[b]	Chirality	10^3M	10^3[Pr(DPM)$_3$], M	$[\theta] \times 10^{-4}$ (nm)[c]
10	3β-Hydroxy-16β-piperidinoandrost-5-en-17-one	(+)	1.1	1.0	+2.1 (312)
			0.9		+0.34 (312)[d]
11	3β,17β-Dihydroxy-16β-piperidinoandrost-5-ene	(+)	1.4	1.4	+2.4 (304)
12	3β,5α-Dihydroxy-6β-piperidinoandrostan-17-one	Diaxial	1.3	1.2	+1.1 (303)
			0.31		+1.1 (305)
13	3β,5β-Dihydroxy-6α-piperidinoandrostan-17-one	(+)	0.74	0.89	+1.24 (303)
			0.74		+0.87 (305)
14	3β,5α,17β-Trihydroxy-6β-piperidinoandrostane	Diaxial	1.4	1.9	−0.0093 (320)
15	3β,5β,17β-Trihydroxy-6α-piperidinoandrostane	(+)	1.35	1.5	+0.44 (309)

[a] See footnote *a* to Table I. [b] Compounds **10–13** were prepared as described by C. L. Hewett and D. S. Savage, *J. Chem. Soc. C*, 484 (1966); 582 (1967). Compounds **14** and **15** were prepared by $NaBH_4$ reduction of compounds **12** and **13**. [c] Only the high wavelength CE is given. [d] This is not the λ_{max} of the CD of **10**. The λ_{max} is ≅290 nm, $[\theta] = 0.56 \times 10^4$.



though, in itself, only four examples might normally be insufficient for the formulation of a definitive rule for predicting a CD sign, the similarity of the 1,2-amino hydroxy steroids in curve shape, and magnitude, to the α-glycol steroids leads us to believe that the effect is general. Entry **12** exhibits a $[\theta]$ of the same magnitude for the diaxial 5α-hydroxy-6β-amine with or without Pr(DPM)$_3$, indicating that the diaxial compound is incapable of the necessary bidentate contact with the metal.[10] Diaxial α-glycols, including cholestane-3β,5α,6β-triol, were also found to show no CE in the presence of Pr(DPM)$_3$.[2] Reduction of **12** to **14** enabled us to again examine the diaxial system in the absence of the interfering CD of the 17-ketone. This compound showed only a very weak CE, attributable to a simple amine in the presence of Pr(DPM)$_3$. Entries **13** and **15** illustrate that the diequatorial isomers corresponding to **12** and **14** do show the expected CD effect. Entry **10** is of particular interest in that it indicates that an α-amino ketone can act as a bidentate for complexing with Pr(DPM)$_3$ and suggests that the sign of the first CE of α-amino ketones follows the same chirality rules as the α-glycols and 1,2-amino alcohols. In the case of the α-amino ketones, the normal Pr(DPM)$_3$ complex CE was superimposed on a broad CE at 380–400 nm, which was attributed to the carbonyl itself.

In summary, we have found that the method for establishing the chirality of cyclic α-glycols[2] with Pr(DPM)$_3$ can be extended to cyclic 1,2-amino alcohols (and possibly for α-amino ketones) and that Pr(DPM)$_3$ can be used in a micromethod for determining the configuration of simple amines. However, application of these methods to a compound of unknown structure should be approached cautiously since it might be possible to mistake a strong amine CE for a weak 1,2-amino alcohol CE (compare entries **9** and **15**).

The investigation of the extension of this method to acylic 1,2-amino alcohols will be reported in a separate communication.

(10) Compound **12** would be expected to show an effect similar to the simple amines shown in Table I. However, this effect is probably obscured by the CE of the 17-ketone function.

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A Study of Optically Active Diastereomeric Charge-Transfer Complexes

Sir:

Charge-transfer complex formation may play an important part in understanding the structure and function of natural products.[1–5] Moser[6] and Briegleb[7] attempted a quantitative study of ORD and CD spectra[8] of optically active charge-transfer complexes. This paper reports the circular dichroism spectra of the charge-transfer (CT) absorption bands of two diastereomeric CT complexes. Of interest to us was the question whether diastereomeric CT complexes show measurably different chiroptical properties.

As the donor molecule we used (+)- and (−)-hexahelicene.[9,10] Its optical purity[9] and absolute configuration[11] have been established. As optically active acceptor (+)-2-(2,4,5,7-tetranitro-9-fluorenylideneaminooxy)propionic acid (TAPA) was used (see Chart I). The resolution of *dl*-hexahelicene (II) using (+)-TAPA (I)[12] is usually interpreted[12] as follows. Diastereomeric charge-transfer complexes are formed and the helicene

(1) E. J. Gabbey, *J. Amer. Chem. Soc.*, **90**, 6574 (1968); E. J. Gabbey and A. de Paolis, *ibid.*, **93**, 562 (1971); J. A. Secrist III and N. J. Leonard, *ibid.*, **94**, 1702 (1972).
(2) J. Verhoeven and P. Schwijzer, *Helv. Chim. Acta*, **55**, 2572 (1972).
(3) M. A. Slifkin and R. H. Walmsley, *Spectrochim. Acta, Part A*, **26**, 1237 (1970).
(4) M. Gouterman and P. E. Stevenson, *J. Chem. Phys.*, **37**, 2266 (1962).
(5) R. H. Sarma, P. Dannies, and N. O. Kaplan, *Biochemistry*, **7**, 4359 (1968).
(6) P. Moser, *Helv. Chim. Acta*, **51**, 1831 (1968).
(7) G. Briegleb, H. G. Kuball, and K. Henschel, *Z. Phys. Chem. (Frankfurt am Main)*, **46**, 229 (1965).
(8) The CD spectra were recorded on a Dichrograph Roussel-Jouan Model CD 185 with a 1-mm cell. The uv spectra were recorded on a Carl Zeiss M4 Q III with a PMQ III recorder. Spectrograde chloroform was used as solvent.
(9) M. S. Newman and D. Lednicer, *J. Amer. Chem. Soc.*, **78**, 4765 (1956).
(10) R. H. Martin, M. J. Marchant, and M. Baes, *Helv. Chim. Acta*, **54**, 358 (1971).
(11) J. Tribout, R. H. Martin, M. Doyle, and H. Wynberg, *Tetrahedron Lett.*, 2839 (1972).
(12) M. S. Newman, W. B. Lutz, and D. Lednicer, *J. Amer. Chem. Soc.*, **77**, 3420 (1955).