formation is

$$\phi_{ox} = \frac{\alpha k_q[\text{diene}]}{k_q[\text{diene}] + 1/\tau_s}$$

and

$$1/\phi_{ox} = 1/\alpha + 1/\alpha k_q[\text{diene}]\tau_s$$

By plotting $1/\phi_{ox}$ against 1/[diene], we will obtain a straight line with $1/\alpha$ as the intercept and $1/\alpha k_q\tau_s$ as the slope. We found experimentally the intercept to be 19.7 ± 1.9 and the slope to be 14.2 ± 1.2 *M*. Therefore, $k_q\tau_s$ is 1.39 ± 0.14 M^{-1} which is in good agreement with the value of $k_q\tau_s$ obtained from the quenching of fluorescence of acetone by 1,3-cyclohexadiene, 1.45 ± 0.15 M^{-1} (Table I). The results indicate that the fluorescence quenching and oxetane formation by dienes proceed *via* the same intermediate and offer experimental support to the kinetic scheme proposed above. However, the data do not exclude a number of alternative pathways, and the detailed discussion will be elaborated in a later publication.

An incidental finding in our investigation is that the Stern–Volmer plot from the quenching of the type I process of pinacolone by 1,3-cyclohexadiene has the appearance of a straight line in spite of the fact that the reaction may take place from both excited states. Dalton and Turro analyzed that the Stern–Volmer plot of a photochemical reaction involving a singlet and a triplet state would have the appearance of a straight line when $k_q^s\tau_s[1 + (\phi_0^t/\phi_0^s)]$ approached $k_q^t\tau_t$.[7] This is apparently the first such case found.

The higher efficiency of 1,3-cyclohexadiene than acyclic dienes as a quencher in photochemical reactions of unsaturated ketones has been reported in several instances,[15] but the nature of these quenching processes is not yet clearly understood.[16]

Acknowledgment. The authors wish to thank the National Science Foundation for the support of this work under Grants GP-16347 and GY-7232, the UniRoyal Company for a fellowship to one of us (M. H. H.), and Professor Nicholas J. Turro for the exchange of some unpublished information.

(15) For recent examples of this phenomenon, see D. I. Schuster and W. V. Curran, *J. Org. Chem.*, **35**, 4192 (1970); D. I. Schuster and N. K. Lau, *Mol. Photochem.*, **1**, 415 (1969); D. I. Schuster, *et al.*, *J. Amer. Chem. Soc.*, **90**, 5027 (1968); D. I. Schuster and A. C. Fabian, *Tetrahedron Lett.*, 1302 (1968).

(16) T. S. Cantrell, *Chem. Commun.*, 1656 (1970).

(17) UniRoyal Fellow, 1970–1971.

(18) National Science Foundation Undergraduate Research Participant, 1970.

N. C. Yang,* Man Him Hui,[17] Sharon A. Bellard[18]
Department of Chemistry, University of Chicago
Chicago, Illinois 60637
Received January 22, 1971

A Simple Method for Determining the Chirality of Cyclic α-Glycols with Pr(DPM)$_3$ and Eu(DPM)$_3$

Sir:

We report an extremely simple method which enables one to determine the chirality of cyclic α-glycols. It involves no derivatization, only a minute amount of the glycol is required, and it is, moreover, applicable to α-glycols containing *tert*-hydroxyl groups.

The so-called nmr shift reagents, *e.g.*, Pr(DPM)$_3$ and Eu(DPM)$_3$, have been widely used[1] for analyzing nmr spectra of compounds containing hydroxyl, amine, and other functional groups. The present method utilizing these complexes is formally an extension of the "aromatic chirality method"[2] (or in a narrower sense the "dibenzoate chirality method"[3]), and merely involves measurement of CD spectra of 1:1 solute and complex mixtures in carbon tetrachloride or chloroform.

A typical CD Cotton effect curve is depicted in Figure 1. The chirality of the glycol moiety is defined as being negative (Figure 1) or positive, respectively, when the Newman projection represents an anticlockwise (left-handedness) or clockwise (right-handedness) rotation from one hydroxyl group to the other.[3] Mixtures of the glycol and complex result in CD curves having two Cotton effects of *opposite* signs at *ca.* 310 and *ca.* 290 nm. Although the amplitudes of these Cotton effects have been found to be dependent on several factors, invariably *the sign of the longer wavelength Cotton effect (first Cotton effect) is in agreement with the chirality of the cyclic α-glycol.* Superficially this observation is exactly what was encountered in the dibenzoate chirality method.[3]

Basic studies pertaining to various factors which influence the CD curves were carried out using 5-cholestene-3β,4β-diol as the substrate and Pr(DPM)$_3$[4] as the complex.

Some factors which influence the twin Cotton effects are the following. (a) The presence of water or alcohol reduces or annihilates the Cotton effects. (b) The $\Delta\epsilon$ is concentration dependent (Figure 2). (c) The $\Delta\epsilon$ is time dependent, *e.g.*, in carbon tetrachloride it almost doubles for a period up to 5–10 hr and then slowly decreases (measurements were made in a stoppered CD cuvette). It should be pointed out that in spite of variations in $\Delta\epsilon$ values, the signs do not change.

On the basis of these studies, the following procedure is recommended for actual measurements. An approximately 1:1 mixture of the glycol and complex is made in dry carbon tetrachloride (or ethanol-free chloroform)[5] so that the solutes are *ca.* 2×10^{-4} *M*. The CD is then measured after 30–60 min. It is preferable to mix the solutions in a drybox in order to obtain larger $\Delta\epsilon$ values; however, this is not mandatory, as the $\Delta\epsilon$ values are already quite strong.

As shown in Table I, measurements of a variety of known glycols under these conditions clearly show that signs of the first Cotton effects agree with the glycol chirality, and hence enable one to establish configurations or conformations of glycol-containing natural products in a straightforward manner. Entry 4 (Table I) shows the application of this method to a compound already possessing strong CD Cotton effects, *i.e.*, at 327 ($\Delta\epsilon$ +1.8) and 248 nm ($\Delta\epsilon$ −3.9) (in ethanol). Similarities in the values of entries 5 and 6 indicate that the distant 3-OH is playing a minor role, if any. It is to be noted that the 5-OH is tertiary,

(1) J. K. M. Sanders and D. H. Williams, *J. Amer. Chem. Soc.*, **93**, 641 (1971), and references therein.

(2) N. Harada and K. Nakanishi, submitted for publication.

(3) N. Harada and K. Nakanishi, *J. Amer. Chem. Soc.*, **91**, 3989 (1969).

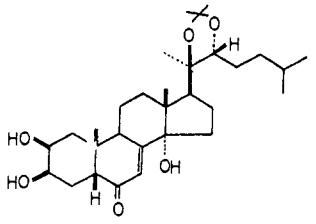
(4) The effect of Eu(DPM)$_3$ is similar to that of Pr(DPM)$_3$ (e.g., a solution of Eu(DPM)$_3$ and 5-cholestene-3β,4β-diol gives the same sign of the Cotton effect and λ_{max} as a solution of Pr(DPM)$_3$ with the glycol).

(5) Solvents were dried over molecular sieves prior to preparation of solutions.

Table I

Entry	Compound	Predicted chirality	M(Pr(DPM)$_3$) $M \times 10^4$	$\times 10^4$	$\Delta\epsilon$ (nm)[d]	Solvent
1	5-Cholestene-3β,4β-diol	(−)	1.8	1.8	−12.6 (312)	CCl_4
2	5α-Cholestane-2β,3β-diol	(+)	1.8	1.8	+9.7 (311)	CCl_4
3	5α-Cholestane-2α,3α-diol	(+)	1.4	1.4	+6.0 (305)	CCl_4
4	Ponasterone A 20,22-acetonide[b]	(−)	1.6	1.7	−5.3 (312)	CCl_4
5	Cholestane-3β,5α,6α-triol	(−)	1.4	1.5	−5.6 (315)	CCl_4
6	Cholestane-3β-acetoxy-5α,6α-triol	(−)	1.4	1.5	−6.0 (314)	CCl_4
7	5α Androstane-3β,16α,17α-triol[a,c]	(+)	3.1	1.9	+5.8 (313)	$CHCl_3$
8	1,3,5(10)-Estratriene-3,16α,17α-triol[a]	(+)	2.4	1.5	+7.6 (315)	CCl_4
9	5-Cholestene-3β-acetox-2α-ol	(−)	1.7	1.7	−1.8 (305)	CCl_4
10	Ponasterone A 2-acetoxy-20,22-acetonide	(−)	1.5	1.5	−1.0 (307)	CCl_4

[a] Samples received from Dr. J. Fried, Syntex Corporation. [b] See **1**. [c] See **2**. [d] CD spectra were measured using a Cary-6001 attachment on a Cary-60 spectropolarimeter.



1

and thus is in a position for which configurational studies are difficult to carry out (due to lack of carbinyl proton and difficulties in derivatization). The result on the steroidal 16α,17α-glycol (entries 7 and 8) defines

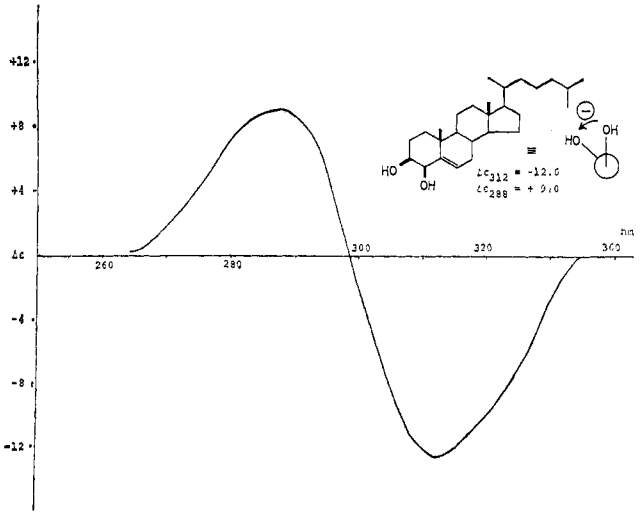
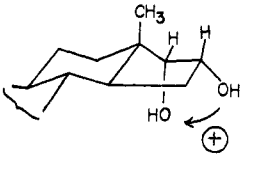


Figure 1. The CD of a mixture of 1.8×10^{-4} M 5α-cholestene-3β,4β-diol and 1.8×10^{-4} M Pr(DPM)$_3$.

the conformation of the D ring under conditions of measurements. Entries 9 and 10 are particularly interesting as they show that the method is applicable to α-glycol monoacetates as well, although the $\Delta\epsilon$ is of diminished intensity under standard conditions.



2

Significantly, steroidal monoalcohols (cholesterol), diaxial α-glycols (cholestane-2β,3α-diol, cholestane-3β,5α,6β-triol), and nonadjacent glycols (cholestane-3β,-6β-diol, 6-oxo-3β,5α-diol derived from diosgenin) gave no CD curves. These results hence suggest that the O···O distance is critical in the observations of CD curves, and that these criteria are met in the nondiaxial α-glycols listed in Table I.

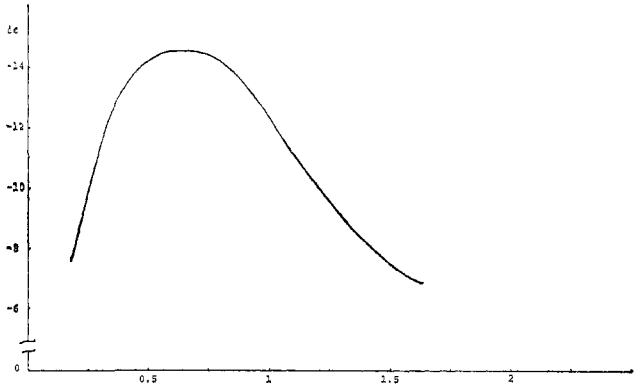


Figure 2. Variation of the $\Delta\epsilon$ at 312 nm for Pr(DPM)$_3$ (1.8×10^{-4} M) and increasing concentration of 5α-cholestene-3β,4β-diol.

The uv λ_{max} of pertinent compounds and mixtures are as follows: (i) dipivaloylmethane, 276 nm (ϵ 13,500, carbon tetrachloride); (ii) Pr(DPM)$_3$, 285 nm (ϵ 33,200, carbon tetrachloride); (iii) 1:1 mixture of 5-cholestene-3β,4β-diol and Pr(DPM)$_3$ in carbon tetrachloride, 20 min after mixing, 282 nm (ϵ *ca.* 31,500), slight shoulder at 305 nm (ϵ 15,000). The first CD extrema of glycol–complex mixtures around 310 nm do not correspond to the uv maxima. On the other hand, the centers of the first and second CD extrema are located around 305 nm and do correspond to the shoulder seen in the uv of the mixture. However, there is so far no evidence that the two extrema are caused by exciton-type splitting.[2,6] The phenomenon observed in the glycols is presumably related to asymmetric induction and/or synthesis,[7,8] and could conceivably result from the expansion of the metal coordination number.[9]

A clear understanding of the results described requires further detailed investigations, but the present method offers a convenient and most simple procedure for

(6) B. Bosnich, *Accounts Chem. Res.*, 2, 266 (1969).
(7) B. Bosnich, *J. Amer. Chem. Soc.*, **89**, 6143 (1967).
(8) U. Doron and W. Durham, *ibid.*, **93**, 889 (1971).
(9) We are grateful to Professor S. Lippard for discussions.

determining the configurations or conformations of α-glycols, and furthermore, it can probably be extended to α-amino alcohols and other similar compounds. Extension of this method to acyclic systems is under investigation.

Acknowledgments. We are grateful to Dr. J. Fried, Syntex Corporation, for a generous gift of steroidal samples. This work was supported by Public Health Service Grant No. CA 11572.

Koji Nakanishi,* James Dillon
Department of Chemistry, Columbia University
New York, New York 10027
Received June 7, 1971

Hydridocobalamin and a New Synthesis of Organocobalt Derivatives of Vitamin B_{12}

Sir:

The Co(I) derivatives of vitamin B_{12} and of other corrins are now well known to exist as the powerful nucleophiles in alkaline medium.[1,2] However, their nature in acidic solution is still not understood. The view that vitamin B_{12s} is a cobalt hydride was first expressed by Müller and Müller,[3] and later by Smith, *et al.*,[4] Dolphin, *et al.*,[5] and Bernhauer, *et al.*[6] However, it was later recognized that all reactions of vitamin B_{12s} cited in support of its hydridic structure were in fact typical of those of the free Co(I) nucleophile.[7] It was subsequently shown that solutions of vitamin B_{12s} slowly decompose into vitamin B_{12r} and molecular hydrogen,[8] indicating that hydridocobalamin, if it exists, must be an unstable or metastable species. This was confirmed by studies in our laboratory, which showed that vitamin B_{12s} decomposition into vitamin B_{12r} and hydrogen in solutions below pH 9.9 could be significantly enhanced by the addition of a platinum catalyst.[1] Absence of definite spectral changes in solutions of vitamin B_{12s} in the pH range between 5 and 14 finally prompted Das, *et al.*,[9] to consider hydridocobalamin a species of altogether questionable existence.

The successful synthesis of the first hydridocobaloximes[10] prompted us to reconsider the possible synthesis or characterization of hydridocobalamin, particularly since the model studies led to the discovery of chemical reactions permitting the distinction of hydridocobalt species from the free Co(I) nucleophiles. Of particular importance in this context are reactions with activated olefins. Ethyl acrylate, for example, reacts with the Co(I) nucleophiles to form the β-carbethoxyethylcobaloxime. With the hydridocobaloximes in buffered neutral or acidic solutions, the α isomers are formed exclusively.[10,11] Vitamin B_{12s} reacts with ethyl acrylate in alkaline medium to yield β-carbethoxyethylcobalamin,[11] readily recognized by its tendency to undergo reversible Co–C bond cleavage in more strongly alkaline solution.[11,12] The formation of α-carbethoxyethylcobalamin has not yet been verified, however. Hydridocobaloximes also react with olefins to form alkylcobaloximes. Generating hydrido(pyridine)cobaloxime from cobaloxime(II) and H_2 *in situ* in polar solvents, we have previously observed the formation of isopropyl(pyridine)cobaloxime.[11] Accordingly, it appeared reasonable to explore the reduction of vitamin B_{12} in acidic media under conditions preventing catalytic destruction of hydridocobalamin. This was achieved by reducing vitamin B_{12a} (hydroxocobalamin) with zinc dust in anhydrous glacial acetic acid under strict exclusion of oxygen. Green solutions formed within a few minutes which turned pink immediately on exposure to air. Rapid decomposition into yellow-brown vitamin B_{12r} and hydrogen was also observed under anaerobic conditions, when a trace of a noble metal catalyst (*e.g.*, platinum oxide or a solution of palladous acetate in glacial acetic acid) was added. Separated from the excess of zinc, the dark green solutions of the reduced cobalamin turn yellow-brown within 15 min of standing at ambient temperature. In the presence of excess zinc the green solutions remain unchanged for several hours, permitting spectroscopic and chemical investigations. In the following we report evidence which demonstrates conclusively that vitamin B_{12} reduced under these conditions is present to a substantial degree in the form of the protonated Co(I) nucleophile, which we designate "hydridocobalamin."[13] The optical absorption spectrum of hydridocobalamin in anhydrous acetic acid is distinctly different from that of vitamin B_{12s} generated by reduction with zinc in aqueous NH_4Cl or with alkaline $NaBH_4$ in water–methanol (Figure 1). The latter two spectra are essentially identical, indicating that reduction of vitamin B_{12a} with zinc in aqueous NH_4Cl buffer produces the Co(I) nucleophile rather than detectable amounts of the hydridocobalamin. The most striking differences between vitamin B_{12s} in the form of the Co(I) nucleophile and the hydride are observed in the chemical reactivities, however. Thus, it has been known for years that vitamin B_{12s} does not react with normal, unactivated olefins. Hydridocobalamin in anhydrous acetic acid, but also in acetic acid–methanol, 1:1, reacts with ethylene rapidly to form ethylcobalamin. After dilution of the reaction solution, the absorption spectrum is identical with that of ethylcobalamin prepared from the nucleophile and ethyl iodide in alkaline solution (Figure 2). The reaction with propylene similarly affords isopropylcobalamin, which is readily distinguished from *n*-propylcobalamin on the basis of the absorption spectrum. In the latter the axial 5,6-dimethylbenzimidazole is attached to cobalt, in the former it is not, causing the spectrum to become similar to that of isopropylcobinamide. Reaction is also observed with cyclohexene, yielding cyclohexylcobalamin, whose ab-

(1) G. N. Schrauzer, E. Deutsch, and R. J. Windgassen, *J. Amer. Chem. Soc.*, **90**, 2441 (1968).
(2) G. N. Schrauzer and E. Deutsch, *ibid.*, **91**, 3341 (1969).
(3) O. Müller and G. Müller, *Biochem. Z.*, **336**, 299 (1962).
(4) E. L. Smith, L. Mervyn, P. W. Muggleton, A. W. Johnson, and N. Shaw, *Ann. N. Y. Acad. Sci.*, **112**, 565 (1964).
(5) D. H. Dolphin, A. W. Johnson, and R. Rodrigo, *ibid.*, **112**, 590 (1964).
(6) K. Bernhauer, O. Müller, and F. Wagner, *Angew. Chem., Int. Ed. Engl.*, **3**, 200 (1964).
(7) G. N. Schrauzer, R. J. Windgassen, and J. Kohnle, *Chem. Ber.*, **98**, 3324 (1965).
(8) J. W. Collat and J. C. Abbott, *J. Amer. Chem. Soc.*, **86**, 2308 (1964).
(9) P. K. Das, H. A. O. Hill, J. M. Pratt, and R. J. P. Williams, *Biochim. Biophys. Acta*, **141**, 644 (1967).
(10) G. N. Schrauzer and R. J. Holland, *J. Amer. Chem. Soc.*, **93**, 1505 (1971).
(11) G. N. Schrauzer and R. J. Windgassen, *ibid.*, **89**, 1999 (1967).
(12) G. N. Schrauzer, J. H. Weber, and T. M. Beckham, *ibid.*, **92**, 7078 (1970).
(13) The axial base 5,6-dimethylbenzimidazole is probably protonated in solutions of hydridocobalamin in glacial acetic acid. Accordingly, the absorption spectrum of hydridocobinamide is similar to that of hydridocobalamin in glacial acetic acid.