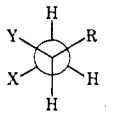
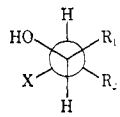
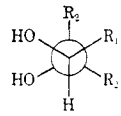
Table IV. Acyclic Glycols and Amino Alcohols

	Classes	Entry	Compound	Sign of the Cotton effect Ni(acac)$_2$ 315/295 nm	Sign of the Cotton effect Pr(dpm)$_3$[a] *ca.* 310 nm
	Prim/sec	**6–8**	X = Y = OH; R = Me[i,l] *i*-Pr,[d,i] Ph[d,i]	(+)/(−)[b]	(+)[b]
		9–13	X = OH; Y = NH_2; R = Me,[f,l] Et,[f,i] *i*-Bu,[e,i] *sec*-Bu,[d,i] CH_2Ph[d,i]	(+)/(−)[b]	(+)[b]
		14	X = NH_2; Y = OH; R = CH_2Cl[d,g]	(−)/(+)[b,m]	(+)[b]
	Sec/sec	**15–17**	X = OH; R_1 = R_2 = Me, Et,[i] CH_2CH_2Br[i,l]	(+)/(−)[b] (+)/(−)[c]	(+)[b]
		18	X = NH_2; R_1 = Ph; R_2 = Me[d]	(−)/(+)[b,m]	(+)[b]
	Sec/tert	**19**	R_1 = R_2 = Me[d,f,h]	(+)/(−)[b]	(+)[c,m]
		20, 21	R_1 = *i*-Bu; R_2 = Me,[e,k] Et[e,k]	(+)/(−)[b]	(−)[c]

[a] Only the longer λ was measured for Pr(dpm)$_3$. [b] In CCl_4. [c] In hexane. [d] The enantiomer was in fact measured. [e] Both enantiomers were measured. [f] Gift from Professor A. Kjaer, Copenhagen. [g] Gift from Dr. R. Paul, Lederle Laboratories. [h] Gift from Professor H. Mosher, Stanford. [i] Prepared by $LiAlH_4$ reduction of the corresponding acid. [j] Prepared according to literature. [k] See ref 2. [l] Only the Ni reagent was measured. [m] See text.

tation, however, is obviated to a great extent by *addition of 0.2 M t-BuOH* to the solution to be measured, Figure 2,[10] and allows lowering of the substrate/Ni ratio to 1:1[11] (usage of *t*-BuOH has other advantages).[7]

Results obtained with a variety of compounds are summarized in Tables III and IV. For the Pr(dpm)$_3$ reagent, it appears that discriminating steric environments, *i.e.*, sec/tert cases, are necessary for it to exhibit CD signs identical with those for cyclic compounds (Table I); the reversal in signs for the prim/sec and sec/sec cases, and the unhindered cyclic and sec/tert cases (entries **4** and **19**, respectively), is presumably caused by this. In contrast, it appears that the angle and steric allowances for the formation of the Ni complex is more restricted and hence the cyclic sec/tert compound **5** gives no CD with Ni(acac)$_2$.

Finally, amines[12] are much more nucleophilic than hydroxyl groups and compounds such as (+)-1-phenyl-1-aminoethane give relatively large CD's with both Pr(dpm)$_3$ and Ni(acac)$_2$ by themselves.[13] Therefore, care must be taken in the interpretation of the results for compounds such as **14** and **18**, where the amino group is much less hindered than the hydroxyl group.

On the basis of these observations and unpublished observations we recommend that in general Pr(dpm)$_3$ be used for cyclic compounds and sterically hindered sec/tert acyclic cases, whereas Ni(acac)$_2$ be used for acyclic cases.[14]

(14) Supported by NSF GP 40087.

J. Dillon, K. Nakanishi*
Department of Chemistry, Columbia University
New York, New York 10027
Received March 6, 1974

higher substrate concentration breaks into monomeric species.[9] The lower molar ratio for amino compounds for Ni reagent is probably due to the greater nucleophilicity of the amino group.

(7) J. S. Ghotra, F. A. Hart, G. P. Moss, and M. L. Staniforth, *J. Chem. Soc., Chem. Commun.*, 113 (1973).

(8) J. P. Fackler and F. A. Cotton, *J. Amer. Chem. Soc.*, **83**, 3775 (1961).

(9) J. P. Fackler, *J. Amer. Chem. Soc.*, **84**, 24 (1962).

(10) The *t*-BuOH helps to break up the Ni(acac)$_2$ trimer. This is not effective for compounds such as entry **3**, Table III, presumably due to the rigid dihedical angle, or entry **8**, Table IV, which has a very hindered hydroxyl group. For these compounds it is necessary to use ratios of 10–20 to 1, glycol to Ni(acac)$_2$.

(11) Lowering the temperature effects results similar to *t*-BuOH addition. A 2:1 D-(−)-butane-2,3-diol:Ni(acac)$_2$ mixture at −3° has a $\Delta\epsilon_{315} = +8.5$ as compared to a value of $\Delta\epsilon_{315} = -2.0$ at room temperature (see Figure 2).

(12) Application of the Pr(dpm)$_3$ method to a limited class of amines and correlation of absolute configuration with the Cahn, Ingold, Prelog nomenclature has recently been published. See G. N. Mitchell and F. I. Caroll, *J. Amer. Chem. Soc.*, **95**, 7912 (1973).

(13) This observation has been extended to a general method for the treatment of isolated hydroxyl groups. J. Dillon and K. Nakanishi, **96**, 4055 (1974).

Use of Complexing Agents for Determining the Absolute Configurations of α-Glycols and α-Amino Alcohols. Applications to Complex Natural Products

Sir:

In our previous paper we reported the use of Ni(acac)$_2$ and Pr(dpm)$_3$ for the determination of the absolute configuration of simple α-amino alcohols and α-glycols,[1] where we used primarily aprotic solvents and the uv CD region. In the following, this technique has been extended to the use of protic solvents and to the d–d region of the CD. This and previously reported methods[1] will be used in the interpretation of more complicated systems.

When Ni(acac)$_2$ is the reagent, varying amounts of *t*-BuOH can be added to CCl_4 (Figure 1), a feature which greatly expands the applicability of this method. Evidently the bulky *t*-Bu group hinders the effective association of *t*-BuOH with Ni(acac)$_2$, so that a 1:1 mixture of *t*-BuOH and CCl_4 is still a suitable solvent. Acetone and acetonitrile, although somewhat inferior to *t*-BuOH, can also be used in this manner.

It was also found that d–d transitions could be used for diagnostic purposes as well (Figure 1 in ref 1 and Table I). Usage of this region has the advantage of usually being free of adsorptions due to the substrate compound. Note that the broad transition at *ca.* 615

(1) J. Dillon and K. Nakanishi, *J. Amer. Chem. Soc.*, **96**, 4057 (1974).

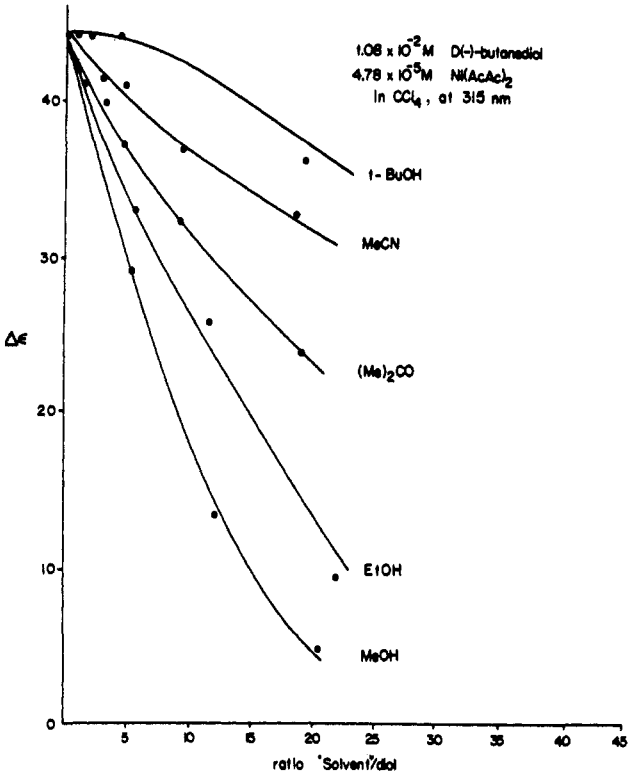
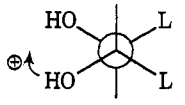


Figure 1. CD observed at 315 nm, when various competing solvents are added to a mixture of 1.08×10^{-2} *M* (2*R*,3*R*)-butane-2,3-diol and 4.78×10^{-5} *M* Ni(acac)$_2$ in CCl_4.

Table I. Comparison of the Signs of the Induced Cotton Effects in the Uv and d–d Regions, for Conformational Unit I in CCl_4



I

L = large substituents

Entry	Compound	315 nm[a]	615 nm (d,d)
1	5α-Cholestan-2α,3α-diol	(−)	(+)
2	(2*S*)-2-Phenylethane-1,2-diol	(−)	(+)
3	(2*S*)-3-Phenylpropane-1-hydroxy-2-amine	(−)	(+)
4	(2*S*,3*S*)-Butane-1,2-diol[b]	(−)	(+)
5	(2*S*)-3-Methylbutane-2,3-diol	(−)	(+)
6	(4*S*)-1-Methyl-5-ethylheptane-4,5-diol	(−)	(+)

[a] The CD consisted of a split Cotton effect centered at 300 nm. Only the longer λ maximum is presented here. See ref 1. [b] The enantiomer was in fact measured.

nm is invariably opposite to that at 315 nm. Also, unlike the uv transition (Figure 2 in ref 1), this maximum does not seem to reverse at low substrate concentrations. This technique, however, does necessitate higher concentrations (10^{-3} *M* Ni(acac)$_2$ and 10^{-2} *M* substrate) and yields smaller Δε's (*ca.* 0.01).

Results of applications to complex natural products are presented in Table II. Comments on the results of Table II (bold face numerals refer to the entries). (**1**) This is a typical case where Pr(dpm)$_3$ is useful. The substrate consists of a bulky sec/tert glycol and an isolated competing hydroxyl. Both of these structural features limit the usefulness of Ni(acac)$_2$. (**2, 3**) Compounds that contain additional enone moieties present

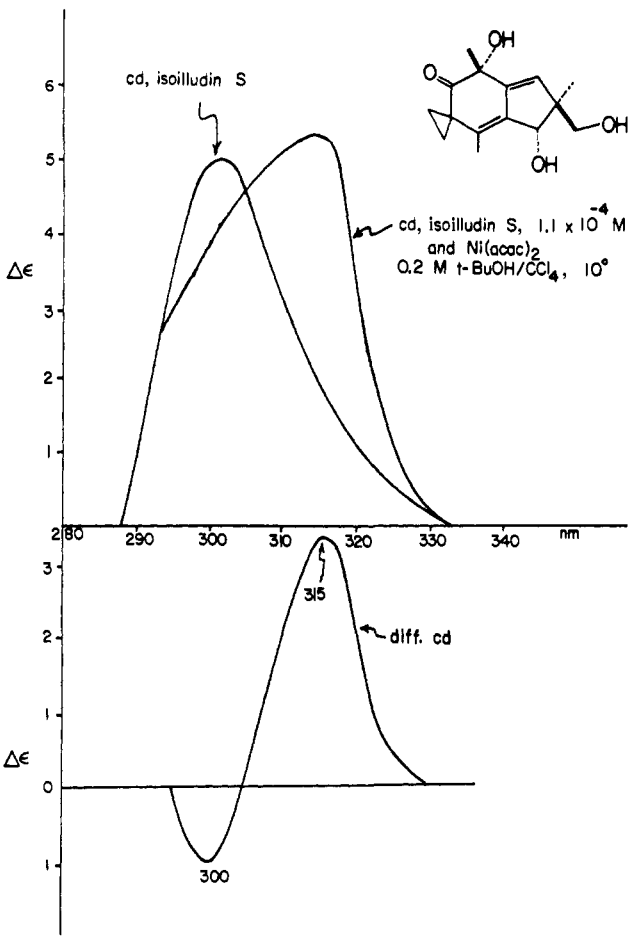


Figure 2. The CD of isoilludin S (1.1×10^{-4} *M*) and that with Ni(acac)$_2$ added as a solid (*ca.* 5×10^{-5} *M*) in a solution of 0.2 *M* *t*-BuOH–CCl_4 at 10°. Below is a differential CD curve.

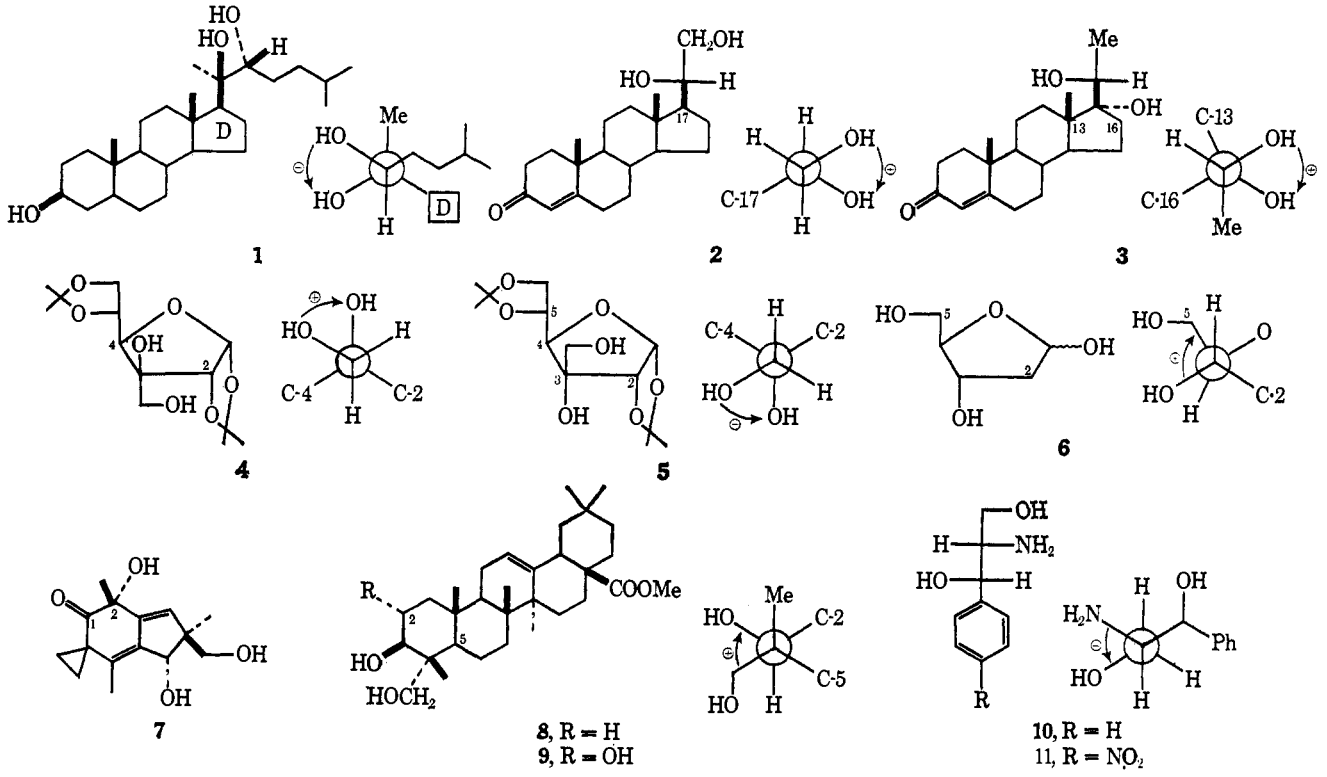
the following difficulties when using Ni(acac)$_2$: (a) since this method requires large substrate/reagent ratios, the induced CD of the Ni–glycol complex is much smaller and hidden in the enone absorption; (b) Ni(acac)$_2$ complexes with the enone itself and affects its CD. These difficulties can be circumvented as follows: (a) the addition of *t*-BuOH and/or the lowering of the solution's temperature allows the use of smaller glycol/Ni ratios; (b) the induced d–d transition can be used as in entries **2** and **9**; (c) in the 310-nm region, simple enones, *e.g.*, cholest-4-en-3-one, are affected differently than glycol-containing enones, entries **2** and **3**.[2] (**4, 5, 6**) The use of *t*-BuOH extends this method to compounds sparingly soluble in CCl_4. (**6, 7, 8, 9**) Ni(acac)$_2$ complexes with 1,3-glycols containing a primary OH and uniquely defines their chiralities. There appears to be no other general method applicable to such systems. (**7**) Neither illudin M[3,4] (Me instead of CH_2OH, and substituents at C-1 and C-2 interchanged) nor D-(−)-pantolactone ((*R*)-α-hydroxy-β,β-dimethyl-γ-butyrolactone) gave an induced CD. The resultant

(2) The differential CD curve between a glycol-containing enone and the same enone system without the glycol moiety (or possibly with a masked glycol moiety such as acetonide) shows extra peaks at 310 nm due to interaction of Ni with the glycol.

(3) Gift of Dr. M. Anchel, Bronx Botanical Gardens. See T. C. McMorris and M. Anchel, *J. Amer. Chem. Soc.*, **85**, 831 (1963).

(4) Pr(dpm)$_3$ is not useful here since it produces CD's with many mono- and bifunctional systems including α-hydroxy ketones.

Table II. Results Obtained upon the Addition of $Pr(dpm)_3$ or $Ni(acac)_2$



Entry	Reagent	Concentration (reagent) (*M*)	Molar ratio (sub/reag)	CD[a]	Method
1	$Pr(dpm)_3$	1.0×10^{-4}	[b]	$\Delta\epsilon_{303} = -8.2$	Hexane
2	$Ni(acac)_2$[d]	5.0×10^{-5}	2/1	$\Delta\epsilon_{311} = -0.6$[c]	0.2 *M* *t*-BuOH-CCl_4 at 10°
		1.0×10^{-3}	2/1	$\Delta\epsilon_{640} = +0.003$	CCl_4
3	$Ni(acac)_2$	2.5×10^{-5}	3/1	$\Delta\epsilon_{319} = -3.0$	0.2 *M* *t*-BuOH-CCl_4
4	$Ni(acac)_2$[f]	5.6×10^{-5}	200/1	$\Delta\epsilon_{316} = -1.0$	50% *t*-BuOH-CCl_4
5	$Ni(acac)_2$[f]	5.6×10^{-5}	200/1	$\Delta\epsilon_{315} = +0.9$	50% *t*-BuOH-CCl_4
6	$Ni(acac)_2$	4.9×10^{-5}	200/1	$\Delta\epsilon_{315} = -0.7$	50% *t*-BuOH-CCl_4
7	$Ni(acac)_2$[d]	5.0×10^{-5}	2/1	$\Delta\epsilon_{315} = +3.3$	0.2 *M* *t*-BuOH-CCl_4 at 10°
8	$Ni(acac)_2$[g]	5.0×10^{-5}	2/1	$\Delta\epsilon_{315} = -1.0$	0.2 *M* *t*-BuOH-CCl_4
9	$Pr(dpm)_3$	1.04×10^{-4}	6/1	$\Delta\epsilon_{313} = +1.5$	CCl_4
	$Ni(acac)_2$	1.0×10^{-3}	9/1	$\Delta\epsilon_{314} = -23.6$	CCl_4
		1.0×10^{-3}	9/1	$\Delta\epsilon_{635} = +0.02$	CCl_4
10	$Ni(acac)_2$	4.7×10^{-5}	15/1	$\Delta\epsilon_{315} = +7.1$	0.2 *M* *t*-BuOH-CCl_4
11	$Ni(acac)_2$	6.0×10^{-5}	10/1	$\Delta\epsilon_{315} = +7.0$[e]	2% *t*-BuOH-CCl_4

[a] The $\Delta\epsilon$ given is based on the concentration of the inorganic complex, unless otherwise noted. For the CD centered at *ca.* 300 only the longer wave maxima is given. [b] A saturated solution of **1** was used. [c] The $\Delta\epsilon$ is based on the concentration of the glycol. [d] The concentration of $Ni(acac)_2$ is approximate since it was added as a solid. [e] The enantiomer was in fact used. [f] Gift of Professor D. Horton, The Ohio State University. [g] Gift of Professor Y. Shimizu, University of Rhode Island.

differential CD (Figure 2), therefore, is due to complexation. (**9**, **10**, **11**) These compounds involve competition between two bidentate systems. Entry **9** consists of both an α- and β-glycol. The result obtained is that for the 1,3-glycol, presumably due to the fact that rotation of the primary OH allows these two hydroxyls to approach closer. In entries **10** and **11**[5] the prim/sec amino alcohol complexes preferentially to that of the sec/sec because of the steric hindrance of the latter. A complex involving just the 1,3-glycol was ruled out since the relatively greater nucleophilicity of the amine should dominate. Finally, in all three cases opposite results would have been obtained if the alternative system were complexing.

(5) A recent publication reports the use of the Cupra-A method in the determination of the absolute configuration of some Chloramphenicol derivatives; see L. A. Mitscher, P. W. Howison, and T. D. Sokolski, *J. Med. Chem.*, **16**, 98 (1972).

The results mentioned clearly demonstrate the general applicability of this method.[6]

(6) Supported by NSF GP 40087.

J. Dillon, K. Nakanishi*
Department of Chemistry, Columbia University
New York, New York 10027
Received March 6, 1974

Stabilization of σ-Delocalized Ions

Sir:

As has been pointed out[1] a 1-phenyl substituent enhances the rate of solvolysis of 2-*exo*-norbornyl deriva-

(1) H. C. Brown, F. J. Chloupek, and M. -H. Rei, *J. Amer. Chem. Soc.*, **86**, 1246 (1964).