8 Hz, Py H5, 1 H), 7.86 (t, J = 8 Hz, Py H4, 1H).

Acylation Kinetics. All volumetric flasks (Kimax) were washed with chromerge, rinsed with water, dilute NH_4OH, and deionized water, and oven dried. Graduated pipets and syringes were used as convenient to transfer liquids. These were washed with acetone and reagent CH_2Cl_2 and blown dry with air. They were also rinsed with liquids to be transferred immediately prior to their use in transferring those same liquids. Small amounts of $CHCl_3$ and $CDCl_3$ were transferred using disposable soda lime glass Pasteur pipets. Spectrophotometer cells (Hellma suprasil) and their Teflon-brand stoppers were washed with spectral grade CH_3CN and dried in a stream of argon. The solvents $CDCl_3$ (pure) and $CHCl_3$ (spectral grade, "stabilized with EtOH") were treated with K_2CO_3 and filtered immediately before use. Dimethylformamide was dried over BaO and distilled at aspirator pressure. Acetonitrile was spectral grade. Tetraphenylboron sodium was Aldrich "Gold Label" (99+%). Diisopropylethylamine was distilled from toluenesulfonyl chloride and stored under nitrogen. The perchlorate salt of this amine was prepared by reacting the amine with 1 equiv of $HClO_4$ in EtOH followed by precipitation of the salt with ether. Sodium perchlorate was used as the monohydrate. Ethanol was dried over 3 Å molecular sieves. Host compounds **7**–**9**[5b] and racemic **10**[6] were available from other studies.

Stock solutions, which were 0.020 M or 0.080 M in diisopropylethylamine, diisopropylethylamine perchlorate salt, or both, were made up by the syringe addition of the amine (0.348 mL, 0.258 g, 2.00 mmol) and/or the transfer of solid salt (0.45 g, 2.00 mmol) into a 100- or 25-mL volumetric flask containing some $CHCl_3$ or $CDCl_3$. The solutions were brought to their final volumes with additional $CHCl_3$ or $CDCl_3$, respectively. A solution 3.0 M in $NaClO_4$ was made in a 5-mL volumetric flask by dissolving 2.1 g of $NaClO_4 \cdot H_2O$ (0.015 mol) in 1 mL of H_2O and adding sufficient DMF to make up the final volume. A stock solution of $NaBPh_4$ (0.075 M) was made by dissolving 256 mg of the salt in 1 mL of DMF and making up the volume to 10 mL with $CDCl_3$. Dimethylformamide solutions 0.015 M in diol **9** were prepared in 2-mL volumetric flasks with the aid of sonication and mild heating, followed by cooling to room temperature, since crystalline **9** (20.5 mg, 0.030 mmol) could not be fully dissolved in 2 mL of DMF by simply mixing the components at room temperature. Host **5** was handled as a 0.0040 M stock solution in $CDCl_3$, prepared by dissolving 15.7 mg of $\mathbf{5} \cdot 2H_2O$ in 5 mL of $CDCl_3$. The racemic binaphthyl cycle **10** was transferred as a 0.0050 M stock solution (13.8 mg in 5.0 mL of $CDCl_3$). Amino acid p-nitrophenyl ester perchlorate stock solutions (0.010 M) were prepared in 5-mL volumetric flasks by dissolving each ester (0.050 mmol) in 0.5–1.0 mL of DMF and making up the volume to 5 mL with $CDCl_3$. Compounds **6** and **7** were weighed and added directly to the reaction mixture. Compound **8** was weighed in a tared flask and transferred as a solution in $CDCl_3$. Ethanol was added to appropriate reaction mixtures with a graduated pipet. All solutions were shaken thoroughly before use, and no solutions were stored more than 24 h.

Reaction mixtures (minus the substrates) were prepared by adding appropriate amounts of reagents and/or stock solutions to volumetric flasks containing some $CDCl_3$, then making the final volume (2 or 5 mL) with $CDCl_3$ ($CHCl_3$ for runs using EtOH as the nucleophile), and shaking. Runs were initiated by the syringe addition of an aliquot (20 or 50 μL) of ammonium ester stock solution to each volumetric flask so that the initial concentration of ester was 1.0×10^{-4} M. The solutions were shaken thoroughly and partially transferred (using Pasteur pipets) into UV cells (1.00-cm light path, 1 or 2.5 mL total volume). These cells were equilibrated and maintained at 24 °C in cell holders which were immersed in a constant-temperature water bath. The cells were fitted with Teflon-brand stoppers.

Absorbances A_t were measured periodically at 350 nm with a Beckman DU quartz spectrometer equipped with a Guilford digital readout, thereby monitoring the formation of p-nitrophenol. Endpoints (A_∞) were noted at 5–8 half-lives and were stable within experimental error. Initial absorbance readings were in the range 0.050–0.200 units, whereas A_∞ was typically 0.300–0.600 units. Table II and its footnotes record the conditions of the runs and the k_1 (and k_2 values where appropriate) values obtained.

Determination of Association Constants and Free Energies of Complexation. The standard method for determining K_a and $-\Delta G°$ values previously reported[6] was applied to hosts **3** and **5** binding Li^+, Na^+, K^+, Rb^+, Cs^+, NH_4^+, $CH_3NH_3^+$, and t-$BuNH_3^+$ picrates. Because of the strongly binding character of these compounds, 0.001 M solutions of host and guest in $CDCl_3$ and D_2O were used, respectively. The limited supply of host **4** allowed only values for Rb^+ and $CH_3NH_3^+$ to be determined. Two values were obtained and averaged for each K_a, once the range was established by preliminary measurements. Deviations between aqueous- and organic-phase determinations of $-\Delta G_a$ ranged from 0.0 to 0.5 kcal/mol, the larger values always being observed at the upper end of the scale in the organic layer or lower end of the scale in the water layer, where errors are greatly magnified. Equilibration of the guest between the two layers was essentially instantaneous on the human time scale. Table I records the K_a and $-\Delta G°$ values for **3**–**5**, as well as values for **8**, **9**, **11**, and **23** obtained earlier, which are listed for comparison purposes.

Registry No. 5, 91084-72-9; **6**, 91084-73-0; **7**, 91084-74-1; **8**, 91084-75-2; **9**, 91084-76-3; **10**, 91084-77-4; **11**, 91084-78-5; **14**, 91084-79-6; **16**, 91084-81-0; **17**, 91084-80-9; **18**, 91084-82-1; **23**, 67191-44-0; **24**, 91084-83-2; **25**, 91084-84-3; **26**, 91084-85-4; **28**, 91084-86-5; **29**, 91084-87-6; **30**, 91084-88-7; **31**, 91084-89-8; **32**, 91084-90-1; **33**, 91110-52-0; 2-bromo-4-methylphenol, 6627-55-0.

Communications to the Editor

Application of Circular Dichroic Spectroscopy for Determination of Chiral Organization of H-Bonded Alcohols

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Received March 7, 1984

Chiral molecules possessing two or more π-electron chromophores located in chiral positions in respect to each other show intramolecular CD exciton coupling effects.[1] We now report on *intermolecular* CD exciton coupling effects exhibited in nonprotic solvents, at low temperatures by hydroxylated chiral molecules possessing only one π-electron chromophore, pointing to their chiral organization in solution.

Circular dichroic spectra of transoid dienes **1** and **2** derived from *trans*-vitamin D_3 (**3**) and vitamin D_3 (**4**), which possess planar diene chromophores, exhibit at room temperature in the region 220–260 nm low-intensity structured Cotton effects. The peaks appear at the same wavelengths as the UV absorption maxima,[2] which doesn't change by lowering the temperature. However, in isopentane/methylcyclohexane (IP/MCH) solution at ca. −100 °C the CD of these dienes changes drastically giving rise to split Cotton effects: negative at 264 and 253 nm, and positive at 250, 242, and 232 nm, whose amplitude increases with lowering temperature and with increased concentration.[3] The shape of the components of these bisignate effects (Figure 1) equidistant from the compounds UV band center, and each possessing vibrational structure, indicates that they originate from exciton coupling.[1] These effects disappear on addition of isopropyl alcohol and do not appear in the acetylated and benzoylated derivatives, showing

(1) "Circular Dichroic Spectroscopy—Excitation Coupling in Organic Stereochemistry"; Harada, N., Nakanishi, K., Eds.; University Science Books: New York, 1983; pp 1–46.

(2) Duraisamy, M., Walborsky, H. M. *J. Am. Chem. Soc.* **1983**, *105*, 3264.

(3) Only Cotton effects due to the long-wavelength $\pi-\pi^*$ transition exhibit a clear bisignate effect.

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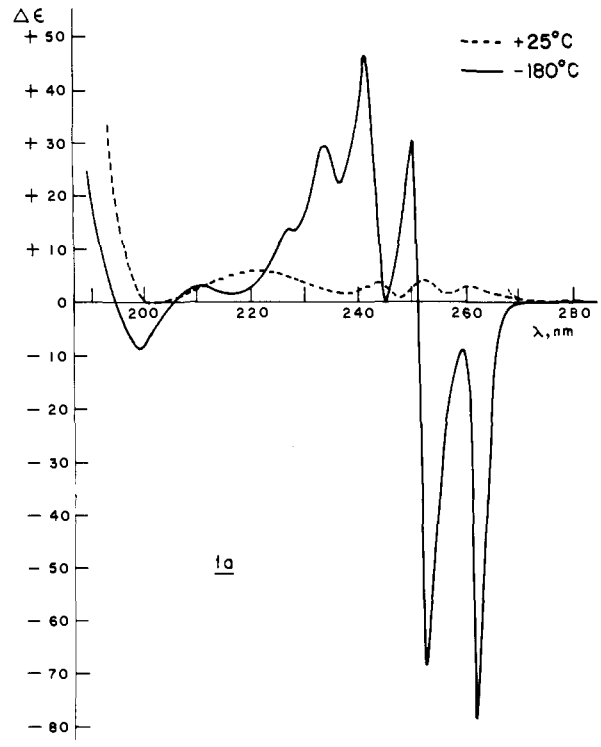
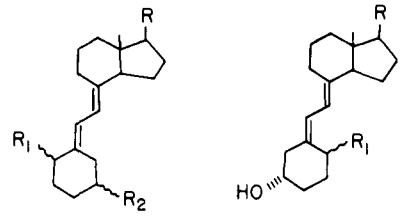


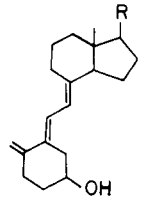
Figure 1. Circular dichroic spectra of diene **1a** at +25 and −180 °C.

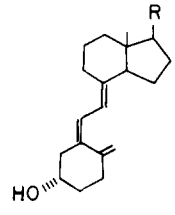
that they derive from intermolecular coupling of the transitions of H-bonded associated species.[4] The amplitudes and the signs of these Cotton effects varied with the structures and substitution patterns: dienes **1a–d** derived from *trans*-vitamin D_3 (**3**) showed



	R_1	R_2
1a:	α CH_3	β OH
b:	β CH_3	α OH
c:	α CH_3	α OH
d:	H	β OH

2a; R_1 = α CH_3
b; R_1 = β CH_3





R = C_8H_{17}

(4) CD exciton coupling effects in protic solvents indicative of non-H-bonded association due to π-electron interactions were reported for cis isomers of astaxanthin diacetate (Noack, K., Thomson, A. J. *Helv. Chim. Acta* **1981**, *64*, 2383) and a number of anthocyanins (Hoshino, T.; Matsumoto, U.; Goto, T. *Tetrahedron Lett.* **1980**, *21*, 1751; *Phytochemistry* **1981**, *20*, 1971. Hoshino, T.; Matsumoto, U.; Harada, N.; Goto, T. *Tetrahedron Lett.* **1981**, *22*, 3621. Hoshino, T.; Matsumoto, U.; Goto, T.; Harada, N. *Ibid.* **1982**, *23*, 433.

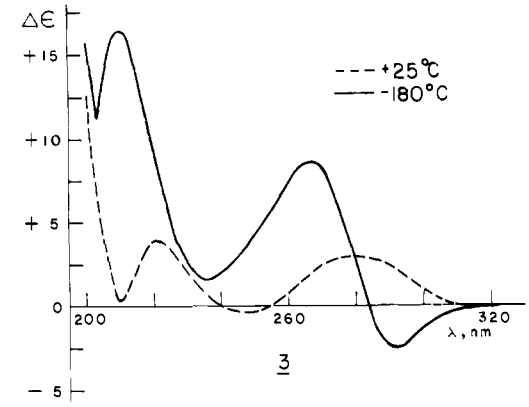
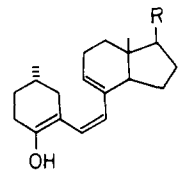
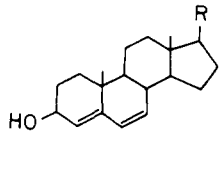


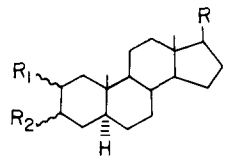
Figure 2. Circular dichroic spectra of *trans*-vitamin D_3 (**3**) at +25 and −180 °C.

negative first Cotton effects ($\Delta\epsilon_{252}$ = −80, −80, −47, and −8, respectively; −175 °C, *c* (0.3–0.6) × 10^{-3} M), while dienes **2a,b** derived from vitamin D_3 (**4**) showed positive effects ($\Delta\epsilon_{252}$ = +20 and +7, respectively; −175 °C, *c* 0.5 × 10^{-3} M).

The parent trienes, *trans*-vitamin D_3 (**3**) and vitamin D_3 (**4**), as well as previtamin D_3 (**5**), also show low-temperature exciton







	R_1	R_2
7a:	α $OCOC_6H_4(OCH_3)p$	α OH
b:	α $OCOCH{=}CHC_6H_5$	α OH
c:	β $OCOC_6H_4(OCH_3)p$	α OH
d:	α OH	α $OCOC_6H_4(OCH_3)p$

R = C_8H_{17}

coupling effects. Thus, comparison of CD of **3** in IP/MCH solution at room temperature and at −175 °C (Figure 2) reveals a negative exciton effect of the 272-nm π–π^* transition ($\Delta\epsilon_{291}$ = −3; *c* 0.6 × 10^{-3} M) and two strong positive peaks which may point to a superposition of two positive exciton effects of the transitions at λ_{max} 250 and 220 nm. Both vitamin D_3 (**4**) and previtamin D_3 (**5**) display, for their highest wavelength π–π^* transition (at λ_{max} 264 and 259 nm, respectively) in IP/MCH solution, positive first Cotton effects[5] ($\Delta\epsilon_{279}$ = +10 and $\Delta\epsilon_{264}$ = +5, respectively; −175 °C, *c* 1.0 × 10^{-3} M).

The above data indicate that the sign of the exciton coupling effect is independent of conformation and configuration of OH group, depending, however, on the relative position of OH group and the diene or triene chromophore.

The following deduction can be reached on the relation between the substitution pattern of monohydroxylated secosteroids and the

(5) The two compounds also display low-temperature π-π^* exciton coupling effects of their other transitions, at lower wavelengths.

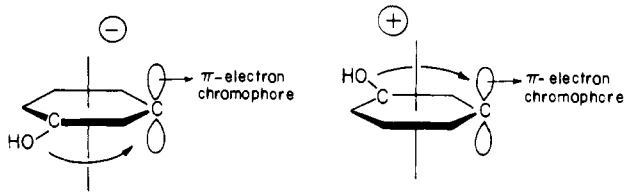


Figure 3. Relation between the substitution pattern of monohydroxylated secosteroids and steroids (β-side pointing upward) and the sign of the intermolecular exciton effect.

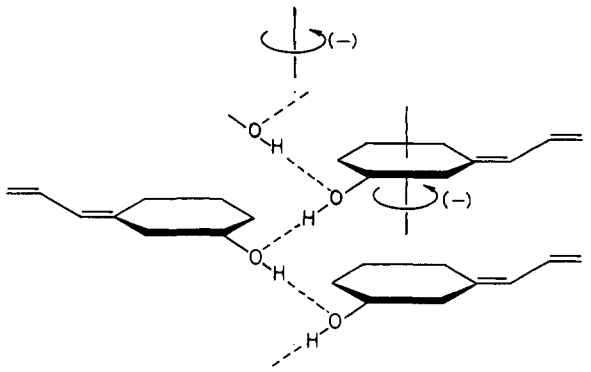


Figure 4. Schematic representation of the assemblies of hydrogen-bonded dienes **1** possessing negative helicity (β-side of the secosteroid pointing upward).

sign of the intermolecular exciton effect: when the shortest direction going from C bearing OH to C bearing the chromophore, relative to an axis perpendicular to the steroidal plane with its β-side pointing upward, is clockwise or counterclockwise, the sign of the exciton effect will be positive or negative, respectively (Figures 3 and 4).

Low-temperature exciton coupling effect was also observed in the steroidal dienol **6**, in IP/MCH solution ($\Delta\epsilon_{232} = -21$; -175 °C, c 0.7×10^{-3} M), whose negative sign is in accordance with the above deduction.

It is reasonable to assume a stepwise concentration-dependent self-association of OH groups, resulting in dimers and oligomers. However, the formation of the energetically more favored helical organization of the oligomers which predominate at low temperatures is determined not only by H bonding but also by intermolecular interaction between molecular surfaces. Chiral patterns of packing occur in crystals of steroids possessing an OH function.[6] This may be exemplified by vitamin D_3 crystals, which are composed of molecules packed in infinite coils, in which OH are H bonded and the trans-diene functions form a positive helix.[7] Positive helical arrangement of the chromophores also exists in vitamin D_3 aggregates, as evidenced by the positive intermolecular exciton effect observed at low temperatures and in hydrocarbon solvents.

Formation of H-bonded oligomers could also be detected in hydrocarbon solution of monoesters of cholestane-1,2-diols **7**, in which OH and the ester function are in close proximity. Thus, cholestane-2α,3α-diol 3-monoanisate (**7a**) exhibits, at low temperatures, a positive exciton effect whose intensity increases with higher concentration and lowered temperature ($\Delta\epsilon_{262} = +28$; -125 °C, c 1.5×10^{-3} M). The positive sign of the effect in **7a** was not changed either by altering the chromophore (**7b**: $\Delta\epsilon_{278} = +15$; -125 °C, c 7.0×10^{-3} M) or its configuration and conformation (**7c**: $\Delta\epsilon_{262} = +14$; -125 °C, c 1.2×10^{-3} M) but was reversed on interchanging both substituents (**7d**: $\Delta\epsilon_{262} = +16$; -150 °C, c 1.0×10^{-3} M). Also in these cases, the relation between the signs of exciton effects and their substitution pattern is in accord with the deduction proposed above for the dienols and trienols.

We have shown that hydroxylated steroids and secosteroids form, in hydrocarbon solvents at low temperature, H-bonded oligomers with a favored helical organization whose chirality can be determined by circular dichroic spectroscopy.

(6) (a) Duax, W. L.; Weeks, C. M.; Rohrer, D. C. *Top. Stereochem.* **1976**, *9*, 289–294. (b) Motherwell, W. D. S.; Riva di Sanseverino, L.; Kennard, O. Abstracts, First European Crystallographic Conference, Bordeaux, France, 1973, Group B6.

(7) Trinh-Toan; DeLuca, H. F.; Dahl, L. F. *J. Org. Chem.* **1976**, *41*, 3476.

Substituent Effects on the Claisen Rearrangement. The Accelerating Effect of a 6-Donor Substituent

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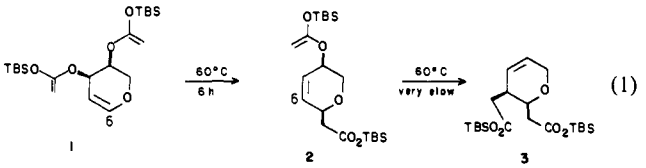
Received March 19, 1984

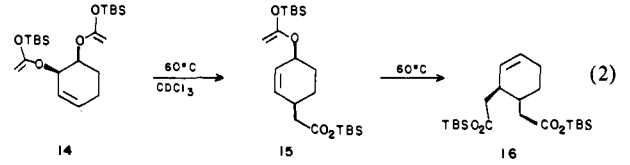
The Claisen rearrangement has emerged as one of the most important carbon–carbon bond-forming reactions in organic synthesis by virtue of its simplicity and selectivity.[2] Despite this, relatively little is known about the effect of various substituents on the rate of the reaction.[3] During the development of a synthetic approach toward pseudomonic acid antibiotics, we recently observed a dramatic example of the synthetic utility of rate differences in Claisen rearrangements (eq 1).[4] We now present



(1)

experimental evidence indicating that this rate difference is the result of an unrecognized accelerating substituent effect. Furthermore, this effect contradicts theoretical predictions based upon Hückel π-electron energies, and we will offer an alternate rational based on the "vinylogously anomeric" nature of the system.

For the factors responsible for the success of the mono-Claisen rearrangement in eq 1 to be elucidated, a series of rate studies was undertaken.[5] As expected, all substrates showed first-order rate behavior. These are collected in Chart I. Also of interest is the cyclohexene analogue (**14**) to the double rearrangement (eq 2). Here accurate rates could not be obtained since both rearrangements proceed at roughly similar rates. For example, after



(2)

16 h at 60 °C, the reaction consisted of **14** (14%), **15** (46%), and **16** (40%). The results indicate that (1) the origin of selectivity

(1) Recipient of a Camille amd Henry Dreyfus Award for New Faculty in Chemistry 1981–1986.

(2) Reviews: (a) Bennett, G. B. *Synthesis* **1977**, 589. (b) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227. (c) Rhoads, S. J.; Raulins, N. R.; *Org. React. (N.Y.)* **1975**, *22*, 1. (d) Rhoads, S. J. In "Molecular Rearrangements"; deMayo, P., Ed.; Wiley-Interscience, New York, 1963; Part I, 655. (e) Tarbell, D. S. *Org. React. (N.Y.)*, *2*, 1. (f) Tarbell, D. S. *Chem. Rev.* **1940**, *27*, 495.

(3) Electron-donating substituents in the 2-position are well-known to accelerate the Claisen rearrangement. (a) Felix, D.; Gschwend-Steen, K.; Wick, A. E.; Eschenmoser, A. *Helv. Chim. Acta* **1969**, *52*, 1030. (b) Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T.; Faulkner, D. J.; Petersen, J. R. *J. Am. Chem. Soc.* **1970**, *92*, 741. (c) Denmark, S. E.; Harmata, M. A. *Ibid.* **1982**, *104*, 4972. See also ref 5. For quantitative studies on the effect of a cyano group at each position, see: Carpenter, B. K.; Burrows, C. J. *J. Am. Chem. Soc.* **1981**, *103*, 6983.

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