maximum) and 8.9×10^4 M^{-1} cm^{-1} for cytochrome *c*(III), or at 417 nm where the $\Delta\epsilon$ is slightly bigger.[19] First-order rate constants, k_{obsd}, were obtained from the slopes of plots of absorbance changes, ln $|A_\infty - A_t|$, against time. A linear dependence of k_{obsd} on the concentration of inorganic complex was observed in each case. Second-order constants defined by the rate law

$$\text{rate} = k[\text{cytochrome } c][\text{complex}]$$

are listed in Table I. The values reported for native cytochrome *c* are in reasonable agreement with those reported in the literature.[18,20]

It is concluded that modifications of lysine-13 and lysine-72 but not of lysine-87 and lysine-60 (Figure 1[21]) have an influence on all the reactions investigated. With the positively charged oxidant Co(phen)$_3^{3+}$ there is an approximately twofold increase in the rate constant when the modification is at positions 13 and 72, consistent with the replacement of a positive by a negative charge. That there is an increase shows that the modified residue probably does not sterically hinder the reaction. All the negatively charged redox partners, whether oxidants or reductants, show an approximately twofold decrease in rate constant with the same modified cytochrome *c*. The rate constants reported for CDNP-Lys-60 and -87 cyctochrome *c* are only slightly different from those for native cytochrome *c*, the small effect most likely being attributable to the change in net charge. These observations indicate that a neutral complex could be expected to show little or no response to modification at positions 13 and 72. The present results unequivocally show that the small inorganic complexes investigated transfer electrons to or at the exposed heme edge.

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Liquid Crystal Characterization of Compounds Chiral by Deuterium Substitution

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Acyclic compounds of the type RCHDR' which are chiral only due to deuterium substitution are very important in studies on chemical and biochemical mechanisms.[1] A major problem faced with the use of these substances is the matter of recognition and characterization of the chirality. Apart from the few cases where optical rotatory dispersion can be observed, the classical optical methods are inapplicable for the characterization of deuterium-labeled chiral compounds because of their low specific optical rotation.

We now present evidence indicating that the determination of the "handedness" of the cholesteric mesophase induced in a nematic liquid by the presence of an asymmetrically deuterated

Table I. Twisting Power (β) of Chiral Deuterium Derivatives Dissolved in a 1:1 (m/m) MBBA–EBBA Mixture

compound	β	compound	β
1a^{a,c}	+0.093 ± 0.006	1b^{a,c}	−0.096 ± 0.007
2a^d	+0.079 ± 0.006	2b^d	−0.075 ± 0.005
3a^{b,e}	−0.113 ± 0.005	3b^{b,e}	+0.109 ± 0.006

^{a} Assumed as enantiomerically pure.[8] ^{b} Assumed to contain ca. 95% of each enantiomer on the basis of the optical purity of the resolved starting hydroxy amines 5 and 6. ^{c} 93% d_1. ^{d} 96% d_1. ^{e} 92% d_1.

compound of the type RCHDR' as solute and of the "twisting power", β, can be used for the characterization of acyclic, RCHDR', chiral compounds.

When a chiral substance is dissolved in a nematic liquid crystal, a cholesteric mesophase is obtained.[2] The cholesteric structure is characterized by its handedness (*P* or *M* helix) and pitch. Equal amounts of enantiomeric solutes of equal optical purity induce helical structures with identical pitch and opposite handedness.[3] Different substances show a different ability to twist the nematic phases. The twisting power of a chiral dopant can be defined as[4]

$$\beta = (pcr)^{-1}$$

where *p* is the pitch (μm), *c* is the concentration (mole of solute/mole of solution), and *r* is the enantiomeric purity of the dopant. The parameter β together with the sign + or − for the *P* helix or *M* helix characterizes the chiral solute in a way similar to the specific optical rotation [α]. However, the physical origin of the two quantities is entirely different.[5]

The origin of the optical rotation depends in fact on the interactions of light with molecules, while the twisting power originates from the interactions between molecules of solute and solvent.

A very small chiral "perturbation" is required in order to induce into a nematic mesophase a cholesteric molecular arrangement which is characterized by its very high macrostructural chirality.

Hence a chirality, not detectable by polarimetric methods owing either to the small quantity of the investigated optically active compound available or to its very low rotatory power, can be, in principle, "amplified" by the phenomenon of the induction of cholesteric mesophases.

Indeed, when the enantiomeric pairs of asymmetrically deuterated compounds **1a–3a** and **1b–3b** were dissolved in nematic solvents, the formation of well-characterized cholesteric mesophases (Table I) was observed.[6] Compound **1a** was prepared by

1a, R = C$_6$H$_5$; R^1 = OCOC$_6$H$_4$NO$_2$-*p*; H$_R$ = H; H$_S$ = ^{2}H
b, R = C$_6$H$_5$; R^1 = OCOC$_6$H$_4$NO$_2$-*p*; H$_R$ = ^{2}H; H$_S$ = H
2a, R = (CH$_2$)$_2$C$_6$H$_5$; R^1 = OH; H$_R$ = H; H$_S$ = ^{2}H
b, R = (CH$_2$)$_2$C$_6$H$_5$; R^1 = OH; H$_R$ = ^{2}H; H$_S$ = H
3a, R = C$_6$H$_5$; R^1 = CH$_2$N(Me)COC$_6$H$_5$; H$_R$ = H; H$_S$ = ^{2}H
b, R = C$_6$H$_5$; R^1 = CH$_2$N(Me)COC$_6$H$_5$; H$_R$ = ^{2}H; H$_S$ = H

esterification (4-NO$_2$C$_6$H$_4$COCl/pyridine/CH$_2$Cl$_2$) of (1*S*)-[1-^{2}H]benzyl alcohol,[8] whereas the 1*R* isomer (**1b**) was prepared as reported for the benzoate[8] by using 4-NO$_2$C$_6$H$_4$CO$_2$H instead of C$_6$H$_5$CO$_2$H. (1*S*)-[1-^{2}H]3-Phenylpropan-1-ol (**2a**) and its 1*R* isomer (**2b**) which were used in the synthesis of (4*S*)- and (4*R*)-[4-^{2}H]D,L-homoserine, were enantiomerically pure, within

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the limits of the ^{1}H NMR spectroscopic method used.^{9} The deuterated amides **3a** and **3b** have been prepared in a study on the stereochemistry of the biological hydroxylation β to the nitrogen atom which is expected to occur in *N*-methyl-2-phenylethylamine in the biosynthesis of the alkaloid halostahine **4** in *Halostachys caspica*,^{10} from β-*S* [β-^{2}H] halostahine **6** and from
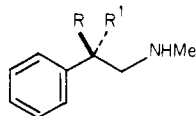
4, R = OH; R^1 = H
5, R = OH; R^1 = ^{2}H
6, R = ^{2}H; R^1 = OH

the β-*R* isomer **5** through palladium-catalyzed ring opening of the oxazolidines **7** and **8**, respectively, a reaction known to proceed with inversion of configuration at the benzylic carbon.^{11}
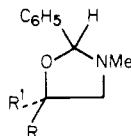
7, R = C$_6$H$_5$; R^1 = ^{2}H
8, R = ^{2}H; R^1 = C$_6$H$_5$

The values of β are about 2 orders of magnitude smaller than those observed for chiral secondary alcohols.^{5} Values of the pitches were determined by means of the Grandjean–Cano method, which is based on the observation of the discontinuity lines appearing when a cholesteric mesophase is inserted in a cell of variable thickness.^{12,13} A drop of cholesteric solution was put between the planoconvex lens and a glass plate,^{14} both previously rubbed with tissue paper; the rubbing directions of the lens and plate were kept parallel to each other.^{16} The preparation was observed with the polarizing microscope and showed the Grandjean–Cano disclinations as concentric circles. The separation of the disclination circles gives the pitch (*P*) through the relation^{16}

$$r^2/2R = (n - \tfrac{1}{2})p/2 \qquad n = 1, 2, 3$$

where *R* is the radius of the lens and *r* the radius of the disclination circles. The handedness of the helices was deduced by placing a drop of the cholesteric solution between a glass plate rubber as before and a lens with concentric surface alignment (circular rubbing). With these boundary conditions, a double-spiral disclination appears; a right-handed helix gives a left-handed double spiral and vice versa.^{17} The measurements were carried out between 16 and 19 °C.^{18}

The concentrations were varied between 6 and 10 (mole of solute/mole of solution). The β values were constant within the experimental errors. No coexistence of cholesteric and isotropic phases were observed below 20 °C. The method requires only two drops of solution and a very small amount of chiral derivative.

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Biosynthetic Intermediates to the Macrocyclic Trichothecenes

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The trichothecene group of terpenoid antibiotics may be classed into two distinct types: simple and macrocyclic.^{1} We recently reported the isolation of trichodermadiene (**1**),^{2} a compound whose structure is intermediate between these two classes in that the C4 ester side chain is analogous in structure to a portion of the macrocyclic ring [as in roridin E (**2**)],^{3} but **1** is not macrocyclic. We now wish to report the isolation of a series of new trichothecenes related to both the simple and macrocyclic trichothecenes. Also, we present evidence that these new trichothecenes lie along the biosynthetic pathway to the macrocyclic trichothecenes.^{4}

During the course of the workup of a large scale fermentation of *Myrothecium verrucaria*,^{6} we isolated three sets of epimeric pairs of new trichothecenes, one set of which upon hydrolysis gave trichodermol (**3**) while the other two sets upon hydrolysis gave verrucarol (**4**). By a combination of ^{1}H and ^{13}C NMR spectroscopy and mass spectroscopy, it was evident that the former pair of isomers was related to trichodermadiene (**1**) in that the pendant C-6′, C-7′ epoxy group was hydrated yielding trichodermadienediols A (**5**) and B (**6**).^{7} The absolute stereochemistry at C-6′ and C-7′ in **5** and **6** was established by transesterification (methanol) to give methyl esters **11** and **12**, respectively, whose absolute configurations have been established by total synthesis.^{8}

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(7) **5**: mp 184–185 °C (EtOAc–petroleum ether); [α]^{28}D +26.3° (*c* 0.39, CHCl$_3$); UV$_{max}$ (MeOH) 260 nm (log ε 4.53); mass spectrum (chemical ionization, methane gas reagent) *m/e* 405.2263 (M$^+$ + H, calcd 405.2277); ^{1}H NMR (CDCl$_3$) δ 0.76 (3 H, s, 14-H), 0.98 (3 H, s, 15-H), 1.13 (3 H, d, *J* = 6 Hz, 8′-H), 1.74 (3 H, s, 16-H), 2.60 (1 H, dd, *J* = 8 and 15 Hz, 3α-H), 3.03 (2 H, AB, *J* = 4 Hz, 13′-H), 3.66 (1 H, d, *J* = 5 Hz, 11-H), 3.87 (1 H, d, *J* = 5 Hz, 2-H), 4.06 (1 H, m, 6′-H), 5.44 (1 H, d, *J* = 5 Hz, 10-H), 5.73 (1 H, d, *J* = 11 Hz, 2′-H), 6.09 (1 H, dd, *J* = 6 and 16 Hz, 5′-H), 6.64 (1 H, dd, *J* = 11 1 and 11 Hz, 3′-H), and 7.65 (1 H, dd, *J* = 11 and 16 Hz, 4′-H). **6**: an oil; [α]^{28}D –15.8° (*c* 0.80, CHCl$_3$); UV$_{max}$ (MeOH) 260 nm (log ε 4.55); mass spectrum (chemical ionization, methane gas) *m/e* 405.2252 (M$^+$ + H calcd 405.2277); ^{1}H NMR (CDCl$_3$) δ 0.74 (3 H, s, 14-H), 0.98 (3 H, s, 15-H), 1.16 (3 H, d, *J* = 6 Hz, 8′-H), 1.73 (3 H, s, 16-H), 2.62 (1 H, dd, *J* = 8 and 15 Hz, 3α-H), 3.04 (2 H, AB, *J* = 4 Hz, 13-H), 3.66 (1 H, d, *J* = H$_s$, 11-H), 3.88 (1 H, d, *J* = 5 Hz, 2-H), 4.30 (1 H, m, 6′-H), 5.44 (1 H, d, *J* = 5 Hz, 10-H), 5.72 (1 H, d, *J* = 11 Hz, 2′-H), 6.16 (1 H, dd, *J* = 6 and 16 Hz, 5′-H), 6.66 (1 H, dd, *J* = 11 and 11 Hz, 3′-H), and 7.64 (1 H, dd, *J* = 11 and 16 Hz, 4′-H).

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