Synthesis and Chiroptical Properties of (1*R*,1′*R*)-[16,16,16,16′,16′,16′-$^2H_6$]-β,β-Carotene

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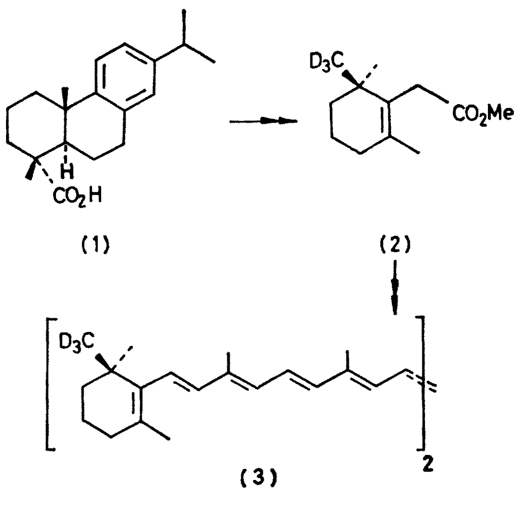
Summary The title compound (**3**) has been prepared from dehydroabietic acid (**1**) in 21 steps and its low temperature c.d. spectra have been found to correspond to those for zeaxanthin (**4**) but with reduced intensities; possible interpretations of the observed c.d. spectrum are discussed.

FOR reasons discussed earlier,[1] we synthetised β,β-carotene and β,ε-carotene, each stereoselectively deuteriated at one CH_3-C(1) and therefore optically active. The starting material, dehydroabietic acid (**1**) was first degraded in 9 steps to the three isomeric homo-α-, β-, and γ-cyclogeranic acids. Methyl (*R*)-[*methyl*-$^2H_3$]homo-β-cyclogeranate (**2**) was converted in 11 steps into the stereoselectively deuteriated optically active (1*R*,1′*R*)-[16,16,16,-16′,16′,16′-$^2H_6$]-β,β-carotene (**3**). The all-(*E*)-compound (**3**) has m.p. 176—177 °C, $\lambda_{max.}$ (hexane) 450 nm (ϵ = 136,000); ^1H n.m.r. and mass spectral data are in agreement with structure (**3**).



(1) (2)

(3)

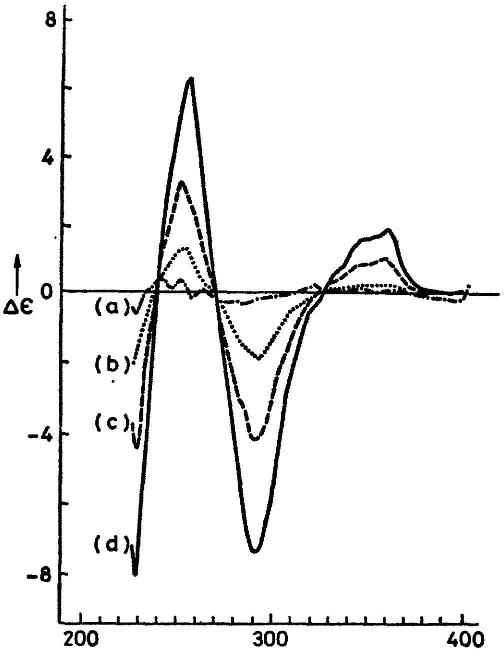
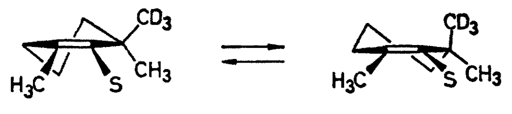


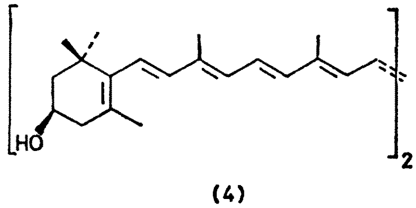
FIGURE. C.d. spectra of all-(*E*)-(1*R*,1′*R*)-$[16,16,16,16',16',16'\text{-}{}^{2}H_6]$-β,β-carotene (**3**) in ether–isopentane–ethanol (5:5:2); (a) +25, (b) −100, (c) −150, (d) −180 °C.

Of special interest is the fact that the optical activity of (**3**), which is solely due to isotopically different substituents not directly attached to the asymmetric carbon, gives rise to a significant c.d. spectrum (Figure). The c.d. spectra of (**3**) at room temperature show only very weak positive and negative maxima. In contrast, at low temperature in EPA [ether–isopentane–ethanol (5:5:2)] they show a quite significant strong spectrum (Figure). The shape of the c.d. curve corresponds exactly to that of all-(*E*)-(3*R*,3′*R*)-zeaxanthin (**4**)[2] (including the position of each positive and negative maximum and each crossing of the zero line). At −180 °C the intensities of the spectrum reach about 10% of the intensities in the corresponding spectrum of zeaxanthin (**4**).

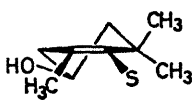
The identically shaped c.d. spectra of (**3**) and (**4**) suggest that we are observing a small contribution from the same intrinsically chiral chromophore in the case of (**3**) as postulated for zeaxanthin (**4**),[2,3] produced by a small stabilisation of the conformer (**3a**) (with a pseudoequatorial CD_3-group), which corresponds to the main conformer (**4a**) of zeaxanthin,[4] over the conformer (**3b**) (with pseudoaxial CD_3-group).



(3a) (3b)



(**4**)



(**4a**)

The reason for the stabilisation of the conformer (**3a**) might be the somewhat smaller steric requirement of the CD_3- than the CH_3-group, well known in a series of kinetic isotope effects of CD_3 *vs.* CH_3.[5] As shown earlier with other cyclohexene derivatives,[6] the more bulky group prefers the pseudoaxial position in the cyclohexene half-chair.

On the other hand, we cannot exclude that the substitution of CH_3 by CD_3 influences not only the conformational equilibrium between the two conformers (**3a**) and (**3b**) (enantiomeric in the absence of isotopes), but also the relative population of the possible conformers around the formal single bond C(6)–C(7)[7] (diastereomeric in the absence of the isotopes). Furthermore, the observed c.d. effect might be due only to an isotopic perturbation of the electron distribution irrespective of conformation, but from the influence of the chiral centres 1 and 1′ on a non-chiral chromophore, we would expect a c.d. spectrum fundamentally different from that observed.

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