ABSOLUTE CONFIGURATION OF SPIROBIPHTHALIDE

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Assignments of absolute configuration to chiral C_2 spirans have been established by chemical and crystallographic methods[1] and theoretical calculations of CD spectra.[2] Chiroptical properties of spirans with fused aromatic rings are of interest to us and we have already reported the properties and the assignment of the absolute configuration of a series of 3,3,3',3'-tetramethyl-1,1'-spirobiindans.[2,3]

3,3'-Spirobiphthalide-6,6'-dicarboxylic acid (1) has already been resolved into two enantiomers by W. H. Mills and C. R. Nodder.[4] This heterocyclic C_2 spiran is conformationally rigid and it is interesting to predict the absolute configuration and to see the spiro conjugation[5] in comparison with the other spirans in which spiro conjugation has been demonstrated.[6]

(+)-1[λ_{nm} ($\Delta\epsilon$): 290 (+1.42), 281 (+1.42), 270 (+2.04), 242 (+24.7), 218 (-121.), 207 (+75.). λ_{nm} (ϵ): 290 (1,730), 282 (1,750), 275 (1,450), 267 (1,290), 232[5] (23,700), 215 (68,200), in CH_3CN] was reduced with diborane to give 6,6'-dihydroxymethyl-3,3'-spirobiphthalide, (-)-(3)*[λ_{nm} ($\Delta\epsilon$): 287 (+3.77), 282 (+3.89), 236 (+26.9), 215 (-150.). λ_{nm} (ϵ): 289 (2,540), 282 (2,490), 227 (16,800), 211 (58,600), 207 (58,600), in CH_3CN] . The CD spectra of (+)-1 and (-)-3 are quite similar except for enhancement of the rotational strength in the longest wavelength region and disappearance of the band in (-)-3 corresponding to that at 207 nm in (+)-1.

In the present case, direct application of the dipole-dipole coupling mechanism[8] in prediction of the absolute configuration is limited both by uncertainty in assigning transition to the A or B category and by spiro conjugation.

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* The diester (+)-(2) was reduced with sodium borohydride in the presence of boron trifluoride etherate,[7] but the product was 3-(1-hydroxymethyl-3-carbomethoxy phenyl)-6-carbomethoxy phthalide instead of the expected spirobi-2-oxaindan.

It is known that a hydroxymethyl group does not have a large influence on the electronic transition of the aromatic chromophore[3] and the same basic pattern of the CD spectra of (+)-1 and (-)-3 shows that the substituents at C-6 and C-6' affect the CD spectrum of the spirobiphthalide to a lesser extent. Therefore, it is not unreasonable to calculate the CD spectrum on unsubstituted phthalide and to predict the absolute configuration comparing the theoretical and the experimental CD spectra.

Our calculation of the optical activity followed the procedure of the composite method,[9] previously described for the spirobiindans,[2] with a few of modifications. The geometry assumed in the calculation
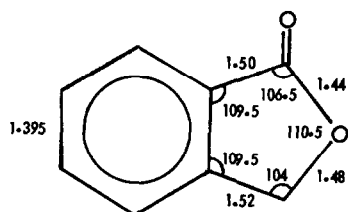

Fig. 1

consists of two planar phthalide residues as illustrated in FIG. 1. The locally excited transition energies were calculated by the normal π-SCF-MO-CI procedure. The spiro resonance integrals, β_{spiro}, were obtained by the equation, $\beta_{spiro} = 0.875$ $(H_\alpha + H_\beta)/2 \cdot S_{\alpha\beta}$, where H_α and H_β were computed from the valence state ionization energies and electron affinities;

$H_\alpha = I_\alpha - A_\alpha$, and $S_{\alpha\beta}$ was the overlap integral between α and β. The dipole and rotational strengths of transitions to the excited states obtained were calculated by the dipole-velocity procedure. The bands corresponding to the n-π* transitions of the lactone groups were not taken into account in the calculation. As even in 1,1'-spirobiindanone the magnitude of the Cotton effect associated with the n-π* transitions is small,[1] the contribution of the n-π* Cotton effect would not be as large as that produced by π-π* transitions in this compound. The theoretical CD curve of spirobiphthalide with S-configuration resembles qualitatively the experimental curve of (-)-3 as shown in FIG. 2.
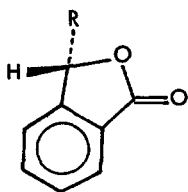

Fig. 3

In chiral phthalides whose absolute configurations are known (phthalideisoquinoline alkaloids and methyl-, butyl-, and di-methylaminomethyl-phthalides[10]), there is notable relation between the chirality at the C-3 position and the sign of the Cotton effect in the longest wave-length region; the configuration depicted in FIG. 3 showed the positive Cotton effect. This empirical information suggests (-)-3 to have S-configuration and the
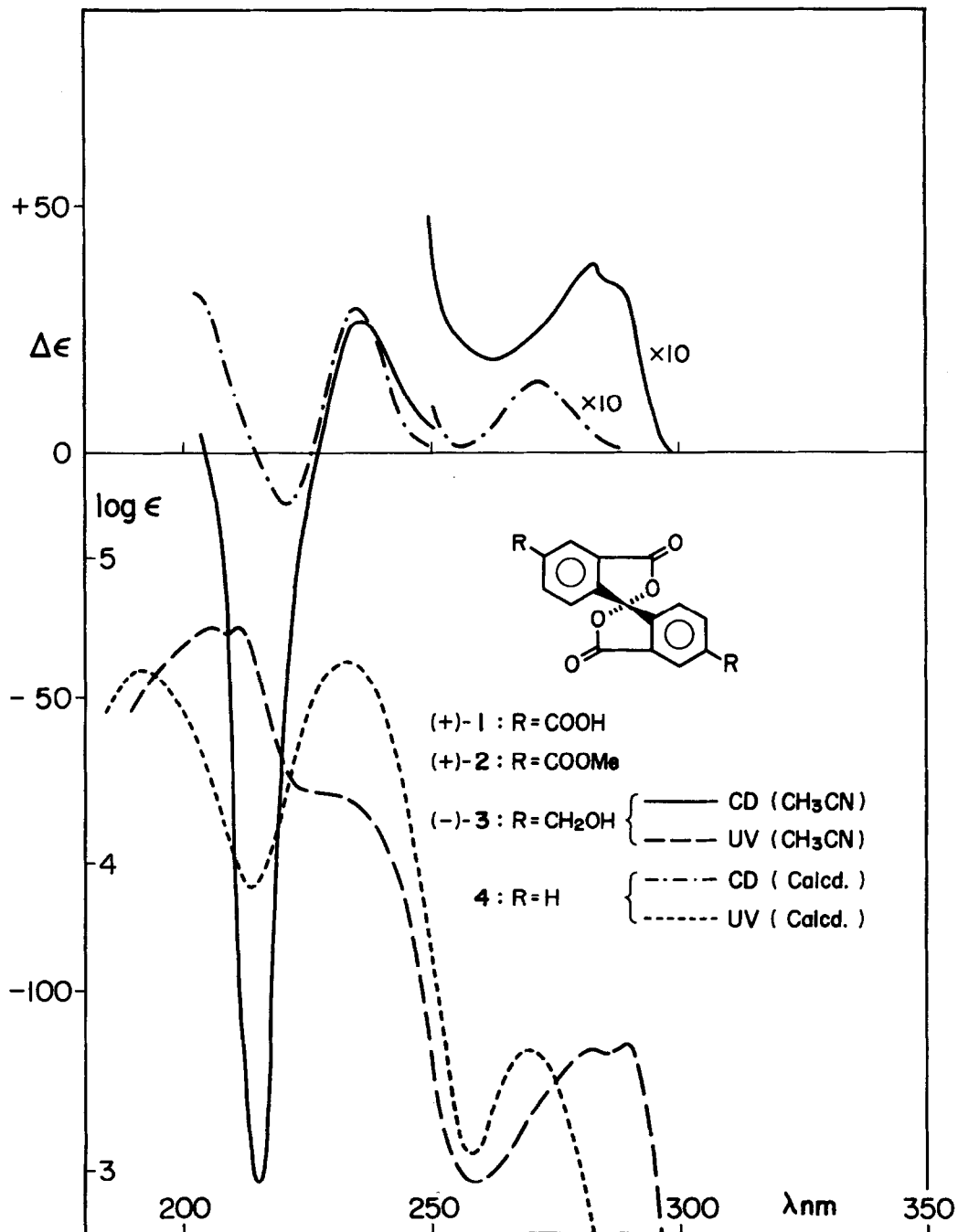
Fig. 2

prediction coincides with the above theoretically obtained one.

Compared with that of phthalide [λ_{nm} (ε) 280 (1,910), 273 (1,910), 227 (11,500) in MeOH[11]] the electronic spectrum of (-)-3 showed a bathochromic shift of several bands, even if the substituent effect of the hydroxy methyl group was taken into consideration, consistent with spiroconjugation. The bathochromic shift is of a similar order to that between spirobiindene and indene[1] but not as large as that between spiro[4.4]nonatetraene and spiro[4.4]nona-1,3,7-triene.[6a]

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