Table I. CD and Uv Data[a]

Compd	Solvent	CD, Δε, nm		Uv, nm (ε)
		π–π*	n–π*	
6	MeOH	−6.0 (232)	+0.18 (316)	227 (15,500)
8	MeOH	−5.3 (230)	+0.50 (317)	228 (28,800)
9	MeOH	−19.0 (238) +3.21 (219) [b]	+0.68 (336)	231 (19,800)
10	MeOH	+38.4 (242) −30.2 (208) [b]	−2.28 (320)	234 (21,300)
13	MeOH	+34.5 (261) −28.0 (229) [b]	−2.34 (317)	245 (24,800)
	0.005 *N* H_2SO_4 in MeOH[c]	+38.1 (263) −30.0 (231) [b]	−1.97 (319)	261 (24,100)
14	MeOH	+25.5 (254) −12.6(221) [b]	−2.19 (323)	241 (28,400)

[a] Data for only one of the enantiomers are given although both were measured. [b] Davydov split Cotton effects centered around uv maxima. [c] Conditions employed in ref 3. The reported values for (+)-ABA in this solvent: +39.5 (262) and −34 (230).

starting material. The CD benzoate **9** (Table I) showed a split Cotton effect due to interaction between the benzoate and enone chromophores. The negative first Cotton effect, in light of the exciton chirality method,[12] indicates a negative chirality (**9a**) between the two axes of electric transition moments. The absolute configuration of the benzoate is hence represented by **9** and that of the diol by **6**.[13]

The more polar MTP ester **5** was likewise hydrolyzed to the *cis*-α-diol **7** (84% yield), which was oxidized with 1.1 mol equiv of Jones reagent in acetone for 30 min to afford the bisenone **10** (71%). The chirality between the two chromophores in **10**, as derived from the twin Cotton effects (Table I), shows 6-OH to be α; this corroborates the conclusion from benzoate **9**.

Optically pure **10** (26 mg) was converted into a mixture of cis and trans esters (**11** and **12**) by a Wittig reaction.[14,15] The mixture was separated into the cis ester **11** (9 mg) and trans ester **12** (12 mg) by preparative tlc (4% *i*-PrOH in hexane) and subsequent purification by lc (1% *i*-PrOH in hexane, Corasil II). Hydrolyses of **11** and **12** with 5% KOH in 50% aqueous MeOH for 5 hr at room temperature, followed by lc purification (70% aqueous MeOH, Poragel PN), gave in quantitative yield the corresponding acids, (+)-ABA **13**,[16] mass spectrum 264.1362 (calcd for $C_{15}H_{20}O_4$, 264.1362), and (+)-*trans*-ABA **14**. The split CD Cotton effects of **13** and **14** (Table I) support the absolute configurations depicted.

The enantiomers of **13** and **14** were similarly prepared from the *cis*-β-diol **6** (see footnote *a* in Table I).

Since violaxanthin **15** has been converted[4] into (+)-*trans*-ABA **13** with retention of the C-6 configuration[17] (as would be expected from the probable mechanism for the opening of the epoxide ring), it should be represented by **15**, as was first believed.[17]

A theoretical treatment of the ORD data of (+)-*trans*-ABA has also arrived at configuration **14**.[18] The regulatory activities of (+)-ABA **13**, (+)-*trans*-ABA **14**, and their enantiomers are under study.[19,20]

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(12) N. Harada and K. Nakanishi, *Accounts Chem. Res.*, **5**, 257 (1972).

(13) This conclusion is valid, independent of the conformation, since although the nmr suggested conformer **9a** (quasiaxial 3-H), molecular models show that the negative chirality remains unchanged in the inverted conformation.

(14) D. L. Roberts, R. A. Heckman, B. P. Hege, and S. A. Bellin, *J. Org. Chem.*, **33**, 3566 (1968).

(15) F. Sondheimer, E. C. Galson, Y. P. Chang, and D. C. Walton, *Science*, **174**, 829 (1971).

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(17) T. E. de Ville, M. B. Hursthouse, S. W. Russell, and B. C. Weedon, *Chem. Commun.*, 1311 (1969).

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(19) Support from National Institutes of Health Grant No. CA 11572 is acknowledged.

(20) NOTE ADDED IN PROOF. Natural (+)-ABA has recently been correlated with (*S*)-malic acid and this has led to the same absolute configuration **13**: G. Ryback: *Chem. Commun.*, 1190 (1972).

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Absolute Configuration of (+)-*trans*-Abscisic Acid as Determined by a Quantitative Application of the Exciton Chirality Method

Sir:

The exciton chirality method,[1,2a] a versatile method for determining absolute configurations of natural products using split type Cotton effects, was applied to *trans*-abscisic acid. A quantitative calculation based on the molecular exciton theory indicates that (+)-*trans*-abscisic acid has the *S* configuration **3**.[2b]

The absolute configuration of (+)-*cis*-abscisic acid has remained obscure in spite of its important role as a plant-growth regulator.[3] Although Cornforth, *et al.*, had assigned an *R* configuration[2b] to (+)-*cis*-abscisic acid by application of Mills' rule,[4] Burden, *et al.*, indicated from their chemical correlation with violaxanthin that the absolute stereochemistry of either abscisic acid or violaxanthin was incorrect.[5]

The CD and ORD spectra of (+)-*cis*-abscisic acid show typical coupling type Cotton effects: CD, $\Delta\epsilon_{262} = +39.5$, $\Delta\epsilon_{230} = -34$, $\Delta\epsilon_{318} = -2.5$;[6] ORD, $[\Phi]_{289} = +63{,}400$, $[\Phi]_{269} = 0$, $[\Phi]_{246} = -182{,}200$, $[\Phi]_{225} = 0$.[7,8] This phenomenon can be interpreted as being due to the transition dipole–dipole coupling between enone and diene–carboxylic acid systems.[9] Therefore, it is expected that the theoretical calculation of absolute signs and amplitudes of split type Cotton effects would permit one to determine the absolute configuration of abscisic acid. It is also important to know the applicability of the exciton chirality method to such conformationally flexible compounds and to com-

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(1) N. Harada and K. Nakanishi, *Accounts Chem. Res.*, **5**, 257 (1972).

(2) (a) N. Harada, S. Suzuki, H. Uda, and K. Nakanishi, *J. Amer. Chem. Soc.*, **93**, 5577 (1971). (b) This is based on the presently accepted nomenclature for assigning *R* and *S* configuration to double bonds: R. S. Cahn, C. K. Ingold, and V. Prelog, *Angew. Chem., Int. Ed. Engl.*, **5**, 385 (1966).

(3) Most recent results suggest that (+)-abscisic acid has the *S* configuration: S. Isoe, S. Be Hyeon, S. Katsumura, and T. Sakan, *Tetrahedron Lett.*, 2517 (1972); T. Oritani and K. Yamashita, *ibid.*, 2521 (1972).

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(9) The shape of the calculated ORD curve for conformation **1** at $\phi = 180°$ is as follows: $[\Phi]_{284} = +30{,}300$, $[\Phi]_{270} = 0$, $[\Phi]_{247} = -118{,}000$, $[\Phi]_{224} = 0$, $[\Phi]_{209} = +41{,}000$.

pare the results with those of a rigid bisenone system, *e.g.*, quassin.[10]

The rotational strength due to the transition dipole coupling of two different chromophores (i and j) can be formulated as follows[11,12] for the longer wavelength transition ($0 \rightarrow \alpha$)

$$E^{\alpha} = (^1/_2)(\sigma_a + \sigma_b) - (^1/_2)\{(\sigma_a - \sigma_b)^2 + 4V^2\}0.5$$

$$\Psi^{\alpha} = C_1{}^{\alpha}\varphi_{ia}\varphi_{j0} + C_2{}^{\alpha}\varphi_{i0}\varphi_{jb}$$

$$R_{\alpha 0} = -C_1{}^{\alpha}C_2{}^{\alpha}\pi(^1/_2)(\sigma_a + \sigma_b)\vec{R}_{ij}\cdot(\vec{\mu}_{i0a} \times \mu_{j0b})$$

where groups i and j exhibit strong π–π^* transitions $0 \rightarrow a$ and $0 \rightarrow b$, respectively. Similar equations can be derived for the shorter wavelength transition ($0 \rightarrow \beta$) as well. Since the values of an oscillator strength computed by the molecular orbital method are generally overestimated, transition lengths r ($\vec{\mu} = e\vec{r}$), as well as $1/e$ widths $\Delta\sigma$ (cm^{-1}) and $\Delta\lambda$ (nm), were obtained from uv spectra of model compounds, 3-methyl-4-ethoxycarbonyl-2-cyclohexenone and cholesterol sorbate: 3-methyl-4-ethoxycarbonyl-2-cyclohexenone, λ_{max} 233.0 nm (ϵ 12,000), r = 0.862 Å, $\Delta\sigma$ 3964.8 cm^{-1}, $\Delta\lambda$ 20.7 nm; cholesterol sorbate, λ_{max} 259.4 nm (ϵ 24,700), r = 1.241 Å, $\Delta\sigma$ 3368.3 cm^{-1}, $\Delta\lambda$ 22.1 nm. CD curves approximated by a Gaussian curve were calculated by setting $R = 2.295 \times 10^{-39}(\pi)^{1/2}\Delta\epsilon_{max}\Delta\sigma/\sigma_{max}$ to be equal to $R_{\alpha 0}$ or $R_{\beta 0}$,[2] and they were then converted into ORD spectra by the Kronig–Kramers theorem.[13]

The W-type long-range coupling observed in the nmr[14] of *trans*-abscisic acid showed that the cyclohexenone ring adopts a half-chair conformation. Moreover, the side-chain conformation at C-8 is mainly s-trans because of the 12.7% NOE observed between H-7 and Me-9.[15] Altogether, there are two possible half-chair conformers and two possible rotamers around the 6–7 single bond for each of the conformers **1t**, **1c**, **2t**, and **2c**.[16] The directions of transition dipoles of diene–carboxylic acid and enone chromophores were calculated by the Pariser–Parr–Pople molecular orbital method to give θ = 41.72° and θ = 44.27°, respectively, as shown in **3**. The positions of point dipoles were assumed to be midpoints of C-9 and C-10 and C-5 and carbonyl oxygen, respectively.

The results of numerical ORD calculations for each conformer are shown in Figure 1, where amplitudes of first and second extrema are plotted against the dihedral angle ϕ between the 6-OH and 7-double bond.[17] Curves for conformation **1** and **2** are similar to each other, and indicate that the first ORD extremum should be negative ($[\Phi]_{284} = -8000$) around $\phi = -30°$ and positive ($[\Phi]_{284} = +35{,}000$) around $\phi = +150°$. The observed amplitude of the first extremum of (+)-*trans*-abscisic acid (see Figure 1) is $[\Phi]_{295} = +34{,}000$.[5] Therefore, in order to satisfy the observed value, (+)-*trans*-abscisic acid should have an S configuration (as in **3**) and a conformation where $\phi \approx +150°$. Similar arguments hold for the case of the second extremum (calcd, $[\Phi]_{247} = +30{,}000$ around $\phi = -30°$, $[\Phi]_{247} = -137{,}000$ around $\phi = +150°$; obsd, $[\Phi]_{245} = -113{,}000$).[9,18]

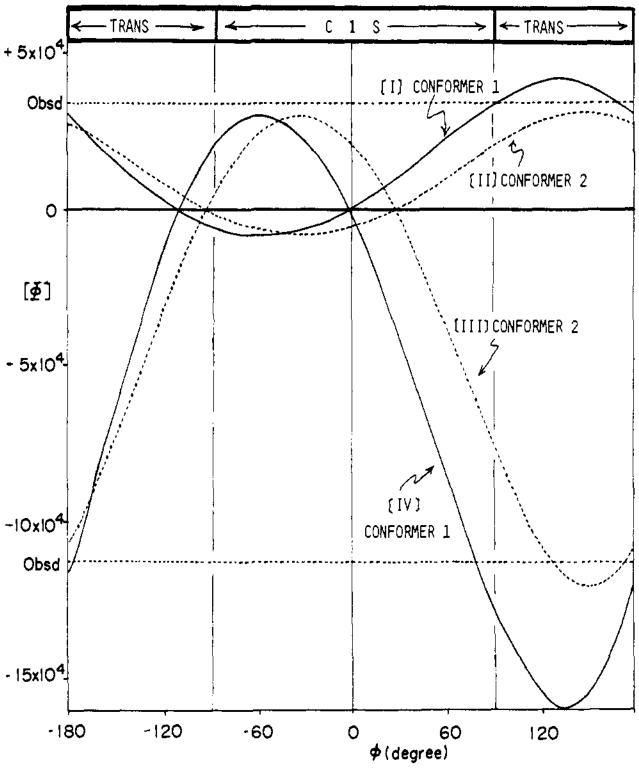
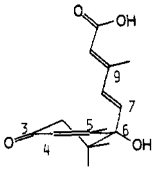
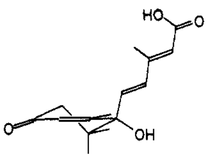


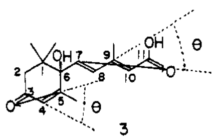
Figure 1. Dependence of calculated ORD Cotton effect extrema on the dihedral angle ϕ[17] between 6-OH and 7-ene. Curves [I] and [IV] are, respectively, traces of first and second (long and short wavelength) extrema for conformer **1**; similarly, curves [II] and [III] represent extrema for conformer **2**. The observed values are adopted from ref 5.



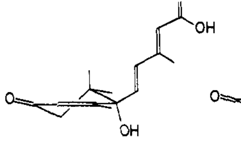
1t



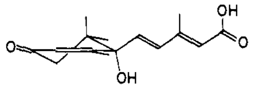
1c



3



2t



2c

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[10] In cases of rigid compounds such as quassin and steroid dibenzoates, an excellent agreement is found between the calculated and observed CD spectra; see ref 2a and M. Koreeda, K. Nakanishi, and N. Harada, manuscript in preparation.

[11] I. Tinoco, Jr., *Advan. Chem. Phys.*, 4, 113 (1962).

[12] The origin of position vectors is set at the middle point between two groups i and j.

[13] C. Djerassi, "Optical Rotatory Dispersion: Application to Organic Chemistry," McGraw-Hill, New York, N. Y., 1960, p 157.

[14] The following W-type long-range coupling was observed in *trans*-abscisic acid in acetone-d_6: Me-1$_{ax}$–H-2$_{ax}$ (J = 0.8 Hz) and H-2$_{eq}$–H-4 (J = 1.0 Hz). Therefore, boat conformations are ruled out.

[15] A portion of the side chain also adopts the s-cis conformation as judged from the small NOE of 6.8% observed between H-8 and Me-9.

[16] Abbreviations t and c mean s-trans and s-cis between 6-OH and the 7-double bond, respectively. These conformations are assumed to have a dihedral angle ϕ of 17.34° between the 4-ene and 3-carbonyl group. The dihedral angles between the 6–7 single bond and 5-methyl group were estimated to be 78.23 and 40.40° for conformations **1** and **2**, respectively.

[17] Plus and minus signs of the dihedral angle ϕ indicate conformations having the diene–carboxylic acid chromophore in the front and rear, respectively.

[18] The angle of transition dipole θ is calculated to be 29.00° when the diene–carboxylic acid moiety has an s-cis conformation about the 10–11 single bond. In this case, the pattern of the dependency of ORD amplitude on the dihedral angle ϕ is similar to that of s-trans in Figure 1, except for the smaller variation in amplitude and the constancy in Cotton effect signs when the side chain is rotated around the 6–7 single bond. Thus, an S configuration is deduced for this case as well. The present discussion is also valid for other s-cis conformations.

Quantitative calculations thus indicate that an S configuration should be assigned to (+)-*trans*-abscisic acid, and therefore to (+)-*cis*-abscisic acid.

As exemplified in the present case, quantitative applications of the exciton chirality method should provide a useful tool for conformational analyses of natural products. An alternative application of the exciton chirality method has also indicated that the configuration of natural (+)-*cis*-abscisic acid should be represented by S.[19,20]

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(20) NOTE ADDED IN PROOF. Natural (+)-ABA has recently been correlated with (S)-malic acid and this has led to the same absolute configuration **13**: G. Ryback, *Chem. Commun.*, 1190 (1972).

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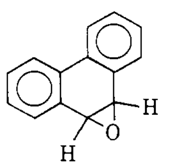
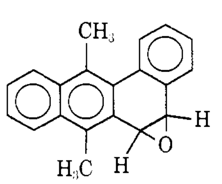
K-Region Arene Oxides of Carcinogenic Aromatic Hydrocarbons

Sir:

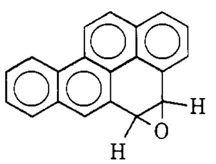
Arene oxides have recently been implicated as primary intermediates in the metabolism of aromatic molecules,[1] and the "K-region" oxides of certain polycyclic hydrocarbons have been shown to induce "malignant transformation" of rodent cells in culture[2] and mutational changes in mammalian cells and bacteriophages.[3] This evidence would appear to support the suggestion of Boyland[4] that epoxides are responsible for the carcinogenic activity of the parent hydrocarbons. However, investigation has been hampered by the synthetic inaccessibility of many of the compounds of greatest interest, *e.g.*, 7,12-dimethylbenz[*a*]anthracene 5,6-oxide (**1b**) and benzo[*a*]pyrene 4,5-oxide (**1c**), the parent hydrocarbons of which are among the most powerful carcinogens.[5] A new general synthesis of arene oxides, and of compounds **1a–c**, in particular, is now reported.



1a



1b



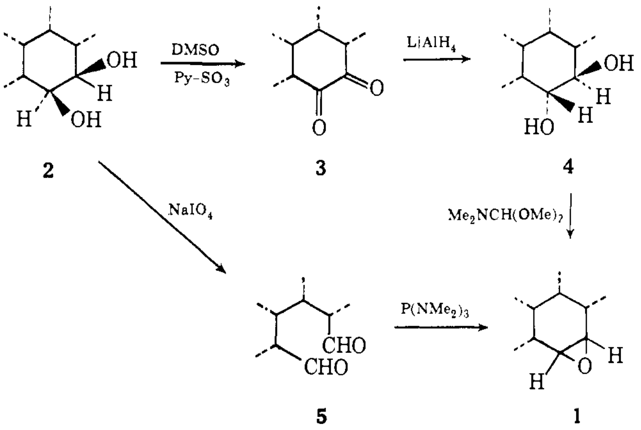
1c

The general synthetic scheme involves the following sequence: (1) generation of the "K-region" *cis*-dihydrodiols (**2**) *via* interaction of the corresponding hydrocarbons with osmium tetroxide,[6] (2) oxidation with dimethyl sulfoxide and sulfur trioxide–pyridine complex[7] to the quinones **3**, (3) reduction with lithium aluminum hydride to yield the related *trans*-dihydrodiols[8] (**4**), and finally (4) cyclization of the latter with the dimethyl acetal of dimethylformamide[9] (DMA–DMF) to afford the desired epoxide (**1**). Good yields of epoxides and intermediates were generally obtained, and the results are summarized in Table I.

Table I. Product Yields (%)[a]

Compd	a	b	c
3	96	49	98
4	87 (93)[b]	85 (55)[b]	44 (96)[b,c]
5		100	68[d]
1 from **4**	71	80	68
1 from **5**	89[e]	75	50

[a] All new compounds show consistent nmr, ir, mass spectral, and microanalytical data. [b] Percentage of trans isomer as determined by nmr on the diacetates is given in parentheses. [c] Isolated as the diacetate, since the diol is susceptible to air oxidation. [d] Lead tetraacetate was employed as the oxidant. [e] M. S. Newman and S. Blum, *J. Amer. Chem. Soc.*, **86**, 5598 (1964).



Oxidation of the *cis*-diols to the corresponding 1,2-diones presented the first synthetic challenge.[10] A number of unsuccessful attempts to transform the *cis*-diol of DMBA (**2b**) to the related quinone **3b** are recorded in the literature.[11,12] Oxidation with dimethyl sulfoxide and acetic anhydride, according to the method of Newman and Davis,[12] gave fair but erratic yields of the quinones. Also, phenanthrene-9,10-dihydro-9,10-diol (**2a**) on treatment with DMSO–Ac$_2$O afforded principally the phenanthrene 9,10-diacetate. In contrast, the sulfur trioxide–pyridine complex in DMSO–triethylamine[7] at room temperature efficiently and

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(12) M. S. Newman and C. C. Davis, *J. Org. Chem.*, **32**, 66 (1967).