Optical Rotatory Dispersion and Circular Dichroism of the Carboxyl Chromophore in Gibbane-10-carboxylic Acids with an Aromatic A Ring, and Their Application to the Stereochemistry of the B Ring of Gibberellins and Their Derivatives

Hiroshi MEGURO, Kiyomi HACHIYA, Katura TUZIMURA, Kenji MORI*
and Masanao MATSUI*

Department of Food Chemistry, Faculty of Agriculture, Tohoku University, Sendai, Japan

**Department of Agricultural Chemistry, The University of Tokyo, Bunkyo-ku, Tokyo, Japan*

Received September 29, 1972

CD and ORD of twelve gibbane-10-carboxylic acid compounds with an aromatic A ring together with two related compounds were measured. The sign of the Cotton effect was found to be positive (negative) when the configuration of the C-10 carboxyl is β (α). The ORD also provided information to determine the configuration at C-4b. The C-10 carboxyl gave a stronger magnitude and redshift of the peak in a *cis* relation with 4b-H compared with that in a *trans* relation.

In our previous communication, an application of circular dichroism (CD) of the lactone chromophore of C₁₉-gibberellins to the stereochemistry and structural elucidation of the A ring was suggested.¹⁾

In studies of the B/C ring junction, the red shift of the CD peak of the ketone chromophore of C-8 keto derivatives of gibberellins has been used to determine the stereochemistry of the 4b hydrogen.²⁾

In this article we report the ORD and CD spectra of the carboxyl chromophore of gibbane-10-carboxylic acids with an aromatic A ring and their application to the study of the stereochemistry in the B ring, especially the configuration at C-10 and C-4b.

types of stereoisomers; four types of C-10- β -carboxyl compounds (A), (B), (C) and (D) and their enantiomers (A'), (B'), (C') and (D'), which are C-10- α -carboxyl compounds and which are shown in Fig. 1.

The compounds (A) and (A') have a C-10-carboxyl which is in a *cis* relation to both carbon bridge of the D-ring and the 4b hydrogen. The compounds (B) and (B') have a C-10 carboxyl which is *cis* to the D-ring and *trans* to the 4b hydrogen. The compounds (C) and (C') have a C-10 carboxyl which is *trans* to the D ring and *cis* to the 4b hydrogen. The compounds (D) and (D') have a C-10 carboxyl which is *trans* to both the D-ring and the 4b hydrogen.

We have measured twelve compounds previously prepared for other purposes³⁻⁸⁾ which belong to (A), (A'), (B), (C'), (D) and two compounds (E) and (F) with an aromatic A ring and a modified C, D ring skeleton, as shown in Fig. 1. Some of these compounds were measured in the form of methyl esters.

MATERIALS AND METHODS

CD and ORD were measured at 22°C on a Japan Spectroscopic Model ORD/UV-5 recording polarimeter with a CD attachment. Sample solutions were prepared by dissolving about 1 mg of the sample in 2 ml of 95% ethanol. Quartz cells with an optical path of 1.0 cm or 0.1 cm were used for the measurements.

According to the stereochemistry of the C-10 carboxyl and B/C ring junction, gibbane-10-carboxylic acids with an aromatic A ring can be classified into eight

RESULTS AND DISCUSSION

Representative CD and ORD spectra of each type of compound, (A), (B), (C) and (D), are shown in Figs. 2, 3, 4 and 5, respectively.

Figure 2 shows the ORD and CD spectra of compound (A)-I as representative. This gave a strong positive CD maximum at 230 nm ($[\theta] = +1.5 \times 10^4$) and a corresponding ORD peak at 236 nm ($M = +1.6 \times 10^4$).

FIG. 1. The Eight Types of Stereoisomers of Gibbane-10-carboxylic Acids with an Aromatic A Ring, and Two Related Compounds.

Figure 3 shows the CD and ORD spectra of compound (B)-III. Both the CD and ORD gave a plain curve indicating an increase of molecular ellipticities below 250 nm due to the C-10 carboxyl and a small negative minimum

at 270 nm, probably due to the aromatic chromophore.

The compounds which belong to (B) gave relatively smaller molecular rotations around the 230 nm wavelength region and in the

FIG. 2. ORD and CD Spectra of (A)-I.
—, ORD; ---, CD.

ORD the background rotation due to the contribution from the skeleton and other chromophores presented some technical difficulties in differentiating the ORD extremum of the C-10 carboxyl. In the CD, however, it was possible to differentiate the sign of the Cotton effect from the sign of plain curve, as shown in Fig. 3.

Figure 4 gives the ORD and CD spectra of (C)-I, which gave a first trough at 234 nm and a CD maximum at 230 nm.

Figure 5 shows the ORD and CD spectra of compound (D)-I as an example of a compound with a ketone in the D ring other than the C-10 carboxyl. In this case, the CD peaks of these two chromophores were distinguished from each other. The ketone gave a CD minimum at a wavelength of 290~300 nm and the C-10 carboxyl gave a plain CD increase at about 230 nm. The ORD also gave a corresponding first peak due to the C-10 carboxyl chromophore at 228 nm. All the compounds,

FIG. 3. ORD and CD Spectra of (B)-III.
—, ORD; ---, CD.

except (B), (E) and (F) gave a strong ORD extremum (in (A) corresponding the CD max.) in the 230~235 nm wavelength region due to the C-10 carboxyl or carbomethoxyl chromophore. It should be noted that the extremely high molecular rotations permitted ORD and CD measurements in dilute solutions to determine the sign and wavelength of the Cotton effect together with the degree of red shift in each compound. The structures, molecular ellipticities and molecular rotations at the CD and ORD extremum around the 230 nm region are shown in Table I. When the ORD and CD gave plain curves or the extrema are not reached, the molecular rotations and molecular ellipticities at the shortest wavelength measured are shown with an asterisk (*). The results may be briefly summarized as follows.

1) *The sign of the Cotton effect.* The sign of the Cotton effect at around the 230 nm

FIG. 4. ORD and CD Spectra of (C')-I.
—, ORD; ---, CD.

region coincided with the stereochemistry of the C-10 carboxyl independent of structural changes in the C/D and B/C ring junctions. This suggests an application of CD and ORD to determine the stereochemistry of C-10 carboxylic acids. Thus, if the CD sign of the first extremum of the ORD around 230 nm is positive, the stereochemistry of the C-10 carboxyl is β and when the sign is negative, it is α .

II) The red shift and rotational strength.

From the position of the ORD extremum (or corresponding CD maximum) the compounds can be divided into two groups; those compounds (A), (A'), (C'), which have the C-10 carboxyl in a *cis* relation with the C-4b hydrogen and another group of compounds (B), (D) which have the C-10 carboxyl in a *trans* relation with the C-4b hydrogen. The former gave ORD extrema with extremely high molecular rotation at about 236 nm (corresponding CD maximum at about 230 nm)

FIG. 5. ORD and CD Spectra of (D)-I.
—, ORD; ---, CD.

and showed distinct red shift compared with the latter. In the latter, compounds (D) gave an ORD extremum at about 228~230 nm with moderate molecular rotation and compounds (B) gave a plain curve with relatively smaller molecular rotation up to 230 nm, indicating the presence of the ORD and CD peaks in a shorter wavelength region than 230 nm. This result suggests that the position of the ORD peak and the molecular rotation may be applied to determine the *cis* or *trans* relation of the C-10 carboxyl and the C-4b hydrogen. Examination with Dreiding models indicates that the conformation of the B, C, D ring system of compounds (A)–(B), (A')–(B') can be expressed as in (a) and (b) in Fig. 6 or their enantiomeric forms. Since the B ring takes an envelope form (d) in this ring system, the C-10 carboxyl in a *cis* relation with the C-4b hydrogen is oriented quasiaxial and that in a *trans* relation is quasi-equatorial.

TABLE I. SIGN AND MAGNITUDE OF THE CD AND ORD PEAKS OF THE CARBOXYL CHROMOPHORE AT C-10, AND THE CORRESPONDING STRUCTURAL RELATIONS

Comp.	Ref.	Con-fig.	Sign C.E.	CD $[\theta] \times 10^{-3}$	(nm)	ORD $[M] \times 10^{-3}$	(nm)	Stereochem. to		Confor-mation	C.E. Red shift
								D ring	4b-H		
(A)-I	(3)	β	+	+15	230 (M)	+16	236 p	<i>cis</i>	<i>cis</i>	q. ax.	○
(A')-I	(4)	α	-	-20	230 (M)	-24	236 t	<i>cis</i>	<i>cis</i>	q. ax.	○
(A')-II	(5)	α	-	-5.1	236 (M)	0	245 t	<i>cis</i>	<i>cis</i>	q. ax.	○
(B)-I	(4) (6)	β	+	+2	232 *	-0.4	240 *	<i>cis</i>	<i>trans</i>	q.e.	^
(B)-II	(7)	β	+	+0.9	232 *	-1	234 *	<i>cis</i>	<i>trans</i>	q.e.	×
(B)-III	(6) (8)	β	+	+2	230 *	+0.8	232 *	<i>cis</i>	<i>trans</i>	q.e.	×
(C')-I	(8)	α	-	-22	230 *	-23	234 t	<i>trans</i>	<i>cis</i>	q.ax.	○
(C')-II	(3)	α	-	-12	230 *	-15	235 t	<i>trans</i>	<i>cis</i>	q.ax.	○
(D)-I	(7)	β	+	+13	226 *	+23	228 p	<i>trans</i>	<i>trans</i>	q.e.	×
(D)-II	(4)	β	+	+12	230 *	+32	228 p	<i>trans</i>	<i>trans</i>	q.e.	×
(D)-III	(7)	β	+	+9	220 *	+18	228 p	<i>trans</i>	<i>trans</i>	q.e.	×
(D)-IV	(5)	β	+	+detected	230 *	+23	230 p	<i>trans</i>	<i>trans</i>	q.e.	×
(E)	(4)	β	+	+1.5	234 *	+5.3	230 *	—	<i>trans</i>	q.e.	×
(F)	(4)	β	+	+2.1	228 *	-0.05	228 *	—	<i>trans</i>	q.e.	×

* $[\theta]$ and $[M]$ measured at the shortest wavelength, shown with asterisk *, should be taken as semiquantitative or qualitative values to determine the sign of the C.E. especially in (B), (E) and (F) due to the large signal-noise ratio.

Stereochemistry of the carboxyl at C-10.

- (a), (A') α , q. axial, *cis* to 4b-H.
 (D) β , q. equatorial, *trans* to 4b-H.
 (b), (B) β , q. equatorial, *trans* to 4b-H.
 (C') α , q. axial, *cis* to 4b-H.
 (c), (E) β , q. equatorial, *trans* to 4b-H.
 (F) β , q. equatorial, *trans* to 4b-H.
 (d), An envelope form of cyclohexene.

FIG. 6. Conformations of the C-10 Carboxyl and 4b-H.

The stronger CD maxima with larger red shift of the quasi-axial carboxyl group than of the quasi-equatorial group can be explained by the formation of a kind of inherently dissymmetric chromophore by analogy with similar compounds such as L-mandelic acid⁹⁾ and α -alkylphenylacetic acids¹⁰⁾ as well as β , γ -unsaturated carbonyl compounds.¹¹⁾ Regarding the interaction of the carboxyl and A ring, the axial carboxyl is expected to interact more effectively than the equatorial one. Thus, the strong red shift associated with the higher molecular rotation of (A) and (C) and the smaller red shift associated with the relatively lower molecular rotation of (B) and (D) are result of the difference in the interaction of the two chromophores in the β , γ -unsaturated carboxyl systems. Finally we should mention the CD and ORD spectra of compounds (E) and (F), both of which have a modified C/D ring which fixes the B ring into an envelope conformation. These are expected to show a similar interaction between π -electrons of the A ring and the C-10 carboxyl, as well as the other types found in our sample. In ORD, their relatively small optical rotation due to the C-10 carboxyl chromophore was over-

lapped by background rotations due to other chromophores and were practically useless for our purpose. In CD they resemble (B), showing a plain increase with smaller molecular ellipticities around at the 230~250 nm region, without the interference of other chromophores which gave maxima in longer wavelength regions. This shows that the sign of the Cotton effect is positive and the interaction with the aromatic A ring should be smaller. As the stereochemistry of the C-10 carboxyl of (E) and (F) is β and equatorial, this is in accord with the results obtained with gibbane-10-carboxylic acids with an aromatic A ring.

REFERENCES

- 1) H. Meguro, K. Tuzimura and N. Takahashi, *Tetrahedron Letters*, **1968**, 6305.
 - 2) A. I. Scott, F. McDapra, F. Comer, S. A. Sutherland, D. W. Young, G. A. Sim and G. Ferguson, *Tetrahedron*, **20**, 1339 (1964).
 - 3) J. F. Grove and T. P. C. Mulholland, *J. Chem. Soc.*, **1960**, 3007.
 - 4) K. Mori, M. Matsui and Y. Sumiki, *Tetrahedron Letters*, **1970**, 429.
 - 5) K. Mori, T. Ogawa, N. Itaya, M. Matsui and Y. Sumiki, *Tetrahedron*, **25**, 1281 (1969).
 - 6) T. P. C. Mulholland, *J. Chem. Soc.*, **1958**, 2693.
 - 7) B. E. Cross, *ibid.*, **1954**, 4670.
 - 8) K. Mori, M. Matsui and Y. Sumiki, *Agr. Biol. Chem.*, **27**, 537 (1963).
 - 9) G. Barth, W. Voelter, H. S. Mosher, E. Bunnerberg and C. Djerassi, *J. Am. Chem. Soc.*, **92**, 875 (1970).
 - 10) J. Cynerman Crig, W. E. Pereira Jr., B. Halpern and J. W. Westley, *Tetrahedron*, **27**, 1173 (1971).
 - 11) A. Moscowitz, K. Mislow, M. A. W. Glass and C. Djerassi, *J. Am. Chem. Soc.*, **84**, 1945 (1962).
-