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Calculations of Cotton Effects in the Vacuum UV Region for Aldonic Acid 1,4-Lactones and Interpretations of Hudson's Lactone Rule

Hiroshi Meguro, Yoshihiro Nishida, and Hiroshi Ohrui*

Department of Food Chemistry, Faculty of Agriculture, Tohoku University
Tsutsumidori-Amamiyamachi 1-1, Sendai 980, Japan

Toshio Konno

Department of Education, Niigata University, Igarashi, Niigata, Japan

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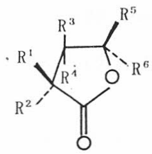
A graphic method of Drude equation was applied to a series of aldonic acid 1,4-lactones *1*—*7* to investigate possible Cotton effects below 200 nm. The calculation shows three bands at 220 nm, 170 nm and 130 nm to reflect the stereochemistries at C-2, C-4 and ring conformations and vicinal OH at C-3 and C-4, respectively. The sum of the rotational contributions at 589 nm of these bands explained the applicability of Hudson's lactone rule in sugar lactones.

In our previous report[1], a series of model lactones were studied on their Cotton effects below the 200 nm region based on the ORD using the Drude equation and they were found to give a second band at *ca.* 170 nm region in addition to the band at 220 nm. The 220 nm band had already been well established to reflect the C-2 configurations[2,3], and the latter band had been revealed to reflect (1) the C-2 configurations *(Rule 1)*[1] as the counter band of the 220 nm band and (2) the C-4 configurations and conformations including ring conformations *(Rule 2)*[1]. The latter band was also suggested to take an essential part of Hudson's lactone rule[4].

In this article we wish to extend the study to a series of aldonic acid 1,4-lactones *1*—*7* (Figure 1). Lactones *2*—*7* are characterized by vicinal hy-



	R^1	R^2	R^3	R^4	R^5	R^6
1	H	OH	Me	Me	H	H
2	H	OH	H	OH	H	H
3	H	OH	H	OH	CH_2OH	H
4	OH	H	H	OH	CH_2OH	H
5	OH	H	OH	H	H	$CH(OH)CH_2OH$
6	H	OH	H	OH	H	$CH(OH)CH_2OH$
7	H	OH	OH	H	H	$CH(OH)CH_2OH$

Figure 1. Model compounds *1*—*7*.

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* To whom correspondence should be addressed.

Table 1 Chiroptical Properties of Aldono-γ-lactones and the Related γ-lactones 1-7.

Compounds	Solvents	λc (nm)	〔θc〕[a] x 10^{-3}	K_C x 10^{-8}	〔Mc〕$_D$[b]	〔M〕$_D$	[M]$_{300}$[c]
D-*Panto.* 1	MeOH	221	-13.1	-0.46	-155	-36	-510
		171	+14.6	+0.38	+119		
		(---------------------)[d]					
D-*Erythro.* 2	MeOH	221	-12.2	-0.40	-135	-53	-533
		170	+14.3	+0.37	+116		
		130	- 6.1	-0.12	- 36		
D-*Ribono.* 3	H_2O	219	-14.3	-0.48	-161	+27	-102
		170	+32.8	+0.89	+280		
		130	-15.6	-0.31	- 94		
	MeOH	221	-13.5	-0.45	-152	+31	- 64
		170	+38.2	+0.99	+311		
		130	-21.2	-0.42	-127		
D-*Arabono.* 4	MeOH	220	+15.4	+0.61	+204	+106	+1004
		(---------------------)[d]					
		128	-18.2	-0.35	-107		
D-*Talono.* 5	MeoH	220	+11.0	+0.42	+139	-112	-252
		170	-23.9	-0.62	-195		
		130	-9.6	-0.19	- 58		
	or[e]	220	+11.0	+0.42	+139	-112	-252
		162	-32.4	-0.80	-250		
		(--------------------)[d]					
D-*Gulono.* 6	MeOH	220	-13.1	-0.46	-154	- 91	-702
		180	+13.9	+0.38	+121		
		110	-11.9	-0.20	- 60		
D-*Galactono.* 7	H_2O	220	-19.4	-0.64	-214	-125	-1151
		(--------------------)[d]					
		141	+12.6	+0.27	+ 83		
	MeOH	223	-16.5	-0.56	-188	-142	-1162
		(--------------------)[d]					
		130	+ 8.1	+0.16	+ 48		

a) Calculated from the Kc values with Kronig-Krammer equation using an assumed Δ value=13.5nm.
b) Rotational contributions of each band to the 〔M〕$_D$ value.
c) Molecular rotations at 300 nm.
d) Not calculated.
e) For D-*talono*-γ-lactone 5, both two and three terms equations were satisfactory with the calculations.

droxyl groups (*vic.* OH) in ring, which are found to make the other bands at 130 nm reflecting the chirality of the *vic.* OH. A mechanistic reationalization for the success of Hudson's rule for aldono-γ-lactones is also attempted.

MATERIALS AND METHODS

Lactones *2*—*7* were purchased from the Wako Chemical Company Co. LTD. in Tokyo and used after recrystallization from ethanol-ethyl ether. ORD and CD measurements and calculations of the Cotton effects below 200 nm were performed according to the previous study[1] except that the lactones *2*, *3*, and *6* fit better with the three term Drude equations. In the three term calculation the λ_{max} value of the first band was taken from the CD measurement, and those of the latter two bands were calculated iteratively with 10 nm steps. The λ_{max} of the latter two bands has a variance of ±20 nm.

RESULTS

The chiroptical data of *2*—*7* are summarized in Table I together with the result of previously studied D-pantolactone *1*[1] for comparison. The table shows the solvents, λ_{max} of three possible bands and their CD ($[\Theta]$) and ORD (Kc) intensities, contributions of each band to the $[M]_D$ ($[Mc]_D$) and molecular rotations at sodium D-line (589 nm) and 300 nm.

The use of the three term Drude equations showed a much better accordance with the ORD data for lactones *2*, *3*, and *6* than the use of the two term one (Figure 2). The calculations gave another Cotton effect at 130 nm, other than the band at 170 nm below 200 nm. For lactones *1*, *4*, *5* and *7* the two term equation gave a better accordance than the three term one to give a single band below the 200 nm region. For lactone *5*, three term equations gave a well accorded result. However, the accordance of the two term equations was better.

Figure 3a and 3b show the ^3E and E_3 conformations of *1*—*7*. At room temperature these sugar lactones in solutions would take a conformational equilibrium between the two conformers.[5,6,7]. Extensive NMR studies by Horton and Walaszek[6-8] showed that sugar lactones favored the conformation with the C-2 hydroxyl group (C2-OH) in a *quasi-equatorial (q. eq)* conformation with exception of D-*glucono*-1,4-lactone. For example, D-*ribono*-γ-lactone *3* was shown to favor a ^3E conformer rather than the E_3. For lactones *4*, *6* and *7* they would take a stable conformation ^3E, E_3 and E_3, respectively, which took both of the C-2 and the C-4 substituents in a *q. eq.* conformation, and the NMR results[7,8] accorded with this speculation. For lactone *4*, which is antipodal to lactone *3*, one may take a E_3 conformation predominantly with the C2-OH in a *q. eq.* conformation.

DISCUSSION

a) Existence of the Band due to vicinal *Hydroxyl Groups (*vic *OH)*

Several sugar lactones showed a new band at 130 nm in addition to the bands at 220 and 170 nm. From the wavelength and the fact that an analogous lactone *1* did not give a band in this region, the new band was postulated to be associated with the *vicinal* hydroxyl groups (*vic.* OH). In order to clarify the effects of the *vic.* OH, a model compound, 1,5-anhydro-D-galactitol (1-deoxy-D-galactopyranose) was studied in a similar way (Figure 4), because the sugar is free from the carbonyl chromophore and its stereochemistry has been established to take a $^4C_1$ conformation[9]. The graphic plot of the Drude

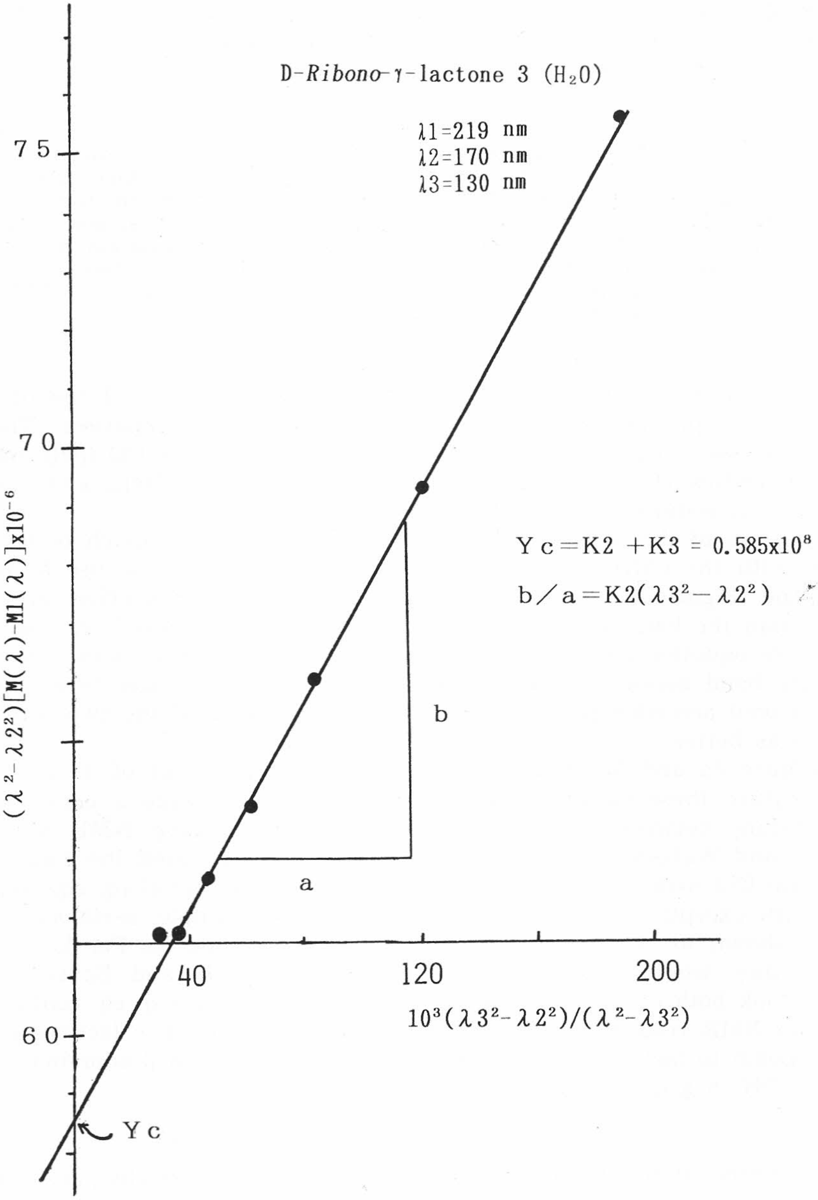
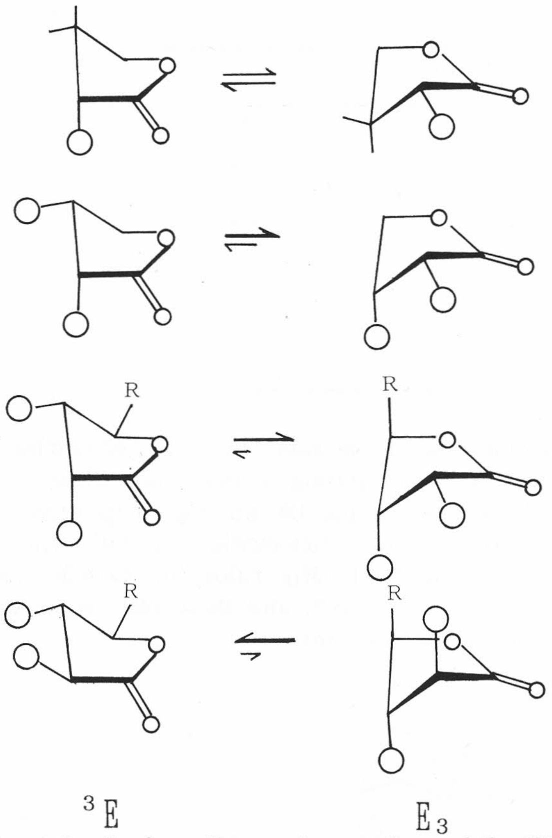


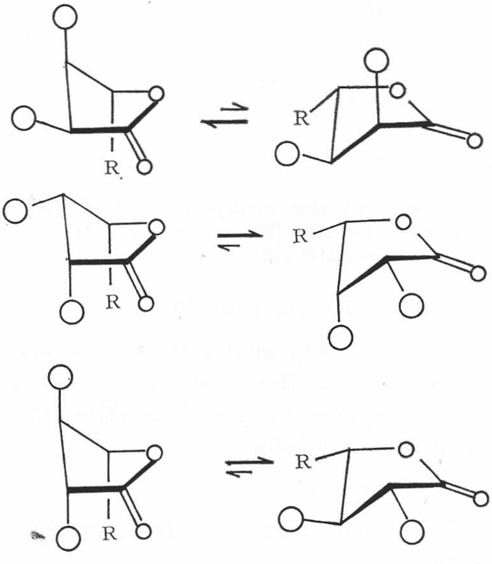
Figure 2. A graphic method of the three term Drude equation for D-*ribono*-γ-lactone *3*.

one term equation gave a single band at $\lambda_{\max} = 130$ nm ($K_c = + 0.41 \times 10^8$). The bands at 170 nm and 220 nm were not found in this compound. This compound takes a stable $^4C_1$ ring conformation with three ring OH in all clockwise relation. The positive Kc of this compound would be mainly associated with the two clockwise *vic.* OH. The sign and the $\lambda_{\max}$ accorded



Compounds	K1(C=O)/K2(Or)/K3(OH)
1	-0.46 / 0.01 / 0
2	-0.40 / 0.05 / -0.12
3 (H₂O)	-0.48 / 0.51 / -0.31
(MeOH)	-0.45 / 0.63 / -0.42
4	+0.61 / 0.49 / -0.35

Figure 3a. Conformations and corrections of the K2 values of model compounds *1—4*. K2 (Or) was calculated from an equation as below K2 (Or) = K2 + 0.8 × K1 (C=O)



Compounds	K1(C=O)/K2(Or)/K3(OH)
5	+0.42 /-0.46 / 0 (two term)
	(+0.42 /-0.28 / -0.19)(three term)
6	-0.46 / 0.01 / -0.41
7 (H₂O)	-0.64 /-0.51 / 0.27
(MeOH)	-0.56 /-0.45 / 0.16

Table 2 ORD Data of Lactones 2-7.

Compounds	Solvent	[M](λ)						
		600	550	500	450	400	350	300
2. erythro.	MeOH	-51	-65	-85	-111	-166	-260	-533
3. ribo.	H_2O	+27	+28	+33	+35	+35	+16	-102
	MeOH	+31	+33	+39	+45	+48	+37	-64
4. Arabo.	MeOH	+102	+123	+149	+209	+294	+487	+1004
5. Talo.	MeOH	-108	-126	-147	-180	-226	-277	-252
6. Gulo.	MeOH	-91	-107	-139	-182	-256	-384	-702
7. Galacto.	H_2O	-124	-155	-197	-269	-378	-587	-1151
	MeOH	-136	-177	-218	-281	-400	-612	-1162

with the third band of sugar lactones with the same *vic.* OH geometries in the assumed conformations. This led to proposing a new rule (*Rule 3* in Figure 5) to correlate the sign of the band in the 130 nm region (positive for the clockwise *vic.* OH and negative for the anticlockwise *vic.* OH). *Rule 3* seems to be closely related to the empirical $[M]_D$ rules for carbohydrate molecules by Whiffen[10], Brewster[11] and Lemieux[12], and these $[M]_D$ rules will be better interpreted by the band at *ca.* 130 nm.

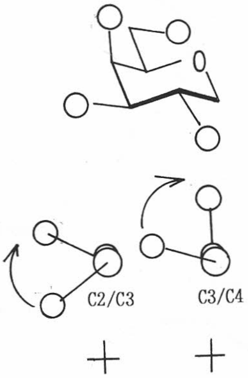


Figure 4. Structure of 1,5-anhydro-D-galactitol and the effects of *vicinal* OH at C2/C3 and C3/C4 on the Cotton effect at 130 nm (Kc = $+0.41 \times 10^8$). Clockwise *vic.* OH gave a positive sign.

b) The Nature of Three bands at 220 nm, 170 nm and 130 nm

The results of the second bands at 170 nm were analyzed as previously[1] by assuming the two transition mechanisms; one is the band due to the carbonyl chromophore and the other due to the ring oxygen. The strength of the former band (K2(C=O)) was calculated by a relation,

$$K2\,(C{=}O) = -0.8 \times K1\,(C{=}O)^1,$$

where K1(C=O) is the strength of the first band at 220 nm. The strength of the latter band K2 (Or) was calculated by

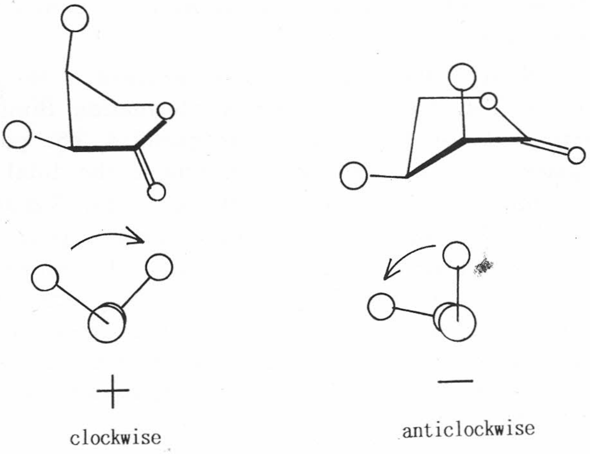


Figure 5. Effects of *vic.* OH on the Cotton effects at 130 nm. *(Rule 3).*

$$K2\,(Or) = K2 - K2\,(C{=}O)$$

where K2 means the total strength of the 170 nm band in Table I.

The calculated K1 (C=O) and K2 (Or) values of *1*—*7* are summarized in Figures 3a and 3b together with the strength of the third band at 130 nm K3 (OH). The results could be summarized as follows.

(1) The K1 (C=O) at 220 nm was positive or negative reflecting the β- or α-configuration at C-2, respectively, as it had already been reported by Okuda *et al.*[2] The intensity was large enough to determine the sign of $[M]_{300}$ (Table I) dependent on the configurations at C-2. However, the contribution at 589 nm ($[M]_D$) was almost cancelled by the counter contribution of K2 (C=O).

(2) The strength of the 170 nm band (Table I) could be well explained by assuming two contributions, K2 (C=O) and K2 (Or)[1]. The sign of K2 (C=O) reflected the configurations at C-2, and was opposite to the sign of K2 (C=O). The K2 (Or) (Figure 4) reflected the configurations at C-4 (β-configuration is positive and the α-one is negative) and the values widely changed depending on the conformations of the C-4 substituent (*q. eq.* showed a smaller effect than the *q. ax.*) and ring conformations (^3E is negative and E_3 is positive).

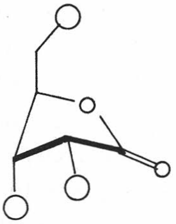
(3) The positive K2 (Or) of *2* (+0.05) suggested its preference of the E_3 conformer to the ^3E, and the negative K3 (OH) (—0.12) showed that the *vic.* OH were anticlockwise to support the E_3 conformation. The large positive K2 (Or) of *3* could be ascribed to the stable E_3 conformation (positive) with *q. ax.* β-configuration at C-4 (positive). The negative K3 (OH) also showed this conformation. An analogous result could be obtained for the antipodal *5*, but lower K2 (Or) and K3 (OH) values of *5* compared with those of *3* suggested the substantial contribution from ^3E which might be stabi-

lized by the large exocyclic side chain in *5*. A similar conformation was reported for D-glucorono 1,4-lactone[8].

The small K2 (Or) (0.01) of *6* could be ascribed to the negative α-configuration (*q. eq.*) at C-4 and a positive E_3 conformation. Similar results to those of *6* were expected also for *7* and its antipodal *4*. The positive K3 (OH) of *7* strongly suggested its E_3 conformation, where the total K2 (Or) would be nearly zero, similarly to the case in *6*. However, the K2(Or) = — 0.45 (MeOH) was too negative for the E_3 conformation. This implies large contributions from the E_3 conformation or from some flattered conformation which would have large negative contributions from the ring and the α-configuration. The larger K1 (C=O) values of *7* (and *4*) than those of the other lactones might originate in this conformational property. Similar results were observed for *4* where the contributions from E_3 or the flattered conformation may bring a large positive K2 (Or) rather than from ^3E.

c) *Interpretations for the Success of Hudson's Rule*

Hudson's lactone rule simply indicates that the sign of $[M_D]$ of aldonic acid 1,4-lactones is determined by the configuration at C-4, and this simple rule has been extended to other types of γ- or δ-lactones by Klyne[13,15]. In our interpretation, the $[M]_D$ values of chiral γ-lactones are the sum of the rotational contributions from K1 (C=O) and its counter K2 (C=O), C-4 configuration and conformation associated band (K2 (Or)), ring conformation associate band K2 (Or)′ and *vic.* OH associted band at 130 nm K3 (OH) (*Rule 4* in Figure 6).



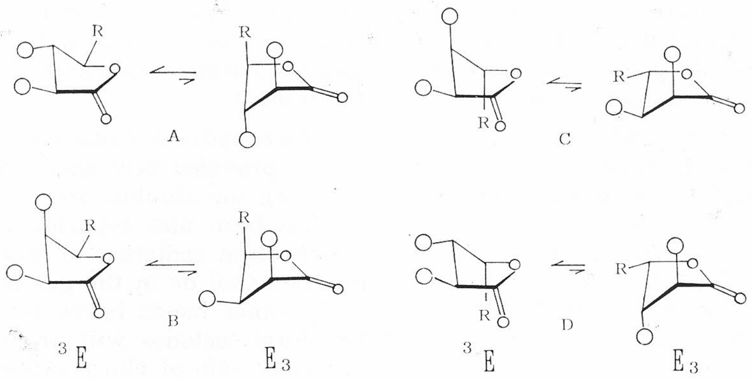
3 (E_3 conformer)

Bands	Rule 1	Rule 2		Rule 3
	C-2β	E_3	C-4 β (q.ax)	anticlock vic. OH
220 nm	—			
170 nm	+	+	++	
130 nm				—
$[M]_D$	Totally Positive			

Figure 6. The sum of the total contributions for lactone *3* and the prediction of the sign of $[M]_D$. (*Rule 4*)

Figure 7 shows the ^3E and E_3 conformations of four possible types of aldono-γ-lactones *A* — *D* with the same β-hydroxyl group at C-2. The model *2*—*7* could be classified into one of these types (however, lactones *2, 3, 6* and *7* are enantiomers of the type of *E, C, B* and *A*, respectively). The signs of each contribution from C-2 (as the sum of K1 (C=O) and K2 (C=O) where |K1 (C=O)| > |K2 (C=O)|), ring chirality, *vic.* OH and C-4, are also given.

Applicability of Hudson's rule depends on whether the sum of these contributions has the same sign as the C-4 contribution to reflect the con-



	3E			⇌	E3				$[M]_D$ Predicted
	C-2	Ring	Vic.OH	C-4	C-2	Ring	Vic.OH	C-4	
A	+	−	−	+	+	+	small	++	positive
B	+	−	+	+	+	+	−	++	positive
C	+	−	+	−−	+	+	−	−	negative
D	+	−	−	−−	+	+	small	−	negative

Figure 7. Four possible types of aldonic acid 1,4-lactones *A—D* and the signs of the rotational contributions from configurations at C-2 configurations, ring conformations, *vic* OH and C-4 configurations.

The accordance of the signs of the total contributions with the signs of the C-4 contributions points to the applicability of the Hudson rule for all *A—D* types.

figuration at C-4 (positive for β-configuration and negative for the α-configuration). These simple aproaches to predict the applicability of Hudson's rule showed that (1) for the lactones in types *B* and *D* (model compound *6*) the predicted signs undoubtedly agreed with the signs of K2 (Or) in the favored ^3E conformation, (2) for the lactones in type *A* (model compounds, *4* and *7*) the total contributions were assumed very small in the ^3E conformation while in the E_3 conformer the contributions would be strongly positive in accordance with K2 (Or). Consequently, the contributions from E_3 would govern the sign of $[M]_D$ in accordance with the rule even if the $^3E/E_3$ ratio was in favor of ^3E, (3) for type *C* (model compounds *3* and *5*), in both conformers the total contributions would be small or small negative. In this sense, the success of the Hudson rule for *3* and *5* seemed to be a lucky result. However, the success was reasonable because they favored the ^3E conformation in which negative contributions from the *ax.* α-substituent at C-4 (K2 (Or)) are large enough to cancel the positive contributions from C-2 and *vic.* OH.

In conclusion, the success of Hudson's lactone rule for all types of aldonic acid 1,4-lactones was rationalized. Here, it should be favorable for Hudson's rule to use the wavelength at 589 nm where the contributions from the band at 220 nm were almost cancelled by the counter peak at 170 nm and the other contributions. If 300 nm were chosen, the contribution of the band at 220 nm would govern the sign of the optical rotations associated to the C-2 configuration as noted from the data of lactone *3*.

This study and our previous ones on carbohydrate molecules[16–18] using a graphic method of the Drude equation have provided new bands below the 200 nm region which are useful for determining the absolute stereochemistry of chiral compounds. A similar approach has been also reported in carbohydrate field using a vacuum-CD with synchrotron radiation to measure the bands in the 170—180 nm region in trifluoroethanol or in the gas phase and also using a Drude equation to measure the other bands below the 170 nm region[19]. The use of the vacuum CD for chiral lactones will provide more detailed explanations for the $[M]_D$ and Hudson's rule of chiral lactones.

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SAŽETAK

Računanje Cottonovih efekata u području ispod 200 nm za 1,4-laktone aldonskih kiselina i interpretacija Hudsonova laktonskog pravila

Hiroshi Meguro, Yoshihiro Nishida, Hiroshi Ohrui i Toshio Konno

Grafička metoda Drudeove jednadžbe primijenjena je na niz 1,4-laktona aldonskih kiselina (*1*—*7*) da bi se istražili mogući Cottonovi efekti ispod 200 nm. Računi su pokazali da tri vrpce (220 nm, 170 nm i 130 nm) odražavaju stereokemiju na C-2, C-4 te vicinalnih OH-skupina na C-3 i C-4, te konformaciju prstena. Suma njihovih rotacijskih doprinosa vrpci kod 589 nm objašnjava primjenljivost Hudsonova laktonskog pravila na laktone šećera.