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The Rotatory Dispersion and Stereochemistry of Organic Compounds. X.[1] Nitrates of α-Hydroxy-carboxylic Acids

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The rotatory dispersion (RD) and ultraviolet absorption of some α-hydroxy-carboxylic acids and their nitrates have been measured and analyzed. A distinct relation has been found between the configuration and the sign of the Cotton effect; namely, nitrates of α-D-hydroxy-carboxylic acids (R-configuration) show positive Cotton effects, while those of α-L-hydroxy-carboxylic acids (S-configuration) show negative Cotton effects. Thus a rotatory contribution by the nitrates of the α-hydroxyl group has been suggested, though it is opposite in sign to the xanthates of the α-hydroxy-carboxylic acids.

In previous papers[1,2] it has been reported, with various nitrates of glucose, that a regular relation exists between the configuration of the carbon atom carrying a nitrate chromophore and the sign of the Cotton effect; namely, α-glucosides with a nitrate chromophore in the D-configuration show negative Cotton effects, while the sign of the Cotton effects of the corresponding β-glucosides is positive. On the contrary, α-glucosides with a nitrate chromophore in the L-configuration show positive Cotton effects, while the sign of the Cotton effects of the corresponding β-glucosides is negative.

This paper will report similar studies made on the nitrate esters of some aliphatic α-hydroxy-carboxylic acids (compounds II—IV, VI, VII, IX—X, XII), namely, tartaric, malic and lactic acids and their alkyl esters, in order to find the sign of the rotatory contribution of the hydroxyl group and, at the same time, to learn that of the carboxyl group, and thus to confirm the view already expressed in earlier papers[3] that the OH group of α-hydroxy-carboxylic acids of the D-configuration contributes to a positive rotation and the COOH group to a negative rotation.

Results and Discussion

Figure 1 collects the RD curves of the derivatives of D(+)-tartaric acid observed in methanol as well

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[1] Part IX: Y. Tsuzuki, K. Tanabe and K. Okamoto, This Bulletin, **39**, 761 (1966).

[2] Y. Tsuzuki, K. Tanabe and K. Okamoto, ibid., **38**, 274 (1965).

[3] a) Y. Tsuzuki, *Sci. Pap. Inst. Phys. Chem. Res. (Tokyo)*, No. 890, Vol. **35**, 432 (1939); b) *J. Chem. Soc. Japan (Nippon Kwagaku Kwaisi)*, **64**, 282 (1943); c) ibid., **64**, 290 (1943) (in Japanese).

TABLE I. HYDROXY-CARBOXYLIC ACIDS AND THEIR NITRATES

	Compound	
I	Diethyl D(+)-tartrate	$\mathrm{COOC_2H_5}$ H-C-OH HO-C-H $\mathrm{COOC_2H_5}$
II	Diethyl D(+)-tartrate mononitrate	$\mathrm{COOC_2H_5}$ $\mathrm{H\text{-}C\text{-}ONO_2}$ HO-C-H $\mathrm{COOC_2H_5}$
III	Diethyl D(+)-tartrate dinitrate	$\mathrm{COOC_2H_5}$ $\mathrm{H\text{-}C\text{-}ONO_2}$ $\mathrm{O_2NO\text{-}C\text{-}H}$ $\mathrm{COOC_2H_5}$
IV	D(+)-Tartaric acid dinitrate	COOH $\mathrm{H\text{-}C\text{-}ONO_2}$ $\mathrm{O_2NO\text{-}C\text{-}H}$ COOH
V	Dimethyl D(+)-tartrate	$\mathrm{COOCH_3}$ H-C-OH HO-C-H $\mathrm{COOCH_3}$
VI	Dimethyl D(+)-tartrate mononitrate	$\mathrm{COOCH_3}$ $\mathrm{H\text{-}C\text{-}ONO_2}$ HO-C-H $\mathrm{COOCH_3}$
VII	Dimethyl D(+)-tartrate dinitrate	$\mathrm{COOCH_3}$ $\mathrm{H\text{-}C\text{-}ONO_2}$ $\mathrm{O_2NO\text{-}C\text{-}H}$ $\mathrm{COOCH_3}$
VIII	Diethyl L(−)-malate	$\mathrm{COOC_2H_5}$ HO-C-H $\mathrm{CH_2COOC_2H_5}$
IX	Diethyl L(−)-malate nitrate	$\mathrm{COOC_2H_5}$ $\mathrm{O_2NO\text{-}C\text{-}H}$ $\mathrm{CH_2COOC_2H_5}$
X	L(−)-Malic acid nitrate	COOH $\mathrm{O_2NO\text{-}C\text{-}H}$ $\mathrm{CH_2COOH}$
XI	Ethyl D(−)-lactate	$\mathrm{COOC_2H_5}$ H-C-OH $\mathrm{CH_3}$
XII	Ethyl D(−)-lactate nitrate	$\mathrm{COOC_2H_5}$ $\mathrm{H\text{-}C\text{-}ONO_2}$ $\mathrm{CH_3}$

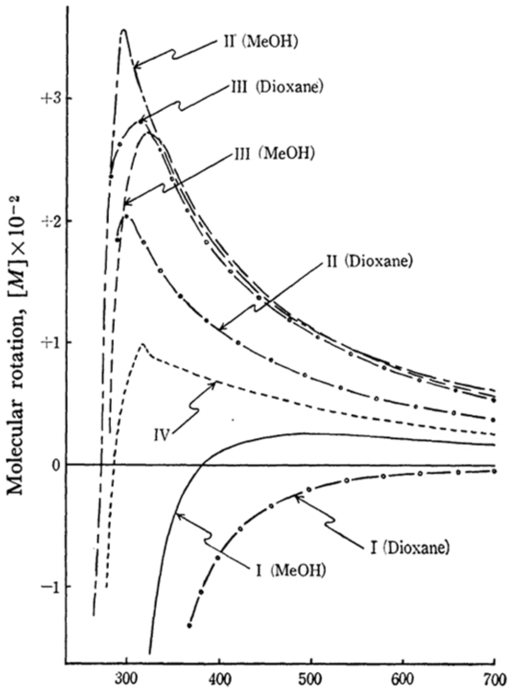

Fig. 1. RD of I—IV.

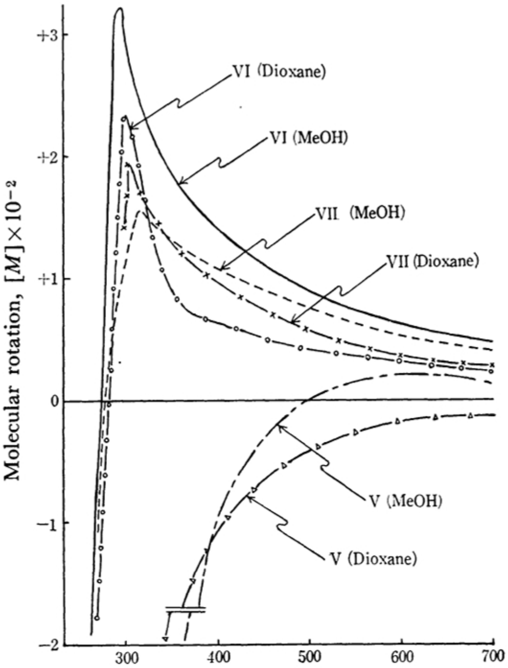

Fig. 2. RD of V—VII.

as in dioxane. The mononitrate (compound II) exhibits a positive Cotton effect with a peak at 294 mμ, and the dinitrates (compounds III and IV) also show positive Cotton effects, the peaks of which both appear at 315 mμ. It should, however, be remarked that some anomalies are visible on the RD curves of these two dinitrates in the region from 330 to 430 mμ, anomalies which can apparently be related to the ultraviolet multiple absorption curves (III and IV) shown in Fig. 4, but the region of the absorption (320—380 mμ) is considerably red-shifted as compared with the peak of the Cotton effect.

In contrast to the dinitrates, a larger decrease in rotation is observed in dioxane than in methanol with the mononitrate (Fig. 1); this decrease is likely to be due to intramolecular hydrogen bond formation in non-polar solvents, as has already been suggested.[3a] Here the intramolecular hydrogen bond may be formed between the OH group and either the carbalkoxy or the nitrate group, whereby the rotatory contribution of the OH group is reduced to a more or less large extent. At any rate, the positive sign of the Cotton effect of the three nitrates agrees with the R-configuration assigned according to the rule of Cahn et al.[4]

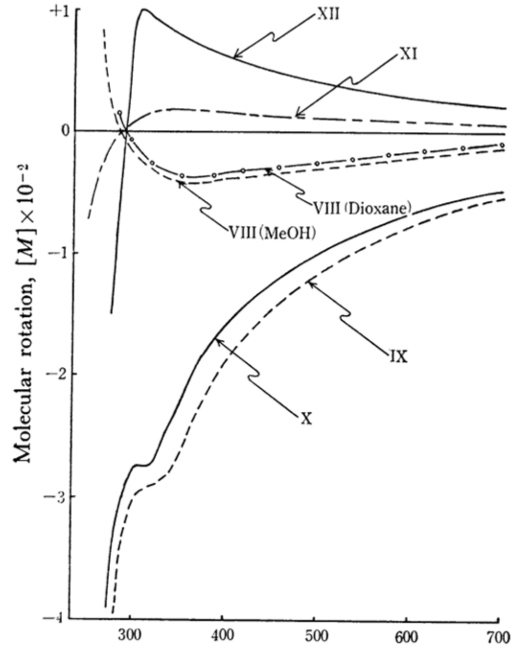

Fig. 3. RD of VIII—XII.

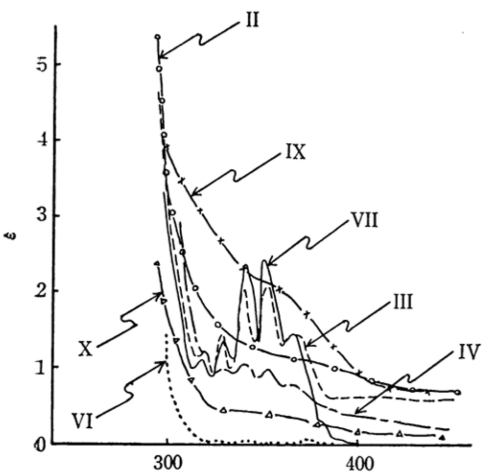

Fig. 4. UV absorption spectra.

In Fig. 2 are shown the RD curves of the mono- and dinitrates of dimethyl D(+)-tartrates (V—VI), observed both in methanol and dioxane. They are not essentially different in their main features from those of Fig. 1. However, the rotation increases in the positive direction in the order:

$$\mathrm{COOH} < \mathrm{COOCH_3} < \mathrm{COOC_2H_5}$$

Figure 3 gives the RD curves of the three derivatives of L(−)-malic acid (VIII—X), as well as those of D(−)-lactic acid (XI—XII). The nitrate of diethyl L(−)-malate (IX) has a feeble negative Cotton effect, with a shoulder in the region from 300 to 320 mμ, the peak being at 303 mμ and the trough at 310 mμ, while the RD curve (IX) can be expressed by the following Drude equation:

$$[M] = \frac{-0.723}{\lambda^2-(0.313)^2} + \frac{-23.82}{\lambda^2-(0.169)^2} \qquad (1)$$

The negative sign of the Cotton effect can also be confirmed by the negative dispersion constant ($A = -0.723$) of the first term of Eq. 1 as well as by the S-configuration of the asymmetric center. The ultraviolet absorption spectrum does not show a fine structure, as do those of the nitrates of tartaric acid, and it has a slight shoulder at 325—380 mμ (IX in Fig. 4).

Thus, it may be concluded that the nitrates of α-hydroxy-carboxylic acids of the D-type (R-configuration) show positive Cotton effects, whereas the nitrates of the L-type (S-configuration) exhibit negative Cotton effects.

It is noteworthy that this conclusion is just the opposite of the observations[5] that all the xanthates of L-hydroxy-carboxylic acids show positive Cotton effects, while those of D-acids exhibit negative Cotton effects. A similar "inversion" of the sign of rotation has been observed in the xanthates of various derivatives of monosaccharides.[6]

As to the correlation between the RD curve and the configuration, lactic acid is expected to provide

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[4] R. S. Cahn, C. K. Ingold and V. Prelog, *Experientia*, **12**, 81 (1956).

[5] A. Fredga, *Svensk. Kem. Tidskr.*, **53**, 221 (1941); **54**, 26 (1942); S. Sjöberg, A. Fredga and C. Djerassi, *J. Am. Chem. Soc.*, **81**, 5002 (1959); C. Djerassi, H. Wolf and E. Bunnenberg, ibid., **84**, 4552 (1962).

[6] Y. Tsuzuki, K. Tanaka and K. Tanabe, This Bulletin, **35**, 1614 (1962); Y. Tsuzuki, K. Tanabe, M. Akagi and S. Tejima, ibid., **37**, 162 (1964); Y. Tsuzuki, K. Tanaka, K. Tanabe, M. Akagi and S. Tejima, ibid., **37**, 730 (1964).

TABLE II. DISPERSION DATA AND CONSTANTS

$$[M] = \frac{A_1}{\lambda^2-\lambda_1^2} + \frac{A_2}{\lambda^2-\lambda_2^2}$$

Compound	Drude's equation				$\lambda_{RD}(\mu)$	Sign of Cotton effect	Configuration4)
	A_1	A_2	$\lambda_1(\mu)$	$\lambda_2(\mu)$			
I	−34.20	+44.68	0.237	0.173			
II	+ 1.29	+27.03	0.312	0.076	0.294	+	R
III	+ 0.815	+29.37	0.303	0.160	0.315	+	R
IV	+ 0.440	+10.3	0.310	0.150	0.315	+	R
V	−36.98	+42.28	0.237	0.173			
VI	+ 0.10	+25.10	0.305	0.207	0.296	+	R
VII	+ 1.58	+15.21	0.300	0.159	0.315	+	R
VIII	+ 2.24	−11.13	0.255	0.000		+	R
XI	− 0.723	−23.82	0.313	0.169		−	S
X	− 1.36	−23.20	0.288	0.000		−	S
XI	− 0.733	+ 3.186	0.255	0.099			
XII	+ 0.496	+ 8.50	0.309	0.158	0.310	+	R

an interesting problem. As may be seen in Fig. 3, ethyl D(−)-lactate really shows a RD curve (XI) quite similar in shape to those of alkyl D(+)-tartrates (I in Fig. 1 and V in Fig. 2); this fact may easily be understood since the lactate coincides with the tartrates in configuration, so that a positive Cotton effect may be expected of the nitrate of D(−)-lactic acid; really, this has already been confirmed with the nitrate of ethyl D(−)-lactate (XII).

Dispersion Constants

The data of the RD measurements were calculated according to a two-term expression of the Drude equation:

$$[M] = \frac{A}{\lambda^2-\lambda_1^2} + \frac{B}{\lambda^2-\lambda_2^2} \tag{2}$$

They have been found to conform to the equation tolerably well, with two exceptions (compounds VIII and X), which can rather better be expressed by an abbreviated form ($\lambda_2=0$).

The dispersion constants of these compounds thus computed are given in Table II, together with some other data on the Cotton effect and on the configuration of the chromophore-bearing asymmetric center.

Experimental

The nitrates of the hydroxy-carboxylic acids and their esters were prepared according to the methods of the literature. The rotatory dispersion was measured with a Rudolph spectropolarimeter over the region from 250 to 700 mμ. The ultraviolet absorption was measured with a Hitachi EPU-II self-recording spectrophotometer. The dispersion constants of the Drude equations were calculated from the data by means of the least-square method with a Fuji FACOM 201 electronic computer.

Diethyl D(+)-Tartrate (Compound I)7)**.**—Colorless syrup, b. p. 157—158°C/11 mmHg. The RD was measured at 17°C in methanol (*c*, 1.3758). $[\alpha]^{17}_{700}$ +8.31°, $[\alpha]_{600}$ +10.7°, $[\alpha]_{589}$ +10.9°, $[\alpha]_{500}$ +14.3°, $[\alpha]_{400}$ +7.12°, $[\alpha]_{350}$ −21.5°, $[\alpha]_{320}$ −75.0°.

Diethyl D(+)-Tartrate Mononitrate (Compound II).8)—Colorless needles, m. p. 46—47°C. The RD was measured at 21°C in methanol (*c*, 0.9970). $[\alpha]^{21}_{700}$ +22.2°, $[\alpha]_{650}$ +27.8°, $[\alpha]_{589}$ +31.6°, $[\alpha]_{500}$ +44.1°, $[\alpha]_{400}$ +69.9°, $[\alpha]_{300}$ +131°, $[\alpha]_{294}$ +142° (peak), $[\alpha]_{280}$ +66.0°, $[\alpha]_{270}$ −39.6°.

Diethyl D(+)-Tartrate Dinitrate (Compound III).7)—Colorless prisms, m. p. 26—27°C. The RD was measured at 20°C in methanol (*c*, 1.1603). $[\alpha]^{20}_{700}$ +20.1°, $[\alpha]_{600}$ +25.9°, $[\alpha]_{589}$ +27.8°, $[\alpha]_{500}$ +35.9°, $[\alpha]_{400}$ +56.8°, $[\alpha]_{315}$ +92.9° (peak), $[\alpha]_{300}$ +74.1°, $[\alpha]_{280}$ +38.6°.

D(+)-Tartaric Acid Dinitrate (Compound IV).9)—White needles, melt with decomp. The RD was measured at 21°C in methanol (*c*, 1.9923). $[\alpha]^{21}_{700}$ +10.4°, $[\alpha]_{600}$ +13.6°, $[\alpha]_{589}$ +14.4°, $[\alpha]_{500}$ +19.6°, $[\alpha]_{400}$ +27.5°, $[\alpha]_{315}$ +41.2° (peak), $[\alpha]_{300}$ +26.1°, $[\alpha]_{280}$ −38.7°.

Dimethyl D(+)-Tartrate (Compound V).7)—Colorless syrup, b. p. 158—158.5°C/12 mmHg. The RD was measured at 18°C in methanol (*c*, 1.2445). $[\alpha]^{18}_{700}$ +2.33°, $[\alpha]_{650}$ +3.70°, $[\alpha]_{589}$ +3.86°, $[\alpha]_{500}$ +0.321°, $[\alpha]_{400}$ −16.6°, $[\alpha]_{330}$ −74.5°.

Dimethyl D(+)-Tartrate Mononitrate (Compound VI).10)—Colorless prisms, m. p. 96—97°C. The RD was measured at 18°C in methanol (*c*, 0.9552). $[\alpha]^{18}_{700}$ +22.0°, $[\alpha]_{600}$ +26.7°, $[\alpha]_{589}$ +27.3°, $[\alpha]_{500}$ +38.4°, $[\alpha]_{400}$ +60.1°, $[\alpha]_{350}$ +79.5°, $[\alpha]_{300}$ +15.3°, $[\alpha]_{290}$ +172° (peak), $[\alpha]_{280}$ +81.8°, $[\alpha]_{270}$ −79.5°, $[\alpha]_{255}$ −706°.

Dimethyl D(+)-Tartrate Dinitrate (Compound VII).10)—Colorless prisms, m. p. 75°C. The RD was measured at 20°C in methanol (*c*, 0.5028). $[\alpha]^{20}_{700}$ +15.6°, $[\alpha]_{600}$ +20.3°, $[\alpha]_{589}$ +21.0°, $[\alpha]_{500}$ +29.6°, $[\alpha]_{400}$ +40.8°, $[\alpha]_{350}$ +47.4°, $[\alpha]_{315}$ +57.4° (peak), $[\alpha]_{295}$ +33.0°, $[\alpha]_{280}$ −9.00°, $[\alpha]_{270}$ −39.8°.

Diethyl L(−)-Malate (Compound VIII).7)—Colorless syrup, b. p. 128°C/10 mmHg. The RD was

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7) E. Fischer and A. Speyer, *Ber.*, **28**, 3255 (1895).

8) P. Frankland, H. L. Heathcote and F. Hartle, *J. Chem. Soc.*, **83**, 157 (1903).

9) A. Lachman, *J. Am. Chem. Soc.*, **43**, 577 (1921).

10) P. Walden, *Ber.*, **35**, 4366 (1902); **36**, 778 (1903).

measured at 19°C in methanol (*c*, 2.6240). $[\alpha]^{19}_{700}$ $-7.67°$, $[\alpha]_{600}$ $-10.6°$, $[\alpha]_{589}$ $-11.1°$, $[\alpha]_{500}$ $-14.8°$, $[\alpha]_{400}$ $-20.7°$, $[\alpha]_{355}$ $-22.4°$, $[\alpha]_{300}$ $-11.5°$, $[\alpha]_{280}$ $+10.3°$, $[\alpha]_{270}$ $+34.0°$.

Diethyl L(−)-Malate Nitrate (Compound IX).[11]—Colorless syrup, b. p. 148°C/25 mmHg. The RD was measured at 21°C in methanol (*c*, 0.6321). $[\alpha]^{21}_{700}$ $-22.3°$, $[\alpha]_{600}$ $-32.3°$, $[\alpha]_{589}$ $-33.8°$, $[\alpha]_{500}$ $-48.2°$, $[\alpha]_{400}$ $-79.1°$, $[\alpha]_{350}$ $-110°$, $[\alpha]_{320}$ $-123°$, $[\alpha]_{300}$ $-127°$, $[\alpha]_{290}$ $-146°$, $[\alpha]_{275}$ $-235°$.

L(−)-Malic Acid Nitrate (Compound X).[12]—White needles, m. p. 111°C at 112°C with decomp. The RD was measured at 21°C in methanol (*c*, 1.1822). $[\alpha]^{21}_{700}$ $-27.1°$, $[\alpha]_{600}$ $-36.4°$, $[\alpha]_{589}$ $-38.0°$, $[\alpha]_{500}$ $-53.8°$, $[\alpha]_{400}$ $-87.5°$, $[\alpha]_{350}$ $-124°$, $[\alpha]_{310}$ $-154°$ (trough), $[\alpha]_{303}$ $-152°$ (peak), $[\alpha]_{300}$ $-154°$, $[\alpha]_{275}$ $-231°$.

Ethyl D(−)-Lactate (Compound XI).[13]—Colorless syrup, b. p. 65—66°C/27 mmHg. A sample of D(−)-lactic acid of 50% optical purity furnished by the Kyowa Hakko Kogyo Co. was esterified with *p*-toluenesulfonic acid.[13] The RD was measured at 20°C in the liquid state. $[\alpha]^{20}_{700}$ $+4.86°$, $[\alpha]_{589}$ $+6.25°$, $[\alpha]_{500}$ $+8.42°$, $[\alpha]_{400}$ $+11.9°$, $[\alpha]_{350}$ $+12.8°$, $[\alpha]_{300}$ $+7.17°$, $[\alpha]_{280}$ $-4.20°$, $[\alpha]_{265}$ $-23.7°$.

Ethyl D(−)-Lactate Nitrate (Compound XII).[14]—Colorless syrup, b. p. 58.0°C/31 mmHg. Optical purity 50%. The RD was measured at 22°C in methanol (*c*, 3.3890). $[\alpha]^{22}_{700}$ $+20.6°$, $[\alpha]_{589}$ $+28.6°$, $[\alpha]_{500}$ $+39.6°$, $[\alpha]_{400}$ $+62.5°$, $[\alpha]_{350}$ $+80.4°$, $[\alpha]_{310}$ $+99.9°$ (peak), $[\alpha]_{300}$ $+92.5°$, $[\alpha]_{290}$ $-1.66°$, $[\alpha]_{275}$ $-97.8°$.

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[11] G. E. Holm and R. Berg, ibid., **61**, 1888 (1928).
[12] A. Lachman, *J. Am. Chem. Soc.*, **43**, 2084 (1921).
[13] Y. Tsuzuki, *J. Chem. Soc. Japan (Nippon Kwagaku Kwaisi)* **64**, 297 (1943) (in Japanese).
[14] L. Henry, *Ber.*, **3**, 529 (1870).