Synthesis of Cyclic Derivatives of Tartaric Acid by Condensing Alkyl *d*-Tartrates with Aliphatic Ketones. (Optical Activity and Chemical Structure in Tartaric Acid. V.*)

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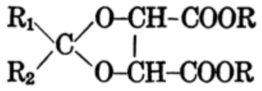
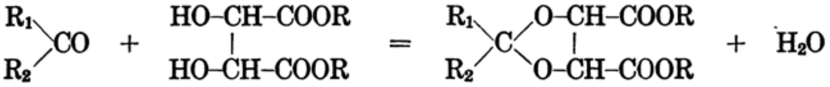
It was reported in the previous communications⁽¹⁾ that various cyclic derivatives of tartaric acid having the constitution


(I)

were synthesized by condensing alkyl *d*-tartrates with some aliphatic aldehydes and ketones as well as with alicyclic ketones. These compounds are suitable materials for the study of the relation between optical activity and chemical structure of tartaric acid, since they are all liquid compounds showing high lævo-rotation and exhibiting simple rotatory dispersion. And, indeed, the author has shown that the groups R_1, R_2 and R exert a certain definite effect on the optical rotatory power of the condensation products, in good agreement with the requirement of the molecular theories of de Mallemann⁽²⁾ as well as of Boys.⁽³⁾

The purpose of the present work is to amplify the materials by condensing alkyl *d*-tartrates with a series of aliphatic ketones, in order to observe how the substituents R_1, R_2 and R influence the optical activity of the resulting compounds.



The following condensations were carried out: ethyl *d*-tartrate with methyl ethyl ketone, methyl propyl ketone, diethyl ketone, methyl amyl ketone, dipropyl ketone and with methyl nonyl ketone, and in addition to these, methyl ethyl ketone with methyl *d*-tartrate, propyl *d*-tartrate and with isopropyl *d*-tartrate. The method of condensation was almost the same as in the cases of alicyclic ketones with ethyl *d*-tartrate⁽⁴⁾ using also in this case phosphorus pentoxide as the condensation reagent. It is, however, to be noted that in the cases of symmetrical ketones, the temperature of the reaction must be lower and the duration of the reaction must accordingly be longer than in the cases of unsymmetrical ketones.

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* Paper IV, this Bulletin, **12** (1937), 487.

(1) Y. Tsuzuki, this Bulletin, **10** (1935), 255; **11** (1936), 362; **11** (1936), 586; **12** (1937), 487.

(2) R. de Mallemann, *Trans. Faraday Soc.*, **26** (1930), 281.

(3) F. S. Boys, *Proc. Roy. Soc.* (London), A, **144** (1934), 655.

(4) Y. Tsuzuki, this Bulletin, **12** (1937), 487.

The condensation proceeds very smoothly in every case. The yield is fairly good, being 30–50% of the theoretical amount. The purification of the product is carried out in the same way as before, i.e. by evaporating off unchanged ketone and by dissolving out unchanged alkyl tartrate with aqueous borax. In the cases of propyl and isopropyl tartrates the purification is somewhat difficult, since these tartrates are not so easily soluble in borate; in these cases the above process of purification must be repeatedly performed, whereby the yield was somewhat impoverished.

The condensation products thus obtained and purified are transparent colourless liquids, showing strong lævo-rotation. Optical rotatory powers have also been measured in ethyl alcohol, in benzene and in cyclohexane. The optical activity and its solvent effect will be discussed in the following paper.

Ethyl methylethylmethylene-*d*-tartrate.

$C_{12}H_{20}O_6$ (260.16). (I) $R_1 = CH_3$, $R_2 = C_2H_5$, $R = C_2H_5$

To a mixture of 15 g. ethyl *d*-tartrate and 15 g. methyl ethyl ketone (Takeda's product, fractionated, b.p. 78.3–79°) was added 8 g. phosphorus pentoxide in portions at 70° during a period of 30 minutes. The liquid coloured pale yellow and the phosphorus pentoxide deeply brownish red. After the whole of phosphorus pentoxide was added, the mixture was maintained at this temperature for 30 minutes, and after cooling, the reaction product was extracted with ether. The ethereal solution was washed several times with a saturated solution of borax to remove unchanged ethyl *d*-tartrate and was finally dried over anhydrous sodium sulphate. After evaporating off the ether, the product was purified by fractional distillation in vacuo. Colourless liquid. Yield 8.5 g. Boiling point 158° (17 mm.), n_D^{20} 1.4361, d_4^{20} 1.0973, M_D 61.99 (62.01), $[\alpha]_D^{20}$ −35.02°, $[M]_D^{20}$ −91.10°. $[\alpha]_D^{20}$ −36.0° (in ethyl alcohol, 4.45%), $[M]_D^{20}$ −91.5° (in ethyl alcohol). $[\alpha]_D^{20}$ −40.2° (in benzene, 5.232%), $[M]_D^{20}$ −104.6° (in benzene). $[\alpha]_D^{20}$ −31.62° (in cyclohexane, 3.265%), $[M]_D^{20}$ −82.25° (in cyclohexane).

Ethyl methylpropylmethylene-*d*-tartrate.

$C_{13}H_{22}O_6$ (274.18). (I) $R_1 = CH_3$, $R_2 = C_3H_7$, $R = C_2H_5$

Ethyl *d*-tartrate (21 g.) and 13 g. methyl propyl ketone (Takeda's product, fractionated, b.p. 100–102°) gave 9 g. pure product. Colourless liquid boiling at 167.5° (20 mm.). n_D^{20} 1.4370, d_4^{20} 1.0770, M_D 66.69 (66.62), $[\alpha]_D^{20}$ −32.05°, $[M]_D^{20}$ −87.88°. $[\alpha]_D^{20}$ −31.8° (in ethyl alcohol, 5.400%), $[M]_D^{20}$ −87.2° (in ethyl alcohol). $[\alpha]_D^{20}$ −36.4° (in benzene, 5.534%), $[M]_D^{20}$ −99.8° (in benzene). $[\alpha]_D^{20}$ −28.86° (in cyclohexane, 3.611%), $[M]_D^{20}$ −79.14° (in cyclohexane).

Ethyl diethylmethylene-*d*-tartrate.

$C_{13}H_{22}O_6$ (274.18). (I) $R_1 = R_2 = C_2H_5$, $R = C_2H_5$

Ethyl *d*-tartrate (21 g.) and 13 g. diethyl ketone (Takeda's product, fractionated, b.p. 100–102°) gave 10.5 g. pure condensation product, when 20 g. P_2O_5 was added to the mixture at 60–70° during 50 minutes. Almost colourless liquid boiling at 169° (22 mm.). n_D^{20} 1.4390, d_4^{20} 1.0850, M_D 66.45 (66.62), $[\alpha]_D^{20}$ −23.06°, $[M]_D^{20}$ −63.23°. $[\alpha]_D^{20}$ −25.3° (in ethyl alcohol, 4.854%),

$[M]_D^{20}$ −69.4° (in ethyl alcohol). $[\alpha]_D^{20}$ −33.0° (in benzene, 5.108%), $[M]_D^{20}$ −90.5° (in benzene). $[\alpha]_D^{20}$ −20.89° (in cyclohexane, 3.631%), $[M]_D^{20}$ −57.27° (in cyclohexane).

Ethyl methylamylmethylene-*d*-tartrate.

$C_{15}H_{26}O_6$ (302.21). (I) $R_1 = CH_3$, $R_2 = C_5H_{11}$, $R = C_2H_5$

To a mixture of 12.6 g. ethyl *d*-tartrate and 7 g. methyl amyl ketone (Takeda's product, fractionated, b.p. 148°) was added 13 g. phosphorus pentoxide at 80–90°, during a period of 50 minutes, and heating was continued for one hour to maintain this temperature. Yield 8 g. Colourless liquid boiling at 180° (15 mm.), n_D^{20} 1.4399, d_4^{20} 1,0478, M_D 76.00 (75.87), $[\alpha]_D^{20}$ −26.59°, $[M]_D^{20}$ −80.36°. $[\alpha]_D^{20}$ −27.33° (in ethyl alcohol, 6.917%), $[M]_D^{20}$ −82.6° (in ethyl alcohol). $[\alpha]_D^{20}$ −31.13° (in benzene, 4.7656%), $[M]_D^{20}$ −94.1° (in benzene). $[\alpha]_D^{20}$ −24.19° (in cyclohexane, 4.2583%), $[M]_D^{20}$ −73.10° (in cyclohexane).

Ethyl dipropylmethylene-*d*-tartrate.

$C_{15}H_{26}O_6$ (302.21). (I) $R_1 = R_2 = C_3H_7$, $R = C_2H_5$

To a mixture of 15 g. ethyl *d*-tartrate and 8.3 g. di-*n*-propyl ketone (prepared from *n*-butyric acid by passing it over ThO_2 at 380–480°, b.p. 142–144°) was added 15 g. P_2O_5 at 80–90°. Yield 6 g. Pure colourless liquid boiling at 175°(16 mm.), n_D^{20} 1.4424, d_4^{20} 1.0521, M_D 76.07 (75.87), $[\alpha]_D^{20}$ −19.77°, $[M]_D^{20}$ −59.74°. $[\alpha]_D^{20}$ −22.45° (in ethyl alcohol, 6.000%), $[M]_D^{20}$ −67.86° (in ethyl alcohol). $[\alpha]_D^{20}$ −28.47° (in benzene, 5.126%), $[M]_D^{20}$ −86.03° (in benzene). $[\alpha]_D^{20}$ −18.17° (in cyclohexane, 5.952%), $[M]_D^{20}$ −54.91° (in cyclohexane).

Ethyl methylnonylmethylene-*d*-tartrate.

$C_{19}H_{34}O_6$ (358.27). (I) $R_1 = CH_3$, $R_2 = C_9H_{19}$, $R = C_2H_5$

To a mixture of 10 g. ethyl *d*-tartrate and 8.5 g. methyl nonyl ketone (Th. Schuchardt) was added 10 g. P_2O_5 in portions at 90° during one hour, and the reaction mixture was further heated at 80° for one hour. Yield 6 g. Colourless liquid boiling at 218° (15 mm.), n_D^{20} 1.4465, d_4^{20} 1.0086, M_D 94.82 (94.34), $[\alpha]_D^{20}$ −21.33°, $[M]_D^{20}$ −76.41°. $[\alpha]_D^{20}$ −21.38° (in ethyl alcohol, 7.5645%), $[M]_D^{20}$ −76.59° (in ethyl alcohol). $[\alpha]_D^{20}$ −26.03° (in benzene, 5.9822%), $[M]_D^{20}$ −93.44° (in benzene). $[\alpha]_D^{20}$ −18.93° (in cyclohexane, 5.4008%), $[M]_D^{20}$ −67.82° (in cyclohexane).

Methyl methylethylmethylene-*d*-tartrate.

$C_{10}H_{16}O_6$ (232.16). (I) $R_1 = CH_3$, $R_2 = C_2H_5$, $R = CH_3$

Methyl *d*-tartrate (15 g.), b.p. 163° (20 mm.), and 15 g. methyl ethyl ketone gave 9 g. pure colourless liquid boiling at 141° (15 mm.). n_D^{20} 1.4420, d_4^{20} 1.1607, M_D 52.92 (52.87), $[\alpha]_D^{20}$ −35.79°, $[M]_D^{20}$ −83.08°.

Propyl methylethylmethylene-*d*-tartrate.

$C_{14}H_{24}O_6$ (288.19). (I) $R_1 = CH_3$, $R_2 = C_2H_5$, $R = C_3H_7$

Propyl *d*-tartrate (15 g.), b.p. 171° (15 mm.), and 15 g. methyl ethyl ketone gave 9 g. pure product. To remove the unreacted propyl *d*-tartrate, the ethereal extract of the mixture must be repeatedly washed with borax solution, since the ester is not so easily soluble in this solution as ethyl *d*-tartrate. Pale yellow liquid. Boiling point 167° (15 mm.). n_D^{20} 1.4399, d_4^{20} 1.0603, M_D 71.62 (71.25), $[\alpha]_D^{20}$ −30.07°, $[M]_D^{20}$ −86.65°.

Isopropyl methylethylmethylene-*d*-tartrate.

$C_{14}H_{24}O_6$ (288.19). (I) $R_1 = CH_3$, $R_2 = C_2H_5$, $R = (CH_3)_2CH$

To a mixture of 15 g. isopropyl *d*-tartrate, b.p. 155° (17 mm.), and 15 g. methyl ethyl ketone was added 15 g. phosphorus pentoxide at 70° in portions during one hour. The phosphorus oxide coloured deep brown but the liquid not so strongly. The liquid was decanted from the dehydrating reagent, and the unchanged ketone was evaporated off. The ethereal extract of the residual liquid was washed with N/2 KBO_2,⁽⁵⁾ in order to remove the unreacted isopropyl tartrate, dried over sodium sulphate, and fractionated in vacuo. This process of purification was repeated once. Yield 8 g. Colourless liquid. Boiling point 115–117° (0.5 mm.). n_D^{20} 1.43321, d_4^{20} 1.0460, M_D 71.63 (71.25), $[\alpha]_D^{20}$ −30.32°, $[M]_D^{20}$ −87.36°.

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(5) The high efficiency of the use of KBO_2 in the separation has been clearly shown by quantitative studies, Y. Tsuzuki, this Bulletin, **13** (1938), 337.