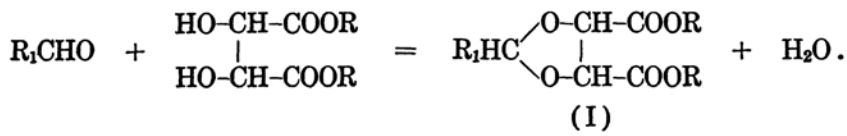
Synthesis of Cyclic Derivatives of Tartaric Acid by Condensing Alkyl *d*-Tartrates with Aromatic Aldehydes. (Optical Activity and Chemical Structure in Tartaric Acid. VI.*)

By Yojiro TSUZUKI.

(Received January 10, 1939.)

In a paper of a series of synthetic studies on the cyclic derivatives of tartaric acid, the author has noticed that a substituent exerts a certain remarkable effect due to the position on the optical activity of the compound, and has pointed out that this effect is closely related with the phenomena of light-absorption, so that it must be considered as a definitely electronic effect.(1)

The purpose of the present work is to prepare cyclic compounds of similar structure by condensing alkyl *d*-tartrates with various aromatic aldehydes, in order to investigate the electronic effect of a substituent on optical activity by observing how the position and the chemical nature of a substituent in the aromatic nucleus of the resulting compounds affect the optical activity.



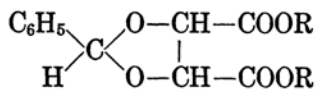
(I)

The condensation of tartaric acid and its esters with benzaldehyde has already been reported by several authors, and the products were used for the study of the optical activity of tartaric acid, since they are strongly

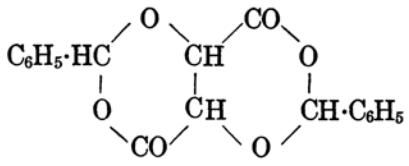
* Paper V: this Bulletin, **14** (1939), 19.

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

lævo-rotatory and their behaviours with respect to the optical activity are simple. Thus B. Jones[2] obtained methyl and ethyl benzylidene-tartrates (II, R = CH_3 and C_2H_5) by condensing respective tartaric esters with benzaldehyde by means of phosphorus pentoxide as dehydrating agent, and showed that their rotatory dispersions are simple. Dibenzylidene-tartrate (III) was obtained by van Ekenstein and Blanksma[3] and its rotatory dispersion was shown by Austin[4] to be also simple. Various derivatives of this compound were prepared by J. W. Pette[5] from tartaric acid and aldehydes by the action of phosphorus pentoxide.



(II)



(III)

The author has carried out the condensations of ethyl *d*-tartrate with *o*-, *m*- and *p*-nitrobenzaldehydes, *o*- and *m*-hydroxybenzaldehydes, *p*-methoxybenzaldehyde, *o*-, *m*- and *p*-chlorobenzaldehydes, piperonal, and with cinnamic aldehyde, and further the condensation of benzaldehyde with propyl, butyl and benzyl *d*-tartrates. Phosphorus pentoxide was always used as the condensing agent with great advantage.

The general method of preparation is analogous to that of the former cases, but the temperature of the reaction must be suitably regulated according to the stability of the aldehyde. In the cases of chlorobenzaldehydes, the temperature is the highest, while in the cases of hydroxybenzaldehydes it is far lower and in the case of cinnamic aldehyde it is the lowest.

Many of the condensation products are solids of low melting points. The optical rotatory power was observed in ethyl alcohol, benzene, and cyclohexane. The magnitudes of their optical activities are found various. Some of them are strongly negative, while some others less negative, and even positive. Discussion will be made on this subject in the next paper.

Ethyl *o*-Nitrobenzylidene-*d*-tartrate (I, R_1 = *o*-$NO_2 \cdot C_6H_4$, R = C_2H_5). To a solution of 7 g. *o*-nitrobenzaldehyde (Kahlbaum) and 10 g. ethyl *d*-tartrate was added 7 g. phosphorus pentoxide in portions at 80–100° in the course of 40 minutes, and the mixture was kept at this temperature for further 15 minutes. The reaction mixture was poured into 50 c.c. water, when the condensation product appeared as a yellow oil, which was solidified on repeatedly rubbing it in fresh water. It was purified by recrystallisation from 80% ethyl alcohol. Pale yellow needles. Yield

(2) B. Jones, *J. Chem. Soc.*, **1933**, 788. H. O. L. Fischer and H. Appel used zinc chloride as the dehydrating agent in preparing the methyl ester, *Helv. Chim. Acta*, **17** (1934), 1581.

(3) *Rec. trav. chim.*, **25** (1906), 162.

(4) T. M. Lowry, "Optical Rotatory Power," 290, London (1935).

(5) J. W. Pette, *Rec. trav. chim.*, **53** (1934), 967.

2.3 g. Melting point 60°. $[\alpha]_D^{20}$ +40.3°, $[M]_D^{20}$ +136.7° (in ethyl alcohol, 3.618%). $[\alpha]_D^{20}$ +34.3°, $[M]_D^{20}$ +116.3° (in benzene, 4.864%). $[\alpha]_D^{20}$ +6.9°, $[M]_D^{20}$ +23.4° (in cyclohexane, 0.6726%). Found: N, 4.21. Calc. for $C_{15}H_{17}NO_8$ (339.14): N, 4.13%.

Ethyl *m*-Nitrobenzylidene-*d*-tartrate. To a mixture of 5 g. *m*-nitrobenzaldehyde (Kahlbaum) and 7 g. ethyl *d*-tartrate was added 8 g. phosphorus pentoxide in portions at 115–125° in the course of 40 minutes and the heating of the mixture was continued at that temperature for 30 minutes. The brown liquid was poured into cold water. The separating brown oil was solidified by repeatedly rubbing in cold water. It was purified by recrystallising four times from absolute alcohol. Pale yellow needles. Melting point 43.5–44°. Yield 3 g. $[\alpha]_D^{20}$ −35.65°, $[M]_D^{20}$ −120.9° (in alcohol, 3.295%). $[\alpha]_D^{20}$ −37.35°, $[M]_D^{20}$ −126.7° (in benzene, 7.638%). $[\alpha]_D^{20}$ −26.1°, $[M]_D^{20}$ −88.3° (in cyclohexane, 1%). Found: N, 4.37. Calc. for $C_{15}H_{17}NO_8$ (339.14): N, 4.13%.

Ethyl *p*-Nitrobenzylidene-*d*-tartrate. Phosphorus pentoxide (8 g.) was added in portions to a mixture of 6 g. *p*-nitrobenzaldehyde (Kahlbaum) and 8.5 g. ethyl *d*-tartrate at 100–108° in the course of 25 minutes, and heating was continued for 15 minutes. Yield 4 g. Pale yellow needles (from absolute alcohol) melting at 59–59.5°. $[\alpha]_D^{20}$ −22.2°, $[M]_D^{20}$ −75.2° (in alcohol, 2.113%). $[\alpha]_D^{20}$ −25.5°, $[M]_D^{20}$ −86.5° (in benzene, 6.136%). $[\alpha]_D^{20}$ −15.4°, $[M]_D^{20}$ −52.3° (in cyclohexane, 0.77%). Found: N, 4.27. Calc. for $C_{15}H_{17}NO_8$ (339.14): N, 4.13%.

Ethyl *o*-Hydroxybenzylidene-*d*-tartrate (I, $R_1 = o\text{-}OH\cdot C_6H_4$, $R = C_2H_5$). To a mixture of 5 g. salicylaldehyde (Takeda) and 8.5 g. ethyl *d*-tartrate was added 7 g. phosphorus pentoxide in portions at 40–50° in the course of 30 minutes. The reaction mixture was poured into cold water. The separating oil resisted solidification. Purification was done by precipitating four times from ethyl alcoholic solution with water, and washing with petroleum ether. Colourless crystals. Yield 2 g. Melting point 59° after sintering. $[\alpha]_D^{20}$ −35.8°, $[M]_D^{20}$ −111.3° (in alcohol, 1.6%). $[\alpha]_D^{20}$ −55.1°, $[M]_D^{20}$ −170.8° (in benzene, 3%). $[\alpha]_D^{20}$ −53.7°, $[M]_D^{20}$ −166° (in cyclohexane, 0.4%). Saponification equivalent: 154.4. Calc. for $C_{15}H_{18}O_7$: 155.07.

Ethyl *m*-Hydroxybenzylidene-*d*-tartrate. To a mixture of 4.7 g. *m*-hydroxybenzaldehyde (Th. Schuchardt) and 8 g. ethyl *d*-tartrate was added 8 g. phosphorus pentoxide in portions at 70–80° in the course of 30 minutes. The reaction product was poured into water, when a brown oil separated out. The oil was purified by precipitating from water–alcohol three times and finally by distilling in vacuum. Colourless crystals. Melting point 37–38.5°. Boiling point 207° (0.5 mm.). Difficultly soluble in cyclohexane. $[\alpha]_D^{20}$ −32.5°, $[M]_D^{20}$ −101° (in alcohol, 5.5%). $[\alpha]_D^{20}$ −26.1°, $[M]_D^{20}$ −80.9° (in benzene, 1.138%). Saponification equivalent: 155.1. Calc. for $C_{15}H_{18}O_7$: 155.07.

Ethyl *p*-Methoxybenzylidene-*d*-tartrate (I, $R_1 = p\text{-}CH_3O\cdot C_6H_4$, $R = C_2H_5$). To a mixture of 7 g. aubepine (Merck) and 10 g. ethyl *d*-tartrate

was added 10 g. phosphorus pentoxide at 50–60° in the course of 30 minutes and the reaction mixture was heated at 65° for one hour. The ethereal extract of the reaction product, washed repeatedly with a concentrated solution of KBO_2, dried over anhydrous sodium sulphate, and fractionated in vacuum, gave 5 g. pale yellow viscous liquid boiling at 183° (0.3 mm.). $[\alpha]_D^{20}$ −27.86°, $[M]_D^{20}$ −90.3° (in alcohol, 3.604%). $[\alpha]_D^{20}$ −26.87°, $[M]_D^{20}$ −87.09° (in benzene, 6.570%). $[\alpha]_D^{20}$ −18.3°, $[M]_D^{20}$ −59.4° (in cyclohexane, 1.364%). Saponification equivalent: 161.0. Calc. for $C_{16}H_{20}O_7$: 162.08.

Ethyl *o*-Chlorobenzylidene-*d*-tartrate (I, R_1 = *o*-Cl·C_6H_4, R = C_2H_5). To a solution of 5.5 g. *o*-chlorobenzaldehyde (Takeda) and 8 g. ethyl *d*-tartrate was added 8 g. phosphorus pentoxide at 100–120° in the course of 40 minutes. The reaction product was poured into cold water. The separating oil, reprecipitated twice from ethyl alcohol with water, suddenly solidified to colourless crystals. Melting point 36–36.5°. Yield 6 g. $[\alpha]_D^{20}$ −15.9°, $[M]_D^{20}$ −52.2° (in alcohol, 4.164%). $[\alpha]_D^{20}$ −28.6°, $[M]_D^{20}$ −94.0° (in benzene, 8.158%). $[\alpha]_D^{20}$ −22.1°, $[M]_D^{20}$ −72.6° (in cyclohexane, 1.358%). Found: Cl, 10.41 (Piria-Schiff). Calc. for $C_{15}H_{17}O_6Cl$ (328.60): Cl, 10.79%.

Ethyl *m*-Chlorobenzylidene-*d*-tartrate. To a mixture of 3.05 g. *m*-chlorobenzaldehyde[6] and 4.50 g. ethyl *d*-tartrate was added 5 g. phosphorus pentoxide at 100° in the course of 40 minutes and the heating was continued for 20 minutes. The liquid was more easily coloured than in the case of the *o*-compound. The reaction product, poured into water, reprecipitated twice from water–alcohol, and finally fractionated in vacuum, gave 3 g. colourless crystals. Boiling point 153° (1 mm.). Melting point 29–30°. $[\alpha]_D^{20}$ −31.44°, $[M]_D^{20}$ −103.3° (in alcohol, 3.455%). $[\alpha]_D^{20}$ −30.16°, $[M]_D^{20}$ −99.10° (in benzene, 2.171%). $[\alpha]_D^{20}$ −18.47°, $[M]_D^{20}$ −60.7° (in cyclohexane, 1.3205%). Found: Cl, 10.64 (Piria-Schiff). Calc. for $C_{15}H_{17}O_6Cl$ (328.60): Cl, 10.79%.

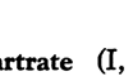
Ethyl *p*-Chlorobenzylidene-*d*-tartrate. To a mixture of 3 g. *p*-chlorobenzaldehyde[7] and 6 g. ethyl *d*-tartrate was added 5 g. phosphorus pentoxide at 110–120° in the course of 40 minutes. The phosphoric acid was coloured reddish, but the liquid only faintly yellow, and the heating was continued for further 30 minutes. The reaction product was extracted with ether. The ethereal solution, shaken thrice with concentrated KBO_2, dried over sodium sulphate, and fractionated in vacuum, gave a viscous pale yellowish liquid (4 g.) boiling at 180° (0.5 mm.). $[\alpha]_D^{20}$ −28.1°, $[M]_D^{20}$ −92.3° (in alcohol, 1.496%). $[\alpha]_D^{20}$ −26.8°, $[M]_D^{20}$ −88.2° (in benzene, 3.955%). $[\alpha]_D^{20}$ −14.7°, $[M]_D^{20}$ −48.3° (in cyclohexane, 1.302%). Found: Cl, 10.42 (Piria-Schiff). Calc. for $C_{15}H_{17}O_6Cl$ (328.60): Cl, 10.79%.

Ethyl Cinnamylidene-*d*-tartrate (I, R_1 = C_6H_5·CH:CH, R = C_2H_5). To a solution of 5.12 g. cinnamic aldehyde (Shuzui) and 8 g. ethyl *d*-

(6) Prepared from *m*-nitrobenzaldehyde (Kahlbaum), b.p. 105° (25 mm.), "Organic Syntheses," **13**, 28.

(7) Prepared from *p*-chlorotoluene, b.p. 98° (18 mm.), m.p. 47°, "Organic Syntheses," **12**, 12.

tartrate was added 8 g. phosphorus pentoxide in portions with gentle warming. The brownish-coloured liquid was poured into water. The separating oil was reprecipitated twice from dilute alcohol, solidified, and recrystallised from petroleum ether. Colourless crystals melting at 54.4°. Yield 1.5 g. $[\alpha]_D^{20}$ −3.70°, $[M]_D^{20}$ −11.9° (in alcohol, 4.046%). $[\alpha]_D^{20}$ −21.0°, $[M]_D^{20}$ −67.3° (in benzene, 4.348%). $[\alpha]_D^{20}$ +12.5°, $[M]_D^{20}$ +40° (in cyclohexane, 0.697%). Saponification equivalent: 161.8. Calc. for $C_{17}H_{20}O_6$: 160.08.

Ethyl 3,4-Methylenedioxybenzylidene-*d*-tartrate (I, $R_1 =$  , $R = C_2H_5$). To a mixture of 5.1 g. piperonal (Merck) and 7 g. ethyl *d*-tartrate was added 6 g. phosphorus pentoxide in portions at 60° in the course of 30 minutes. The deeply coloured liquid was poured into water and repeatedly rubbed in water. The solidified product was recrystallised from ethyl alcohol four times. Colourless silky needles. Yield 1 g. Melting point 40.5–41.5°. $[\alpha]_D^{18}$ −32.6°, $[M]_D^{18}$ −110° (in alcohol, 2.715%). $[\alpha]_D^{18}$ −31.0°, $[M]_D^{18}$ −105° (in benzene, 4.010%). $[\alpha]_D^{20}$ −18.9°, $[M]_D^{20}$ −63.8° (in cyclohexane, 0.958%). Saponification equivalent: 169.6. Calc. for $C_{16}H_{18}O_8$: 169.07.

Propyl Benzylidene-*d*-tartrate (I, $R_1 = C_6H_5$, $R = C_3H_7$). To a solution of dipropyl *d*-tartrate (16 g.) and freshly distilled benzaldehyde (15 g.) was added 15 g. phosphorus pentoxide in portions at 60–70°. The liquid was coloured deeply brown. The product was extracted with ether. The ethereal solution was washed by shaking with KBO_2 solution five times. After evaporating off ether and benzaldehyde, the residue was fractionated in vacuum. This process of purification was once repeated. Colourless liquid boiling at 169° (0.3 mm.). Yield 9 g. d_4^{20} 1.1333. n_D^{20} 1.4882, M_D 81.93 (81.50). $[\alpha]_D^{20}$ −35.87°, $[M]_D^{20}$ −115.6° (homog.). Found: C, 63.50; H, 6.96. Calc. for $C_{17}H_{22}O_6$ (322.18): C, 63.32; H, 6.88%.

Butyl Benzylidene-*d*-tartrate (I, $R_1 = C_6H_5$, $R = C_4H_9$). To a solution of dibutyl *d*-tartrate (15 g.) and freshly distilled benzaldehyde (8 g.) was added 10 g. phosphorus pentoxide in portions at 60° in the course of 30 minutes, and thereafter heated at 60–70° further for 30 minutes. The liquid mixture was deeply coloured. The ethereal extract was shaken with N/2 KBO_2 four times and once with water, and dried over sodium sulphate. After evaporating off ether, the residue was fractionally distilled. Almost colourless liquid. Yield 9 g. Purification is effected by shaking the ethereal solution with N/2 KBO_2 several times, drying over sodium sulphate, and by fractional distillation in vacuum. This process was once repeated. Colourless liquid. Boiling point 189–190° (0.2 mm.). d_4^{20} 1.1004, d_4^{25} 1.0974. n_D^{25} 1.4830, M_D 91.14 (90.74). $[\alpha]_D^{20}$ −31.22°, $[M]_D^{20}$ −109.3° (homog.). Found: C, 65.08; H, 7.24. Calc. for $C_{19}H_{26}O_6$ (350.21): C, 65.10; H, 7.48%.

Benzyl Benzylidene-*d*-tartrate (I, $R_1 = C_6H_5$, $R = C_6H_5{\cdot}CH_2$). To a mixture of benzyl *d*-tartrate (10 g.) and freshly distilled benzaldehyde

(3.22 g.) was added 7 g. phosphorus pentoxide in portions at 70° in the course of 60 minutes. The resulted fatty mass was poured into water, and the separating solid was recrystallised from absolute alcohol three times. White crystals. Yield 4 g. Melting point 86°. $[\alpha]_D^{20}$ −39.7°, $[M]_D^{20}$ −166° (in alcohol, 1.356%). $[\alpha]_D^{20}$ −39.38°, $[M]_D^{20}$ −164.8° (in benzene, 12.18%). Found: C, 71.64; H, 5.30. Calc. for $C_{25}H_{22}O_6$ (418.18): C, 71.74; H, 5.30%.

Musashi Higher School,
Itabashiku, Tokyo