Revision of Stereochemical Assignments of Dimethyl 2,3-Diphenyltartrates

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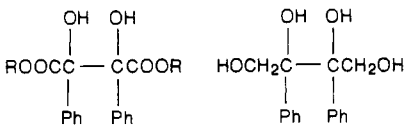
Stereochemical assignments of (±)- and *meso*-dimethyl 2,3-diphenyltartrates (**1**) (and corresponding acids **2**), initially based tentatively[1] on the Stern proposal (higher melting meso-isomer)[2] and subsequently adopted in various studies,[3-5] including stereoselective reactions,[4] are shown to be incorrect. Correct assignments were made by chromatographic resolution of the esters and confirmed by demonstrating the identity of (±)-tetrol **3** from reduction of (±)-dimethyl ester **1** with that from the corresponding (±)-diethyl ester.[6] Persistence of the incorrect stereochemical assignments for ca. 30 years, the importance of tartaric acid derivatives to the foundation of stereochemistry and the significant implications of the revised stereoselectivities prompt this report.

Dimethyl esters **1** precipitated from a solution of methyl phenylglyoxylate in 2-propanol during sunlight irradiation. The high-melting isomer crystallized from methanol–water (10:1), mp 159–61 °C. The low-melting isomer was isolated from the filtrates and recrystallized from methanol–water (4:1), mp 124–5 °C.



The isomers were subjected to chromatographic resolution on a cellulose tris[(3,5-dimethylphenyl)carbamate] column using hexane–2-propanol (90:10) as eluent.[7] The high-melting ester was completely resolved into (+)- and (−)-isomers; whereas, the low-melting isomer was eluted unchanged.

Assignment of (±)-configuration to the high-melting isomer was confirmed by comparison of the tetrols **3**, obtained from reduction ($LiAlH_4$) of (±)- and *meso*-esters **1**, with tetrol **3** from reduction of (±)-diethyl 2,3-diphenyltartrate. The (±)-diethyl ester was isolated from asymmetric hydrogenation of ethyl phenylglyoxylate.[6] The tetrols from (±)-dimethyl and -diethyl esters were found to be identical.

These results require revision of the tentative (±)- and *meso*-2,3-diphenyltartaric acid (**2**) assignments to the predominant product from electrochemical pinacolization of phenylglyoxylic acid in buffered acid and alkaline media, respectively.[1] This revision is significant since the results with phenylglyoxylic acid[1] are now in accord with enhanced (±)/*meso* ratios in alkaline relative to acid media, generally observed for both electrochemical and photochemical pinacolization.[8]

The required revision of stereoselectivity reported for pinacolization of methyl phenylglyoxylate utilizing titanium trichloride in acetic acid[4] also brings these results into accord with the common stereoselectivity observed in electrochemical and photochemical pinacolizations,[8] namely favored (±)-configuration.[9]

Experimental Section

General Methods. ^1H NMR were obtained utilizing a Varian EM-390 90-MHz spectrometer. Elemental Analyses were performed by MicAnal Organic Microanalysis, Tucson, AZ.

(±)- and *meso*-Dimethyl 2,3-Diphenyltartrates (1). A solution of methyl phenylglyoxylate (50 g, 0.30 mol) in 2-propanol (160 mL) was irradiated in sunlight for ca. 1 week; precipitation of the product began within 1–2 days. Filtration provided an isomeric mixture of the tartrates (41.7 g, 0.25 mol), mp 122–5 °C. Two recrystallizations from methanol–water (10:1 by vol) afforded the higher melting isomer (16.5 g), mp 159–61 °C (lit.[5] mp 158–9 °C). The lower melting isomer (11.1 g) was obtained from the supernatants by recrystallization from methanol–water (4:1 by vol), mp 124–5 °C (lit.[5] mp 122–4 °C).

IR and NMR spectral data for the isomers have been reported.[4] Chromatographic resolution of 5-mg samples were carried out under pressure (81 kg cm^{-1}) with a flow rate of 9.9 mL min^{-1} on a cellulose tris[(3,5-dimethylphenyl)carbamate] column (50 × 2.0 cm) using hexane–2-propanol (90:10) as eluent. The high-melting (±)-isomer (159–61 °C) was completely resolved into (+)- and (−)-isomers, mp 116–9 °C, $[\alpha]^{25}_D$ +182°, elution time, 27 min, and mp 115–9 °C, $[\alpha]^{25}_D$ −183°, elution time, 37 min, respectively. The low-melting *meso*-isomer (124–5 °C) was eluted (38 min) unchanged.

(±)-2,3-Diphenyl-1,2,3,4-butanetetrol (3). A solution of (±)-dimethyl ester **1** (14.0 g, 0.042 mol), in tetrahydrofuran (175 mL), was added dropwise (over a period of 1.5 h) to a stirred suspension of lithium aluminum hydride (6.7 g, 0.18 mol) in diethyl ether (350 mL). The reaction mixture was stirred an additional 20 min at room temperature and 2.5 h at reflux. Subsequently, while the mixture was cooled in an ice bath, ethyl acetate (15 mL) followed by water (50 mL) was added. The mixture was then poured into an ice-cold solution of 11% HCl (400 mL). The aqueous layer was extracted with chloroform, and the combined organic layers were dried over anhydrous sodium sulfate. Following evaporation of solvent, the tetrol was recrystallized from chloroform–hexane to yield 10.6 g (76%): mp 131–2 °C; NMR (pyridine-d_5) δ 4.10, 4.23, 4.77, 4.90 (4 H, CH_2, 2 d, J = 12 Hz), 6.43 (4 H, OH, s), 7.1–7.3 (6 H, Ar H, m), 7.5–7.8 (4 H, Ar H, m).

Analogous reduction of (±)-diethyl 2,3-diphenyltartrate,[6b] mp 123–4 °C (lit.[6a] mp 124 °C), provided the identical (±)-2,3-diphenyl-1,2,3,4-butanetetrol obtained from the (±)-dimethyl ester.

***meso*-2,3-Diphenyl-1,2,3,4-butanetetrol (3).** *meso*-Dimethyl-ester **1** was converted, as described above, into *meso*-**3**: mp 161–2 °C; NMR (pyridine-d_5) δ 4.30, 4.43, 4.53, 4.67 (4 H, CH_2, AB q), 5.97 (4 H, OH, s), 7.2–7.4 (6 H, Ar H, m), 7.8–8.0 (4 H, Ar H, m).

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.1; H, 6.6. Found: C, 70.0; H, 6.6.

Registry No. (±)-**1**, 81390-15-0; *meso*-**1**, 81390-14-9; (±)-**2**, 103595-78-4; *meso*-**2**, 103595-79-5; (±)-**3**, 115533-56-7; *meso*-**3**, 115533-57-8.

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