

560. The Phthalates of 3 : 5 : 5-Trimethylhexan-1-ol.

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Di-(3 : 5 : 5-trimethylhexyl) phthalate prepared from racemic 3 : 5 : 5-trimethylhexanol slowly deposits the racemic diester at 0°.

Racemic 3 : 5 : 5-trimethylhexanol has been optically resolved and the (++)-, (---)-, racemic, and *meso*-forms of di-(3 : 5 : 5-trimethylhexyl) phthalate have been synthesised.

EVIDENCE has been presented (E. E. Turner and L. Turner, *J.*, 1951, 2543) that 3 : 5 : 5-trimethylhexan-1-ol, synthesised from a mixture of 2 : 4 : 4-trimethylpent-1- and -2-ene (*diisobutylene*), carbon monoxide, and hydrogen by the "oxo" reaction, is free from isomeric alcohols. The alcohol used in the present work was prepared by the "oxo" procedure and was fractionally distilled (b. p. 193.6°, reflux ratio 80 : 1) through a column of one hundred theoretical plates before use.

The work described below originated when a sample of di-(3 : 5 : 5-trimethylhexyl) phthalate prepared from phthalic anhydride and racemic 3 : 5 : 5-trimethylhexanol deposited a solid form of the diester. This, when purified (m. p. 26—29°), was thought to be either the racemic or the *meso*-dialkyl phthalate. E. E. Turner and L. Turner (*J.*, 1952, 1761) had already described the isolation of (+)-3 : 5 : 5-trimethylhexan-1-ol, by way of the brucine salt of racemic 3 : 5 : 5-trimethylhexyl hydrogen phthalate. This partial resolution has been completed (cf. Gilman and Blatt, "Organic Syntheses," Wiley, New York, Coll. Vol. I, 2nd Edn., p. 418). Hydrolysis of the (+)- and the (---)-hydrogen phthalate gave (+)- and (---)-3 : 5 : 5-trimethylhexan-1-ol respectively. On acid-catalysed esterification of (+)-3 : 5 : 5-trimethylhexyl hydrogen phthalate with (+)-3 : 5 : 5-trimethylhexanol, (++)-di-(3 : 5 : 5-trimethylhexyl) phthalate was obtained, and the (---)-diester was prepared in the same way. Recrystallisation of an equimolar mixture of the (++)- and the (---)-diester from methanol provided racemic di-(3 : 5 : 5-trimethylhexyl) phthalate (m. p. 26—29°), identical with the crystalline product isolated from the original mixture of racemic and *meso*-diesters.

Acid-catalysed esterification of (+)-3 : 5 : 5-trimethylhexyl hydrogen phthalate with (---)-3 : 5 : 5-trimethylhexanol would bring about ester exchange and give a mixture of racemic and *meso*-diesters. Therefore, *meso*-di-(3 : 5 : 5-trimethylhexyl) phthalate was synthesised by treating the silver salt of (+)-3 : 5 : 5-trimethylhexyl hydrogen phthalate with the iodide derived from (---)-3 : 5 : 5-trimethylhexanol. Unfortunately the *meso*-diester was obtained only as an oil. Since racemic di-(3 : 5 : 5-trimethylhexyl) phthalate remains unaffected by 2 hr.' heating at 200° it is unlikely that a thermal ester interchange has transformed the *meso*-di-(3 : 5 : 5-trimethylhexyl) phthalate into a mixture of racemic and *meso*-diester.

Haller (*Compt. rend.*, 1889, **108**, 410, 456) prepared (++)- and (---)-dibornyl succinate and phthalate, in addition to the optically inactive mixture of racemic and *meso*-diesters given by the esterification of succinic or phthalic acid with racemic borneol. However, neither the *meso*-dibornyl succinate nor the corresponding phthalate was isolated. In a similar manner Quist (*Annalen*, 1918, **417**, 296) reported the synthesis of (++)-, (---)-, and racemic difenchyl oxalates. Despite the extensive use of hydrogen phthalates for

resolution of alcohols (Hewitt and Kenyon, *J.*, 1925, 1094; Kenyon and Snellgrove, *ibid.*, p. 1169) no instance was known to the authors in which the four possible diesters of an asymmetric alcohol with a dibasic acid have been recorded.

EXPERIMENTAL

Optical rotations were measured in a 4-dm. tube.

Di-(3 : 5 : 5-trimethylhexyl) Phthalate.—Phthalic anhydride (1 mol.), racemic 3 : 5 : 5-trimethylhexanol (4 mols.), and alumina (2% by wt. of the alcohol) were refluxed for 6 hr. in a glass apparatus, and the water (1 mol.) entrained in the refluxing alcohol was separated. The product was washed with dilute alkali, then water, and steam-distilled, to leave a viscous mixture of stereoisomeric *di*-(3 : 5 : 5-trimethylhexyl) phthalates, which were decanted from water and dried at 100° under reduced pressure (yield 90%) (Found : C, 74.3; H, 10.0; acid val., 0; sap. val., 264 mg. of KOH per g. C₂₆H₄₂O₄ requires C, 74.6; H, 10.1%; acid val. 0; sap. val. 268 mg.).

After being kept for some months at -5° the mixture of stereoisomers slowly began to crystallise. It was pressed on a porous plate at -10°, then allowed to warm to 20°, and the residual crystals were recrystallised five times from methanol and then three times from acetone to provide colourless needles of constant m. p. 26—29° (Found : C, 74.3; H, 9.9; acid val. 0; sap. val. 267 mg. of KOH per g.).

Hydrolysis of the crystalline phthalate gave phthalic acid, m. p. 195° (anhydride, m. p. 130°, imide, m. p. 233°) and racemic 3 : 5 : 5-trimethylhexan-1-ol. The latter was identified as the 3 : 5-dinitrobenzoate, lemon-yellow plates, m. p. 62° [from light petroleum (b. p. 40—60°)] undepressed on admixture with an authentic sample of the same m. p.

Racemic 3 : 5 : 5-Trimethylhexyl Hydrogen Phthalate and its Resolution.—Prepared following the method of E. E. Turner and L. Turner (*J.*, 1951, 2544), this ester had m. p. 52° (Found : C, 69.9; H, 8.1. Calc. for C₁₇H₂₄O₄ : C, 69.9; H, 8.2%).

A solution of it (70 g.) and anhydrous brucine (83.1 g.) in warm acetone (100 c.c.), on storage overnight, deposited rhombs (120.5 g.), m. p. 70—75°, which after crystallisation from acetone (250 c.c.) had m. p. 90—92° (74 g.). The first and the second acetone mother-liquors were combined. Two further recrystallisations of the brucine salt from acetone gave colourless prisms (60 g.) of unchanged m. p. and optical rotation. The (+)-3 : 5 : 5-trimethylhexyl hydrogen phthalate recovered from the brucine salt of m. p. 90—92° crystallised in colourless plates, m. p. 69° [from light petroleum (b. p. 40—60°)] (18.6 g.), [α]_D²⁰ +7.0° ± 0.5° (*c* 4.0 in CHCl₃) (Found : C, 69.8; H, 8.2%).

Acetone was removed from the combined first and second mother-liquors, and the crude (-)-ester was retrieved. Three crystallisations from light petroleum (b. p. 40—60°) yielded (-)-3 : 5 : 5-trimethylhexyl hydrogen phthalate (15 g.), m. p. 69°, [α]_D²⁰ -7.0° ± 0.5° (*c* 4.3 in CHCl₃) (Found : C, 70.1; H, 8.5%).

(+) and (-)-3 : 5 : 5-Trimethylhexan-1-ol.—Alkaline hydrolysis of the (+)- and the (-)-hydrogen phthalate gave (+)- and (-)-3 : 5 : 5-trimethylhexan-1-ol, respectively, b. p. 190—192°, [α]_D²⁰ +4.5° ± 0.3° and -4.5° ± 0.3° (*c* 4.0 in CHCl₃) [Found : (+)-alcohol, C, 75.2; H, 13.7. (-)-alcohol, C, 74.8; H, 13.7. C₉H₂₀O requires C, 75.0; H, 13.9%].

(+) and (-)-3 : 5 : 5-Trimethylhexyl 3 : 5-dinitrobenzoate were obtained as pale lemon-yellow needles, m. p. 56° [from light petroleum (b. p. 40—60°)], [α]_D²⁰ +0.5° ± 0.3° and -0.5° ± 0.3° respectively (*c* 4.0 in CHCl₃) [Found : (+)-ester, C, 57.1; H, 6.6; N, 8.3. (-)-ester, C, 57.0; H, 6.6; N, 8.1. C₁₆H₂₂O₆N₂ requires C, 56.8; H, 6.5; N, 8.3%].

(++)-*Di*-(3 : 5 : 5-Trimethylhexyl) Phthalate.—(++)-3 : 5 : 5-trimethylhexan-1-ol (1.2 g.) and (+)-3 : 5 : 5-trimethylhexyl hydrogen phthalate (2 g.) in toluene (25 c.c.) were treated with concentrated sulphuric acid (1 drop). This mixture was refluxed for 4 hr. (Soxhlet), the toluene-water distillate being dried by magnesium sulphate in the thimble. After the toluene solution had been washed with dilute alkali, acid, and water, it was steam-distilled, and the residue was dried under reduced pressure at 100° and then sublimed (bath 180°/0.02 mm.). Two recrystallisations of the sublimate from the minimum of methanol gave colourless needles (2.0 g.) of (++)-*di*-(3 : 5 : 5-trimethylhexyl) phthalate, m. p. 37—38°, [α]_D²⁰ +4.4° ± 0.3° (*c* 4.8 in CHCl₃), unchanged by further crystallisation (Found : C, 74.7; H, 10.2. C₂₆H₄₂O₄ requires C, 74.6; H, 10.1%).

(--)-*Di*-(3 : 5 : 5-trimethylhexyl) Phthalate.—Prepared as outlined above for the (++)-isomer, this ester crystallised in colourless needles, m. p. 37—38°, [α]_D²⁰ -4.4° ± 0.3° (*c* 4.7 in CHCl₃) (Found : C, 74.6; H, 10.2%).

Racemic Di-(3 : 5 : 5-trimethylhexyl) Phthalate. Equal quantities of (+ +)- and (— —)-di-(3 : 5 : 5-trimethylhexyl) phthalate were dissolved in, and crystallised from, the minimum of methanol at -60° , giving a colourless microcrystalline precipitate of racemic di-(3 : 5 : 5-trimethylhexyl) phthalate, m. p. and mixed m. p. $26-29^{\circ}$. It had m. p. $25-27^{\circ}$ after 2 hr. at 200° under nitrogen.

(+)-3 : 5 : 5-Trimethylhexyl Iodide [from (—)-Alcohol].—Red phosphorus (0.19 g.) and powdered iodine (2.13 g.) were added to (—)-3 : 5 : 5-trimethylhexanol (2 g.) at 0° and left overnight. This mixture was then warmed to 70° for 3 hr. and the iodide distilled off under reduced pressure (b. p. $62^{\circ}/2$ mm.). An ethereal solution of this red distillate was washed with sodium hydrogen sulphite solution, followed by sodium hydrogen carbonate solution, and finally water. Fractional distillation provided 3 : 5 : 5-trimethylhexyl iodide as a colourless oil, b. p. $68^{\circ}/4$ mm., $[\alpha]_D^{20} +11.9^{\circ} \pm 0.5^{\circ}$ (*c* 3.5 in CHCl_3) (Found : C, 42.3; H, 7.4; I, 49.7. $\text{C}_9\text{H}_{19}\text{I}$ requires C, 42.5; H, 7.5; I, 50.0%).

meso-Di-(3 : 5 : 5-trimethylhexyl) Phthalate.—(+)-3 : 5 : 5-Trimethylhexyl hydrogen phthalate (2 g.), dissolved in the theoretical quantity of dilute aqueous ammonia, was treated with an excess of silver nitrate (2 g.) in water. The resultant white precipitate (2.6 g.) of silver (+)-3 : 5 : 5-trimethylhexyl phthalate was filtered off, washed with water, and dried under reduced pressure in the dark.

Excess of 3 : 5 : 5-trimethylhexyl iodide (2 g.) [from (—)-alcohol] was treated in "AnalaR" benzene (40 c.c.) with silver (+)-3 : 5 : 5-trimethylhexyl phthalate (2.6 g.), refluxed for 1 hr., cooled, and filtered. The filtrate was steam-distilled, and an ethereal solution of the residue was washed with sodium hydrogen carbonate solution, followed by water. Solvent and moisture were removed at 100° under reduced pressure and the residue, of colourless meso-di-(3 : 5 : 5-trimethylhexyl) phthalate, was distilled (bath $170^{\circ}/0.01$ mm.), to yield a colourless mobile oil, $\alpha 0^{\circ}$, which could not be crystallised (Found : C, 74.1; H, 9.8%).

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