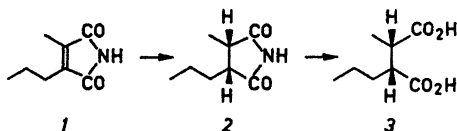


## Some Methods for Stereospecific or Stereoselective Preparation of *erythro*-2-Methyl-3-propylsuccinic Acid

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In connection with work on the synthesis of ( $\pm$ )-roccellic acid,<sup>1</sup> we have studied various methods for the synthesis of *erythro*-2-methyl-3-propylsuccinic acid (3). The highest yield of this compound was obtained by catalytic reduction of methylpropylmaleimide (1) to *cis*-2-methyl-3-propylsuccinimide (2), followed by acid hydrolysis to (3) (cf. Ref. 2).



In this manner methylpropylsuccinic acid was obtained in an *erythro:threo* ratio of 9:1.

Partial alkaline hydrolysis of the imide (2) to the *mono*-amide followed by deamination with nitrogen tetroxide<sup>1,3</sup> gave methylpropylsuccinic acid in an *erythro:threo* ratio of 6.5:3.5. This relatively low *erythro:threo* ratio is probably due to isomerisation during the hydrolysis since roccellic acid *mono*-amide was deaminated without appreciable racemisation. In this connection it is interesting to note that methylpropylsuccinimide does not appear to react with nitrogen tetroxide.

The reduction of methylpropylmaleic anhydride by zinc and acetic acid<sup>4</sup> was found to give a high yield of methylpropylsuccinic acid in an *erythro:threo* ratio of 7:3. This reaction thus seems to offer a simple method for the stereoselective synthesis of *erythro*-2,3-dialkylsuccinic acids.

Attempted diimine reduction<sup>5,6</sup> of methylpropylmaleic acid gave only a trace of reduced material even when a large excess of diimine was used.

Since the preparation of *erythro*-2-methyl-3-propylsuccinic acid was originally intended as a model reaction for the

synthesis of ( $\pm$ )-roccellic acid,<sup>1</sup> methylpropylmaleic anhydride was synthesised by bromination of a mixture of *cis*- and *trans*-methylpropylsuccinic anhydride, followed by dehydrobromination. Addition of hydrogen cyanide to ethyl propylacetoacetate followed by hydrolysis and dehydration<sup>4</sup> is probably a more convenient method for the synthesis of methylpropylmaleic anhydride. However, this method could not be used in the synthesis of methyl-dodecylmaleic anhydride for steric reasons.<sup>1</sup>

*Experimental.* 2-Methyl-3-propylsuccinic anhydride. Triethyl 2,3,3-hexanetricarboxylate<sup>7</sup> (30 g), prepared by sodium hydride catalysed condensation of diethyl propylmalonate and ethyl 2-bromopropionate in dimethyl sulphoxide solution, was hydrolysed and partially decarboxylated by heating in concentrated sulphuric acid (300 ml) for 15 min at 85°. The solution was poured onto ice and then extracted continuously with ether for 24 h. The ether was evaporated, the product distilled to effect decarboxylation and then refluxed with acetyl chloride for 1 h. Removal of excess acetyl chloride followed by distillation gave methylpropylsuccinic anhydride (12 g), b.p. 131–133°/12 mm in an *erythro:threo* ratio of 2.5:7.5.

2-Bromo-2-methyl-3-propylsuccinic anhydride. A mixture of 2-methyl-3-propylsuccinic anhydride (7.1 g) and red phosphorus (1.0 g) was heated on a boiling water bath and dry bromine (23 g) added from a dropping funnel. The heating was continued overnight; the mixture was then slowly poured into boiling water. Isolation of the product in the usual manner gave 2-bromo-2-methyl-3-propylsuccinic anhydride (8.5 g) which was used in the next step without purification. (Found: Br 34.3. Calc. for C<sub>8</sub>H<sub>11</sub>BrO<sub>3</sub>: Br 34.0).

Methylpropylmaleic anhydride. a) A mixture of 2-bromo-2-methyl-3-propylsuccinic anhydride (8.5 g), lithium bromide (3.6 g) and lithium carbonate (3.6 g) in dry dimethyl formamide (200 ml) was kept at 50° for 2.5 h. After cooling, water (300 ml) was added and the solution extracted with a mixture of light petroleum (7 parts) and ether (3 parts). Distillation gave methylpropylmaleic anhydride (3.2 g). For unknown reasons, the yields were occasionally very low. A small amount was purified by preparative gas chromatography. (Found: C 62.1; H 6.8. Calc. for C<sub>8</sub>H<sub>10</sub>O<sub>3</sub>: C 62.3; H 6.5).

b) 2-Bromo-2-methyl-3-propylsuccinic anhydride (4.0 g) was twice slowly distilled at reduced pressure to give methylpropylmaleic anhydride (1.6 g), essentially free from bromine.

*Methylpropylmaleimide* (1) was prepared from urea and methylpropylmaleic anhydride (cf. Ref. 2), m.p. 55–56° (sublimed) (lit.<sup>4</sup> 56–57°). NMR (CDCl<sub>3</sub>,  $\delta$ -units relative to tetramethylsilane as internal standard): 0.95 (t, C–CH<sub>3</sub>), 1.3–1.7 (m, C–CH<sub>2</sub>), 1.97 (s, C=C–CH<sub>3</sub>), 2.32 (t, C=C–CH<sub>2</sub>). (Found: C 62.4; H 7.1. Calc. for C<sub>8</sub>H<sub>11</sub>NO<sub>2</sub>: C 62.7; H 7.2).

*Cis-2-methyl-3-propylsuccinimide* (2). The maleimide (1, 1.01 g) in ethanol (60 ml) was reduced catalytically using palladium on charcoal (Engelhardt, 10% Pd, 0.06 g) as catalyst. The reduction was very slow, the theoretical amount of hydrogen being absorbed only after 12 h. Isolation of the product in the usual manner followed by recrystallisation from light petroleum gave *cis-2-methyl-3-propylsuccinimide* (2, 0.91 g), m.p. 49–50°. Tschugaeff<sup>7</sup> gives m.p. 51–53° for a product which is probably predominantly the *trans*-isomer of (2). NMR: 0.95 (m, C–CH<sub>3</sub>), 1.22

(d, C–CH<sub>3</sub>), 1.5 (m, CH<sub>2</sub>), 2.88 (m, O=C–CH–). (Found: C 61.8; H 8.5. Calc. for C<sub>8</sub>H<sub>13</sub>NO<sub>2</sub>: C 61.9; H 8.4).

*Erythro-2-methyl-3-propylsuccinic acid*. The *cis*-imide (2, 0.086 g) was refluxed in concentrated hydrochloric acid (1 ml) for 1 h. The hydrochloric acid was removed using a rotatory evaporator to give methylpropylsuccinic acid (0.090 g), m.p. 135–148° in an *erythro:threo* ratio of 9:1. Recrystallisation from dilute hydrochloric acid gave *erythro-2-methyl-3-propylsuccinic acid* (3, 0.040 g), m.p. 158–160°. Lit. m.p. for the high melting isomer of methylpropylsuccinic acid 156–158°<sup>4</sup> (cf. Ref. 7). (Found: C 55.4; H 8.0. Calc. for C<sub>8</sub>H<sub>14</sub>O<sub>4</sub>: C 55.2; H 8.1).

The *erythro:threo* ratio was determined by gaschromatography of the methyl esters.

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## Formation of Dibenzofuran from 2,2'-Dihydroxybiphenyl via the Cyclic Phosphorane

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During experiment aimed at the synthesis of lichen acids of the dibenzofuran type, the following observation was made.

2,2'-Dihydroxybiphenyl reacted with dibromotriphenylphosphorane to give the cyclic phosphorane (1). When this compound was heated under reduced pressure, rapid decomposition occurred and a fair yield of dibenzofuran (2) was obtained.

This reaction appears to be of some interest in connection with the synthesis of carboxylated dibenzofurans, e.g. the lichen acids pannaric acid<sup>1</sup> and porphyritic acid,<sup>2</sup> which are decarboxylated under the strongly acidic conditions generally required for the ringclosure of 2,2'-dihydroxybiphenyls to dibenzofurans.<sup>3,4</sup>

The formation of dibenzofuran from the phosphorane (1) is probably related to the reactions whereby bromobenzene derivatives are produced by thermal decomposition of bromophenoxytriphenylphosphoranes<sup>5</sup> and chlorobenzene by decomposition of dichlorotriphenoxyphosphorane.<sup>6</sup> The replacement of hydroxyl by halogen by boiling with phosphorus oxychloride or phosphorus pentachloride, frequently used for heterocyclic compounds, appears also to be a related reaction.

