

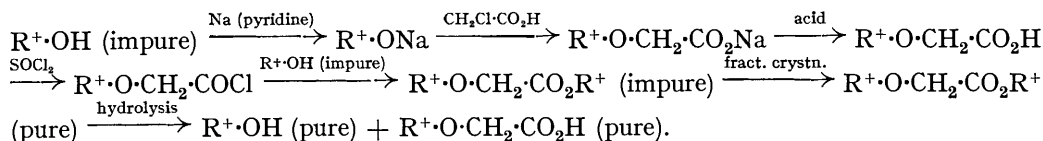
391. *New Methods in Stereochemistry. Part I. A New Method for preparing Pure d- and l-Borneol.*

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THE purification of crude *d*- or *l*-borneol, obtained directly from natural sources or by reducing *d*- or *l*-camphor, usually falls into two stages: (*a*) the separation of borneol from *isoborneol*, and (*b*) the stereochemical purification of the resulting borneol. This problem has been examined in detail by Haller (*Ann. chim.*, 1892, **27**, 392), Tschugaev (*J. Russ. Phys. Chem. Soc.*, 1904, **36**, 1096), McKenzie (J., 1907, **91**, 1225; *Biochem. Z.*, 1929, **208**, 474), Pickard and Littlebury (J., 1907, **91**, 1974), Ikeda and Fujita (*Bull. Inst. Phys. Chem. Research, Tokyo*, 1928, **7**, 48), and others.

We now show that crude *d*- and *l*-borneol may be effectively purified by a species of auto-catalytic process, fundamentally similar to the optical resolution of *dl*-menthol by means of an initial quantity of *l*-menthol (Read and Grubb, *J. Soc. Chem. Ind.*, 1932, **51**,

329T). Thus, a specimen of commercial *d*-borneol, m. p. 200—201°, $[\alpha]_D + 21.5^\circ$ (alcohol), was converted into impure *d*-bornoxyacetic acid; the impure *d*-bornyl *d*-bornoxyacetate obtained by esterifying this acid with some of the original *d*-borneol yielded stereochemically pure *d*-bornyl *d*-bornoxyacetate when fractionally recrystallised; and upon differential hydrolysis this ether-ester yielded pure *d*-borneol, m. p. 204.5—205°, $[\alpha]_D + 37.6^\circ$ (toluene), and pure *d*-bornoxyacetic acid, m. p. 76°, $[\alpha]_D + 59.1^\circ$ (alcohol). In the following summary of the processes, R represents the bornyl radical:



The pure *d*-bornoxyacetic acid may be recovered and used repeatedly in an improved process.

In a similar way, pure *l*-borneol, m. p. 205°, $[\alpha]_D - 37.9^\circ$ (toluene), and pure *l*-bornoxyacetic acid were prepared from a specimen of commercial *l*-borneol having m. p. 190—197°, $[\alpha]_D - 33.6^\circ$ (alcohol).

In both instances, the only fundamental stereochemical agent required is some of the impure alcohol which it is desired to purify in bulk. The results indicate that the complete optical resolution of indefinite quantities of *dl*-borneol could probably be effected by the successive application of limited amounts of *d*- and *l*-bornoxyacetic acid, prepared in turn from commercial specimens of *d*- and *l*-borneol (compare Read and Grubb, *loc. cit.*, p. 330T). The method permits also of the preparation of stereochemically pure *l*-camphor from commercial *l*-borneol.

EXPERIMENTAL.

Preparation of Pure d-Borneol.—(1) Owing to the high melting point of borneol it was necessary to use a solvent in preparing sodium bornoxide (compare sodium menthoxide; *J. Soc. Chem. Ind.*, 1932, 51, 330T). Sodium (5 g.) was added to a solution of commercial *d*-borneol (35 g.; m. p. 200—201°, $[\alpha]_D + 21.5^\circ$, *c* 2.5, absolute alcohol) in dry pyridine (85 c.c.) boiling under reflux; solution was complete in 20 minutes. Chloroacetic acid (10 g.) was added gradually, frequent shaking causing the sodium salt to separate as a smooth paste. After 14 hours' heating (wire gauze), the mixture was poured into an excess of dilute sulphuric acid. The acid liquor was extracted with ether. The ether was washed with water, alkali, and water, dried over sodium sulphate, and distilled, the unused borneol being thereby recovered. The alkaline washing was mixed with the succeeding water washing and acidified: crude *d*-bornoxyacetic acid separated as an oil, which was extracted with ether. Three such preparations yielded 32 g. of impure *d*-bornoxyacetic acid, m. p. 70—72°, $[\alpha]_D + 34.0^\circ$ (*c* 2.0, alcohol); unused borneol was recovered almost quantitatively (79 g.).

A solution of the above impure *d*-bornoxyacetic acid (28 g.) in thionyl chloride (35 c.c.) was warmed for an hour on the water-bath; the excess of thionyl chloride was then distilled away. The crude *d*-bornoxyacetyl chloride (29.6 g.) distilled at 130—135°/13 mm.

The acid chloride (29.5 g.) was added to a solution of the above commercial *d*-borneol (18.5 g.) in dry pyridine (50 c.c.). On the following day the mixture was poured into an excess of dilute sulphuric acid. The ethereal extract of the precipitated ester was washed twice each with acid, alkali, and water. The recovered ester was steam-distilled for 30 minutes to remove unchanged borneol; it was then redissolved in ether, dried, and isolated (35 g.): it had $[\alpha]_D + 47.0^\circ$ (*c* 2.0, chloroform), and melted indefinitely at about 70°.

The crude ester was very soluble in most of the usual organic solvents. It was recrystallised twice from a mixture of methyl alcohol (2 parts) and water (1 part), and then three times from methyl alcohol, until the specific rotatory power of the crystalline separation was the same as that of the residue in the mother-liquor; the yield was 27% of the original crude ester. Pure *d*-bornyl *d*-bornoxyacetate forms small transparent prisms, m. p. 72°, $[\alpha]_D + 63.3^\circ$ (*c* 2.0, chloroform) (Found: C, 75.6; H, 10.5. $\text{C}_{22}\text{H}_{36}\text{O}_3$ requires C, 75.8; H, 10.4%).

The ester (7.8 g.) was completely hydrolysed when heated for 2 hours with 1% alcoholic potassium hydroxide (200 c.c.). The resulting *d*-borneol, after isolation by steam distillation and extraction with ether, had m. p. 204.5—205°, $[\alpha]_D + 37.6^\circ$ (*c* 5.9, toluene): it was therefore

stereochemically pure (*Biochem. Z.*, 1929, **208**, 474). Pure *d*-bornoxyacetic acid was obtained by extracting the acidified non-volatile residue with ether; after distillation at 0.65 mm. from a bath at 150°, it formed transparent prisms, m. p. 76°, $[\alpha]_D + 59.1^\circ$ (*c* 2.0, alcohol) (Found: C, 68.3; H, 9.1. $C_{12}H_{20}O_3$ requires C, 67.9; H, 9.4%). It is too soluble in the ordinary organic solvents to permit of recrystallisation; it dissolves only slightly in water.

(2) In a similar way, a specimen of commercial *d*-borneol having m. p. 203–204°, $[\alpha]_D + 28.4^\circ$ (*c* 2.6, alcohol), yielded an impure *d*-bornoxyacetic acid with m. p. 71–72°, $[\alpha]_D + 45.8^\circ$ (*c* 2.0, alcohol). The derived impure *d*-bornoxyacetyl chloride reacted in dry pyridine with pure *l*-menthol to yield a stereochemically impure *l*-menthyl *d*-bornoxyacetate, $[\alpha]_D - 17.9^\circ$ (*c* 2.0, chloroform), as a mobile oil (Found: C, 75.0; H, 10.6. $C_{22}H_{38}O_3$ requires C, 75.4; H, 10.8%).

Preparation of Pure l-Borneol.—The commercial *l*-borneol used in this work had m. p. 190–197°, $[\alpha]_D - 33.6^\circ$ (*c* 4.7, alcohol).

(1) When treated in pyridine with impure *d*-bornoxyacetyl chloride made from commercial *d*-borneol having $[\alpha]_D + 28.4^\circ$ (*c* 2.6, alcohol), the above impure *l*-borneol yielded an impure *l*-bornyl *d*-bornoxyacetate: this was a solid with an indefinite melting point, $[\alpha]_D - 15.0^\circ$ (*c* 2.0, chloroform), and was too soluble to admit of purification by fractional crystallisation. This result indicates that commercial *d*-borneol cannot be used, according to the method now adumbrated, for purifying commercial *l*-borneol. Accordingly, commercial *l*-borneol was applied as below.

(2) Commercial *l*-borneol, $[\alpha]_D - 33.6^\circ$ (*c* 4.7, alcohol), was converted into impure *l*-bornoxyacetic acid, according to the method described above for the impure *d*-acid: the acid had m. p. 72–73°, $[\alpha]_D - 53.1^\circ$ (*c* 2.0, alcohol), and was too soluble to permit of recrystallisation. The corresponding crude *l*-bornoxyacetyl chloride distilled at 140–143°/17 mm. (Found: C, 62.6; H, 8.5. $C_{12}H_{19}O_2Cl$ requires C, 62.5; H, 8.3%).

When esterified in dry pyridine with some of the original commercial *l*-borneol, this acid chloride yielded impure *l*-bornyl *l*-bornoxyacetate, m. p. 55–60°, $[\alpha]_D - 57.6^\circ$ (*c* 2.0, chloroform). Four recrystallisations from methyl alcohol gave a 37% yield of pure *l*-bornyl *l*-bornoxyacetate, m. p. 72°, $[\alpha]_D - 63.3^\circ$ (*c* 2.0, chloroform). Hydrolysis with 1% alcoholic potassium hydroxide, in the way described above, furnished pure *l*-borneol, m. p. 205°, $[\alpha]_D - 37.9^\circ$ (*c* 4.2, toluene), and pure *l*-bornoxyacetic acid, m. p. 76°, $[\alpha]_D - 59.0^\circ$ (*c* 2.0, alcohol).

The purification of commercial specimens of *d*- and *l*-borneol by the above method may be greatly facilitated by the direct application of pure *d*- and *l*-bornoxyacetyl chloride, respectively, in preparing the requisite crystalline esters.

Attempted Use of l-Menthoxycetic Acid in preparing Pure d- and l-Borneol.—*l*-Menthoxycetyl chloride (*J. Soc. Chem. Ind.*, 1932, **51**, 330r) reacted in pyridine with commercial *d*-borneol, $[\alpha]_D + 28.4^\circ$ (*c* 2.0, alcohol), to yield the corresponding stereochemically impure *d*-bornyl *l*-menthoxyacetate: this distilled from a bath at 206–208° under 0.5 mm. as a mobile oil with $[\alpha]_D - 37.7^\circ$ (*c* 2.2, chloroform), $n_D^{15} 1.4803$.

Similarly, commercial *l*-borneol, $[\alpha]_D - 33.6^\circ$ (*c* 4.7, alcohol), yielded stereochemically impure *l*-bornyl *l*-menthoxyacetate as a viscid liquid, with $[\alpha]_D - 76.1^\circ$ (*c* 2.7, chloroform), $n_D^{15} 1.4805$ (Found: C, 75.8; H, 10.7. $C_{22}H_{38}O_3$ requires C, 75.4; H, 10.9%).

Thus, the *l*-menthoxyacetic esters cannot be applied effectively in purifying such specimens of *d*- or *l*-borneol.

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