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Proton-Mobility in the Indene Ring-System

V.* Syntheses of Optically Active Alkyl-Substituted Indenes

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Some optically active alkyl-indenes have been synthesized. Their absolute configurations were established by correlation with β-phenylbutyric acid.

In connection with current investigations on the steric courses of tautomeric rearrangements,[1] the authors synthesized some optically active indene derivatives (VI—VIII). β-Phenylbutyric acid (I) was the common starting material. The absolute configuration of the latter was determined by Prelog and Scherrer,[2] by chemically relating its (−)-antipode to (+)-S-hydratropic acid. The optically pure (−)-β-phenylbutyric acid is usually obtained *via* the menthol ester.[3] However, Eliel *et al.*[4] obtained partial resolution of the acid using (+)-α-phenylethylamine. By repeated recrystallization of the phenylethylamine salt we were able to isolate the acid in high optical purity. Furthermore, since both antipodes of α-phenylethylamine are available, this method makes it possible to obtain both forms of the acid.

The 3-methyl-1-indanone (II) resulting from the Friedel-Crafts synthesis, had an optical rotation of $[\alpha]_D^{25} = +3.80°$ (neat), when β-phenylbutyric acid with $[\alpha]_D^{25} = +52.3°$ (benzene) was used. It is possible that this step involves some racemization, and therefore, it is uncertain whether our final indenes are optically pure. However, the rotation of the hydroxy compound (III) was as high as −39.2 °(benzene). No attempts were made to determine the proportion of the *cis*- and/or the *trans*-form in the product (III). The syntheses of (VI) and (VII) have been previously described in detail for the racemic substances.[5] In order to obtain (VIII) in a fair yield, it was necessary to modify the previously described method by substituting benzene for tetrahydrofuran in the Grignard reaction. The final reactions are unlikely to involve racemization to any appreciable extent, since rearranged products could not be detected. Further, the optical rotation

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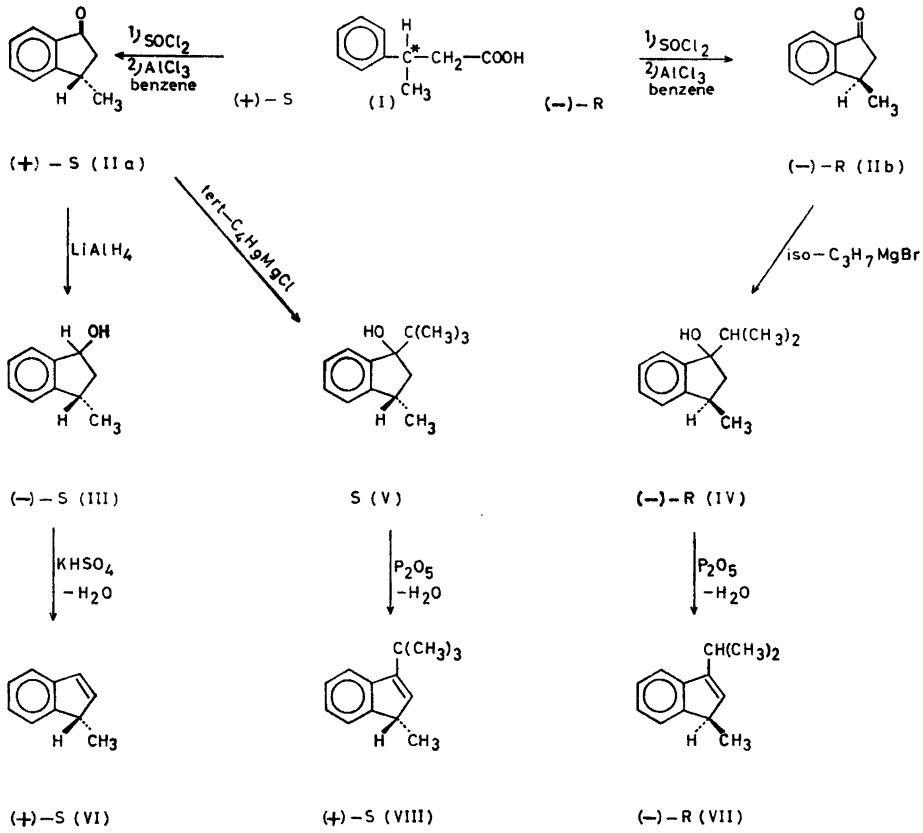

Fig. 1.

of the final products (VI—VIII) are quite satisfactory (for example $[\alpha]_D^{25} = +182.1°$ (benzene) for VI) for our purpose of following rearrangement rates.

Since the absolute configuration of β-phenylbutyric acid is known, and no inversion could possibly occur during the synthetic routes described, the absolute configurations of the alkylindenes (VI—VIII) are established (Fig. 1).

EXPERIMENTAL

Racemic β-phenylbutyric acid (I) was prepared from crotonic acid and benzene;[6] b.p. 153—154° (10 mm), m.p. 37—39° (from petroleum ether), yield 76 %.

(+)- *and* (–)-*β-Phenylbutyric acid.* 34.4 g (0.285 moles) of (–)-α-phenylethylamine were added to a solution of 46.6 g (0.285 moles) of rac. β-phenylbutyric acid in 127 ml of ethanol and 136 ml of water. After standing at room temperature overnight, the salt was collected and dried. It was recrystallized from ethanol and water and, after each recrystallization, the acid was liberated from a small amount of the salt and its rotation determined in benzene solution (Table 1).

Table 1.

Crystallization	Ethanol (ml)	Water (ml)	Salt obtained (g)	m.p. of salt	$[\alpha]_D^{25}$ of acid (in benzene)
1	127	136	32.5	135–140°	–
2	45	45	25.5	142–143.5°	+41.5°
3	25	35	19.7	144–145.5°	+48.5°
4	20	40	16.8	144.5–146°	+52.2°

From 16.8 g of α-phenylethylamine salt the acid was liberated. The resulting (+)-β--phenylbutyric acid (9.1 g 20 % $[\alpha]_D^{25} = +52.3°$) was used in the subsequent reactions without further purification. From the combined mother liquors, (−)-β-phenylbutyric acid (13.5 g, 0.082 moles, $[\alpha]_D^{25} = -30.8°$) was liberated. It was dissolved in 37 ml of ethanol and 39 ml of water. 9.6 g (0.082) moles) of (+)-α-phenylethylamine were added. The collected salt was recrystallized from ethanol and water (Table 2). Liberation of the acid gave 6.6 g (14 %) of (−)-β-phenylbutyric acid, $[\alpha]_D^{25} = -51.1°$.

Table 2.

Crystallization	Ethanol (ml)	Water (ml)	Salt obtained (g)	m.p. of salt	$[\alpha]_D^{25}$ of acid (in benzene)
1	37	39	15.1	142.5–144°	−48.2°
2	20	40	12.7	144–145.5°	−51.2°

(+)-*3-methyl-1-indanone* (*II a*) 9.0 g (0.055 moles) of (+)-β-phenyl-butyric acid were heated with 20 g (0.168 moles) of freshly distilled thionylchloride at 80° for 3 h. Excess reagent was removed in vacuum; dry benzene was added and the evaporation process was repeated. The acid chloride was dissolved in 30 ml of dry benzene and slowly added to 20 g of anhydrous aluminium chloride in 70 ml of dry benzene The resulting mixture was refluxed for 1.5 h, cooled and poured on to ice and concentrated hydrochloric acid. The benzene layer was separated, the aqueous layer extracted with benzene and the combined organic layers were washed with water and dried. Evaporation of the solvent and distillation gave 6.5 g (81 %) of (+)-3-methyl-1-indanone, b.p. 112–113.5° (9 mm), $[\alpha]_D^{25} = +3.8°$ (neat).

(−)-*1-Hydroxy-3-methylindane* (*III*) (+)-3-methyl-1-indanone (6.2 g, 0.043 moles) were reduced with $LiAlH_4$ as described for the racemic substance,[7] yielding 6.0 g (94 %) of (−)-1-hydroxy-3-methylindane, m.p. 86.5–87.0° (from petroleum ether). $[\alpha]_D^{25} = -39.2°$ (benzene).

(+)-*1-Methylindene* (*VI*). 5.9 g (0.040 moles) of (III) were dehydrated by distillation over 7.0 g of potassium bisulphate,[7] yielding 2.5 g (48 %) of (+)-1-methylindene, b.p. 67.0–67.5°, $[\alpha]_D^{25} = +182.1°$ (benzene), $[\alpha]_D^{25} = +173.0°$ (pyridine).

(−)-*1-Methyl-3-isopropylindene* (*VII*). (−)-3-Methyl-1-indanone (II b) (4.9 g, 0.034 moles, 83 %) was prepared from 6.6 g (0.040 moles) of (−)-β-phenylbutyric acid as described for the other antipode above; $[\alpha]_D^{25} = -4.1°$, b.p. 114–115° (9 mm). Reaction with isopropyl magnesium bromide, as in the preparation of the racemic compound[5] gave 5.6 g (0.030 moles) of the crude alcohol, (−)-1-hydroxy-1-isopropyl-3-methylindane (IV), $[\alpha]_D^{25} = -33.1°$ (benzene). Dehydration with phosphorus pentoxide in benzene gave 2.5 g (43 %, calculated on 3-methyl-1-indanone), of 1-methyl-3-isopropylindene b.p. 54–56° (0.15 mm). 1.5 g of the product were chromatographed on 80 g of silicic acid (Mallinckrodt). Elution with petroleum ether (b.p. 60–75°) gave in the first fraction the pure product $[\alpha]_D^{25} = -111.0°$ (benzene). The subsequent fractions, however, con-

tained some 1-methyl-3-isopropylidene indane. The optical rotations were determined for some fractions containing different amounts of 1-methyl-3-isopropylidene indane. From these data the specific rotation of 1-methyl-3-isopropylidene indane was calculated to approximately +90°.

(+)-*1-Methyl-3-tert-butylindene* (*VIII*). *tert*-Butyl magnesium chloride was prepared from 4.8 g (0.052 moles) of *tert*-butylchloride and 1.2 g (0.052 g at.) of magnesium in 35 ml of dry tetrahydrofuran under nitrogen. After complete addition of the chloride, the product was refluxed for 30 min. 5.0 g (0.034 moles) of (+)-3-methyl-1-indanone in 15 ml of dry tetrahydrofuran were added at room temperature over a period of 20 min. The resulting mixture was kept under reflux in a nitrogen atmosphere for 5 h and left standing at room temperature overnight. The complex was decomposed by the addition of 40 ml of a saturated aqueous ammonium chloride solution. The product was extracted with ether, and the ether solution dried and evaporated. The crude alcohol (7.7 g) thus obtained, was dissolved in 30 ml of dry benzene and treated with 7.0 g of phosphorus pentoxide at reflux temperature for 10 min. The benzene layer was repeatedly washed with water and dried. Evaporation of the solvent gave 5.6 g of crude (+)-1-methyl-3-*tert*-butylindene, which were purified chromatographically on silicic acid (Mallinckrodt). Elution with petroleum ether gave the pure compound, yield 30 %, $n_D^{25} = 1.5292$, $[\alpha]_D^{25} = +110.2°$ (benzene).

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