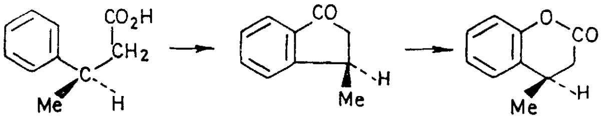
Preparation and Absolute Configuration of the Enantiomeric 3,4-Dihydro-4-methylcoumarins

By J. **Grimshaw"** and **P. 6. Pillar,** Department of Chemistry, Queen's University, Belfast BT9 5AG

Enantiomers of 3-phenylbutyric acid have been converted into 3,4-dihydro-4-methylcoumarin. (-t-)-(I?)-3,4-d{-hydro-4-methylcoumarin has [alD20 +35" (c 1 in benzene).

THE value of the specific rotation of 3,4-dihydro-4-methylcoumarin was required for comparison with the results described in the preceding paper.l Some attempts were made to resolve 3-(o-methoxyphenylj-butyric acid, which could then be demethylated to give the dihydrocoumarin, but no crystalline salt of the acid with an optically active amine could be obtained. Enantiomers of the dihydrocoumarin were eventually prepared from active 3-phenylbutyric acid. Resolution of 3-phenylbutyric acid 2 proceeds readily on crystallisation of its salts with active 1-phenylethylamine. The absolute configuration of (-)-(RR)-3-phenylbutyric acid 3 (I) has been determined by relating this acid chemically to (+)-(S)-hydratropic acid. The S-phenylbutyric acid was converted into 3-methylindan-l-one, which afforded 3,4-dihydro+methylcoumarin after oxidation with a peroxy-acid.

Weidler and Bergson 4 have prepared both enantiomers of 3-methylindan-l-one from the active 3-phenylbutyric acids by treating the acid chlorides with aluminium chloride in dry benzene. However, Eliel and his co-workers 2 have shown that active 2-phenylbutane is rapidly racemised by aluminium chloride at 0". We therefore employed warm polyphosphoric acid to cyclise the 3-phenylbutyric acid. 5 To ensure that racemisation was not taking place under these conditions the c.d. of (R)-3-methylindan-l-one, in dioxan, was measured after treatment with polyphosphoric acid under the same conditions as used in the cyclisation reaction. Comparison with the c.d. measured before this treatment showed no significant difference.



(1) (-l-(W PI) (+)-P) (III) (+f-w

Sign of rotation for solution in benzene at 589 nm.

The preparation of 3,4-dihydrocoumarin by oxidation of indan-l-one with peroxy-acids has been reported.6

EXPERIMENTAL

Attempted Resolution of 3-(o-Methoxyphenyl)butyriG Acid. -Equimolar quantities of the acid and each of several optically active amines [cinchonine, codeine, yohimbine, sparteine, and (-)-1-phenylethylamine] were dissolved in aqueous ethanol. K'o crystalline salts could be obtained.

(-j-)-(S)- and (-)-(R)-3-Phenylbztty~ic Acid.--S-Phenylbutyric was resolved by use of (**f**)- and ( )-l-phenylethylamines.l The diastereoisomeric salts crystallised from aqueous ethanol and the recovered acids had the following properties: (+)-(S)-acid [a],2o +-52" (c 1 in benzene), (-)-@)-acid *[a],,"" -51"* (c **1** in benzene) {lit.,' [a],2o -57.2 (G 9 in benzene), *[a],""* *-5S.5* (c *2* in benzene)).

3-Mcthylindan- I-one.-3-Phenylbutyric acid (10 g.) and polyphosphoric acid (29 g.) were mixed at 50" and kept at 95" for 90 min.; the colour changed from yellow to *red.* The mixture was then poured on crushed ice (ca. 40 g.) and triturated until the polyphosphoric acid had decomposed. The organic product was extracted with benzene, washed with dilute sodium hydroxide and water, dried WEm*) | and evaporated. Distillation of the residue afforded 3-methylindan-l-one (6.4 g., 72%), b.p. 116-**llS"/lO** mm. (lit., 4 **112-113"/9** mm.). (+)-(S)-S-Phenylbutyric acid gave (S)-3-methylindan-l-one, *[a],"0* — l-4" (c **1** in benzene) and j-16" (c 2 in acetone); (-)-(R)-3-phenylbutyric acid gave (K)-3-methylindan-l-one (II) [a],"0 +2*0" (c 1 in benzene) and – 20" (c **1** in acetone), broad negative c.d. with at least three partially resolved peaks, &,. 350 (AE -0*495), 340 (-l-05), and 325 nm. (AC **-1.11).**

*Enantiomers of 3,4-Dihy&o-4-methylcownavin.-3-Methyl*indan-l-one (1.5 g., 0.01~) and peroxylauric acid (4.3 g., 0.0211) in dichloromethane (25 ml.) containing methanesulphonic acid (**1** g.) were heated under reflux in the dark **for 24** h. The mixture was then gently swirled with an excess of cold dilute sodium hydroxide solution, and the dichloromethane layer was washed with dilute hydrochloric acid and water, dried (MgSO,), and evaporated. The residue was distilled to yield 3,4-dihydro-4-methylcoumarin, b.p. **S7-90'/0*1** mm. (1.6 g., SO%), whose purity was determined by g.1.c. analysis [Perkin-Elmer Fl 1 instrument; fluorosilicone oil column (2 m.) ; temp. 130'1. The principal impurity was unchanged methylindanone and a calibration graph was made for methylindanone-dihydromethylcoumarin mixtures. (R)-3-lMethylindan-l-one gave a mixture with [a],"O +24" (c **1** in benzene) of dihydrocoumarin (75%) and indanone (25%). Thus the pure (+)-(R)-3,4-dihydro-4-methylcoumarin (III) had *[a],""* + *32"* (c **1** in benzene).

(S)-3-Methylindan-l-one gave a mixture *[a],""* — *23"* (c 1 in benzene) of dihydrocoumarin (76%) and indanone (24%). Thus (-)-(S)-3,4-dihydro-4-methylcoumarin had [a],"" -30" (c **1** in benzene).

---

l R. N. Gourley, J. Grimshaw, and P. G. Millar, preceding paper.

2 E. L. Eliel, P. H. Wilken, and F. T. Fang, *J. Org. Chem.*, 1957, 22, 231.

3 V. Prelog and H. Scherrer, *H&v. Chim. Acta*, 1959, 42, 2227.

4 A. M. Weidler and G. Bergson, Acta Cham. &and., 1964, 18, 1484.

5 H. R. Snyder and F. X. Werber, *J. Anzer. Chem. SOL, 1950, 72*, 2965.

6 M. Clerc-Bory and C. Mentzer, *Camp. rend., 1955, 241,* 1316.

' H. Rupe, *Annalen*, 1909, 369, 325; D. J. Cram, *J. Amer, Chem. SOL, 1952, 74,* 2138.

In a third experiment the oxidation was continued for 48 hr., and a pure sample (g.l.c. analysis) of (+)-(*R*)-3,4-dihydro-4-methylcoumarin was obtained after chromatography of the product on neutral alumina; $[\alpha]_D^{20}$ +31° (*c* 1 in benzene), o.r.d. (*c* 0·8 in hexane): $[\alpha]_{590}$ +12·1°, $[\alpha]_{400}$ 30·5°, $[\alpha]_{350}$ 56°, $[\alpha]_{300}$ 135°, extremum $[\alpha]_{285}$ +315°, $[\alpha]_{270}$ ±0°, $[\alpha]_{260}$ −935°.

If the maximum specific rotation of (−)-(*R*)-3-phenylbutyric acid is taken as −58° (benzene), pure (+)-(*R*)-3,4-dihydro-4-methylcoumarin has $[\alpha]_D^{20}$ +35° (*c* 1 in benzene).

We thank the Ministry of Education, N. Ireland, for a studentship (to P. G. M.), and Dr. D. N. Jones (Sheffield) for the o.r.d. measurement.

[0/446 *Received, March* 20*th*, 1970]