ABSOLUTE CONFIGURATION OF (1*R*,2*S*,4*R*,6*S*,7*R*)-(+)-3--OXOTRICYCLO[2,2,1,$0^{2,6}$]HEPTANE-7-CARBOXYLIC ACID*

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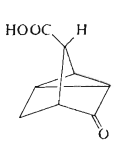
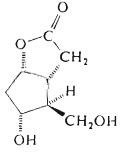
The title acid was assigned absolute configuration on the basis of stereoselective condensation with optically active amines.

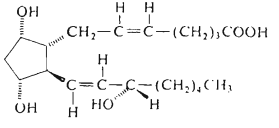
One of the syntheses leading to prostaglandins starts from norbornadiene[1] which is converted by Prins reaction into diformate of 3-hydroxymethyltricyclo[2,2,1,$0^{2,6}$]-heptan-5-ol. Its oxidation afforded the keto acid I which was resolved into its enantiomers with (−)-1-phenylethylamine. The (+)-enantiomer was converted by a series of stereospecific reactions into the Corey lactone *II* and further into the natural prostaglandin $PGF_{2\alpha}$ (*III*). The absolute configuration of compound *III* has been determined by X-ray diffraction and degradation to (*S*)-(+)-2-hydroxyheptanoic acid[2].



I



II



III

* Part LX in the series Asymmetric Reactions; Part LIX: This Journal *48*, 1618 (1983).

Since absolute configuration of the acid *I* follows only indirectly from the mentioned reaction sequence, we assigned it in this paper using the method elaborated in our laboratory[3,4]. Reaction of the racemic keto acid *I* with optically active (*S*)-(−)-1-phenyl-1-methylaminoethane or (*S*)-(+)-1-phenyl-2-methylaminopropane in the ratio 1·5 : 1 in the presence of N,N′-dicyclohexylcarbodiimide in tetrahydrofurane afforded – after removal of N,N′-dicyclohexylurea and amide of *I* – the unreacted optically active levorotatory keto acid *I*. If one assumes that the keto group containing part of the molecule represents a sterically more bulky substituent than the three-membered ring moiety, the levorotatory enantiomer of the acid *I* has the 7*S* configuration. This determined also the configuration of the other chiral centers (1*S*, 2*R*, 4*S* and 6*R*).

EXPERIMENTAL

(±)-3-Oxotricyclo[2,2,1,$0^{2,6}$]heptane-7-carboxylic Acid (*I*)

Norbornadiene (79·2 g) was added at 15–25°C during 50 min to a stirred solution of paraformaldehyde (24 g) and conc. sulfuric acid (9 ml) in formic acid (480 ml). After 2 h the mixture was decomposed with ice-cold water (700 ml) and the aqueous phase was extracted with ether (3 × × 440 ml). The ethereal extracts were combined, washed four times with saturated solution of sodium chloride and dried over sodium sulfate. Distillation *in vacuo* afforded 74 g (44%) of 3-hydroxymethyltricyclo[2,2,1,$0^{2,6}$]heptan-5-ol diformate, b.p. 85–90°C/40 Pa.

The diformate (40 g) was dissolved in acetone (690 ml) and oxidized with Jones reagent (310 ml) at −10°–0°C. The mixture was stirred at this temperature for 13 h during which time further Jones reagent (100 ml) was added. After decomposition with 2-propanol (107 ml) and addition of sodium chloride (340 g), the solid material was filtered and washed with ethyl acetate (5 × × 110 ml). The aqueous phase was separated and the organic one dried over magnesium sulfate and taken down. The obtained racemic acid *I* (9 g; 29%) was crystallized from ethyl acetate; m.p. 143–144·5°C.

Asymmetric Transformation of Racemic Acid *I*

To a solution of the racemic acid *I* (1·14 g; 7·5 mmol) in tetrahydrofuran (3 ml) was added dicyclohexylcarbodiimide (1·03 g; 5 mmol), followed by a solution of 5 mmol of (*S*)-(−)-1-phenyl-1-methylaminoethane (*a*) or (*S*)-(+)-1-phenyl-2-methylaminopropane (*b*) in tetrahydrofuran (3 ml). After standing for 24 h at room temperature, ether (50 ml) was added and the mixture was filtered. The unreacted acid was extracted from the filtrate with 10% aqueous sodium hydroxide, liberated by acidification with sulfuric acid and taken up in ether. After drying over sodium sulfate and removal of the solvent, the obtained acid melted at 139–141°C; for (*a*) $[\alpha]_D^{20}$ −8·4° (*c* 1, methanol), for (*b*) $[\alpha]_D^{20}$ −6·2° (*c* 1, methanol).

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4. Červinka O., Hub L.: This Journal *32*, 2295 (1967); 33, 2927, 2933 (1968).

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