Formation of a Chiral β-Lactam by Photocyclisation of an Achiral Oxo Amide in its Chiral Crystalline State

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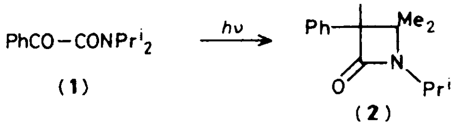
Chiral crystals of the achiral oxo amide *N,N*-di-isopropylphenylglyoxylamide, prepared in large quantities, were irradiated in the solid state to give the optically active β-lactam 3-hydroxy-1-isopropyl-4,4-dimethyl-3-phenylazetidin-2-one in high optical and chemical yields.

Optically active β-lactams are important antibiotics, and have long been a target of organic synthesis. In all cases, however, a chiral source is essential for enantiomeric control. We have found that the achiral oxo amide *N,N*-di-isopropylphenylglyoxylamide (**1**) forms chiral crystals, which upon irradiation in the solid state give the optically active Norrish Type II photocyclisation product, 3-hydroxy-1-isopropyl-4,4-dimethyl-3-phenylazetidin-2-one (**2**) in high optical and chemical yields.

Recrystallisation of the oxo amide (**1**), prepared according to the reported method,[1] from benzene afforded colourless prisms. That each crystal (5—10 mg) was chiral was shown by photochemical conversion into the optically active lactam (**2**). Crystals of (**1**) which gave (+)- or (−)-(**2**) on photocyclisation are tentatively identified as (+)- and (−)-(**1**), respectively. Crystals of (+)- and (−)-(**1**) can easily be prepared in large quantities by seeding with finely powdered crystals of (+)- and (−)-(**1**) during recrystallisation of (**1**) from benzene. Seeding with (−)-(**1**) during recrystallisation of (+)-(**1**) gives (−)-(**1**), and *vice versa*.

Irradiation of crystals of (+)-(**1**) (200 mg) with a high-pressure mercury lamp, with occasional grinding (agate pestle and mortar) at room temperature for 40 h gave (+)-(**2**) {74% yield, $[\alpha]_D$ +123° (*c* 0.5 in $CHCl_3$), 93% enantiomeric excess (e.e.), m.p. 149—150 °C} after purification by column chromatography on silica gel. The optical purity of (**2**) was determined by h.p.l.c. on an optically active solid phase.† Irradiation of (−)-(**1**) under the same conditions gave (−)-(**2**) with 93% e.e. in 75% yield. Purification to 100% e.e. can



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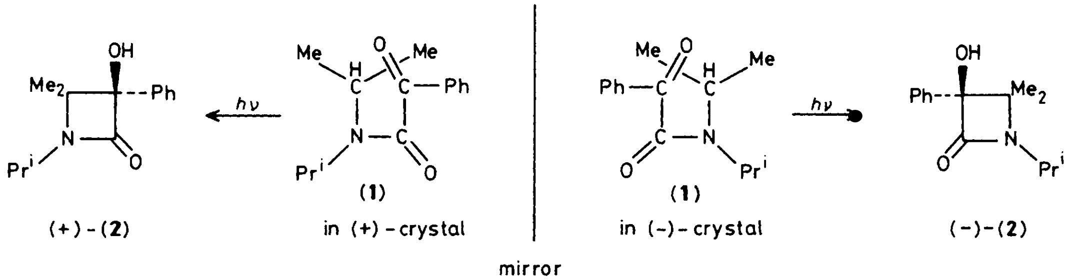
† Chiralcel OC, from Daicel Chemical Industries, Ltd., Himeji, Japan.



Scheme 1. A possible mode of formation of optically active (**2**) from achiral (**1**) in its chiral crystal. The relationship between the depicted absolute configuration and sign of $[\alpha]_D$ is arbitrary.

easily be achieved by recrystallisation from benzene. The structure of the optically active (**2**) was determined by comparison of spectral data with those reported for racemic (**2**).[2]

The foregoing results are valuable in that an optically active compound is produced in bulk from achiral material. Only a few successful examples of photochemical conversion of achiral into chiral material in the absence of a chiral source have been reported hitherto,[3] and in these cases the conversion was carried out only on a fragment of chiral crystal. In our case, chiral crystals are available in bulk, and mass product of the chiral product is possible. Moreover, the present data may throw some light on the generation of optically active amino acids on Earth.[4,5] Photocyclisation of (**1**) proceeds efficiently in sunlight and hydrolysis of the optically active (**2**) gives an optically active β-amino acid.

A possible mode of formation of optically active (**2**) from achiral (**1**) in the chiral crystal is shown in Scheme 1. Since in the crystal lattice the molecular motion of (**1**) is restrained, Norrish Type II reactions in the chiral (+)- and (−)-crystals proceed stereoselectively.

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