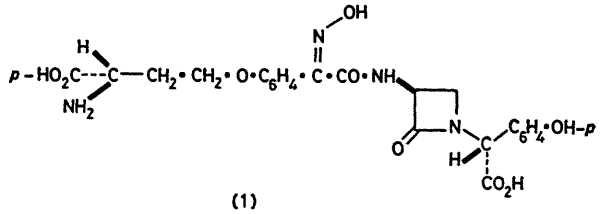
Preparation of 3-Phenylacetamidoazetidine-2,4-diones

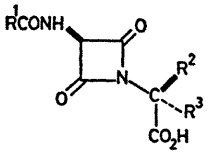
By ARUN C. KAURA and RICHARD J. STOODLEY*
(*Department of Organic Chemistry, The University, Newcastle upon Tyne* NE1 7RU)

Summary *trans*-3-Phenylacetamido-4-pyruvoyloxyazetidin-2-ones, prepared by the reaction of 3-benzyl-7-oxo-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-enes with pyruvic acid, are converted into 3-phenylacetamidoazetidine-2,4-diones when irradiated in benzene.

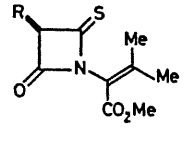
THE nocardicins, *e.g.* (**1**), reveal that appropriate monocyclic azetidinones can display significant antibacterial activity.[1] As part of a programme aimed at the synthesis of monocyclic derivatives incorporating an electronically activated β-lactam linkage, we have been interested in preparing azetidine-2,4-diones of type (**2**). Although related compounds, *e.g.* (**3**), have been described by other groups,[2-4] the recent report by Bachi and his co-workers,[5] in which the thione (**3b**) was converted into the dione (**4b**) by oxidation with ozone or *m*-chloroperbenzoic acid, prompts us to report our results. Binkley has shown that pyruvoyl esters of secondary alcohols are converted into ketones,



(1)

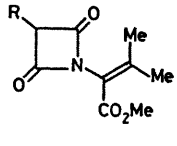


(2)



(3)

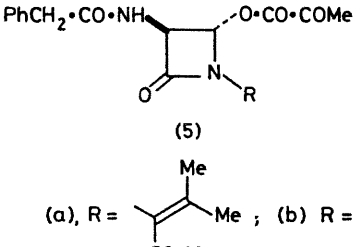
(a) R = $PhCH_2 \cdot CO \cdot NH$
(b) R = phthalimido



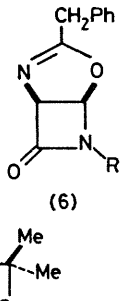
(4)

(a) R = $PhCH_2 \cdot CO \cdot NH$
(b) R = phthalimido

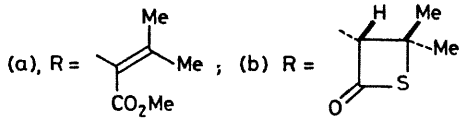
acetaldehyde, and carbon monoxide, when irradiated in benzene.[6] Consequently, we investigated the feasibility of deriving azetidine-2,4-diones from compounds of type (5).

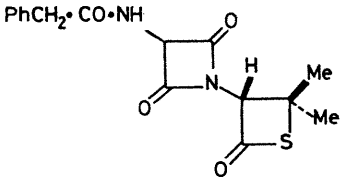


(5)



(6)





(7)

Previously, we have shown[7] that oxazoline-azetidinones of type (6) react with acetic acid with rupture of the 4,5-bond to give *trans*-acetoxyazetidinones. When treated with pyruvic acid, compound (**6a**)[8] was converted (72%) into the azetidinone (**5a**),† $[\alpha]_D$ −55° (EtOH). Irradiation of a 1% solution of the pyruvate (**5a**) in benzene with a Hanovia u.v. lamp for 48 h, and purification of the product by silica gel chromatography, afforded the dione (**4a**)† (87%), m.p. 130—131 °C. In common with other azetidine-2,4-diones,[9] the compound (**4a**) showed a weak i.r. absorption at 1883 cm^{-1} and a strong one at 1745 cm^{-1} for the ring carbonyl groups. The 3-hydrogen atom appeared as a doublet (J 7 Hz) at δ 4·80.

The pyruvate (**5b**),† $[\alpha]_D$ −64° ($CHCl_3$), prepared in 88% yield by treatment of the oxazoline-azetidinone (**6b**)[10] with pyruvic acid, was similarly converted into the dione (**7**); the product was isolated as a chromatographically homogeneous syrup (43%),† $[\alpha]_D$ −19° ($CHCl_3$), after silica gel chromatography.

The foregoing results are of interest in that they reveal that the Binkley photoreaction can be employed to generate a carbonyl group adjacent to a β-lactam nitrogen atom; this comprises a new route to azetidine-2,4-diones. Moreover, the procedure makes available, for the first time, azetidine-2,4-diones bearing an acylamino-group at position 3.

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† The compositions of new compounds were confirmed by elemental analysis and/or mass spectroscopy; their spectral properties were in accordance with the assigned structures.

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