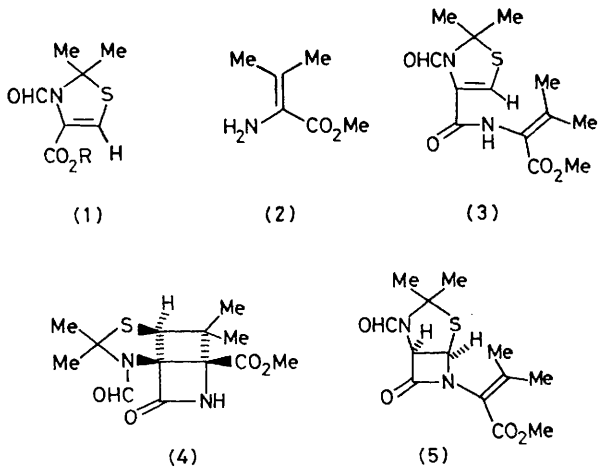
Photochemical Synthesis of a Novel β-Lactam

By PRABIR K. SEN, CHRISTOPHER J. VEAL, and DOUGLAS W. YOUNG*

Summary The dehydrovaline acrylamide (**3**) has been photolysed to yield the novel fused β-lactam system (**4**); this finding opens up a possible route to compounds which may be of interest in the light of current views on the mode of action of β-lactam antibiotics.

IT has been suggested that the antibacterial action of β-lactam antibiotics is related to the reactivity of the strained β-lactam ring towards nucleophiles.[1] It is, therefore, of interest to consider how additional ring strain in penicillins and cephalosporins might affect the biological activity of compounds of this type. We now report a method of synthesis of 3-oxo-2-azabicyclo[2.2.0]hexanes which may afford entry to the penicillin and cephalosporin analogues.

The ester (**1**, R = Me)[2] was hydrolysed to the acid (**1**, R = H)† using methanolic sodium hydroxide. The acid was converted into a mixed anhydride using ethyl chloroformate and condensed with methyl dehydrovalinate (**2**)[3] to yield the dehydrovaline acrylamide (**3**).† When a solution of the acrylamide in either dioxan or pyridine was irradiated using a Hanovia 125 W medium pressure lamp and a Pyrex filter, a product was obtained in 6% yield which had the characteristic carbonyl absorption of a β-lactam group at 1780 cm^{-1} in the i.r. spectrum. This product, $C_{13}H_{18}N_2O_4S$,‡ m.p. 148—150 °C, had but end absorption in the u.v. spectrum and the ^1H n.m.r. spectrum showed the presence of four singlet *C*-methyl groups, one methoxy group, and one formyl group. The olefinic proton of the starting material had been replaced by a singlet at τ 6·1 and there was an exchangeable (NH) proton at τ 3·02. Ions at *m/e* 270 (M^+ − CO) and 255 (M^+ − CONH) in the mass spectrum supported the β-lactam structure.[4] The structure (**4**) is in accord with these data and would result from a $\pi 2_s + \pi 2_s$ cycloaddition reaction of the diene forming a cyclobutane ring and at the same time creating a β-lactam ring. It is of interest to note that when the acrylamide



chromophore is not protected as the thiazoline, such photolyses take an alternative path.[5] There was no evidence for the presence of the alternative β-lactam (**5**) among the reaction products. This would have arisen by a pathway such as that noted by Chapman and Adams.[6]

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† These compounds had the expected analytical and spectroscopic data.

‡ Molecular formula is based on accurate mass measurement of the ion at *m/e* 270, and observation of a strong parent ion at *m/e* 298 in the field desorption mass spectrum. The compound is isomeric with the starting material.

[1] See for example, R. B. Morin, B. G. Jackson, R. A. Mueller, E. R. Lavagnino, W. B. Scanlon, and S. L. Andrews, *J. Amer. Chem. Soc.*, 1969, **91**, 1401.
[2] D. W. Young, D. J. Morecombe, and P. K. Sen, *European J. Biochem.*, 1977, **75**, 133.
[3] C. J. Veal and D. W. Young, *J.C.S. Perkin I*, 1975, 2086.
[4] P. V. De Marco and R. Nagarajan, 'Cephalosporins and Penicillins, Chemistry and Biology,' Academic Press, New York, 1972, p. 311 *et seq.*
[5] C. J. Veal and D. W. Young, *Tetrahedron Letters*, 1976, 2985.
[6] O. L. Chapman and W. R. Adams, *J. Amer. Chem. Soc.*, 1968, **90**, 2333.