Oxidation of Clavulanic Acid and a Ready Synthesis of the 7-Oxo-4-oxa-1-azabicyclo[3.2.0]hept-2-ene Ring System

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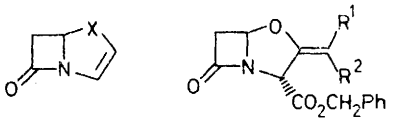
Summary Pyridinium chlorochromate oxidation of benzyl clavulanate gave the *Z*- and *E*-aldehydes (**3**) and (**4**), whereas attempted Pfitzner–Moffat oxidation resulted in the formation of the diene (**5**).

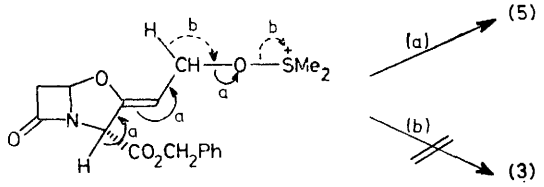
CURRENT knowledge concerning the degree of strain which may be accommodated by fused, bicyclic β-lactam systems has been extended by recent reports of structural types (**1**, X = CH_2)[1,2] and (**1**, X = S).[3] We now describe a simple, high-yielding preparation[4] of the analogous 7-oxo-4-oxa-1-azabicyclo[3.2.0]hept-2-ene system (**1**, X = O) arising out of our attempts to oxidise benzyl clavulanate (**2**).

When (**2**) was oxidised using pyridinium chlorochromate in methylene chloride (20 min; room temp.), clean conversion into a less polar product was observed (t.l.c.); fractionation on silica gel gave the required aldehyde (**3**) and the *E*-isomer (**4**) as an inseparable mixture† in the ratio (**3**):(**4**) of 1:1·2 (n.m.r.). The low (10%) isolated yield reflects the instability of the products towards chromatography.

An alternative attempt to convert (**2**) into (**3**) using the Pfitzner–Moffat method (dimethyl sulphoxide–dicyclohexylcarbodi-imide–orthophosphoric acid in benzene) resulted in the formation of a less polar material (71% after silica gel chromatography) which was not the expected (**3**) but the u.v.-fluorescent diene (**5**)† [ν_{max} ($CHCl_3$) 1805 (β-lactam CO), 1710 (ester CO), and 1635 cm^{-1} (C=C); λ_{max} (MeCN) 317 nm]. Formation of (**5**) presumably arises by a 1,4-elimination process (a)‡ from the intermediate (**6**) rather than the normal 1,2-elimination (b).



(1) (2) $R^1 = CH_2OH$; $R^2 = H$ (3) $R^1 = CHO$; $R^2 = H$ (4) $R^1 = H$; $R^2 = CHO$ (5)



(6)

The diene (**5**) polymerises on standing but may be stored for several weeks at <0 °C in ethyl acetate containing 0·01% hydroquinone.

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† Full spectral data and precise mass measurement were obtained.
‡ This elimination process has been effected subsequently with a variety of *O*-substituted clavulanic acid derivatives.

[1] U.S.P. 3,950,357; Abstracts, Sixteenth Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, 1976.
[2] A. G. Brown, D. F. Corbett, A. J. Eglington, and T. T. Howarth, *J.C.S. Chem. Comm.*, 1977, 523.
[3] R. B. Woodward in 'Recent Advances in the Chemistry of β-Lactam Antibiotics,' ed. J. Elks, Chemical Society Special Publication No. 28, 1977.
[4] The total synthesis of this novel, bicyclic ring system has recently been reported, A. J. Eglington, *J.C.S. Chem. Comm.*, in the press.