Journal of

The Chemical Society,

Chemical Communications

NUMBER 9/1973 9 MAY

Synthesis and Some Properties of an Oxa-penam

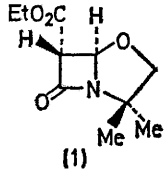
By Bernard T. Golding† and David R. Hall

(*Department of Molecular Sciences, University of Warwick, Coventry* CV4 7AL)

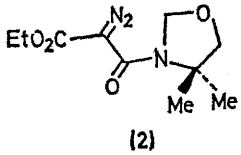
Summary Photolysis of *N*-(ethoxycarbonyl)diazoacetyl-4,4-dimethyloxazolidine (**2**) gives as major product the oxa-penam ethyl (*trans*-5H,6H)-2,2-dimethyl-7-oxo-4-oxa-1-azabicyclo[3,2,0]heptane-6-carboxylate (**1**), the β-lactam function of which is cleaved readily by nucleophilic reagents.

Analogues of the penicillins and cephalosporins derived by replacing their sulphur atom by oxygen are interesting from the standpoint of current theories[1] on the mode of action of these antibiotics. We present the synthesis[2] of a 1-oxa-analogue of a penicillin—the azaoxabicycloheptanone (**1**)—and our findings on its behaviour towards nucleophiles.

Following essentially the procedure of Lowe and his co-workers,[3] the diazoamide (**2**)‡ was prepared, and a dilute

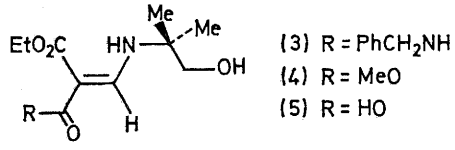


(**1**)



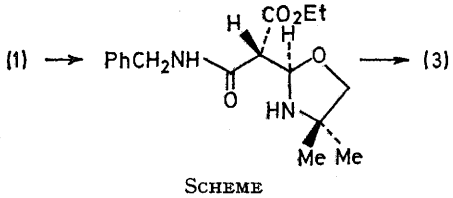
(**2**)

solution in CCl_4 was photolysed under nitrogen using a medium-pressure Hg u.v. lamp. Monitoring by i.r. spectroscopy showed the disappearance of absorptions from the starting-material (**2**) at 2135 ($N{\equiv}N^+-$), 1712 (ester C=O), and 1630 cm^{-1} (amide C=O) within 2 h, concomitant with the appearance of new bands at 1790 and 1737 cm^{-1}. These absorptions are assigned to the carbonyl group of the β-lactam function and ester function, respectively, of the



(**3**) R = $PhCH_2NH$
(**4**) R = MeO
(**5**) R = HO

(Probable configuration shown)



Scheme

oxa-penam (**1**). The n.m.r. spectrum of the solution obtained on evaporation of the reaction mixture *in vacuo* to 0·5 ml showed absorptions at τ 4·69 (d, *J* 1 Hz, 5-H), 5·82 (q, OCH_2Me), 6·19 and 6·38 (ABq, *J* 8·0 Hz, OCH_2CMe_2), 6·29 (d, *J* 1 Hz, 6-H) (collapses to sharp s on irradiation at τ 4·69), and 8·47 and 8·80 (singlets, Me_2C), 8·70 (t, OCH_2Me). These signals are assigned to the *trans*-5H,6H-stereoisomer (**1**) (stereochemistry as depicted), the small coupling constant between 5-H and 6-H indicating this stereochemistry.[4] Integration shows that this component comprises *ca.* 55% of product.

† *Present address:* Research School of Chemistry, Australian National University, P.O. Box 4, Canberra, ACT 2600, Australia.

‡ Satisfactory analytical and spectroscopic data were obtained for this compound.

Compound (**1**) could neither be directly crystallised nor further purified owing to its instability. However, we submit that the following degradative evidence taken with the spectroscopic data, shows that the oxa-penam (**1**) is the principal product from photolysis of compound (**2**). Addition of 1 mol. equiv. of benzylamine to the reaction mixture from photolysis of compound (**2**) brought about rapid formation of the benzylamide (**3**)‡ [m.p. 87—88°, τ — 0·66 br (d, J 14·0 Hz, NH), 0·78 br (CONH), 1·87 (d, J 14·0 Hz, HC=), 2·68 (s, Ph), 5·49 (d, J 6·0 Hz, CH_2OH), 5·82 (q, J 7·0 Hz, OCH_2Me), 6·56 (s, CH_2Ph), 7·27br (OH), 8·72 (s, Me_2), and 8·73 (t, J 7·0 Hz, OCH_2Me)]. This compound probably arises from the oxa-penam (**1**) by nucleophilic opening of the β-lactam and eliminative fragmentation of the resulting oxazolidine ring (*cf.* Scheme). A comparable reaction is known in penicillin chemistry.[5] Compound (**3**) was obtained in 60% yield, which correlates well with the value of 55% deduced from an n.m.r. spectrum (see above) as the yield of oxa-penam (**1**) from the photolysis. Similar products to (**3**)—compounds (**4**)‡ and (**5**),‡ respectively—were obtained on methanolysis of (**1**) and by attempted chromatography of (**1**) on silica gel.

We thank Dr. G. Lowe for a helpful discussion, and the S.R.C. and Pfizer Ltd. for a C.A.P.S. studentship (to D.R.H.)

(*Received, 29th January* 1973; *Com.* 114.)

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