Synthesis of β-Lactams by Photolytic Wolff Rearrangement

By GORDON LOWE* and DAMON D. RIDLEY

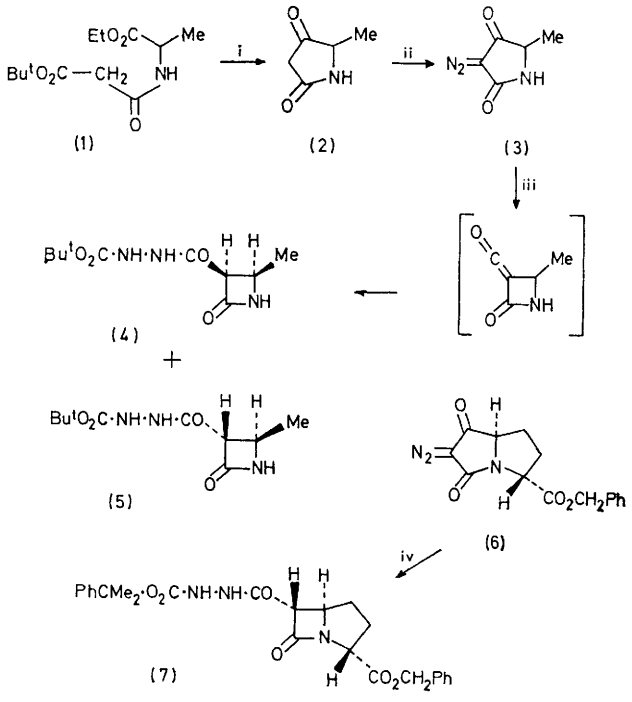
(*The Dyson Perrins Laboratory, Oxford University, South Parks Road, Oxford* OX1 3QY)

Summary A new method for the synthesis of β-lactams has been developed, using a photolytically induced ring contraction of 3-diazopyrrolidine-2,4-diones.

ALTHOUGH the Wolff rearrangement is capable of generating derivatives of cyclobutanecarboxylic acids by photolytically or thermally induced ring contraction of α-diazocyclopentanones,[1] the generation of β-lactams by the ring contraction of diazopyrrolidinediones has not hitherto been reported. The expectation that this method might be capable of generating highly strained fused β-lactam-heterocyclic systems has been realised.

N-(t-Butoxycarbonylacetyl)-DL-alanine ethyl ester (**1**), prepared by coupling DL-alanine ethyl ester and t-butyl hydrogen malonate in the presence of dicyclohexylcarbodiimide, was cyclised with potassium t-butoxide in benzene solution. The product (without purification) when heated in refluxing xylene for 1·5 h gave 5-methylpyrrolidine-2,4-dione (**2**),[2] m.p. 114–115·5° (60% overall). Diazo-transfer with methanesulphonyl azide in the presence of triethylamine[3] gave 3-diazo-5-methylpyrrolidine-2,4-dione (**3**), m.p. 115—115·5°, ν_{max} ($CHCl_3$) 2130 (CN_2) and 1700—1690 cm^{-1} (ketone and amide) in 95% yield. Photolysis of the diazo-compound (**3**) in benzene, in the presence of t-butyl carbazate (1·1 equiv.) with a medium-pressure mercury lamp in a Pyrex vessel for 1 h at room temperature, gave the *cis*-β-lactam (**4**), (36% isolated yield), ν_{max} (Nujol) 1755 (β-lactam), 1708 (O_2C·NH), and 1675 cm^{-1} (hydrazide), and the *trans*-β-lactam (**5**), (55% isolated yield), ν_{max} ($CHCl_3$) 1760 (β-lactam), 1730 (O_2C·NH), and 1695 cm^{-1} (hydrazide). The stereochemical assignments were made by ^1H n.m.r. spectroscopy.

Dibenzyl *trans*-pyrrolidine-2,5-dicarboxylate was prepared from the corresponding dicarboxylic acid,[4] and converted by steps analogous to those described above, into benzyl 3-diazo-2,4-dioxopyrrolizidine-8-carboxylate (**6**), ν_{max} ($CHCl_3$) 2160 (CN_2), 1740 (ester), and 1700—1690 cm^{-1} (ketone and amide). Photolysis in ether at −70° in the presence of αα-dimethylbenzyl carbazate (1 equiv.) gave the 1-azabicyclo[3,2,0]heptan-7-one derivative (**7**), ν_{max} ($CHCl_3$)



Reagents: i, (a) KOBu^t, (b) heat; ii $MeSO_2N_3$ + NEt_3; iii $h\nu$ > 300 nm + Bu^tO_2C·NH·NH_2; iv $h\nu$ > 300 nm + Ph·CMe_2·O_2C·NH·NH_2.

1770 (β-lactam), 1750 ($O_2C{\cdot}NH$), 1730 (ester), and 1700 cm^{-1} (hydrazide). The stereochemistry of the new chiral centre was deduced from the coupling constant of 2·0 Hz observed for the H-6 signal in the ^1H n.m.r. spectrum.[5]

Extension of this method to the synthesis of nuclear analogues of the penicillins and cephalosporins is in progress.

The assistance of Miss Janet E. Hamilton and the award of a Perkin Research Fellowship (to D.D.R.) are acknowledged.

(*Received, 2nd March* 1973; *Com.* 283.)

[1] L. Horner and E. Spietschka, *Chem. Ber.*, 1955, **88**, 934; M. P. Cava, R. L. Little, and D. R. Napier, *J. Amer. Chem. Soc.*, 1958, **80**, 2257; J. Meinwald, G. G. Curtius, and P. G. Gassman, *ibid.*, 1962, **84**, 116; P. R. Brook and B. V. Brophy, *Tetrahedron Letters*, 1969, 4187.
[2] Y. Isowa and M. Ohta, *Bull. Chem. Soc. Japan*, 1962, **35**, 1941.
[3] M. Regitz, *Angew. Chem. Internat. Edn.*, 1967, **6**, 733.
[4] G. Cignarella and G. Nathansohn, *J. Org. Chem.*, 1961, **26**, 1500.
[5] H. B. Kagan, J. J. Basselier, and J. L. Luche, *Tetrahedron Letters*, 1964, 941; K. D. Barrow and T. M. Spotswood, *ibid.*, 1965, 3325.