Synthesis of β-Lactams by Photolytic Wolff Rearrangement

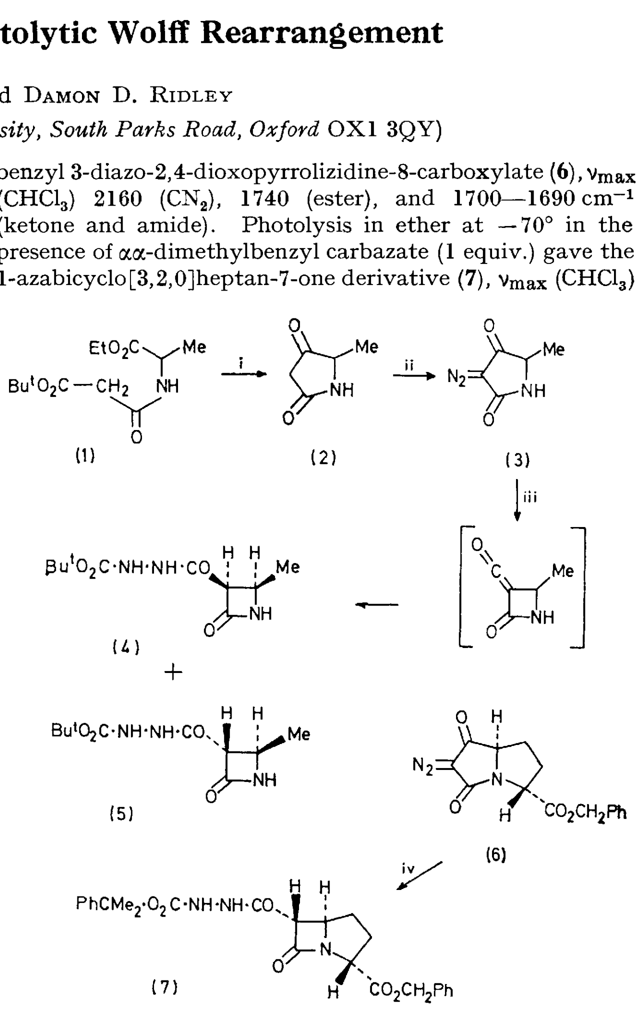
By Gordon Lowe* and Damon D. Ridley
(*The Dyson Perrins Laboratory, Oxford University, South Parks Road, Oxford* OX1 3QY)

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$_2$C·NH), and 1675 cm^{-1} (hydrazide), and the *trans*-β-lactam (**5**), (55% isolated yield), ν_{max} (CHCl$_3$) 1760 (β-lactam), 1730 (O$_2$C·NH), and 1695 cm^{-1} (hydrazide). The stereochemical assignments were made by ^{1}H 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 $\alpha\alpha$-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$_2$N$_3$ + NEt$_3$; iii $h\nu$ > 300 nm + Bu^{t}O$_2$C·NH·NH$_2$; iv $h\nu$ > 300 nm + Ph·CMe$_2$·O$_2$C·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 ^{1}H n.m.r. spectrum.[5]

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

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