

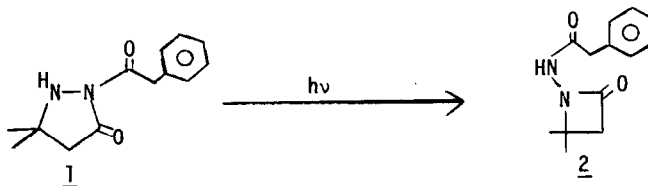
## A MODEL FOR THE PHOTOCHEMICAL FORMATION OF 6-AZA PENICILLIN ISOMERS.<sup>1</sup>

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(Received in USA 23 April 1974; received in UK for publication 20 June 1974)

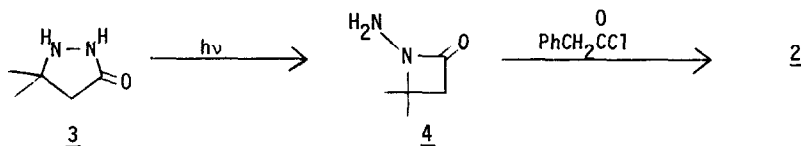
As part of our approach to the syntheses of penicillin isomers containing nitrogen in the six position (such as 12) we hope to use a novel ring contraction reaction involving the photolysis of 2-acylpyrazolidin-3-ones to introduce the  $\beta$ -lactam functionality. As a model system for the ring contraction we have investigated the photolysis of 2-phenylacetyl-5,5-dimethylpyrazolidin-3-one, 1<sup>2</sup> (mp 62-63°), which contains the side chain of penicillin G.

While initial experiments on the photochemistry of 1 indicated the formation of the desired  $\beta$ -lactam 2, they were hampered by low yields of 2 and the presence of numerous side products apparently resulting from reactions directed by the benzene ring. After experimentation, we found we were able to deal effectively with both of these difficulties. Namely, irradiation<sup>3</sup> thru corex of a non-degassed solution of 1 in *t*-butyl alcohol produced a crude reaction mixture which was shown by GLC to contain almost exclusively 2 and from which 2 could be isolated by column chromatography (silicic acid, elution with Et<sub>2</sub>O/EtOH (90/10)) in 40-50% yield.

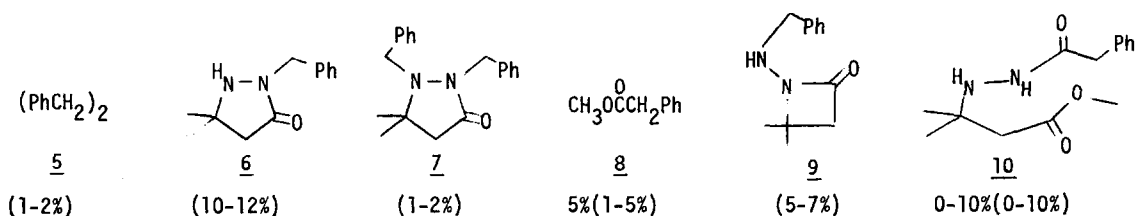


Compound 2 was assigned the structure shown on the basis of its physical data: mp 137-138°; ir (CCl<sub>3</sub>H) 3380 (N-H), 1765 ( $\beta$ -lactam), 1700 (amide) cm<sup>-1</sup>; nmr (CCl<sub>3</sub>D)  $\delta$  1.31 (s,6), 2.61 (s,2), 3.49 (s,2), 7.29 (s,5); mass spectrum (70/eV) m/e (rel intensity) 232 (M<sup>+</sup>, trace); camphor depression determined m.w. 248; analysis correct for C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>.

N-acylamino  $\beta$ -lactam 2 was also obtained by acylation of azetidin-2-one 4<sup>4</sup>, which was formed in 15% isolated (30% by nmr) yield upon irradiation<sup>3</sup> for 20 hours thru vycor of a degassed methanolic solution of freshly distilled 3.<sup>5</sup> Treatment of 4 with one equivalent of phenylacetyl chloride and one equivalent of triethylamine in benzene for several hours gave, in good yield, azetidin-2-one, 2, which was identical by NMR and IR with the major photoproduct of 1.

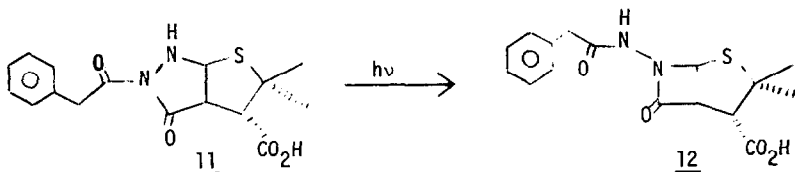


The yields of the side products from the photolysis of 1 varied considerably depending on the experimental conditions. For example, products 5 thru 10 were obtained from irradiation<sup>3</sup> thru vycor of a degassed methanolic solution of 1 in the yields shown below. The yields in brackets are GLC determined, based on the isolated yield of 2 which was 15% under these conditions.



The structural assignments of 5 thru 8 are based on comparison to samples of these molecules synthesized in our laboratories, while 9 and 10 were identified on the basis of their spectra.<sup>6</sup>

The application of these photolysis results toward the synthesis of 12 is currently under study and will be reported at a later time.



We wish to thank the National Institutes of Health (AI 10389) and the NIH Biomedical Science Support Program (S 505-RR 07041) for support of this work.

#### References

1. Presented in part at the 5th Northeast Regional Meeting of the American Chemical Society, October 17, 1973.
2. This molecule was prepared by a general procedure worked out in our laboratories. See, C.E. Hatch and P.Y. Johnson, *Tetrahedron Lett.*, 2153 (1973).
3. All irradiations were carried out at .5 to 1% w/v concentration for 2-3 hours with a Hanovia 450 watt immersion lamp.
4. This type of molecule has also been synthesized thermally starting from an azetidin-2-one. See F.D. Greene, R.L. Camp, V.P. Abegg and G.O. Pierson, *Tetrahedron Lett.*, 4091 (1973).
5. H. Stetter and K. Findeisen, *Chem. Ber.*, 98, 3228 (1965).
6. This data will be reported at a later time.