

SYNTHESIS OF OXYGEN ANALOGS OF THE PENICILLINS.

I. PHOTOCYCLIZATION OF 2-OXOAMIDES TO 3-CARBOMETHOXY-6-HYDROXYPENAMS<sup>1</sup>

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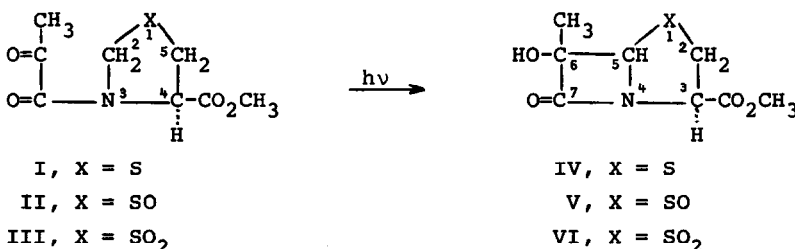
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It has recently been shown that 2-oxoamides may be photocyclized to  $\beta$ -lactams<sup>2</sup> in a manner analogous to the formation of hydroxycyclobutanones by ultraviolet irradiation of  $\alpha$ -diketones.<sup>3</sup> In the course of our investigation of synthetic approaches to penicillin derivatives, we have prepared several side-chain oxygen analogs of the penicillins lacking the gem-dimethyls by the photoisomerization of the corresponding 2-oxoamides.

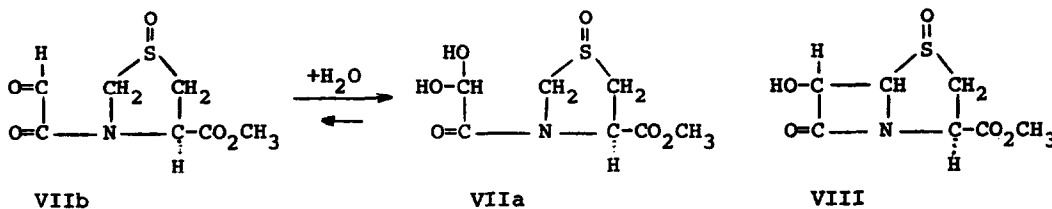
Coupling of pyruvic acid with L-4-carbomethoxythiazolidine using dicyclohexylcarbodiimide, followed by silica gel chromatography, led to a 50% yield of 3-pyruvoyl-4-carbomethoxythiazolidine<sup>4</sup> (I) [ir (film) 1750, 1710, 1650  $\text{cm}^{-1}$ ; nmr ( $\text{CDCl}_3$ )  $\delta$  2.41 (overlapping singlets,  $\text{COCH}_3$ ), 3.17-3.5 (m,  $\text{SCH}_2\text{C}$ ), 3.75 (s,  $\text{OCH}_3$ ), 4.66-5.44 (m,  $\text{SCH}_2\text{NCH}$ )]. Oxidation of I with sodium metaperiodate led to a mixture of diastereomeric sulfoxides II (mp 114-138°) whereas oxidation with potassium permanganate gave sulfone III (mp 120-121° dec).



Irradiation (Hanovia 200-watt lamp, pyrex filter) of the 2-oxoamides I, II, and III at 0-10° in dry benzene under nitrogen yielded, respectively, 3-carbomethoxy-6-hydroxy-6-methylpenam (IV) [ir (film) 1770, 1750  $\text{cm}^{-1}$ ; nmr ( $\text{CDCl}_3$ )  $\delta$  1.4 (s, 6- $\text{CH}_3$ ), 2.9-3.65 (m, 2- $\text{CH}_2$  and 3-CH), 3.75 (s,  $\text{OCH}_3$ ), 5.05

(overlapping singlets, OH and 5-CH); 11% yield], 3-carbomethoxy-6-hydroxy-6-methylpenam sulfoxide (V) [mp 151-152° dec; ir (KBr) 3250, 1760 (broad), 1070  $\text{cm}^{-1}$ ; nmr ( $\text{CD}_3\text{COCD}_3$ )  $\delta$  1.65 (s, 6- $\text{CH}_3$ ), 3.46 (d,  $J=4$  Hz, 2- $\text{CH}_2$ ), 3.75 (overlapping signals,  $\text{OCH}_3$  and 3-CH), 4.05 (s, OH), 4.85 and 5.08 (singlets, 5-CH); 8% isolated yield, 40% estimated by ir and nmr], and 3-carbomethoxy-6-hydroxy-6-methylpenam sulfone (VI) [mp 144-147° dec; ir (KBr) 3410, 1790, 1730  $\text{cm}^{-1}$ ; nmr ( $\text{CDCl}_3$ )  $\delta$  1.65 (s, 6- $\text{CH}_3$ ), 3.33 (s, OH), 3.55 (d, 2- $\text{CH}_2$ ), 3.99 (m,  $\text{OCH}_3$  and 3-CH), 4.7 and 4.9 (singlets, 5-CH); 70% yield].

To extend this method to an analog more closely resembling the penicillins, 3-glyoxylyl-4-carbomethoxythiazolidine sulfoxide hydrate (VII) was synthesized from L-4-carbomethoxythiazolidine and isolated as a hygroscopic solid VIIa [ir (KBr) 3400, 1745, 1660, 1040  $\text{cm}^{-1}$ ;  $M^+$  219.020,  $\text{C}_7\text{H}_9\text{NO}_5\text{S}$  (VIIb) requires 219.021; elemental analysis indicates a hydrate,  $\text{C}_7\text{H}_9\text{NO}_5\text{S}\cdot\text{H}_2\text{O}$  (VIIa)]. Preliminary photolyses of VII over molecular sieves in dry tetrahydrofuran at 0° resulted in the disappearance of the 1660  $\text{cm}^{-1}$  amide band with the concomitant appearance of a 1785  $\text{cm}^{-1}$   $\beta$ -lactam band (40% estimated yield) but the product (presumably VIII) has not been isolated.



#### FOOTNOTES AND REFERENCES

1. See J. C. Sheehan, K. R. Henery-Logan, and D. A. Johnson, *J. Amer. Chem. Soc.*, **75**, 3292 (1953) for naming system.
2. B. Åkermark, N.-G. Johansson, and B. Sjöberg, *Tetrahedron Letters*, 371 (1969).
3. W. H. Urry and D. J. Trecker, *J. Amer. Chem. Soc.*, **84**, 118 (1962); W. H. Urry, D. J. Trecker and D. A. Winey, *Tetrahedron Letters*, 609 (1962); N. J. Turro and T.-J. Lee, *J. Amer. Chem. Soc.*, **91**, 5651 (1969); R. G. Zepp and P. J. Wagner, *ibid.*, **92**, 7466 (1970).
4. All new compounds gave satisfactory analytical and spectroscopic (ir, nmr) data.