

## A New Oxidative Two-atom Expansion of the $\beta$ -Lactam Ring of a 6 $\beta$ -Aminopenicillanate

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Methyl 6 $\beta$ -(dihydro-4*H*-1,3,5-dioxazin-5-yl)penicillanate is converted into methyl (6*S*,9*S*)-8,8-dimethyl-2-oxo-5-oxa-7-thia-1,4-diazabicyclo[4.3.0]non-3-ene-9-carboxylate by the action of potassium permanganate in aqueous acetic acid.

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Recently, we have shown<sup>1</sup> that penicillanate 1,1-dioxides, *e.g.* (**1a**), react by an epimerisation- $\beta$ -elimination sequence, in the presence of 1,5-diazabicyclo[4.3.0]non-5-ene, to give azetidinesulphonic acids, *e.g.* (**2**). In the hope that it would undergo the  $\beta$ -elimination reaction without epimerisation, we at-

tempted to prepare the sulphone (**1b**). We now report an unprecedented rearrangement which occurred as a consequence of oxidation of the penicillanate (**3a**) with potassium permanganate.

When the acid (**3b**) was stirred with 41% aqueous formalde-

hyde-ether and the crude product (isolated from the ether layer) treated with diazomethane, the penicillanate (**3a**), m.p. 125–127 °C,  $[\alpha]_D^{25} +233^\circ$  (EtOH), was obtained (51% after  $\text{SiO}_2$  chromatography).

The penicillanate (**3a**) reacted with potassium permanganate (2.2 mol. equiv.) in 80% aqueous acetic acid (conditions that are usually effective for transforming penicillanates into penicillanate 1,1-dioxides<sup>2</sup>) to give compound *A* (56% after  $\text{SiO}_2$  chromatography), m.p. 149–151 °C,  $[\alpha]_D^{25} -310^\circ$  (EtOH). The constitution of compound *A*, as  $\text{C}_9\text{H}_{12}\text{N}_2\text{O}_4\text{S}$ , was established by elemental analysis and mass spectroscopy. Spectroscopic considerations revealed the presence of a  $-\text{CO}_2\text{Me}$  group [ $\nu_{\text{max}}$  1750  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  3.78 (3H, s);  $\delta_{\text{C}}$  52.7 (q) and 168 p.p.m. (s)], an unstrained  $-\text{C}(\text{O})\text{N}<$  moiety [ $\nu_{\text{max}}$  1690  $\text{cm}^{-1}$ ;  $\delta_{\text{C}}$  151 p.p.m. (s)], and a  $-\text{CH}: \text{N}-$  function [ $\delta_{\text{H}}$  7.76 (1H, s);  $\delta_{\text{C}}$  147 p.p.m. (d)], suggesting that compound *A* was bicyclic. Additionally, compound *A* incorporated a  $\text{CMe}_2$  moiety [ $\delta_{\text{H}}$  1.47 and 1.70 ( $2 \times 3\text{H}$ , s);  $\delta_{\text{C}}$  23.6 and 33.5 ( $2 \times \text{q}$ ), and 53.9 p.p.m. (s)] and two CH groups [ $\delta_{\text{H}}$  4.80 and 6.52 ( $2 \times 1\text{H}$ , s);  $\delta_{\text{C}}$  69.9 and 95.1 p.p.m. ( $2 \times \text{d}$ )]. In common with the penicillanate (**3a**), compound *A* showed in the mass spectrum a base peak at  $m/z$  174 attributable to the ion (**4**). On the basis of the foregoing information, compound *A* was considered to possess either the structure (**5**) or (**6**).

In the hope of differentiating between the two structures, compound *A* was treated with sodium borohydride in ethanol. Following silica gel chromatography a dihydro-derivative, m.p. 134–136 °C (decomp.),  $[\alpha]_D^{25} +44^\circ$  (EtOH), was isolated (81%). The 360 MHz  $^1\text{H}$  n.m.r. spectrum of this material indicated that it possessed the structure (**7a**). In particular, the chemical shift of the bridgehead proton ( $\delta$  6.68) was very similar to that of compound *A* ( $\delta$  6.52); furthermore, the methylene proton at  $\delta$  4.07 was coupled ( $J$  8 Hz) to the amino-proton at  $\delta$  6.24, as well as ( $J$  16 Hz) to the methylene proton at  $\delta$  3.67.

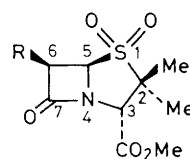
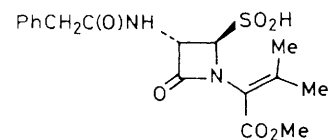
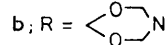
It is well established that *N*- and *O*-acylhydroxylamines can be differentiated by i.r. spectroscopy.<sup>3</sup> Corroboratory evidence that the dihydro-derivative possessed the structure (**7a**) was deduced by its conversion into the *N*-acetyl compound (**7b**) (96%), m.p. 167–169 °C (decomp.),  $[\alpha]_D^{25} -26^\circ$  (EtOH) [ $\nu_{\text{max}}$  1750 (ester CO), 1680, and 1665  $\text{cm}^{-1}$  (amide CO)], in the presence of acetic anhydride and pyridine.

On the basis of the aforementioned evidence, the structure (**5**) must be assigned to the product of oxidation of the penicillanate (**3a**) with potassium permanganate (*i.e.*, compound *A*).

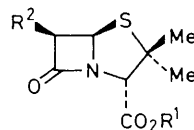
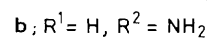
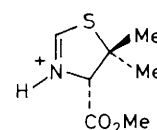
One feature of the oxathiadiazabicyclononene derivative (**5**), *i.e.* the stereochemistry of the bridgehead methine group, remained to be established. Although no diagnostic effects were observed with the compound (**5**), nuclear Overhauser effect (n.O.e.) experiments with the derived sulphone, m.p. 123–125 °C,  $[\alpha]_D^{25} -260^\circ$  (EtOH) [prepared (98%) by oxidation of the compound (**5**) with potassium permanganate] suggested that it possessed the stereostructure (**8a**). Thus the intensity of the 9-proton at  $\delta$  4.86 was increased by 10% when the methyl group at  $\delta$  1.51 was irradiated and by 2% when the methyl group at  $\delta$  1.60 was irradiated; on this evidence, the signal at  $\delta$  1.51 was assigned to the  $8\beta$ -methyl group. The intensity of the 6-proton at  $\delta$  5.91 was unaffected by irradiation of the  $8\beta$ -methyl group but was increased by 2% when the  $8\alpha$ -methyl group was irradiated.

The conversion of the penicillanate (**3a**) into the oxathiadiazabicyclononene derivative (**8b**) provides a rare example of a penicillanate rearrangement involving rupture of the 5,6-bond.<sup>4</sup> Loss of the *N*-protecting group probably does not occur until after oxidation of the nitrogen atom since, under the reaction conditions, the amine (**3c**)<sup>5</sup> was not converted into the compound (**8b**).

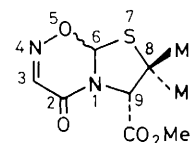
It is noteworthy that the dihydro- and tetrahydro-oxadia-

(1) a; R = PhCH<sub>2</sub>C(O)NH

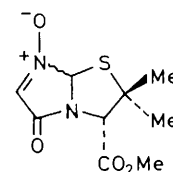
(2)

(3) a; R<sup>1</sup> = Me, R<sup>2</sup> = b; R<sup>1</sup> = H, R<sup>2</sup> = NH<sub>2</sub>c; R<sup>1</sup> = Me, R<sup>2</sup> = NH<sub>2</sub>

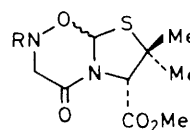
(4)



(5)

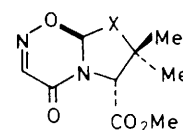


(6)



(7) a; R = H

b; R = MeCO



(8) a; X =

b; X = S

zine rings, present respectively in the compounds (**7**) and (**8a,b**), are hitherto unknown entities. Furthermore, the array of reactive functionality incorporated into the compounds, in addition to ensuring diverse chemistry, is likely to be exploitable in a synthetic context.

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