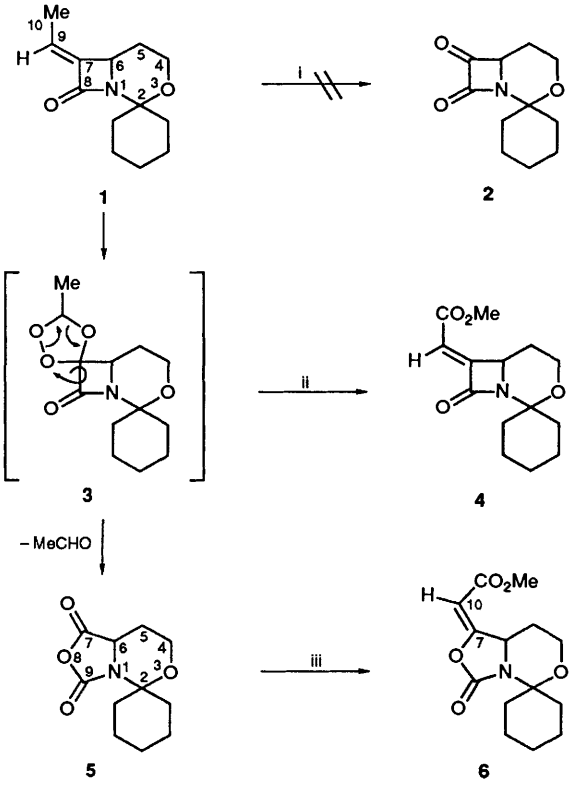
Olivanic Acid Analogues. Part 11.[1] Ozonolysis of α-Ethylideneazetidinones: Ozonide Fragmentation to α-Amino Acid-*N*-carboxyanhydrides

John H. Bateson,* Stephen C. M. Fell, Arun C. Kaura and Robert Southgate
SmithKline Beecham Pharmaceuticals, Research Division, Brockham Park, Betchworth, Surrey, RH3 7AJ, UK

Ozonolysis of (*E*)-7-ethylidene[3-oxa-1-azabicyclo[4.2.0]octane-2-spirocyclohexan]-8-one failed to provide the α-oxoazetidinone **2**, but afforded an α-amino acid-*N*-carboxyanhydride [3,8-dioxa-1-azabicyclo[4.3.0]nonane-2-spirocyclohexane]-7,9-dione **5**. [3-Oxa-1-azabicyclo[4.2.0]octane-2-spirocyclohexane]-7,8-dione **2** was instead obtained from the *trans*-ketone **9** by a sequence involving Baeyer–Villiger oxidation of the azido ketone **10**.

In continuation of our studies of synthetic precursors of molecules related to the olivanic acids, we turned our attention to the preparation of functionalised alkylidene β-lactams (*cf.* compound **4**, Scheme 1). Such compounds are potential precursors of the asparenomycin series of naturally occurring carbapenem antibiotics.[2] The readily accessible ethylideneazetidinone **1**,[3] which is obtained from the *trans*-substituted methyl ketone **9**[4] (*cf.* Scheme 3) provides a useful starting point for an 'alkene transposition' strategy leading to analogues of type **4**. We now describe in full[5] the results of some investigations into the ozonolysis of the alkene **1**, with subsequent reconstruction of a modified double bond system using Wittig methodology.



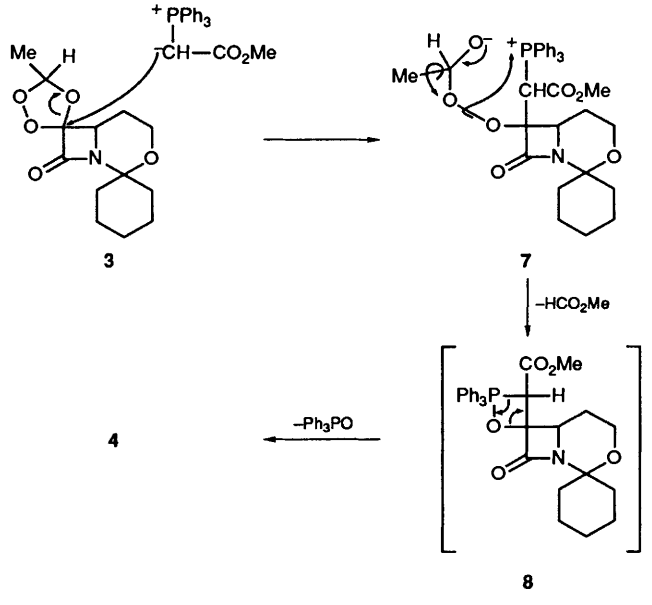
Scheme 1 *Reagents:* i, O_3, EtOAc, −70 °C, 3 min; ii, $Ph_3P{=}CHCO_2Me$ (1.2 or 2.4 mol equiv.), −70–0 °C, 1 h; iii, $Ph_3P{=}CHCO_2Me$, EtOAc, heat, 30 min

Azetidine-2,3-diones (α-keto-β-lactams) have been obtained in many areas of β-lactam chemistry. Although some monocyclic examples have been reported,[6–8] the majority of such studies comprises the chemistry of 6-oxopenicillins[9–16] and, to a lesser degree, that of 7-oxocephalosporins.[14,15,17] These materials have found utility as reactive intermediates for the synthesis of other substituted lactam systems. For example, Chiba has examined the use of a monocyclic α-oxoazetidinone as a substrate for amination reactions leading to the nocardicins.[18] Other groups have reported transformations affording a variety of vinylidene β-lactam derivatives.[8,11,16,19,20] Baldwin has also discovered an interesting ring expansion of benzyl 6-oxopenicillanate whereby treatment with an excess of diazomethane gave a bicyclic oxo-γ-lactam.[21]

We anticipated that the α-oxoazetidinone **2** would prove to be a suitable intermediate for alkene transpositions. To our surprise, however, ozonolysis of the protected (*E*)-ethylideneazetidinone **1**, followed by work-up with dimethyl sulfide or triphenylphosphine, failed to provide the expected derivative **2**. The colourless product contained an extra oxygen atom ($C_{11}H_{15}NO_4$, CHN, precise mass MS measurement). Although the IR spectrum exhibited carbonyl group bands (ν_{max}/cm^{-1} 1850 and 1780) similar to those reported for benzyl 6-oxopenicillanate (ν_{max}/cm^{-1} 1830 and 1780), their intensity profile resembled that of an anhydride. There was no significant UV absorption. Later experiments showed that the reaction proceeded in the absence of a reducing agent; the ozonide gave the product cleanly merely on warming to room temperature. The foregoing evidence supports a cyclic α-amino acid-*N*-carboxyanhydride structure **5**, and its formation may be explained (Scheme 1) by the occurrence of an acyl migration, ring expansion process during fragmentation of the ozonide **3**. Such a mechanism has been proposed[22] by Bailey to account for the products of the so-called 'anomalous' ozonolysis reactions of acyclic enones and enoates. Preferred acyl migration to peroxide oxygen is proposed by analogy with the Baeyer–Villiger rearrangement and this leads, with loss of acetaldehyde (arrows), to the *N*-carboxyanhydride **5** (83%). The isolation of this compound adds strong support to Bailey's rationale.

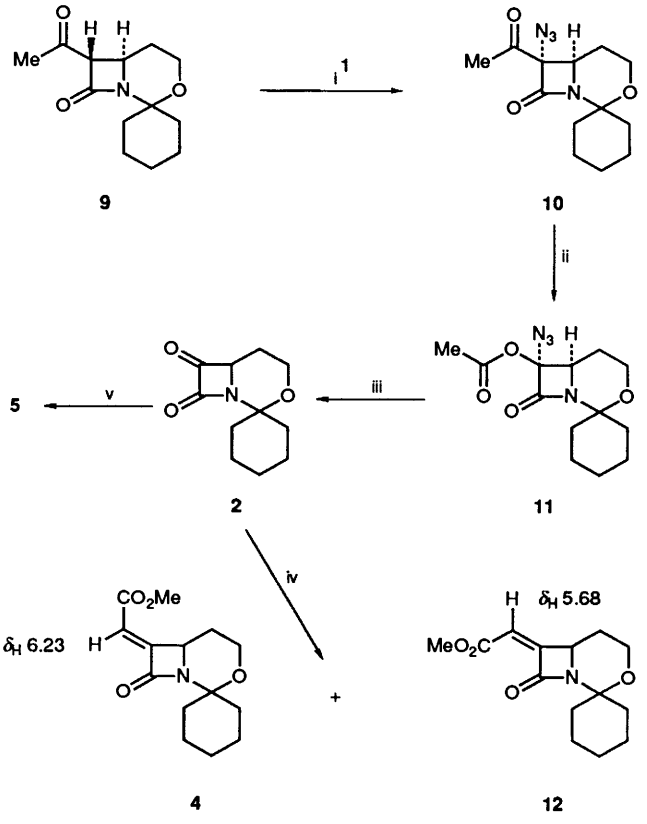
The anhydride **5** failed to react with methyl (triphenylphosphoranylidene)acetate at room temperature, and this provides further evidence for the absence of the reactive α-keto-β-lactam functionality. At reflux temperature a single 'acrylate' isomer **6** was obtained (81%) (λ_{max}/nm 238; ν_{max}/cm^{-1} 1800, 1710 and 1665). In contrast, when the stabilised phosphorane (1.2 or 2.4 mol equiv.) was added to the cold (−70 °C) ozonide solution and the mixture was then allowed to warm to room temperature, a single isomer **4** of a different acrylate compound was obtained (57%) (λ_{max}/nm) 266 and 218; ν_{max}/cm^{-1} 1750, 1730 and 1710). Formally, this is the expected derivative of the α-keto-β-lactam **2** (*vide infra*). A small amount of the anhydride **5** was also obtained. Owing to the propensity for precursor

ozonide **3** to rearrange/fragment to the anhydride **5**, we believe that acrylate **4** arises by reaction of phosphorane directly at C-7 of the ozonide. This view gains support from a recent study by Hon and his co-workers,[23] who observed a similar alkene transposition reaction of stabilised Wittig reagents with ozonides derived from mono-substituted alkenes; attack of the ylide occurred exclusively at the most highly substituted ozonide carbon atom. Similarly, in the present work, reaction at the β-lactam 'peroxy-acetal' carbon atom of the ozonide is favoured. Furthermore, even in the presence of an excess of ylide, we have never detected the formation of methyl crotonate in our reaction mixtures. This product would arise from reaction at the 'acetaldehyde' terminal of the ozonide. The absence of this compound may be explained by a mechanism (Scheme 2) involving heterolysis of the C(7)–ether oxygen bond of ozonide **3** in the expected manner. This gives rise to the Baeyer–Villiger-type intermediate **7**, which collapses with methyl migration producing the oxaphosphetane **8** together with methyl formate. The *E*-geometry of products **4** and **6**, assigned initially on steric grounds, was proven in the former case by an alternative synthesis (*vide infra*).



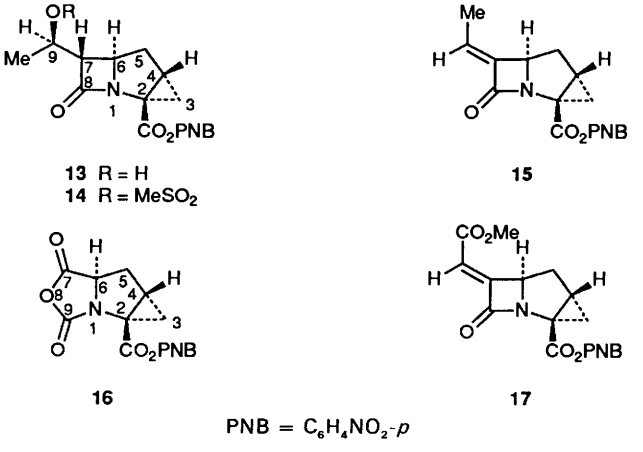
Scheme 2

Access to the 7-oxoazetidinone **2** was achieved in an unexpected manner (Scheme 3). Baeyer–Villiger oxidation with *m*-chloroperbenzoic acid (*m*CPBA) of the azido ketone **10**,[1] derived from the *trans*-ketone **9**,[4] gave a stable α-acetoxy azide **11** (95%). This was hydrolysed under mild conditions using ammonia in methanol; spontaneous α-elimination of azide ion from the intermediate alkoxide produced the α-oxo-β-lactam **2** in high yield (89%); ν_{max}/cm^{-1} 1830 and 1760). Satisfactory and consistent carbon microanalytical data could not be obtained owing, we believe, to the readiness of the keto group to hydrate; the $[M - CO]^+$ ion observed in the mass spectrum (EI) yielded a precise mass measurement. Compound **2** was, therefore, characterised by reaction with methyl (triphenylphosphoranylidene)acetate at room temperature, giving the *E*-acrylate compound **4** as the major (least polar) product. This was identical in all respects with the isomer prepared by low temperature trapping of the ozonide **3** (*vide supra*). The *Z*-isomer **12** was also obtained (5%). Comparison of the respective 9-H chemical shifts (δ_H 6.23 and 5.68) permits conclusive assignment of the double bond geometries, since in the *E*-isomer **4**, this proton is proximate to the deshielding plane of the β-lactam carbonyl group.[3]



Scheme 3 *Reagents:* i, KOH, $MeSO_2N_3$, THF–H_2O, room temp., 48 h, 36%; ii, *m*CPBA, $NaHCO_3$, CH_2Cl_2, room temp., 48 h, 95%; iii, NH_3, MeOH, room temp., 30 min, 89%; iv, $Ph_3P{=}CHCO_2Me$, CH_2Cl_2, room temp., 30 min, **4**, 74%, **12**, 5%; v, *m*CPBA, CH_2Cl_2, −30 °C, 67%

We have also obtained evidence for the occurrence of anomalous ozonide fragmentation in another polycyclic azetidinone series. The homochiral, tricyclic cyclopropane **15** was



PNB = $C_6H_4NO_2$-*p*

obtained by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) elimination of methanesulfinic acid from the mesylate **14** of alcohol **13**.[3] The latter compound was prepared from (3*R*,4*R*)-4-acetoxy-3-[(1*R*)-1-dimethyl-*tert*-butylsilyloxy)ethyl]azetidin-2-one* using established methods.[24,25] Ozonolysis of the highly strained system **15**, as before, gave an unstable product (ν_{max}/cm^{-1} 1850, 1800 and 1735), which decomposed in solution at room temperature, liberating carbon dioxide (ν_{max}/cm^{-1} 2335).[26] Once more, this indicates the formation

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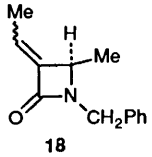
of an α-amino acid-*N*-carboxyanhydride **16**, rather than the corresponding α-oxoazetidinone. Again, direct trapping of the ozonide at low temperature with methyl (triphenylphosphoranylidene)acetate provided an isolable acrylate derivative **17**. This was obtained consistently, albeit in low yield (5%). The outcome of the ozonolysis reactions of compounds **1** and **15** is clearly at variance with results reported[27] by Tufariello, who obtained the expected azetidine-2,3-dione **19** from a monocyclic ethylideneazetidinone **18**. We therefore recommend caution in extending such reaction sequences to polycyclic systems.



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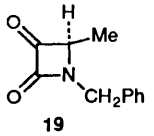

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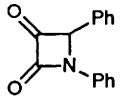

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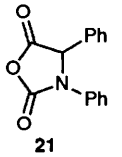

21

Monocyclic α-amino acid-*N*-carboxyanhydrides (*e.g.* **21**) have also been obtained[7] by Palomo using *m*-chloroperbenzoic acid oxidation of azetidine-2,3-diones (*e.g.* **20**). When α-oxoazetidinone **2** was oxidised at −30 °C using this reagent, the *N*-carboxyanhydride **5** was once more obtained in 67% yield.

Anhydrides of type **21** are readily opened by nucleophiles[7] and are known precursors of α-amino acid derivatives.[28]

Experimental

The experimental techniques, chromatographic materials, solvents and spectroscopic instrumentation employed in this work were as described in Parts 2,[29] 4[25] and 8[3] of the series. UV and IR spectra were obtained for solutions in ethanol and chloroform, respectively. NMR spectra were determined for solutions in $CDCl_3$ using tetramethylsilane as internal standard. Coupling constant values *J* are given in Hz.

Compounds **1**–**12** are racemic.

Ozonolysis of (E)-7-*Ethylidene*[3-*oxa*-1-*azabicyclo*[4.2.0]*octane*-2-*spirocyclohexan*]-8-*one* **1**

[3,8-*Dioxa*-1-*azabicyclo*[4.3.0]*nonane*-2-*spirocyclohexane*-7,9-*dione*] **5**.—The (*E*)-olefin[3] **1** (1.36 g) in ethyl acetate (150 cm^3) was ozonolysed at −70 °C for 12 min. The cold solution was purged with argon (15 min) and then allowed to warm to room temperature, when it was washed with brine and dried ($MgSO_4$). Evaporation and crystallisation (EtOAc–Et_2O–hexane) gave the *N*-carboxyanhydride **5** (1.155 g, 83%) as colourless rods, m.p. 130–132 °C (gas evolution) (Found: C, 58.5; H, 7.0; N, 6.2%; M^+, 225.1001. $C_{11}H_{15}NO_3$ requires C, 58.7; H, 6.7; N, 6.2%; *M*, 225.1001); ν_{max}/cm^{-1} 1850, 1780st and 940; δ_H(250 MHz) 1.2–2.25 (11 H, m, 5-H and c-C_6H_{10}), 2.50 (1 H, ddd, *J* 14, 12, 4.5, 5-H), 3.94 (2 H, ddm, *J* 8, 4, 4-H) and 4.44 (1 H, dd, *J* 12, 4.5, 6-H); *m*/*z* (EI) 225, 182, 153, 138 and 110.

Similar experiments, employing addition of triphenylphosphine or dimethyl sulfide (each 1.1 mol equiv.) after ozonolysis of compound **1**, also gave the anhydride **5** as the only product.

Methyl (E)-8-*Oxo*[1-*oxa*-1-*azabicyclo*[4.2.0]*octane*-2-*spirocyclohexan*]-7-*ylideneacetate* **4**.—The (*E*)-olefin **1** (0.156 g) in ethyl acetate (15 cm^3) was ozonolysed and purged as described above. (An aliquot, warmed to room temperature, had ν_{max}/cm^{-1} 1850, 1780.) Solid methyl (triphenylphosphoranylidene)-acetate (0.267 g, 1.1 mol equiv.) was added to the cold solution. The suspension was stirred at −70 °C for 15 min and allowed to warm to room temperature. The mixture was evaporated and the residue chromatographed on silica gel (Art. 9385, 6 × 3 cm) eluting with ethyl acetate–hexane (1:1) to give a gum (0.136 g) containing *ca.* 10% of anhydride **5** (IR spectrum). Rechromatography, eluting with chloroform, followed by crystallisation from chloroform (trace)–hexane gave the title *E*-enoate **4** as prisms (0.107 g, 57%), m.p. 110–112 °C (Found: C, 63.4; H, 7.3; N, 5.2%; M^+, 265.1312. $C_{14}H_{19}NO_4$ requires C, 63.4; H, 7.2; N, 5.3%; *M*, 265.1314); λ_{max}/nm 266w and 218; ν_{max}/cm^{-1} 1750, 1730sh and 1710w; δ_H(250 MHz) 1.44–1.93 (10 H, m), 2.17 (1 H, m) and 2.35 (1 H, m, 5-H_2), 3.77 (3 H, s, OMe), 3.90 (2 H, ddd, *J* 12, 5, 3, 4-H), 4.42 (1 H, ddd, *J* 10.7, 4.7, 1.3, 6-H) and 6.23 (1 H, d, *J* 1.3, 9-H); *m*/*z* (EI) 265, 222, 205 and 169.

A similar experiment utilising a larger excess of methyl (triphenylphosphoranylidene)acetate (2.4 mol equiv.) gave compound **4** still as the only alkenic product, in improved yield (68%).

Methyl [(E)-9-*Oxo*[3,8-*dioxa*-1-*azabicyclo*[4.3.0]*nonane*-2-*spirocyclohexan*]-7-*ylideneacetate* **6**.—The *N*-carboxyanhydride **5** (0.050 g) in ethyl acetate (5 cm^3) was stirred with a suspension of methyl (triphenylphosphoranylidene)acetate (0.088 g, 1 mol equiv.) at room temperature for 2 h. No reaction occurred. The mixture was heated at reflux temperature in an argon atmosphere for 30 min. The homogeneous mixture was cooled and chromatographed on silica gel (Art. 9385, 6 × 2 cm), eluting with ethyl acetate–hexane (1:1). Crystallisation from diethyl ether–hexane gave the title *E*-enoate **6** as prisms (0.052 g, 81%), m.p. 103–104 °C (Found: C, 59.9; H, 6.8; N, 5.0%; M^+, 281.1264. $C_{14}H_{19}NO_5$ requires C, 59.8; H, 6.8; N, 5.0%; *M*, 281.1263); λ_{max}/nm 238; ν_{max}/cm^{-1} 1800, 1710, 1665 and 1140; δ_H(90 MHz) 1.2–2.55 (12 H, m), 3.67 (3 H, s), 3.97 (2 H, dm, *J* 13, 4-H), 5.19 (1 H, ddd, *J* 12, 4, 2, 6-H) and 5.57 (1 H, d, *J* 2, 10-H); *m*/*z* (EI) 281, 238, 183 and 152.

Synthesis of [3-*Oxa*-1-*azabicyclo*[4.2.0]*octane*-2-*spirocyclohexane*]-7,8-*dione* **2**

7-*Acetoxy*-7-*azido*[3-*oxa*-1-*azabicyclo*[4.2.0]*octane*-2-*spirocyclohexan*]-8-*one* **11**.—(6*RS*,7*SR*)-7-Acetyl-7-azido[3-oxa-1-azabicyclo[4.2.0]octane-2-spirocyclohexan]-8-one **10**[1] (0.5 g, 1.8 mmol) in dry CH_2Cl_2 (5 cm^3) was cooled to 0 °C and treated with *m*-chloroperbenzoic acid (0.616 g, 3.6 mmol) and then with sodium hydrogencarbonate (0.3 g, 3.6 mmol). The reaction mixture was stirred at room temperature for 48 h. Triethylamine (0.497 cm^3, 3.6 mmol) was added and the solution washed with brine. Evaporation of the solvent and chromatography of the residue on silica gel, eluting with CH_2Cl_2, afforded the azido acetate **11** as a pale yellow crystalline solid (0.501 g, 95%), m.p. 105 °C (hexane) (Found: C, 53.1; H, 6.2; N, 18.8. $C_{13}H_{18}N_4O_4$ requires C, 53.05; H, 6.2; N, 19.0%); ν_{max}/cm^{-1} 2120, 1770 and 1775sh; δ_H(250 MHz) 1.45–1.91 (11 H, 5-H and c-C_6H_{10}), 2.23 (3 H, s, MeCO), 2.23–2.36 (1 H, m, 5-H) and 3.85–4.00 (3 H, m, 4-H_2 and 6-H); *m*/*z* (EI) $M^+ - N_2$, 266.1269. $M - N_2$, 266.1267.

[3-*Oxa*-1-*azabicyclo*[4.2.0]*octane*-2-*spirocyclohexane*]-7,8-*dione* **2**.—The azido acetate **11** (0.3 g, 1.0 mmol) was added to methanol (15 cm^3) which was saturated with ammonia and the solution was then diluted (a further 15 cm^3 of methanol). After the mixture had been stirred at room temperature for 30 min, the solvent and excess of ammonia were removed under reduced pressure and the residue was chromatographed on silica gel, eluting with ethyl acetate–hexane (3:2), to give the title oxoazetidinone **2** as colourless plates (0.19 g, 89%), m.p. 117–

118 °C (ethyl acetate–hexane) (Found: C, 62.3; H, 7.15; N, 6.6. $C_{11}H_{15}NO_3$ requires C, 63.1; H, 7.2; N, 6.7%); ν_{max}/cm^{-1} 1830 and 1760; δ_H(250 MHz) 1.48–2.03 (11 H, m, 5-H and c-C_6H_{10}), 2.42 (1 H, m, 5-H), 3.91–3.96 (2 H, m, 4-H) and 4.28 (1 H, dd, *J* 7.2, 9.6, 6-H); *m/z* (EI) $M^+ - CO$, 181.1104. *M* − CO, 181.1102.

Reaction of the Oxoazetidinone **2** *with Methyl (Triphenylphosphoranylidene)acetate.*—The oxoazetidinone **2** (0.158 g, 0.76 mmol) in CH_2Cl_2 (5 cm^3) was treated with methyl (triphenylphosphoranylidene)acetate (0.84 mmol) at room temperature for 30 min. The solvent was removed under reduced pressure and the residue chromatographed on silica gel. Elution with ethyl acetate–hexane (2:3) gave the *E*-acrylate isomer **4** (0.148 g, 74%), m.p. 110.5–111.5 °C (ethyl acetate–hexane). This compound was identical (CHN, IR, NMR, MS) with the sample prepared *via* ozonolysis of the ethylidene derivative **1** (*vide supra*).

Continued elution of the column provided the *Z*-isomer **12** as a solid (0.010 g, 5%); ν_{max}/cm^{-1} 1755, 1720 and 1685; δ_H(250 MHz) 1.41–1.96 (11 H, m, 5-H and c-C_6H_{10}), 2.41 (1 H, m, 5-H), 3.83–3.98 (5 H, m, 4-H) and (s, OMe), 4.09 (1 H, dd, *J* 10.2 and 5.0, 6-H) and 5.86 (1 H, d, *J* 1.0, 9-H).

Oxidation of the Oxoazetidinone **2** *with* m-*Chloroperbenzoic Acid.*—The oxoazetidinone **2** (0.050 g, 0.24 mmol) CH_2Cl_2 (3 cm^3) was cooled to −30 °C. MCPBA (85%; 0.054 g, 1.1 mol equiv.) in CH_2Cl_2 (1 cm^3) was added, and the mixture was stirred for 1 h. The precipitate was redissolved by dilution with CH_2Cl_2 (10 cm^3), and the solution was washed well with brine and dried. Recovery gave a residue which was chromatographed rapidly on silica gel (Art. 9385, 2 × 1 cm). Elution with CH_2Cl_2 gave the *N*-carboxyanhydride **2**. Crystallisation (EtOAc–Et_2O–hexane) provided material (36 mg, 67%) identical (IR, NMR) with the sample prepared by ozonolysis of *E*-olefin **1** (*vide supra*).

Ozonolysis of p-*Nitrobenzyl* (2S,4R,6R,E)-7-*Ethylidene*-8-*oxo*-1-*azatricyclo*[4.2.0.0^{2,4}]*octane*-2-*carboxylate* **15**

p-*Nitrobenzyl* (2S,4R,6R,7S,9R)-7-(1-*Hydroxyethyl*)-8-*oxo*-1-*azatricyclo*[4.2.0.0^{2,4}]*octane*-2-*carboxylate* **13**.—The title cyclopropane **13** was prepared from (3*R*,4*R*)-4-acetoxy-3-[(1*R*)-(1-dimethyl-*tert*-butylsilyloxy)ethyl]azetidin-2-one using methods reported from these laboratories[25] and elsewhere;[24] $\nu_{max}(CHCl_3)/cm^{-1}$ 3600, 3450, 1765 and 1725; δ_H(400 MHz) 1.29 (1 H, t, *J* 6.2, 3-H_α), 1.31 (3 H, d, *J* 6.3, 10-H), 1.41 (1 H, ddd, *J* 9.2, 6.2, 1.2, 3-H_β), 1.73 (1 H, br d, *J* 4.6, 9-H), 1.94 (1 H, dddd, *J* 13.1, 8.3, 4.8, 1.2, 5-H_β), 2.32 (1 H, dd, *J* 13.1, 7.1, 5-H_α), 2.42 (1 H, ddd, *J* 9.2, 6.2, 4.8, 4-H_β), 2.86 (1 H, dd, *J* 6.3 and 1.8, 7-H_β), 3.58 (1 H, ddd, *J* 8.3, 7.1, 1.8, 6-H_α), 4.17 (1 H, td, *J* 6.3, 4.6, MeC*H*OH), 5.29 (1 H, *J* 13.4) and 5.40 (1 H, *J* 13.4, ABq, ArCH_2O), 7.66 (2 H, d, *J* 8.7) and 8.23 (2 H, d, *J* 8.7) (AA′BB′); *m/z* (positive ion FAB, thioglycerol) 347 (MH^+).

p-*Nitrobenzyl* (1′R,2S,4R,6R,7S)-7-[(1-*Methylsulfonyloxy*)-*ethyl*]-8-*oxo*-1-*azatricyclo*[4.2.0.0^{2,4}]*octane*-2-*carboxylate* **14**.—The alcohol **13** (0.78 g) in CH_2Cl_2 (10 cm^3) was stirred with methanesulfonyl chloride (0.387 g) and triethylamine (0.47 cm^3) at ambient temperature for 45 min. The solution was diluted with CH_2Cl_2, washed with saturated aqueous ammonium chloride, dried, concentrated to *ca.* 2 cm^3 and chromatographed on silica gel (Art. 7729). Elution with ethyl acetate–hexane (gradient) gave the mesylate **14** as a white foam (0.91 g, 96%); ν_{max}/cm^{-1} 1770, 1725, 1350 and 1175; δ_H(400 MHz) 1.32 (1 H, t, *J* 6.3, 3-H_α), 1.4–1.5 (1 H, m, 3-H_β), 1.54 (1 H, d, *J* 6.3, 10-H_3), 1.9–2.0 (1 H, m, 5-H_β), 2.37 (1 H, dd, *J* 13.3, 7.1, 5-H_α), 2.4–2.5 (1 H, m, 4-H_β), 3.0–3.1 (together 4 H, m, 7-H_β and SO_2Me; s at 3.03 discernible), 3.66 (1 H, m, 6-H_α), 5.04 (1 H, dq, *J* 6.3 and 4.5, 9-H), 5.29 (1 H, *J* 13.4) and 5.38 (1 H, *J* 13.4) (ABq, ArCH_2O) and 7.64 (2 H, d, *J* 8.48) and 8.23 (2 H, d, *J* 8.48) (AA′BB′); *m/z* (positive ion FAB; 3-nitrobenzyl alcohol–NaOAc) 447 (MNa^+).

p-*Nitrobenzyl* (2S,4R,6R,E)-7-*Ethylidene*-8-*oxo*-1-*azatricyclo*[4.2.0.0^{2,4}]*octane*-2-*carboxylate* **15**.—A solution of DBU (0.024 g) in CH_2Cl_2 (0.5 cm^3) was added at ambient temperature to a stirred solution of the methanesulfonate **14** (0.045 g) in the same solvent (2 cm^3). The mixture was stirred for a further 20 h and then diluted with CH_2Cl_2 (5 cm^3), washed with 50% saturated aqueous ammonium chloride (3 cm^3), dried and evaporated. The residue was chromatographed on a short silica gel column (Art. 7729) to give the title olefin **15** as a mixture of *E*- and *Z*-isomers (7:1) (0.028 g, 80%); ν_{max}/cm^{-1} 1765, 1730 and 1610; *m/z* 328 (M^+) and 329 (MH^+). In a repeat of this experiment careful chromatography afforded, as well as the mixture, small quantities of the pure isomers.

(*E*)-Ethylidene; δ_H(400 MHz) 1.21 (1 H, t, *J* 6.1, 3-H_α), 1.45 (1 H, ddd, *J* 7.5, 6.1 and 1.4, 3-H_β), 1.73 (1 H, dd, *J* 7.2, 0.7, 10-H_3), 1.93 (1 H, dddd, *J* 12.9, 8.0, 5.0 and 1.3, 5-H_β), 2.29 (1 H, dd, *J* 12.9 and 7.5, 5-H_α), 2.43 (1 H, m, 4-H_β), 4.11 (1 H, br t, *J* 8.0, 6-H_α), 5.30 (1 H, *J* 13.4), 5.42 (1 H, *J* 13.4, ABq, ArCH_2O), 6.19 (1 H, dq, *J* 7.2, 1.4, 9-H), 7.70 (2 H, d, *J* 8.7) and 8.24 (2 H, d, *J* 8.7) (AA′BB′).

(*Z*)-Ethylidene; δ_H(400 MHz) 1.20 (1 H, t, *J* 6.1, 3-H_α), 1.42 (1 H, ddd, *J* 8.0, 6.1, 1.4, 3-H_β), 1.92 (1 H, dddd, *J* 13.0, 7.1, 5.2, 1.7, 5-H_β), 2.02 (1 H, dd, *J* 7.2 and 1.0, CHCH_3), 2.24 (1 H, dd, *J* 13.0, 7.5, 5-H_α), 2.42 (1 H, m, 4-H_α), 3.99 (1 H, m, H-6$_\alpha$), 5.32 (1 H, *J* 13.4), 5.39 (1 H, *J* 13.4, ABq), 5.67 (1 H, dq, *J* 7.2, 1.1, C*H*Me), 7.70 (2 H, d, *J* 8.7) and 8.25 (2 H, d, *J* 8.7) (AA′BB′).

Ozonolysis of the Ethylidene Compound **15**.—The ethylidene derivative **15** (0.030 g) in CH_2Cl_2 (5 cm^3) was ozonolysed at −70 °C until the solution turned blue. Excess of ozone was removed by purging with argon and the mixture was then stirred at 0 °C for 30 min. The solution was carefully monitored (IR spectrum) and showed strong bands ν_{max}/cm^{-1} 1850, 1800, 1735, 1495 and 1350, believed to be due to the unstable *N*-carboxyanhydride **19**. A weak band ν_{max}/cm^{-1} 2335 gradually increased in intensity as the solution warmed to ambient temperature over 45 min. A concomitant loss of the 'anhydride' bands at ν_{max}/cm^{-1} 1850 and 1800 was observed; the solution finally exhibited strong bands ν_{max}/cm^{-1} 2335, 1735, 1495 and 1350. We attribute the appearance of the high frequency band to the formation of carbon dioxide[26] during decomposition of anhydride **16**. Evaporation of the solution gave an intractable yellow residue.

p-*Nitrobenzyl* (2S,4R,6R)-7-(1-*Methoxycarbonylmethylene*)-8-*oxo*-1-*azatricyclo*[4.2.0.0^{2,4}]*octane*-2-*carboxylate* **17**.—A solution of the ethylidene derivative **15** (0.065 g) in CH_2Cl_2 (3 cm^3) was cooled to −70 °C and the solution ozonolysed until it turned blue. The colour was then discharged by the passage of argon, dimethyl sulfide (0.013 g) was added and the stirred reaction mixture was warmed to ambient temperature. After 10 min at that temperature the solvent was removed under reduced pressure, the residue dissolved in benzene (1 cm^3) and this solution treated at ambient temperature with a solution of methyl (triphenylphosphoranylidene)acetate (0.066 g) in benzene (2 cm^3). After 15 min, the solvent was evaporated and the residue purified on silica gel (Art. 7729) to afford the title acrylate **17** as a gum (0.004 g, 5%); ν_{max}/cm^{-1} 1770 and 1725; δ_H (250 MHz) *inter alia* 1.28 (1 H, t, *J* 6.3, 3-H_α), 1.5–1.6 (1 H, partially obscured by H_2O, 3-H_β), 1.9–2.05 (1 H, m, 5-H_β), 2.35–2.6 (together 2 H, m, 4-H_β and 5-H_α), 3.78 (3 H, s, CO_2Me), 4.41 (1 H, br t, *J* 7.5, 6-H_α), 5.31 (1 H, *J* 13.5), 5.42 (1 H, *J* 13.5,

ABq, ArCH_2O), 6.21 (1 H, d, *J* 1.1, C*H*CO_2Me), 7.68 (2 H, d, *J* 8.7) and 8.24 (2 H, d, *J* 8.7) (AA'BB'); *m/z* (positive ion FAB; thioglycerol) 373 (MH^+).

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