An Oxidative Rearrangement of t-Butyl (3*RS*,5*SR*)-2-Ethoxycarbonylcarbapen-1-em-3-carboxylate to t-Butyl (1*RS*,5*SR*,7*RS*,8*SR*)-8-Ethoxycarbonyl-8-hydroxy-3-oxo-2-oxa-6-azabicyclo[3.3.0]octane-7-carboxylate[1,†]

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The title reaction [(**1a**) ⟶ (**10a**)] is induced by the action of osmium(VIII) oxide. Presumably, the diol (**12**), formed by the addition of the elements of hydrogen peroxide to the *endo*-face of the 1,2-double bond of the precursor (**1a**), is an intermediate in the reorganisation. The rearrangement product is shown to possess structure (**10a**) [rather than (**11a**) as proposed in the preliminary communication of this work] by *X*-ray crystallography. Compound (**10a**) undergoes dehydrogenation in the presence of lead(IV) acetate or chromium(VI) oxide to give t-butyl (1*RS*,5*SR*,8*SR*)-8-ethoxycarbonyl-8-hydroxy-3-oxo-2-oxa-6-azabicyclo[3.3.0]oct-6-ene-7-carboxylate (**13a**). Unusual results are encountered when compound (**10a**) is subjected to methylsulphonylation conditions. Thus, with methanesulphonyl chloride and triethylamine in dichloromethane, it reacts to give the *O*-methanesulphonate (**10d**) as the major product and (depending upon the experimental conditions) either the *N*-methylsulphonylmethylsulphonyl-*O*-methylsulphonyl derivative (**10f**) or the *N*-methylsulphonylmethylsulphonyl derivative (**10h**). The last-cited compound is the major product when the oxazabicyclo-octane (**10a**) is added to an 'aged' mixture of methanesulphonyl chloride and triethylamine in acetonitrile. In the presence of methanesulphonyl chloride in pyridine, compound (**10a**) is transformed into the *N*-methylsulphonyl derivative (**10c**). A study of the 300 MHz ^{1}H n.m.r. spectra of oxazabicyclo-octanes of type (**10**) and oxazabicyclo-octenes of type (**13**) reveals some unexpected downfield shifts of the 1-hydrogen atoms as a consequence of *O*-substitution.

Recently, we described[2] the preparation of carbapenems of type (**1**). Our interest in such compounds stemmed from the hope that they could be induced to undergo an oxidative rearrangement to carbapenems of type (**2**), representatives of which might possess antibacterial activity. Earlier, we showed[2] that the alkene function of compound (**1a**) underwent addition of hydrogen mainly from the *endo*-face to give the carbapenam (**3**) and addition of diazomethane predominantly from the *exo*-face to afford the cycloadduct (**4**). We envisaged that osmium(VIII) oxide would attack largely from the *exo*-face to give the diol (**5**) which, under appropriate conditions, would be convertible into the carbapenem (**2a**). The unexpected outcome of the hydroxylation reaction and its consequences are the subject of this paper.

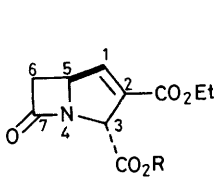
Results and Discussion

When treated with osmium(VIII) oxide (1.1 mol equiv.) in pyridine followed by aqueous sodium metabisulphite, the carbapenem (**1a**) was converted into a crystalline product, with the molecular formula $C_{14}H_{21}NO_7$, in 85% yield. The material, designated compound (**A**), was clearly derived from its precursor (**1a**) by the addition of the elements of hydrogen peroxide. The i.r. spectrum of compound (**A**), which featured absorptions at 3 420, 3 320, and 1 775 cm^{-1}, was in accord with the expected carbapenam structure (**5**). However, the 360 MHz ^{1}H n.m.r. spectrum ($CDCl_3$) exhibited two one-proton double doublets at δ 2.59 (*J* 19 and 2.5 Hz) and 2.83 (*J* 19 and 9 Hz), that would have to be attributable to the 6β- and 6α-hydrogen atoms of the diol (**5**). The coupling constants contrast with those of the carbapenam (**6**) which is reported[3] to possess signals corresponding to the 6β- and 6α-hydrogen atoms at δ 2.66 (*J* 15.5 and 2 Hz) and 3.05 (*J* 15.5 and 5 Hz).

If compound (**A**) possessed the diol structure (**5**), it would be expected to react with lead(IV) acetate to give compound (**7**) which, it was envisaged, would spontaneously cyclise to the oxacarbacephem (**8**). When treated with the oxidant in dichloromethane, compound (**A**) was rapidly transformed into a new crystalline product. The material, designated compound (**B**) and isolated in 61% yield, possessed the molecular formula expected for the oxacarbacephem (**8**). Although its i.r. spectrum, which showed absorptions at 3 400, 1 785, 1 725, 1 715, and 1 655 cm^{-1}, was compatible with the structure (**8**), its u.v. and ^{1}H n.m.r. spectra were not. Thus, the u.v. spectrum displayed only weak absorptions at 255 (ε 560) and 250 nm (ε 150); typically, the oxacarbacephem chromophore appears at *ca.* 270 nm (ε *ca.* 10 000).[4] The 360 MHz ^{1}H n.m.r. spectrum ($CDCl_3$) incorporated two one-proton doublets at δ 2.85 (*J* 19 and 3 Hz) and 3.02 (*J* 19 and 10 Hz); the 7β- and 7α-hydrogen atoms of the carbacephem (**9**) are reported[5] to absorb ($CDCl_3$) at δ 2.64 (*J* 15.2 and 2.3 Hz) and 3.28 (*J* 15.2 and 5 Hz).

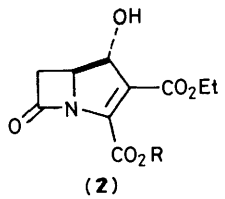
A further examination of compound (**A**) revealed that it was a basic material and that it gave a crystalline salt (55% yield) when treated with toluene-*p*-sulphonic acid in acetone–diethyl ether. This result excluded the carbapenam structure (**5**) and suggested that compound (**A**) was either the fused γ-lactone (**10a**) or the fused δ-lactone (**11a**). Evidently, the *cis*-hydroxylation had occurred from the *endo*-face of the carbapenem (**1a**) to give the *cis*-diol (**12**), which had spontaneously rearranged to

† Part of this work was carried out in the Department of Organic Chemistry at the University of Newcastle upon Tyne.



(1)

a; R = Bu^t



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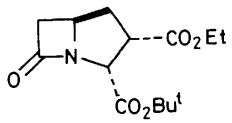

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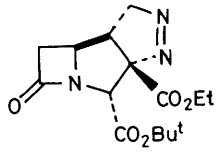

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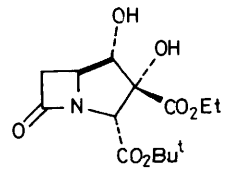
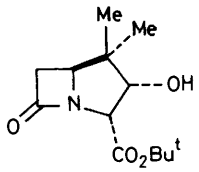


(5)



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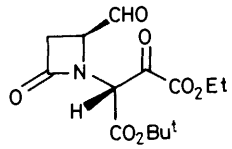

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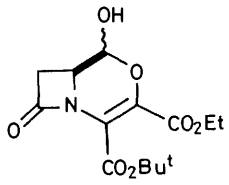

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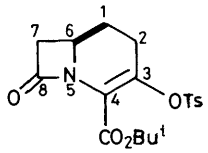

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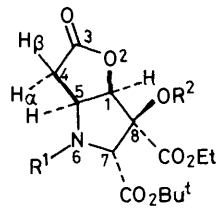


(10)

a; $R^1 = R^2 = H$

b; $R^1 = R^2 = Ac$

c; $R^1 = SO_2Me$, $R^2 = H$

d; $R^1 = H$, $R^2 = SO_2Me$

e; $R^1 = Ac$, $R^2 = SO_2Me$

f; $R^1 = SO_2CH_2SO_2Me$, $R^2 = SO_2Me$

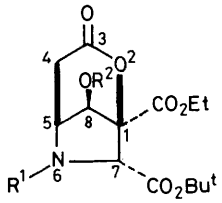
g; $R^1 = SO_2Me$, $R^2 = SO_2CH_2SO_2Me$

h; $R^1 = SO_2CH_2SO_2Me$, $R^2 = H$

i; $R^1 = H$, $R^2 = SO_2CH_2SO_2Me$

j; $R^1 = SO_2CH_2SO_2Me$, $R^2 = Ac$

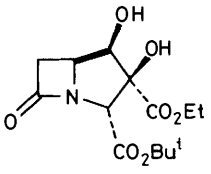
k; $R^1 = R^2 = SO_2Me$



(11)

a; $R^1 = R^2 = H$

b; $R^1 = R^2 = Ac$



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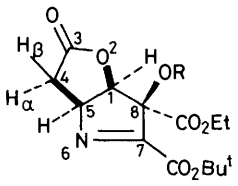
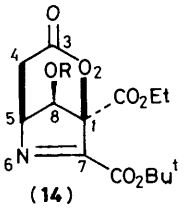


(13)

a; R = H

b; R = Ac

c; R = SO_2Me



(14)

a; R = H

b; R = Ac

the product, *i.e.* either (**10a**) or (**11a**). In consequence, compound (**B**) was formulated as the fused pyrroline (**13a**) or (**14a**).

It is well established that γ- and δ-lactones absorb in the i.r. region at *ca.* 1 770 and 1 745 cm^{-1}, respectively.[6] Accordingly, the fused γ-lactones (**10a**) and (**13a**) appeared to be the favoured structures for compounds (**A**) and (**B**). This view was seemingly supported by the lack of coupling between the oxygenated methine and hydroxy hydrogen atoms in the ^{1}H n.m.r. spectra of compounds (**A**) and (**B**). However, these inferences should be treated with caution. By virtue of their strained nature, the δ-lactones (**11a**) and (**14a**) are likely to absorb in the i.r. region at a higher wavenumber than normal. Moreover, the lack of coupling between the oxygenated methine and hydroxy hydrogen atoms may also be accommodated by the structures (**11a**) and (**14a**) in which a near-orthogonal relationship exists between the protons in question. Finally, it is worth noting that, on the basis of a Dreiding model, the tertiary alcohol function of the intermediate *cis*-diol (**12**) appears to be better disposed to react with the β-lactam carbonyl function (the closest interatomic distances between the β-lactam carbonyl carbon atom and the 1- and 2-oxygen atoms are *ca.* 3.5 Å and 3.25 Å, respectively).

The methine hydrogen atom of a secondary alcohol is known to absorb at significantly higher field (often *ca.* 1 p.p.m.) than that of its *O*-acetyl derivative.[7] Accordingly, it was expected that the structural issue would be resolved by acetylation studies. If compounds (**A**) and (**B**) were the fused γ-lactones (**10a**) and (**13a**), the chemical shifts of the 1-hydrogen atoms would not be expected to be substantially altered in their acetyl derivatives (**10b**) and (**13b**). Conversely, if the compounds were the fused δ-lactones (**11a**) and (**14a**), a marked downfield shift of the 8-hydrogen atoms would be expected in their acetyl derivatives (**11b**) and (**14b**).

Compound (**A**) reacted with acetic anhydride in pyridine to give a crystalline diacetyl derivative in 90% yield after silica-gel chromatography. Although the 360 MHz ^{1}H n.m.r. spectrum ($CDCl_3$) of the product was complex due to the presence of a 1.5:1 mixture of rotamers (arising from restricted rotation about the amide linkage), the oxygenated methine hydrogen atom appeared as two doublets at δ 5.59 (*J* 8 Hz) and 5.68 (*J* 7 Hz). In compound (**A**), the oxygenated methine hydrogen atom appeared as a doublet at δ 4.84 (*J* 6 Hz). This result suggested that the diacetyl derivative possessed the structure (**11b**) rather than the structure (**10b**) and, therefore, that compound (**A**) was the fused δ-lactone (**11a**) rather than the fused γ-lactone (**10a**).

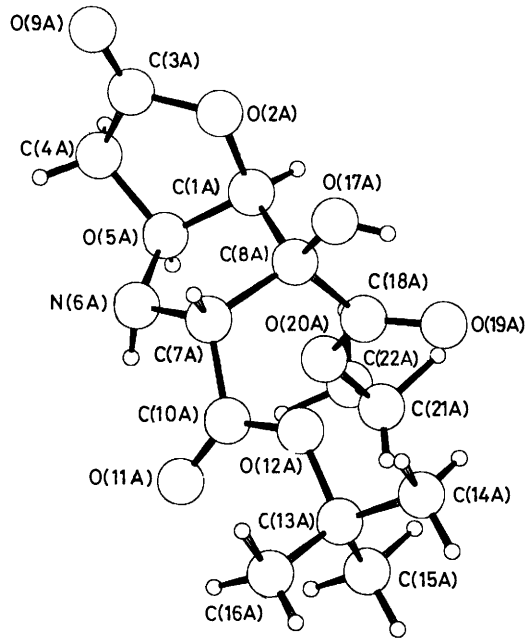


Figure. The molecular structure of compound (**10a**)

Compound (**B**) was transformed into a crystalline *O*-acetyl derivative, isolated in 83% yield after silica-gel chromatography, on treatment with acetic anhydride in pyridine. In the 360 MHz ^{1}H n.m.r. spectrum ($CDCl_3$) of the product, the oxygenated methine hydrogen atom absorbed as a doublet at δ 5.43 (*J* 5 Hz). In compound (**B**), the corresponding hydrogen atom appeared as a doublet at δ 4.88 (*J* 5 Hz). Seemingly, therefore, the *O*-acetyl derivative possessed the structure (**14b**) and compound (**B**) was the fused δ-lactone (**14a**).

At this stage (and on the basis of other results which are presented below), we were reasonably confident that compound (**A**) and (**B**) were the fused δ-lactones (**11a**) and (**14a**) and, indeed, these were the structures proposed in the preliminary communication of this work.[1] However, as further evidence unfolded, the reliability of the 'acylation shift' as a structural probe came into question. An *X*-ray crystallographic investigation of compound (**A**) was therefore undertaken. The molecular structure (see Experimental section for crystal data and other information) is shown in the Figure together with its crystallographic numbering. Refined atomic co-ordinates are included in Table 1 and selected bond lengths and bond angles are presented in Table 2. Each hydrogen atom associated with a heteroatom is within hydrogen bonding distance of two other heteroatoms, one intramolecular and the other intermolecular (see Table 3). Clearly, compound (**A**) was the fused γ-lactone (**10a**)* rather than the fused δ-lactone (**11a**) that we had favoured. Obviously, therefore, compound (**B**) was the fused γ-lactone (**13a**)

On the basis of the aforecited evidence, it is apparent that osmium(VIII) oxide had effected the *cis*-hydroxylation of the carbapenem (**1a**) from the *endo*-face to give the *cis*-diol (**12**). This stereochemical outcome matches that observed in the hydrogenation reaction but contrasts with that observed for the 1,3-dipolar cycloaddition involving diazomethane. Presumably, in the oxidation and reduction reactions, the t-butoxycarbonyl group exerts a steric dominance and impedes attack from the *exo*-face. The spontaneous rearrangement of the *cis*-diol (**12**) to the fused γ-lactone (**10a**) is of interest. We assume that the process is triggered by attack of the 1β-hydroxy group on the β-lactam carbonyl entity. Analogous reorganisations of 2β-hydroxymethylclavams,[8] 2β-hydroxymethylpenams,[9] and 3β-hydroxycephams[10] have been reported.

The oxidation of the fused pyrrolidine (**10a**) to the fused pyrroline (**13a**), induced by lead(IV) acetate, is also deserving of comment. Although this oxidant has been used to convert dibenzylamine into *N*-benzylidenebenzylamine in low yield,[11] we are unaware of its application in effecting the dehydrogenation of compounds incorporating the $NHCH(CO_2R)$ function. Probably, in the substrate in question, this oxidation is particularly facile. Thus the (**10a**) ⟶ (**13a**) transformation was also effected in 50% yield using chromium(VI) oxide–pyridine–acetic anhydride.

During the course of the structural studies involving compound (**A**), some unexpected reactions were encountered

Table 1. Fractional atomic co-ordinates (× 10^4) for compound (**10a**) with estimated standard deviations (e.s.d.s) in parentheses

Atom	*x/a*	*y/b*	*z/c*
C(1A)	3 565(2)	8 453(3)	6 400(1)
O(2A)	2 725(1)	8 874(2)	6 601(1)
C(3A)	2 846(3)	10 045(3)	6 825(2)
C(4A)	3 820(2)	10 465(3)	6 808(2)
C(5A)	4 134(2)	9 593(3)	6 342(2)
N(6A)	3 803(2)	9 970(2)	5 637(1)
C(7A)	3 215(2)	9 014(2)	5 244(1)
C(8A)	3 239(2)	7 885(3)	5 701(1)
O(9A)	2 216(2)	10 548(2)	7 003(1)
C(10A)	3 507(2)	8 773(3)	4 608(2)
O(11A)	4 072(2)	9 383(2)	4 409(1)
O(12A)	3 055(2)	7 808(2)	4 310(1)
C(13A)	3 239(3)	7 291(3)	3 694(2)
C(14A)	2 568(4)	6 212(4)	3 575(2)
C(15A)	4 276(3)	6 932(4)	3 815(2)
C(16A)	2 924(4)	8 207(4)	3 137(2)
O(17A)	2 336(1)	7 354(2)	5 578(1)
C(18A)	3 991(2)	6 975(3)	5 629(1)
O(19A)	3 832(2)	5 919(2)	5 505(1)
O(20A)	4 839(2)	7 496(2)	5 733(1)
C(21A)	5 693(3)	6 741(4)	5 779(2)
C(22A)	6 444(5)	7 164(9)	6 321(5)
C(23A)	6 118(24)	6 557(32)	6 533(13)
C(1B)	7 615(2)	6 796(3)	3 833(1)
O(2B)	6 624(1)	6 432(2)	3 582(1)
C(3B)	6 574(3)	5 357(3)	3 249(2)
C(4B)	7 565(2)	4 923(3)	3 278(1)
C(5B)	8 210(2)	5 668(3)	3 824(1)
N(6B)	8 322(2)	5 103(2)	4 485(1)
C(7B)	8 087(2)	5 975(2)	4 951(1)
C(8B)	7 802(2)	7 194(2)	4 571(1)
O(9B)	5 816(2)	4 921(3)	2 979(1)
C(10B)	8 900(2)	6 058(3)	5 579(1)
O(11B)	9 596(2)	5 416(2)	5 687(1)
O(12B)	8 730(1)	6 914(2)	5 983(1)
C(13B)	9 451(3)	7 223(3)	6 611(2)
C(14B)	8 941(3)	8 186(4)	6 905(2)
C(15B)	10 344(3)	7 722(4)	6 441(2)
C(16B)	9 653(3)	6 123(4)	7 064(2)
O(17B)	7 004(1)	7 669(2)	4 745(1)
C(18B)	8 618(2)	8 099(3)	4 689(1)
O(19B)	8 547(2)	9 144(2)	4 815(1)
O(20B)	9 410(1)	7 580(2)	4 610(1)
C(21B)	10 250(2)	8 330(3)	4 614(2)
C(22B)	10 368(7)	8 477(12)	3 962(3)
C(23B)	10 714(19)	7 830(24)	4 112(16)

* For the *X*-ray analysis of a related system (the hydrobromide salt of ethyl {(1*S*,5*R*,8*R*)-8-hydroxy-3-oxo-2-oxa-6-azabicyclo[3.3.0]octan-6-yl}acetate), see: J. F. Richardson and V. K. Yadav, *Acta Cryst., Sect. C*, 1985, **41**, 1687.

Table 2. Selected bond lengths (Å) and bond angles (°) for compound (**10a**) with e.s.d.s in parentheses

(*a*) Bond lengths

C(1A)–O(2A)	1.448(4)	C(1A)–C(5A)	1.524(4)
C(1A)–C(8A)	1.540(4)	O(2A)–C(3A)	1.372(4)
C(3A)–C(4A)	1.482(5)	C(3A)–O(9A)	1.197(5)
C(4A)–C(5A)	1.513(5)	C(5A)–N(6A)	1.477(4)
N(6A)–C(7A)	1.465(3)	C(7A)–C(8A)	1.561(4)
C(7A)–C(10A)	1.505(5)	C(8A)–O(17A)	1.387(3)
C(8A)–C(18A)	1.510(4)	C(10A)–O(11A)	1.206(4)
C(10A)–O(12A)	1.318(4)	O(12A)–C(13A)	1.483(4)
C(13A)–C(14A)	1.514(6)	C(13A)–C(15A)	1.499(6)
C(13A)–C(16A)	1.517(5)	C(18A)–O(19A)	1.205(4)
C(18A)–O(20A)	1.314(4)	O(20A)–C(21A)	1.467(5)
C(21A)–C(22A)	1.423(9)	C(21A)–C(23A)	1.540(26)
C(1B)–O(2B)	1.442(3)	C(1B)–C(5B)	1.515(4)
C(1B)–C(8B)	1.548(4)	O(2B)–C(3B)	1.367(4)
C(3B)–C(4B)	1.487(5)	C(3B)–O(9B)	1.192(4)
C(4B)–C(5B)	1.513(4)	C(5B)–N(6B)	1.477(4)
N(6B)–C(7B)	1.462(4)	C(7B)–C(8B)	1.562(4)
C(7B)–C(10B)	1.516(4)	C(8B)–O(17B)	1.389(4)
C(8B)–C(18B)	1.514(4)	C(10B)–O(11B)	1.201(4)
C(10B)–O(12B)	1.326(4)	O(12B)–C(13B)	1.484(4)
C(13B)–C(14B)	1.506(6)	C(13B)–C(15B)	1.504(6)
C(13B)–C(16B)	1.520(6)	C(18B)–O(19B)	1.194(4)
C(18B)–O(20B)	1.320(4)	O(20B)–C(21B)	1.462(4)
C(21B)–C(22B)	1.415(9)	C(21B)–C(23B)	1.478(33)

(*b*) Bond angles

C(5A)–C(1A)–O(2A)	105.0(2)	C(8A)–C(1A)–O(2A)	109.0(2)
C(8A)–C(1A)–C(5A)	107.6(3)	C(3A)–O(2A)–C(1A)	110.9(2)
C(4A)–C(3A)–O(2A)	109.1(3)	O(9A)–C(3A)–O(2A)	120.1(3)
O(9A)–C(3A)–C(4A)	130.8(3)	C(5A)–C(4A)–C(3A)	104.5(3)
C(4A)–C(5A)–C(1A)	102.9(3)	N(6A)–C(5A)–C(1A)	105.5(2)
N(6A)–C(5A)–C(4A)	112.3(2)	C(7A)–N(6A)–C(5A)	110.0(2)
C(8A)–C(7A)–N(5A)	108.5(2)	C(10A)–C(7A)–N(6A)	111.5(2)
C(10A)–C(7A)–C(8A)	114.9(2)	C(7A)–C(8A)–C(1A)	101.6(2)
C(5B)–C(1B)–O(2B)	105.8(2)	C(8B)–C(1B)–O(2B)	110.2(2)
C(8B)–C(1B)–C(5B)	106.7(2)	C(3B)–O(2B)–C(1B)	110.3(2)
C(4B)–C(3B)–O(2B)	109.4(3)	O(9B)–C(3B)–O(2B)	120.9(3)
O(9B)–C(3B)–C(4B)	129.7(4)	C(5B)–C(4B)–C(3B)	104.6(3)
C(4B)–C(5B)–C(1B)	102.5(2)	N(6B)–C(5B)–C(1B)	105.5(2)
N(6B)–C(5B)–C(4B)	111.5(2)	C(7B)–N(6B)–C(5B)	110.1(2)
C(8B)–C(7B)–N(6B)	108.1(2)	C(10B)–C(7B)–N(6B)	110.6(2)
C(10B)–C(7B)–C(8B)	115.3(2)	C(7B)–C(8B)–C(1B)	102.2(2)

O(2A)–C(1A)–C(5A)–N(6A)	−92.6(2)
C(8A)–C(1A)–C(5A)–C(4A)	141.3(3)
O(2B)–C(1B)–C(5B)–N(6B)	−90.6(2)
C(8B)–C(1B)–C(5B)–C(4B)	143.5(2)

Table 3. Hydrogen bonding geometry (X–H ··· Y) for compound (**10a**) with e.s.d.s in parentheses

	Atoms		Distances (Å)		
	X	Y	X ··· Y	X–H	H ··· Y
Intra	O(17A)	O(19A)	2.704(6)	0.79(3)	2.21(6)
	N(6A)	O(11A)	2.749(6)	0.88(3)	2.30(6)
	O(17B)	O(19B)	2.724(7)	0.81(3)	2.47(6)
	N(6B)	O(11B)	2.713(6)	0.95(2)	2.24(5)
Inter	N(6A)	O(11A)^{I}	3.158(7)	0.88(3)	2.35(6)
	O(17A)	N(6B)^{II}	2.869(7)	0.79(3)	2.22(6)
	N(6B)	O(11B)^{III}	3.150(7)	0.95(2)	2.31(6)
	O(17B)	N(6A)^{I}	2.880(7)	0.81(3)	2.14(5)

Roman numeral superscripts refer to the following equivalent positions which should be applied to the co-ordinate of the second atom: I $1-x$, $2-y$, $1-z$; II $1-x$, $1-y$, $1-z$; III $2-x$, $1-y$, $1-z$

under methylsulphonylation conditions. Thus when treated in dichloromethane at 0 °C with methanesulphonyl chloride (2.2 mol equiv.) and triethylamine (2 mol equiv.), compound (**10a**) was transformed into two products which were separated by silica-gel chromatography. The major product, isolated in 51% yield after recrystallisation, possessed the molecular formula $C_{15}H_{25}NO_9S$. The minor product, designated compound (**C**), was obtained in 5% yield after recrystallisation and analysed for $C_{17}H_{27}NO_{13}S_2$.

The major product was clearly a monomethylsulphonyl derivative of compound (**10a**) and therefore possessed structure (**10c**) or (**10d**). That the latter structure was the correct one was revealed by the reaction of the material with acetic anhydride–pyridine. The acetylated product (**10c**), isolated in 53% yield after silica-gel chromatography and recrystallisation, featured an amide carbonyl absorption [$\nu_{max.}$(KBr) 1 650 cm^{-1}] in the i.r. region. Moreover [like its relative (**10b**)] the material was present in deuteriochloroform as a 1.5:1 mixture of rotamers. Compound (**10d**) underwent oxidation with lead(IV) acetate in dichloromethane to give the fused pyrroline (**13c**) in 47% yield. The last-cited material was also produced in 74% yield by treatment of the fused pyrroline (**13a**) with methanesulphonyl chloride and triethylamine in dichloromethane at 0 °C.

On the basis of its 300 MHz ^{1}H n.m.r. spectroscopic properties, compound (**C**) was considered to possess structure (**10f**) or (**10g**). Thus the spectrum ($CDCl_3$) featured two three-proton singlets at δ 3.18 and 3.29 for the two methylsulphonyl entities and a two-proton AB quartet (*J* 15 Hz) centred at δ 4.90 attributed to the bis(sulphonyl)methylene function. Whilst no distinction between the possible structures was possible by spectral analysis, subsequent findings established that compound (**C**) was the *N*-methylsulphonylmethylsuphonyl derivative (**10f**).

When methanesulphonyl chloride (2.2 mol equiv.) was added to a solution of the fused γ-lactone (**10a**) in a 1:1 mixture of dichloromethane and triethylamine, two new materials were produced. The minor product, isolated in 15% yield by fractional crystallisation of the mixture, was designated compound (**D**); it possessed the molecular formula $C_{16}H_{25}NO_{11}S_2$. Silica-gel fractionation of the mother liquor led to the isolation of the *O*-methanesulphonate (**10d**) in 46% yield together with a further quantity (5%) of compound (**D**).

The 360 MHz ^{1}H n.m.r. spectrum ($CDCl_3$) of compound (**D**) incorporated a three-proton singlet at δ 3.22 for a methylsulphonyl moiety and two one-proton doublets (*J* 15 Hz) at δ 4.65 and 4.84 attributed to the bis(sulphonyl)methylene group, suggesting that compound (**D**) possessed the structure (**10h**) or (**10i**). The relationship between compounds (**C**) and (**D**) was established by the finding that the latter material was transformed into the former on treatment with methanesulphonyl chloride and triethylamine in dichloromethane at 0 °C.

That compound (**D**) possessed structure (**10h**) was revealed by its reaction with acetic anhydride–pyridine. The resultant acetyl derivative, isolated in 37% yield after recrystallisation, showed no amide carbonyl absorption in the i.r. region, indicating that it was the *O*-acetyl derivative (**10j**). In consequence, compound (**C**) possessed structure (**10f**).

When treated in pyridine at 0 °C with methanesulphonyl chloride (5 mol equiv.), compound (**10a**) was converted into the *N*-methanesulphonate (**10c**) (48% yield after recrystallisation). The last-cited compound underwent *O*-methylsulphonylation with methanesulphonyl chloride either in dichloromethane containing triethylamine or in pyridine. The recrystallised product

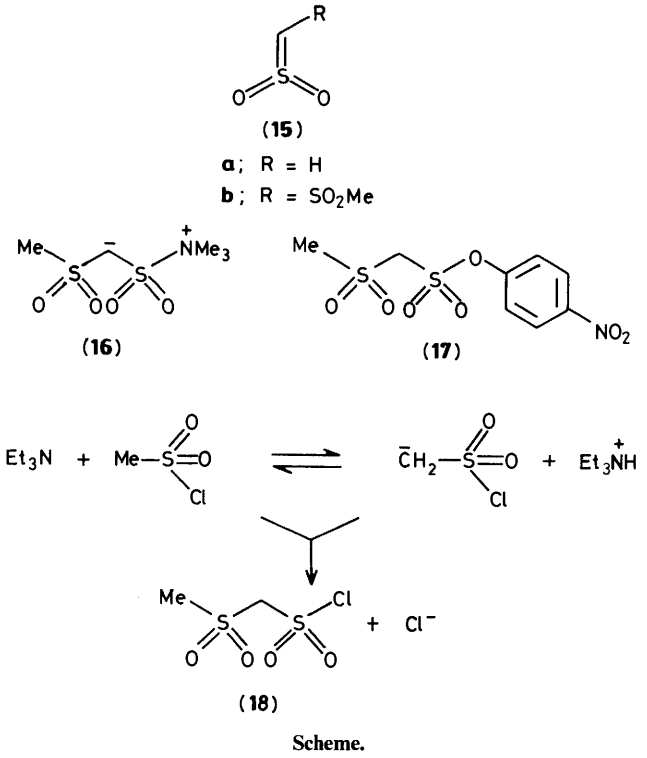
(**10k**) was isolated in 57% yield from the former reaction and in 34% yield from the latter.

The reactions of compound (**10a**) with methanesulphonyl chloride are of interest in a number of respects. Although *O*- and *N*-methylsulphonylations by the reagent are well documented, we are unaware of any studies in which differentiation between alcohols and amines has been reported.* Presumably, in the presence of triethylamine and dichloromethane (conditions devised by Crossland and Servis[12]), sulphene (**15a**) is the reactive species, whereas in pyridine, methanesulphonyl chloride is involved. Compounds (**10d, f, k**) are uncommon examples of tertiary *O*-methanesulphonates. The conditions used for the formation of product (**10k**) are of note; normally, methanesulphonates of tertiary alcohols are accessible only under the Crossland-Servis conditions.

The conversion of the oxazabicyclo-octane (**10a**) into the sulphonamides (**10f, h**) represent rare instances of methylsulphonylmethylsulphonylations induced by methanesulphonyl chloride and triethylamine. Opitz and his co-workers[13] provided the first examples of this reaction. Thus simple amines and *p*-nitrophenol, when introduced into a mixture which had been prepared by the addition of methanesulphonyl chloride (2 mol equiv.) to a solution of triethylamine (3 mol equiv.) in acetonitrile at −40 °C and 'aged' for 1 h, were transformed into their methylsulphonylmethylsulphonyl derivatives. The German workers provided evidence for the involvement of the sulphene (**15b**) and, indeed, they were able to isolate a crystalline trimethylamine complex to which they assigned structure (**16**).

When subjected to Opitz's conditions, the oxazabicyclo-octane (**10a**) was transformed into the sulphonamide (**10h**) (68% yield after recrystallisation).

If compound (**10a**) undergoes *O*-methylsulphonylation by way of the species (**15a**) [to give the product (**10d**)] and *N*-methylsulphonylmethylsulphonylation by way of the species (**15b**) [to give the product (**10h**)], it is necessary to invoke an opposite selectivity of the sulphenes (**15a, b**) towards the alcohol and amino functions of the substrate. Conceivably, compound (**10h**) arises by a thermodynamically controlled reaction *via* the intermediate (**10i**). However, when a mixture of the sulphonate (**17**)[13] [prepared in 30% yield (after SiO_2 chromatography and recrystallisation) from the reaction of *p*-nitrophenol with an 'aged' mixture of $MeSO_2Cl$ and Et_3N in MeCN at −40 °C] and the oxazabicyclo-octane (**10a**) was left in the presence of triethylamine, no reaction occurred. We therefore consider that the reaction leading to the sulphonamide (**10h**) is under kinetic control. An alternative explanation for the formation of the last-cited compound, which we prefer, is that it arises by way of methylsulphonylmethanesulphonyl chloride (**18**), formed from methanesulphonyl chloride by the route outlined in the Scheme.



Scheme.

Chemical Shift and Conformational Considerations.—It is appropriate to summarise the effects of *N*- and *O*-substitution upon the chemical shifts of the ring protons of oxazabicyclo-octanes of type (**10**) and oxazabicyclo-octanes of type (**13**). The results are collected in Tables 4 and 5.

In the case of oxazabicyclo-octanes of type (**10**) (Table 4), the following conclusions may be drawn. The 1-proton experiences a significant downfield shift when an *O*-sulphonyl group is present (0.53 p.p.m.), when an *N*-sulphonyl entity is present (0.56—0.63 p.p.m.), and when both *O*- and *N*-sulphonyl/acyl functions are present (0.63—0.75 p.p.m.). The 4α-proton is relatively insensitive to either *N*- or *O*-substitution and to both *N*- and *O*-substitution. Although little affected by the presence of an *O*-sulphonyl group or both *N*-acyl and *O*-sulphonyl/acyl substituents, the 4β-proton is deshielded by an *N*-sulphonyl function (0.34—0.42 p.p.m.) and by both *N*-sulphonyl and *O*-sulphonyl/acyl entities (0.42—0.70 p.p.m.). The 5-proton suffers a notable downfield shift in the presence of an *N*-sulphonyl moiety (0.45—0.79 p.p.m.) and both *O*- and *N*-sulphonyl/acyl groups (0.58—0.89 p.p.m.); however, it is not markedly influenced by the presence of an *O*-sulphonyl substituent. The 7-proton behaves in a similar fashion to the 5-proton, being significantly deshielded when an *N*-sulphonyl entity is present (0.59—0.79 p.p.m.) and when both *O*- and *N*-sulphonyl/acyl groups are present (0.76—1.21 p.p.m.); it is unaffected by the presence of an *O*-sulphonyl substituent.

With oxazabicyclo-octenes of type (**13**) (Table 5), it is clear that *O*-sulphonyl/acyl substituents have little effect upon the chemical shifts of the 4α-, 4β-, and 5-protons but that they cause deshielding of the 1-protons (0.44—0.55 p.p.m.).

The coupling constants of the 1-, 4-, and 5-hydrogen atoms of oxazabicyclo-octanes of type (**10**) and oxazabicyclo-octenes of types (**13**) are summarised in Table 6. In the former compounds, the values for $J_{4\alpha,5}$ (8—9 Hz) are essentially constant whereas those for $J_{1,5}$ (6—9 Hz) and $J_{4\beta,5}$ (2—7 Hz) vary with the nature of the substituents R^1 and R^2. In the latter compounds, the values for $J_{1,5}$ (5 Hz), $J_{4\alpha,5}$ (8—10 Hz), and $J_{4\beta,5}$ (3 Hz) show little variation. These results imply that compounds of type (**10**) can adopt different conformations whereas compounds of type (**13**) share a common conformation. According to Dreiding models, two conformational extremes, represented by the types (**19**) and (**20**), are feasible. In conformation (**19**), the dihedral angles (θ) between H_1 and H_5, $H_{4\alpha}$ and H_5, and $H_{4\beta}$ and H_5 are *ca.* 30, 30, and 90° [which correspond to *J* values of 7.5, 7.5, and 0 Hz, using a modified Karplus equation ($J = 10\cos^2\theta$)[14]], whereas in conformation (**20**), the corresponding dihedral angles are ca. 30, 30, and 150° (which represent *J* values of 7.5, 7.5, and 7.5 Hz). It would appear that compounds (**10a, d, f, j**) tends towards a geometry of type (**19**), whereas compounds (**10b, c, e, h**) favour a geometry of type (**20**).

* Selective *O*-methylsulphonylations (see: D. H. Ball and T. W. Parrish, *Adv. Carbohydr. Chem.*, 1968, **23**, 233) and *N*-methylsulphonylations (see: M. G. Stout, M. J. Robins, R. K. Olsen, and R. K. Robins, *J. Med. Chem.*, 1969, **12**, 658) are known.

Table 4. Chemical shifts (p.p.m.; in $CDCl_3$) of the 1-, 4-, 5-, and 7-hydrogen atoms of oxazabicyclo-octanes of type (**10**)

Compd.	1-H	4α-H[a]	4β-H	5-H	7-H
(**10a**)	4.84	2.83	2.59	*ca.* 4.3	3.82
(**10b**)[b]	5.59	3.04	2.71	*ca.* 4.9	4.68
(**10c**)	5.47	2.87	2.93	4.75	4.41
(**10d**)	5.37	2.90	2.59	*ca.* 4.4	3.87
(**10e**)[b]	5.51	3.07	2.72	4.88	5.03
(**10f**)	5.47	2.98	3.29	5.19	4.63
(**10h**)	5.40	2.90	3.01	5.09	4.61
(**10j**)	5.56	2.97	3.26	5.16	4.58
(**10k**)	5.51	2.94	3.09	4.88	4.74

[a] The proton with the large vicinal coupling constant is assumed to be that at the 4α-position; this assignment is not unequivocal in all cases. [b] Only the chemical shifts of the protons of the major rotamer are quoted.

Table 5. Chemical shifts (p.p.m.; in $CDCl_3$) of the 1-, 4-, and 5-hydrogen atoms of oxazabicyclo-octanes of type (**13**)

Compd.	1-H	4α-H	4β-H	5-H
(**13a**)	4.88	3.02	2.85	5.04
(**13b**)	5.43	3.02	2.95	5.09
(**13c**)	5.32	3.05	2.99	5.12

Table 6. Coupling constants (Hz) of the 1-, 4-, and 5-hydrogen atoms of bicycles of types (**10**) and (**13**)

Compd.	$J_{1,5}$	$J_{4\alpha,4\beta}$	$J_{4\alpha,5}$	$J_{4\beta,5}$
(**10a**)	6	19	9	2.5
(**10b**)[a]	8	19	9	5
(**10c**)	9	18	9	7
(**10d**)	6	19	9	2
(**10e**)[a]	8	19	9	6
(**10f**)	6	19	8	2
(**10h**)	8	19	9	7
(**10j**)	6	19	8	2
(**10k**)	7	19	8	4
(**13a**)	5	19	10	3
(**13b**)	5	19	8	3
(**13c**)	5	19	8	3

[a] Only the coupling constants of the protons of the major rotamer are quoted.

The pertinent torsion angles of compound (**10a**), obtained from *X*-ray analysis and calculated from spin-spin coupling constants, are summarised in Table 7. Clearly, in the crystal state, a conformation of type (**19**) is adopted. Apparently, in deuteriochloroform solution, some distortion of this conformation is in evidence.

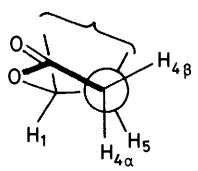
It was of interest to examine whether the downfield shift of the 1-proton of compounds (**10b, j**) (in comparison with that of their parent) and of compound (**13b**) [in comparison with that of its relative (**13a**)] would be duplicated in simpler systems. Accordingly, the synthesis of compounds (**21a, b**) and (**22a, b**) was undertaken.

Ethyl 2-oxocyclopentanecarboxylate was converted into the cyclopentenecarboxylate (**23**), isolated as a colourless oil in 67% yield (after SiO_2 chromatography), by sequential reactions involving sodium borohydride in methanol, methanesulphonyl chloride in pyridine, and boiling triethylamine–chloroform. A similar preparation (but using $POCl_3$ in place of $MeSO_2Cl$ and Et_3N) has been reported in a patent.[15] Hydroxylation of the cyclopentene (**23**) was achieved with osmium(VIII) oxide either under catalytic conditions (*N*-methylmorpholine *N*-oxide[16]) or stoicheiometric conditions; the yield (after SiO_2 purification) of the *cis*-diol (**21c**) was 22% under the former conditions and 30% under the latter. In acetic anhydride–pyridine, the diol (**21c**) was converted into a 4:1 mixture of the monoacetate (**21b**) and the diacetate (**21a**), which were separable by silica-gel chromatography. The diacetate (**21a**) was isolated as a colourless oil in 4% yield and the monoacetate (**21b**) as a clear oil in 54% yield.

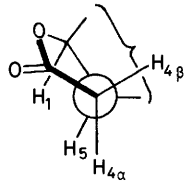
Table 7. Selected torsion angle (°) of compound (**10a**) determined from *X*-ray analysis and spin-spin coupling constants[a]

	Angle (from *X*-ray)	Angle (from *J*)
H_1,H_5	31	40
$H_{4\alpha},H_5$	35	18
$H_{4\beta},H_5$	88	60

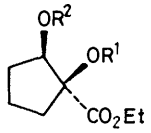
[a] The spin-spin coupling constants (*J*) were converted into torsion angles (θ) by using the Karplus relationship: $J = 10\cos^2\theta$



(**19**)

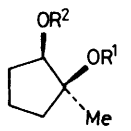


(**20**)



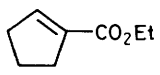
(**21**)

a; $R^1 = R^2 = Ac$
b; $R^1 = H, R^2 = Ac$
c; $R^1 = R^2 = H$



(**22**)

a; $R^1 = R^2 = Ac$
b; $R^1 = H, R^2 = Ac$
c; $R^1 = R^2 = H$



(**23**)

When treated overnight with acetic anhydride–pyridine at ambient temperature, the diol (**22c**)[17] was converted into a 2:1 mixture of the diacetate (**22a**) and the monoacetate (**22b**); only the former material was isolated in a pure state (16% yield) following silica-gel fractionation. The monoacetate (**22b**) was obtained in 56% yield when the diol (**22c**) was treated for 3 h at 0 °C with acetic anhydride–pyridine.

In the 300 MHz ^1H n.m.r. spectra of the diacetates (**21a**) and

(**22a**), the respective 2-hydrogen atoms appeared as a triplet (*J* 6 and 6 Hz) at δ 5.46 and a double doublet (*J* 6 and 4 Hz) at δ 5.05. The corresponding protons of the monoacetates (**21b**) and (**22b**) resonated as triplets at δ 5.13 (*J* 8 and 8 Hz) and δ 4.70 (*J* 7 and 7 Hz) respectively. Clearly, the replacement of the hydrogen atom of the 1-hydroxy group by an acetyl function induces a downfield shift of *ca.* 0.34 p.p.m. of the *anti*-disposed methine hydrogen atom at position 2. Although significant, the deshielding effect is less than that observed in the oxazabicyclo-octanes and the oxazabicyclo-octene.

Experimental

Dry solvents, referred to in the ensuing experiments, were prepared as follows: pyridine and triethylamine were stored over sodium hydroxide pellets; dichloromethane was stored over anhydrous calcium chloride flakes; acetonitrile was left over 4 Å molecular sieves. Light petroleum refers to that fraction boiling in the range 40—60 °C.

T.l.c. was performed on Schleicher and Schull plastic sheets coated with silica gel (F1500 LS254); the chromatograms were initially examined under u.v. light and then developed either with iodine vapour or an aqueous potassium permanganate spray. Column chromatography was effected, under pressure, using Merck Kieselgel H (Type 60).

Evaporations were carried out using a Buchi rotary evaporator or a Buchi cold-finger rotary evaporator. M.p.s were determined using a Kofler hot-stage apparatus and were uncorrected. I.r. spectra were recorded using a Hilger and Watts Infrascan. A Unicam SP800 spectrometer was employed to determine u.v. spectra. ^{1}H N.m.r. spectra were run using tetramethylsilane as internal standard; spectra were measured at 60 MHz, using either a Varian EM360 or a Hitachi–Perkin-Elmer R24B spectrometer, at 300 MHz on a Bruker AC300 spectrometer, and at 360 MHz on a Bruker WM360 spectrometer. Electron impact (e.i.) mass spectra were determined using an A.E.I. MS9 spectrometer operating at 70 e.v.; chemical ionisation (c.i.) spectra were recorded with a Kratos MS45 instrument using ammonia as the carrier gas. Microanalyses were performed using a Carlo Erba 1106 elemental analyser.

Preparation of t-Butyl (1RS,5SR,7RS,8SR)-8-*Ethoxycarbonyl*-8-*hydroxy*-3-*oxo*-2-*oxa*-6-*azabicyclo*[3.2.0]*octane*-7-*carboxylate* (**10a**).—Osmium(VIII) oxide (1.35 g, 5.31 mmol) was added to a stirred solution of the carbapenem (**1a**) [2] (1.35 g, 4.80 mmol) in dry pyridine (30 cm^3) at 0 °C. After 0.5 h, a solution of sodium metabisulphite (1.57 g, 8.26 mmol) in water (90 cm^3) was added and the mixture was stirred at room temperature for 12 h. The mixture was extracted with ethyl acetate (4 times) and the combined extracts were dried ($MgSO_4$). Evaporation, addition of toluene to the residue, and re-evaporation, left a light-brown solid. Recrystallisation of the material from chloroform–diethyl ether gave the *title compound* (**10a**) (1.28 g, 85%) as a white solid, m.p.121 °C; $\nu_{max.}$(KBr) 3 420br and 3 320 (OH and NH), 1 775 (γ-lactone C=O), and 1 750 and 1 720 cm^{-1} (ester C=O); $\lambda_{max.}$(EtOH) 213 nm (ε 630); δ(360 MHz; $CDCl_3$) 1.32 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.44 (9 H, s, CMe_3), 2.59 (1 H, dd, *J* 19 and 2.5 Hz, 4-H), 2.83 (1 H, dd, *J* 19 and 9 Hz, 4-H), 3.0br and 3.5br (each 1 H, s, OH and NH), 3.82 (1 H, s, 7-H), 4.23—4.35 (3 H, m, OCH_2Me and 5-H), and 4.84 (1 H, d, *J* 6 Hz, 1-H); *m/z* (e.i.) 259 ($C_{10}H_{13}NO_7^+$), 241, 214 ($C_9H_{12}NO_5^+$, base peak), 172, 140, and 57 ($C_7H_7^+$) (Found: C, 53.1; H, 6.7; N, 4.6. $C_{14}H_{21}NO_7$ requires C, 53.3; H, 6.7; N, 4.45%).

* See 'Instructions for Authors (1989),' *J. Chem. Soc., Perkin Trans. 1*, 1989, Issue 1.

Crystal data. $C_{14}H_{21}NO_7$, *M* = 315.3. Monoclinic, *a* = 14.356(2), *b* = 11.057(2), *c* = 20.732(3) Å, β = 104.68(1)°, *U* = 3 183 Å (by least-squares refinement on setting angles of 25 accurately centred reflections 6.2 < θ < 11.1°), λ = 0.710 69 Å, space group $P2_1/c$ (No. 14), *Z* = 8 (2 molecules in asymmetric unit), D_c = 1.32 g cm^{-3}. Crystal dimensions: 0.3 × 0.3 × 0.5 mm, μ(Mo-K_α) = 0.67 cm^{-1}.

Data collection and processing. CAD4 diffractometer using graphite-monochromated Mo-K_α radiation in a ω/2θ scan mode with ω scan width = 0.60 + 0.35 tanθ, and ω scan speed in the range 1.1—5° min^{-1} depending on the intensity gathered in a pre-scan; 4 033 reflections measured ($I > 0$, $0 < \theta < 25°$; $\pm h$, $+k$, $+l$) yielding 2 935 unique structure factors [R_{int} = 0.012, $F \geqslant 3\sigma(F)$]. Negligible change in intensity standards (−6 0 2; −2 0 6; 0 4 0) measured repeatedly at 2.5 hourly intervals. Lorenz and polarisation corrections were applied but absorption effects were ignored.

Structure analysis and refinement. Direct methods (MULTAN-80 [18]) were used to solve the structure and difference Fourier maps, produced during the course of blocked matrix least-squares refinement (SHELX-76 [19]), were employed to locate the hydrogen atoms. Slight disorder of the terminal ethyl carbon atoms over the two sites [C(22A): C(23A), 0.85(2): 0.15(2); C(22B): (C23B), 0.87(2): 0.13(2)] necessitated the application of constants to the associated hydrogen atoms. A final *R* value of 0.048 was obtained {R_w = 0.045, $w = 1.2394/[\sigma^2(|F_o|) + 0.0003F_o^2]$, $\sigma|F_o|$ from counting statistics} with all atoms anisotropic except for C(23A), C(23B), and the associated hydrogen atoms; these were subjected to isotropic refinement. Scattering factors were obtained from 'International Tables for *X*-Ray Crystallography'; [20] computations were carried out on the joint CDC 7600/Amdahl 470 system of the University of Manchester Regional Computing Centre. Complete listings of the bond lengths and angles, the hydrogen atom co-ordinates, and thermal parameters are available on request from the Cambridge Crystallographic Data Centre.*

Preparation of t-Butyl (1RS,5SR,8SR)-8-*Ethoxycarbonyl*-8-*hydroxy*-3-*oxo*-2-*oxa*-6-*azabicyclo*[3.3.0]*oct*-6-*ene*-7-*carboxylate* (**13a**).—(*a*) Lead(IV) acetate (0.282 g, 0.64 mmol) was added to a stirred solution of compound (**10a**) (0.100 g, 0.32 mmol) in dry dichloromethane (2 cm^3). After 15 min, the mixture was diluted with dichloromethane and washed with aqueous potassium hydrogen carbonate (2 ×). Evaporation of the dried ($MgSO_4$) organic layer and recrystallisation of the brown solid from dichloromethane–diethyl ether gave the *title compound* (**13a**) (0.061 g, 61%) as a white solid, m.p. 140—141 °C (with softening at 136 °C); $\nu_{max.}$(KBr) 3 400br (OH), 1 785 (γ-lactone C=O), 1 725 and 1 715 (ester C=O), and 1 655 cm^{-1} (C=N); $\lambda_{max.}$(EtOH) 225 (ε 560) and 250sh nm (150); δ(360 MHz; $CDCl_3$) 1.29 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.53 (9 H, s, CMe_3), 2.85 (1 H, dd, *J* 19 and 3 Hz, 4-H), 3.02 (1 H, dd, *J* 19 and 10 Hz, 4-H), 3.89 (1 H, s, OH), 4.27—4.38 (2 H, m, OCH_2Me), 4.88 (1 H, d, *J* 5 Hz, 1-H), and 5.04 (1 H, ddd, *J* 10, 5, and 3 Hz, 5-H); *m/z* (e.i.) 298 ($C_{13}H_{16}NO_7^+$), 257 ($C_{10}H_{11}NO_7^+$), 212 ($C_9H_{10}NO_5^+$), 184, 167, and 57 ($C_4H_9^+$, base peak) (Found: C, 53.6; H, 6.0; N, 4.4. $C_{14}H_{19}NO_7$ requires C, 53.65; H, 6.1; N, 4.45%).

(*b*) Dry pyrdine (0.204 cm^3, 2.52 mmol) was added to a stirred solution of chromium(VI) oxide (0.218 g, 1.28 mmol) in dry dichloromethane (4 cm^3). To this mixture was added a solution of compound (**10a**) (0.100, g, 0.32 mmol) in dry dichloromethane (4 cm^3) followed by acetic anhydride (0.12 cm^3, 1.27 mmol). After 3 h, the mixture was diluted with dichloromethane and washed with dilute hydrochloric acid. Evaporation of the dried ($MgSO_4$) organic layer and purification of the residue by silica-gel chromatography gave a white solid (0.097 g) which was recrystallised from dichloromethane–diethyl ether. The i.r. and

360 MHz ^{1}H n.m.r. spectra of the product (0.050 g, 50%) were identical with those of compound (**13a**).

Preparation of the Toluene-p-*sulphonic Acid Salt of t-Butyl* (1RS,5SR,7RS,8SR)-8-*Ethoxycarbonyl*-8-*hydroxy*-3-*oxo*-2-*oxa*-6-*azabicyclo*[3.3.0]*octane*-7-*carboxylate* (**10a**).—Toluene-*p*-sulphonic acid monohydrate (0.012 g, 0.063 mmol) was added to a solution of compound (**10a**) (0.020 g, 0.063 mmol) in acetone (1 cm^3). Evaporation and recrystallisation of the material from chloroform–diethyl ether gave the *title compound* (0.017 g, 55%), m.p. 120—128 °C (with softening at 82 °C); $\nu_{max.}$(KBr) 3 440br and 3 220br (OH and NH), 1 805 (γ-lactone C=O), and 1 745 cm^{-1} (ester C=O); $\lambda_{max.}$(EtOH) 230 (ε 1 400), 256 (200), 262 (230), and 268 nm (200); δ(360 MHz; $CDCl_3$) 1.26 (3 H, t, *J* 7 Hz, CH_2Me), 1.35 (9 H, s, CMe_3), 2.35 (3 H, s, C_6H_4Me), 2.87 (1 H, dd, *J* 19 and 10 Hz, 4-H), 3.23 (1 H, dd, *J* 19 and 5 Hz, 4-H), 4.19—4.28 (2 H, m, OCH_2Me), 4.83—4.89 (2 H, m, 5- and 7-H), 5.32 (1 H, d, *J* 8 Hz, 1-H), 5.7br (1 H, s, OH), and 7.17 and 7.30 (each 2 H, d, separation 8 Hz, ArH); *m/z* (e.i.) 241, 229, 214, 172, 152, 91 (base peak), and 44 (Found: C, 51.5; H, 5.9; N, 3.0. $C_{21}H_{29}NO_{10}S$ requires C, 51.75; H, 6.0; N, 2.85%).

Preparation of t-Butyl (1RS,5SR,7RS,8SR)-8-*Acetoxy*-6-*acetyl*-8-*ethoxycarbonyl*-3-*oxo*-2-*oxa*-6-*azabicyclo*[3.3.0]-*octane*-7-*carboxylate* (**10b**).—Acetic anhydride (1 cm^3) was added to a solution of compound (**10a**) (0.050 g, 0.16 mmol) in dry pyridine (1 cm^3). After 12 h, ice was added. After a further 15 min, the mixture was partitioned between ethyl acetate and dilute hydrochloric acid. The organic layer was then washed with aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and concentrated. Purification of the resultant syrup by silica-gel chromatography [light petroleum–EtOAc (1:1) as eluant] gave the *title compound* (**10b**) (0.057 g, 90%) as a white solid. After recrystallisation from diethyl ether, the sample (0.013 g, 21%) possessed m.p. 135—136 °C (with softening at 101 °C); $\nu_{max.}$(KBr) 1 795 (γ-lactone C=O), 1 760 and 1 740 (ester C=O), and 1 670 cm^{-1} (amide C=O); $\lambda_{max.}$(EtOH) 220 nm (ε 800); δ(360 MHz; $CDCl_3$) 1.26 and 1.28 (1.8 and 1.2 H, each t, *J* 7 Hz, CH_2Me), 1.46 and 1.47 (3.6 and 5.4 Hz, each s, CMe_3), 2.00 and 2.09 (1.8 and 1.2 H, each s, NCOMe), 2.13 and 2.14 (1.8 and 1.2 H, each s, OCOMe), 2.71 (1 H, dd, *J* 19 and 5 Hz, 4-H), 3.02 and 3.04 [0.4 H (dd, *J* 18 and 8 Hz) and 0.6 H (dd, *J* 19 and 9 Hz), 4-H], 4.12—4.32 (2 H, m, OCH_2Me), 4.65 and 4.68 (0.4 and 0.6 H, each s, 7-H), 4.84—4.97 (1 H, m, 5-H), 5.59 and 5.68 [0.6 H (d, *J* 8 Hz) and 0.4 H (d, *J* 7 Hz), 1-H]; *m/z* (e.i.) 326 ($M^+ - C_3H_5O_2$), 298 ($M^+ - C_5H_9O_2$), 256, 239, 214, 197, and 57 ($C_4H_9^+$, base peak) (Found: C, 54.1; H, 6.2; N, 3.3. $C_{18}H_{25}NO_9$ requires C, 54.15; H, 6.3; N, 3.5%).

Preparation of t-Butyl (1RS,5SR,8SR)-8-*Acetoxy*-8-*ethoxycarbonyl*-3-*oxo*-2-*oxa*-6-*azabicyclo*[3.3.0]*oct*-6-*ene*-7-*carboxylate* (**13b**).—Acetic anhydride (1 cm^3) was added to a solution of compound (**13a**) (0.050 g, 0.16 mmol) in pyridine (1 cm^3). After 12 h, ice was added. After a further 15 min, the mixture was partitioned between ethyl acetate and dilute hydrochloric acid. The organic layer was then washed with aqueous potassium hydrogen carbonate, dried ($MgSO_4$), and evaporated. Purification of the residue by silica-gel chromatography [light petroleum–EtOAc (1:1) as eluant] gave the *title compound* (**13b**) (0.047 g, 83%) as a white solid. After recrystallisation from diethyl ether, the sample (0.025 g, 44%) displayed m.p. 126—131 °C; $\nu_{max.}$(KBr) 1 790 (γ-lactone C=O) and 1 770, 1 755, and 1 735 cm^{-1} (ester C=O); $\lambda_{max.}$(EtOH) 218 nm (ε 1 200); δ(360 MHz; $CDCl_3$) 1.27 (3 H, t, *J* 7 Hz, CH_2Me), 1.54 (9 H, s, CMe_3), 2.19 (3 H, s, OCOMe), 2.95 (1 H, dd, *J* 19 and 3 Hz, 4-H), 3.02 (1 H, dd, *J* 19 and 8 Hz, 4-H), 4.21—4.33 (2 H, m, OCH_2Me), 5.07—5.11 (1 H, m, 5-H), and 5.43 (1 H, d, *J* 5 Hz, 1-H); *m/z* (e.i.) 355 (M^+), 340 ($M^+ - CH_3$), 212, 185, 177, and 57 ($C_4H_9^+$, base peak) (Found: C, 54.1; H, 5.8; N, 3.9. $C_{16}H_{21}NO_8$ requires C, 54.1; H, 5.95; N, 3.95%).

Reaction of Compound (**10a**) *with Methanesulphonyl Chloride–Triethylamine*.—(*a*) To a stirred solution of compound (**10a**) (0.270 g, 0.86 mmol) in dry dichloromethane (9 cm^3) at 0 °C was added methanesulphonyl chloride (0.146 cm^3, 1.89 mmol) followed by dry triethylamine (0.241 cm^3, 1.73 mmol). After 15 min, ice was added and the mixture was partitioned between dichloromethane and dilute hydrochloric acid. The organic layer was then washed with aqueous potassium hydrogen carbonate, dried ($MgSO_4$), and concentrated. Fractionation of the resultant syrup by silica-gel chromatography (light petroleum–EtOAc, gradient elution) gave two fractions.

The first-eluted fraction (0.247 g), isolated as a white solid, was recrystallised from dichloromethane–diethyl ether to give *t-butyl* (1RS,5SR,7RS,8SR)-8-*ethoxycarbonyl*-8-*methylsulphonyloxy*-3-*oxo*-2-*oxa*-6-*azabicyclo*[3.3.0]*octane*-7-*carboxylate* (**10d**) (0.172 g, 51%), m.p. 122—124 °C; $\nu_{max.}$(KBr) 3 360 (NH), 1 790 (γ-lactone C=O), and 1 755 and 1 725 cm^{-1} (ester C=O); $\lambda_{max.}$(EtOH) 217 nm (ε 425); δ(360 MHz; $CDCl_3$) 1.32 (3 H, t, *J* 7 Hz, CH_2Me), 1.48 (9 H, s, CMe_3), 2.59 (1 H, dd, *J* 19 and 2 Hz, 4-H), 2.90 (1 H, dd, *J* 19 and 9 Hz, 4-H), 3.29 (SO_2Me), 3.87 (1 H, s, 7-H), 4.11—4.16 and 4.35—4.44 (1 and 2 H, each m, OCH_2Me and 5-H), and 5.37 (1 H, d, *J* 6 Hz, 1-H); *m/z* (e.i.) 292 ($M^+ - C_5H_9O_2$), 140, and 57 ($C_4H_9^+$, base peak) (Found: C, 45.5; H, 5.6; N, 3.4. $C_{15}H_{25}NO_9S$ requires C, 45.8; H, 5.9; N, 3.55%).

The second-eluted fraction (0.052 g), isolated as a colourless solid, was recrystallised from chloroform–light petroleum to give *t-butyl* (1RS,5SR,7RS,8SR)-8-*ethoxycarbonyl*-6-*methylsulphonylmethylsulphonyl*-8-*methylsulphonyloxy*-3-*oxo*-2-*oxa*-6-*azabicyclo*[3.3.0]*octane*-7-*carboxylate* (**10f**) (0.024 g, 5%), m.p. 122—123 °C; $\nu_{max.}$(KBr) 1 800 (γ-lactone C=O), and 1 760 and 1 745 cm^{-1} (ester C=O); $\lambda_{max.}$(EtOH) 232 (ε 370) and 260 nm (350); δ(360 MHz; $CDCl_3$) 1.36 (3 H, t, *J* 7 Hz, CH_2Me), 1.50 (9 H, s, CMe_3), 2.98 (1 H, dd, *J* 19 and 8 Hz, 4-H), 3.18 (3 H, s, SO_2Me), 3.29 (1 H, dd, *J* 19 and 2 Hz, 4-H), 3.29 (3 H, s, OSO_2Me), 4.24—4.44 (2 H, m, OCH_2Me), 4.63 (1 H, s, 7-H), 4.90 (2 H, ABq, *J* 15 Hz, separation of inner lines 22 Hz, $SO_2CH_2SO_2$), 5.17—5.22 (1 H, m, 5-H), and 5.47 (1 H, d, *J* 6 Hz, 1-H); *m/z* (e.i.) 353, 335, 308, 196, and 152 (base peak) (Found: C, 37.2; H, 4.8, N, 2.5. $C_{17}H_{27}NO_{13}S_2$ requires C, 37.15; H, 4.95; N, 2.55%).

(*b*) Methanesulphonyl chloride (0.135 cm^3, 1.74 mmol) was added to a stirred ice-cooled solution of compound (**10a**) (0.249 g, 0.79 mmol) in a 1:1 mixture of dry dichloromethane and dry triethylamine (10 cm^3). After 0.5 h, ice was added to the mixture which was partitioned between dichloromethane and dilute hydrochloric acid. The organic layer was washed with dilute hydrochloric acid followed by aqueous potassium hydrogen carbonate, dried ($MgSO_4$), and evaporated. Addition of chloroform to the residue (0.214 g) gave a white solid which was collected by filtration. Recrystallisation of the material from ethanol–ethyl acetate gave *t-butyl* (1RS,5SR,7RS,8SR)-8-*ethoxycarbonyl*-8-*hydroxy*-6-*methylsulphonylmethylsulphonyl*-3-*oxo*-2-*oxa*-6-*azabicyclo*[3.3.0]*octane*-7-*carboxylate* (**10h**) (0.055 g, 15%), m.p. 165—167 °C; $\nu_{max.}$(KBr) 3 460 (OH), 1 800 (γ-lactone C=O), and 1 735 cm^{-1} (ester C=O); $\lambda_{max.}$(EtOH) 220 (ε 500) and 265 nm (100); δ(360 MHz; $CDCl_3$) 1.36 (3 H, t, *J* 7 Hz, CH_2Me), 1.48 (9 H, s, CMe_3), 2.90 (1 H, dd, *J* 19 and 7 Hz, 4-H), 3.22 (3 H, s, SO_2Me), 3.7br (1 H, s, OH), 4.25—4.29 and 4.39—4.44 (each 1 H, m, OCH_2Me), 4.61 (1 H, s, 7-H), 4.65 and 4.84 (each 1 H, d, *J* 15 Hz, $SO_2CH_2SO_2$), 5.06—5.13 (1 H, m, 5-H), and 5.40 (1 H, d, *J* 8 Hz, 1-H) (addition of D_2O caused the signal at δ 3.7 to disappear); *m/z* (e.i.) 370 ($M^+ - C_5H_9O_2$), 214, and 57 ($C_4H_9^+$, base peak) (Found: C, 40.8; H, 5.5; N, 3.1. $C_{16}H_{25}NO_{11}S_2$ requires C, 40.75; H, 5.35; N, 2.95%).

Evaporation of the filtrate and fractionation of the residue by silica-gel chromatography (light petroleum–EtOAc, gradient elution) gave two products. The first-eluted material, obtained as a pale-yellow foam (0.143 g, 46%), was identical with compound (**10d**) on the basis of 360 MHz ^{1}H n.m.r. spectroscopy. The second fraction, isolated as a white solid (0.017 g, 5%), was identical with compound (**10h**) on the basis of i.r. and 360 MHz ^{1}H n.m.r. spectroscopy.

(c) Methanesulphonyl chloride (0.141 cm^3, 1.82 mmol) was added to a cooled (MeCN–solid CO_2) stirred solution of triethylamine (0.375 cm^3, 2.69 mmol) in dry acetonitrile (10 cm^3). After 1 h, a solution of compound (**10a**) (0.190 g, 0.60 mmol) in dry acetonitrile (2 cm^3) was added. The mixture was allowed to warm up to room temperature after a further 10 min and then diluted with ethyl acetate and washed sequentially with brine, dilute hydrochloric acid, and aqueous potassium hydrogen carbonate. Evaporation of the dried ($MgSO_4$) organic layer left a yellow solid (0.174 g) which was recrystallised from dichloromethane to give a white material (0.155 g, 68%), m.p. 164—165 °C, that was identical to compound (**10h**) by i.r. and 360 MHz ^{1}H n.m.r. spectroscopy.

Preparation of t-Butyl (1RS,5SR,7RS,8SR)-6-*Acetyl*-8-*ethoxycarbonyl*-8-*methylsulphonyloxy*-3-*oxo*-2-*oxa*-6-*azabicyclo*[3.3.0]*octane*-7-*carboxylate* (**10e**).—Acetic anhydride (1 cm^3) was added to a solution of compound (**10d**) (0.079 g, 0.20 mmol) in pyridine (1 cm^3). After 1 h, ice was added to the solution. After a further 15 min, the mixture was partitioned between ethyl acetate and dilute hydrochloric acid. The organic layer was then washed with aqueous potassium hydrogen carbonate, dried ($MgSO_4$), and concentrated. Purification of the product by silica-gel chromatography [light petroleum–EtOAc (1:1) as eluant] gave a pale-green solid (0.094 g) which was recrystallised from dichloromethane–diethyl ether to give the *title compound* (**10e**) (0.046 g, 53%) as a white solid, m.p. 148—152 °C (decomp.); $\nu_{max.}$(KBr) 1 800 (γ-lactone C=O), 1 750 and 1 735 (ester C=O), and 1 650 cm^{-1} (amide C=O); $\lambda_{max.}$(EtOH) 218 nm (ε 860); δ(360 MHz; $CDCl_3$) 1.36 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.46 and 1.49 (3.6 and 5.4 H, each s, CMe_3), 2.05 and 2.10 (1.8 and 1.2 H, each s, NCOMe), 2.72 and 2.80 [0.6 H, (dd, *J* 19 and 6 Hz) and 0.4 H (dd, *J* 18 and 5 Hz), 4-H], 2.99 and 3.07 [0.4 H (dd, *J* 18 and 8 Hz) and 0.6 H (dd, *J* 19 and 9 Hz), 4-H], 3.24 and 3.26 (1.8 and 1.2 H, each s, SO_2Me), 4.31—4.39 (2 H, m, OCH_2Me), 4.82—4.94 (1 H, m, 5-H), 4.86 and 5.03 (0.4 and 0.6 H, each s, 7-H), and 5.51 and 5.62 [0.6 H (d, *J* 8 Hz) and 0.4 H (d, *J* 7 Hz), 1-H]; *m/z* (e.i.) 362 ($M^+ - C_3H_5O_2$), 334 ($M^+ - C_5H_9O_2$), 293, 239, 197, 152, and 57 ($C_4H_9^+$, base peak) (Found: C, 46.6; H, 5.7; N, 3.3. $C_{17}H_{25}NO_{10}S$ requires C, 46.9; H, 5.8; N, 3.2%).

Preparation of t-Butyl (1RS,5SR,8SR)-8-*Ethoxycarbonyl*-8-*methylsulphonyloxy*-3-*oxo*-2-*oxa*-6-*azabicyclo*[3.3.0]*oct*-6-*ene*-7-*carboxylate* (**13c**).—(*a*) Lead(IV) acetate (0.153 g, 0.35 mmol) was added to a stirred solution of compound (**10d**) (0.068 g, 0.17 mmol) in dry dichloromethane (5 cm^3). After 12 h, water (1 cm^3) was added to the mixture which was diluted with dichloromethane and filtered. The filtrate was washed with aqueous potassium hydrogen carbonate, dried ($MgSO_4$), and concentrated. Crystallisation of the resultant foamy product (0.063 g) from dichloromethane–diethyl ether gave the *title compound* (**13c**) (0.032 g, 47%), m.p. 137 °C; $\nu_{max.}$(KBr) 1 790 (γ-lactone C=O), 1 760 and 1 745 (ester C=O), and 1 655 cm^{-1} (C=N); $\lambda_{max.}$(EtOH) 221 nm (ε 790); δ(360 MHz; $CDCl_3$) 1.32 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.55 (9 H, s, CMe_3), 2.99 (1 H, dd, *J* 19 and 3 Hz, 4-H), 3.05 (1 H, dd, *J* 19 and 8 Hz, 4-H), 3.34 (3 H, s, SO_2Me), 4.24—4.43 (2 H, m, OCH_2Me), 5.09—5.14 (1 H, m, 5-H), and 5.32 (1 H, d, *J* 5 Hz, 1-H); *m/z* (e.i.) 376 ($M^+ - CH_3$), 336, 292, 290 ($M^+ - C_5H_9O_2$), 287, 212, 152, 140, 132, 118, and 57 ($C_4H_9^+$, base peak) (Found: C, 46.0; H, 5.3; N, 3.5. $C_{15}H_{21}NO_9S$ requires C, 46.05; H, 5.4; N, 3.6%).

(*b*) To a stirred solution of compound (**13a**) (0.090 g, 0.29 mmol) in dichloromethane (4 cm^3) at 0 °C was added methanesulphonyl chloride (0.037 cm^3, 0.48 mmol) followed by dry triethylamine (0.065 cm^3, 0.47 mmol). After 10 min, ice was added and the mixture partitioned between dichloromethane and dilute hydrochloric acid. The organic layer was washed with aqueous potassium hydrogen carbonate, dried ($MgSO_4$), and concentrated. Recrystallisation of the resultant solid from dichloromethane–diethyl ether gave a material (0.083 g, 74%) that was identical with compound (**13c**) by 60 MHz ^{1}H n.m.r. spectroscopy.

Reaction of Compound (**10h**) *with Methanesulphonyl Chloride–Triethylamine.*—Triethylamine (0.092 cm^3, 0.66 mmol) followed by methanesulphonyl chloride (0.051 cm^3, 0.66 mmol) were added to a stirred solution of compound (**10h**) (0.155 g, 0.33 mmol) in dry dichloromethane (10 cm^3). After 0.5 h, ice was added to the mixture which was then diluted with dichloromethane and washed with dilute hydrochloric acid (2 ×) followed by aqueous potassium hydrogen carbonate (2 ×). Evaporation of the dried ($MgSO_4$) organic layer and purification of the residue by silica-gel chromatography [light petroleum–EtOAc (2:3) as eluant] gave a white solid (0.153 g). The material (0.099 g, 55%), m.p. 123—124 °C, obtained after recrystallisation from chloroform–diethyl ether, was indistinguishable from compound (**10f**) on the basis of i.r. and 360 MHz ^{1}H n.m.r. spectroscopy.

Preparation of t-Butyl (1RS,5SR,7RS,8SR)-8-*Acetoxy*-8-*ethoxycarbonyl*-6-*methylsulphonylmethylsulphonyl*-3-*oxo*-2-*oxa*-6-*azabicyclo*[3.3.0]*octane*-7-*carboxylate* (**10j**).—Acetic anhydride (1 cm^3) was added to a stirred solution of the alcohol (**10h**) (0.040 g, 0.085 mmol) in dry pyridine (1 cm^3). After 24 h, ice was added to the mixture which, after a further 15 min, was partitioned between ethyl acetate and dilute hydrochloric acid. The organic layer was washed with aqueous potassium hydrogen carbonate, dried ($MgSO_4$), and concentrated to leave an off-white residue (0.047 g). Crystallisation of the material from dichloromethane–diethyl ether gave the *title compound* (**10j**) (0.016 g, 37%) as a white solid, m.p. 112—114 °C; $\nu_{max.}$(KBr) 1 795 (γ-lactone C=O) and 1 740 cm^{-1} (ester C=O); $\lambda_{max.}$(EtOH) 209 nm (ε 430); δ(360 MHz; $CDCl_3$) 1.28 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.49 (9 H, s, CMe_3), 2.17 (3 H, s, CO_2Me), 2.97 (1 H, dd, *J* 19 and 8 Hz, 4-H), 3.18 (3 H, s, SO_2Me), 3.26 (1 H, dd, *J* 19 and 2 Hz, 4-H), 4.16—4.33 (2 H, m, OCH_2Me), 4.58 (1 H, s, 7-H), 4.92 (2 H, AB q, *J* 15 Hz, separation of inner lines 16 Hz, $SO_2CH_2SO_2$), 5.14—5.18 (1 H, m, 5-H), and 5.56 (1 H, d, *J* 6 Hz, 1-H); *m/z* (e.i.) 412 ($M^+ - C_5H_9O_2$), 353, 256, 214, and 57 ($C_4H_9^+$, base peak) (Found: C, 42.4; H, 5.2; N, 2.8. $C_{18}H_{27}NO_{12}S_2$ requires C, 42.1; H, 5.3; N, 2.75%).

Preparation of t-Butyl (1RS,6SR,7RS,8SR)-8-*Ethoxycarbonyl*-8-*hydroxy*-6-*methylsulphonyl*-3-*oxo*-2-*oxa*-6-*azabicyclo*[3.3.0]*octane*-7-*carboxylate* (**10c**).—To a stirred solution of compound (**10a**) (0.050 g, 0.15 mmol) in dry pyridine (1 cm^3) at 0 °C was added methanesulphonyl chloride (0.062 cm^3, 0.80 mmol). The mixture was allowed to warm up to room temperature and, after 10 min, ice was added. The mixture was then partitioned between ethyl acetate and dilute hydrochloric acid. After washing with aqueous potassium hydrogen carbonate, the organic layer was dried ($MgSO_4$) and concentrated. Purification of the residue by silica-gel chromatography [light petroleum–EtOAc (1:1) as eluant] and recrystallisation of the product (0.069 g) from diethyl ether gave the *title compound* (**10c**) (0.030 g, 48%) as a white solid, m.p. 145—147 °C; $\nu_{max.}$(KBr) 3 520 (OH), 1 805 and 1 785 (γ-lactone C=O), and

1 735 cm^{-1} (ester C=O); $\lambda_{max.}$(EtOH) 220 nm (ε 330); δ(360 MHz; $CDCl_3$) 1.35 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.47 (9 H, s, CMe_3), 2.87 (1 H, dd, *J* 18 and 9 Hz, 4-H), 2.93 (1 H, dd, *J* 18 and 7 Hz, 4-H), 2.99 (3 H, s, SO_2Me), 3.8br (1 H, s, OH), 4.21—4.30 and 4.37—4.46 (each 1 H, m, OCH_2Me), 4.41 (1 H, s, 7-H), 4.72—4.79 (1 H, m, 5-H), and 5.47 (1 H, d, *J* 9 Hz, 1-H) (addition of D_2O caused the signal at δ 3.8 to disappear); *m/z* (e.i.) 292 ($M^+ - C_5H_9O_2$) and 57 ($C_4H_9^+$, base peak) (Found: C, 45.6; H, 5.9; N, 3.7. $C_{15}H_{23}NO_9S$ requires C, 45.8; H, 5.9; N, 3.55%).

Preparation of t-Butyl (1RS,5SR,7RS,8SR)-8-*Ethoxycarbonyl*-6-*methylsulphonyl*-8-*methylsulphonyloxy*-3-*oxo*-2-*oxa*-2-*azabicyclo*[3.3.0]*octane*-7-*carboxylate* (**10k**).—(*a*) Methanesulphonyl chloride (0.033 cm^3, 0.43 mmol) was added to a stirred solution of compound (**10c**) (0.088 g, 0.22 mmol) in dry dichloromethane (2 cm^3) and dry triethylamine (0.5 cm^3) at 0 °C. After 30 min, ice was added to the mixture which was then diluted with dichloromethane and washed with dilute hydrochloric acid (2 ×). The organic layer was then washed with aqueous potassium hydrogen carbonate, dried ($MgSO_4$), and concentrated. Recrystallisation of the product (0.097 g) from dichloromethane–diethyl ether gave the *title compound* (**10k**) (0.060 g, 57%) as a white solid, m.p. 124—126 °C; $\nu_{max.}$(KBr) 1 795 (γ-lactone C=O), and 1 755 and 1 740 cm^{-1} (ester C=O); $\lambda_{max.}$(EtOH) 212 nm (ε 260); δ(360 MHz; $CDCl_3$) 1.36 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.50 (9 H, s, CMe_3), 2.94 (1 H, dd, *J* 19 and 8 Hz, 4-H), 3.05 (3 H, s, SO_2Me), 3.09 (1 H, dd, *J* 19 and 4 Hz, 4-H), 3.28 (3 H, s, OSO_2Me), 4.26—4.39 (2 H, m, OCH_2Me), 4.74 (1 H, s, 7-H), 4.85—4.90 (1 H, m, 5-H), and 5.51 (1 H, d, *J* 7 Hz, 1-H); *m/z* (e.i.) 370 ($M^+ - C_5H_9O_2$), 292, 275, 109, 105, 87, and 85 (base peak) (Found: C, 40.6; H, 5.3; N, 3.1. $C_{16}H_{25}NO_{11}S_2$ requires C, 40.75; H, 5.35; N, 2.95%).

(*b*) Methanesulphonyl chloride (0.018 cm^3, 0.23 mmol) was added to a stirred solution of compound (**10c**) (0.044 g, 0.11 mmol) in dry pyridine (2 cm^3). After 12 h, ice was added to the mixture which was then partitioned between ethyl acetate and dilute hydrochloric acid. The organic layer was washed with aqueous potassium hydrogen carbonate, dried ($MgSO_4$), and concentrated. Crystallisation of the resultant residue (0.040 g) from dichloromethane–diethyl ether gave a white solid (0.018 g, 34%), m.p. 122—124 °C, that was identical to compound (**10k**) by 360 MHz ^1H n.m.r. spectroscopy.

Preparation of p-*Nitrophenyl Methylsulphonylmethanesulphonate* (**17**).—Methanesulphonyl chloride (7.78 cm^3, 0.10 mmol) was added to a cooled (MeCN–solid CO_2) stirred solution of dry triethylamine (20.84 cm^3, 0.15 mol) in dry acetonitrile (150 cm^3). After 1 h, the mixture was filtered and *p*-nitrophenol (6.95 g, 0.05 mmol) was added to the filtrate. The mixture was then allowed to warm up to room temperature and filtered. Concentration of the filtrate left a syrupy solid which was dissolved in chloroform. The solution was washed with dilute hydrochloric acid (2 ×) followed by brine (2 ×). Evaporation of the dried ($MgSO_4$) organic layer and recrystallisation of the residue from chloroform–light petroleum gave the title compound (**17**) (4.37 g, 30%) as a white solid, m.p. 122 °C; $\nu_{max.}$(KBr) 1 525 and 1 360 (NO_2), and 1 335, 1 325, and 1 150 cm^{-1} (SO_2); $\lambda_{max.}$(EtOH) 213 (ε 5 300) and 260 nm (8 200); δ(60 MHz; CD_3SOCD_3) 3.35 (3 H, s, SO_2Me), 5.93 (2 H, s, $SO_2CH_2SO_2$), and 7.73 and 8.48 (each 2 H, d, separation 7 Hz, ArH); *m/z* (e.i.) 295 (M^+) and 157 ($C_2H_5O_4S_2^+$, base peak) (Found: C, 32.6; H, 2.9; N, 4.6. Calc. for $C_8H_9NO_7S_2$: C, 32.55; H, 3.05; N, 4.75%).

Preparation of Ethyl Cyclopent-1-*enecarboxylate* (**23**).—To a stirred ice-cooled solution of 97% ethyl 2-oxocyclopentanecarboxylate (3.00 g, 18.6 mmol) in methanol (50 cm^3) was added sodium borohydride (1.09 g, 28.8 mmol) in portions over 30 min. After a further 30 min, the solution was poured into 1M hydrochloric acid (50 cm^3) and the mixture was extracted with dichloromethane. The organic extract was washed with water, dried ($MgSO_4$), and concentrated to leave a colourless oil which was dissolved in pyridine (5 cm^3). This solution was stirred in an ice-bath whilst methanesulphonyl chloride (1.35 cm^3, 17.4 mmol) added dropwise over 10 min. After 2 h, the mixture was poured onto water and extracted with dichloromethane. The organic extract was then washed with dilute hydrochloric acid followed by water and dried ($MgSO_4$). Evaporation left a clear oil which was heated under reflux for 1 h with a 1:1 mixture of triethylamine and chloroform (10 cm^3). The mixture was diluted with dichloromethane and washed with dilute hydrochloric acid and water. Evaporation of the dried ($MgSO_4$) organic layer and purification of the product by silica-gel chromatography [light petroleum–Et_2O (4:1) as eluant] gave the title compound (**23**) (1.75 g, 67%) as a colourless oil; $\nu_{max.}$(film) 1 720 (unsaturated ester C=O) and 1 640 cm^{-1} (C=C); δ(300 MHz; $CDCl_3$) 1.23 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.82—1.98 (2 H, 5 lines, 4-H_2), 2.38—2.58 (4 H, m, 3- and 5-H_2), 4.14 (2 H, q, *J* 7 Hz, OCH_2Me), and 6.70—6.77 (1 H, m, 2-H).

Preparation of Ethyl (2SR,3RS)-1,2-*Dihydroxycyclopentanecarboxylate* (**21c**).—(*a*) 2% Aqueous osmium(VIII) oxide (0.5 cm^3) was added to a stirred solution of the alkene (**23**) (1.00 g, 7.1 mmol) and *N*-methylmorpholine *N*-oxide (1.25 g, 1.07 mmol) in a 4:1 mixture of acetone–water (25 cm^3). After 20 h, the solution was diluted with dichloromethane and washed with saturated aqueous sodium metabisulphite. The organic phase was washed with dilute hydrochloric acid and water and dried ($MgSO_4$). Evaporation of the solvent and purification of the residue by silica-gel chromatography [light petroleum–Et_2O (2:3) as eluant] gave the *title diol* (**21c**) (0.264 g, 22%) as a colourless oil; $\nu_{max.}$(film) 3 450 (OH) and 1 730 cm^{-1} (ester C=O); δ(300 MHz; $CDCl_3$) 1.30 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.57—1.71, 1.80—1.92, and 2.04—2.21 (each 2 H, m, 3-, 4-, and 5-H_2), 2.45br (1 H, d, *J* 8 Hz, 2-OH), 3.60 (1 H, s, 1-OH), and 4.25 (2 H, q, *J* 7 Hz, 1-OH); *m/z* (e.i.) 174 (M^+, 16%), 156 ($M^+ - H_2O$, 18), 128 (31), 127 (12), 117 (21), 101 (78), and 100 (100) (Found: M^+, 174.0892. $C_8H_{14}O_4$ requires *M*, 174.0892).

(*b*) 2% Aqueous osmium(VIII) oxide (20 cm^3, 1.57 mmol) was added to a stirred solution of the alkene (**23**) (0.270 g, 1.93 mmol) in tetrahydrofuran (20 cm^3). After 18 h, saturated aqueous sodium metabisulphite (10 cm^3) was added and, after a further 1 h, the mixture was extracted with dichloromethane. The organic extract was washed with water, dried ($MgSO_4$), and concentrated. Removal of the solvent and purification of the residue by silica-gel chromatography [light petroleum–Et_2O (1:1) as eluant] gave a colourless oil (0.083 g, 30%) that was identical by 300 MHz ^1H n.m.r. spectroscopy with the diol (**21c**).

Reaction of the Diol (**21c**) *with Acetic Anhydride*.—A solution of the diol (**21c**) (0.390 g, 2.24 mmol) in a 1:1 mixture of acetic anhydride–pyridine (2 cm^3) was left overnight and then poured onto ice. The mixture was extracted with dichloromethane and the extract was washed with dilute hydrochloric acid followed by saturated aqueous sodium hydrogen carbonate. Evaporation of the dried ($MgSO_4$) organic layer left a syrup which was mainly a 4:1 mixture of the monoacetate (**21b**) and the diacetate (**21a**). Fractionation of the product by silica-gel chromatography [light petroleum–Et_2O (4:1) as eluant] gave two fractions.

The first-eluted material (0.025 g, 4%), isolated as a colourless oil, was *ethyl* (2SR,3RS)-1,2-*diacetoxycyclopentanecarboxylate* (**21a**); $\nu_{max.}$(film) 1 750 cm^{-1} (ester C=O); δ(300 MHz; $CDCl_3$) 1.24 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.65—1.75, 1.77—1.90, 2.10—2.23, and 2.35—2.47 (1, 2, 2, and 1 H, each m, 3-, 4-, and 5-H_2), 2.04 and 2.11 (each 3 H, s, 2 × COMe), 4.18 (2 H, q, *J* 7 Hz,

OCH_2Me), and 5.46 (1 H, t, J 6 and 6 Hz, 2-H); m/z (c.i.) 259 (MH^+, 1%), 216 ($M^+ - C_2H_2O$, 39), 174 ($M^+ - C_4H_8O_2$, 76), 156 ($M^+ - C_4H_6O_3$, 94), and 143 ($M^+ - C_5H_7O_3$, 100) (Found: MH^+, 259.1172. $C_{12}H_{19}O_6$ requires m/z 259.1182).

The second-eluted material (0.261 g, 54%), isolated as a colourless oil, was *ethyl* (2SR,3RS)-2-*acetoxy*-1-*hydroxycyclopentanecarboxylate* (**21b**); $\nu_{max.}$(film) 3 500 (OH) and 1 740 cm^{-1} (ester C=O); δ(300 MHz; $CDCl_3$) 1.30 (3 H, t, J 7 Hz, CH_2Me), 1.64—1.78, 1.80—1.97, and 2.10—2.26 (1, 3, and 2 H, each m, 3-, 4-, and 5-H_2), 2.07 (3 CH, s, OMe) 3.22 (1 H, s, 2-OH), 4.24 (2 H, q, J 7 Hz, OCH_2Me), and 5.13 (1 H, t, J 8 and 8 Hz, 2-H); m/z (c.i.) 234 (MNH_4^+, 6%), 217 (MH^+, 1), 200 ($MH^+ - HO$, 16), 199 ($MH^+ - H_2O$, 100), and 174 ($MH^+ - C_2H_2O$, 67) (Found: C, 55.9; H, 7.8. $C_{10}H_{16}O_5$ requires C, 55.55; H, 7.45%. MNH_4^+, 234.1397. $C_{10}H_{21}NO_5$ requires m/z 234.1341. MH^+, 217.1076. $C_{10}H_{17}O_5$ requires m/z 217.1076).

Reaction of the Diol (**22c**) *with Acetic Anhydride.*—(*a*) A solution of the diol (**22c**)[16] (0.050 g, 0.43 mmol) in a 1:1 mixture of acetic anhydride–pyridine (2 cm^3) was left overnight and then poured onto ice. The mixture was extracted with dichloromethane and the extract was washed with dilute hydrochloric acid followed by saturated aqueous sodium hydrogen carbonate and water. Evaporation of the dried ($MgSO_4$) organic layer gave a clear syrup which was a 2:1 mixture of compounds (**22a**) and (**22b**). Fractionation of the mixture by silica-gel chromatography (light petroleum–Et_2O, gradient elution) led to the isolation of (1SR,2RS)-1,2-*diacetoxy*-1-*methylcyclopentane* (**22a**) (0.014 g, 16%) as a clear oil; $\nu_{max.}$(film) 1 740 cm^{-1} (ester C=O); δ(300 MHz; $CDCl_3$) 1.46 (3 H, s, 1-Me), 1.53—2.07 and 2.13—2.23 (5 and 1 H, each m, 3-, 4-, and 5-H_2), 2.00 and 2.05 (each 3 H, s, 2 × $MeCO_2$), and 5.05 (1 H, dd, J 6 and 4 Hz, 3-H); m/z (c.i.) 218 (MNH_4^+, 4%), 201 (MH^+, 1), 157 (22), 141 (91), 115 (77), and 99 (100) (Found: C, 59.7; H, 8.3. $C_{10}H_{16}O_4$ requires C, 60.0; H, 8.05%. MNH_4^+, 218.1383. $C_{10}H_{20}NO_4$ requires m/z 218.1392. MH^+, 201.1129. $C_{10}H_{17}O_4$ requires m/z 201.1127).

(*b*) The diol (**22c**)[16] (0.056 g, 0.48 mmol) was left in a 1:1 mixture of acetic anhydride–pyridine (2 cm^3) at 0 °C for 3 h. Work-up as before gave (1SR,2RS)-2-*acetoxy*-1-*methylcyclopentanol* (**22b**) (0.043 g, 56%) as a clear oil; $\nu_{max.}$(film) 3 460 (OH) and 1 730 cm^{-1} (ester C=O); δ(300 MHz; $CDCl_3$) 1.26 (3 H, s, 1-Me), 1.55—1.95 and 2.03—2.13 (5 and 1 H, each m, 3-, 4-, and 5-H_2), 2.11 (3 H, s, $MeCO_2$), 3.53br (1-OH), and 4.70 (1 H, t, J and 7 Hz, 2-H); m/z (c.i.) 159 (MH^+, 2%), 115 (40), and 98 (100) (Found: MH^+, 159.1019. $C_8H_{15}O_3$ requires m/z 159.1021).

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