74. Asymmetric Synthesis of Diazepino-β-lactams by [2 + 2] Cycloaddition of an '*Evans-Sjogren*' Ketene with 1*H*-1,2-Diazepines

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The ketene derivative of the chiral oxazolidinone **1** underwent non-concerted stereospecific [2 + 2] cycloadditions with the (*Z*)-imine moiety of diazepines **2**, leading thereby with good diastereoselection to the *trans*-β-lactam adducts **3** (major) and **4** (minor). The absolute configuration of the major cycloadduct **3a** was determined by an X-ray analysis. Its formation is discussed in terms of minimisation of steric interaction in the two transition states which give sequencially the zwitterionic intermediates and the final cycloadducts.

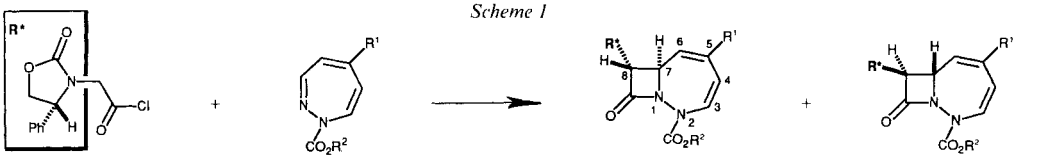
Introduction. – The (*Z*)-imine moiety of 1*H*-1,2-diazepines **2** is known to undergo easily [2 + 2] cycloadditions either with ketenes [1] or with acyl chlorides in the presence of an amine base, giving thereby *trans*-β-lactams [2] [3]. Using these latter experimental conditions *Lynch et al.* [4] investigated the reaction of (*E*)-imines with acyl chlorides. They concluded from kinetic data that the *cis*-β-lactams they isolated arose exclusively from cycloaddition with the ketene intermediates and not *via* direct acylation of the imines with the acyl chloride.

The cycloaddition of ketenes with imines, *i.e.* the '*Staudinger* reaction', is thought to proceed in two steps, most probably *via* a zwitterionic intermediate [5]. As to the stereospecific outcome of the non-concerted [2 + 2] cycloadditions between imines and mono-substituted ketenes, it appears as a rule that (*Z*)-imines lead to *trans*-azetidinones [2] [6], whereas (*E*)-imines give *cis*-β-lactams [4] [7–10]. Last but not least, the asymmetric synthesis of β-lactams was achieved with chiral imines [10] or with chiral ketenes [4] [7] [8], this latter approach being used more often than the first one. Along these lines, *Evans* and *Sjogren* [7] as well as *Ojima et al.* [8] found that the reaction of the chiral acetyl chloride **1** with (*E*)-imines in the presence of an amine base led to the expected *cis*-β-lactams with high asymmetric induction.

We describe herein a similar series of non-concerted [2 + 2] cycloadditions of 1,2-diazepines **2** (*i.e.* (*Z*)-imines) with the '*Evans-Sjogren*' ketene which was obtained *in situ* by a base treatment of 2-oxo-4-phenyloxazolidine-3-acetyl chloride (**1**). An X-ray analysis, as performed with one of the major cycloadducts, permitted the correlation between the absolute configuration of the chiral ketene inductor (one asymmetric center) and the absolute configuration of this major cycloadduct (3 asymmetric centers).

Asymmetric Synthesis of Diazepino-β-Lactams. – The optically active acyl chloride **1** was synthesized in 5 steps and in good overall yield (55%) according to [7], the chiral asymmetric inductor being (*R*)-phenylalanine. Reaction of **1** with a tertiary amine (Et_3N)

Scheme 1



1 **2a–d** **3a–d** (major) **4a–d** (minor)

a R^1 = Me, R^2 = Et; **b** R^1 = Me, R^2 = Bn; **c** R^1 = H, R^2 = Me; **d** R^1 = H, R^2 = *t*-Bu

Table 1. *Major and Minor β-Lactam Adducts* **3** *and* **4**, *Respectively, Obtained on Reaction of Chiral Acyl Chloride* **1** *with Diazepines* **2a–d** *in the Presence of* Et_3N

Product	Overall yield [%]	Relative yields [%]		d.e. [%]
		major adduct **3**	minor adduct **4**	
3a/4a	50	93	7	86
3b/4b	65	89	11	78
3c/4c	53	91	9	82
3d/4d	50	87	13	74

in CH_2Cl_2 solution at low temperature gave the short-lived ketene to which diazepines **2** were added. This led in all instances and in moderate yields (50–65%) to the expected *trans-β*-lactams **3** (major cycloadducts) and **4** (minor cycloadducts) which were obtained with good asymmetric induction (d.e. 74–86%; *Scheme 1* and *Table 1*). Major and minor cycloadducts could easily be distinguished by ^{1}H- and ^{13}C-NMR spectra. In the major adducts **3**, H–C(8) (*d*) appears at *ca.* 4.8 ppm and H–C(7) (*m*) at *ca.* 3.9 ppm, whereas in the minor adducts **4**, the chemical shifts of these two protons are roughly reversed (see *Exper. Part, Table 3*). These data are best explained by assuming a shielding effect of the Ph moiety upon H–C(7) in the major cycloadducts, and upon H–C(8) in the minor cycloadducts. Furthermore, it is worth noticing that all minor cycloadducts are strongly levorotatory as compared to the isomeric major cycloadducts (see *Exper. Part*).

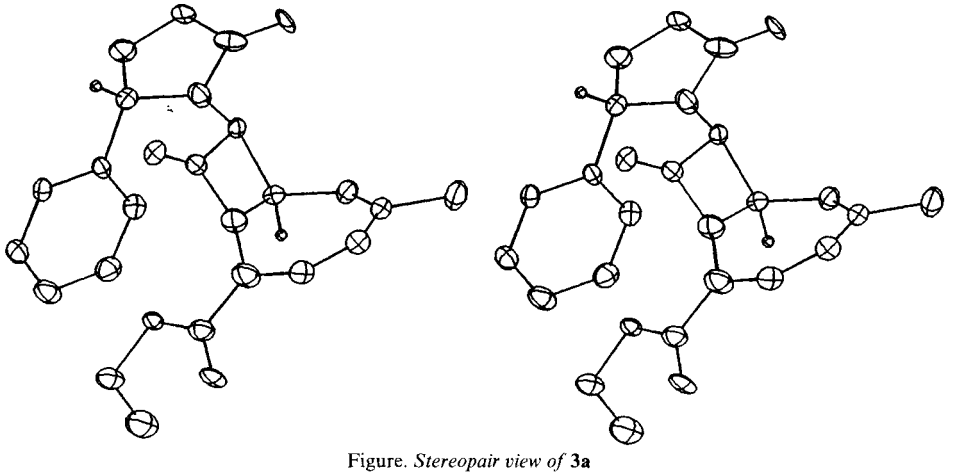


Figure. *Stereopair view of* **3a**

Table 2. *Crystallographic Data of* **3a**

Formula	$C_{20}H_{21}N_3O_5$	Θ_{max} [°]	27
Space group	Triclinic, $P\bar{1}$	Radiation [Å]	MoK_α ($\lambda = 0.71069$)
a [Å]	5.991 (2)	Scan mode	$\omega/2\Theta$
b [Å]	9.112 (3)	Collected intensities	$\pm h, \pm k, +l$
c [Å]	9.231 (3)	Absorption [cm^{-1}]	5.8
α [°]	102.81 (3)	No. of ind. reflections	2040
β [°]	99.33 (3)	No. of refl. used in ref.	1707 ($F > 4\sigma(F)$)
γ [°]	90.19 (3)	No. of variables	256
V [$Å^3$]	484.4 (3)	Observations/parameter	6.7
Z	1	Max. and min. $\Delta\rho$ [$e \cdot Å^{-3}$]	0.33, −0.29
F(000)	202	Final R (unit weights)	0.082[a])
Temp. [K]	293		

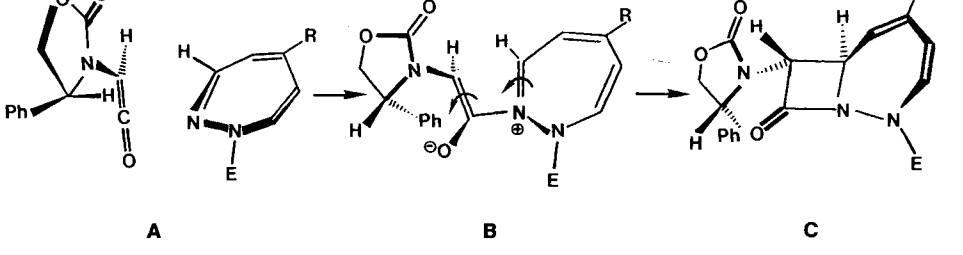
[a]) High R value due to bad crystals.

The absolute configuration of the major cycloadduct **3a** was established by an X-ray diffraction analysis (see the *Fig.* and *Table 2*) which confirmed the above cited NMR data as well as the *trans*-configuration of H–C(7)/H–C(8). Since the NMR data of all major cycloadducts **3b–d** are consistent with those of **3a**, it follows that their absolute configuration is (7*R*,8*R*). Similar NMR considerations for the minor cycloadducts **4** lead to the conclusion that they occur in the (7*S*,8*S*)-configuration.

X-Ray Structure Determination for 3a. – Reflection intensities were collected at room temperature on a four-circle diffractometer *Enraf-Nonius CAD4* equipped with a graphite monochromator and using Mo$K\alpha$ radiation. Unit-cell parameters were determined from 25 accurately centered, independent, and strong reflexions by least-squares method. Four standard reflexions monitored every 3600s during data collection showed no intensity loss. The usual corrections except for absorption were applied. The structure was solved by direct methods with SHELXS-86 [11] and refined with SHELXS-76 [12]. Non-H-atoms were refined anisotropically. The positions for H-atoms were calculated. Details of crystal data and parameters of data collection are given in *Table 2*. Crystallographic data are deposited at the *Cambridge Crystallographic Data Centre*, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England.

Discussion. – Assuming a zwitterion to occur as an intermediate during the non-concerted [2 + 2] cycloaddition of ketenes with imines [13], the stereoselective formation of the major β-lactam cycloadducts **3** is best explained as follows in terms of absolute configuration. Let us assume an orthogonal approach of the *in situ* formed ketene of **1** toward the imine double bond of **2**, as indicated in *Scheme 2* (see **A**). Such a topology keeps steric interactions at a minimum and is akin to the nowadays accepted transition state geometry of the concerted [$2\pi_s + 2\pi_a$] cycloaddition of ketenes to olefins [14]. After

Scheme 2



acylation of N(1), the resulting zwitterionic intermediate **B** undergoes a counterclockwise rotation around – and in the direction of – the C(9)–C(8) bond. This leads to the symmetry-allowed conrotation [10] [15] as indicated in *Scheme 2* which gives the major cycloadduct **C** (= **3**). A similar stereodynamic mechanism can also explain the absolute configuration of the major β-lactam cycloadducts which were obtained by *Evans* and *Sjogren* [7] and by *Ojima et al.* [8] [9].

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Experimental Part

General. Flash chromatography (FC): silica gel (*Merck 60*, 230–400 mesh). TLC: alumina roll (*Merck 60* F_{254}). M.p.: *Kofler* hot bench or *Büchi SMP 20* apparatus; corrected. $[\alpha]_D$: *Perkin-Elmer-PE-241* polarimeter. UV spectra (λ_{max} in nm (ε)): *Varian Techtron 635*. IR spectra (cm^{-1}): *Perkin-Elmer-157-G* spectrophotometer. ^{1}H- and ^{13}C-NMR spectra: *Bruker-WP-80-DS* (80 MHz), *Bruker-AC-F-250* (250 MHz), and *Bruker-WM-400* (400 MHz) apparatus using double-irradiation techniques; tetramethylsilane (TMS; ^{1}H-NMR) and $CDCl_3$ (δ 77.00 with respect to TMS; ^{13}C-NMR) as internal references; δ in ppm and J in Hz. High-resolution (HR)MS were measured on a *MAT-311* spectrometer at the University of Rennes. Microanalyses were carried out by the Service Central de Microanalyses of the CNRS.

(4S)-2-Oxo-4-phenyloxazolidine-3-acetyl Chloride (**1**) was prepared according to [7].

Methyl 1H-1,2-Diazepine-1-carboxylate (**2c**). To a stirred soln. of hydroxylamine *O*-sulfonic acid (23 g, 0.20 mol) in H_2O (50 ml) at 0° were successively added KOH (12 g) in H_2O (20 ml) and pyridine (25 ml). After 2 d of continuous stirring at r.t., K_2CO_3 (14 g) was added portionwise. After 2 h, the precipitated solids were filtered off, and the soln. was concentrated *i.v.*; EtOH (*ca.* 400 ml) was added whereby some additional solids precipitated which were removed. To the resulting EtOH soln. were added K_2CO_3 (40 g) and methyl chloroformate (16 ml), the latter one dropwise. The mixture was kept at r.t. for 24 h and then filtered over sintered glass. The resulting soln. was evaporated and the crude residue purified by FC (AcOEt/EtOH 8:2): [(methoxycarbonyl)imino]pyridinium ylide as a colourless oil (9.6 g, 31%). A soln. of this ylide (9.15 g, 60 mmol) in toluene (8.0 l) was irradiated for 10.5 h under N_2 using a 'falling-film'-type photoreactor [16], equipped with 2 1000-W medium-pressure Hg-vapour lamps, the reaction being monitored by UV until complete disappearance of the pyridinium-ylide absorption band. After evaporation, the oily residue was purified by FC (AcOEt/cyclohexane 6:4) leading to **2c**. Orange oil (6.4 g, 70%). IR ($CHCl_3$): 1720, 1615, 1440. UV (MeOH): 359 (280). ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.43 (*dd*, H–C(3)); 6.57 (*dddd*, H–C(5)); 6.28 (*ddt*, H–C(4)); 6.24 (*dd*, H–C(7)); 5.79 (*ddd*, H–C(6)); 3.89 (*s*, CO_2Me); $J(3,4) = 3.4$, $J(3,5) = 0.9$, $J(4,5) = 11.2$, $J(4,6) = 1.1$, $J(4,7) = 1.1$, $J(5,6) = 5.5$, $J(5,7) = 0.6$, $J(6,7) = 7.4$. HR-MS: 152.0594 ($C_7H_8N_2O_2$, M^+, calc. 152.05857).

Benzyl 5-Methyl-1H-1,2-diazepine-1-carboxylate (**2b**). Same procedures as above using hydroxylamine *O*-sulfonic acid (45.2 g, 0.40 mol), H_2O (100 ml), KOH (24 g) in H_2O (40 ml), 4-methylpyridine (60 ml), K_2CO_3 (24 g), and benzyl chloroformate (150 ml). The [(benzyloxycarbonyl)imino]pyridinium ylide was recrystallized. M.p. 95–115° (AcOEt/toluene). ^{1}H-NMR ($CDCl_3$, 250 MHz): 8.61 (*d*, $J = 7.0$, H–C(2), H–C(6)); 7.45 (*d*, $J = 7.3$, H_o); 7.36 (*d*, $J = 7.0$, H–C(3), H–C(5)); 7.33 (*t*, $J = 7.3$, H_m); 7.28 (*t*, $J = 6.7$, H_p); 5.16 (*s*, PhCH_2); 2.49 (*s*, Me–C(4)).

A soln. of the ylide (2.02 g, 8.3 mmol) was irradiated as described above in toluene (1 l). After FC (AcOEt/cyclohexane 4:6), **2b** (1.78 g, 88%) was obtained as orange crystals. M.p. 62–62.5° (hexane). IR (KBr): 1686, 1647, 1613, 1592, 1411, 1350, 1336. UV (MeOH): 350 (330). ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.44–7.32 (*m*, 5 H, Ph); 7.30 (*dq*, H–C(3)); 6.20 (*d*, H–C(7)); 6.03 (*m*, H–C(4)); 5.59 (*dd*, H–C(6)); 5.31 (*s*, PhCH_2); 1.91 (*t*, Me–C(5)); $J(3,4) = 3.8$, $J(3,Me) = 0.8$, $J(4,6) = 1.8$, $J(4,7) = 0.9$, $J(4,Me) = 1.0$, $J(6,7) = 7.6$. Anal. calc. for $C_{14}H_{14}N_2O_2$ (242.27): C 69.40, H 5.83, N 11.56; found: C 69.5, H 5.8, N 11.6.

General Procedure for the Synthesis of β-Lactams of Type **3** *and* **4**. To a stirred soln. of **1** (1–2 mmol) and Et_3N (1.5 equiv.) in anh. CH_2Cl_2 (3–6 ml) under Ar at −60° was added dropwise a soln. of **2** (1 equiv.) in CH_2Cl_2 (1 ml per mmol). After 20 min at −60°, the temp. was raised to 0° and allowed to react for 2 h. The mixture was filtered through silica gel with AcOEt. After evaporation, the residue was separated by FC at low pressure (*Jobin-Yvon* apparatus, AcOEt/cyclohexane) or by prep. TLC, leading to diastereoisomers **3** and **4**. Typical NMR data in *Table 3*.

Table 3. *^{1}H- and ^{13}C-NMR Data of the [2 + 2] Cycloadducts* **3** (major) *and* **4** (minor). δ in ppm and J in Hz; rel. to TMS (^{1}H) or $CDCl_3$ (= 77.0 ppm; ^{13}C (62.9 MHz)).

	3a	**3b**	**3c**	**3d**	**4a**	**4b**	**4c**	**4d**
δ(H–C(7))	3.89	3.80	4.01	4.01	4.76	4.76	4.82	4.89
δ(H–C(8))	4.73	4.78	4.72	4.67	3.89	3.93	3.90	3.76
^3J(7,8)	1.8	2.0	2.0	br. *s*	2.0	2.0	2.0	2.0
δ(C(8))	62.16	62.71	61.93	61.22	60.70	61.66	61.13	60.46
δ(C(4′))	58.22	58.11	58.51	58.04	61.45	60.48	60.80	60.81

3a *and* **4a** *from* **2a**. Reaction of **1** (485 mg, 2 mmol), Et_3N (420 µl, 3 mmol), and **2a** [17] (462 mg, 2.6 mmol) gave, after FC (AcOEt/cyclohexane 6:4), **3a** (414 mg, 52%) and **4a** (28 mg, 1%).

Ethyl (4′R,7R,8R)-5-Methyl-9-oxo-8-(2′-oxo-4′-phenyl-1′,3′-oxazolidin-3′-yl)-1,2-diazabicyclo[5.2.0]nona-3,5-diene-2-carboxylate (**3a**). Colourless crystals. M.p. 138–139°. $[\alpha]_D^{20} = +7.0$ (c = 1.0, $CHCl_3$). IR (KBr): 2979, 1792, 1756, 1720, 1652, 1461, 1405, 1369, 1319, 1270, 1241, 1219, 1158, 1116, 1089, 1033, 764, 708. ^{1}H-NMR ($CDCl_3$, 250 MHz, 313 K): 7.48–7.37 (*m*, 5 arom. H); 6.68 (*dt*, J = 9.5, 1.7, H–C(3)); 5.56 (*m*, H–C(6)); 4.94 (*dd*, J = 8.9, 4.8, H–C(5′)); 4.90 (*dd*, J = 9.1, 1.1, H–C(4)); 4.73 (*d*, J = 1.8, H–C(8)); 4.72 (*t*, J = 8.9, H–C(5′)); 4.30, 4.26 (*dq*, J = 14.1, 7.1, CH_3CH_2); 4.23 (*dd*, J = 8.9, 4.8, H–C(4′)); 3.89 (*m*, H–C(7)); 1.82 (*t*, J = 1.7, Me–C(5)); 1.31 (*t*, J = 7.1, CH_3CH_2). ^{13}C-NMR ($CDCl_3$, 62.9 MHz, 323 K): 158.59 (*sdd*, C(9)); 157.16 (*sm*, C(2′)); 150.64 (*st*, *C*OOEt); 138.72 (*sm*, C_{ipso}); 130.78 (*sm*, C(5)); 129.07 (*dd*, J = 161.8, C_m); 128.97 (*dt*, J = 159.5, C_p); 127.45 (*dd*, J = 174.6, C(3)); 126.66 (*dquint.*, J = 158.8, C_o); 124.80 (*dm*, J = 157.7, C(6)); 110.43 (*dm*, J = 156.2, C(4)); 70.72 (*td*, J = 156.3, C(5′)); 63.41 (*tq*, J = 148.8, CH_3CH_2); 62.57 (*ddd*, J = 159.5, C(7)); 62.16 (*dt*, J = 163.4, C(8)); 58.22 (*dm*, J = 147.5, C(4′)); 26.12 (*qdd*, J = 127.3, *Me*–C(5)); 14.05 (*qt*, J = 127.4, CH_3CH_2). Anal. calc. for $C_{20}H_{21}N_3O_5$ (383.39): C 62.65, H 5.52, N 10.96; found: C 62.6, H 5.6, N 10.8.

Ethyl (4′R,7S,8S)-5-Methyl-9-oxo-8-(2′-oxo-4′-phenyl-1′,3′-oxazolidin-3′-yl)-1,2-diazabicyclo[5.2.0]nona-3,5-diene-2-carboxylate (**4a**). Colourless oil. $[\alpha]_D^{20} = -163$ (c = 1.75, $CHCl_3$). IR (film): 2982, 2922, 1793, 1750, 1730, 1650, 1619, 1477, 1420, 1372, 1311, 1272, 1226, 1182, 1109, 839, 820, 760, 704. ^{1}H-NMR ($CDCl_3$, 250 MHz, 328 K): 7.47–7.35 (*m*, 5 arom. H); 6.73 (*dt*, J = 9.5, 1.7, H–C(3)); 5.34 (*m*, H–C(6)); 4.94 (*dd*, J = 8.6, 4.6, H–C(5′)); 4.91 (*dd*, J = 9.5, 1.0, H–C(4)); 4.76 (*d*, J = 2.0, H–C(7)); 4.71 (*t*, J = 8.6, H–C(5′)); 4.31, 4.29 (*dq*, J = 10.5, 7.1, CH_3CH_2); 4.29 (*dd*, J = 8.6, 4.6, H–C(4′)); 3.89 (*d*, J = 2.0, H–C(8)); 1.77 (*t*, J = 1.7, Me–C(5)); 1.35 (*t*, J = 7.1, CH_3CH_2). ^{13}C-NMR ($CDCl_3$, 62.9 MHz, 323 K): 158.33 (*s*, C(9)); 156.76 (*s*, C(2′)); 151.42 (*s*, *C*OOEt); 137.99 (*s*, C_{ipso}); 131.33 (*s*, C(5)); 129.46 (*d*, C_p); 129.40 (*d*, C_m); 127.83 (*d*, C(3)); 127.13 (*d*, C_o); 124.77 (*d*, C(6)); 110.92 (*d*, C(4)); 70.51 (*t*, C(5′)); 63.86 (*t*, CH_3CH_2); 63.26 (*d*, C(7)); 61.45 (*d*, C(4′)); 60.70 (*d*, C(8)); 26.63 (*q*, *Me*–C(5)); 14.27 (*q*, CH_3CH_2).

3b *and* **4b** *from* **2b**. Reaction of **1** (542 mg, 2.26 mmol), Et_3N (480 µl, 3.39 mmol), and **2b** (580 mg, 2.37 mmol) gave, after FC (AcOEt/cyclohexane 1:1), **3b** (662 mg, 60%) and **4b** (57 mg, 6%), besides **2b** (129 mg, 22%).

Benzyl (4′R,7R,8R)-5-Methyl-9-oxo-8-(2′-oxo-4′-phenyl-1′,3′-oxazolidin-3′-yl)-1,2-diazabicyclo[5.2.0]-nona-3,5-diene-2-carboxylate (**3b**). Resinous material. M.p. 90–100°. $[\alpha]_D^{20} = -23$ (c = 1.1, $CHCl_3$). IR (KBr): 1793, 1755, 1739, 1415, 1309, 1270, 1216, 1113, 757. ^{1}H-NMR ($C_2D_2Cl_4$, 400 MHz, 341 K): 7.49–7.24 (*m*, 10 arom. H); 6.75 (*dm*, J = 9.4, H–C(3)); 5.66 (*m*, H–C(6)); 5.34, 5.25 (*d*(*AB*), J = 12.2, PhCH_2); 4.97 (*dd*, J = 9.4, 0.8, H–C(4)); 4.79 (*d*, J = 8.8, 4.9, H–C(5′)); 4.75 (*d*, J = 2.0, H–C(8)); 4.66 (*t*, J = 8.8, H–C(4′)); 4.18 (*dd*, J = 8.4, 4.9, H–C(4′)); 3.92 (*m*, H–C(7)); 1.86 (*t*, J = 1.6, Me–C(5)). ^{13}C-NMR ($CDCl_3$, 62.9 MHz, 323 K): 158.95 (*sdd*, C(9)); 157.46 (*sm*, C(2′)); 150.87 (*st*, *C*OOBn); 139.21 (*sm*, C_{ipso} of Ph–C(4′)); 135.02 (*sm*, C_{ipso} of Bn); 131.06 (*sm*, C(5)); 129.28 (*dd*, J = 160.5, C_m of Ph–C(4′)); 129.12 (*dt*, J = 160, C_p of Ph–C(4′)); 128.61 (*dt*, J = 160, C_p of Bn); 128.55 (*dd*, J = 160, C_m of Bn); 128.31 (*dquint.*, J = 159.5, C_o of Bn); 127.54 (*ds*, J = 184, C(3)); 126.70 (*dquint.*, J = 159, C_o of Ph–C(4′)); 125.05 (*dm*, J = 158, C(6)); 110.94 (*dm*, J = 157, C(4)); 70.90 (*td*, J = 156, C(5′)); 69.26 (*tt*, J = 149.5, PhCH_2); 62.71 (*ddd*, J = 158, C(8)); 62.67 (*dd*, J = 156, C(7)); 58.11 (*dm*, J = 147, C(4′)); 26.26 (*qdd*, J = 127, *Me*–C(5)). Anal. calc. for $C_{25}H_{23}N_3O_5 \cdot H_2O$ (463.47): C 64.78, H 5.44, N 9.07; found: C 65.0, H 5.3, N 8.6.

Benzyl (4′R,7S,8S)-5-Methyl-9-oxo-8-(2′-oxo-4′-phenyl-1′,3′-oxazolidin-3′-yl)-1,2-diazabicyclo[5.2.0]nona-3,5-diene-2-carboxylate (**4b**). Resinous material. $[\alpha]_D^{20} = -203$ (c = 0.9, $CHCl_3$). IR (KBr): 1798, 1756, 1740, 1420, 1310, 1272, 1219, 1111, 756, 698. ^{1}H-NMR (C_6D_6, 80 MHz, 343 K): 7.16 (*m*, 5 arom. H); 7.04 (*m*, 5 arom. H); 6.68 (*dt*, J = 9.4, 1.0, H–C(3)); 5.30 (*qt*, J = 1.6, 1.0, H–C(6)); 5.07 (*s*, PhCH_2); 4.66 (*dqd*, J = 1.7, 1.6, 1.0, H–C(7)); 4.51 (*dd*, J = 9.4, 1.0, H–C(4)); 4.35 (*dd*, J = 8.4, 4.5, H–C(5′)); 3.82 (*t*, J = 8.4, H–C(5′)); 3.72 (*d*, J = 1.7, H–C(8)); 3.60 (*dd*, J = 8.4, 4.5, H–C(4′)); 1.41 (*t*, J = 1.6, Me–C(5)). ^{13}C-NMR ($CDCl_3$, 62.9 MHz, 323 K):

158.37 (*s*, C(9)); 157.03 (*s*, C(2′)); 151.38 (*s*, *C*OOBn); 138.08 (*s*, C_{ipso} of Ph–C(4′)); 135.26 (*s*, C_{ipso} of Bn); 131.50 (*s*, C(5)); 129.34 (*d*, C_m of Ph–C(4′)); 129.34 (*d*, C_p of Ph–C(4′)); 128.59 (*d*, C_m of Bn); 128.53 (*d*, C_p of Bn); 128.37 (*d*, C_o of Bn), 127.88 (*d*, C(3)); 127.11 (*d*, C_o of Ph–C(4′)); 125.33 (*d*, C(6)); 111.44 (*d*, C(4)); 70.64 (*t*, C(5′)); 69.24 (*t*, Ph*C*H_2); 63.47 (*d*, C(7)); 61.66 (*d*, C(8)); 60.48 (*d*, C(4′)); 26.52 (*q*, *Me*–C(5)).

3c *and* **4c** *from* **2c**. Reaction of **1** (175 mg, 0.73 mmol), Et_3N (200 µl, 1.5 mmol), and **2c** (120 mg, 0.73 mmol) gave, after prep. TLC (AcOEt/cyclohexane 6:4), **3c** (125 mg, 47%) and **4c** (12 mg, 5%), besides some **2c**.

*Methyl (4′*R,*7*R,*8*R*)-9-Oxo-8-(2′-oxo-4′-phenyl-1′,3′-oxazolidin-3′-yl)-1,2-diazabicyclo[5.2.0]nona-3,5-diene-2-carboxylate* (**3c**). Colourless resin. $[\alpha]_D^{20} = +30.5$ (*c* = 1.8, $CHCl_3$). IR (KBr): 2957, 1788, 1748, 1735, 1638, 1608, 1472, 1452, 1434, 1412, 1354, 1319, 1263, 1212, 1146, 1118, 1096, 1032, 995, 753, 708, 695. ^{1}H-NMR ($CDCl_3$, 250 MHz, 323 K): 7.48–7.36 (*m*, 5 arom. H); 6.74 (*d*, *J* = 9.3, H–C(3)); 5.87 (*ddt*, *J* = 11.8, 2.0, 1.0, H–C(6)); 5.78 (*ddd*, *J* = 11.8, 7.7, 1.7, H–C(5)); 5.07 (*ddd*, *J* = 9.3, 7.7, 1.0, H–C(4)); 4.95 (*dd*, *J* = 8.8, 5.0, H–C(5′)); 4.72 (*d*, *J* = 2.0, H–C(8)); 4.70 (*t*, *J* = 8.8, H–C(5′)); 4.20 (*dd*, *J* = 8.8, 5.0, H–C(4′)); 4.01 (*m*, H–C(7)); 3.81 (*s*, MeO). ^{13}C-NMR ($CDCl_3$, 62.9 MHz, 323 K): 158.86 (*sdd*, C(9)); 157.53 (*st*, C(2′)); 151.54 (*sq*, *C*OOMe); 138.97 (*sm*, C_{ipso}); 130.15 (*ddm*, *J* = 160, C(6)); 129.73 (*dm*, *J* = 186, C(3)); 129.38 (*dd*, *J* = 160, C_m); 129.34 (*dm*, *J* = 160, C_p); 126.94 (*dm*, *J* = 160, C_o); 123.25 (*dddd*, *J* = 158, C(5)); 106.80 (*ddm*, *J* = 160, C(4)); 71.09 (*td*, *J* = 156, C(5′)); 64.27 (*dddd*, *J* = 160, C(7)); 61.93 (*dd*, *J* = 154, C(8)); 58.51 (*dm*, *J* = 147, C(4′)); 54.17 (*qs*, *J* = 148, MeO). Anal. calc. for $C_{18}H_{17}N_3O_5$ (355.35): C 60.84, H 4.82, N 11.83; found: C 60.5, H 5.0, N 11.4.

*Methyl (4′*R,*7*S,*8*S*)-9-Oxo-8-(2′-oxo-4′-phenyl-1′,3′-oxazolidin-3′-yl)-1,2-diazabicyclo[5.2.0]nona-3,5-diene-2-carboxylate* (**4c**). Yellow oil. $[\alpha]_D^{20} = -220$ (*c* = 0.4, $CHCl_3$). IR (film): 2955, 1791, 1746, 1735, 1645, 1432, 1420, 1318, 1266, 1215, 1102, 1031, 756, 708, 697. ^{1}H-NMR ($CDCl_3$, 250 MHz, 300 K): 7.48–7.33 (*m*, 5 arom. H); 6.79 (*d*, *J* = 9.3, H–C(3)); 5.71 (*ddd*, *J* = 11.8, 8.0, 1.8, H–C(5)); 5.45 (*dm*, *J* = 11.8, H–C(6)); 5.09 (*dd*, *J* = 9.3, 8.0, H–C(4)); 4.93 (*dd*, *J* = 8.6, 4.9, H–C(5′)); 4.82 (*m*, H–C(7)); 4.75 (*t*, *J* = 8.6, H–C(5′)); 4.32 (*dd*, *J* = 8.6, 4.9, H–C(4′)); 3.90 (*d*, *J* = 2.0, H–C(8)); 3.87 (*s*, MeO). ^{13}C-NMR ($CDCl_3$, 62.9 MHz, 323 K): 158.35 (*s*, C(9)); 156.89 (*s*, C(2′)); 152.08 (*s*, *C*OOMe); 137.96 (*s*, C_{ipso}); 130.03 (*d*, C(3)); 129.99 (*d*, C(6)); 129.56 (*d*, C_p); 129.48 (*d*, C_m); 127.16 (*d*, C_o); 123.65 (*d*, C(5)); 106.92 (*d*, C(4)); 70.63 (*t*, C(5′)); 64.30 (*d*, C(7)); 61.13 (*d*, C(8)); 60.80 (*d*, C(4′)); 54.34 (*q*, MeO).

3d *and* **4d** *from* **2d**. Reaction of **1** (240 mg, 1.05 mmol), Et_3N (350 µl, 2.5 mmol), and **2d** [18] (240 mg, 1.24 mmol) gave, after prep. TLC (AcOEt/cyclohexane 3:7), **3d** (177 mg, 45%) and **4d** (20 mg, 5%), besides some **2d**.

tert-*Butyl (4′*R,*7*R,*8*R*)-9-Oxo-8-(2′-oxo-4′-phenyl-1′,3′-oxazolidin-3′-yl)-1,2-diazabicyclo[5.2.0]nona-3,5-diene-2-carboxylate* (**3d**). Colourless crystals. M.p. 117–119°. $[\alpha]_D^{20} = +62.3$ (*c* = 4.8, $CHCl_3$). IR (KBr): 2975, 2928, 1783, 1770, 1729, 1642, 1610, 1476, 1458, 1423, 1394, 1372, 1330, 1274, 1217, 1183, 1163, 1109, 1032, 850, 833, 759, 712, 703. ^{1}H-NMR (C_6D_6, 250 MHz, 348 K): 7.26–7.03 (*m*, 5 arom. H); 6.67 (*d*, *J* = 9.4, H–C(3)); 5.42 (*ddm*, *J* = 11.6, 1.6, H–C(6)); 5.32 (*ddd*, *J* = 11.6, 7.9, 1.8, H–C(5)); 4.60 (*dd*, *J* = 9.4, 7.9, H–C(4)); 4.55 (*dd*, *J* = 8.8, 5.2, H–C(5′)); 4.45 (*s*, H–C(8)); 4.07 (*m*, H–C(7)); 3.84 (*t*, *J* = 8.8, H–C(5′)); 3.58 (*dd*, *J* = 8.8, 5.2, H–C(4′)); 1.39 (*s*, *t*-Bu). ^{13}C-NMR ($CDCl_3$, 62.9 MHz, 323 K): 158.42 (*s*, C(9)); 157.14 (*s*, C(2′)); 148.99 (*s*, *C*OO(*t*-Bu)); 138.71 (*sm*, C_{ipso}); 129.44 (*dm*, *J* = 180, C(3)); 129.18 (*dm*, *J* = 160, C(6)); 129.12 (*dd*, *J* = 162, C_m); 129.12 (*dm*, *J* = 160, C_p); 126.99 (*dm*, *J* = 160, C_o); 123.08 (*dddd*, *J* = 157, C(5)); 104.98 (*ddm*, *J* = 160, C(4)); 84.05 (*sm*, Me_3C); 70.78 (*td*, *J* = 156, C(5′)); 63.22 (*dtm*, *J* = 159, C(7)); 61.22 (*d*, *J* = 152, C(8)); 58.04 (*dm*, *J* = 150, C(4′)); 27.79 (*qsept*. *J* = 127, Me_3). Anal. calc. for $C_{21}H_{23}N_3O_5$ (397.43): C 63.46, H 5.83, N 10.58; found: C 63.6, H 6.1, N 10.2.

tert-*Butyl (4′*R,*7*S,*8*S*)-9-Oxo-8-(2′-oxo-4′-phenyl-1′,3′-oxazolidin-3′-yl)-1,2-diazabicyclo[5.2.0]nona-3,5-diene-2-carboxylate* (**4d**). Yellow oil. $[\alpha]_D^{20} = -273$ (*c* = 0.8, $CHCl_3$). IR (film): 2980, 2925, 1796, 1762, 1730, 1640, 1611, 1458, 1418, 1394, 1370, 1323, 1272, 1258, 1157, 1104, 1039, 844, 711, 706. ^{1}H-NMR ($CDCl_3$, 250 MHz, 300 K): 7.46–7.35 (*m*, 5 arom. H); 6.79 (*dt*, *J* = 9.3, 2.0, H–C(3)); 5.70 (*ddd*, *J* = 11.7, 8.0, 1.9, H–C(5)); 5.45 (*dm*, *J* = 11.7, H–C(6)); 5.01 (*dd*, *J* = 9.3, 8.0, H–C(4)); 4.94 (*dd*, *J* = 8.6, 4.6, H–C(5′)); 4.89 (*m*, H–C(7)); 4.70 (*t*, *J* = 8.6, H–C(5′)); 4.30 (*dd*, *J* = 8.6, 4.6, H–C(4′)); 3.76 (*d*, *J* = 2.0, H–C(8)); 1.56 (*s*, *t*-Bu). ^{13}C-NMR ($CDCl_3$, 62.9 MHz, 323 K): 157.87 (*sm*, C(9)); 156.45 (*sm*, C(2′)); 149.79 (*s*, *C*OO(*t*-Bu)); 137.96 (*sm*, C_{ipso}); 129.74 (*ddm*, *J* = 185, C(3)); 129.42 (*dm*, *J* = 160, C(6)); 128.38 (*dm*, *J* = 160, C_p); 128.38 (*dd*, *J* = 161, C_m); 127.00 (*dm*, *J* = 160, C_o); 123.34 (*ddd*, *J* = 155, C(5)); 105.56 (*ddm*, *J* = 159, C(4)); 84.17 (*sm*, Me_3C); 70.36 (*td*, *J* = 155, C(5′)); 64.15 (*dddd*, *J* = 162, C(7)); 60.81 (*d*, *J* = 148, C(4′)); 60.46 (*ddm*, *J* = 153, C(8)); 27.93 (*qsept*., *J* = 127, Me_3).

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