Asymmetric Synthesis of Pentono- and 6-Deoxyhexono-δ-lactams *via* Hetero-*Diels-Alder* Reactions with Nitroso Dienophile

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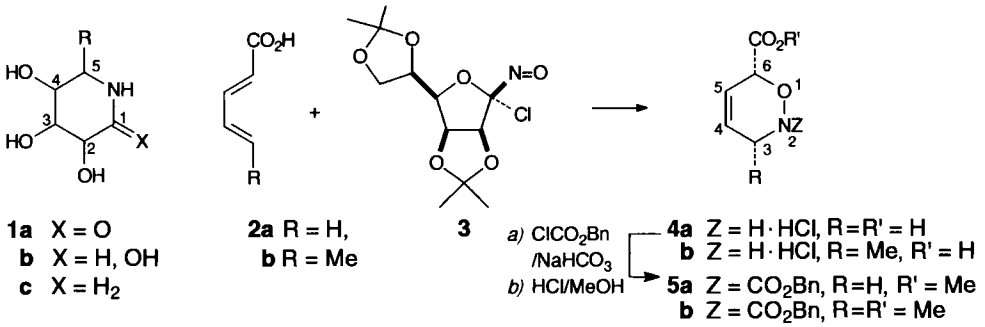
Asymmetric *Diels-Alder* reaction of the pentadienoic and hexadienoic acids **2a,b** with the chiral chloro-nitroso derivative **3** gave the primary adducts **4a,b** with good-to-excellent enantioselectivity. Subsequent *cis*- or *trans*-dihydroxylation and hydrogenolytic cleavage of the N–O bond led to the 5-amino-5-deoxy-pentono-δ-lactams **13a**, **14**, **15a**, and **16** in the D-ribose, L-arabinose, D-xylose, and L-lyxose series, respectively, and to the 5-amino-5,6-dideoxyhexono-δ-lactams **13b** and **15b** in the D-allose and D-glucose series, respectively.

Introduction. – 5-Amino-5-deoxyhexono-δ-lactams **1a** are stable amino-sugars which were easily synthesized. They possess some glycosidase inhibitory properties [1][2], but, except in the D-mannose and D-rhamnose series [3–5], they are in general weaker inhibitors when compared to the corresponding 5-amino-5-deoxy-D-hexoses **1b** or to their 1-deoxy derivatives **1c** in the D-glucose [6], D-gulose [7], D-galactose [8], L-rhamnose [4], or L-fucose [9] series (*Scheme 1*). δ-Lactams are important intermediates for the synthesis of more potent inhibitors like 1-deoxy-amino-sugars [4][7][9–11], amidines [12–15], amidrazones [14–16], amidoximes [15][17], pyrrolo- and imidazolo-sugars [18], or polyhydroxyindolizines [19]. In the pyrrolidinone series, amidrazones, which are obtained from D-ribono-γ-lactam, are potent nucleotide hydrolase inhibitors [20].

We describe herein a straightforward synthesis of 5-amino-5-deoxypentono- and 5-amino-5,6-dideoxyhexono-δ-lactams **13a**, **14**, **15a**, **16**, **13b**, and **15b** in the D-ribose, L-arabinose, D-xylose, L-lyxose, D-allose, and D-glucose series, respectively, starting from the readily available (*E*)-pentadienoic acid **2a** [21] and from the commercial (*E,E*)-hexadienoic acid (= sorbic acid) **2b**. The synthetic methodology has already been presented by us for the preparation of 6-deoxy-amino-sugars and of their 1-deoxy derivatives from hexadienal dimethyl acetal or *O*-methyloxime [22][23] and consisted of an asymmetric hetero-*Diels-Alder* reaction with the chiral chloro-nitroso derivative **3** of D-mannose [24], followed by *cis*- or *trans*-dihydroxylation and cleavage of the oxazine ring by hydrogenolysis. This reaction scheme starting from methyl sorbate has been described in the racemic series by *Belleau* and *Au-Young* in 1963 to give linear 5-amino-5,6-dideoxyhexonic acids in the allonic and allegedly gulonic, in fact gluconic series [25].

5-Amino-5-deoxypentono-δ-lactams in the D-ribose [26–28], D-xylose [27][29], D-lyxose [27], D- and DL-arabinose [27][30] series were already known compounds. A preliminary communication of these results appeared previously [31].

Scheme 1



Asymmetric *Diels-Alder* Reaction and Optical Purity (*Scheme 1*). – Asymmetric *Diels-Alder* reaction of chloro-nitroso compound **3** with the dienoic acids **2a**, **b** was carried out according to *Kresze*'s conditions, *i.e.*, in CH_2Cl_2/EtOH solutions at $-10°$ overnight [24]; the adducts **4a**, **b** crystallized as hydrochlorides in *ca.* 75% yield after addition of dry Et_2O. In both cases, one chiral regioisomer only was formed, the 3,6-disubstituted one, **4b**, having the 3,6-*cis*-configuration. These compounds are stable but base-sensitive.

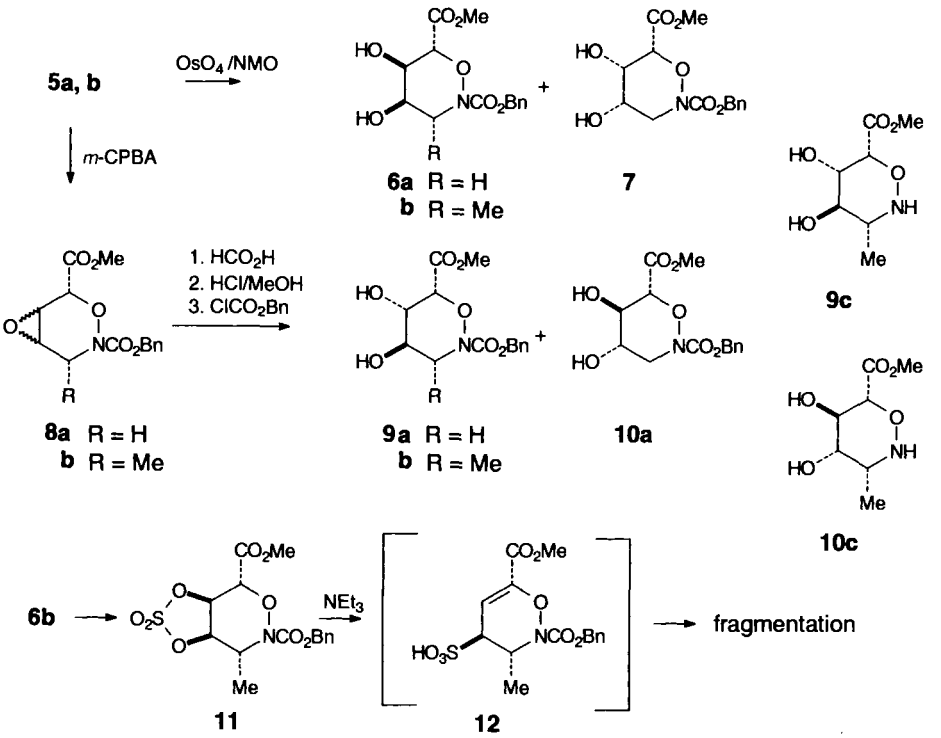
The adducts were *N*-protected with $ClCO_2Bn/NaHCO_3$ in MeOH and esterified with dry HCl/MeOH to give the protected adduct derivatives **5a**, **b** in *ca.* 90% yield. These latter ones are moderately stable, and their partial aromatization into pyrrole derivatives by chromatography, as described by *Kresze* and coworkers [32] in similar cases, was not studied any further.

Kresze and coworkers had proven the (3*R*,6*R*)-configuration for the adduct of ethyl sorbate with dienophile **3** [24][33]; the same configuration was deduced for adduct **4b** and **5b** by analogy. The (6*R*)-configuration for the monosubstituted adduct **4a** and **5a** was corroborated by comparison of the physical data of the final pentono-δ-lactams with those of the literature [26–29].

The optical purity of the adducts **4a**, **b** was determined by HPLC on chiral columns (*Chiralpack AD* or *Chiralcel OD*) with their protected derivatives **5a**, **b**, racemic (±)-**5a**, **b** being used as references. These racemates were synthesized by *Diels-Alder* reaction of the acids **2a**, **b** with acyl-nitroso dienophile BnO–CO–N=O (prepared by *in situ* oxidation of the corresponding hydroxamic acid with periodate salts in CH_2Cl_2 [34]), followed by esterification with HCl/MeOH. Enantiomeric proportions for the monosubstituted adduct derivative **5a** were found to be 93:7, corresponding to 86% enantiomeric excess (ee) which rose to 96% ee after one recrystallization of **4a**. The disubstituted adduct derivative **5b** was enantiomerically pure, with ee > 98%, as already observed in similar cases [22][23][33].

Dihydroxylation (*Scheme 2*). – *cis*-Dihydroxylation of adducts with catalytic amounts of OsO_4 in acetone/H_2O with 4-methylmorpholine 4-oxide (NMO) as co-oxidant [22][35][36] was uneffective with **4a**, **b**. Carried out with the protected derivatives **5a**, **b**, it gave easily the dihydroxy esters **6a**, **b** and **7** in 65–70% overall yield. As observed with other sorbic-acid derivatives [23][34], the disubstituted derivative **5b** gave only one dihydroxy ester **6b**; to the contrary, the monosubstituted derivative **5a** yielded the two

Scheme 2



crystalline dihydroxy esters **6a** and **7** in a 4:1 ratio which were easily separated by chromatography. In both cases, the two *cis*-arranged OH groups in the major dihydroxy esters **6a,b** proved to be in *trans*-position with respect to the carboxylate group.

The formation of both dihydroxy compounds was not observed with other monosubstituted 3,6-dihydro-2*H*-oxazines [37][38], but there are some examples in the 2,5-dihydro-1*H*-pyrrole series [39].

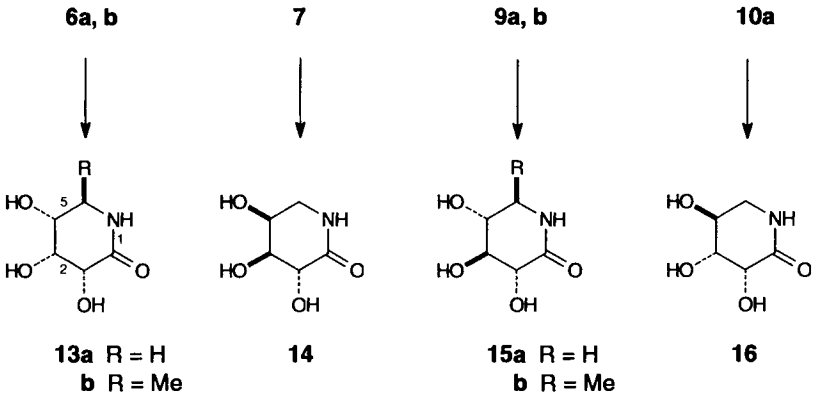
trans-Dihydroxylation was carried out by acid-catalyzed opening of the appropriate epoxy derivative as described earlier in the racemic *N*-benzoyl series by *Belleau* and *Au-Young* [25]. Epoxidation of the protected adduct derivatives **5a,b** with *m*-chloroperbenzoic acid (*m*-CPBA) led in a clean reaction in 5 days to epoxy esters **8a,b** as a 1:1 and 3:2 diastereoisomer mixture, respectively. These epoxy esters were difficult to purify and were thus characterized as the dihydroxy esters obtained in the following step. Acidic opening of the epoxide moiety with 90% formic acid at 90° and methanolysis of the formed isomeric formates with 10% HCl/MeOH afforded the *trans*-dihydroxy esters; partial *N*-deprotection required final treatment with $ClCO_2Bn/NaHCO_3$. As already mentioned above, the selectivity of this hydroxylation varied strongly with the series, epoxy ester **8a** gave both crystalline *trans*-dihydroxy esters **9a** and **10a** in *ca.* 70% overall yield and in a 65:35 ratio; they were easily separated by chromatography. Opening of epoxy ester **8b** was stereospecific but led to *trans*-dihydroxy ester **9b** in moderate yield only. In both cases, the OH groups of the major dihydroxy ester **9a,b** are in a *trans*-diaxial position as a result of a *trans*-diaxial opening of the epoxide ring [23][40].

Attemps to obtain the *trans*-dihydroxy ester by inversion of one OH group of the *cis*-dihydroxy ester *via* the cyclic sulfate [23][40] were undertaken with **6b**. Crystalline cyclic sulfate **11** was easily obtained by the *Sharpless* method [41] but led quickly to a base-catalyzed β-elimination to the unstable 3,4-dihydro-2*H*-oxazine intermediate **12**, as observed by ^{1}H-NMR (H–C(6) disappeared and H–C(5) became an olefinic proton). On warming, compound **12** seemed to undergo a *retro-Diels-Alder* fragmentation (*cf.* [42]) with formation of acetaldehyde, a reaction which was not further studied.

Belleau and *Au-Young* had followed a similar reaction scheme starting from methyl sorbate in the racemic series with *N*-benzoyl compounds [25]. Surprisingly, the (*N*-unprotected) dihydroxy ester isolated after epoxide opening was claimed to be **10c**. We repeated the opening of the *N*-benzoyl-epoxy ester according to the conditions described in [25] and obtained the *N*-deprotected dihydroxy ester **9c** which, on treatment with $ClCO_2Bn$/$NaHCO_3$, gave dihydroxy ester **9b**, identical to the compound obtained from **8b** (see above). Therefore, the linear amino acid which *Belleau* and *Au-Young* finally obtained must also belong to the gluconic and not to the gulonic series.

δ-Lactams. – The isolated chiral dihydroxy esters **6a,b**, **7**, **9a,b**, and **10a** were stable but base-sensitive compounds which underwent readily a base-catalyzed rearrangement to pyrrolidine compounds [43]. Their hydrogenolysis in neutral medium, *i.e.*, in MeOH over Pd/C, cleaved both the *N*-carbamate group and the N–O bond, and the ensuing linear amino ester cyclized at once and in good yield (*ca.* 80%) to give the 5-amino-5-deoxy-δ-lactams in the D-ribonic (**13a**), 6-deoxy-D-allonic (**13b**), L-arabinonic (**14**), D-xylonic (**15a**), 6-deoxy-D-gluconic (**15b**), and L-lyxonic series (**16**), respectively (*Scheme 3*). For completion of the reaction, it was best to add the catalyst twice [23]. Physical data of the known δ-lactams were in good agreement with literature data for D-ribonolactam **13a** [26–28], D-xylonolactam **15a** [27][29], or with those of the D-enantiomer for L-arabinonolactam **14** [27] and L-lyxonolactam **16** [27].

Scheme 3



Structure Determinations. – The absolute configuration of the primary adducts **4a,b** as established above agreed well with that of the final known δ-lactams which showed data consistent with literature.

The regiospecificity of the hetero-*Diels-Alder* addition was assumed to be the same as for other sorbic-acid derivatives as determined by *Kresze et al.* [24][33] or by us [22][23][34], *i.e.*, the O-atom of the nitroso compound is bound to the α-position of the carboxylic group. Direct determination was possible by $^1H,^{13}C$-NMR correlation.

For adducts **4a** and **5a**, the CH_2 signal appears at *ca.* 45 ppm in ^{13}C-NMR; for **4b** and **5b** the CH signal bearing the Me group appears at *ca.* 51 ppm; both CH_2 and CH moieties are also bound to the N(2) atom. In all cases, the C-atom in α-position to the carboxylic group appears at *ca.* 76 ppm and is also bound to the O(1) atom.

Table 1. *^1H-NMR Data* ($CDCl_3$) *of* 2H-*Oxazines* **5a,b**, **6a,b**, **7**, **8a,b**, **9a,b** *and* **10a**. At 250 MHz and 300 K; δ in ppm, *J* in Hz.

	H_a–C(3)	H_b–C(3)[a]	H–C(4)	H–C(5)	H–C(6)	CH_2[b]	CO_2Me
5a	4.15	4.15	6.01	6.01	5.06	5.23 5.26	3.74
5b	4.53	1.38	5.97	5.91	5.17	5.18 5.25	3.81
6a[c])	4.30	3.54	4.06	4.01	4.66	5.20 5.25	3.85
6b[d])	4.52	1.33	3.90	4.13	4.60	5.19 5.23	3.84
7[e])	4.07	3.45	3.81	4.23	4.48	5.21	3.81
8a[f])	4.00	3.97	3.55	3.65	4.83	5.21 5.22	3.80
8a[g])	4.20	3.90	3.39	3.66	4.93	5.21	3.81
8b (maj.)	4.59	1.45	3.15	3.62	4.97	5.18 5.23	3.85
8b (min.)	4.47	1.39	3.54	3.60	4.76	5.16 5.23	3.81
9a[d])[h])		3.88–4.00			4.86	5.21	3.78
9b	4.29	1.49	3.88	4.07	4.86	5.22 5.24	3.84
10a[d])[i])	4.29	3.23	3.70	3.82	4.16	5.20 5.23	3.82

	^2J(3a,3b)[j])	^3J(3a,4)	^3J(3b,4)	^3J(4,5)	^3J(5,6)	Others *J*
5a[k])	[l])	3.1		10.2	3.0	$^4J(3,5) = 2.1$, $^5J(3,6) = 3.0$, $^4J(4,6) = 2.2$
5b	6.7	4.2		10.3	1.4	$^4J(3,5) = 1.2$, $^5J(3,6) = 2.9$, $^4J(4,6) = 2.3$
6a[c])	14.5	3.2	1.8	3.1	9.4	
6b[d])	7.1	2.3		3.2	10.1	
7	13.0	5.2	10.2	3.2	1.8	
8a[f])	14.5	1.4	3.0	4.1	2.7	
8a[g])	14.7	1.1	2.2	4.1	1.0	$^4J(3,5) = 0.6$
8b (maj.)	7.0	1.3		4.1	0	$^4J(4,6) = 0.8$
8b (min.)	6.7	5.2		4.1	1.0	
9a[d])	[l])	[l])	[l])	[l])	1.8	
9b	7.3	1.9		3.3	2.0	$^4J(3,5) = 1.1$
10a[d])[i])	13.4	5.2	10.0	8.1	9.1	

[a]) Me–C(3) for **5b**, **6b**, **8b**, and **9b**. [b]) PhCH_2, $J = 12.3$; arom. H: 7.33–7.36. [c]) 2.59 (*t*, OH–C(4)), 3.44 (*d*, OH–C(5)), *J* (3b, OH–C(4)) = 1.8, *J* (4, OH–C(4)) = 1.8, *J* (5, OH–C(5)) = 3.4. [d]) 330 K. e) 3.14 (*d*, OH–C(4)), 3.25 (*d*, OH–C(5)), *J* (4, OH–C(4)) = 8.0, *J* (5, OH–C(5)) = 5.5. [f]) Isomer with R_f 0.21. [g]) Isomer with R_f 0.32. [h]) 2 OH: 1.92 (*d*, $J = 2.8$), 2.62 (*d*, $J = 6.6$). [i]) 2.46 (*d*, OH–C(4)), 3.00 (*d*, OH–C(5)), *J* (4, OH–C(4)) = 3.2, *J* (5, OH–C(5)) = 2.8. [j]) ^3J(3, Me) for **5b**, **6b**, **8b**, and **9b**. [k]) Measured in C_6D_6. [l]) Not determined.

Configuration and *conformation* of the adducts and dihydroxy esters were determined from the ^1H-NMR data (*Table 1*) and shown in the *Figure*. *N*-Disubstituted carbamates RR'N–CO_2R are known to present a hindered rotation around the N–CO bond whose energy barrier is lower than the one of the corresponding amides (*ca.* 2–3 kcal) [44]; thus the coalescence temperatures of the signals of the groups near the carbamate moiety is

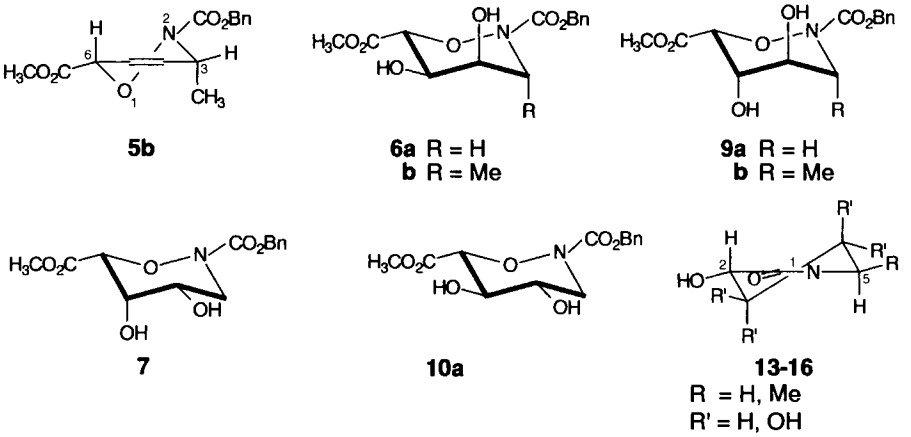


Figure. *Configuration and conformation of* **5a,b**, **6a,b**, **7**, **9a,b**, **10a**, *and* **13–16**

close to 300 K [45]. The NMR spectra of the studied adducts and dihydroxy esters show effectively at this temperature either one species or only a broadening of some signals which disappears at *ca.* 330 K to give well-resolved spectra. As previously discussed with similar adducts or dihydroxy compounds [22][23][34], the conformation of the 3,6-disubstituted *N*-acyl compounds is fixed by the steric interaction of the vicinal acyl–N(2) and Me–C(3) groups [46], this latter one being pseudo-axial in adduct **4b** and **5b** or axial in dihydroxy ester **6b** and **9b**.

The 3,6-*cis* configuration of the disubstituted **4b** and **5b** results directly from the coupling values of the protected compound **5b**. The small values of $^3J(5,6)$ and $^4J(3,5)$ and the larger values of $^3J(3,4)$ and $^4J(4,6)$ correspond to a pseudo-equatorial H–C(3) and a pseudo-axial H–C(6) in the half-chair conformation [34].

Both major *cis*-dihydroxy esters **6a,b** are characterized by large values of $^3J(5,6)$ and small values of $^3J(4,5)$ which correspond to *trans*-diaxial H–C(5) and H–C(6) and equatorial H–C(4) in a chair conformation as shown in the *Figure*; the diol moicty is *anti* to the Me and COOMe groups. For the minor all-*cis*-dihydroxy ester **7**, the large $^3J(3\,b,4)$ and small $^3J(4,5)$ values correspond to axial H–C(4) and equatorial H–C(5).

As to the major *trans*-dihydroxy esters **9a,b**, the ^{1}H-NMR spectrum of **9b** is the only one which could be analysed: all coupling constants are small, and a long-range W-coupling $^4J(3,5)$ indicates the equatorial position of H–C(3) and H–C(5). Structure and conformation for this latter diol could be deduced from these NMR data; however, the structures of **9a,b** result simply from the ones of the corresponding δ-lactams **15a,b**. Coupling constants $^3J(4,5)$ and $^4J(5,6)$ in the minor *trans*-dihydroxy ester **10a** are large and correspond to axial H–C(4), H–C(5), and H–C(6), all substituents being in equatorial position. The spectra of dihydroxy ester **9c** [25] (see *Exper. Part*) is close to the one of **9b**.

In all dihydroxy esters, the equatorial COOMe and (in **6b** and **9b**) the axial Me groups control the conformations.

The ^{1}H-NMR data of the δ-lactams are presented in *Table 2*. The data of **13a** and **15a** are in good agreement with the published data [28][29]. The structure of the lactams **13a,b**, **14**, and **16** results from the ones of the dihydroxy esters **6a,b**, **7**, **10a**, respectively.

The conformation of **13a,b** was deduced from a large coupling constant $^3J(4,5a)$ between axial H–C(4) and H_a–C(5), the Me group in allonolactam **13b** being then equatorial, and from a long-range W-coupling between equatorial H–C(3) and H_b–C(5) in **13a**. Large $^3J(2,3)$ and small $^3J(3,4)$ coupling constants in the arabinonolactam **14** determine structure and conformation with axial H–C(2) and H–C(3) and equatorial H–C(4). Likewise, the xylono- and gluconolactams **15a,b** show large $^3J(2,3)$, $^3J(3,4)$, and $^3J(4,5a)$, and therefore, all substituents are equatorial. The lyxonolactam **16** presents only small couplings, therefore, H–C(4) is equatorial.

Table 2. *^{1}H-NMR Data* (D_2O) *of the δ-Lactams* **13a,b**, **14**, **15a,b** *and* **16**. At 250 MHz and 300 K; δ in ppm, *J* in Hz.

	H–C(2)	H–C(3)	H–C(4)	H_a–C(5)	H_b–C(5)[a])	*J*(2,3)	*J*(3,4)	*J*(4,5a)	*J*(4,5b)	*J*(5a,5b)[b])	*J*(2,5a)
13a	4.24	4.24	4.22	3.33	3.43	[c])	2.1	9.5	6.4	11.8	
13a[d])	3.81	3.88	3.85	3.10	3.01	2.8	1.8	10.0	6.4	10.8	0.7
13b	4.27	4.21	3.72	3.56	1.28	3.1	2.0	9.1		6.3	0.8
14	4.22	3.95	4.26	3.53	3.33	9.5	2.5	3.0	2.8	13.8	0.7
15a	4.02	3.70	3.96	3.13	3.51	9.2	9.0	8.9	5.7	12.4	0.8
15b	4.02	3.71	3.46	3.36	1.28	9.6	9.4	9.0		6.2	0.8
16	4.41	4.17	4.19	3.69	3.24	2.9	4.8	3.6	3.7	13.9	[c])

[a]) Me(6) in **13b** and **15b**. [b]) ^3J(5,Me) in **13b**, and **15b**. [c]) Not determined. [d]) In (D_6)DMSO at 400 MHz: *J*(3,5b) = 0.8, 7.28 (*s*, NH), 4.95 (*d*, *J* = 3.4, OH), 4.92 (*d*, *J* = 6.2, OH), 4.59 (*d*, *J* = 4.4, OH).

Most of the lactams present a weak homoallylic ^5J(2,5a) coupling constant between axial H–C(2) and H_a–C(5) protons.

The ^{1}H-NMR data are in agreement with a half-chair conformation for all lactams **13**–**16** (see *Fig.*), OH–C(2) and (for **13b** and **15b**) Me–C(5) being equatorial. The conformation of the lactams seems also to be determined by the H-bond between OH–C(2) and the C(1)-carbonyl group which fixes this OH group in its equatorial position, as also (for **13b** and **15b**) by the equatorial C(5) substituent. Both these effects determine also the same half-chair conformation of δ-lactams in the D-gluconic [6][47] and D-galactonic [48] series, and can explain the unexpected twist-boat conformation which was observed for the D-mannono-δ-lactam [3].

Conclusion. – An easy and straightforward synthesis of some δ-lactams is described starting by an asymmetric hetero-*Diels-Alder* addition of dienoic acids to give, on the major reaction pathways, D-ribono-δ-lactam **13a** in 35% and D-xylono-δ-lactam **15a** in 25% yield from pentadienoic acid **2a**, and 6-deoxy-D-allono-δ-lactam **13b** in 45% and 6-deoxy-D-glucono-δ-lactam **15b** in 25% yield from sorbic acid (**2b**).

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Experimental Part

1. General. Benzyl chloroformate, 5% Pd/C catalyst, 5.1M aq. 4-methylmorpholine 4-oxide (NMO), OsO_4, *tert*-butyl hydroperoxide, *m*-chloro-perbenzoic acid and tetrapropylammonium periodate were purchased from *Fluka*, $RuCl_3 \cdot n\,H_2O$ from *Aldrich*, formic acid from *Prolabo*, and sorbic acid (**2b**) from *EGA-Chemie*; thionyl chlorid was distilled. Usual solvents were freshly distilled, dry EtOH and MeOH distilled over Mg/MgI_2; CH_2Cl_2 was kept over Na_2CO_3. (*E*)-Penta-2,4-dienoic acid (**2a**) was prepared according to [21]. Standard OsO_4 soln. was prepared according to [34][49] (OsO_4 (1 g) and 70% *t*-BuOOH (1 ml) in *t*-BuOH (200 ml)). Flash chromatography (FC): silica gel (*Merck 60*, 230–400 mesh). TLC: Al-roll silica gel (*Merck 60*, F_{254}). M.p.: *Kofler* hot bench or *Büchi-SMP20* apparatus; corrected. $[\alpha]_D$: *Schmidt-Haensch-Polartronic-Universal* polarimeter. HPLC: liquid chromatograph *Hewlett-Packard 190*. IR Spectra (ν in cm^{-1}): *Perkin-Elmer 157G*. ^{1}H- and ^{13}C-NMR (62.9 MHz) Spectra: *Bruker AC-F250* for most spectra or *Bruker DSX 400*; $SiMe_4$ or sodium 3-(trimethylsilyl) (D_4)propanoate ((D_4)TSP) in D_2O (^{1}H-NMR), and $CDCl_3$ or CD_3OD, or (in D_2O) MeOH, or dioxane (δ($CDCl_3$) = 77.0,

$\delta(CD_3OD)$ = 49.0, in D_2O $\delta(Me_3OH)$ = 50.0, δ(dioxane) = 67.4 with respect to $SiMe_4$ (^{13}C-NMR)) as internal references; δ in ppm and J in Hz; ^{13}C attributions ascertained by ^{1}H,^{13}C correlation. High resolution (HR)-MS: *MAT-311* spectrometer; *m/z* (rel.%); measured at the University of Rennes. Microanalyses were carried out by the 'Service Central de Microanalyses' of the CNRS, F-69390 Vernaison, or by the 'Service de microanalyse de l'ICSN-CNRS', F-91198 Gif s/Yvette.

2. Diels-Alder *Adducts. (6R)-3,6-Dihydro-2*H*-1,2-oxazine-6-carboxylic Acid Hydrochloride* (**4a**). To a stirred soln. of **3** [24] (10 g, 32.5 mmol) in CH_2Cl_2 (74 ml) under Ar at $-10°$, **2a** (3.5 g, 35.7 mmol, 1.1 equiv.) in dry EtOH (19 ml) was added. After 16 h at $-10°$, the soln. was stirred at 0° for 3 h, diluted with dry Et_2O (130 ml) to precipitate **4a** as fine crystals, and stirred for further 2 h at 0°. Adduct **4a** (3.86 g, 72%) was isolated by filtration and washed with dry Et_2O.

4a: Colourless crystals. M.p. 157–158° (dec.; MeOH/Et_2O). $[\alpha]_D^{22} = +128$ (c = 1.0, H_2O). IR (KBr): 3000–2870, 2740, 2690, 2610, 1750, 1575, 1420, 1390, 1375, 1355, 1220, 1195, 1165, 1070, 1030, 930, 805, 745, 660. ^{1}H-NMR (D_2O, 300 K): 4.04 (*dq*, H_a–C(3)); 3.89 (*ddt*, H_b–C(3)); 6.12 (*ddt*, H–C(4)); 6.26 (*dddd*, H–C(5)); 5.24 (*m*, H–C(6)); J(3a,3b) = 17.2, J(3a,4) = 2.4, J(3a,5) = 2.2, J(3a,6) = 2.5, J(3b,4) = 4.1, J(3b,5) = 1.4, J(3b,6) = 1.6, J(4,5) = 10.8, J(4,6) = 2.4, J(5,6) = 3.5. ^{13}C-NMR (D_2O, 300 K): 172.0 (CO_2H); 122.6, 120.6 (C(4), C(5)); 76.1(C(6)); 43.7(C(3)). Anal. calc. for $C_5H_8ClNO_3$ (165.58): C 36.27, H 4.87, Cl 21.41, N 8.46, found: C 36.2, H 4.9, Cl 21.0, N 8.2.

*(3R,6R)-3,6-Dihydro-3-methyl-2*H*-1,2-oxazine-6-carboxylic Acid Hydrochloride* (**4b**). As described for **4a** with **3** (2.5 g, 8.12 mmol), **2b** (1 g, 8.92 mmol, 1.1 equiv.) in CH_2Cl_2 (18 ml), and EtOH (4.5 ml): **4b** (0.97 g, 67%). The mother liquors were left to stand for 2.5 days at 0° to give a second crop (0.17 g, 11%). Colourless crystals. M.p. = 170–172° (dec.; MeOH/Et_2O). $[\alpha]_D^{20} = +125$ (c = 1.0, H_2O). IR (KBr): 2900–2650, 2520, 2370, 1750, 1560, 1440, 1407, 1230, 1100, 1065, 1045, 1002, 902, 867, 822, 780, 742, 710. ^{1}H-NMR (D_2O, 300 K): 4.24 (*m*, H–C(3)); 6.22 (*m*, H–C(4)); 6.05 (*m*, H–C(5)); 5.19 (*m*, H–C(6)); 1.42 (*d*, Me–C(3)); J(3,4) = 2.1; J(3,5) = 2.5; J(3,6) = 2.5; J(3,Me) = 7.0; J(4,5) = 10.7; J(4,6) = 3.1; J(5,6) = 2.7. ^{13}C-NMR (D_2O, 300 K): 171.7 (CO_2H); 126.5, 122.2 (C(4), C(5)); 76.3 (C(6)); 51.3 (C(3)); 15.2 (*Me*–C(3)). Anal. calc. for $C_6H_{10}ClNO_3$ (179.64): C 40.11, H 5.61, Cl 19.74, N 7.80; found: C 40.1, H 5.7, Cl 19.8, N 7.8.

*2-Benzyl 6-Methyl (6R)-3,6-Dihydro-2*H*-1,2-oxazine-2,6-dicarboxylate* (**5a**). To a stirred soln. of **4a** (3.17 g, 19.1 mmol) in MeOH (36 ml) under Ar, $NaHCO_3$ (6.42 g, 76.5 mmol, 4 equiv.) and slowly $ClCO_2Bn$ (3.25 ml, 22.9 mmol, 1.2 equiv.) were added. After 5 h at r.t., the solids were removed by centrifugation, 10% HCl in MeOH (36 ml) was added to the soln. and the soln. stirred for 0.5 h. Insoluble material was centrifuged off and washed with MeOH. The solvents were evaporated to give crude **5a** (7.3 g) which was used for the next reactions. Purification for analysis by FC (CH_2Cl_2/Et_2O 9:1) gave **5a** (5.3 g, quant). Yellowish oil. $[\alpha]_D^{17} = +115$ (c = 1.0, $CHCl_3$). R_f 0.58 (CH_2Cl_2/Et_2O 6:4). ^{1}H-NMR: *Table 1*. ^{1}H-NMR (C_6D_6, 300 K): 3.80 (*ddd*, 2 H–C(3)); 5.25 (*ddt*, H–C(4)); 5.63 (*ddt*, H–C(5)); 4.80 (quint., H–C(6)); 5.07, 5.13 (*2d*, J = 12.4, PhCH_2); 7.14 (*m*, 5 arom. H); 3.18 (*s*, OMe); J(3,4) = 3.1, J(3,5) = 2.1, J(3,6) = 3.0, J(4,5) = 10.2, J(4,6) = 2.2, J(5,6) = 3.0. ^{13}C-NMR ($CDCl_3$, 300 K): 168.3 (CO_2Me); 155.6 (CO_2Bn); 135.8, 128.5, 128.3, 128.2, (Ph); 124.6, 122.6 (C(4), C(5)); 76.3 (C(6)); 67.9 (PhCH_2); 52.5 (MeO); 45.1 (C(3)). The product was too unstable for elemental analysis.

*2-Benzyl 6-Methyl (3R,6R)-3,6-Dihydro-3-methyl-2*H*-1,2-oxazine-2,6-dicarboxylate* (**5b**). As described for **5a** with **4b** (1.93 g, 10.7 mmol), MeOH (20 ml), $NaHCO_3$ (3.61 g, 43.0 mmol, 4 equiv.), and $ClCO_2Bn$ (1.82 ml, 12.9 mmol, 1.2 equiv.). Purification by FC (CH_2Cl_2) gave **5b** (3.12 g, 99%). Yellowish oil. $[\alpha]_D^{17} = -55$ (c = 1.0, $CHCl_3$). R_f 0.24 (CH_2Cl_2). IR ($CHCl_3$): 3020, 2955, 1740, 1700, 1437, 1405, 1315, 1275, 1115, 1070, 1025, 695. ^{1}H-NMR: *Table 1*. ^{13}C-NMR ($CDCl_3$, 300 K): 167.7 (CO_2Me); 154.7 (CO_2Bn); 130.6 (C(4)); 135.9, 128.5, 128.3, 128.1 (Ph); 121.9 (C(5)); 76.1 (C(6)); 67.7 (CH_2Ph); 52.6 (OMe); 50.5 (C(3)); 17.9 (Me–C(3)). The product was too unstable for elemental analysis.

rac-*2-Benzyl 6-Methyl 3,6-Dihydro-2*H*-1,2-oxazine-2,6-dicarboxylate* ((±)-**5a**). According to [23][37]: To a stirred soln. of **2a** (0.663 g, 6.76 mmol) at 0° in CH_2Cl_2 (10 ml) containing 4 Å molecular sieves (*ca.* 30 beads), $(Pr_4N)IO_4$ (1.69 g, 4.48 mmol, 0.66 equiv.) was added, followed portionwise by benzyl *N*-hydroxycarbamate [37] (2.248 g, 13.4 mmol, 2 equiv.). After 1 h at r.t., some $NaHSO_3$ was added to remove the brown colour. The soln. was diluted with AcOEt (50 ml) and washed twice with 0.5N aq. HCl and H_2O, dried ($MgSO_4$), and evaporated. The resulting oil was stirred in MeOH (5 ml) and 10% HCl in MeOH (5 ml) at r.t. for 1 h. Evaporation and FC (CH_2Cl_2/Et_2O 9:1, 60 g of silica gel) gave (±)-**5a** (0.92 g, 49%).

rac-*2-Benzyl 6-Methyl 3,6-Dihydro-*r*-3-methyl-2*H*-1,2-oxazine-2,*c*-6-dicarboxylate* ((±)-**5b**). As described for **5a**, with **2b** (0.5 g, 4.46 mmol), CH_2Cl_2 (15 ml), $(Pr_4N)IO_4$ (1.12 g, 2.97 mmol, 0.66 equiv.), and benzyl *N*-hydroxycarbamate (1.49 g, 8.92 mmol, 2 equiv.). Purification by FC (CH_2Cl_2) gave (±)-**5b** (0.8 g, 60%).

HPLC Determination of Enantiomeric Excess (ee). For **5a**: *Chiralpak AD Daicel* column, i-PrOH/heptane 5:95 (k'_1 = 5.43, k'_2 = 5.97, k'_2/k'_1 = 1.10, resolution 1.36, flow rate 0.8 ml/min; det. at λ = 254 nm, temp. 26.9°);

retention time (intensity) for (±)-**5a**: (+)-**5a** at $t_R(1)$ 19.9 min (230), (−)-**5a** at $t_R(2)$ 21.5 min (228); for the chiral **5a**: $t_R(1)$ 19.8 min (295), $t_R(2)$ 21.6 min (22); ee 86%. After recrystallization of **1a** from MeOH/Et_2O: ee 95.5.

For **5b**: *Chiralcel OD Daicel* column, i-PrOH/heptane 30:70 ($k'_1 = 1.53$, $k'_2 = 2.14$, $k'_2/k'_1 = 1.4$, resolution 1.59, flow rate 0.8 ml/min; det. at $\lambda = 260$ nm, temp. 26°); retention time (intensity) for (±)-**5b**: (+)-**5b** at $t_R(1)$ 8.2 min (148), (−)-**5b**, $t_R(2)$ 10.2 min (163); for the chiral **5b**: $t_R(1)$ 8.0 min (3.3), $t_R(2)$ 10.3 min (407), > 98%.

3. *Tetrahydro-dihydroxy-2*H*-oxazine Derivatives. 2-Benzyl 6-Methyl (4*R*,5*R*,6*R*)-Tetrahydro-4,5-dihydroxy-2*H*-1,2-oxazine-2,6-dicarboxylate* (**6a**) *and 2-Benzyl 6-Methyl (4*S*,5*S*,6*R*)-Tetrahydro-4,5-dihydroxy-2*H*-1,2-oxazine-2,6-dicarboxylate* (**7**). To a stirred soln. of **5a** (2.42 g, 8.75 mmol) in acetone (22 ml) and H_2O (9 ml), 5.1M aq. NMO (3.5 ml, 17.8 mmol, 2 equiv.) and the OsO_4 soln. (8.75 ml, 0.17 mmol) were added. After 5 h at 40°, some $Na_2S_2O_7$ was added, the acetone evaporated, H_2O (40 ml) added, and the soln. extracted with CH_2Cl_2 (5 × 20 ml). The combined org. phase was dried ($MgSO_4$) and evaporated and the crude product (4.0 g) separated by FC (CH_2Cl_2/Et_2O 6:4, 100 g of silica gel): **6a** (1.50 g, 55%) and **7** (0.375 g, 14%), ratio 4:1.

Data of **6a**: Colourless crystals. M.p. 84–87° (i-Pr_2O). $[\alpha]_D^{24} = -40$ ($c = 1.0$, $CHCl_3$). R_f 0.15 (CH_2Cl_2/Et_2O, 9:1). IR ($CHCl_3$): 3560, 1720, 1440, 1400, 1330, 1230, 1135, 1090. ^{1}H-NMR: *Table 1*. ^{13}C-NMR ($CDCl_3$, 300 K): 169.4 (*C*O_2Me); 156.5 (*C*O_2Bn); 135.6, 128.5, 128.3, 128.0 (Ph); 76.0 (C(6)); 68.1 (Ph*C*H_2); 68.0 (C(4)); 64.9 (C(5)); 53.0 (MeO); 50.4 (C(3)). Anal. calc. for $C_{14}H_{17}NO_7$ (311.29): C 54.02, H 5.51, N 4.50; found: C 53.8, H 5.3, N 4.4.

Data of **7**: Colourless crystals. M.p. 132–134° (i-PrOH). $[\alpha]_D^{23} = -21$ ($c = 1.0$, $CHCl_3$). R_f 0.15 (CH_2Cl_2/Et_2O, 9:1). IR (KBr): 3460, 2960, 1710, 1700, 1440, 1410, 1365, 1340, 1300, 1262, 1220, 1085, 1070, 1010. ^{1}H-NMR: *Table 1*. ^{13}C-NMR ($CDCl_3$, 300 K): 167.5 (*C*O_2Me); 155.2 (*C*O_2Bn); 135.5, 128.6, 128.5, 128.2 (Ph); 80.0 (C(6)); 68.3 (Ph*C*H_2); 67.6 (C(5)); 65.4 (C(4)); 52.8 (MeO); 47.0 (C(3)). Anal. calc. for $C_{14}H_{17}NO_7$ (311.29): C 54.02, H 5.51, N 4.50; found: C 53.7, H 5.5, N 4.4.

*2-Benzyl 6-Methyl (3*R*,4*R*,5*R*,6*R*)-Tetrahydro-4,5-dihydroxy-3-methyl-2*H*-1,2-oxazine-2,6-dicarboxylate* (**6b**). As described for **6a**/**7**, with **5b** (3.02 g, 10.4 mmol), aq. NMO soln. (4.1 ml, 20.7 mmol, 2 equiv.), OsO_4 soln. (10 ml), acetone (26 ml), and H_2O (10 ml); for 6.5 h at 40°: **6b** (2.19 g, 65%). Yellowish oil. $[\alpha]_D^{17} = -38$ ($c = 1.0$, $CHCl_3$). R_f 0.20 (CH_2Cl_2/Et_2O 6:4). IR ($CHCl_3$): 3570, 3045, 2970, 1735, 1452, 1415, 1310, 1145, 1098, 1050, 1032, 705. ^{1}H-NMR: *Table 1*. ^{13}C-NMR ($CDCl_3$, 333 K): 169.4 (*C*O_2Me); 156.2 (*C*O_2Bn); 136.1, 128.5, 128.2, 127.9 (Ph); 76.5 (C(6)); 69.3 (C(4)); 68.0 (Ph*C*H_2); 65.7 (C(5)); 56.4 (MeO); 52.7 (C(3)); 14.2 (Me – C(6)). Anal. calc. for $C_{15}H_{19}NO_7$ (325.32): C 55.38, H 5.89, N 4.31; found: C 55.5, H 6.1, N 4.5.

*2-Benzyl 6-Methyl (6*R*)-4ξ,5ξ-Epoxytetrahydro-2*H*-1,2-oxazine-2,6-dicarboxylate* (= *4-Benzyl 2-Methyl (1aξ,2*R*,5aξ)-Tetrahydro-2*H*-oxireno[2,3-*d*][1,2]oxazine-2,4-dicarboxylate*; **8a**). To a stirred soln. of crude **5a** (from **4a** (1.95 g, 11.7 mmol)) in CH_2Cl_2 (15 ml) under Ar, 70% *m*-CPBA (4.06 g, 17.0 mmol of pure peracide, 1.4 equiv.) was added and the same quantity after 2 days at r.t. After 5 days at r.t., sodium metabisulfite (4.48 g, 23.5 mmol, 2 equiv.) was added, the solids were removed by centrifugation, and the soln. was washed with 1M aq. Na_2CO_3 (2 × 15 ml) and H_2O (2 × 15 ml). The aq. phases were extracted with CH_2Cl_2 (10 ml) and the org. phases dried ($MgSO_4$) and evaporated: crude **8a** (3.43 g, quant.) as a 1:1 mixture of two isomeric epoxides which were unstable on chromatography and not further purified. Yellowish oil, R_f 0.21 and 0.32 (AcOEt/cyclohexane 1:1). ^{1}H-NMR: *Table 1*.

*2-Benzyl 6-Methyl (3*R*,6*R*)-4ξ,5ξ-Epoxytetrahydro-3-methyl-2*H*-1,2-oxazine-2,6-dicarboxylate* (= *4-Benzyl 2-Methyl (1aξ,2*R*,5*R*,5aξ)-Tetrahydo-5-methyl-2H-oxireno[2,3-*d*][1,2]oxazine-2,4-dicarboxylate*; **8b**). As described for **8a** with **5b** (2.2 g, 7.57 mmol), 70% *m*-CPBA (4.35 g, 18 mmol pure peracide, 2.4 equiv.), and CH_2Cl_2 (10 ml; for 5.5 days): **8b** (2.0 g, 86%) as a 3:2 isomer mixture which was not further purified. Yellow oil. R_f 0.31 and 0.40 (AcOEt/cyclohexane 1:1). IR ($CHCl_3$): 1730, 1700, 1575, 1440, 1410, 1290, 1260, 1125, 1075. ^{1}H-NMR: *Table 1*.

*2-Benzyl 6-Methyl (4*R*,5*S*,6*R*)-Tetrahydro-4,5-dihydroxy-2*H*-1,2-oxazine-2,6-dicarboxylate* (**9a**) *and 2-Benzyl 6-Methyl (4*S*,5*R*,6*R*)-Tetrahydro-4,5-dihydroxy-2*H*-1,2-oxazine-2,6-dicarboxylate* (**10a**). A soln. of crude **8a** (3.43 g, from **4a**, (1.95 g, 11.7 mmol)) in formic acid (35 ml) and H_2O (3.5 ml) was heated at 90° for 1 h and then evaporated. The residue was dissolved in dry MeOH (15 ml) and 11.5% HCl in MeOH (7.5 ml, 23.4 mmol, 2 equiv.), and the soln. stirred at 0° for 0.5 h and at r.t. for another 0.5 h, and then evaporated. The residue was stirred in MeOH (15 ml) at r.t. and treated with $ClCO_2Bn$ (0.55 ml, 3.90 mmol, 0.33 equiv.) and $NaHCO_3$ (4.42 g, 52.6 mmol, 4.5 equiv.) for 0.5 h. The solids were removed by centrifugation. The soln. was evaporated and the oil (4.19 g) separated by FC (AcOEt, 110 g of silica gel): **9a** (1.02 g), **10a** (0.65 g), and mixed fractions (total 2.53 g, 69% yield from **4a**; **9a**/**10a** 65:35).

Data of **9a**: Beige crystals. M.p. 151–153° (i-PrOH). $[\alpha]_D^{25} = -28$ ($c = 1.0$, MeOH). R_f 0.13 (AcOEt/cyclohexane 7:3). IR (KBr): 3520, 3380, 2930, 1755, 1695, 1420, 1360, 1340, 1210, 1115, 1095, 1080, 1050, 745, 695. ^{1}H-NMR: *Table 1*. ^{13}C-NMR ($CDCl_3$, 330 K): 168.5 (*C*O_2Me); 156.5 (*C*O_2Bn); 136.1, 128.6, 128.4, 128.1 (Ph);

76.5 (C(6)); 68.8, 68.2, 66.6 (C(4), C(5), PhCH$_2$); 52.5 (MeO); 48.4 (C(3)). Anal. calc. for $C_{14}H_{17}NO_7$ (311.29): C 54.02, H 5.51, N 4.50; found: C 53.8, H 5.5, N 4.5.

Data of **10a**: Colourless crystals. M.p. 88–91° (i-Pr$_2$O). R_f 0.17 (AcOEt/cyclohexane 7:3). IR ($CHCl_3$): 3440, 3000, 2940, 2920, 1720, 1440, 1400, 1340, 1225, 1185, 1080, 695. ^{1}H-NMR: *Table 1*. ^{13}C-NMR ($CDCl_3$, 330 K): 168.4 (*C*O$_2$Me); 155.1 (*C*O$_2$Bn); 135.5, 128.6, 128.5, 128.2 (Ph); 80.0 C(6); 72.5, 69.0 (C(4), C(5)); 68.4 (PhCH$_2$); 53.1 (MeO); 49.8 (C(3)). Anal. calc. for $C_{14}H_{17}NO_7$ (311.29): C 54.02, H 5.51, N 4.50; found: C 53.8, H 5.4, N 4.8.

*2-Benzyl 6-Methyl (3*R*,4*R*,5*S*,6*R*)-Tetrahydro-4,5-dihydroxy-3-methyl-2*H*-1,2-oxazine-2,6-dicarboxylate* (**9b**). As described for **9a**/**10a**, with crude **8b** (2.0 g, 6.51 mmol), 90% formic acid (22 ml; 1.25 h at 90°), dry MeOH (10 ml), 11.5% HCl/MeOH (4.1 ml), $NaHCO_3$ (2.54 g, 30.3 mmol, 4 equiv.), and $ClCO_2Bn$ (0.27 ml, 1.89 mmol, 0.25 equiv.). FC (AcOEt, 100 g of silica gel): by-product (*ca.* 0.2 g, *ca.* 10%) and **9b** (1.30 g, 53%).

Data of **9b**: Colourless crystals. M.p. (dec.) 124–128°. $[\alpha]_D^{20} = -5.5$ ($c = 1.0$, $CHCl_3$). R_f 0.15 (AcOEt/cyclohexane 7:3). IR (KBr): 3520, 2950, 2900, 1740, 1725, 1455, 1390, 1350, 1297, 1250, 1225, 1135, 1115, 1060, 1045, 760, 735, 698. ^{1}H-NMR: *Table 1*. Anal. calc. for $C_{15}H_{19}NO_7$ (325.31): C 55.38, H 5.89, N 4.31; found: C 55.3, H 5.7, N 4.0.

Data of By-product R_f 0.5. ^{1}H-NMR ($CDCl_3$, 300 K): similar to that of **9b**; it was not further studied; 7.34 (*m*, 5 arom. H); 5.19, 5.23 (2*d*, $J = 12$, PhC*H*$_2$); 5.07 (*d*, H–C(6)); 4.31 (*tq*, H–C(3)); 4.24 (*dt*, H–C(5)); 4.06 (br. *s*, H–C(4)); 3.83 (*s*, MeO); 2.83 (*s*, OH–C(4)); 1.55 (*d*, Me–C(3)); J(3,4) = 1.6, J(3,5) = 1.2, J(3, Me–C(3)) = 7.4, J(4,5) = 2.7, J(5,6) = 2.3.

*Methyl Tetrahydro-*t*-4,*c*-5-dihydroxy-*r*-3-methyl-2*H*-1,2-oxazine-*c*-6-carboxylate* (**9c**). According to [25], from methyl sorbate, an oil was obtained which was essentially **9c** (*ca.* 50% yield from epoxide), only characterized by ^{1}H-NMR (CD_3OD, 300 K): 5.13 (*d*, H–C(6)); 4.05 (*m*, H–C(5)); 3.90 (*m*, H–C(4)); 3.81 (*s*, MeO); 3.52 (*ddq*, H–C(3)); 1.59 (*d*, Me–C(3)); J(3, Me) = 7.3, J(3,4) = 2.5, J(3,5) = 1.1, J(4,5) = 3.9, J(5,6) = 2.3. Acylation of **9c** by $ClCO_2Bn$/$NaHCO_3$ gave a derivative identical to **9b** by ^{1}H-NMR.

*2-Benzyl 6-Methyl (3*R*,4*R*,5*S*,6*R*)-Tetrahydro-3-methyl-4,5-(sulfonyldioxy)-2*H*-1,2-oxazine-2,6-dicarboxylate (= 6-Benzyl 4-Methyl (3a*S*,4*R*,7*R*,7a*R*)-Tetrahydro-7-methyl-4*H*-1,3,2-dioxthiolo[4,5-d][1,2]oxazine-4,6-dicarboxylate 2,2-Dioxide*; **11**). To a stirred soln. of **6b** (0.457 g, 1.40 mmol) in CH_2Cl_2 (4.5 ml) at 0°, Et_3N (0.78 ml, 5.5 mmol, 4 equiv.) was added, and then dropwise within 10 min a soln. of $SOCl_2$ (0.15 ml, 2.05 mmol, 1.5 equiv.) in CH_2Cl_2 (0.4 ml). The soln. was diluted with Et_2O (15 ml) and washed with H_2O (3 × 5 ml), dried ($MgSO_4$) and evaporated. The resulting oily cyclic sulfites (0.436 g, 85%) were dissolved in MeCN (4 ml) and H_2O (6 ml) and vigourously stirred at 0° in the presence of $RuCl_3$ (30 mg, 0.1 mmol) and $NaIO_4$ (0.523 g, 2.44 mmol, 2 equiv.). After 1.5 h, the soln. was diluted with Et_2O (15 ml) and the org. phase washed with H_2O, dried ($MgSO_4$), and evaporated: **11** (0.40 g, 73% from **6b**). Pink oil which crystallized slowly. Colourless crystals. M.p. 97–98° (EtOH). $[\alpha]_D^{20} = -55$ ($c = 1$, $CHCl_3$). R_f 0.38 (AcOEt/cyclohexane 1:1). IR (KBr): 2990, 1740, 1452, 1390, 1340, 1294, 1260, 1210, 1120, 1015, 1000, 975, 888, 838, 782, 700. ^{1}H-NMR ($CDCl_3$, 300 K): 7.36 (*s*, 5 arom. H); 5.29 (*dd*, H–C(5)); 5.27, 5.25 (2*d*, $J = 12.3$, PhC*H*$_2$); 5.00 (*dd*, H–C(4)); 4.84 (*dq*, H–C(3)); 4.82 (*d*, H–C(6)); 3.88 (*s*, MeO); 1.42 (*d*, Me–C(3)); J(3,Me) = 7.3, J(3,4) = 1.6, J(4,5) = 4.8, J(5,6) = 9.6. Anal. calc. for $C_{15}H_{17}NO_9S$ (387.36): C 46.51, H 4.42, N 3.62, S 8.28; found: C 46.8, H 4.4, N 3.7, S 8.4.

Reaction of **11** at r.t. with ammonium benzoate in DMF for 3 h, or at once in $CDCl_3$ with Et_3N, gave *2-benzyl 6-methyl (3*R*,4*S*)-3,4-Dihydro-3-methyl-4-sulfo-2*H*-1,2-oxazine-2,6-dicarboxylate* (**12**) which was characterized in soln. by ^{1}H-NMR ($CDCl_3$, 300 K): 7.29 (*m*, 5 arom. H); 6.32 (*dd*, H–C(5)), 5.17 (*s*, PhCH$_2$), 4.89 (*q*, H–C(3)); 4.69 (*dd*, H–C(4)); 3.73 (*s*, OMe); 1.14 (*d*, Me–C(3)); J(3,Me) = 7.2, J(3,4) = 1.2, J(3,5) = 1.3, J(4,5) = 5.7.

At 335 K in $CDCl_3$, **12** was transformed into another species (9.78 (*d*, $J = 2.8$, MeC*H*O); 8.65 (*d*, $J = 3.5$, 1 H); 7.36 (*m*, arom. H); 6.34 (*d*, $J = 3.5$, 1 H); 5.11 (*s*, PhC*H*$_2$); 3.86 (*s*, MeO); 2.17 (*d*, $J = 2.8$, *Me*CHO)) which was not further studied.

4. *δ-Lactams. General Procedure (GP):* A stirred soln. of tetrahydrodihydroxy-2*H*-oxazine derivative (1 mmol) in MeOH (4.5 ml) was hydrogenolysed over 5% Pd/C (20 mg and another 20 mg after 8 h) at 40° for 24 h. The catalyst was then removed by centrifugation and washed with MeOH/H_2O 1:1; the solns. were evaporated and the residues crystallized and washed in EtOH to give pure δ-lactams.

*5-Amino-5-deoxy-*D*-ribono-1,5-lactam* (= *(3*R*,4*R*,5*R*)-3,4,5-Trihydroxypiperidin-2-one*; **13a**). According to the *GP*, with **6a** (0.484 g, 1.55 mmol): **13a** (201 mg, 88%). Colourless crystals. M.p. 250–251° (dec.; EtOH). $[\alpha]_D^{23} = +33$ ($c = 0.5$, H_2O) ([26]: m.p. 240–242° (dec.), $[\alpha]_D^{23} = +33$ ($c = 0.3$, H_2O); [27]: m.p. 244–250°, $[\alpha]_D^{20} = +33.6$ ($c = 0.5$, H_2O). [28]: M.p. 219° (AcOEt), $[\alpha]_D^{20} = +29$ ($c = 2$, H_2O)). IR (KBr): 3350–3240, 2910, 1650, 1495, 1405, 1350, 1290, 1270, 1150, 1105, 1075, 1040, 775. ^{1}H-NMR: *Table 2*; data in (D_6) DMSO identical to those in [28]. ^{13}C-NMR (D_2O, 300 K): 43.2 (C(5)); 65.4(C(4)); 68.9, 71.6 (C(2), C(3)); 174.0 (C(1)).

*5-Amino-5,6-dideoxy-*D*-allono-1,5-lactam* (= *(3*R*,4*R*,5*R*,6*R*)-3,4,5-Trihydroxy-6-methylpiperidin-2-one*; **13b**). According to the *GP*, with **6b** (156 mg, 0.48 mmol): **13b** (69 mg, 90%). Colourless crystals. M.p. 222–224° (EtOH). $[\alpha]_D^{20} = +53$ ($c = 1.0$, H_2O). IR (KBr): 3280, 2900, 1653, 1610, 1460, 1380, 1322, 1297, 1270, 1155, 1060, 998, 820, 715, 635. ^{1}H-NMR: *Table 2*. ^{13}C-NMR (D_2O, 300 K): 19.2 (Me(6)); 50.8 (C(5)); 72.3 (C(4)); 72.6 (C(3)); 69.5 (C(2)); 174.3 (C(1)). Anal. calc. for $C_6H_{11}NO_4 \cdot 0.5\ H_2O$ (170.16): C 42.35, H 7.11, N 8.23; found: C 42.5, H 6.9, N 7.9.

*5-Amino-5-deoxy-*L*-arabinono-1,5-lactam* (= *(3*R*,4*S*,5*S*)-3,4,5-Trihydroxypiperidin-2-one*; **14**). According to the *GP*, with **7** (234 mg, 0.75 mmol): **14** (91 mg, 83%). Colourless crystals. M.p. 186–188° (EtOH). $[\alpha]_D^{22} = +130$ ($c = 0.5$, H_2O) ([27]: m.p. 178°, $[\alpha]_D = -172$ ($c = 1$, H_2O) for the D-enantiomer). IR (KBr): 3360–3220, 1645, 1495, 1437, 1350, 1137, 1105, 1095, 1070, 815. ^{1}H-NMR: *Table 2*. ^{1}H-NMR (CD_3OD, 300 K): 4.11 (*dt*, H–C(4)); 4.10 (*d*, H–C(2)); 3.78 (*dd*, H–C(3)); 3.37 (*dd*, H_a–C(5)); 3.26 (*dd*, H_b–C(5)); $J(2,3) = 8.4$, $J(3,4) = 2.5$, $J(4,5a) = 3.5$, $J(4,5b) = 3.9$, $J(5a,5b) = 13.1$; data identical to those in [30]. ^{13}C-NMR (D_2O, 300 K): 45.6 (C(5)); 67.6 (C(4)); 72.4 (C(3)); 70.1 (C(2)); 174.1(C(1)). Anal. calc. for $C_5H_9NO_4$ (147.13): C 40.81, H 6.17, N 9.52; found: C 40.8, H 6.3, N 9.5.

*5-Amino-5-deoxy-*D*-xylono-1,5-lactam* (= *(3*R*,4*S*,5*R*)-3,4,5-Trihydroxypiperidin-2-one*, **15a**). According to *GP*, with **9a** (488 mg, 1.57 mmol): to give **15a** (175 mg, 76%). Colourless crystals. M.p. 176–177° (EtOH). $[\alpha]_D^{20} = +7$ ($c = 0.5$, H_2O) ([29]: m.p. 172–173°, $[\alpha]_D^{20} = +7.4$ ($c = 1$, H_2O); [27]: m.p. 176–177°. $[\alpha]_D + 6$ ($c = 1$, H_2O). IR (KBr): 3430–3230, 1675, 1485, 1435, 1295, 1115, 1040, 1005, 720. ^{1}H-NMR: *Table 2*; data identical to those in [29]. ^{13}C-NMR (D_2O, 300 K): 44.6 (C(5)); 68.1 (C(4)); 75.3 (C(3); 71.9 (C(2)); 174.1 (C(1)), data identical to those in [29]. Anal. calc. for $C_5H_9NO_4$ (147.13): C 40.81, H 6.17, N 9.52; found: C 40.9, H 6.1, N 9.7.

*5-Amino-5,6-dideoxy-*D*-glucono-1,5-lactam* (= *(3*R*,4*S*,5*R*,6*R*)-3,4,5-Trihydroxy-6-methylpiperidin-2-one*; **15b**). According to *GP*, with **9b** (0.24 g): **15b** (86 mg, 71%). Colourless crystals. M.p. 227–229° (EtOH/H_2O). $[\alpha]_D^{20} = +63$ ($c = 1$, H_2O). IR (KBr): 3480–3200, 2900, 1660, 1628, 1450, 1323, 1240, 1130, 1112, 1068, 1032, 1020, 1002, 882, 720, 675. ^{1}H-NMR: *Table 2*. ^{13}C-NMR (D_2O, 300 K): 19.1 (Me(6)); 52.4 (C(5)); 74.2 (C(4)); 74.7 (C(3)); 72.3 (C(2)); 173.7 (C(1)). Anal. calc. for $C_6H_{11}NO_4 \cdot 1/3H_2O$ (167.16): C 43.50, H 7.03, N 8.34; found: C 43.4, H 6.8, N 8.3.

*5-Amino-5-deoxy-*L*-lyxono-1,5-lactam* (= *(3*R*,4*R*,5*S*)-3,4,5-Trihydroxypiperidin-2-one*; **16**). According to *GP*, with **10a** (428 mg, 1.37 mmol): **16** (159 mg, 79%). Colourless crystals. M.p. 192–193° (EtOH). $[\alpha]_D^{22} = +54$ ($c = 0.5$, H_2O) ([27]: m.p. = 188–189°. $[\alpha]_D = -54.7$ ($c = 1$, H_2O) for the D-enantiomer). IR (KBr): 3300–3200, 1665, 1435, 1090, 750. ^{1}H-NMR: *Table 2*. ^{13}C-NMR (D_2O, 300 K): 45.0 (C(5)); 67.3, 67.7 (C(3), C(4)); 71.3 (C(2)); 174.4 (C(1)). Anal. calc. for $C_5H_9NO_4$ (147.13): C 40.81, H 6.17, N 9.52; found: C 40.9, H 6.2, N 9.7.

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