2-(2,3,3,4,4,5,5,6,6,7,7,7-dodecafluorohept-1-enyl)-2,3-dihydrobenzo-1,4-dioxine (23). A solution of **10** (0.1 g, 0.14 mmol) in dry THF (10 mL) was treated with a 1M solution of tetrabutylammonium fluoride in THF (0.14 mL, 0.14 mmol) at -78°C. This temperature was maintained for 1h and then was allowed to rise to room temperature overnight. The reaction mixture was quenched with water and extracted with diethyl ether. Organic layer was dried over Na_2SO_4. Solvent was removed and the crude product was purified by flash chromatography (petroleum ether- CH_2Cl_2 97/ 3) to give **23** (55 mg, 88% yield, pure Z) as an oil.
^1H NMR δ 4.07 (dd, 1H, J_{gem} = 11.5 Hz, ^3J = 6.5 Hz, O-C*H*$_2$-CH), 4.32 (dd, 1H, J_{gem} =11.5 Hz, ^3J = 2.3 Hz, O-C*H*$_2$-CH), 5.21 (dddd, 1H, ^3J = 7.6 Hz, ^3J = 6.5 Hz, ^3J = 2.3 Hz, $^4J_{HF}$ = 1.5 Hz, CH-C=C), 5.85 (dd, 1H, $^3J_{HF}$ = 32.8 Hz, ^3J = 7.6 Hz, CH=C); ^{13}C NMR δ 66.1 (O-CH_2), 66.8 (O-CH), 111.8 (*C*H=C), 117.4 and 117.5 (C-Ar), 122.1 (C-Ar), 142.0 et 142.7 (quaternary C-Ar), 148.1 (dt, $^1J_{CF}$ = 270 Hz, $^2J_{CF}$ = 29.5 Hz, *C*F-CF_2); ^{19}F NMR δ -81.4 (t, 3F, ^3J = 9.5, CF_3), -118.2 (m, 2F, F_3), -123.1 (2F, F_4), -123.3 (2F, F_5), -123.6 (m, 1F, F_2), -126.5 (2F, F_6); IR (film): 2930, 2878, 1715, 1597, 1497 (s), 1356, 1238 (s), 1204 (s), 1144 (s), 1074, 748 cm^{-1}; MS m/e (%) 448 (M^+, 100), 428 (M^+- HF, 11), 321 (8), 259 (10), 229 (4), 209 (8), 139 (6), 129 (17), 151 (7), 121 (95), 108 (64).

2-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)-octahydrobenzo-1,4-dioxine (24).
DBH (0.119 g, 0.42 mmol) was added to a solution of **6** (0.500 g; 0.83 mmol) in acetonitrile (10 mL). The reaction mixture was stirred at room temperature for 1,75 h, then diluted in diethyl ether and washed with an aqueous solution of $Na_2S_2O_3$. The aqueous layer was extracted with diethyl ether. The organic layers were combined and washed with brine. After drying over Na_2SO_4, removal of the solvent gave crude **24** as a mixture of two diasteromers (**24a/24b** =70/30 (NMR)). Flash chromatography (petroleum ether-AcOEt 95/5) gave pure **24a** as a white solid and pure **24b** as a liquid (**24a+24b** = 0.25 g, 62%).
A similar procedure using NBS (1 eq, 2.25 h at rt in the dark) gave **24** (**24a/24b** = 65/35) in 69% yield .
24a. mp = 59°C; ^1H NMR δ 1.25-1.38 (m, 4H, CH_2-C*H*$_2$-C*H*$_2$-CH_2), 1.73-1.75 (m, 2H, C*H*$_2$-CH_2-CH_2-C*H*$_2$), 1.86-1.88 (m, 2H, C*H*$_2$-CH_2-CH_2-C*H*$_2$), 1.95-2.43 (m, 2H, CH_2-CF_2), 3.09 (m, 1H, CH_2-C*H*-O-CH_2), 3.25 (m, 1H, CH_2-C*H*-O-CH), 3.42 (dd, 1H, $J_{gem} \sim {}^3J \sim 11$, O-C*H*$_2$-CH), 3.87 (dd, 1H, J_{gem} = 11, ^3J = 2.7, O-C*H*$_2$-CH), 4.09 (ddt, 1H, ^3J = 2.7, ^3J = 10.5, ^3J = 5.9, C*H*-CH_2-CF_2); ^{13}C NMR δ 24.2 (CH_2-*C*H$_2$-CH_2-CH_2), 30.1 and 30.2 (*C*H$_2$-CH_2-CH_2-*C*H$_2$), 33.7 (t, $^2J_{CF}$ = 21.7 Hz, *C*H$_2$-CF_2), 69.23 (*C*H-CH_2-CF_2), 71.3 (O-*C*H$_2$-CH), 79.5 and 80.2 (2x CH_2-*C*H-O); ^{19}F NMR δ -81.4 (t, $^4J_{FF}$ = 10 Hz, CF_3), -111.8 (dm, 1F, J_{AB} = 271 Hz, F_2), -113.3 (dm, 1F, J_{AB} = 271 Hz, F_2), -122.2 (2F, F_3), -123.3 (2F, F_4), -124.0 (2F, F_5), -126.6 (2F, F_6); IR (KBr): 2942 (s), 2869, 2859, 1464, 1370 (s), 1319 (s), 1238 (vs), 1190 (vs), 1165 (vs), 1144 (vs), 1098 (vs), 1061 (s), 1020 (s), 920, 903, 708 (vs), 635 (vs) cm^{-1}; MS m/z (%) 474 (100, M^+), 433 (12), 357 (6), 127 (13), 98 (14), 81 (33), 67 (28); Anal. calc. for $C_{15}H_{15}O_2F_{13}$: C, 37.99; H, 3.19. Found: C, 37.75; H, 2.75.
24b: ^1H NMR δ 1.26-1.36 (m, 4H, CH_2-C*H*$_2$-C*H*$_2$-CH_2), 1.73-1.88 (m, 4H, C*H*$_2$-CH_2-CH_2-C*H*$_2$), 2.43-2.90 (m, 2H, CH_2-CF_2), 3.19 (m, 1H, CH_2-C*H*-O-CH_2), 3.38 (m, 1H, CH_2-C*H*-O-CH), 3.72 (d, 1H, J_{AB} = 12 Hz, $^3J \sim 0$, O-C*H*$_2$-CH), 3.97 (dd, 1H, J_{AB} = 12 Hz, ^3J = 3.3 Hz, O-C*H*$_2$-CH), 4.24 (dt, 1H, ^3J = 3.3 Hz, ^3J = 6.5 Hz, C*H*-CH_2-CF_2); ^{13}C NMR δ 24.3 (CH_2-*C*H$_2$-CH_2-CH_2), 30.2 and 30.3 (*C*H$_2$-CH_2-CH_2-*C*H$_2$), 30.9 (t, $^2J_{CF}$ = 21.2 Hz, *C*H$_2$-CF_2), 66.4 (*C*H-CH_2-CF_2), 69.8 (O-*C*H$_2$), 73.3 (*C*H-O-CH), 81.0 (*C*H-O-CH_2); ^{19}F NMR δ -81.3 (t, 3F, $^4J_{FF}$ = 9.5 Hz, CF_3), -114.0 (dm, 1F, J_{AB} = 280 Hz, F_2), -115.1 (dm, 1F, J_{AB} = 280 Hz, F_2), -122.2 (2F, F_3), -123.3 (2F, F_4), -124.0 (2F, F_5), -126.6 (2F, F_6); IR (film): 2944 (s), 2869 (s), 1456, 1362, 1238 (vs), 1198 (vs), 1167 (vs), 1144 (vs), 1061, 1020, 849, 708 cm^{-1}; MS m/z (%) 474 (M^+, 86), 433 (8), 141 (17), 112 (15), 97 (15), 81 (100), 67 (100); Anal. calc. for $C_{15}H_{15}O_2F_{13}$: C, 37,99; H, 3,19. Found: C, 38.08; H, 2.76.

2-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)-tetrahydropyran (25). The reaction of **16** (0.273 g, 0.5 mmol) following the same procedure afforded after chromatography (petroleum ether) **25** as an oil in 59% yield.
^1H NMR δ 1.33-1.89 (m, 6H, CH_2), 2.00-2.47 (m, CH_2-CF_2), 3.47 (m, 1H, O-CH_2), 3.75 (m, 1H, O-CH_2), 3.99 (m, 1H, O-CH); ^{13}C NMR δ 23.3 (C_4), 25.5 (C_5) , 32.5 (C_3), 37.6 (t, $^2J_{CF}$ = 21 Hz, *C*H$_2$-CF_2), 68.6 (C_6), 71.1 (C_2); ^{19}F NMR δ -81.4 (t, $^4J_{FF}$ = 9.5 Hz, CF_3), -113.1 (2F, F_2), -122.3 (2F, F_3), -123.3 (2F, F_4), -124.2 (2F, F_5), -126.6 (m, 2F, F_6). IR (film): 2944 (br), 2857 (br), 1443, 1395, 1358, 1240 (s, br), 1208 (s, br), 1146 (s), 1094, 1053, 812, 731, 708, 654 cm^{-1}.

Acknowledgements.

The authors thank Elf-Atochem for the gift of F-alkyl iodides, the "Ministère de l'Education Nationale, de l'Enseignement Supérieur et de la Recherche" for a fellowship (GF), The "Département de la Marne" for financial support, and Henri Baillia and Sylvie Lanthony for their help in NMR and Elemental Analysis.

References and notes

1- a/ *Chemistry of Organic Fluorine Compounds*, Hudlicky, M. Ed.; Ellis Horwood, 1976.
b/ "*Organofluorine chemistry. Principles and Commercial Applications*". R. E. Banks, B. E. Smart, J.C. Tatlow, Eds.; Plenum 1994.
c/ Riess, J. G.; Greiner, J. in "*Carbohydrates as Organic Raw Materials II*", Descotes, G. Ed., VCH, 1993, p 209.
d/ Huang, W.-Y. *J. Fluorine Chem.*, **1992**, 58, 1-8.

2- a/ Brace, N. O. *J. Org. Chem.*, **1962**, 27, 3033-3038.
b/ Traverso, E.; Rinaldi. A. *Eur. Pat. Appl.* EP 444,752. *Chem. Abstr.* **1991**, 115, 255609.
c/ Rong, G. B.; Keese, R. *Tetrahedron Lett.*, **1990**, 31, 5615-5616.
d/ Huang, B. N.; Wang, K.-Y.; Huang, W.-Y.; Prescher, D. *Chin. J. Chem.*, **1993**, 11, 169-173.
e/ Guo, C.; Wang, S. Youji Huaxue, 1994, 14,171-176. *Chem. Abstr.* **1994**, 121, 82457h.

3- a/ Huang, W.-Y.; Lü, L.; Zhang, Y.-Z. *Chin. J. Chem.*, **1990**, 68-74.
b/ Miura, K.; Takeyama, Y.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.*, **1991**, 64, 1542-1553.
c/ Sasahoka, S.-I.; Uno, M.; Joh, T.; Imasaki, H.; Takahashi, S. *J. Chem. Soc. Chem. Commun.*, **1991**, 86-87.

4- a/ Chen, Q.-Y.; Yang, Z.- Y. *J. Chem. Soc. Chem. Commun.*, **1986**, 498-499.
b/ Huang, W.-Y.; Zhuang, J.-L. *Chin. J. Chem.*, **1991**, 9, 351-359.
c/ Wang, Z.; Lu, X. *Tetrahedron*, **1995**, 51, 2639-2658.

5- a/ Greiner, J.; Milius, A.; Riess, J. G. *J. Fluorine Chem.*, **1992**, 56, 285-293.
b/ Kotora, M.; Hàjek, M.; Ameduri, B.; Boutevin, B. *J. Fluorine Chem.*, **1994**, 68, 49-56.

6/ a/ Krahler, S. E. *U. S. Patent* 4,489,006. *Chem. Abstr.* **1985**, 102, 221011.
b/ Laurent, P.; Blancou, H.; Commeyras, A. *J. Fluorine Chem.*, **1993**, 64, 125-127.
c/ see also ref. 2e.

7/ Bergeron, S.; Brigaud, T.; Foulard, G.; Plantier-Royon, R.; Portella, C. *Tetrahedron Lett.*, **1994**, 35, 1985-1989.

8/ To our knowledge only one example of F-alkylmethyl-1,4-dioxane has been detected as a minor product in a cationic F-alkylation process: Umemoto, T.; Kuriu, Y.; Nakayama, S.-I. *Tetrahedron Lett.*, **1982**, 23, 1169-1172.

9/ a/ Brown, H. C.; Midland, M. M. *Angew. Chem. Int. Ed Engl.*, **1972**, 8, 692-700.
b/ see also ref. 3b.

10/ Irradiation of H-2 induced an enhancement of H-6 (10 %) and the vinylic (3.5 %) proton signals.

11/ For a review on the intramolecular $S_{N'}$ reaction, see Paquette L. A. and Sterling C. J. M. *Tetrahedron*, **1992**, 48,7383-7423.

12/ Thiéry, V.; Coudert, G.; Morin-Allory, L.; Guillaumet, G. *Tetrahedron*, **1995**, 2619-2628 and ref. therein

13/ Noyes, R. M.; Körös, E. *Accounts Chem. Res.*, **1971**, 4, 233-239.

14/ a/ Kartha, K. P. R. *Tetrahedron Lett.*, **1986**, 27, 3415-3416.
b/ Szarek, W. A.; Zamojski, A.; Tiwari, K. N.; Ison, E. R. *Tetrahedron Lett.*, **1986**, 27, 3827-3830.
c/ Kouaklieva, M. I.; Dahl, M. L.; Turos, E. *Tetrahedron Lett.*, **1992**, 33, 7093-7096.
d/ Banik, B. K.; Manhas, M. S.; Bose A. K. *J. Org. Chem.*, **1994**, 59, 4714-4716.

15/ a/ Masaki, Y.; Miura, T. Ochiai, M. Synlett **1993**, 847-849.
b/ Posner, G. H.; Rogers, D. Z. J. Am. Chem. Soc. **1977**, 99, 8208-8214.

(*Received in Belgium* 7 *December* 1995; *accepted* 23 *February* 1996)

Pergamon

Tetrahedron, Vol. 52, No. 17, pp. 6201-6214, 1996

0040-4020/96 $15.00 + 0.00

S0040-4020(96)00269-4

Stereoselective Synthesis of D,L-Erythrose-, and of D,L-1,4-Dideoxy-4-Aminoerythrose Derivatives Bearing a β-Lactam at C-4.

Théophile TSCHAMBER[a)]*, Charles J. CRAIG[b)], Marc MULLER[a)], and Jacques STREITH[a)].

a) Ecole Nationale Supérieure de Chimie, CNRS-URA-135, Université de Haute-Alsace, 3, rue Alfred Werner, F-68093 MULHOUSE CEDEX, France.
b) ROCHE PRODUCTS Ltd, WELWYN GARDEN CITY, Hertf. AL7 3AG, ENGLAND.

Key Words : Hetero Diels-Alder, nitroso dienophiles, β-lactams, erythrose and aminoerythrose derivatives

Summary. *- Acylnitroso dienophiles react with azetidinodiazepines 1, with high stereoselectivity from the α-side, to give cycloadducts 2 and 3. Catalytic osmylation of these latter compounds proceeded with total face-selectivity to give diols 4 and 8, respectively. Hydrogenolysis, followed by molecular rearrangements, ultimately led to dideoxyaminoerythrose derivatives 6 (from 4) and to erythrose derivatives 10 (from 8). The hydrochlorides of 6a and 6b were assessed for their anti-HIV in vitro activity ; they were found to be less potent than castanospermine.*

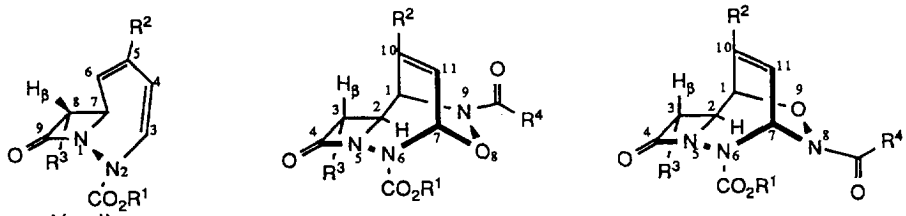
Introduction. - Azetidinodiazepines **1** have been shown to undergo facial selective, but regio non-selective cycloaddition reactions with nitrosodienophiles, leading thereby in high yield to direct[1] **2**, and to inverse[1] cycloadducts **3**.[2] Furthermore, the inverse cycloadduct **3a**, when reacted with osmium tetroxide, led stereospecifically to a rather unstable *cis*-diol which is *syn* with respect to the N-O bridge, whereas the direct adduct **2a** did not react at all. This lack of reactivity is most probably due to a more pronounced steric crowding of **2a** [steric interference of OsO_4 both with Me-C(10) and with Bz-N(9)] as compared to **3a**. (*Scheme 1*).

We describe herein the osmylation products obtained with type **2** and with type **3** cycloadducts which are devoid of any methyl group at C(10). For that reason adducts **2** were expected to react with OsO_4. We describe furthermore the transformation of the ensuing diols into dideoxyaminoerythrose **6** and into erythrose **10** derivatives.[4]

Diels-Alder cycloadducts. - In a previous publication it was shown that nitrosodienophiles react face selectively with the convexe α-side of type **1a** azetidinodiazepines, to give the direct [1] **2a** and the inverse[1] **3a** cycloadducts in high yield.[2] Very similar results are described herein. They were obtained with azetidinodiazepines **1b-d** which led in close to quantitative yields to the regioisomers **2b-d** and **3b-d** (*Scheme 1*). These results agree with the previously described high face selectivity of the Diels-Alder process. The

acylnitrosodienophiles[3] -*i.e.* benzoylnitroso- and benzyloxycarbonylnitrosodienophiles - were prepared *in situ* from the corresponding hydroxamic acids, according to some known procedures,[5,6] and reacted at once with the diene components.

Scheme 1



1(a-d) **2(a-e) direct adducts** **3(a-d) inverse adducts**

	R^1	R^2	R^3	R^4
a	Et	Me	Me	Ph
b	Me	H	Me	OBn
c	Me	H	H	OBn
d	tBu	H	N_3	OBn
e	tBu	H	NHCOBn	OBn

The azido group of the direct cycloadduct **2d** was reduced to the corresponding primary amine and thence acylated to give the phenylacetamide derivative **2e**, according to the procedure of Carrié *et al.*.[7]

Chemical shifts and coupling constants of H-C(1), H-C(7), and H-C(11) led easily to the differentiation between the direct **2**, and the inverse adducts **3**. The differentiation is even more pronounced when considering the chemical shifts of the corresponding C-atoms, *i.e.* C(1), C(7), and C(11) (see *Experimental*). Structural analyses, which are based on such ^{1}H- and ^{13}C-NMR data, are very similar to those discussed in detail in a previous publication for **2a** and **3a**.[2]

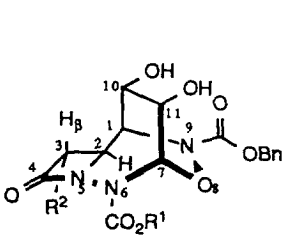
Osmylation of direct cycloadducts 2. Synthesis of 2-azetidinone-dideoxyamino-erythrose derivatives 6 and 7. - Catalytic osmylation of direct cycloadducts **2b**, **2c**, and **2e**, in the presence of the cooxidant N-methylmorpholine N-oxide (NMO), gave in excellent yield the expected *cis* diols **4a**, **4b**, and **4c**, respectively. These were transformed into the corresponding acetonide derivatives, *i.e.* **5a**, **5b**, and **5c** (*Scheme 2*). One-pot hydrogenolyses (H_2/Pd/C) of the single N-O bond and of the benzyloxycarbonyl moiety of compounds **4** and **5** triggered molecular rearrangements which led ultimately to pyrrolidine derivatives. For example **4b** gave the rather unstable dihydroxypyrrolidine **6a** which was isolated as its hydrochloride **6a•HCl**.

The formation of **6** results from a mechanistically straightforward multistep sequence : after hydrogenolysis of the O-Bn and of the N-O bonds (of type **5** compounds), followed by decarboxylation, the hemiaminal functionality breaks up leading to an aldehyde which condenses at once with the primary NH_2-C(1) amine. The ensuing Δ^1 pyrroline is then hydrogenated (Pd/C) to give pyrrolidine **6**. This multistep mechanism is akin to the one we had observed during catalytic hydrogenolysis of a trihydroxytetrahydroxazine which led also

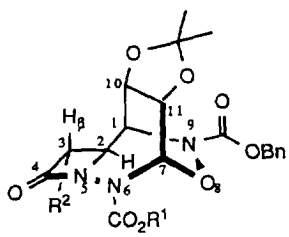
to a dihydroxypyrrolidine.[8] The above described one-pot multistep hydrogenolysis/hydrogenation sequence was also encountered with the acetonide derivatives **5a** and **5c** which gave the corresponding dihydroxypyrrolidines **7a** and **7c** as unstable species. They were isolated as N-benzyloxycarbonyl derivatives **7b** and **7d**, respectively. Compound **7b** was deprotected in aqueous acid medium to the corresponding dideoxyaminoerythrose derivatives **6c** (*Scheme 2*) ; hydrogenolysis (Pd/C) of **6c** followed by acidification (HCl) gave **6b**, as its hydrochloride.

Structure and stereochemistry of azetidinopyrrolidine derivatives **6a**, **6b**, **7b**, and **7d** could be ascertained unequivocally by IR spectroscopy and by ^{1}H-NMR (see *Experimental*). One notices in particular a strong C=O absorption band between 1768 and 1800 cm^{-1}, which proves that the β-lactam rings have been retained.

Scheme 2

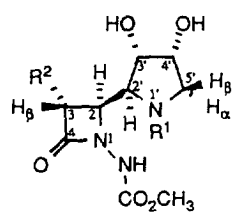


4(a-c)



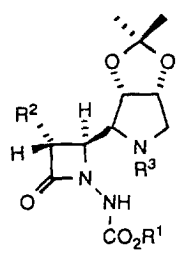
5(a-c)

	R^1	R^2
a	Me	Me
b	Me	H
c	tBu	NHCOBn



6

	R^1	R^2
a	H	H
b	H	Me
c	CO_2Bn	Me



7

	R^1	R^2	R^3
a	Me	Me	H
b	Me	Me	CO_2Bn
c	tBu	NHCOBn	H
d	tBu	NHCOBn	CO_2Bn

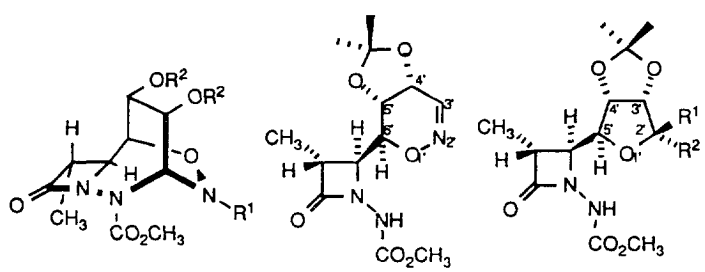
Osmylation of the inverse cycloadduct 3b. Synthesis of type 10 2-azetidinone-erythrose derivatives. - Osmylation of the inverse cycloadduct **3b** gave in good yield *cis* diol **8a** as the only detectable product. As already observed with direct adducts **2**, osmylation occurs with total face selectivity from the least hindered side, *i.e. syn* with respect to the N-O bridge. Hydrogenolysis of the benzyloxycarbonyl moiety (Pd/C) of derivative **8b** led directly to 6'*H*-4',5'-dihydro-1',2'-oxazine **9**, which is akin to a very similar oxazinylazetidinone we had described in a previous publication.[2] The formation of **9** results obviously from the

break-up of the free aminal **8c**. As a matter of fact the ^{1}H-NMR spectrum of **9**, as measured in dilute $CDCl_3$ solution, shows that this oxazine equilibrates with the postulated tricyclic precursor **8c**. Hydrogenolysis (Raney nickel) of the single N-O bond of **8c/9** in the presence of ammonia, followed by aqueous acid treatment, gave directly the erythrose **10a** (34 %), and **10b** (66 %) in 60 % overall yield.

The postulated mechanism which accounts best for the formation of the erythrose derivatives **10a** and **10b** should be as follows : Raney nickel promotes the cleavage of the oxazine ring along the N-O bond, whereby an unstable imine is formed. Addition of ammonia to this imine (formation of an aminal) prevents it from being hydrogenated.[9] Acid catalysed hydrolysis of the imine/aminal gives the corresponding aldehyde, an open-chain erythrose derivative, *i.e.* a carbohydrate derivative.

The stereostructures of the azetidinoerythrose derivatives **10a** and **10b** follow from their ^{1}H-NMR data (see *Experimental*). For example the β-lactam is clearly *trans* ($J_{2,3}$=2.5 Hz). The α-anomer **10a** appears with $J_{2',3'}$=4 Hz indicating a *cis* relationship of H-C(2') and H-C(3'), whereas for the β-anomer **10b** $J_{2',3'}$=0. These results agree well with literature data for erythrofuranose anomers.[10]

Scheme 3



8 **9** **10**

	R^1	R^2
a	CO_2Bn	H
b	CO_2Bn	R^2-R^2 = CMe_2
c	H	R^2-R^2 = CMe_2

	R^1	R^2
a	H	OH
b	OH	H

Anti HIV assays. - It has been known for some time that aminosugar derivatives which inhibit glycoprotein processing have potential activity against HIV.[11] These naturally occurring aminodeoxysugars derive either from piperidines, from pyrrolidines, from pyrrolizines, or from octahydroindolizines, and are deprived of the anomeric OH group. Compounds **6a** and **6b** (hydrochlorides), which are derivatives of (±) amino erythrose, fall within the pyrrolidine group. As a consequence they were tested for their anti-HIV activity. These compounds were evaluated in two separate experiments in duplicate in a primary screen against HIV (Strain GB 8) in JM cells (3 day assay). Activity was measured by syncytium formation[12] and cytotoxicity[13] in an MTT assay, castanospermine being the reference compound. In these assays **6a** and **6b** (hydrochlorides) showed some antiviral activity which was less pronounced than that of castanospermine (reference substance)[14].

Acknowledgements. - The support of the *Centre National de la Recherche Scientifique* (URA-135) is gratefully acknowledged. We wish also to thank the *Ministère de la Recherche et de la Technologie* for a research

grant to M. Muller and Miss L. Whittaker of the *Roche-Welwyn Research Centre (U.K.)* for her efficient cooperation in the *in vitro* anti-HIV inhibition assays.

Experimental part

General. - Flash chromatography (FC) : silica gel (**Merck 60** ; 230-400 mesh). TLC : Al sheets silica gel (**Merck 60** F_{254}) ; detection : UV or spraying i) with a 5 % $H_3[P(Mo_3O_{10})_4]$ solution in EtOH followed by heating, or ii) with a solution of $KMnO_4$ (2 g) and Na_2CO_3 (4 g) in H_2O (100 ml) followed by heating. M.p. : **Kofler** hot bench or **Büchi SMP 20** apparatus : corrected. UV spectra : **Perkin-Elmer 550SE.** IR spectra (cm^{-1}) : **Perkin-Elmer 157-G** and **580-B.** ^1H- and ^{13}C-NMR spectra : **Bruker WP-80-DS**, and **AC-F-250** using double irradiation techniques : tetramethysilane TMS (^1H-NMR) and $CDCl_3$ (^{13}C-NMR ; d($CDCl_3$) = 77.0 ppm with respect to TMS) 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, Vernaison. All compounds reported in this work are racemic. **OsO_4 solution** : OsO_4 (1 g) in t-butanol (200 ml) and t-butylhydroperoxyide (1 ml).

Methyl *trans*-8-methyl-9-oxo-1,2-diazabicyclo[5.2.0]-3,5-nonadiene-2-carboxylate 1b, and methyl 9-oxo-1,2-diazabicyclo[5.2.0]-3,5-nonadiene-2-carboxylate 1c. - The pyrolysis gas of acetone generated in a ketene lamp[15] was left to react with a solution of methyl 1*H*-1,2-diazepine-1-carboxylate (6.58 g ; 43.3 mmol)[14] in toluene (70 ml) at r.t. After 15 h the starting material had been consumed (TLC ; AcOEt/cyclohexane 1:1). After evaporation of the solvent the residue was separated by FC (AcOEt/cyclohexane 3:7) and gave **1b** (3.53 ; 39 %) and **1c** (4.70 g ; 56 %).

Azetidinodiazepine 1b : yellow oil. UV (MeOH) : 275 (5 600).IR($CHCl_3$) : 3015, 1780 (C=O β-lactam), 1738 (C=O carbamate), 1643, 1612, 1447, 1333, 1277, 1212 (br), 1147, 974, 930. ^1H-NMR (80 MHz, $CDCl_3$) : 6.85 (*dm*, *J*=9.1, H-C(3)) ; 5.94 (*dm*, *J*=11.3, H-C(6)) ; 5.80 (*dddd*, *J*=11.3, 6.8, 1.6, 0.6, H-C(5)) ; 5.11 (*ddd*, *J*=9.1, 6.8, 1.8, H-C(4)) ; 4.17 (*m*, H-C(7)) ; 3.86 (*s*, CH_3-O), 2.67 (*qd*, *J*=7.2, 1.9, H-C(8)) ; 1.42 (*d*, J=7.2 ; CH_3-C(8)). HR-MS : 208.0841 ($C_{10}H_{12}N_2O_3$, $M^{+\cdot}$, calc. 208.08479).

Azetidinodiazepine 1c : Colourless crystals. M.p. 100 °C (CH_2Cl_2/diisopropylether). UV(MeOH) : 274(8600). IR(KBr) : 1775 (C=O β-lactam), 1733 (C=O carbamate), 1645, 1611, 1443, 1399, 1328 (br), 1285, 1249, 1206, 1163, 1126, 1092, 1028, 953, 829, 790, 766, 752, 719, 705. ^1H-NMR (80 MHz, $CDCl_3$) : 6.86 (*dm*, *J*=9.4, H-C(3)) ; 5.90 (*dm*, *J*=11.4, H-C(6)) ; 5.83 (*ddm*, *J*=11.4, 6.0, H-C(5)) ; 5.13 (ddm, *J*=9.4, 6.0, H-C(4)) ; 4.55 (*dm*, *J*=5.4, H-C(7)) ; 3.85 (*s*, CH_3-O) ; 3.04 (*dd*, *J*=14.0, 5.4, Hα-C(8)) ; 2.44 (*dd*, *J*=14.0, 2.2, Hβ-C(8). Anal calc. for $C_9H_{10}N_2O_3$ (194.18) : C 55.67, H 5.19, N 14.43 ; found : C 55.5, H 5.27, N 14.5.

t-Butyl [7α,8α]-8-azido-9-oxo-1,2-diazabicyclo[5.2.0]-3,5-nonadiene-2-carboxylate 1d. - To a soln. of t-butyl (1H)-1,2-diazepine-1-carboxylate[17] (2.55 g ; 13.1 mmol) and of NEt_3 (3.65 ml ; 26.3 mmol) in anhydr. ether (30 ml) were added 1 drop of oxalyl chloride and thence dropwise a soln. of azidoacetic acid chloride (3.4 g ; 33.6 mmol) in anhydr. ether (20 ml). After 15 min at r.t. the reaction mixture is filtered and the soln. evaporated to dryness. The residue was purified by FC (AcOEt/cyclohexane 4:6) and gave **1d** (3.60 g ; 99 %) as an orange oil. IR(film) : 2975, 2925, 2098 (N_3), 1791(β-lactam), 1728(carbamate), 1638, 1604, 1583, 1433, 1390, 1368, 1317, 1254, 1150. ^1H-NMR (80 MHz, C_6D_6) ; 6.84 (*dm*, *J*=9.2, H-C(3)) ; 5.37 (*dddd*,

J=11.5, 7.7, 1.7, 0.6, H-C(5)) ; 5.11 (*ddt*, *J*=11,5, 1.7, 1.0, H-C(6)) ; 4.64 (*ddd*, *J*=9.2, 7.7, 1.0, H-C(4)) ; 3.86 (*t*, *J*=1.7, H-C(7)) ; 3.35 (*d*, *J*=1.7, H-C(8)) ; 1.38 (*s*, $C(CH_3)_3$. HR-MS calc. for : $[M\text{-}CO_2tBu + H]^+$ $C_7H_7N_5O$: 177.06506 ; found : 177.0651 ; for $[M\text{-}OtBu\text{-}N_2]^+$ $C_8H_6N_3O_2$: 176.04600, found : 176.0455.

Methyl [1α,2β,3β,7α]-9-benzyloxycarbonyl-3-methyl-4-oxo-8-oxa-5,6,9-triazatricyclo-[5.2.2.0^{2,5}]-undec-10-ene-6-carboxylate 2b and methyl[1α,2β,3β,7α] 8-benzyloxycarbonyl-3-methyl-4-oxo-9-oxa-5,6,8-triazatricyclo[5.2.2.0^{2,5}]-undec-10-ene-6-carboxylate 3b. - To a stirred soln. of **1b** (3.53 g ; 17.0 mmol) and nPr_4NIO_4 (2.24 g ; 5.31 mmol) in CH_2Cl_2 (20 ml) which was cooled to 0°C, was added portionwise over 45 min N-benzyloxycarbonyl hydroxamic acid (3.53 g ; 23.4 mmol). After 1 h the reaction mixture was left to warm up to r.t., washed with an 5 % aqueous soln. of sodium thiosulfate, dried over $MgSO_4$, and evaporated. The residue was separated by FC(AcOEt/cyclohexane 7:3) leading to **3b** (2.24 g ; 35 %) and to **2b** (3.84 g ; 60 %).

Tricyclic 2b : colourless crystals. M.p. 136 °C. (AcOEt/cyclohexane). IR(KBr) : 3018, 2960, 1783 (C=O β-lactam), 1738 (C=O, carbamate), 1680, 1450, 1346, 1315, 1297, 1278, 1254, 1114, 1082, 972, 941, 929, 766, 754, 698. ^{1}H-NMR (80 MHz, C_6D_6, 323 K) : 7.15 (*m*, 5*H*Ph) ; 6.22 (*dm*, *J*=6.0, H-C(7)) ; 5.81 (*ddd*, *J*=9.2, 6.4. 1.0, H-C(10)) ; 5.57 (*ddd*, *J*=9.2, 6.0, 1.5, H-C(11)) ; 5.09 and 4.99 (*d*(AB), *J*=12.5, O-CH_2-Ph) ; 4.76 (*ddd*, J=6.4, 1.5, 1.4, H-C(1)) ; 3.71 (*dd*, J=1.8, 1.4, H-C(2)) ; 3.30 (s, O-CH_3) ; 1.97 (*qdm*, *J*=7.2, 1.8, H-C(3)) ; 0.90 (*d*, *J*=7.2, CH_3-C(3)). ^{13}C-NMR (20.1 MHz, $CDCl_3$) : 170.9 (s sext, C(4)) ; 155.9 (st, O=C-O-CH_2Ph) ; 154.75 (sq, O=*C*-OCH_3) ; 135.2 (sm, *C*(s)Ph) ; 130.7 (*dddd*, ^1J=172, C(10)) ; 128.3 (dm, ^1J=161, *C*(m)Ph) ; 128.2 (*dm*, ^1J=160, *C*(p)Ph) ; 127.9 (*dm*, ^1J=160, *C*(o)Ph)) ; 127.2 (*dt*, ^1J=176, C(11)) ; 81.5 (*dd*, ^1J=170, C(7)) ; 68.2 (*tm*, ^1J=149, O-*C*H_2) ; 67.3 (*dm*, ^1J=160, C(2)) ; 56.7 (dtd, ^1J=147, C(1)) ; 54.0 (*qs*, ^1J=148, O-*C*H3) ; 45.1 (*dq*, ^1J=139, C(3)) ; 12.8 (qt, ^1J=128, *C*H_3-C(3)). Anal. calc. for $C_{18}H_{19}N_3O_6$ (373.34) : C 57.91, H 5.13, N 11.26 ; found : C 57.5, H 5.1, N 11.2.

Tricyclic 3b : colourless crystals. M.p. 112 °C. (AcOEt/cyclohexane). IR(KBr) : 3058, 3038, 2978, 2960, 2942, 1780 (C=O β-lactam), 1730 (br, C=O carbamates), 1500, 1446, 1394, 1345, 1294 (br), 1270 (br), 1221, 1092, 1078, 998, 927. ^{1}H-NMR (80 MHz, $CDCl_3$) : 7.35 (*s*, 5*H*Ph) ; 6.76 (*dd*, *J*=6.2, 1.9, H-C(7)) ; 6.59 (*ddd*, *J*=8.8, 5.4, 1.9, H-C(10)) ; 6.48 (*ddd*, *J*=8.8, 6.2, 1.6, H-C(11)) ; 5.20 (*s*, O-CH_2) ; 5.02 (*ddd*, *J*=5.4, 1.8, 1.6, H-C(1)) ; 4.10 (*t*, *J*=1.8, H-C(2)) ; 3.78 (*s*, O-CH_3) ; 2.61 (*qd*, *J*=7.3, 1.8, H-C(3)) ; 1.41 (*d*, *J*=7.3, CH_3-C(3)). ^{13}C-NMR (20.1 MHz, $CDCl_3$) : 171.30 (*s sext*, C(4)) ; 154.6 (*sm*, O=*C*-OBn) ; 154.1 (sq, O=*C*-OCH_3) ; 134.9 (*sm*, *C*(s)Ph) ; 129.0 (*qd*, ^1J=171, C(10)) ; 128.1 (*dt*, ^1J=176, C(11)) ; 128.1 (*dm*, ^1J=160, *C*(m)Ph) ; 128.0 (*dm*, ^1J=160, *C*(p)Ph) ; 127.7 (*dm*, ^1J=160, *C*(o)Ph) ; 75.1 (*dm*, ^1J=154, C(1)) ; 68.5 (*dm*, ^1J=160, C(2)) ; 68.0 (*tm*, ^1J=149, O-*C*H_2-Ph) ; 66.9 (*dt*, ^1J=162, C(7)) ; 53.6 (*qs*, ^1J=148, O-*C*H_3) ; 44.1 (*dq*, ^1J=139, C(3)) ; 12.6 (*qt*, ^1J=128, *C*H_3-C(3)). Anal. calc. for $C_{18}H_{19}N_3O_6$ (373.34) : C 57.91, H 5.13, N 11.26 ; found : C 58.2, H 5.0, N 11.1.

Methyl [1α,2β,7α]-9-benzyloxycarbonyl-4-oxo-8-oxa-5,6,9-triazatricyclo[5.2.2.0^{2,5}]-undec-10-ene-6-carboxylate 2c and methyl [1α,2β,7α]-8-benzyloxycarbonyl-4-oxo-9-oxa-5,6,8-triazatricyclo[5.2.2.0^{2,5}]-undec-10-ene-6-carboxylate 3c. - Similar procedure as for **2b** and **3b** : to a stirred soln. of **1c** (4.81 g ; 24.5 mmol) and of Pr_4NIO_4 (3.60 g, 8.58 mmol) in CH_2Cl_2 (30 ml), which was cooled to 0 °C, was added portionwise N-benzyloxycarbonylhydroxamic acid (6.50 g, 33.1 mmol). The residue was separated by FC(AcOEt/cyclohexane 7:3) and give **3c** (3.68 g ; 41 %) and **2c** (4.81 g ; 59 %).

Tricyclic 2c : Colourless resin. IR(KBr) 2950, 1790(β-lactam), 1730(carbamate), 1440, 1290, 1262, 1200, 1110, 1080. ^{1}H-NMR (80 MHz, C_6D_6) : 7.15 (*m*, 5*H*Ph) ; 6.19 (*dm*, *J*=5.6, H-C(7)) ; 5.79 (*ddd*, *J*=9.2, 6.2, 1.3, H-C(10)) ; 5.53 (*ddd*, *J*=9.2, 5.6, 1.9, H-C(11)) ; 5.16 and 5.13 (*d* (AB), J=12.5, O-C*H*$_2$-Ph) ; 4.66 (*ddd*, J=6.2, 1.9, 1.3, H-C(1)) ; 3.88 (*ddd*, *J*=5.2, 2.2, 1.3, H-C(2)) ; 3.30 (*s*, O-C*H*$_3$) ; 2.16 (*dd*, *J*=15.0, 5.2, Hα-C(3)) ; 1.57 (*dd*, *J*=15.0, 2.2, Hβ-C(3)). ^{13}C-NMR (50 MHz, $CDCl_3$) : 168.6 (*s*, C(4)) ; 156.0 (*s*, O=*C* carbamate) ; 154.9 (*s*, O=*C* carbamate) ; 135.3 (*s*, *C*(s)Ph) ; 130.3 (*d*, C(10)) ; 128.6 (*d*, *C*(m)Ph) ; 128.5 (*d*, *C*(p)Ph) ; 128.2 (*d*, *C*(o)Ph) ; 128.1 (*d*, C(11)) ; 81.6 (*d*, C(7)) ; 68.4 (*t*, O-*C*H$_2$-Ph) ; 60.0 (*d*, C(2)) ; 57.0 (*d*, C(1)) ; 54.1 (*q*, O-*C*H$_3$) ; 36.8 (*t*, C(3)). Anal. calc. for $C_{17}H_{17}N_3O_6$ (359.31) : C 56.83, H 4.77, N 11.69 ; found : 56.6, H 4.9, N 11.4.

Tricyclic 3c : colourless crystals. M.p. 139 °C. (CH_2Cl_2/diisopropylether). IR(KBr) : 3070, 3030, 2955, 1785 (C=O β-lactam), 1730 *and* 1703 (carbamates) ; 1448, 1415, 1386, 1356, 1339, 1306, 1292, 1283, 1266, 1217, 1111, 1072, 1038, 1020, 909, 847, 792, 773, 758, 750, 702. ^{1}H-NMR (80 MHz, C_6D_6) : 7.15 (*m*, 5*H* Ph) ; 6.81 (*dd*, *J*=6.8, 1.0, H-C(7)) ; 5.93 (*ddd*, *J*=9.2, 6.8, 1.0, H-C(11)) ; 5.43 (*ddd*, *J*=9.2, 6.2, 1.0, H-C(10)) ; 4.98 (*s*, O-C*H*$_2$-Ph) ; 4.05 (*ddd*, *J*=6.2, 2.0, 1.0, H-C(1)) ; 3.81 (*dt*, *J*=5.2, 2.0, H-C(2)) ; 3.36 (*s*, O-C*H*$_3$) ; 2.04 (*ddd*, *J*=15.1, 5.2, 0.5, Hα-C(3)) ; 1.43 (*dd*, *J*=15.1, 2.0, Hβ-C(3)). ^{13}C-NMR (50 MHz ; $CDCl_3$) ; 169.1 (s, C(4)) ; 155.0 (s, *C*=O carbamate) ; 154.4 (s, *C*=O carbamate) ; 135.1 (s, *C*(s) Ph) ; 129.2 (d, C(10)) ; 128.7 (d, C(11)) ; 128.5 (d, *C*(m)Ph) ; 128.4 (d, *C*(p)Ph) ; 128.1 (d, *C*(o)Ph) ; 75.7 (d, C(1)) ; 68.3 (t, O-*C*H$_2$Ph) ; 67.1 (d, C(7)) ; 61.1 (d, C(2)) ; 53.9 (q, O-*C*H$_3$) ; 35.9 (t, C(3)). Anal. calc. for $C_{17}H_{17}N_3O_6$ (359.31) : C 56.83, H 4.77, N 11.69 ; found : C 56.8, H 4.7, N 11.7.

t-Butyl [1α,2β,3β,7α]-3-azido-9-benzyloxycarbonyl-8-oxa-4-oxo-5,6,9-triazatricyclo [5.2.2.0^{2,5}]-undec-10-ene-6-carboxylate 2d and t-butyl[1α,2β,3α,7α]-3-azido-8-benzyloxycarbonyl-9-oxa-4-oxo-5,6,8-triazatricyclo[5.2.2.0$^{2.5}$]-undec-10-ene-6-carboxylate 3d. - Same procedure as for **2b** and **3b** : **1d** (2.65 g ; 9.6 mmol), and nPr_4NIO_4 (1.14 g ; 3.44 mmol) in CH_2Cl_2 (15 ml), N-benzyloxycarbonylhydroxamic acid (2.07 g ; 12.3 mmol). FC of the residue (AcOEt/cyclohexane 1:1) gave **3d** (2.14 g ; 51 %) and **2d** (1.83 g ; 43 %).

Tricyclic 2d : Colourless crystals. M.p. 127°C. (AcOEt/cyclohexane). IR(KBr) : 2978, 2105(N_3), 1795(β-lactam), 1730(carbamate), 1493, 1450, 1390, 1366, 1285(br), 1252(br), 1149, 1080(br), 1005(br), 842. ^{1}H-NMR (80 MHz, C_6D_6, 313 K) : 7.14 (*m*, 5*H*Ph) ; 6.21 (*dd*, *J*=5.8, 1.0, H-C(7)) ; 5.69 (*ddd*, *J*=9.2, 6.3, 1.0, H-C(10)) ; 5.47 (*ddd*, *J*=9.2, 5.8, 1.6, H-C(11)) ; 5.00 (s, C*H*$_2$-Ph) ; 4.65 (*ddd*, *J*=6.3, 1.6, 1.2, H-C(1)) ; 3.98 (*dd*, *J*=1.6, 1.2, H-C(2)) ; 3.27 (*d*, *J*=1.6, H-C(3)) ; 1.32 (*s*, C(C*H*$_3$)$_3$. ^{13}C-NMR (62.9 MHz, $CDCl_3$, 323 K) : 163.5 (st, C(4)) ; 155.8 (st,O=*C*-O-CH$_2$Ph) ; 152.4 (s, O=*C*-O-C(CH$_3$)$_3$) ; 135.3 (sm, *C*(s)Ph) ; 129.7 (dq, ^{1}J=174, C(10)) ; 128.5 (dd, ^{1}J=160, *C*(m)Ph) ; 128.4 (dm, J=160, *C*(p)Ph) ; 128.3 (dt, J=177, C(11)) ; 128.0 (*d quint*, ^{1}*J*=160, C(o)Ph) ; 84.3 (*sm*, *C*(CH$_3$)$_3$) ; 81.8 (*dtm*, ^{1}*J*=172, C(7)) ; 68.5 (*tm*, ^{1}*J*=149, O-*C*H$_2$) ; 67.8 (*ds(br)*, ^{1}*J*=163, C(2)) ; 64.07 (*dm*, ^{1}*J*=156, C(3)) ; 56.1 (*dtd*, ^{1}*J*=149, C(1)) ; 27.8 (*q sept*, ^{1}*J*=127, C(*C*H$_3$)$_3$). Anal. calc. for $C_{20}H_{22}N_6O_6$ (442.40) : C 54.30, H 5.01, N 19.00 ; found : C 54.6, H 4.9, N 19.0.

Tricyclic 3d : colourless crystals. M.p. 180 °C. (CH_2Cl_2/diisopropylether). IR(KBr) : 3040, 3003, 2987, 2938, 2100(N_3), 1786(b-lactam), 1729 and 1720(carbamates), 1687, 1498, 1458, 1412, 1389, 1369, 1338, 1311, 1287, 1273, 1208, 1160, 1070, 894, 879, 851, 825, 806, 768, 755(br), 698, 600. ^{1}H-NMR (80 MHz, C_6D_6) : 7.15 (*m*, 5*H* Ph) ; 6.71 (*dd*, *J*=6.8, 1.0, H-C(7)) ; 5.76 (*ddd*, *J*=9.2, 6.8, 1.0, H-C(11) ; 5.34 (*ddd*, *J*=9.2,

6.0, 1.0, H-C(10)) ; 5.00 and 4.94 (*d* (AB), *J*=12.2, CH_2 Ph) ; 4.07 (*ddd*, *J*=6.0, 1.6, 1.0, H-C(1)) ; 3.90 (*t*, *J*=1.6, H-C(2)) ; 3.10 (*d*, *J*=1.6, H-C(3)) ; 1.37 (s, $C(CH_3)_3$. ^{13}C-NMR (62.9 MHz, $CDCl_3$, 323 K) : 163.9 (*st*, C(4)) ; 155.1 (*st*, O=*C*-O-CH_2Ph) ; 152.1 (*s*, O=*C*-O-tBu) ; 135.3 (*sm*, *C*(s)Ph) ; 129.7 (*dt*, ^1J=177, C(11)) ; 128.8 (*dm*, ^1J=160, *C*(m)Ph) ; 128.4 (*dq*, ^1J=173, C(10)) ; 128.1 (*dm*, *J*=160, *C*(p)Ph) ; 128.1 (*dm*, ^1J=160, *C*(o)Ph) ; 84.0 (sm, $C(CH_3)_3$; 74.3 (*dtd*, ^1J=155, C(1)) ; 69.0 (*ds(br)*, ^1J=164, C(2)) ; 68.5 (*tm*, ^1J=146, O-CH_2) ; 67.7 (*dt*, ^1J=163, C(7)) ; 63.3 (*dd*, ^1J=156, C(3)) ; 27.8 (*q sept*, ^{1}J=127, $C(CH_3)_3$). Anal. calc. for $C_{20}H_{22}N_6O_6$ (442.40) : C 54.30, H 5.01, N 19.00 ; found : C 54.3, H 5.0, N 18.8.

***t*-Butyl [1α,2β,3β,7α]-9-benzyloxycarbonyl-8-oxa-4-oxo-3-phenyl-acetamido-5,6,9-triazatricyclo-[5.2.2.0^{2,5}]-undec-10-ene-6-carboxylate 2e**. - To a stirred soln. of **2d** (1.00 g ; 2.26 mmol) in THF/H_2O 40:1 (20 ml) at r.t. were successively added PPh_3 (650 mg ; 2.49 mmol), phenylacetic acid (385 mg ; 2.83 mmol) and dicyclohexylcarbodiimide (700 mg ; 3.39 mmol). After 1 h the reaction was complete according to TLC (AcOEt/cyclohexane 1:1), the solvents were evaporated, the residue was purified by FC (AcOEt/cyclohexane 6:4) which led to **2e** (1.00 g ; 83 %) as colourless crystals. M.p. 139 °C (AcOEt/cyclohexane). IR(KBr) : 3298, 3060, 3030, 3005, 2975, 2955, 2930, 1790 and 1760(β-lactam), 1727(carbamate)1678, 1541, 1491, 1452, 1390, 1367, 1344, 1330, 1317, 1305, 1288, 1268, 1249, 1204, 1157, 1139, 1112, 1075, 1060, 1002. ^{1}H-NMR (80 MHz, C_6D_6, 323 K) : 7.11 (*m*, 2 Ph) ; 6.19 (*d(br)*, *J*=7.0, N-H) ; 6.12 (*dm*, *J*=6.0, H-C(7)) ; 5.91 (*ddd*, *J*=9.2, 6.5, 0.9 H-C(10)) ; 5.55 (*ddd*, J=9.2, 6.0, 1.4, H-C(11)) ; 5.24 (*dt*, *J*=6.5, 1.4, H-C(1)) ; 5.02 and 4.95 (d(AB), J=12.4, O-CH_2-Ph) ; 4.62 (*dd*, *J*=7.0, 1.8, H-C(3)) ; 4.19 (*dd*, J=1.8, 1.4, H-C(2)) ; 3.14 (*s*, CH_2-Ph) ; 1.33 (s, $C(CH_3)_3$). Anal. calc. for $C_{28}H_{30}N_4O_7$ (534.53) ; C 62.92, H 5.66, N 10.48 ; found : C 63.0, H 5.6, N 10.5.

Methyl [1α,2β,3β,7α,10α,11α]-9-benzyloxycarbonyl-10,11-dihydroxy-3-methyl-8-oxa-4-oxo-5,6,9-triaza-tricyclo[5.2.2.0^{2,5}]-undecane-6-carboxylate 4a. - To a stirred soln. of **2b** (362 mg ; 0.97 mmol) in THF/*t*BuOH 1:1 (9 ml) was added NMO (197 mg ; 1.48 mmol). To this soln. cooled to 0 °C was added the catalytic OsO_4 soln. (1 ml). After 2 h **2b** was consumed (TLC), the solvent was evaporated and the residue purified by FC(AcOEt) which led to **4a** (360 mg ; 91 %) as a colourless resin. IR(KBr) : 3420(br), 2950, 2930, 1775(β-lactam), 1738(carbamate), 1439, 1325(br), 1270(br), 1207, 1075(br), 942. ^{1}H-NMR (80 MHz, $CDCl_3$) : 7.36 (s, 5*H* Ph) ; 6.05 (s(br), H-C(7)) ; 5.21 (s, O-CH_2) ; 4.86 (*dm*, *J*=1.7, H-C(1)) ; 4.10 (*s(br)*, H-C(10) and H-C(11) ; 3.89 (*t*, *J*=1.7, H-C(2)) ; 3.85 (*s(br)*, O-*H*) ; 3.78 (s, O-CH_3) ; 2.97 (*qdm*, *J*=7.2, 1.8, H-C(3)) ; 1.43 (d, J=7.2, CH_3-C(3)).

Methyl [1α,2β,7α,10α,11α]-9-benzyloxycarbonyl-10,11-dihydroxy-8-oxa-4-oxo-5,6,9-triazatricyclo-[5.2.2.0^{2,5}]-undecane-6-carboxylate 4b. - Same procedure as for **4a** : **2c** (314 mg ; 0.87 mmol), THF/t-BuOH 1:1 (6 ml), NMO (176 mg ; 1.30 mmol), catalytic OsO_4 soln. (0.9 ml). FC of the crude residue (AcOEt) gave **4b** (340 mg, 99 %) as a colourless oil. IR(KBr) : 3450(br), 2958, 1780 (C=O b-lactam), 1730, 1440, 1415(br), 1326(br), 1277(br), 1205, 1095, 1075, 750, 693.^{1}H-NMR (80 MHz, $CDCl_3$) : 7.34 (s, 5*H* Ph) ; 6.00 (s(br), H-C(7)) ; 5.20 (s, -O-CH_2 Ph) ; 4.87 (s(br), H-C(1)) ; 4.62 (s(br), H-O) ; 4.20 (m, H-C(2)) ; 4.20 (dm, J=7.0, H-C(10)) ; 4.07 (dm, J=7.0, H-C(11)) ; 3.78 (s, O-CH_3) ; 3.12 (dd, J=15.2, 5.0, Ha-C(3)) ; 2.81 (dd, J=15.2, 2.0, Hb-C(3)) ; 2.45 (s, H-O).

t-Butyl [1α,2β,3β,7α,10α,11α]-9-benzyloxycarbonyl-10,11-dihydroxy-3-phenylacetamido-8-oxa-4-oxo-5,6,9-triazatricyclo[5.2.2.0^{2,5}]undecane-6-carboxylate 4c. - Same procedure as for **4a** : **2d** (625 mg ; 1.17mmol), THF/t-BuOH 1:1 (15 ml), NMO (237 mg ; 1.75 mmol), catalytic OsO_4 soln. (1.2 ml). After 4 h the reaction was complete, the crude residue was separated by FC(AcOEt) which gave **4c** (630 mg, 95 %) as colourless crystals. M.p. 145-150 °C (AcOEt/cyclohexane). IR(KBr) : 3400(br), 3325, 3028, 2975, 1785, 1740, 1660, 1530, 1491, 1450, 1369, 1320(br), 1257, 1153. ^{1}H-NMR (250 MHz, $CDCl_3$, 297 K) : 7.31 (m, 10*H* Ph) ; 7.02 (s(br), H-N) ; 5.84 (s(br), H-C(7)) ; 5.17 (s, O-CH_2) ; 4.99 (t, J=1.8, H-C(1)) ; 4.92 (m, H-C(3)) ; 4.55 (s(br), H-O) ; 4.13 (dd, J=8.0, 1.8, H-C(10)) ; 4.06 (s(br), H-O) ; 3.98 (t, J=1.8, H-C(2)) ; 3.96 (dd, J=8.0, 0.9, H-C(11)) ; 3.56 (s,O=C-CH_2 Ph) ; 1.43 (s, C(CH_3)$_3$). Anal. calcd. for $C_{28}H_{32}N_4O_9$ (568.54) : C 59.15, H 5.65, N 9.85 ; found : C 58.9, H 5.8, N 9.6.

Methyl [1α,2β,3β,7α,10α,11α]-9-benzyloxycarbonyl-10,11-*O,O*-isopropylidene-3-methyl-8-oxa-4-oxo-5,6,9-triazatricyclo[5.2.2.0^{2,5}]undecane-6-carboxylate 5a. - A soln. of **4a** (345 mg ; 0.85 mmol) in 2,2-dimethoxypropane (DMP)/MeOH 12:2 (14 ml) containing some Amberlyst 15 beads was stirred overnight at r.t.. After filtration and evaporation of the solvents the residue was recrystallised in CH_2Cl_2/cyclohexane and gave **5a** (331 mg ; 79%) as colourless crystals. M.p. 170°C. IR(KBr) : 2920, 2843, 1778(β-lactam), 1732 and 1700(carbamate), 1448, 1414, 1380, 1315(br), 1279(br), 1210, 1167, 1122, 1085, 1079. ^{1}H-NMR (80 MHz, $CDCl_3$) : 7.36 (*s*, 5*H* Ph) ; 6.00 (*s(br)*, H-C(7)) ; 5.21 (*s*, CH_2 Ph) ; 5.03 (*m*, H-C(1)) ; 4.43 (s(br), H-C(10) and H-C(11)) ; 3.95 (t, J=1.6, H-C(2)) ; 3.81 (s, O-CH_3) ; 2.99 (qdm), J=7.2, 1.6, H-C(3)) ; 1.47 (d, J=7.2, CH_3-C(3)) ; 1.42 and 1.32 (2*s*, 2xCH_3 acetonide). ^{13}C-NMR (20.1 MHz, $CDCl_3$) : 167.4 (s sext, C(4)) ; 154.8 (st, O=*C*-O-Bn) ; 154.2 (sq ; O=*C*-O-CH_3) ; 135.3 (sm, C(s) Ph) ; 129.2 (dm, ^{1}J=160, C(m)Ph) ; 128.1 (dm, ^{1}J=160, C(p) and C(o) Ph) ; 110.9 (s sept, *C*(CH_3)$_2$) ; 84.1 (dm, ^{1}J=169, C(7)) ; 71.01 (dm, ^{1}J=157, C(11)) ; 67.9 (tm, ^{1}J=148, O-*C*H_2-Ph) ; 67.7 (dm, ^{1}J=154, C(10)) ; 63.6 (dm, ^{1}J=160, C(2)) ; 56.8 (dm, ^{1}J=147, C(1)) ; 54.2 (qs, J=148, O-*C*H_3) ; 45.5 (dm, ^{1}J=140, C(3)) ; 25.0 (qq, J=128, CH_3 aceton.) ; 23.6 (qq, ^{1}J=128, CH_3 aceton.) ; 13.0 (qt, J=129, *C*H_3-C(3)). Anal. calc. for $C_{21}H_{25}N_3O_8$ + 0.5 C_6H_{12} (489.51) : C 58.88, H 6.38, N 8.58 ; found : C 59.0, H 6.7, N 8.1.

Methyl [1α,2β,7α,10α,11α]-9-benzyloxycarbonyl-10,11-*O,O*-isopropylidene-8-oxa-4-oxo-5,6,9-triaza-tricyclo[5.2.2.0^{2,5}]undecane-6-carboxylate 5b. - Same procedure as for **5a** : **4b** (557 mg ; 1.41 mmol), DMP/MeOH 5:2 (14 ml). After recrystallisation the crude residue gave **5b** (575 mg ; 93 %) as colourless crystals. M.p. 165 °C (CH_2Cl_2/Ether). IR(KBr) : 3040, 2994, 2958, 2923, 1777 (C=O β-lactam), 1752 and 1711 (C=O carbamates), 1449, 1410, 1383, 1359, 1331, 1318, 1303, 1279, 1248, 1213, 1156, 1130, 1093, 1063, 1030, 975, 968, 897, 867, 832, 768, 757, 742, 733. ^{1}H-NMR (80 MHz, C_6D_6) : 7.20 (m, 5*H* Ph) ; 6.01 (d, J=1.2, H-C(7)) ; 5.15 (s, CH_2Ph) ; 4.85 (dd, J=2.1, 1.6, H-C(1)) ; 4.30 (dd, J=8.0, 1.2, H-C(11)) ; 4.14 (dd, J=8.0, 2.1, H-C(10)) ; 3.82 (ddd, J=5.2, 2.2, 1.6, H-C(2)) ; 3.26 (s, O-CH_3) ; 2.18 (dd, J=15.2, 5.2, Hα-C(3)) ; 1.75 (dd, J=15.2, 2.2, Hβ-C(3)) ; 1.44 (s(br), CH_3 acet.) ; 1.04 (s(br), CH_3 acet.). ^{13}C-NMR (20.1 MHz, $CDCl_3$) : 164.9 (sq, C(4)) ; 154.8 (st, C=*C*-OCH_2Bn) ; 154.2 (sq, O=*C*-OCH_3) ; 135.5 (sm, *C*(s) Ph) ; 128.3 (dm, ^{1}J=160, C(m) Ph) ; 128.1 (dm, J=160, C(p)Ph) ; 128.1 (dm, ^{1}J=160, C(o) Ph) . 111.1 (s sept, *C*(CH_3)$_2$) ; 84.3 (dm, J=170, C(7)) ; 71.1 (dt, ^{1}J=155, C(11)) ; 67.9 (tm, ^{1}J=148, *C*H_2 Ph) ; 67.3 (dm, ^{1}J=152, C(10)) ; 57.1 (dm, ^{1}J=146, C(1)) ; 56.2 (dm, ^{1}J=159, C(2)) ; 54.2 (qs, ^{1}J=148, O*C*H_3) ; 37.3 (tm, ^{1}J=143, C(3)) ; 25.2 (qq, ^{1}J=127, *C*H_3 acet.) ; 23.8 (qq, J=126, *C*H_3 acet.). Anal. calc. for

$C_{20}H_{23}N_3O_8$ (433.38) : C 55.43, H 5.35, N 9.70 ; found : C 55.5, H 5.2, N 9.4.

t-Butyl [1α,2β,3β,7α,10α,11α]-9-benzyloxycarbony-10,11-*O,O*-isopropylidene-3-phenylacetamido-8-oxa-4-oxo-5,6,9-triazacyclo[5.2.2.0^{2,5}] undecane-6-carboxylate 5c. - Same procedure as for **5a** : **4c** (473 mg ; 0.84 mmol), DMP (10 ml). The crude residue was separated by FC(AcOEt/cyclohexane 1:1) and gave **5c** (315 mg, 62 %) as colourless crystals. M.p. 163 °C (CH_2Cl_2/diisopropyl ether). IR(KBr) : 3380, 3070, 3037, 2986, 2943, 1795 and 1777(β-lactam), 1735(carbamate), 1706, 1672, 1539, 1497, 1456, 1400, 1384, 1373, 1323, 1306, 1271, 1257, 1214, 1154, 1123, 1100, 1072, 1031, 975, 877, 848, 815, 755, 730, 698. ^{1}H-NMR (250 MHz, $CDCl_3$, 323 K) : 7.33 (m, 10 *H* Ph) ; 6.20 (s(br), N-H) ; 5.86 (s(br), H-C7)) ; 5.18 (s, C*H*$_2$-Ph) ; 5.15 (dd, J=1.8, 1.6, H-C(1)) ; 4.97 (d(br), J=7.2, H-C(3)) ; 4.44 (dd, J=8.1, 1.8, H-C(10)) ; 4.35 (dd, J=8.1, 1.3, H-C(11)) ; 4.02 (t, J=1.6, H-C(2)) ; 3.61 (s, O=C-C*H*$_2$-Ph) ; 1.45 (s, C(C*H*$_3$)$_3$) ; 1.41 (s, C*H*$_3$ aceton.) ; 13.2 (s, CH_3 aceton). ^{13}C-NMR (62.9 MHz, $CDCl_3$, 323 K) : 171.4 (stt, NH-*C*=O) ; 162.7 (sm, C(4)) ; 154.6 (st, O=*C*-O-CH_2Ph) ; 152.2 (s, O=*C*-O-tBu) ; 135.5 (sm, C(s) O-CH_2*Ph*) ; 134.2 (s quint, C(s) O-C-CH_2*Ph*) ; 123.2 (d quint, ^{1}J=158, C(o) O-C-CH_2*Ph*) ; 128.5 (dd, ^{1}J=160, C(m) O-C-CH_2*Ph*) ; 128.2 (dm, ^{1}J=161, C(m) O-CH_2-*Ph*) ; 128.0 (dm, ^{1}J=160, C(p), O-CH_2*Ph*) ; 128.0 (dm, J=160, C(o) O-CH_2*Ph*) ; 126.9 (dt, ^{1}J=160, C(p) O-C-CH_2*Ph*) ; 111.0 (s sept, *C*(CH$_3$)$_2$) ; 84.6 (sm, *C*(CH$_3$)$_3$) ; 84.3 (dm, ^{1}J=173, C(7)) ; 71.1 (dt, ^{1}J=156, C(11)) ; 67.8 (dm, ^{1}J=154, C(10)) ; 67.7 (tt, ^{1}J=148, O-*C*H$_2$Ph) ; 64.8 (d, ^{1}J=162, C(2)) ; 56.7 (d(br), ^{1}J=152, C(3)) ; 56.6 (dm, ^{1}J=148, C(1)) ; 42.5 (tm, ^{1}J=129, O-C-*C*H$_2$ Ph) ; 27.7 (q ssept, ^{1}J=127, C(*C*H$_3$)$_3$; 25.0 (qq, ^{1}J=127, C(*C*H$_3$)) ; 23.7 (qq, ^{1}J=127, C(*C*H$_3$)). Anal. calcd. for $C_{31}H_{36}N_4O_9$ + 0.5 $C_6H_{14}O$ (659.71) : C 61.90, H 6.57, H 8.49 ; found : C 61.7, H 6.5, H 8.5.

Methyl [2'α,3'β,4'β(2S*)]-2-[3',4'-dihydroxypyrrolidine-2'-yl]-4-oxoazetidine-1-carbamate hydrochloride 6a.HCl. - A stirred solution of **4b** (629 mg ; 1.61 mmol) in 96 % EtOH (15 ml) containing some 5 % Pd/C was put under H_2 pressure (1 atm) for 4 h at 45 °C. After filtration over Celite, followed by rinsing with AcOEt, the soln. was evaporated to dryness and the residue purified by percolation over an acidic Amberlist CG-120 resin (H_2O followed by 2N NH_4OH). After evaporation of NH_3 under *vac.* over a dessicator containing conc. H_2SO_4, the remaining soln. was neutralised with 1N HCl to *ca.* pH 6.8 and then submitted to liophilisation which leads to **6a•HCl** (319 mg ; 68 %) as a colourless foam. M.p. 230-250 °C dec. IR(KBr) : 3450(br), 1765(β-lactam), 1728(carbamate), 1660(br). ^{1}H-NMR (250 MHz, D_2O, 297K, ref. TSPA) : 4.42 (ddd, J=5.8, 5.4, 2.6, H-C(2)) ; 4.38 (ddd, J=4.0, 3.6, 2.0, H-C(4')) ; 4.32 (dd, J=8.0, 4.0, H-C(3')) ; 3.86 (dd, J=8.0, 5.8, H-C(2')) ; 3.79 (s, O-C*H*$_3$) ; 3.50 (dd, J=12.8, 3.6, H-C(5')) ; 3.41 (dd, J=12.8, 2.0, H-C(5')) ; 3.25 (dd, J=15.4, 5.4, Hα-C(3)) ; 2.90 (dd, J=15.4, 2.6, Hβ-C(3)). ^{13}C-NMR (D_2O, 62.9 MHz, 297K, ref dioxane 67.8 ppm) ; 171.1 (s, C(4)) ; 158.5 (s, O=*C*-O-CH$_3$) ; 74.3 (d, C(3')) ; 70.9 (d, C(4')) ; 61.4 (d, C(2')) ; 57.3 (q, O-*C*H$_3$) ; 55.1 (d, C(2')) ; 51.4 (t, C(5')) ; 38.1 (t, C(3)).

Methyl [2'α,3'β,4'β(2S*,3R*)]-2-[3',4',*O,O*-isopropylidene-pyrrolidine-2'-yl]-3-methyl-4-oxoazetidine-1-carbamate 7a and methyl [2'a,3'b,4'b (2S*, 3R*)]-2-[1'-benzyloxycarbonyl-3',4'-*O,O*-isopropylidene pyrrolidine-2'-yl]-3-methyl-4-oxoazetidine-1-carbamate 7b. - A stirred solution of **5a** (1.0 g ; 2.05 mmol) in 96 % EtOH containing some 5 % Pd/C (40 mg) was put under H_2 (1 atm) at 50 °C for 5h. After filtration over Celite, the solvent was evaporated to give crude **7a**. **7a** was treated

with a saturated aqueous soln. of $NaHCO_3$ (10 ml) and with benzylchloroformate (0.65 ml ; 4.1 mmol) for 2 h at r.t. After acidification with HCl to pH 2, the soln. was successively extracted with AcOEt (10 ml) and with CH_2Cl_2 (10 ml). The combined organic solns were dried over $MgSO_4$ and evaporated to give a residue which was crystallised : **7b** (682 mg ; 77 %) as colourless crystals.

Pyrrolidine 7a : colourless oil. IR ($CHCl_3$) : 1787 (C=O β-lactam), 1739 (C=O carbamate). ^{1}H-NMR ($CDCl_3$, 80 MHz) : 7.30 (s(br) ; N(H)) ; 4.74 (ddd, J=6.0, 4.0, 2.0, H-C(4')) ; 4.51 (dd, J=6.0, 2.0, H-C(3')) ; 3.77 (s, O-CH_3) ; 3.45 (dd, J=7.6, 2.2, H-C(4)) ; 3.28 (dd, J=7.6, 2.0, H-C(2')) ; 3.07 (dd, J=13.2, 4.0, Hβ-C(5')) ; 2.98 (dd, J=13.2, 2.0, Hα-C(5')) ; 2.91 (qd, J=7.4, 2.2, H-C(3)) ; 2.45 (s, NH) ; 1.36 (d, J=7.4, CH_3-C(3)) 1.31 and 1.48 (2s, 2 CH_3 acetonide).

Pyrrolidine 7b : Colourless crystals. M.p. 164 °C. IR(KBr) : 3182(br), 2980, 1772(β-lactam), 1743 and 1732(carbamates), 1696, 1522, 1452, 1416, 1281, 1252, 1221, 1157, 1100. ^{1}H-NMR ($CDCl_3$, 80 MHz, 328 K) : 7.32 (s, Ph) ; 7.30 (s(br), N(H)) ; 5.17 and 5.11 (d(AB), J=12.5, O-CH_2-Ph) ; 4.72 (ddd, J=5.8, 5.0, 1.5, H-C(4')) ; 4.53 (dd, J=5.8, 1.5, H-C(3')) ; 4.33 (dd, J=4.0, 1.5, H-C(2')) ; 4.02 (dd, J=13.0, 1.5, Hα-C(5')) ; 3.75 (dd, J=4.0, 1.8, H-C(2)) ; 3.74 (s, O-CH_3) ; 3.48 (dd, J=13.0, 5.0, Hβ-C(5')) ; 2.68 (qd, J=7.2, 1.8, H-C(3)) ; 1.42 and 1.31 (2q, J=0.5, CH_3 acetonide) ; 1.32 (d, J=7.2, CH_3-C(3)) ; ^{13}C-NMR ($CDCl_3$, 20.1 MHz) : 170.3 (sm, C(4)) ; 155.4 (st, O=*C*-O-CH_2Ph) ; 155.3 (O=*C*-OCH_3) ; 136.0 (sm, C(s) Ph) ; 128.2 (dm, ^{1}J=159, C(m) Ph) ; 127.8 (dm, ^{1}J=160, C(p) Ph) ; 127.3 (dm, ^{1}J=160, C(o) Ph) ; 112.1 (sm, *C*$(CH_3)_2$) ; 80.7 (dm, ^{1}J=153, C(3')) ; 78.7 (dm, ^{1}J=154, C(4')) ; 67.1 (tm, ^{1}J=148, O-*C*H_2-Ph) ; 64.1 (dm, ^{1}J=152, C(2)) ; 64.0 (dm, ^{1}J=148, C(2')) ; 52.7 (qs, ^{1}J=146, O-*C*H_3) ; 52.5 (tm, ^{1}J=143, C(5')) ; 44.2 (dm, ^{1}J=138, C(3)) ; 26.7 and 24.7 (2qq, ^{1}J=126, C(*C*$H_3)_2$) ; 12.2 (qt, ^{1}J=128, *C*H_3-C(3)). Anal. calc. for $C_{21}H_{27}N_3O_7$ (433.47) : C 58.20, H 6.28, N 9.69 ; found : C 58.0, H 6.3, N 9.8.

t-Butyl [2'α,3'β,4'β(2R*,3R*)]-2-[1'-benzyloxycarbonyl-3'-4'-*O*,*O*-isopropylidene pyrrolidine-2'-yl]-4-oxo-3-phenylacetamidoazetidine-1-carbamate 7d. - Same procedure as for **7b** : **5c** (822 mg, 1.35 mmol), 96 % EtOH (30 ml), 5 % Pd/C (100 mg). After 6 h crude **7c** was isolated and treated with benzylchloroformate (1 ml ; 8.55 mmol) in the presence of $NaHCO_3$. FC of the crude residue (AcOEt/cyclohexane 4:6) gave **7d** (695 mg ; 86 %) as a colourless resin. IR(KBr) : 3320(br), 2994, 2938, 1799(β-lactam), 1736(carbamate), 1690, 1498, 1457, 1418, 1371, 1249, 1216, 1160, 1125, 1060. ^{1}H-NMR ($CDCl_3$, 250 MHz, 293 K) : 7.49 (s(br), H-N) ; 7.33-7.22 (m, two Ph) ; 6.79 (s(br) ; H-N amide) ; 5.16 and 5.12 (d(AB), J=12.6, O-CH_2-Ph) ; 5.00 (dd, J=6.0, 4.7, H-C(4')) ; 4.58 (dd, J=6.0, 1.2, H-C(3')) ; 4.47 (d(br), J=7.0, H-C(3)) ; 4.32 (t, J=1.8, H-C(2)) ; 4.09 (d(br), J=13.4, H-C(5'α)) ; 3.82 (m, H-C(2')) ; 3.75 (dd, J=13.4, 4.7, H-C(5'β)) ; 3.57 (s, CH_2-Ph) ; 1.45 (s, C(C$H_3)_3$) ; 1.42 and 1.29 (2s, C(C$H_3)_2$). ^{13}C-NMR ($CDCl_3$, 62.9 MHz, 297 K) : 171.9 (sm, O=*C*-CH_2 Ph) ; 165.6 (sm, C(4)) ; 156.3 (s(br), O=*C*-O-CH_2 Ph) ; 153.9 (sd, O=*C*-O tBu) ; 135.9 (sm, C(s) Ph carbamate) ; 134.1 (s quint, C(s) Ph amide) ; 129.0 (d quint, ^{1}J=158, C(o) Ph amide) ; 128.6 (dd, ^{1}J=160, C(m) Ph) ; 128.4 (dm, ^{1}J=160, C(m) Ph) ; 127.9 (dt, ^{1}J=160, C(p) Ph carb.) ; 127.1 (d quint, ^{1}J=160, C(o) Ph carb.) ; 127.0 (dm, ^{1}J=160, C(p) Ph amide) ; 112.0 (sm, *C*$(CH_3)_2$) ; 82.2 (sm, *C*$(CH_3)_3$) ; 81.6 (dt(br), ^{1}J=157, C(3')) ; 79.4 (dd(br), ^{1}J=159, C(4')) ; 67.4 (tt, ^{1}J=148, O-*C*H_2Ph) ; 66.4 (ds(br), ^{1}J=154, C(2)) ; 62.2 (ds(br), ^{1}J=144, C(2')) ; 54.9 (dm, ^{1}J=152, C(3)) ; 53.7 (tm, ^{1}J=143, C(5')) ; 42.7 (tt, ^{1}J=129, O=C-*C*H_2 Ph) ; 27.9 (q sept, ^{1}J=127, C(*C*$H_3)_3$) ; 26.9 and 24.7 (2qm, ^{1}J=129, C(*C*$H_3)_2$). Anal. calc. for $C_{31}H_{38}N_4O_8$ (594.65) : C 62.61, H 6.44, N 9.42 ; found : C 62.8, H 6.4, N 8.8.

Methyl [2'α,3'β,4'β(2S*,3R*)]-2-[1'-benzyloxycarbonyl-3',4'-dihydroxy-pyrrolidine-2'-yl]-3-methyl-4-oxoazetidine-1-carbamate 6c. - A soln. of **7b** (283 mg ; 0.64 mmol) in aq. 1N HCl/THF 6:5 (11 ml) was stirred at r.t. over 2 d. After evaporation of the solvents the residue was separated by FC(AcOEt) which leads to unreacted **7b** (85 mg ; 30 %) and **6c** (155 mg, 62 %) as colourless crystals. M.p. 110-130 °C (AcOEt/cyclohexane). IR(KBr) : 3400(br), 2945, 1768, (O=C β-lactam), 1724(br), 1680, 1492, 1445, 1410, 1347, 1246, 1137, 1086. ^{1}H-NMR ($CDCl_3$, 80 MHz) : 7.64 (s(br), H-N) ; 7.32 (s, Ph) ; 5.10 (s, O-C*H*$_2$ Ph) ; 4.14 (dd, J=4.0, 3.0, H-C(2')) ; 4.11 (dd, J=5.0, 3.0, H-C(3')) ; 4.01 (ddd, J=5.0, 4.8, 3.6, H-C(4')) ; 3.78 (dd, J=4.0, 2.6, H-C(2)) ; 3.71 (s, O-C*H*$_3$) ; 3.67 (dd, J=12.0, 3.6, H-C(5'α)) ; 3.56 (dd, J=12.0, 4.8, H-C(5'β)) ; 2.94 (qd, J=7.2, 2.6, H-C(3)) ; 2.93 (s(br), O-*H*) ; 1.28 (d, J=7.2, CH_3-C(3)). Anal. calc. for $C_{18}H_{23}N_3O_7$ (393.38) : C 54.96, H 5.89, N10.68 ; found : C 54.8, H 6.2, N 10.9.

Methyl [2'α,3'β,4'β(2S*,3R*)]-2-[3',4'-dihydroxypyrrolidine-2'-yl]-3-methyl-4-oxoazetidine-1-carbamate hydrochloride 6b HCl. - A stirred soln. of **6c** (99 mg, 0.25 mmol) in 96 % EtOH (5 ml) containing some 5 % Pd/C was put under H_2 (1 atm) at 45 °C for 2 h. After filtration over Celite and evaporation of the solvent, the crude residue was purified by percolation over acidic Amberlist CG-120 (H_2O followed by 2N NH_4OH). Then same procedure as for **6a•HCl** which leads after liophilisation to **6b•HCl** (55 mg ; 74 %) as a colourless foam. M.p. 195-200 °C. IR(KBr) : 3440(br), 3200, 1779 (O=C β-lactam), 1728 (O=C carbamates) , 1402, 1266, 1110, 1063. ^{1}H-NMR (D_{20}, 250 MHz, 303 K, ref HDO à 4.80 ppm) : 4.36 (ddd, J=4.0, 3.7, 1.6, H-C(4')) ; 4.30 (dd, J=8.6, 4.0, H-C(3')) ; 4.10 (dd, J=5.3, 2.6, H-C(2)) ; 3.87 (dd, J=8.6, 5.3, H-C(2')) ; 3.74 (s, O-C*H*$_3$) ; 3.30 (dd, J=13.0, 3.7, H-C(5'β)) ; 3.22 (dd, J=13.0, 1.6, H-C(5'α)) ; 3.16 (qd, J=7.4, 2.6, H-C(3)) ; 1.36 (d, J=7.4, C*H*$_3$-C(3)).

Methyl [1α,2β,3β,7α,10α,11α]-8-benzyloxycarbonyl-10,11-dihydroxy-3-methyl-9-oxa-4-oxo-5,6,8-triaza-tricyclo[5.2.2.0^{2,5}]undecane-6-carboxylate 8a.- Same procedure as for **4a** : **3b** (290 mg ; 0.78 mmol), THF/t-BuOH 1:1 (5 ml), NMO (157 mg ; 1.17 mmol), catalytic OsO_4 soln. (0.7 ml). FC of the crude residue (AcOEt) gave **8a** (304 mg ; 96 %) as a colourless resin. IR(KBr) : 3450(br), 2962, 2939, 1778 (C=O β-lactam), 1733, 1500, 1446, 1410, 1348, 1282, 1218, 1110, 1085, 1052. ^{1}H-NMR ($CDCl_3$, 80 MHz) : 7.35 (s, Ph) ; 6.43 (d, J=2.4 ; H-C(7)) ; 5.20 (s, O-C*H*$_2$Ph) ; 4.63 (d, J=1.0, H-C(1)) ; 4.28 (dd, J=7.6, 2.4, H-C(11)) ; 4.28 (s(br), H-O) ; 3.92 (dd, J=1.7, 1.0, H-C(2)) ; 3.89 (dm, J=7.6, H-C(10)) ; 3.65 (s, O-C*H*$_3$) ; 2.93 (qd, J=7.2, 1.7, H-C(3)) ; 1.42 (d, J=7.2, CH_3-C(3)).

Methyl [1α,2β,3β,7α,10α,11α]-8-benzyloxycarbonyl-10,11-*O*,*O*-isopropylidene-3-methyl-9-oxa-4-oxo-5,6,8-triazatricyclo[5.2.2.0^{2,5}]-undecane-6-carboxylate 8b. - Same procedure as for **5a** : **8a** (277 mg ; 0.68 mmol), DMP/MeOH 5:1 (12 ml). The crude was recrystallised to give **8b** (277 mg ; 77 %). M.p. 213-214 °C (CH_2Cl_2/iPr_2O). IR(KBr) : 3020, 2978, 2959, 2922, 1768, 1743,1697, 1446, 1406, 1347, 1280, 1242, 1210, 1163, 1138, 1084. ^{1}H-NMR ($CDCl_3$, 80 MHz) : 7.36 (s, Ph), 6.55 (d, ^{1}J=2.2, H-C(7)) ; 5.29 and 5.18 (d(AB), J=12.3, O-CH_2 Ph) ; 4.56 (t, J=1.2, H-C(1)) ; 4.56 (dd, J=7.9, 2.2, H-C(11)) ; 4.32 (dd, J=7.9, 1.2, H-C(10)) ; 3.99 (dd, J=1.7, 1.2, H-C(2)) ; 3.73 (s, O=C-O-C*H*$_3$) ; 2.91 (qdm, J=7.2, 1.7, H-C(3)) ; 1.48 (d, J=7.2, C*H*$_3$-C(3)) ; 1.42 and 1.32 (2s, C(CH_3)$_2$). Anal. calc. for $C_{21}H_{25}N_3O_8$ (447.40) : C 56.38, H 5.63, N 9.39 ; found : C 56.2, H 5.7, N 9.5.