REGIOSELECTIVITY OF 1,3-DIPOLAR CYCLOADDITION OF 3-OXIDOPYRIDINIUM BETAINES TO OLEFINS AND STEREOSELECTIVE SYNTHESIS OF 6-ALKYLOXY-5-OXA-9-AZATRICYCLO[5.2.1.$0^{4,8}$]DECAN-2-ONE DERIVATIVES

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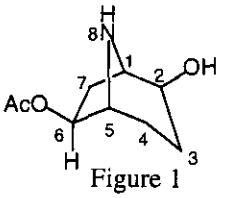
Abstract - A new method to obtain the four isomers of tropane skeleton by dipolar addition of 3-oxidopyridinium betaines to activated olefins is described, and a general synthetic strategy for tricyclic tropane homologues is also reported.

Bao Gong Teng A is an alkaloid isolated from the chinese herb, Erycibe obtusifolia.[1,2] This natural product showed antiglaucoma properties.[3] This molecule, presented in Figure 1, has a nortropane skeleton with a 6-*exo*-acetoxy group.[4] Its asymmetric synthesis was described,[5] but no pharmacological study concerning dia- and regioisomers was reported.

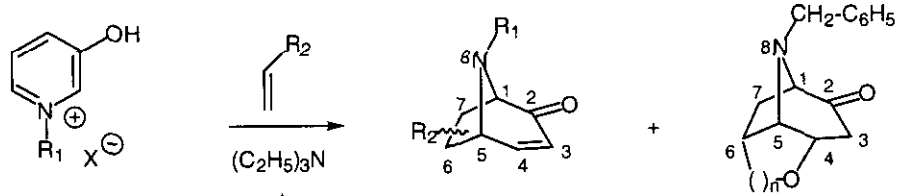


(-)

Figure 1

Moreover, tropane analogs have a propensity to bind to monoamine transporters, particularly the dopamine transporter.[6,7] Compounds with high pharmacological specificity for particular neurotransmitter transporters, as well as chemical stability and ability to carry radioactive atoms without loss of pharmacological activity or selectivity are of interest as research tools. So, we present here an original method to obtain the different isomers of azabicyclooctene structure from the main synthesis step to access to tropane skeleton : an 1,3-dipolar cycloaddition of dipolarophiles to pyridinium betaines. We describe also a new synthetic approach to access in one-pot reaction to tricyclic tropane homologues.

The 1,3-dipolar cycloaddition of pyridinium betaines is a well-known synthetic method which is largely used for preparing tropane derivatives. Particularly, the regioselective preparation of azabicyclo[3.2.1]oct-3-ene compounds is recognized as a very significant methodology, and reactions with different N-substituants and dipolarophiles were reported.[8] Although there are four conceivable products that could be formed by reaction of 1-methyl-3-pyridiniumolate with acrylonitrile, methyl acrylate, methyl vinyl ketone or methyl methacrylate, only the two diastereoisomers 6-*endo* and 6-*exo* were detected.[9] In a few cases, the 7-*endo* cycloadduct from 3-oxidopyridiniums with acrylonitrile was described,[10-12] but the formation of the 7-*exo* compound has never been demonstrated. In this regard, we realized the cycloaddition of N-benzyl (or -methyl)-3-hydroxypyridinium salts with different dipolarophiles (Scheme 1).



1a,b
a : $R_1 = CH_2\text{-}C_6H_5$
b : $R_1 = CH_3$

2a-f

3a,b
a : n = 1
b : n = 2

a : $R_1 = CH_2\text{-}C_6H_5$; $R_2 = CN$
b : $R_1 = CH_2\text{-}C_6H_5$; $R_2 = CO_2CH_3$
c : $R_1 = CH_2\text{-}C_6H_5$; $R_2 = CH_2OH$
d : $R_1 = CH_2\text{-}C_6H_5$; $R_2 = C_2H_4OH$
e : $R_1 = CH_3$; $R_2 = CN$
f : $R_1 = CH_3$; $R_2 = CO_2CH_3$

Scheme 1

In the ^{1}H-NMR spectrum, we observe eight aromatic signals (except the phenyl group) : four doublets and four doublets of doublets (Figure 2). For the product (**2a**) (Scheme 1), an analytical HPLC confirms the formation of four compounds. We have demonstrated the formation of the 6,7-*endo* and 6,7-*exo* isomers by ^{1}H and ^{13}C NMR spectral data.

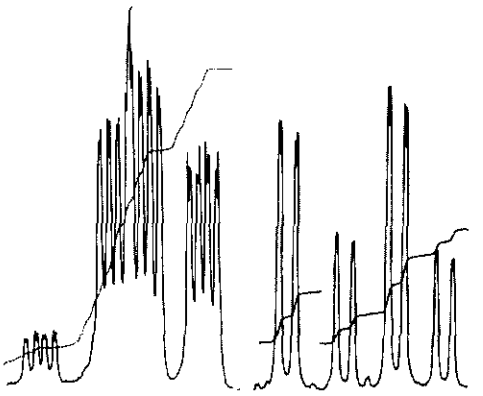


Figure 2

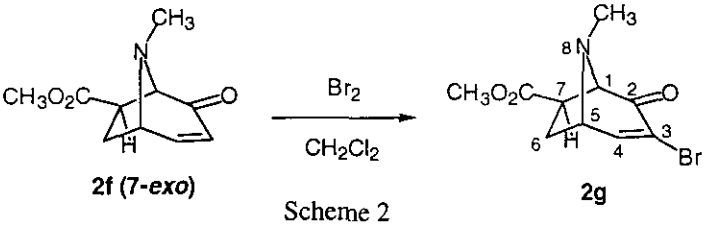
For all compounds (Scheme 1), the different stereoisomers are separated by chromatography on a silica gel column : the eluent is a mixture of ethyl acetate and hexanes. The proportion of each isomer is based on the

integral's intensity of the ethylenic protons. Results are summarized in Table 1. In a general way, H-5 is a doublet ($J_{4,5}$ = 5 Hz) for the 6-*exo* structure. For the 7-*exo* compound, H-1 appears as a singlet. For both 6,7-*endo* isomers, the respective protons 7,6$_{exo}$ are doublet of doublet of doublet. Still the coupling constant between H-1 and H-7$_{exo}$ is 8 Hz, while it is 6 Hz between H-5 and H-6$_{exo}$.

Entry / ABO[1]	6-*endo*	6-*exo*	7-*endo*	7-*exo*	Eluent (v/v) $AcOC_2H_5/C_6H_{12}$
2a	4	4	1	1	7/3
2b[2]	4	4	1	2	-
2c	-	2	2	1	7/3
2d	-	2	1	1	7/3
2e[3]	2	2	1	1	7/3
2f[3]	4	5	1	4	9/1

Table 1. [1] ABO = azabicyclooctene. [2] The compounds (**2b**) were not separated. [3] Underlined compounds were not isolated.

So, treatment of the cycloadduct (**2f**) (7-*exo*) with bromine in methylene chloride[13] gives the 3-bromo derivative (**2g**) (Scheme 2) as crystallized product.



2f (7-*exo*) **2g**

Scheme 2

The racemic structure (Figure 3) of stereoisomer (**2g**) was established by X-Ray crystallography and confirmed that the ester group attached at C-7 is in exo configuration.

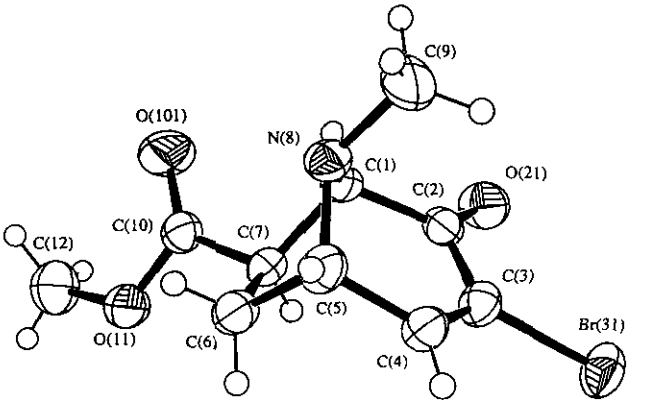
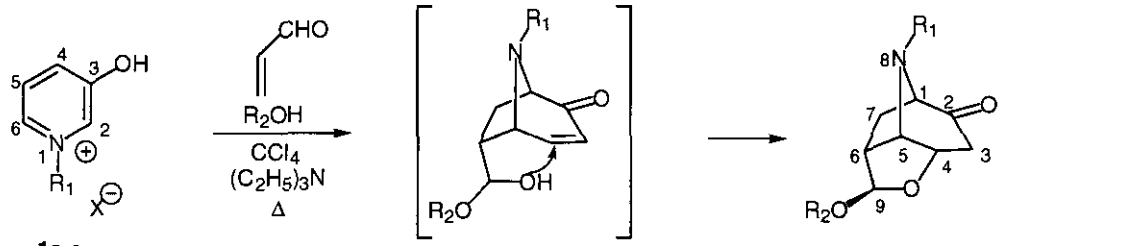


Figure 3. ORTEP diagram of compound (**2g**)

The compound (**3a**) (6-*endo*) is a tricyclic product in which the hydroxy group has added to the α,β-unsaturated carbonyl function.[14,15] The same reactivity is observed with 3-butenol for the 6-*endo*

isomer. The 7-*endo* bicyclic compound (**3b**) was isolated, then the sterically conceivable cyclisation from 7 to 4 position did not occur. We took the reactivity of the hydroxy group into account, and we initially investigated the possibility of generating *in situ* an hemiacetal intermediate which can spontaneously cyclise. So, we developed a novel stereoselective method of protecting the double bond of the azabicyclooctene. With acrolein and an alcohol, in the presence of triethylamine, the addition of pyridinium betaines (generated *in situ* from their salt) gives an hemiacetal intermediate which is spontaneously cyclised to the corresponding 9-*exo* tricyclic compound (Scheme 3). The formation of the 9-*endo* isomer is not observed : it is disadvantageous from the steric standpoint. The *exo* configuration of the C-9 substituent is confirmed by the multiplicity of the H-9 proton signal. It appears as a singlet because it doesn't couple with H-6 : the dihedral angle H6-C6-C9-H9 is about 90°. With an alcohol functionalized by an halogeno or an ester group, acrolein reacts to produce the corresponding tricyclic cycloadduct as well.

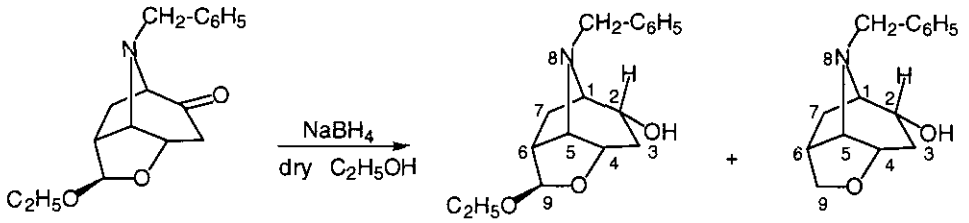


1a-c
a : $R_1 = CH_2\text{-}C_6H_5$
b : $R_1 = CH_3$
c : $R_1 = CH_2\text{-}C_6H_4F$

4a-h
a : $R_1 = CH_2\text{-}C_6H_5$; $R_2 = C_2H_5$
b : $R_1 = CH_2\text{-}C_6H_5$; $R_2 = CH(CH_3)_2$
c : $R_1 = CH_2\text{-}C_6H_5$; $R_2 = C_2H_4CH_2Cl$
d : $R_1 = CH_2\text{-}C_6H_5$; $R_2 = CH_2C(CH_3)_2CO_2CH_3$
e : $R_1 = CH_3$; $R_2 = C_2H_5$
f : $R_1 = CH_3$; $R_2 = CH(CH_3)_2$
g : $R_1 = CH_2\text{-}p\text{-}FC_6H_4$; $R_2 = C_2H_5$
h : $R_1 = CH_2\text{-}p\text{-}FC_6H_4$; $R_2 = CH(CH_3)_2$

Scheme 3

When the compound (**4a**) is reduced by sodium borohydride (Scheme 4), the 2-*endo* alcohol (**5a**) is obtained in 52% yield. The corresponding 2-*exo* alcohol is not formed, but the product (**5b**) with the cleaved ether functional group is isolated (yield : 5 %).



4a **5a** **5b**

Scheme 4

The formation of four isomers, and more particularly the 7-*endo*/*exo* isomers by 1,3-dipolar cycloaddition of pyridinium betaines was demonstrated. The 7-*exo* compound which has never been decribed was isolated, and its structure was confirmed by X-Ray crystallography. Moreover, a novel stereoselective synthesis of oxazatricyclic compounds was developed on the basis of hydroxy group's reactivity : 1,3-

dipolar cycloaddition of acrolein, in the presence of alcohol, gives a 6-alkyloxy-5-oxa-9-azatricyclo[5.2.1.$0^{4,8}$]decan-2-one compound.

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EXPERIMENTAL

General. TLC was carried out on Al_2O_3 (Neutral alumina 60 F_{254}, Merck, type E) or SiO_2 (Kieselgel 60 F_{254}), and the spots were located with UV light. Column chromatography was carried out on Al_2O_3 (Merck aluminium oxyde 90) and/or SiO_2 (Chromagel 60 ACC). Melting points were determined on a Kofler hot-plate melting point apparatus and are not corrected. IR spectra were obtained on a Beckman AccuLab 2 spectrometer. Absorption bands are expressed in cm^{-1} and only noteworthy absorptions are listed. ^1H and ^{13}C-NMR spectra were recorded on a Brüker AC-400 spectrometer working at 400 MHz (^1H-NMR) and 100 MHz (^{13}C-NMR). Chemical shifts are reported in ppm downfield δ from TMS. Coupling constants, J, are given in Hz. MS spectrometry was done on HEWLETT PACKARD 5985B - 5989A instruments. Elemental analyses were performed by Microanalytical Center, ENSCM, Montpellier (France). 1-Benzyl-3-hydroxypyridinium chloride (**1a**)[5] and 1-methyl-3-hydroxypyridinium iodide (**1b**)[16] are known compounds.

1-p-Fluorobenzyl-3-hydroxypyridinium chloride (1c) : 3-Hydroxypyridine (2 g, 21 mmol) was added to 4-fluorobenzyl chloride (15 mL, 125 mmol). The mixture was heated to 150 °C for 30 min. On cooling a precipitate was obtained. It was then filtered and washed with acetone (Yield : 70%) : mp 148-150°C (recrystallization solvent : acetonitrile); ^1H-NMR (400 MHz, DMSO-d_6) δ 5.87 (s, 2H, CH_2), 7.28 (t, 2H, $J_{Hortho,Hmeta} = J_{Hortho,F} = 8.5$ Hz, 2 x H_{rothoF}), 7.71 (dd, 2H, $J_{Hmeta,Hortho} = 8.5$ Hz, $J_{Hmeta,F} = 5.5$ Hz, 2 x H_{metaF}), 7.98 (dd, 1H, $J_{5,4} = 8.5$ Hz, $J_{5,6} = 6$ Hz, H-5), 8.17 (d, 1H, $J_{4,5} = 8.5$ Hz, H-4), 8.83 (d, 1H, $J_{6,5} = 6$ Hz, H-6), 8.93 (s, 1H, H-2) ; ^{13}C-NMR (100 MHz, DMSO-d_6) δ 62.08 (CH_2), 116.00 (d, $^2J_{CF} = 22$ Hz, 2 x C_{orthoF}), 128.74 (CH), 130.68 (C_{paraF}), 131.38 (d, $^3J_{CF} = 8$ Hz, 2 x C_{metaF}), 132.03 (CH), 131.73 (CH), 132.52 (CH), 157.51 (C-3), 162.49 (d, $^1J_{CF} = 246.5$ Hz, C-F) ; Anal. Calcd for $C_{12}H_{11}NOFCl$: C, 60.13 ; H, 4.59 ; N, 5.85. Found : C, 60.01 ; H, 4.57 ; N, 5.84.

Typical procedure (A) for synthesis of 8-azabicyclo[3.2.1]oct-3-ene (6,7-*endo*, 6,7-*exo*) compounds (**2a-f**) : 3-Hydroxypyridinium salt (50 mmol), triethylamine (10 g, 0.1 mol) and a small amount of hydroquinone in dipolarophile (0.5 mol) were heated under reflux. After cooling, the solvent was evaporated under reduced pressure. The mixture was diluted in water and extracted with CH_2Cl_2. The organic layer was separated and dried (Na_2SO_4). The solvent was evaporated under reduced pressure and the residual oil was chromatographed (silica gel, ethyl acetate / hexanes).

Compounds **(2a)** : These compounds are obtained from the typical procedure A with N-benzyl-3-hydroxypyridinium chloride and acrylonitrile (time reaction : 16 h ; Yield : 70%). The ratio of ethyl acetate / hexanes for the chromatography is 7/3 v/v.

8-Benzyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-*endo*-carbonitrile (2a) : oil ; Rf 0.83 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v) ; IR (CCl_4) ν_{max} 2250, 1695 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.95 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 6 Hz, H-7_{endo}), 2.86 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 10.5 Hz, $J_{7exo,1}$ = 8Hz, H-7_{exo}), 3.38 (ddd, 1H, $J_{6,7exo}$ =10.5 Hz, $J_{6,7endo}$ = 6 Hz, $J_{6,5}$ = 6 Hz, H-6), 3.65 (dd, 1H, $J_{1,7exo}$ = 8 Hz, $J_{1,3}$ = 1.5 Hz, H-1), 3.71 (AB pattern, 2H, J = 13 Hz, CH_2), 3.97 (dd, 1H, $J_{5,6}$ = 6 Hz, $J_{5,4}$ = 5 Hz, H-5), 6.32 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1.5 Hz, H-3), 7.07 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5 Hz, H-4), 7.20 (m, 2H, Ph), 7.32 (m, 3H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 29.82 (C-7), 30.49 (C-6), 52.99 (CH_2-Ph), 58.81 (C-5), 68.09 (C-1), 119.44 (CN), 127.64 (CH-Ph), 128.41 (2 x CH-Ph), 128.50 (2 x CH-Ph), 129.63 (C-3), 136.71 (C-Ph), 146.01 (C-4), 197.08 (C=O); MS m/z (relative intensity) 238 ($M^{+\bullet}$, 2.7), 209 (2.2), 147 (40.2), 91 (100) ; Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.63 ; H, 5.88 ; N, 11.76. Found : C, 75.93 ; H, 5.86 ; N, 11.81.

8-Benzyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-*exo*-carbonitrile (2a) : mp 92-94°C (recrystallization solvent : ethyl acetate/hexane, 7/3) ; Rf 0.72 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v) ; IR (KBr) ν_{max} 2250, 1695; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.10 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 9.5 Hz, H-7_{endo}), 2.71 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,1}$ = 8 Hz, $J_{7exo,6}$ = 3.5 Hz, H-7_{exo}), 2.97 (dd, 1H, $J_{6,7endo}$ = 9.5 Hz, $J_{6,7exo}$ = 3.5 Hz, H-6), 3.71 (dd, 1H, $J_{1,7exo}$ = 8 Hz, $J_{1,3}$ = 1.5 Hz, H-1), 3.83 (AB pattern, 2H, J = 13 Hz, CH_2), 4.02 (d, 1H, $J_{5,4}$ = 5 Hz, H-5), 6.12 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1.5 Hz, H-3), 6.88 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5 Hz, H-4), 7.32 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 30.28 (C-7), 31.24 (C-6), 52.04 (CH_2-Ph), 60.84 (C-5), 67.77 (C-1), 121.12 (CN), 127.52 (CH-Ph), 128.21 (2 x CH-Ph), 128.43 (2 x CH-Ph), 128.51 (C-3), 136.96 (C-Ph), 145.47 (C-4), 197.20 (C=O) ; MS m/z (relative intensity) 238 ($M^{+\bullet}$, 4.1), 209 (2.4), 147 (35.4), 91 (100) ; Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.63 ; H, 5.88 ; N, 11.76. Found : C, 75.48 ; H, 5.87 ; N, 11.78.

8-Benzyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-7-*endo*-carbonitrile (2a) : oil isolated as a pure product from a mixture of **2a** (6-*exo* and 7-*endo*) by chromatography (Al_2O_3 / CH_2Cl_2) ; Rf 0.64 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v), 0.55 (Al_2O_3 / CH_2Cl_2) ; IR (CCl_4) ν_{max} 2250, 1695 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.12 (dd, 1H, $J_{6endo,6exo}$ = 12.5 Hz, $J_{6endo,7}$ = 4 Hz, H-6_{endo}), 2.67 (ddd, 1H, $J_{6exo,6endo}$ = 12.5 Hz, $J_{6exo,7}$ = 11 Hz, $J_{6exo,5}$ = 6 Hz, H-6_{exo}), 3.54 (ddd, 1H, $J_{7,6exo}$ = 11 Hz, $J_{7,1}$ = 7.5 Hz, $J_{7,6endo}$ = 4 Hz, H-7), 3.69 (AB pattern, 2H, J = 13 Hz, CH_2), 3.78 (dd, 1H, $J_{5,6exo}$ = 6 Hz, $J_{5,4}$ = 5.5 Hz, H-5), 3.85 (dd, 1H, $J_{1,7}$ = 7.5 Hz, $J_{1,3}$ = 1.5 Hz, H-1), 6.21 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1.5 Hz, H-3), 7.14 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5.5 Hz, H-4), 7.30 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 28.05 (C-7), 34.64 (C-6), 53.71 (CH_2-Ph), 57.60 (C-5), 73.27 (C-1), 119.10 (CN), 127.19 (C-3), 127.86 (CH-Ph), 128.40 (2 x CH-Ph), 128.65 (2 x CH-Ph), 136.96 (C-Ph), 150.15 (C-4), 194.31 (C=O) ; MS

m/z (relative intensity) 238 ($M^{+\bullet}$, 4.9), 209 (1.2), 147 (25.9), 91 (100) ; Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.63 ; H, 5.88 ; N, 11.76. Found : C, 75.78 ; H, 5.90 ; N, 11.74.

8-Benzyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-7-*exo*-carbonitrile (2a) : oil ; Rf 0.62 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v) ; IR (CCl_4) ν_{max} 2250, 1695 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.30 (dd, 1H, $J_{6endo,6exo}$ = 12.5 Hz, $J_{6endo,7}$ = 9.5 Hz, H-6_{endo}), 2.55 (ddd, 1H, $J_{6exo,6endo}$ = 12.5 Hz, $J_{6exo,7}$ = 6 Hz, $J_{6exo,5}$ = 6 Hz, H-6_{exo}), 2.86 (dd, 1H, $J_{7,6endo}$ = 9.5 Hz, $J_{7,6exo}$ = 6 Hz, H-7), 3.81 (AB pattern, 2H, J = 13 Hz, CH_2), 3.88 (dd, 1H, $J_{5,6exo}$ = 6 Hz, $J_{5,4}$ = 5.5 Hz, H-5), 3.92 (d, 1H, $J_{1,3}$ = 1.5 Hz, H-1), 6.05 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1.5 Hz, H-3), 7.08 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5.5 Hz, H-4), 7.30 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 28.04 (C-7), 34.64 (C-6), 53.70 (CH_2-Ph), 58.11 (C-5), 73.24 (C-1), 121.01 (CN), 127.15 (C-3), 127.82 (CH-Ph), 128.64 (2 x CH-Ph), 128.74 (2 x CH-Ph), 136.95 (C-Ph), 150.92 (C-4), 194.49 (C=O) ; MS m/z (relative intensity) 238 ($M^{+\bullet}$, 4.9), 209 (1.5), 147 (27.8), 91 (100) ; Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.63 ; H, 5.88 ; N, 11.76. Found : C, 75.33 ; H, 5.90 ; N, 11.71.

Methyl 8-Benzyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6,7-*endo*- and -6,7-*exo*-carboxylate (2b) : These compounds are obtained from the typical procedure A with N-benzyl-3-hydroxypyridinium chloride and methyl acrylate (reaction time: 5 hours ; Yield : 78%). The different isomers were not separated ; Rf 0.80 (CH_2Cl_2 / Al_2O_3) ; IR ($CHCl_3$) ν_{max} 1730 (br) ; MS m/z (relative intensity) 271 ($M^{+\bullet}$, 12.9), 242 (15.1), 180 (100), 91 (100).

Compounds (3a) : These compounds are obtained from the typical procedure A with N-benzyl-3-hydroxypyridinium chloride and allyl alcohol (reaction time: 95 hours ; Yield : 70%). The ratio of ethyl acetate / hexanes for the chromatography is 7/3, v/v. A mixture of 6,7-*exo* compounds was obtained : they were separated by second chromatography (Al_2O_3 / CH_2Cl_2).

9-Benzyl-5-oxa-9-azatricyclo[5.2.1.0^{4,8}]decan-2-one (3a) : oil ; Rf 0.70 (SiO_2 / ethyl acetate/ hexanes, 7/3, v/v) ; IR (CCl_4) ν_{max} 1730 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.42 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 3 Hz, H-7_{endo}), 2.28 (dd, 1H, $J_{3endo,3exo}$ = 16 Hz, $J_{3endo,4}$ = 1 Hz, H-3_{endo}), 2.55 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 10.5 Hz, $J_{7exo,1}$ = 8.5 Hz, H-7_{exo}), 2.79 (dd, 1H, $J_{3exo,3endo}$ = 16 Hz, $J_{3exo,4}$ = 5 Hz, H-3_{exo}), 2.89-2.94 (m, 1H, H-6), 3.50 (d, 1H, $J_{1,7exo}$ = 8.5 Hz, H-1), 3.58 (AB pattern, 2H, J = 13 Hz, CH_2-Ph), 3.72-3.80 (m, 2H, 2 x H-9), 3.96 (m, 1H, H-5), 4.44 (ddd, 1H, $J_{4,5}$ = 6 Hz, $J_{4,3exo}$ = 5 Hz, $J_{4,3endo}$ = 1 Hz, H-4), 7.27-7.36 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 32.98 (C-7), 39.17 (C-6), 41.70 (C-3), 56.97 (CH_2-Ph), 68.85 (C-5), 70.80 (C-1 or C-4), 71.45 (C-9), 72.11 (C-1 or C-4), 127.31 (CH-Ph), 128.36 (2 x CH-Ph), 128.43 (2 x CH-Ph), 138.08 (C-Ph), 211.40 (C=O) ; MS m/z (relative intensity) 243 ($M^{+\bullet}$, 1), 215 (31.6), 152 (7.8), 91 (100) ; Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.07 ; H, 7.00 ; N, 5.76. Found : C, 73.92 ; H, 6.99 ; N, 5.77.

8-Benzyl-6-*exo*-(hydroxymethyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (2c) : : oil ; Rf 0.56 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v), 0.53 (Al_2O_3 / CH_2Cl_2); IR (CCl_4) ν_{max} 3620, 1690 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.83 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 9 Hz, H-7_{endo}), 2.24 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 11 Hz, $J_{7exo,1}$ = 8 Hz, H-7_{exo}), 2.34 (m, 1H, H-6), 3.59 (dd, 1H, $J_{1,7exo}$ = 8 Hz, $J_{1,3}$ = 1.5 Hz, H-1), 3.65-3.70 (m, 2H, CH_2OH), 3.78-3.86 (m, 3H, CH_2Ph, H-5), 6.13 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1.5 Hz, H-3), 6.94 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5 Hz, H-4), 7.23-7.36 (m, 5H, Ph); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.83 (C-7), 43.30 (C-6), 51.43 (CH_2-Ph), 60.43 (C-5), 65.86 (CH_2OH), 67.82 (C-1), 127.42 (C-3 or CH-Ph), 128.49 (C-3 or CH-Ph), 128.57 (4 x CH-Ph), 138.57 (C-Ph), 147.16 (C-4), 199.68 (C=O) ; MS m/z (relative intensity) 244 ($M^{+\bullet}$+1, 5.8), 215 (27.7), 152 (54.3), 91 (100) ; Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.07 ; H, 7.00 ; N, 5.76. Found : C, 73.78 ; H, 7.02 ; N, 5.74.

8-Benzyl-7-*exo*-(hydroxymethyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (2c) : oil ; Rf 0.55 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v), 0.29 (Al_2O_3 / CH_2Cl_2); IR (CCl_4) ν_{max} 3630, 1685 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.99 (dd, 1H, $J_{6endo,6exo}$ = 12 Hz, $J_{6endo,7}$ = 9 Hz, H-6_{endo}), 2.09 (m, 1H, H-6_{exo}), 2.23 (d, 1H, $J_{7,6endo}$ = 9 Hz, H-7), 3.02 (m, 1H, OH), 3.73-3.78 (m, 2H), 3.82-3.90 (m, 3H), 6.16 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1.5 Hz, H-3), 7.06 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5 Hz, H-4), 7.26-7.38 (m, 5H, Ph); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 32.88 (C-6), 40.29 (C-7), 51.87 (CH_2-Ph), 56.92 (C-5), 65.88 (C-9), 72.03 (C-1), 127.26 (C-3 or CH-Ph), 127.50 (C-3 or CH-Ph), 128.57 (2 x CH-Ph), 128.61 (2 x CH-Ph), 137.91 (C-Ph), 150.44 (C-4), 197.17 (C=O) ; MS m/z (relative intensity) 244 ($M^{+\bullet}$+1, 6.9), 215 (18.6), 152 (39.2), 91 (100) ; Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.07 ; H, 7.00 ; N, 5.76. Found : C, 74.37 ; H, 7.02 ; N, 5.74.

8-Benzyl-7-*endo*-(hydroxymethyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (2c) : oil ; Rf 0.19 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v) ; IR (CCl_4) ν_{max} 3600, 1680 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.36 (dd, 1H, $J_{6endo,6exo}$ = 12.5 Hz, $J_{6endo,7}$ = 5 Hz, H-6_{endo}), 2.43 (ddd, 1H, $J_{6exo,6endo}$ = 12.5 Hz, $J_{6exo,7}$ = 10.5 Hz, $J_{6exo,5}$ = 6.5 Hz, H-6_{exo}), 2.59 (m, 1H, OH), 3.02 (m, 1H, H-7), 3.33 (m, 1H, CH_2OH), 3.54 (m, 1H, CH_2OH), 3.73-3.81 (m, 4H, CH_2Ph, H-1, H-5), 6.20 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1 Hz, H-3), 7.15 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5 Hz, H-4), 7.28-7.36 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 31.03 (C-6), 40.04 (C-7), 53.04 (CH_2-Ph), 57.32 (C-5), 63.42 (CH_2OH), 71.63 (C-1), 127.29 (C-3), 128.11 (CH-Ph), 128.39 (2 x CH-Ph), 128.59 (2 x CH-Ph), 137.74 (C-Ph), 152.48 (C-4), 199.11 (C=O) ; MS m/z (relative intensity) 244 ($M^{+\bullet}$+1, 6.4), 215 (16.4), 152 (39.8), 91 (100) ; Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.07 ; H, 7.00 ; N, 5.76. Found : C, 74.37 ; H, 6.97 ; N, 5.78.

Compounds **(3b)** : These compounds are obtained from the typical procedure A with N-benzyl-3-hydroxypyridinium chloride and 3-buten-1-ol (reaction time: 77 hours ; Yield : 62%). The ratio of ethyl acetate / hexanes for the chromatography is 7/3 (v/v).

10-Benzyl-5-oxa-10-azatricyclo[6.2.1.$0^{4,9}$]undecan-2-one (3b) : oil ; Rf 0.72 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v) ; IR (CCl_4) ν_{max} 1725 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.43 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 6 Hz, H-7_{endo}), 1.64 (m, 1H, H-9_{endo}), 1.96 (m, 1H, H-9_{exo}), 2.40 (dd, 1H, $J_{3endo,3exo}$ = 19 Hz, $J_{3endo,4}$ = 2.5 Hz, H-3_{endo}), 2.57 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 11 Hz, $J_{7exo,1}$ = 8.5 Hz, H-7_{exo}), 2.74 (m, 1H, H-6), 2.97 (dd, $J_{3exo,3endo}$ = 19 Hz, $J_{3exo,4}$ = 10.5 Hz, H-3_{exo}), 3.33-3.57 (m, 4H, H-5, H-1, 2 x H-10), 3.73 (s, 2H, CH_2-Ph), 4.51 (ddd, 1H, $J_{4,3exo}$ = 10.5 Hz, $J_{4,5}$ = 8 Hz, $J_{4,3endo}$ = 2.5 Hz, H-4), 7.24-7.35 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 25.91 (C-9), 30.12 (C-6), 39.94 (C-7), 54.77 (CH_2OH), 54.87 (CH_2Ph), 57.80 (C-5), 67.85 (C-4), 69.45 (C-1), 127.28 (CH-Ph), 128.32 (2 x CH-Ph), 128.36 (2 x CH-Ph), 138.27 (C-Ph), 210.95 (C=O) ; MS m/z (relative intensity) 257 ($M^{+\bullet}$, 1.2), 229 (27), 166 (5.4), 91 (100) ; Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.71 ; H, 7.39 ; N, 5.45. Found : C, 75.01 ; H, 7.41 ; N, 5.43.

8-Benzyl-6-*exo*-(2-hydroxyethyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (2d) : oil ; Rf 0.34 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v) ; IR (CCl_4) ν_{max} 3630, 1680 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.78-1.89 (m, 3H, H-7_{endo}, 2 x H-9), 2.16 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,1}$ = 8 Hz, $J_{7exo,6}$ = 3.5 Hz, H-7_{exo}), 2.35-2.41 (m, 1H, H-6), 3.49 (d, 1H, $J_{5,4}$= 5 Hz, H-5), 3.57 (dd, 1H, $J_{1,7exo}$ = 8 Hz, $J_{1,3}$ = 1.5 Hz, H-1), 3.60-3.76 (m, 2H, CH_2OH), 3.76-3.85 (AB pattern, 2H, J = 13 Hz, CH_2-Ph), 6.11 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1.5 Hz, H-3), 6.97 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5 Hz, H-4), 7.24-7.35 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 29.82 (C-7), 37.21 (C-9), 39.57 (C-6), 51.86 (CH_2-Ph), 60.05 (CH_2OH), 61.73 (C-5), 68.41 (C-1), 126.99 (C-3 or CH-Ph), 127.48 (C-3 or CH-Ph), 128.56 (2 x CH-Ph), 128.71 (2 x CH-Ph), 137.76 (C-Ph), 148.58 (C-4), 198.56 (C=O) ; MS m/z (relative intensity) 258 ($M^{+\bullet}$+1, 3.2), 229 (7.8), 166 (28.5), 91 (100) ; Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.71 ; H, 7.39 ; N, 5.45. Found : C, 75.01 ; H, 7.36 ; N, 5.47.

8-Benzyl-7-*exo*-(2-hydroxyethyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (2d) : oil ; Rf 0.19 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v) ; IR (CCl_4) ν_{max} 3635, 1685 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.18-2.04 (m, 4H, H-6_{endo}, H-6_{exo}, 2 x H-9), 2.23 (m, 1H, H-7), 3.37 (s, 1H, H-1), 3.49-3.84 (m, 5H, H-5, CH_2Ph, CH_2OH), 6.10 (dd, 1H, $J_{3,4}$= 10 Hz, $J_{3,1}$= 1 Hz, H-3), 7.10 (dd, 1H, $J_{4,3}$= 10 Hz, $J_{4,5}$= 5 Hz, H-4), 7.25-7.36 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 34.78 (C-6 or C-9), 35.53 (C-7), 36.80 (C-6 or C-9), 52.07 (CH_2-Ph), 57.36 (C-5), 60.53 (CH_2OH), 73.53 (C-1), 127.06 (C-3 or CH-Ph), 127.51 (C-3 or CH-Ph), 128.60 (2 x CH-Ph), 128.68 (2 x CH-Ph), 137.92 (C-Ph), 149.24 (C-4), 198.56 (C=O) ; MS m/z (relative intensity) 258 ($M^{+\bullet}$+1, 3.8), 229 (5.1), 166 (24.2), 91 (100) ; Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.71 ; H, 7.39 ; N, 5.45. Found : C, 75.01 ; H, 7.36 ; N, 5.47.

8-Benzyl-7-*endo*-(2-hydroxyethyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (2d) : oil ; Rf 0.07 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v) ; IR (CCl_4) ν_{max} 3640, 1675 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.39 (dd, 1H, $J_{6endo,6exo}$ = 12.5 Hz, $J_{6endo,7}$= 4.5 Hz, H-6_{endo}), 1.44-1.56 (m, 2H, 2 x H-9), 2.11 (m, 1H, OH), 2.51 (ddd, 1H, $J_{6exo,6endo}$ = 12.5 Hz, $J_{6exo,7}$ = 10 Hz, $J_{6exo,5}$ = 7 Hz, H-6_{exo}), 2.80 (m, 1H, H-7), 3.55-3.71

(m, 4H, H-1, H-5, CH_2OH), 3.70-3.79 (AB pattern, 2H, J = 13 Hz, CH_2-Ph), 6.10 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1 Hz, H-3), 7.10 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5.5 Hz, H-4), 7.25-7.36 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 34.42 (C-7), 34.54 (C-6 or C-9), 35.30 (C-6 or C-9), 53.25 (CH_2-Ph), 57.33 (C-5), 61.85 (CH_2OH), 73.10 (C-1), 127.34 (C-3 or CH-Ph), 128.08 (C-3 or CH-Ph), 128.47 (2 x CH-Ph), 128.69 (2 x CH-Ph), 138.18 (C-Ph), 152.56 (C-4), 199.31 (C=O) ; MS m/z (relative intensity) 258 ($M^{+\bullet}$+1, 4.1), 229 (4.9), 166 (22.1), 91 (100) ; Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.71 ; H, 7.39 ; N, 5.45. Found : C, 75.41 ; H, 7.42 ; N, 5.43.

Compounds (2e) : These compounds are obtained from the typical procedure A with N-methyl-3-hydroxypyridinium iodide and acrylonitrile (reaction time: 20 hours ; Yield : 73%). The ratio of ethyl acetate / hexanes for the chromatography is 7/3 (v/v).

8-Methyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-*exo*-carbonitrile (2e) : mp 95-97°C (recrystallization solvent : CH_2Cl_2) ; Rf 0.50 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v) ; IR (KBr) ν_{max} 2240, 1680; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.09 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 9.5 Hz, H-7_{endo}), 2.52 (s, 3H, NCH_3), 2.70 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,1}$ = 8 Hz, $J_{7exo,6}$ = 3.5 Hz, H-7_{exo}), 2.98 (dd, 1H, $J_{6,7endo}$= 9.5 Hz, $J_{6,7exo}$= 3.5 Hz, H-6), 3.65 (d, 1H, $J_{1,7exo}$ = 8 Hz, H-1), 4.01 (d, 1H, $J_{5,4}$ = 5 Hz, H-5), 6.06 (d, 1H, $J_{3,4}$ = 10 Hz, H-3), 6.93 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5 Hz, H-4); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 30.53 (C-7), 31.65 (C-6), 35.73 (NCH_3), 63.81 (C-5), 69.79 (C-1), 121.34 (CN), 128.42 (C-3), 145.41 (C-4), 197.40 (C=O) ; MS m/z (relative intensity) 162 ($M^{+\bullet}$, 24.8), 133 (25.9), 81 (100) ; Anal. Calcd for $C_9H_{10}N_2O$: C, 66.67 ; H, 6.17 ; N, 17.28. Found : C, 66.53 ; H, 6.18 ; N, 17.31.

8-Methyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-7-*exo*-carbonitrile (2e) : oil ; Rf 0.42 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v) ; IR ($CHCl_3$) ν_{max} 2260, 1690 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.29 (dd, 1H, $J_{6endo,6exo}$ = 12.5 Hz, $J_{6endo,7}$ = 9.5 Hz, H-6_{endo}), 2.51 (s, 3H, NCH_3), 2.57 (ddd, 1H, $J_{6exo,6endo}$ = 12.5 Hz, $J_{6exo,5}$ = 6 Hz, $J_{6exo,7}$ = 5.5 Hz, H-6_{exo}), 2.83 (dd, 1H, $J_{7,6endo}$ = 9.5 Hz, $J_{7,6exo}$ = 5.5 Hz, H-7), 3.85 (s, 1H, H-1), 3.88 (dd, 1H, $J_{5,6}$ = 6 Hz, $J_{5,4}$ = 5.5 Hz, H-5), 6.00 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1 Hz, H-3), 7.09 (dd, 1H, $J_{4,3}$= 10 Hz, $J_{4,5}$= 5.5 Hz, H-4); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.92 (C-7), 34.38 (C-6), 37.17 (NCH_3), 60.58 (C-5), 75.17 (C-1), 121.09 (CN), 126.57 (C-3), 150.96 (C-4), 194.80 (C=O) ; MS m/z (relative intensity) 162 ($M^{+\bullet}$, 26.2), 133 (17.3), 81 (100) ; Anal. Calcd for $C_9H_{10}N_2O$: C, 66.67 ; H, 6.17 ; N, 17.28. Found : C, 66.94 ; H, 6.19 ; N, 17.21.

8-Methyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-*endo*-carbonitrile (2e) : oil ; Rf 0.27 (SiO_2 / ethyl acetate/hexanes, 7/3, v/v) ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.89 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 6 Hz, H-7_{endo}), 2.38 (s, 3H, NCH_3), 2.82 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 10.5 Hz, $J_{7exo,1}$ = 7.5 Hz, H-7_{exo}), 3.39 (td, 1H, $J_{6,7exo}$ = 10.5 Hz, $J_{6,5}$ = $J_{6,7endo}$ = 6 Hz, H-6), 3.55 (dd, 1H, $J_{1,7exo}$ = 7.5 Hz, $J_{1,3}$ = 1.5 Hz, H-1), 3.98 (dd, 1H, $J_{5,6}$ = 6 Hz, $J_{5,4}$ = 5 Hz, H-5), 6.22 (dd, 1H,

$J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1.5 Hz, H-3), 7.08 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5 Hz, H-4); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 29.96 (C-7), 30.59 (C-6), 36.42 (NCH_3), 61.52 (C-5), 70.11 (C-1), 119.54 (CN), 129.27 (C-3), 146.07 (C-4), 197.15 (C=O) ; MS m/z (relative intensity) 162 ($M^{+\bullet}$, 24.6), 133 (25.3), 81 (100) ; Anal. Calcd for $C_9H_{10}N_2O$: C, 66.67 ; H, 6.17 ; N, 17.28. Found : C, 66.82 ; H, 6.16 ; N, 17.24.

Compounds **(2f)** : These compounds are obtained from the typical procedure A with N-methyl-3-hydroxypyridinium iodide and methyl acrylate (reaction time: 24 hours ; Yield : 87%). The ratio of ethyl acetate / hexanes for the chromatography is 9/1 (v/v).

Methyl 8-Methyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-*exo*-carboxylate (2f) : oil ; Rf 0.54 (SiO_2 / ethyl acetate/hexanes, 9/1, v/v) ; IR (CCl_4) ν_{max} 1735, 1690 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.88 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 9.5 Hz, H-7_{endo}), 2.42 (s, 3H, NCH_3), 2.83 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,1}$ = 8 Hz, $J_{7exo,6}$ = 3.5 Hz, H-7_{exo}), 2.93 (dd, 1H, $J_{6,7endo}$ = 9.5 Hz, $J_{6,7exo}$ = 3.5 Hz, H-6), 3.53 (dd, 1H, $J_{1,7exo}$ = 8 Hz, $J_{1,3}$ = 1.5 Hz, H-1), 3.74 (s, 3H, OCH_3), 4.07 (d, 1H, $J_{5,4}$ = 5 Hz, H-5), 6.02 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1.5 Hz, H-3), 6.99 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5 Hz, H-4); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.90 (C-7), 35.33 (C-6), 47.23 (NCH_3), 52.43 (OCH_3), 62.55 (C-5), 70.17 (C-1), 127.43 (C-3), 147.27 (C-4), 183.14 ($C=O_{ester}$), 198.91 ($C=O_{ketone}$) ; MS m/z (relative intensity) 195 ($M^{+\bullet}$, 28.2), 167 (7.5), 82 (100) ; Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.54 ; H, 6.67 ; N, 7.18. Found : C, 61.79 ; H, 6.70 ; N, 7.15.

Methyl 8-Methyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-7-*exo*-carboxylate (2f) : oil ; Rf 0.41(SiO_2 / ethyl acetate/hexanes, 9/1, v/v) ; IR (CCl_4) ν_{max} 1740, 1690 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.10 (dd, 1H, $J_{6endo,6exo}$ = 12.5 Hz, $J_{6endo,7}$ = 9.5 Hz, H-6_{endo}), 2.42 (s, 3H, NCH_3), 2.53 (ddd, 1H, $J_{6exo,6endo}$ = 12.5 Hz, J = 6.5 Hz, $J_{6exo,7}$ = 6 Hz, H-6_{exo}), 2.79 (dd, 1H, $J_{7,6endo}$ = 9.5 Hz, $J_{7,6exo}$ = 6 Hz, H-7), 3.72 (s, 3H, OCH_3), 3.78 (m, 2H, H-1, H-5), 5.95 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1.5 Hz, H-3), 7.03 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5 Hz, H-4) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 32.42 (C-6), 36.43 (C-7), 43.21 (NCH_3), 52.40 (OCH_3), 60.53 (C-5), 73.67 (C-1), 126.14 (C-3), 150.39 (C-4), 173.14 ($C=O_{ester}$), 197.12 ($C=O_{ketone}$) ; MS m/z (relative intensity) 195 ($M^{+\bullet}$, 34.3), 167 (5.4), 82 (100) ; Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.54 ; H, 6.67 ; N, 7.18. Found : C, 61.78 ; H, 6.64 ; N, 7.21.

Methyl 8-Methyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-*endo*-carboxylate (2f) : oil ; Rf 0.24 (SiO_2 / ethyl acetate/hexanes, 9/1, v/v) ; IR (CCl_4) ν_{max} 1740, 1690 ; ^{1}H-NMR (400 MHz, $CDCl_3$) 1.98 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 6 Hz, H-7_{endo}), 2.38 (s, 3H, NCH_3), 2.60 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 10 Hz, $J_{7exo,1}$ = 7 Hz, H-7_{exo}), 3.49 (dd, 1H, $J_{1,7exo}$ = 10 Hz, $J_{1,3}$ = 1.5 Hz, H-1), 3.55 (ddd, 1H, $J_{6,7exo}$ = 10 Hz, $J_{6,7endo}$ = 6 Hz, $J_{6,5}$ = 5.5 Hz), 3.66 (s, 3H, OCH_3), 3.96 (dd, 1H, $J_{5,6}$ = 5.5 Hz, $J_{5,4}$ = 5 Hz, H-5), 6.04 (dd, 1H, $J_{3,4}$ = 10 Hz, $J_{3,1}$ = 1.5 Hz, H-3), 6.92 (dd, 1H, $J_{4,3}$ = 10 Hz, $J_{4,5}$ = 5 Hz, H-4) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 26.90 (C-7), 36.52 (C-6), 46.96 (NCH_3), 52.02 (OCH_3), 61.69 (C-5), 70.75 (C-1), 128.27 (C-3), 147.29 (C-4), 171.56 ($C=O_{ester}$), 198.06 ($C=O_{ketone}$) ; MS m/z (relative

intensity) 195 ($M^{+\bullet}$, 29.1), 167 (7.1), 82 (100) ; Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.54 ; H, 6.67 ; N, 7.18. Found : C, 61.42 ; H, 6.66 ; N, 7.19.

Methyl 3-Bromo-8-methyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-7-*exo*-carboxylate (2g) : Bromine (1.13 g, 5.79 mmol) in CH_2Cl_2 (10 mL) was added dropwise to the adduct (**2f**) (7-*exo*) (930 mg, 5.81 mmol) in CH_2Cl_2 (100 mL). The solution was stirred at rt for 17 h. The solution was then filtered, and the precipitate was dissolved in water. The solution was basified (Na_2CO_3), extracted with CH_2Cl_2 and the extract was dried (Na_2SO_4). The solvent was evaporated under reduced pressure, and the residual product was chromatographed (alumina, CH_2Cl_2). This product was crystallized in methylene chloride (460 mg, 29 %) ; mp 104-106 °C; Rf 0.51 (Al_2O_3 / CH_2Cl_2) ; IR (KBr) ν_{max} 1740, 1690 ; ^{1}H-NMR (400 MHz, $CDCl_3$) 2.18 (dd, 1H, $J_{6endo,6exo}$ = 13 Hz, $J_{6endo,7}$ = 9.5 Hz, H-6_{endo}), 2.45 (s, 3H, NCH_3), 2.51 (ddd, 1H, $J_{6exo,6endo}$ = 13 Hz, $J_{6exo,7}$ = 6.5 Hz, $J_{6exo,5}$ = 6 Hz, H-6_{exo}), 2.81 (dd, 1H, $J_{7,6endo}$ = 9.5 Hz, $J_{7,6exo}$ = 6.5 Hz, H-7), 3.73 (s, 3H, OCH_3), 3.83 (dd, 1H, $J_{5,6exo}$ = 6 Hz, $J_{5,4}$ = 5 Hz, H-5), 4.06 (s, 1H, H-1), 7.41 (d, 1H, $J_{4,5}$ = 5 Hz, H-4) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 32.65 (C-6), 36.21 (C-7), 43.04 (NCH_3), 52.66 (OCH_3), 62.69 (C-5), 73.31 (C-1), 120.45 (C-3), 150.67 (C-4), 172.26 ($C{=}O_{ester}$), 190.15 ($C{=}O_{ketone}$) ; Anal. Calcd for $C_{10}H_{12}NO_3Br$: C, 43.80 ; H, 4.38 ; N, 5.11. Found : C, 43.71 ; H, 4.36 ; N, 5.09 ; Single crystal X-Ray structure analyses (crystallyzed from CH_2Cl_2). Empirical formula : $C_{10}H_{12}NO_3Br$, molecular mass : 274.12 g.mol^{-1}, crystal size : 0.07 x 0.31 x 0.42 mm, monoclinic, $P2_1/c$ (n° 14), a= 10.084(1) Å, b= 8.623(4) Å, c= 12.945(2) Å, β= 107.46 (1)°, V= 1073.8(5) Å^3, T= 293 K, d_{calcd}= 1.696 g.cm^{-3}, μ= 3.78 mm^{-1}, F(000)= 552 e, Z= 4, λ= 0.71073 Å, 4707 measured reflections [+/-h, +h, +l], [sin θ/λ]max= 0.807 Å^{-1}, Empirical absorption correction *via* ψ scans, 2069 observed reflections [I>2σ(I)], 185 refined parameters, H atoms were refined in the final refinement by least squares, R= 0.045, R_ω= 0.047, maximal residual electron density 0.576 e.Å^{-3} (near Br 31) ; Leg. dessin : ORTEP drawing of $C_{10}H_{12}BrNO_3$ showing 50 % probability displacement ellipsoids ; Ref. dessin : M.N. Burnett and C.K. Johnson, ORTEP III, report ORNL-6895, Oak Ridge National laboratory, Tennesee, USA, 1996.

Typical procedure (B) for synthesis of oxazatricyclic compounds (**4a-h**) : 3-Hydroxypyridinium salt (10 mmol), alcohol (170 mmol) and acrolein (170 mmol) were heated under reflux. Triethylamine (10 g, 0.1 mol) was added and the mixture was refluxing for 1.5 h. After cooling, the solvent was evaporated under reduced pressure. The mixture was diluted in water and extracted with CH_2Cl_2. The organic layer was separated, dried (Na_2SO_4) and evaporated under reduced pressure. The residual oil was chromatographed (alumina, CH_2Cl_2) to give the corresponding tricyclic compound as colorless oil.

9-Benzyl-6-*exo*-ethoxy-5-oxa-9-azatricyclo[5.2.1.0^{4,8}]decan-2-one (4a) : This compound is obtained from the typical procedure B with 1-benzyl-3-hydroxypyridinium chloride and ethanol (Yield : 35%) ; Rf 0.76 (Al_2O_3 / CH_2Cl_2) ; IR (CCl_4) ν_{max} 1730 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.19 (t, 3H, J = 7 Hz, CH_3), 1.40 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 3 Hz, H-7_{endo}), 2.29 (dd, 1H, $J_{3endo,3exo}$ = 15.5 Hz, $J_{3endo,4}$ = 1.5 Hz, H-3_{endo}), 2.47 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 11 Hz, $J_{7exo,1}$ = 8.5 Hz, H-7_{exo}), 2.82 (dd, 1H, $J_{3exo,3endo}$ = 15.5 Hz, $J_{3exo,4}$ = 4 Hz, H-3_{exo}), 2.80-2.86 (m, 1H, H-6), 3.43-3.75 (m, 5H, OCH_2, CH_2Ph, H-1), 4.23 (ddd, 1H, $J_{5,4}$ = 8.5 Hz, $J_{5,6}$ = 6 Hz, $J_{5,1}$ = 1.5 Hz, H-5), 4.60 (ddd, 1H, $J_{4,5}$ = 8.5 Hz, $J_{4,3exo}$ = 4 Hz, $J_{4,3endo}$ = 1.5 Hz, H-4), 4.93 (s, 1H, H-9), 7.28-7.39 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 15.12 (CH_3), 29.88 (C-7), 41.02 (C-3), 44.95 (C-6), 57.11 (CH_2-Ph), 62.47 (OCH_2), 67.35 (C-5), 70.32 (C-1), 71.97 (C-4), 105.30 (C-9), 127.34 (CH-Ph), 128.39 (2 x CH-Ph), 128.46 (2 x CH-Ph), 138.10 (C-Ph), 210.77 (C=O) ; HRMS calcd for $C_{17}H_{22}NO_3$ (MH^+) : 288.16006. Found : 288.15982 ; Anal. Calcd for $C_{17}H_{21}NO_3$: C, 71.08 ; H, 7.32 ; N, 4.88. Found : C, 70.94 ; H, 7.31 ; N, 4.89.

9-Benzyl-6-*exo*-1-methylethoxy-5-oxa-9-azatricyclo[5.2.1.0^{4,8}]decan-2-one (4b) : This compound is obtained from the typical procedure B with 1-benzyl-3-hydroxypyridinium chloride and isopropanol (Yield : 30%) ; Rf 0.68 (Al_2O_3 / CH_2Cl_2) ; IR (CCl_4) ν_{max} 1730 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.15 (m, 6H, 2 x CH_3), 1.40 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 3.5 Hz, H-7_{endo}), 2.28 (dd, 1H, $J_{3endo,3exo}$ = 15.5 Hz, $J_{3endo,4}$ = 1.5 Hz, H-3_{endo}), 2.45 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 10.5 Hz, $J_{7exo,1}$ = 8.5 Hz, H-7_{exo}), 2.82 (dd, 1H, $J_{3exo,3endo}$ = 15.5 Hz, $J_{3exo,4}$ = 4 Hz, H-3_{exo}), 2.79-2.85 (m, 1H, H-6), 3.46-3.60 (m, 3H, CH_2Ph, H-1), 3.87 (m, 1H, $CH(CH_3)_2$), 4.21 (ddd, 1H, $J_{5,4}$ = 8 Hz, $J_{5,6}$ = 6 Hz, $J_{5,1}$ = 1.5 Hz, H-5), 4.56 (ddd, 1H, $J_{4,5}$ = 8 Hz, $J_{4,3exo}$ = 4 Hz, $J_{4,3endo}$ = 1.5 Hz, H-4), 5.00 (s, 1H, H-9), 7.27-7.35 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.61 (CH_3), 23.50 (CH_3), 29.87 (C-7), 40.93 (C-3), 45.14 (C-6), 57.07 (CH_2Ph), 67.48 (C-5 or $CH(CH_3)_2$), 68.41 (C-5 or $CH(CH_3)_2$), 70.29 (C-1), 71.92 (C-4), 103.52 (C-9), 127.26 (CH-Ph), 128.32 (2 x CH-Ph), 128.39 (2 x CH-Ph), 138.13 (C-Ph), 210.72 (C=O) ; MS m/z (relative intensity) 302 ($M^{+\bullet}$+1, 2.9), 273 (17.8), 242 (4.6), 210 (4.4), 91 (100) ; Anal. Calcd for $C_{18}H_{23}NO_3$: C, 71.76 ; H, 7.64 ; N, 4.65. Found : C, 71.90 ; H, 7.67 ; N, 4.64.

9-Benzyl-6-*exo*-3-chloropropoxy-5-oxa-9-azatricyclo[5.2.1.0^{4,8}]decan-2-one (4c) : This compound is obtained from the typical procedure B with 1-benzyl-3-hydroxypyridinium chloride and 3-chloro-1-propanol (Yield : 28%). For the compound (**4c**), a second chromatography is required (SiO_2 / ethyl acetate/hexanes, 2/8, v/v) ; Rf 0.45 (SiO_2 / ethyl acetate/hexanes, 2/8, v/v) ; IR (CCl_4) ν_{max} 1730 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.40 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 3.5 Hz, H-7_{endo}), 2.01 (q, 2H, J = 6 Hz, $OCH_2CH_2CH_2Cl$), 2.30 (dd, 1H, $J_{3endo,3exo}$ = 16 Hz, $J_{3endo,4}$ = 1.5 Hz, H-3_{endo}), 2.47 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 11 Hz, $J_{7exo,1}$ = 8.5 Hz, H-7_{exo}), 2.82 (dd, 1H, $J_{3exo,3endo}$ = 16 Hz,

$J_{3exo,4}$ = 4 Hz, H-3_{exo}), 2.83-2.88 (m, 1H, H-6), 3.48-3.70 (m, 6H), 3.76-3.82 (m, 1H), 4.18 (ddd, 1H, $J_{5,4}$ = 8.5 Hz, $J_{5,6}$ = 6 Hz, $J_{5,1}$ = 1.5 Hz, H-5), 4.58 (ddd, 1H, $J_{4,5}$ = 8.5 Hz, $J_{4,3exo}$ = 4 Hz, $J_{4,3endo}$ = 1.5 Hz, H-4), 4.90 (s, 1H, H-9), 7.28-7.37 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 29.74 ($OCH_2CH_2CH_2Cl$), 32.35 (C-7), 40.92 (C-3 or CH_2Cl), 41.71 (C-3 or CH_2Cl), 44.83 (C-6), 57.04 (CH_2Ph), 63.23 (OCH_2), 67.26 (C-5), 70.22 (C-1), 72.06 (C-4), 105.45 (C-9), 127.32 (CH-Ph), 128.36 (2 x CH-Ph), 128.41 (2 x CH-Ph), 138.02 (C-Ph), 210.62 (C=O) ; Anal. Calcd for $C_{18}H_{22}NO_3Cl$: C, 64.38 ; H, 6.56 ; N, 4.17. Found : C, 64.25 ; H, 6.58 ; N, 4.16.

9-Benzyl-6-*exo*-(methoxycarbonyl-2-methylpropoxy)-5-oxa-9-azatricyclo[5.2.1.$0^{4,8}$]-decan-2-one (4d) : This compound is obtained from the typical procedure B with 1-benzyl-3-hydroxypyridinium chloride and methyl 2,2-dimethyl-3-hydroxypropionate (Yield : 26%) ; Rf 0.78 (Al_2O_3 / CH_2Cl_2) ; IR (CCl_4) ν_{max} 1730 (br) ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.18-1.24 (m, 6H, $C(CH_3)_2$), 1.37 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 3 Hz, H-7_{endo}), 2.27 (dd, 1H, $J_{3endo,3exo}$ = 16 Hz, $J_{3endo,4}$ = 1.5 Hz, H-3_{endo}), 2.43 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 11 Hz, $J_{7exo,1}$ = 8.5 Hz, H-7_{exo}), 2.81 (dd, 1H, $J_{3exo,3endo}$ = 16 Hz, $J_{3exo,4}$ = 4 Hz, H-3_{exo}), 2.78-2.87 (m, 1H, H-6), 3.36-3.48 (m, 3H), 3.59-3.72 (m, 5H), 4.13 (ddd, 1H, $J_{5,4}$ = 8 Hz, $J_{5,6}$ = 6 Hz, $J_{5,1}$ = 1.5 Hz, H-5), 4.54 (ddd, 1H, $J_{4,5}$ = 8 Hz, $J_{4,3exo}$ = 4 Hz, $J_{4,3endo}$= 1.5 Hz, H-4), 4.86 (s, 1H, H-9), 7.27-7.41 (m, 5H, Ph); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 22.26 (CH_3), 22.41 (CH_3), 29.58 (C-7), 40.92 (C-3), 44.87 (C-6), 51.72 (OCH_3), 57.08 (CH_2Ph), 67.52 (C-5), 72.07 (C-1), 73.05 (C-4), 73.39 ($C(CH_2)$), 105.46 (C-9), 127.34 (CH-Ph), 128.17 (2 x CH-Ph), 128.41 (2 x CH-Ph), 138.09 (C-Ph), 176.44 ($C=O_{ester}$), 210.70 ($C=O_{ketone}$) ; MS m/z (relative intensity) 374 ($M^{+\bullet}$+1, 1.2), 345 (14.1), 282 (10.7), 242 (8.3), 91 (100) ; Anal. Calcd for $C_{21}H_{27}NO_5$: C, 67.56 ; H, 7.24 ; N, 3.75. Found : C, 67.83 ; H, 7.26 ; N, 3.73.

6-*exo*-Ethoxy-9-methyl-5-oxa-9-azatricyclo[5.2.1.$0^{4,8}$]decan-2-one (4e) : This compound is obtained from the typical procedure B with 1-methyl-3-hydroxypyridinium iodide and ethanol (Yield : 21.5%) ; Rf 0.63 (Al_2O_3 / CH_2Cl_2) ; IR (CCl_4) ν_{max} 1740 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.14 (t, 3H, J = 7 Hz, CH_3), 1.28 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 3.5 Hz, H-7_{endo}), 2.20 (dd, 1H, $J_{3endo,3exo}$ = 16 Hz, $J_{3endo,4}$ = 1.5 Hz, H-3_{endo}), 2.25 (s, 3H, NCH_3), 2.38 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 11 Hz, $J_{7exo,1}$ = 8.5 Hz, H-7_{exo}), 2.63 (dd, 1H, $J_{3exo,3endo}$ = 16 Hz, $J_{3exo,4}$ = 4 Hz, H-3_{exo}), 2.67-2.74 (m, 1H, H-6), 3.34 (d, 1H, $J_{1,7exo}$ = 8 Hz, H-1), 3.37 (m, 1H, OCH_2), 3.65 (m, 1H, OCH_2), 4.07 (ddd, 1H, $J_{5,4}$ = 8.5 Hz, $J_{5,6}$ = 6 Hz, $J_{5,1}$ = 1.5 Hz, H-5), 4.51 (ddd, 1H, $J_{4,5}$ = 8.5 Hz, $J_{4,3exo}$ = 4 Hz, $J_{4,3endo}$ = 1.5 Hz, H-4), 4.83 (s, 1H, H-9) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 15.11 (CH_3), 29.22 (C-7), 40.67 (C-3), 40.70 (NCH_3), 44.53 (C-6), 62.45 (OCH_2), 69.52 (C-5), 71.88 (C-1), 72.42 (C-4), 105.22 (C-9), 210.55 (C=O) ; MS m/z (relative intensity) 211 ($M^{+\bullet}$, 0.5), 183 (7.8), 166 (3.2), 82 (100) ; Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.56 ; H, 8.06 ; N, 6.64. Found : C, 62.31 ; H, 8.09 ; N, 6.61.

6-*exo*-(1-Methylethoxy)-9-methyl-5-oxa-9-azatricyclo[5.2.1.0^{4,8}]decan-2-one (4f) : This compound is obtained from the typical procedure B with 1-methyl-3-hydroxypyridinium iodide and isopropanol (Yield : 18%) ; Rf 0.55 (Al_2O_3 / CH_2Cl_2) ; IR (CCl_4) ν_{max} 1730 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.10-1.16 (m, 6H, 2 x CH_3), 1.31 (dd, 1H, $J_{7endo,7exo}$ = 14.5 Hz, $J_{7endo,6}$ = 3.5 Hz, H-7_{endo}), 2.23 (dd, 1H, $J_{3endo,3exo}$ = 16 Hz, $J_{3endo,4}$ = 1.5 Hz, H-3_{endo}), 2.27 (s, 3H, NCH_3), 2.41 (ddd, 1H, $J_{7exo,7endo}$ = 14.5 Hz, $J_{7exo,6}$ = 11 Hz, $J_{7exo,1}$ = 8.5 Hz, H-7_{exo}), 2.66 (dd, 1H, $J_{3exo,3endo}$ = 16 Hz, $J_{3exo,4}$ = 4.5 Hz, H-3_{exo}), 2.73-2.78 (m, 1H, H-6), 3.36 (d, 1H, $J_{1,7exo}$ = 8.5 Hz, H-1), 3.84 (m, 1H, $CH(CH_3)_2$), 4.11 (ddd, 1H, $J_{5,4}$ = 8.5 Hz, $J_{5,6}$ = 6 Hz, $J_{5,1}$ = 1.5 Hz, H-5), 4.54 (ddd, 1H, $J_{4,5}$ = 8.5 Hz, $J_{4,3exo}$ = 4.5 Hz, $J_{4,3endo}$ = 1.5 Hz, H-4), 4.96 (s, 1H, H-9) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.74 (CH_3), 23.65 (CH_3), 29.38 (C-7), 40.76 (C-3), 40.93 (NCH_3), 44.89 (C-6), 68.58 ($CH(CH_3)_2$), 69.77 (C-5), 71.77 (C-1), 72.58 (C-4), 103.57 (C-9), 210.71 (C=O) ; MS m/z (relative intensity) 225 ($M^{+\bullet}$, 0.7), 197 (9.2), 138 (18.7), 82 (100) ; Anal. Calcd for $C_{12}H_{19}NO_3$: C, 64.00 ; H, 8.44 ; N, 6.22. Found : C, 64.25 ; H, 8.41 ; N, 6.25.

6-*exo*-Ethoxy-9-(4-fluorobenzyl)-5-oxa-9-azatricyclo[5.2.1.0^{4,8}]decan-2-one (4g) : This compound is obtained from the typical procedure B with 1-p-fluorobenzyl-3-hydroxypyridinium chloride and ethanol (Yield : 33%) ; Rf 0.80 (Al_2O_3 / CH_2Cl_2) ; IR (CCl_4) ν_{max} 1730 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.17 (t, 3H, J = 7 Hz, CH_3), 1.38 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 3.5 Hz, H-7_{endo}), 2.26 (dd, 1H, $J_{3endo,3exo}$ = 16 Hz, $J_{3endo,4}$ = 1.5 Hz, H-3_{endo}), 2.43 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 11 Hz, $J_{7exo,1}$ = 8.5 Hz, H-7_{exo}), 2.77 (dd, 1H, $J_{3exo,3endo}$ = 16 Hz, $J_{3exo,4}$ = 4 Hz, H-3_{exo}), 2.80 (ddd, 1H, $J_{6,7exo}$ = 11 Hz, $J_{6,5}$ = 6 Hz, $J_{6,7endo}$ = 3.5 Hz, H-6), 3.39-3.53 (m, 4H, H-1, CH_2-p-FC_6H_4, OCH_2), 3.68 (m, 1H, OCH_2), 4.15 (dd, 1H, $J_{5,4}$ = 8.5 Hz, $J_{5,6}$ = 6 Hz, H-5), 4.55 (ddd, 1H, $J_{4,5}$ = 8.5 Hz, $J_{4,3exo}$ = 4 Hz, $J_{4,3endo}$= 1.5 Hz, H-4), 4.88 (s, 1H, H-9), 7.01 (t, 2H, J = 8.5 Hz, 2xH_{orthoF}), 7.29 (dd, 2H, J= 8.5 Hz, J= 5.5 Hz, 2xH_{metaF}) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 15.16 (CH_3), 29.89 (C-7), 41.02 (C-3), 44.99 (C-6), 56.43 (CH_2-p-FC_6H_4), 62.58 (OCH_2), 67.33 (C-5), 70.29 (C-1), 71.98 (C-4), 105.32 (C-9), 115.27 (d, $^2J_{CF}$= 21 Hz, 2 x C_{orthoF}), 130.03 (d, $^3J_{CF}$= 8 Hz, 2 x C_{metaF}), 133.85 (C_{paraF}), 163.36 (d, $^1J_{CF}$= 245 Hz, C-F), 210.70 (C=O) ; MS m/z (relative intensity) 306 ($M^{+\bullet}$+1, 3.2), 277 (20.2), 260 (3.9), 196 (9), 109 (100) ; Anal. Calcd for $C_{17}H_{20}NO_3F$: C, 66.89 ; H, 6.56 ; N, 4.59. Found : C, 66.75 ; H, 6.57 ; N, 4.60.

6-*exo*-(1-Methylethoxy)-9-(4-fluorobenzyl)-5-oxa-9-azatricyclo[5.2.1.0^{4,8}]decan-2-one (4h) : This compound is obtained from the typical procedure B with 1-p-fluorobenzyl-3-hydroxypyridinium chloride and isopropanol (Yield : 27%). The compound **(4g)** was also detected (in a ratio of 1 to 4). It was probably due to the presence of ethanol as stabilizing agent ; Rf 0.84 (Al_2O_3 / CH_2Cl_2) ; IR (CCl_4) ν_{max} 1730 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.12 (d, 3H, J = 6 Hz, CH_3), 1.15 (d, 3H, J = 6 Hz, CH_3), 1.38 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 3 Hz, H-7_{endo}), 2.27 (dd, 1H, $J_{3endo,3exo}$ = 15.5

Hz, $J_{3endo,4}$ = 1.5 Hz, H-3_{endo}), 2.42 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 11 Hz, $J_{7exo,1}$ = 8.5 Hz, H-7_{exo}), 2.77 (dd, 1H, $J_{3exo,3endo}$ = 15.5 Hz, $J_{3exo,4}$ = 4 Hz, H-3_{exo}), 2.80 (m, 1H, H-6), 3.39-3.56 (m, 3H, H-1, CH_2-p-FC_6H_4), 3.85 (m, 1H, $CH(CH_3)_2$), 4.16 (ddd, 1H, $J_{5,4}$ = 8.5 Hz, $J_{5,6}$ = 6 Hz, $J_{5,1}$ = 1.5 Hz, H-5), 4.54 (ddd, 1H, $J_{4,5}$ = 8.5 Hz, $J_{4,3exo}$ = 4 Hz, $J_{4,3endo}$ = 1.5 Hz, H-4), 4.99 (s, 1H, H-9), 7.02 (t, 2H, J = 8.5 Hz, 2 x H_{orthoF}), 7.29 (dd, 2H, J = 8.5 Hz, J = 5.5 Hz, 2 x H_{metaF}) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.75 (CH_3), 23.64 (CH_3), 30.00 (C-7), 41.08 (C-3), 45.06 (C-6), 56.51 (CH_2-p-FC_6H_4), 67.40 (C-5), 68.67 ($CH(CH_3)_2$), 70.37 (C-1), 72.05 (C-4), 105.39 (C-9), 115.35 (d, $^2J_{CF}$= 21.5 Hz, 2 x C_{orthoF}), 130.08 (d, $^3J_{CF}$ = 7.5 Hz, 2 x C_{metaF}), 133.60 (C_{paraF}), 162.19 (d, $^1J_{CF}$= 246 Hz, C-F), 210.81 (C=O) ; MS m/z (relative intensity) 320 ($M^{+\bullet}$+1, 1.2), 291 (13.9), 260 (3.6), 210 (3.6), 109 (100) ; Anal. Calcd for $C_{18}H_{22}NO_3F$: C, 67.71 ; H, 6.90 ; N, 4.39. Found : C, 67.98 ; H, 6.92 ; N, 4.37.

Compounds (**5a**) and (**5b**) : Sodium borohydride (174 mg, 4.60 mmol) was added dropwise to a solution of compound (**4a**) (660 mg, 2.30 mmol) in CH_2Cl_2 (15 mL). The suspension was stirred at rt for 1 h. The solvent was evaporated under reduced pressure. The residual product was dissolved in water, extracted with CH_2Cl_2 and the extract was dried (Na_2SO_4). The solvent was evaporated under reduced pressure, and the residual oil was chromatographed (Al_2O_3 / CH_2Cl_2).

9-Benzyl-6-*exo*-ethoxy-5-oxa-9-azatricyclo[5.2.1.0^{4,8}]decan-2-*endo*-ol (5a) : oil ; Rf 0.58 (Al_2O_3/ CH_2Cl_2) ; IR (CCl_4) ν_{max} 3590 ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.20 (t, 3H, J = 7 Hz, CH_3), 1.61 (dd, 1H, $J_{3endo,3exo}$ = 15 Hz, $J_{3endo,4}$ = 2 Hz, H-3_{endo}), 1.84 (dd, 1H, $J_{7endo,7exo}$ = 14.5 Hz, $J_{7endo,6}$ = 3.5 Hz, H-7_{endo}), 2.04 (m, 2H, H-3_{exo}, H-7_{exo}), 2.43 (m, 1H, OH), 2.80 (ddd, 1H, $J_{6,7exo}$ = 11 Hz, $J_{6,5}$ = 6 Hz, $J_{6,7endo}$ = 3.5 Hz, H-6), 3.39-3.55 (m, 4H, H-1, CH_2Ph, OCH_2), 3.70 (m, 1H, OCH_2), 3.90 (ddd, 1H, $J_{5,4}$ = 8 Hz, $J_{5,6}$ = 6 Hz, $J_{5,1}$ =1.5 Hz, H-5), 4.27 (t, 1H, $J_{2,3exo}$ = $J_{2,1}$= 7.5 Hz, H-2), 4.45 (m, 1H, H-4), 5.00 (s, 1H, H-9), 7.27-7.37 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 15.04 (CH_3), 23.59 (C-7), 32.39 (C-3), 45.11 (C-6), 58.16 (CH_2-Ph), 62.19 (OCH_2), 63.39 (C-1), 66.55 (C-5), 68.33 (C-2), 76.97 (C-4), 106.03 (C-9), 126.82 (CH-Ph), 128.09 (2 x CH-Ph), 128.15 (2 x CH-Ph), 139.12 (C-Ph); MS m/z (relative intensity) 289 ($M^{+\bullet}$, 1.9), 244 (15.6), 198 (40.9), 91 (100) ; Anal. Calcd for $C_{17}H_{22}NO_3$: C, 70.59 ; H, 7.96 ; N, 4.84. Found : C, 70.44 ; H, 7.93 ; N, 4.82.

9-Benzyl-5-oxa-9-azatricyclo[5.2.1.0^{4,8}]decan-2-*endo*-ol (5b) : Rf 0.39 (CH_2Cl_2 / Al_2O_3) ; IR (CCl_4) ν_{max} 3580 cm^{-1} ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.61 (dd, 1H, $J_{3endo,3exo}$= 15 Hz, $J_{3endo,4}$ = 2 Hz, H-3_{endo}), 1.83 (dd, 1H, $J_{7endo,7exo}$ = 14 Hz, $J_{7endo,6}$ = 3 Hz, H-7_{endo}), 2.06 (ddd, 1H, $J_{3exo,3endo}$ = 15 Hz, $J_{2,3exo}$ = 7.5 Hz, $J_{3exo,4}$ = 4 Hz, H-3_{exo}), 2.15 (ddd, 1H, $J_{7exo,7endo}$ = 14 Hz, $J_{7exo,6}$ = 11 Hz, $J_{7exo,1}$ = 7.5 Hz, H-7_{exo}), 2.67 (m, 1H, OH), 2.85 (m, 1H, H-6), 3.40 (t, 1H, $J_{1,7exo}$ = $J_{1,2}$ = 7.5 Hz, H-1), 3.52 (s, 2H, CH_2Ph), 3.64 (dd, 1H, $J_{5,4}$ = 7.5 Hz, $J_{5,6}$ = 6.5 Hz, H-5), 3.69 (dd, 1H, $J_{9exo,9endo}$ = 9 Hz, $J_{9exo,6}$ = 4 Hz, H-9_{exo}), 3.92 (d, 1H, $J_{9endo,9exo}$= 9 Hz, H-9_{endo}), 4.24 (t, 1H, $J_{2,3exo}$ = $J_{2,1}$= 7.5 Hz, H-2), 4.30 (m, 1H, H-4), 7.26-7.38 (m, 5H, Ph) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 26.64 (C-7), 32.59 (C-3), 39.72 (C-6), 58.31 (CH_2-Ph), 64.23 (C-1), 68.24 (C-5), 68.70 (C-2), 72.25 (C-9), 77.23 (C-4), 127.09 (CH-Ph),

128.29 (2 x CH-Ph), 128.41 (2 x CH-Ph), 139.15 (C-Ph) ; MS m/z (relative intensity) 245 ($M^{+\bullet}$, 2.2), 154 (76.2), 91 (100) ; Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.47 ; H, 7.76 ; N, 5.71. Found : C, 73.62 ; H, 7.75 ; N, 5.75.

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