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Aggregative Activation and Heterocyclic Chemistry II[1a] Nucleophilic condensations of ketone enolates on dehydrodihydropyran generated by Complex Bases

Brigitte Jamart-Grégoire,[†] Sophie Mercier-Girardot,[†] Sandra Ianelli,[#] Mario Nardelli[#] and Paul Caubère,[†*]

[†]Laboratoire de Chimie Organique I, URA CNRS 457, INCM FU CNRS 0008, Faculté des Sciences Université H. Poincaré, Nancy I, BP 239, F-54506 Vandoeuvre-les-Nancy, France

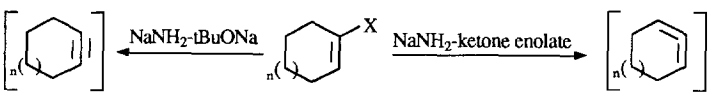
[#]Istituto di Chimica Generale, Universita degli Studi di Parma, Centro di Studio CNR per la Strutturistica Diffrattometrica, Viale delle Scienze, I-43100 Parma, Italy

Abstract: 3,4-dehydrodihydropyran has been easily generated from 5-bromo-3,4-dihydropyran and nucleophilic or non nucleophilic complex bases. Under such conditions ketone enolates have been condensed for the first time on the short lived intermediate leading to heterocyclic derivatives under mild conditions and with good yields. The reactivity of dehydrodihydropyran is discussed.

Introduction

Base promoted elimination-additions (BPEA) are particularly useful to perform nucleophilic functionalisation of organic halides. Thus, inter-as well as intramolecular nucleophilic arynic[1] and hetarynic[2] condensations continue to be developed. A similar chemistry could be devised starting from appropriate cyclic halogenovinyl halides, since, transient strained cycloalkynes and cycloallenes could be generated from the corresponding vinyl halide and potassium tert-butoxide or organolithium compounds.[3] However, it was found under these conditions, that condensations of nucleophiles were impeded by competitive attack of the base.[3b] This problem was solved in our laboratory with the help of complex bases[4] which are unimetal superbases[5] resulting from aggregative activation[1e] of two (or more) bases or nucleophiles (Scheme 1).

Scheme 1

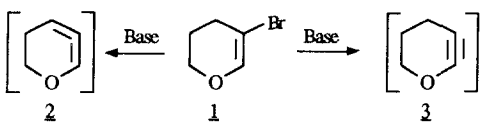


These studies also showed that the nature of the main intermediate formed during the nucleophilic condensations of 1-chlorocyclohexene strongly depends on the nature of the base and nucleophile.[1e] Thus the nucleophilic complex bases $NaNH_2$-ketone enolates generated 1,2-cyclohexadiene as main intermediate,[6] while cyclohexyne was the reactive species with the non nucleophilic complex bases $NaNH_2$-tBuONa.[7]

To the best of our knowledge, the chemical behaviour of the short lived heterocyclic intermediates is practically unknown.[8]

Thus we have examined the reaction of complex bases with 1 which could lead to the formation of 2 and/or 3[9] (Scheme 2). As a result of the presence of the oxygen in the ring and for a given base, the nature of the main intermediate could be different from that observed with 1-chlorocyclohexene.

Scheme 2



2 1 3

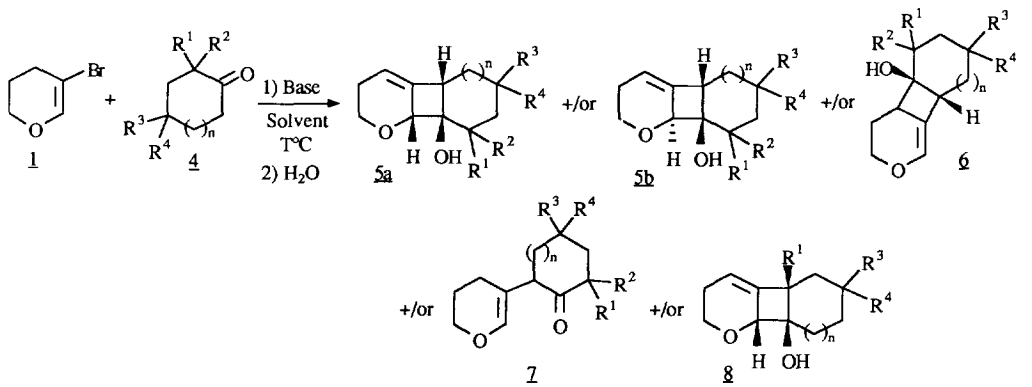
Another aspect of the study concerns the reactivity of these short lived species 2 and 3. Nucleophilic attack on cyclohexyne is obvious, and we showed that ketone enolates condensed on the central carbon atom of the 1,2-cyclohexadiene.[7] However the electronic structures of these intermediates are not well known[3] and still less information exists about 2 and 3. Thus the possible directing effect of the oxygen atom in the condensation considered cannot be easily anticipated and comparison with linear alkynes, allenes and their corresponding alkoxy derivatives is useless. Indeed unactivated alkynes and propargylic ethers are unreactive in nucleophilic condensations and in the allene series the situation is very confusing.[10,11]

Condensation of ketone enolates with 5-bromo-3,4-dihydropyran

Drawing on our experience with 1-chlorocyclohexene and aryne chemistry we investigated the condensation of a number of representative cycloalkanone enolates in THF or DME, in the presence of $NaNH_2$, $NaNH_2$-tBuONa and of the very strong complex base $NaNH_2$-Et$(OCH_2CH_2)_2$ONa ($NaNH_2$-MEDEGNa).[4]

For sake of simplicity, we present in Scheme 3 the products which may be observed in these reactions.

Scheme 3



1 4 5a 5b 6 7 8

The most significated results stemming from a systematic study are shown in Table I.

Table I

Run	n	R^1	R^2	R^3	R^4	Base (solvent)	T°C	t (h)	5a[a] %	5b[a] %	6[a] %	7[a] %	8[a] %	Overall yield %
1	0	H	H	H	H	$NaNH_2$ (THF)	20	36	-	13	-	30	-	43
2	0	H	H	H	H	$NaNH_2$ (DME)	20	24	-	29	-	37	-	66
3	0	H	H	H	H	$NaNH_2$ (DME)	-15	216	18	23	-	16	-	57
4	0	H	H	H	H	$NaNH_2$ (DME)	-30	336	24	15	-	-	-	39
5	1	H	H	H	H	$NaNH_2$ (THF)	20	72	43	-	11	13	-	67
6	1	H	H	H	H	$NaNH_2$ (DME)	20	48	-	-	-	40	-	40
7	1	H	H	H	H	$NaNH_2$ (DME)	0	66	26	-	16	8	-	50
8	1	H	H	H	H	$NaNH_2$ (DME)	-15	320	46	-	7	8	-	61
9	2	H	H	H	H	$NaNH_2$ (DME)	40	3	-	-	-	35	-	35
10	2	H	H	H	H	$NaNH_2$ (DME)	20	18	17	13	-	17	-	47
11	2	H	H	H	H	$NaNH_2$ (THF)	20	24	11	28	-	9	-	48
12	2	H	H	H	H	$NaNH_2$ (DME)	-15	184	20	30	-	10	-	60
13	3	H	H	H	H	$NaNH_2$ (DME)	40	3	-	26	-	60	-	86
14	3	H	H	H	H	$NaNH_2$ (THF)	20	96	-	19	-	52	-	71
15	3	H	H	H	H	$NaNH_2$ (DME)	20	6	-	13	-	66	-	79
16	3	H	H	H	H	$NaNH_2$ (DME)	-15	240	25	17	-	17	-	59
17	1	Me	H	H	H	$NaNH_2$-MEDEGNa (THF)	20	48	17	25	-	-	16	58
18	1	OMe	H	H	H	$NaNH_2$-tBuONa (THF)	0	240	-	-	-	-	30	30
19	1	SMe	H	H	H	$NaNH_2$ (THF)	20	24	-	-	-	-	40	40
20	1	O-$(CH_2)_3$-O		H	H	$NaNH_2$-tBuONa (THF)	0	120	47	-	-	-	-	47
21	1	H	H	Me	H	$NaNH_2$-tBuONa (DME)	0	24	42	9	-	-	-	51
22	1	H	H	O-$(CH_2)_3$-O		$NaNH_2$-MEDEGNa (THF)	-10	72	70	-	-	-	-	70

[a] Isolated yield calculated from 1.

To obtain some clues about the mechanism of this reaction, we merely determined the stereochemistry of the ring junctions (see experimental part).

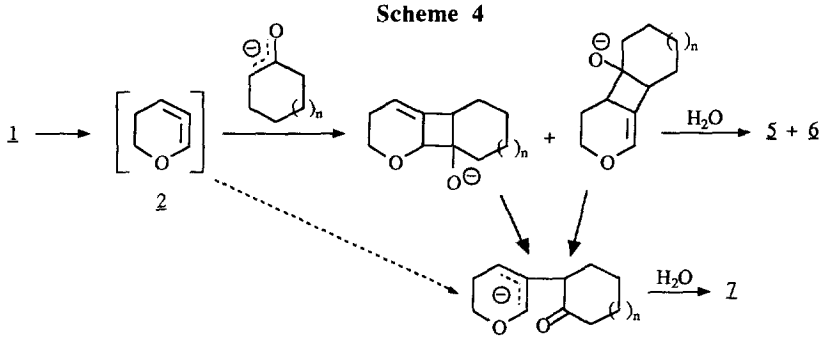
From these data a number of interesting facts emerge. Overall yields vary from fair to excellent, so it may be concluded that the reactive intermediate was nicely generated under our conditions. Actually whatever the yield was, 1 was always consumed and the lower yields (runs 9, 18) seemed partly due to a lack of reactivity of the ketone enolate and above all to the instability of the products as evidenced by the large amount of by-products formed.

The nature of the short lived intermediate may be deduced from the following remarks : the only hydroxy compounds isolated were methylene cyclobutanols 5a-b, 6 and 8 whose formation was favoured by low temperatures in THF. This observation is reminiscent of what was observed during the condensation of ketone enolates with 1,2-cyclohexadiene[7] and led us to conclude that dehydrodihydropyran 2 was the main (if not the only) intermediate.

Such an hypothesis was supported by the following arguments : i) if 3 had been the intermediate, alcohols 5a-b should have been formed from the isomerization of the corresponding cyclobutenols which were never observed even in traces. Such alcohols were observed during the condensation of ketone enolates with cyclohexyne under similar conditions.[12] ii) although observed only once, alcohol 6 can be formed only from 2. Note that alcohol 6 is very unstable and polymerizes rapidly certainly by cross condensation of the hydroxyl group of a given molecule with the dihydropyran part of another. Sampling during condensation of run 3

showed after hydrolysis that the first formed alcohols 5a and 5b slowly evolved toward the corresponding ketones 7. In other words, most if not all, of the ketones come from the opening of the alkoxide corresponding to 5. This was confirmed by opening alcohols 5 (n = 0, 3 ; $R^1 = R^2 = R^3 = R^4 = H$) into the corresponding ketones 7 with $NaNH_2$ in THF (see experimental part). According to these remarks we propose the mechanism of Scheme 4 to account for our results.

Scheme 4

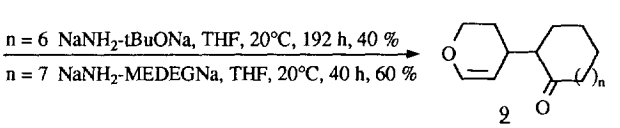


The junction between the four membered ring and the carbocycle always being cis, we favour, as in the cyclohexene series,[13] a cycloaddition with a strongly polarized transition state instead of a two step sequence.

That 2 was the intermediate was confirmed by the condensations described below which, considering the results obtained till now, are completely unexpected.

We had firmly established that during the condensation of cycloalkanone enolates with arynes or 1,2-cycloallenes[6c,14] the amount of four membered ring derivatives obtained depended on the ring size of the starting ketone. The larger the cycloalkanone ring the less probable the four membered ring. So we decided to study the condensation of eleven and twelve membered cycloalkanones. Moreover, curiously, unreported experiment showed that THF led to a higher overall yield than DME. Furthermore, whatever the conditions used, the only product observed corresponded to a nucleophilic attack on the C_4 position. We have reported the most significant results in Scheme 5.

Scheme 5



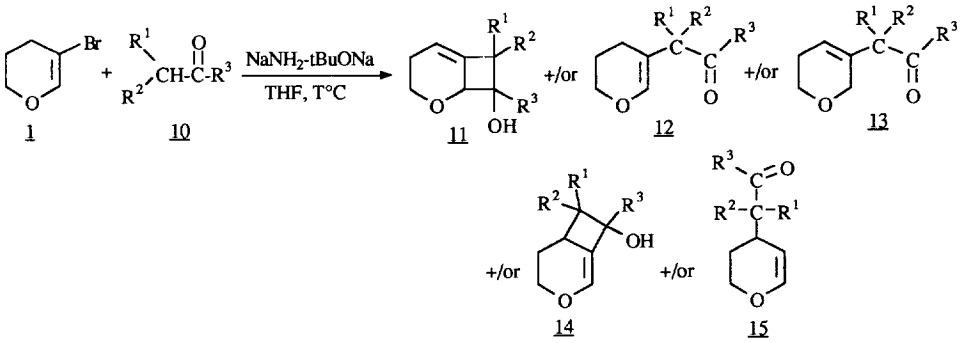
Such a nucleophilic attack should be expected during the condensation of any nucleophile with 2 since it corresponds to a negative charge developed on the C_3 position which could be stabilized by the inductive -I effect of the oxygen. In fact this situation corresponds to the meta directing effect of electron-withdrawing groups in arynic chemistry.

The divergent reactivities of ketones reported in Table I and Scheme 3 are not easy to explain.

We thought that the main difference lay in the stereochemistry of the enolate. Indeed five to seven membered ketones lead only to E enolates while Z stereochemistry must be considered with eleven and twelve

membered rings.[15] In other words the behaviour of large ring cycloalkanones would be closely similar to that of linear ketones. A few condensations with such substrates were performed in order to verify such an assertion. The reactions observed with representative substrates are summarized in Scheme 6 and the most significant results reported in Table II.

Scheme 6



1 10 11 12 13 14 15

Table II

Run	R1	R2	-R3	T°C	t (h)	11 % a)	12 % a)	13 % a)	14 % a)	15 % a)	Overal yield %
1	H	Me	-Ph	20	72	13	-	-	27	-	40
2	H	H		20	48	-	-	10	-	34	44
3	H	Me	-Et	20	120	-	-	-	60	23	83
4	Me	Me	-iPr	20	168	11	18	-	27	-	56
5	Me	Me	-iPr	40	49	-	-	-	27	20	47

a) Isolated yields calculated from 1

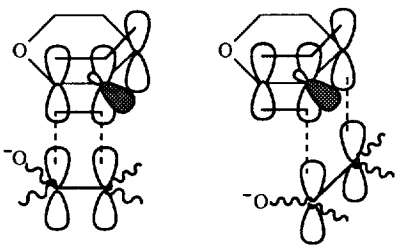
A few exploratory experiments rapidly showed that the complex base $NaNH_2$-tBuONa had to be prefered to $NaNH_2$ and THF to DME.

Interestingly as suggested above attacks on C_3 and C_4 positions were observed. These results support 2 as being the intermediate in our condensations. However no information may be drawn from the ratios 11+12+13/14+15. Indeed, under our experimental conditions the stabilities of the products formed are unknown and some of them may be destroyed or rearranged during the condensations invalidating any conclusion. For example comparison of runs 4 and 5 shows that changing the reaction temperature from 20°C to 40°C led to the unique formation of products due to condensation on the C_4 position. In fact when 11+12 of run 4 were placed in the presence of $NaNH_2$-tBuONa at 0°C then warmed to 30°C a complete degradation took place explaining why these products were not observed in run 5. Moreover it appears as highly improbable that products coming from attack on the C_3 position were transformed into products coming from attack on the C_4 one and conversely. The above control experiment supports this conclusion since neither 14 nor 15 were observed during warming.

Concerning the intimate mechanisms of the condensations a number of conclusions may be drawn from the present work. As suggested before, the ketones obtained during these condensations seemed to be generated from the corresponding alkoxide of the methylene cyclobutanols. Let us now consider the formation of the

methylene cyclobutanols. Since a cis junction between the four membered ring and the homocycle was always observed, a syn addition of the ketone enolates on 2 must take place. The most favourable approach of the two reagents necessitates a good overlap of the orbitals of the enolates and of 2 in a concerted or quasi-concerted mechanism. Among the few orbital descriptions of cyclic allenes given in the literature[8a] that fitting best with our observation would contain a sp^2 or pseudo sp^2 orbital on the central atom and a conjugated π system as given in Scheme 7 where approaches of the reactants were symbolized.

Scheme 7



If we admit that the sp^2 orbital is electron rich, there remains a conjugated electron deficient π system favouring nucleophilic condensations. This interpretation could explain the nucleophilic attacks taking place on the C_3 position in spite of the negative charge formally born by this center.

Of course this picture does not take into account a number of parameters such as the possible complexation of the cation of the ketone enolates (or of their aggregates with the bases present in the reaction medium) with the oxygen of the heterocycle. We have shown elsewhere[1a] that aggregates may play an important part in elimination-additions but no clear clue appears for the present time.

Moreover we are unable to interpret why some ketone enolates condense on the C_3 position and others on the C_4 one. In fact we think that these reactions are frontier orbital controlled and that a rigorous interpretation of the results obtained necessitates an accurate theoretical approach.

Conclusion

The present work highlight a new interesting synthetic consequence of aggregative activation. Thus it has been shown for the first time that nucleophiles may be easily condensed with 3,4-dehydrodihydropyran generated under very mild conditions from 5-bromo-3,4-dihydropyran and easily prepared complex bases.

The reactivity of the short lived intermediate is not completely understood but useful clues on its chemical properties have been obtained. Works are in progress in order to improve our knowledge on these interesting species and to extend these first results.

Finally a number of the pyran derivatives presently obtained are good starting materials for the synthesis of polycyclic oxygenated heterocycles. Such developments will be published in a near future.

Experimental

General Methods. Melting points were determined on a Totoli melting point apparatus and are uncorrected. ^{13}C NMR spectra were recorded with a Bruker AM 400 or a Bruker 300 MHz spectrometer. ^1H NMR spectra were recorded on a Jeol PMX 60 at 60 MHz, or a Bruker AM 400 instrument at 400 MHz. Me_4Si was the internal standard. Infrared (IR) spectra of thin liquid films between NaCl plates or KBr pellets were recorded

with a Perkin-Elmer 841 instrument.X ray analysis was performed by Centro di Studio C.N.R. per la Strutturistica Diffratometrica of Parma (Italy). Elemental analyses were performed by CNRS Laboratory (Vernaison) and by E.N.S.C.M Microanalysis Departement of Montpellier. Mass spectra were recorded on Hewlett Packard 5971A instrument or by the Laboratory of Mass Spectroscopy, Faculté de Pharmacie (Nancy). Thin-layer chromatography (TLC) was performed with plates coated with kieselgel G (Merck). The plates were developed with petroleum ether/EtOAc. The silica gels used for column chromatography and flash chromatography were kieselgels of 0.063-0.2 mm and 0.04-0.063 mm particle size, respectively. High pressure liquid chromatography was performed with a Waters PREP 500 chromatograph equipped with a silica gel column.

Materials. Sodium amide powder was obtained commercially (Merck). Reagent-grade tetrahydrofuran (THF) (BASF) was distilled from sodium benzophenone ketyl. 1,2-Dimethoxyethane (DME) was distilled from sodium and was stored under sodium until used.

Typical procedures

a) Procedure involving complex base "$NaNH_2$-alcoholate"

Preparation of the complex base and enolate formation : to a suspension of $NaNH_2$ (200 mmol) in the reaction solvent (20 ml), alcohol (tBuOH or EtO-$(OCH_2$-$CH_2)_2$-OH) (50 mmol) in 5 ml of the same solvent was added dropwise at room temperature. The mixture was stirred 2h at 40-45 °C. The ketone (50 mmol) diluted with 5ml of the reaction solvent was then added and the mixture was stirred 2h at 40-45°C or 4h at 20°C for the cyclopentanone.

Condensation : 5-Bromo-3,4-dihydropyran[16] (25 mmol) diluted in the solvent reaction (10 ml) was added to the complex base and enolate prepared as below .The reaction was performed for the time and at the temperature given in Table.The reaction time was determined by disappearance of 5-bromo-3,4-dihydropyran followed by G.P.C. (decane was used as internal standard). After completion the mixture was poured on ice and extracted with 3 x 75 ml of ether.The different products thus obtained were separated by HPLC.

b) Procedure involving complexe base "$NaNH_2$-enolate":

Preparation of the complex base : to a suspension of $NaNH_2$ (150 mmol) in the reaction solvent (20 ml), ketone (50 mmol) diluted with 10 ml of the same solvent was added dropwise at room temperature or at -17°C for cyclopentanone.The mixture was stirred 2h at 40-45 °C or 12h at -17°C for the cyclopentanone.

Condensation : 5-Bromo-3,4-dihydropyran[16] (25 mmol) diluted in the solvent reaction (10 ml) was added to the complex base and the reaction was performed for the time and at the temperature given in table.The reaction time was determined by disappearance of 5-bromo-3,4-dihydropyran followed by G.P.C. (decane was used as internal standard). After completion the mixture was poured on ice and extracted with 3 x 75 ml of ether.The different products thus obtained were separated by HPLC chromatography.

All compounds were identified by IR, ^1H NMR, ^{13}C NMR, melting point and combustion analysis or mass spectra. In the case of very instable products IR and ^1H NMR were only recorded.

X Rays diffraction analysis permit us to determine the stereochemistry of compound 5a (n=0, R^1=R^2=R^3=R^4=H), 5a (n=1, R^1=R^2=R^3=R^4=H), 5b (n=2, R^1=R^2=R^3=R^4=H), 5a (n=3, R^1=R^2=R^3=R^4=H), 5b (n=3, R^1=R^2=R^3=R^4=H), 8 (n=1, R^1=SMe, R^3=R^4=H) and 14 (R^1=Me, R^2=H, R^3=C_6H_5). The stereochemistry of the remaining compounds was deduced by comparison of the ^{13}C NMR data of the carbones (CH-O), (C-OH) and (CR^1-C=) of the ring junction.

(1RS,2RS,8SR) 3-oxatricyclo [6.3.0.0 2,7] undec-6-en-1-ol 5a (n=0, R^1=R^2=R^3=R^4=H)

IR (NaCl) : 3600-3200 cm^{-1} (OH).^1H NMR (CCl_4) δ ppm : 5.50 (pt, 1H, CH=C), 4.33-4.56 (m, 1H, CH-O), 3.50-4.20 (m, 3H, CH_2-O and OH exchanged with D_2O), 3.10 (pt, 1H, CH-C=C), 1.00-2.83 (m, 8H, aliph. H and CH_2-C=C). ^{13}C NMR ($CDCl_3$) δ ppm : 136.4 (C=), 116.5 (CH=), 85.8 (C-OH), 81.8 (CH-O), 63.7 (CH_2-O), 53.4 (CH-C=C), 32.8 (CH_2-C=C), 28.6, 26.5, 25.4 (3xCH_2). mp 64°C. Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.48. Found : C, 72.30; H, 8.34. X Rays spectroscopic data have been collected.[17]

(1RS,2SR,8SR) 3-oxatricyclo [6.3.0.0 2,7] undec-6-en-1- ol 5b (n=0, R^1=R^2=R^3=R^4=H)

IR (NaCl) : 3600-3200 cm^{-1} (OH).^1H NMR (CCl_4) δ ppm : 5.57 (pt, 1H, CH=C),3.50-4.27 (m, 3H, CH_2-O-CH), 3.20 (s, 1H, OH exchanged with D_2O), 3.00 (pt, 1H, CH-C=C), 1.33-2.66 (m, 8H, aliph.H and CH_2-C=C). ^{13}C NMR ($CDCl_3$) δ ppm : 141.1 (C=), 116.9 (CH=), 85.1 (C-OH), 77.9 (CH-O), 63.3 (CH_2-O), 53.3 (CH-C=), 37.2 (CH_2-C=), 29.0, 25.0, 24.9 (3x CH_2). MS Calcd. for $C_{10}H_{14}O_2$ m/e 166. Anal.Calcd. for the acetate derivative prepared using a procedure described in the literature.[18] $C_{12}H_{16}O_3$: C, 69.23 ; H, 7.69. Found : C, 69.06; H, 7.62.

(1RS,2RS,8SR) 3-oxatricyclo [6.4.0.0^{2,7}] dodec-6-en-1- ol 5a (n=1, R^1=R^2=R^3=R^4=H)
IR (NaCl) : 3600-3200 cm^{-1} (OH). ^{1}H NMR (CCl_4) δ ppm : 5.41 (pt, 1H, CH=C),4.55 (m, 1H, OH exchanged with D_2O), 3.33-4.31(m, 3H, CH_2-O-CH), 2.83 (pt, H, CH-C=C), 0.78-2.47 (m, 10H, aliph. H, CH_2-C=C). ^{13}C NMR ($CDCl_3$) δ ppm : 134.4 (C=), 112.9 (CH=), 83.4 (CH-O), 72.9 (C-OH), 63.9 (CH_2O), 44.9 (CH-C=C), 29.5 (CH_2-C=C), 28.5, 24.9, 20.7, 19.8 (4xCH_2). MS: $C_{11}H_{16}O_2$ m/e 180.

Anal. Calcd. for the para-nitrobenzoate derivative $C_{18}H_{19}NO_5$: C, 65.64 ; H, 5.81 ; N, 4.25. Found : C, 65.62 ; H, 5.85 ; N, 4.17. X Rays spectroscopic data have been collected on epoxyde derivative.[17,11]

(1RS,2RS,8SR) 5-oxatricyclo [6.4.0.0^{2,7}] dodec-6-en-1- ol 6 (n=1, R^1=R^2=R^3=R^4=H)
Identification was made on para-nitrobenzoate derivative.
IR (KBr) : 1710 cm^{-1} (C=O). ^{1}H NMR (CCl_4) δ ppm : 8.13 (ps, 4H, arom. H), 6.36 (pt, 1H, CH=), 2.88-4.6 (m,4H, CH_2-O, 2xCH-C=C), 1.03-2.46 (m, 10H, aliph.H).^{13}C NMR ($CDCl_3$) δ ppm : 169,0 (C=O), 145,0 (OCH=), 163.6, 150.4, 136.6, 136.3, 130.5, 123.4 (arom.C), 108.5 (C=), 80.3 (C-O-C=O), 63.8 (CH_2-O), 47.8, 47.5 (2xCH-C=CH), 25.9, 22.8, 21.9, 20.6, 19.9 (5xCH_2). mp 134°C. Anal. Calcd. for $C_{18}H_{19}NO_5$: C, 65.64; H, 5.81; N, 4.25. Found : C, 65.15;H, 5.72; N, 4.31.

(1RS,2RS,8SR) 3-oxatricyclo [6.5.0.0^{2,7}] tridec-6-en-1- ol 5a (n=2, R^1=R^2=R^3=R^4=H)
IR (KBr) : 3600-3200 cm^{-1} (OH). ^{1}H NMR (CCl_4) δ ppm : 5.47 (pt, 1H, CH=C), 3.17-4.33 (m, 4H, CH_2-O-CH, OH exchanged with D_2O), 2.82 (pt, 1H, CH=C), 0.67-2.50 (m, 12H, aliph. H,CH_2-C=). ^{13}C NMR ($CDCl_3$) δ ppm : 139.5 (C=),113.1 (CH=), 82.7 (CH-O), 78.8 (C-OH), 63.6 (CH_2-O), 52.2 (CH-C=), 32.2 (CH_2-C=), 30.8, 28.7, 25.7, 25.2, 23.0 (5x CH_2). mp 118°C. Anal. Calcd. for $C_{12}H_{18}O_2$: C, 73.43 ; H, 9.60. Found : C,73.49 ; H, 9.41.

(1RS,2SR,8SR) 3-oxatricyclo [6.5.0.0^{2,7}] tridec-6-en-1- ol 5b (n=2, R^1=R^2=R^3=R^4=H)
IR (NaCl) : 3600-3200 cm^{-1} (OH). ^{1}H NMR (CCl_4) δ ppm : 5.53 (pt, 1H, CH=C), 3.10-4.33 (m, 4H, CH_2-O-CH, OH exchanged with D_2O), 2.55 (pt, 1H, CH-C=), 0.65-2.33 (m, 12H, aliph. H, CH_2-C=). ^{13}C NMR ($CDCl_3$) δ ppm : 140.5 (CH=), 116.73 (C=), 79.7 (CH-O), 78.7 (C-OH), 63.5 (CH_2-O),56.4 (CH-C=), 40.2 (CH_2-C=), 31.7, 31.2, 30.3, 25.0, 24.3 (5xCH_2). MS Calcd. for $C_{12}H_{18}O_2$ m/e 194. Anal. Calcd. for the acetate derivative $C_{14}H_{20}O_3$: C, 71.18 ; H, 8.47. Found : C, 71.24 ; H, 8.76. X Rays spectroscopic data have been collected on *(1RS,2SR,6SR,7SR,8SR)1-acetoxy-3-oxatricyclo [6.5.0.0^{2,7}] tridecan-6,7-diol* obtained after esterification (procedure described in the literature[18]) following by a bishydroxylation (procedure described in the literature[19]) (yield 51% from the corresponding 5b).

(1RS,2RS,8SR) 3-oxatricyclo [6.6.0.0^{2,7}] tetradec-6-en-1-ol 5a (n=3, R^1=R^2=R^3=R^4=H)

IR (NaCl): 3600-3200 cm^{-1} (OH). ^{1}H NMR (CCl_4) δ ppm : 5.33 (pt, 1H, CH=C), 3.4-4.26 (m, 4H, CH_2-O-, CH-O and OH exchanged with D_2O), 1.06-3.06 (m, 15H , aliph. H and CH_2-CH=C , CH-C=). ^{13}C NMR ($CDCl_3$) : δ 138.0 (C=), 112.8 (CH=), 83.9 (CH-O), 76.5 (C-OH), 63.6 (CH_2-O), 52.0 (CH-C=), 26.3 (CH_2-C=), 26.0, 25.2, 24.7, 24.3, 23.9, 23.5 (6xCH_2). mp epoxyde derivative : 105 °C. Anal. Calcd. for the epoxyde derivative $C_{13}H_{20}O_3$. 1.43 % H_2O : C, 68.64 ; H, 9.04.Found : C, 69.08 ; H, 8.95. X Rays spectroscopic data have been collected for *(1RS,2RS,6RS,7RS,8SR) 1-acetoxy-3-oxatricyclo [6.6.0.0^{2,7}] tetradec-6-an-6,7-diol* obtained after esterification (procedure described in the literature[18]) following by a bishydroxylation (procedure described in the literature[19]) (yield 55% from the corresponding 5a).

(1RS,2SR,8SR) 3-oxatricyclo [6.6.0.0^{2,7}] tetradec-6-en-1-ol 5b (n=3, R^1=R^2=R^3=R^4=H)
IR (NaCl): 3600-3200 cm^{-1} (OH). ^{1}H NMR (CCl_4) δ ppm : 5.43 (pt, 1H , CH=C), 3.26-4.16 (m, 4H, CH_2-O, CH-O-, OH exchanged with D_2O), 2.26-2.50 (pt, 1H, CH-C=C), 0.80-2.20 (m, 14H, aliph.H and CH_2-CH=C). ^{13}C NMR ($CDCl_3$) δ ppm : 142.68 (C=), 115.0 (CH=), 78.9 (CH-O), 74.4 (C-OH), 63.5 (CH_2-O), 56.0 (CH-C=), 31.3 (CH_2-C=), 30.6, 30.6, 25.5, 24.9, 24.2, 23.1 (6xCH_2). mp 63°C. MS $C_{13}H_{20}O_2$ m/e 208. X Rays spectroscopic data have been collected for *(1RS,2RS,6SR,7SR,8SR) 1-acetoxy-3-oxatricyclo [6.6.0.0^{2,7}] tetradecan-6,7-diol* obtained after esterification (procedure described in the literature[18]) following by a bishydroxylation (procedure described in the literature[19]) (yield 40% from the

corresponding 5b).

5-(2-oxocyclopentyl)-3,4-dihydropyran 7 (n=0, R^1=R^2=R^3=R^4=H)

IR (NaCl) : 1743 cm^{-1} (C=O),1 664 cm^{-1} (C=C). ^1H NMR (CCl_4) δ ppm : 6.10 (s, 1H, O-CH=), 3.66-4.00 (m, 2H, CH_2-O), 1.63-2.53 (m, 11 H, aliph.H). ^{13}C NMR ($CDCl_3$) : δ 218.1 (C=O), 140.8 (O-CH=), 108.3 (C=C), 64.4 (O-CH_2), 52.2 (CH-C=O), 37.4 (CH_2-C=O), 27.8, 21.4, 20.0, 19.8 (4xCH_2). Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26 ; H, 8.49. Found : C, 71.86 ; H, 8.47.

5-(2-oxocyclohexyl)-3,4-dihydropyran 7 (n=1, R^1=R^2=R^3=R^4=H)

IR (NaCl) : 1712 cm^{-1} (C=O), 1665 cm^{-1} (C=C). ^1H NMR (CCl_4) δ ppm : 6.00 (s, 1H ,O-CH=), 3.70-4.00 (m, 2H, CH_2-O), 1.50-2.33 (m, 13H, aliph.H). ^{13}C NMR ($CDCl_3$) δ ppm : 210.7 (C=O), 140.4 (O-CH=), 110.5 (C=C), 65.1 (O-CH_2), 54.2 (CH-C=O), 41.7 (CH_2-C=O), 31.9, 27.7, 24.8, 22.0, 21.3 (5xCH_2). Anal. Calcd. for the para-dinitrobenzoate derivative $C_{18}H_{18}O_7N_2$: C, 57.75 ; H, 4.81 ; N, 7.48. Found : C, 57.48 ; H, 5.42 ; N, 7.62.

5-(2-oxocycloheptyl)-3,4-dihydropyran 7 (n=2, R^1=R^2=R^3=R^4=H)

IR (NaCl) : 1704 cm^{-1} (C=O), 1657 cm^{-1} (C=C). ^1H NMR (CCl_4) δ ppm : 6.10 (s, 1H, O-CH=), 3.76 (pt, 2H, CH_2-O), 1.36-2.50 (m, 15 H, H aliph). ^{13}C NMR ($CDCl_3$) δ ppm : 210.0 (C=O), 141.0 (O-CH=), 110,7 (C=C), 65.4 (O-CH_2), 56.6 (CH-C=O), 42.1 (CH_2-C=O), 30.2, 29.3, 28.3, 25.5, 22.4, 22.1 (6xCH_2). Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19 ; H, 9.34. Found : C, 74.43 ; H, 9.32.

5-(2-oxocyclooctyl)-3,4-dihydropyran 7 (n=3, R^1=R^2=R^3=R^4=H)

IR (NaCl) : 1702 cm^{-1} (C=O), 1659 cm^{-1} (C=C). ^1H NMR (CCl_4) δ ppm : 6.20 (s, 1H, O-CH=), 3.80 (pt, 2H, CH_2-O), 1.30-2.53 (m, 17H, aliph. H). ^{13}C NMR ($CDCl_3$) δ ppm : 210.0 (C=O), 144.7 (O-CH=), 108.8 (C=C), 65.3 (O-CH_2), 49.4 (CH-C=O), 36.2 (CH_2-C=O), 29.1, 25.2, 24.8, 24.0, 21.9, 21.4, 18.4 (7xCH_2). Anal. Calcd. for $C_{13}H_{20}O_2$: C, 74.96 ; H, 9.68. Found : C, 74.43 ; H, 9.48.

Compounds 7 (n=0,3, R^1=R^2=R^3=R^4=H) can also be prepared by reacting the corresponding alcohols 5 (1eq.) with $NaNH_2$ (1.2 eq.) in THF at room temperature to give respectively 20% and 50% yield.

(1RS,2RS,8SR) 8-methylthio-3-oxatricyclo [6.4.0.$0^{2,7}$] dodec-6-en-1-ol 8 (n=1, R^1=SMe, R^3=R^4=H)

IR (NaCl) : 3600-3200 cm^{-1} (OH). ^1H NMR (CCl_4) δ ppm : 5.63 (pt, 1H, CH=C), 3.26-4.46 (m, 4H, CH_2-O-CH, OH exchanged with D_2O), 2.00 (s, 3H, SCH_3), 1.00-2.50 (m, 10H, aliph. H). ^{13}C NMR ($CDCl_3$) δ ppm : 134.2 (C=), 116.9 (CH=), 83.7 (CH-O), 75.3 (C-OH), 63.3 (CH_2-O), 59.4 (C-SMe), 30.1 (CH_2-C=C), 28.3, 24.8, 22.0, 19.3 (4xCH_2), 12.4 (S-CH_3). mp 82°C. Anal. Calcd. for $C_{12}H_{18}O_2S$: C, 63.71 ; H, 7.96 ; S, 14.15. Found: C, 63.47 ; H, 7.90 ; S, 14.06. X Rays spectroscopic data have been collected.

(1RS,2RS,8SR) 8-methoxy-3-oxatricyclo [6.4.0.$0^{2,7}$] dodec-6-en-1-ol 8 (n=1, R^1=OMe, R^3=R^4=H)

IR (NaCl) : 3600-3200 cm^{-1} (OH). ^1H NMR (CCl_4) δ ppm : 5.70 (pt, 1H, CH=C), 3.40-4.26 (m, 4H, CH_2-O-CH, OH exchanged with D_2O), 3.20 (s, 3H, OCH_3), 0.93-2.50 (m, 10H, aliph. H). ^{13}C NMR ($CDCl_3$) δ ppm : 134.0 (C=), 120.3 (CH=), 84.9 (CH-O), 83.3 (C-OMe), 74.4 (C-OH), 63.5 (CH_2-O), 51.8 (CH_3-O), 27.5 (CH_2-C=C),25.9, 25.1, 22.7, 19.7 (4xCH_2). mp 73°C. Anal. Calcd. for $C_{12}H_{18}O_3$: C, 68.55 ; H, 8.63. Found : C, 68.03; H, 8.28.

(1RS,2RS,8SR) 10-methyl-3-oxatricyclo [6.4.0.$0^{2,7}$] dodec-6-en-1-ol 5a (n=1, R^1=R^2=R^4=H, R^3=Me)

IR (NaCl) : 3600-3200 cm^{-1} (OH). ^1H NMR (CCl_4) δ ppm : 5.36 (pt, 1H, CH=C), 3.26-4.46 (m, 4H, CH_2-O-CH, OH exchanged with D_2O), 2.80 (m, 1H, CH-C=C), 0.80-2.40 (m, 9H, aliph. H, CH_2-C=C), 0.80 (pd, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ ppm : 134.3 (C=), 112.3 (CH=), 82.8 (CH-O), 72.1 (C-OH), 63.5 (CH_2-O), 45.6 (CH-C=C), 29.4 (CH_2-C=C), 28.4, 28.3, 24.6 (3xCH_2),26.8 (CH-CH_3), 22.0 (CH_3). mp 122°C. Anal. Calcd. for the para-dinitrobenzoate derivative $C_{19}H_{20}O_7N_2$: C, 58.76 ; H, 5.19 ; N,7.21. Found : C, 58.53 ; H, 5.25 ; N, 7.20.

(1RS,2SR,8SR) 10-methyl-3-oxatricyclo[6.4.0.0^{2,7}]dodec-6-en-1-ol 5b *(n=1, R^1=R^2=R^4=H , R^3=Me)*

IR (NaCl) : 3600-3200 cm^{-1} (OH). ^{1}H NMR (CCl_4) δ ppm : 5.43 (pt, 1H, CH=C), 3.26-4.53 (m, 3H, CH_2-O-CH), 3.20 (m, 1H, OH exchanged with D_2O), 0.70-2.70 (m, 13H, aliph. H, CH_3, CH_2-C=C, CH-C=C). ^{13}C NMR ($CDCl_3$) δ ppm : 140.6 (C=), 113.7 (CH=), 74.4 (CH-O), 72.8 (C-OH); 63.2 (CH_2-O); 48.1 (CH-C=C); 35.3 (CH_2-C=C); 32.1, 31.1, 24.1 (3xCH_2), 8,5 (CH-CH_3), 21.4 (CH_3). mp 110°C. Anal. Calcd. for the para-dinitrobenzoate derivative $C_{19}H_{20}O_7N_2$: C, 58.76; H, 5.15; N, 7.21. Found : C, 58.72; H, 5.28; N, 6.92.

(1RS,2RS,8SR) 12-methyl-3-oxatricyclo[6.4.0.0^{2,7}]dodec-6-en-1-ol 5a *(n=1, R^3=R^2=R^4=H, R^1=Me)*

IR (NaCl) : 3600-3200 cm^{-1} (OH). ^{1}H NMR (CCl_4) δ ppm : 5.40 (pt, 1H, CH=C), 3.26-4.33 (m, 4H, CH_2-O-CH, OH exchanged with D_2O), 2.76 (m, 1H, CH-C=C), 1.06-2.43 (m, 9H, aliph. H, CH_2-CH=C), 0.93 (pd, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ ppm : 134.4 (C=), 112.3 (CH=), 83.2 (CH-O), 74.7 (C-OH), 63.3 (CH_2-O), 45.3 (CH-C=C), 30.2 (CH-CH_3), 27.7 (CH_2-CH=C), 24.4, 21.0, 20.2 (3xCH_2), 15.7 (CH_3). MS $C_{12}H_{18}O_2$ m/e 194.

(1RS,2SR,8SR) 12-methyl-3-oxatricyclo[6.4.0.0^{2,7}] dodec-6-en-1-ol 5b *(n=1, R^3=R^2=R^4=H, R^1=Me)*

IR (NaCl) : 3600-3200 cm^{-1} (OH). ^{1}H NMR (CCl_4) δ ppm : 5.36 (pt, 1H, CH=C), 3.40-4.36 (m, 4H, CH_2-O-CH, OH exchanged with D_2O), 2.60 (m, 1H, CH-C=C), 0.80-2.40 (m, 12H, aliph. H, CH_2-C=C, CH_3). ^{13}C NMR ($CDCl_3$) δ ppm : 139.4 (C=), 113.9 (CH=), 74.4 (C-OH), 73.0 (CH-O), 63.4 (CH_2-O), 48.3 (CH-C=C), 36.6 (CH-CH_3), 35.6 (CH_2-CH=C), 24.2, 22.6, 20.7 (3xCH_2), 15.2 (CH_3). MS $C_{12}H_{18}O_2$ m/e 194.

(1RS,2RS,8SR) 8-methyl-3-oxatricyclo [6.4.0.0^{2,7}] dodec-6-en-1-ol 8 *(n=1, R^3=R^4=H, R^1=Me)*

IR (NaCl) : 3600-3200 cm^{-1} (OH). ^{1}H NMR (CCl_4) δ ppm : 5.23 (pt, 1H, CH=C), 3.40-4.33 (m, 3H, CH_2-O-CH), 3.20 (s, 1H, OH exchanged with D_2O), 1.16-2.33 (m, 10H, aliph. H, CH_2-CH=), 1.10 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ ppm : 138.8 (C=), 112.7 (CH=), 83.0 (CH-O), 73.7 (C-OH), 63.4 (CH_2-O), 47.1 (C-CH_3), 30.6 (CH_2-CH=C), 29.0, 24.4, 21.2, 19.6 (4xCH_2), 22.3 (CH_3). MS $C_{12}H_{18}O_2$ m/e 194. Anal. Calcd. for the derivative*(1RS,2RS,6SR,7SR,8SR) 8-methyl-3-oxatricyclo [6.4.0.0^{2,7}] dodecan-6,7,1-triol* prepared using a procedure described in the literature[19] (yield:15%) $C_{12}H_{20}O_4$: C, 63.15; H, 8.77. Found : C, 63.16; H, 8.88.

(1RS,2RS,8SR) 3-oxatricyclo [6.4.0.0^{2,7}] dodec-6-en-10 (spiro-2'-[1,3]-dioxolan)-1-ol 5a *(n=1, R^1=R^2=H, R^3R^4=O-$(CH_2)_2$-O)*

IR (NaCl) : 3600-3200 cm^{-1} (OH). ^{1}H NMR (CCl_4) δ ppm : 5.43 (pt, 1H, CH=C), 3.30-4.30 (m, 8H, CH_2-O-CH, O-CH_2-CH_2-O, OH exchanged with D_2O), 2.83 (m, 1H, CH-C=C), 1.46-2.16 (m, 8H, aliph. H). ^{13}C NMR ($CDCl_3$) δ ppm : 134.4 (C=CH), 114.0 (CH=), 108.5 (C-O), 82.0 (CH-O), 72.3 (C-OH), 63.8, 63.4, 63.1 (3xOCH_2), 45.5 (CH-C=), 30.0, 29.4, 25.7, 25.2 (4xCH_2). mp 83°C. Anal. Calcd. for $C_{13}H_{18}O_4$, 7.39 % H_2O : C, 60.72 ; H, 7.81. Found : C, 60.71 ; H, 8.03.

(1RS,2RS,8SR) 3-oxatricyclo [6.4.0.0^{2,7}] dodec-6-en-12 -(spiro-2'-[1,3]-dioxan)-1- ol 5a *(n=1, R^1R^2=O-$(CH_2)_3$-O, R^3=R^4=H)*

IR (NaCl) : 3600-3200 cm^{-1} (OH). ^{1}H NMR (CCl_4) δ ppm : 5.33 (pt, 1H, CH=C),3.50-4.43 (m, 7H, CH_2-O-CH, 2xO-CH_2), 3.23 (m, 1H, OH exchanged with D_2O), 1.40-2.23 (m, 11H, aliph. H, CH_2-CH=C). ^{13}C NMR ($CDCl_3$) δ ppm : 138.9 (C=), 113.7 (CH=), 86.02 (O,O), 82.3 (CH-O), 65.0 (C-OH), 59.8, 59.9, 59.7 (3xCH_2-O), 49.4 (CH-C=), 25.8 (CH_2-CH=C), 25.6, 19.7, 19.0, 16.4 (4xCH_2). mp 116°C. Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.66 ; H, 7.99. Found : C, 66.92 ; H, 7.93.

4-(2-oxocycloundecyl) -3,4-dihydropyran 9 *(n=6)*

IR (NaCl) : 1703 cm^{-1} (C=O), 1644 cm^{-1} (C=C). ^{1}H NMR (CCl_4) δ ppm : 6.36 (d, 1H, OCH=), 4.66 (d, 1H, CH=), 4.4 (td, 2H, CH_2-O), 2.33-2.76 (m, 3H, CH-C=O-CH_2), 1.16-2.16 (m, 19H, aliph.H). ^{13}C NMR

($CDCl_3$) : δ 216.0 (C=O), 143.8 (O-CH=), 102.2 (CH=), 64.8 (OCH_2), 57.3 (CH-C=O), 42.8 (CH_2-C=O), 32.9 (CH-CH=), 27.7, 27.1, 25.4, 25.2, 25.2, 25.1, 24.1, 23.9, 22.3 (9xCH_2). Anal. Calcd. for $C_{16}H_{28}O_2$, 0.46% H_2O : C, 75.84 ; H, 11.19. Found : C, 75.23 ; H, 11.15. MS $C_{16}H_{26}O_2$ m/e 250.

4-(2-oxocyclododecyl)-3,4-dihydropyran 9 (n=7)
IR (NaCl) : 1709 cm^{-1} (C=O), 1645 cm^{-1} (C=C). ^1H NMR (CCl_4) δ ppm : 6.33 (d, 1 H, OCH=), 4.6 (d, 1H, CH=), 3.93 (t, 2H, OCH_2), 2.26-2.66 (m, 3 H, CH-C-O-CH_2), 1.16-2.0 (m, 21 H, aliph. H). ^{13}C NMR ($CDCl_3$) : δ 213.0 (C=O), 143.2 (O-CH=), 101.3 (CH=), 63.6 (OCH_2), 56.5 (CH-C=), 38.1 (CH_2-C=O), 29.5 (CH-C=O), 27.0, 26.0, 25.7, 23.4, 23.5, 23.2, 23.0, 21.8, 21.6, 21.3 (10xCH_2). MS $C_{17}H_{28}O_2$ m/e 264.

(1SR,7SR,8RS) 1-phenyl-8-methyl-4-oxabicyclo [4.2.0^{2,7}] oct-2-en-1-ol 14 (R^1=Me, R^2=H, R^3=C_6H_5)

IR (NaCl) : 3600-3200 cm^{-1} (OH). ^1H NMR (CCl_4) δ ppm : 6.90-7.96 (m, 5H, arom. H), 6.53 (ps, 1H, CH=O), 3.23-4.30 (m, 2H, CH_2-O), 3.03 (ps, 1H, OH exchanged with D_2O), 2.36-2.83 (m, 2H, CH-C=, CH-CH_3), 0.70-1.70 (m, 5H, aliph. H) . ^{13}C NMR ($CDCl_3$) δ ppm : 144.5 (OCH=), 136.6 (C= arom.), 128.5, 128.4, 128.3, 127.4, 126.3 (5xarom. CH=), 120.5 (C=), 81.9 (C-OH), 64.4 (CH_2-O), 43.8 (CH-C=), 31.8 (CH-CH_3), 20.1 (CH_2), 8.7 (CH_3). X Rays spectroscopic data have been collected.

1-phenyl-8-methyl-3-oxabicyclo [4.2.0^{2,7}] oct-6-en-1-ol 11 (R^1= Me, R^2=H, R^3=C_6H_5)

IR (NaCl) : 3600-3200 cm^{-1} (OH). ^1H NMR (CCl_4) δ ppm : 7.0–8.0 (m, 5H, arom. C), 5.50 (pt, 1H, CH=), 3.40-4.40 (m, 4H, CH_2-O-CH, OH exchanged with D_2O), 1.0-2.80 (m, 6H, aliph. H). Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.77 ; H, 7.40. Found : C, 77.66 ; H, 7.36.

1-ethyl-8-methyl-4-oxabicyclo [4.2.0^{2,7}] oct-2-en-1-ol 14 (R^1= Me, R^2=H, R^3=C_2H_5)
IR (NaCl) : 3600-3200 cm^{-1} (OH). ^1H NMR (CCl_4) δ ppm : 6.33 (ps, 1H, OCH=), 3.00-4.33 (m, 3H, CH_2-O, CH=), 2.73 (ps, 1H, OH exchanged with D_2O), 0.86-2.60 (m, 11H, aliph. H) .

4-(1-methyl-2-oxobutyl)-3,4-dihydropyran 15 (R^1= Me, R^2=H, R^3=C_2H_5)
IR (NaCl) : 1713 cm^{-1} (C=O), 1644 cm^{-1} (C=C). ^1H NMR (CCl_4) δ ppm : 6.23 (dd, 1H, O-CH=), 4.50 (dd, 1H, CH=CH-O), 3.53-4.13 (m, 2H, CH_2-O), 0.53-2.70 (m, 12H, aliph. H). ^{13}C NMR ($CDCl_3$) δ ppm : 213.3 (C=O), 144.0 (O-CH=), 101.2 (CH=), 63.8 (O-CH_2), 49.9 (CH-C), 31.9 (CH-CH_3), 34.9, 26.9 (2xCH_2), 13.2, 7.0 (2xCH_3). Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39 ; H, 9.58. Found : C, 71.23 ; H, 9.49.

(1SR,2RS) 1-isopropyl-8,8-dimethyl-3-oxabicyclo [4.2.0^{2,7}] oct-6-en-1ol 11 (R^1=Me, R^2=Me, R^3=iPr)
IR (NaCl) : 3600-3200 cm^{-1} (OH). ^1H NMR (CCl_4) δ ppm : 5.30 (pt, 1H, CH=C), 3.30-4.30 (m, 4H, CH2-O-CH, OH exchanged with D_2O), 0.96-2.46 (m, 15H, aliph. H, CH_2-C=C). ^{13}C NMR ($CDCl_3$) δ ppm : 146.0 (C=), 111.8 (CH=), 79.9 (C-OH), 77.7 (O-CH), 63.9 (CH_2), 49.7 (CH_2-CH=), 32.3 (CH-$(CH_3)_2$); 26.6 (C-$(CH_3)_2$), 22.5, 19.8, 16.3, 15.7 (4xCH_3). MS $C_{12}H_{20}O_2$ m/e 196.

5-(1,1,3-trimethyl-2-oxobutyl)-3,4-dihydropyran 12 (R^1=Me, R^2=Me, R^3=iPr)
IR (NaCl) : 1702 cm^{-1} (C=O), 1647 cm^{-1} (C=C). ^1H NMR (CCl_4) : δ 6.43 (ps, 1H, O-CH=), 3.86 (pt, 2H, CH2-O), 0.53-2.70 (m, 17H, aliph. H). ^{13}C NMR ($CDCl_3$) δ ppm : 219.3 (C=O), 141.5 (O-CH=), 113.3 (C=), 65.3 (CH_2-O), 50.2 (C-$(CH_3)_2$), 34.2 (CH-$(CH_3)_2$), 26.4, 24.4 (2xCH_2), 20.5, 20.0, 20.2, 19.9 (4xCH_3). MS $C_{12}H_{20}O_2$ m/e 196.

1-isopropyl-8,8-dimethyl-4-oxabicyclo [4.2.0^{2,7}] oct-2-en-1-ol 14 (R^1=Me, R^2=Me, R^3=iPr)
IR (NaCl) : 3600-3200 cm^{-1} (OH). ^1H NMR (CCl_4) δ ppm : 6,20 (ps, 1H, CH=O), 3.16-4.33 (m, 4H, CH_2-O, CH-CH=, OH exchanged with D_2O), 0.50-2.50 (m, 15H, aliph. H).

4-(1,1,3-trimethyl-2-oxobutyl)-3,4-dihydropyran 15 (R^1=Me, R^2=Me, R^3=iPr)

IR (NaCl) : 1702 cm^{-1} (C=O), 1644 cm^{-1} (C=C). ^1H NMR (CCl_4) δ ppm : 6.23 (dd,1H, O-CH=), 4.26 (dd, 1H, CH=C), 3.66-4.13 (m, 2H, CH_2-O-), 0.71-1.86 (m, 16H, aliph. H). ^{13}C NMR ($CDCl_3$) δ ppm : 219.0 (C=O), 144.6 (O-CH=), 101.2 (CH=), 65.0 (O-CH_2), 49.9 (C-$(CH_3)_2$), 35.9, 33.9 (2xCH), 24.1 (CH_2),

20.5, 20.4, 20.2, 19.9 (4xCH3). Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.43 ; H, 10.27. Found : C, 73.13 ; H, 10.19.

5-(2-cyclopropyl-2-oxoethyl)-2,3-dihydropyran 13 (R^1=R^2=H, R^3=C_3H_5)

IR (NaCl) : 1698 cm^{-1} (C=O). ^1H NMR (CCl_4) δ ppm : 5.26 (pt, 1H, CH=), 3.43-4.03 (m, 4H, CH_2OCH_2), 3.00 (ps, 2 H, =C-CH_2-C=O), 0.56-2.36 (m, 7H, aliph.H). ^{13}C NMR ($CDCl_3$) δ ppm : 208.2 (C=O),131.4 (C=), 123.1 (CH=), 67.6, 63.9 (2xOCH2), 48.7 (CH2-C=O), 25.4 (CH2-CH=), 19.8 (CH), 2x11.2 (2xCH2). MS $C_{10}H_{14}O_2$ m/e 166.

4-(2-cyclopropyl-2-oxoethyl)-3,4-dihydropyran 15 (R^1=R^2=H, R^3=C_3H_5)

IR (NaCl) : 1695 cm^{-1} (C=O), 1643 cm^{-1} (C=C). ^1H NMR (CCl_4) δ ppm : 6.16 (dd, 1H, OCH=), 4.4 (dd, 1 H, CH=), 3.83 (t, 2H, OCH_2), 2.96 (m, 1H, CH-CH=), 0.4-2.33 (m, 9H, aliph. H). ^{13}C NMR ($CDCl_3$) δ ppm : 208.9 (C=O), 143.2 (O-CH=), 103.8 (CH=), 63.6 (OCH_2), 49.2 (CH2-C=O), 28.3, 20.2, 10.3 (3xCH_2), 25.5, 14.6 (2xCH). Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.28 ; H, 8.43. Found : C, 72.26 ; C, 8.23. MS m/e 166.

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