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Enzymatic resolution of bicyclo[n.1.0]alkan-1-ols derivatives: Preparation of optically active α-substituted α-methylcycloalkanones.

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Abstract : Optically active α-methyl α-substituted cycloalkanones are prepared by a chemoenzymatic sequence which involves a Lipozyme® -catalyzed transesterification of 1-(chloroacetoxy)bicyclo[n.1.0]alkanes and ring opening of these cyclopropanol derivatives.

Optically active α,α-disubstituted cycloalkanones are useful intermediates for the synthesis of natural and/or biologically active compounds bearing a quaternary chiral carbon atom.[1,2,3] Such optically active cycloalkanones [4,5,6] could be prepared by alkylation of ketonic compounds in the presence of a chiral catalyst [7] or using a chiral base,[8] by alkylation of ketone enolate derivatives with alkylating agents bearing a chiral group,[9] by reaction of metallated [10] or unmetallated [11] chiral enamines or imines derivatives with alkylating agents, by addition of allyl derivatives to β-dicarbonyl compounds in the presence of palladium complexes bearing chiral ligands, by asymmetric Claisen rearrangement [12] and by enzymatic reduction of 2,2-disubstituted 1,3-diketones.[13,14] In fact most of these methods gave access to cycloalkanones bearing on the quaternary carbon atom an activating group (ester, ketone, nitrile, phenyl, ...) and/or an alkyl chain with an electron withdrawing group in β-position. The former groups were introduced in order to allow the alkylation of a α-monosubstituted cycloalkanone and/or to obtain a regioselective addition and the latter groups came from the addition of electron poor alkenic reactants. When focus was put on α-substituted α-methylcycloalkanones, the synthesis using these methods should necessitate various reactions including protecting and deprotecting steps in order to obtain the substituents in the proper oxidation state and with the desired chain length.

Recently it has been reported that lipase-catalysed transesterification of bicyclo[4.1.0]heptan-1-yl chloroacetates allows the preparation of optically active bicyclo[4.1.0]heptan-1-ol derivatives which can be transformed into enantiomerically enriched 2-methylcyclohexanones by the well known cleavage of cyclopropanols in basic medium. When an alkyl substituent was present on the bicyclic junction carbon atom α to the hydroxyl or to the chloroacetoxy group, α-substituted α-methylcyclohexanones were obtained and no epimerisation was observed during the cyclopropanic bond cleavage.[15]

This approach to α-substituted α-methylcycloalkanones seems interesting because the substituent R introduced during the synthesis of the bicycloalkanyl chloroacetate precursor could present the desired

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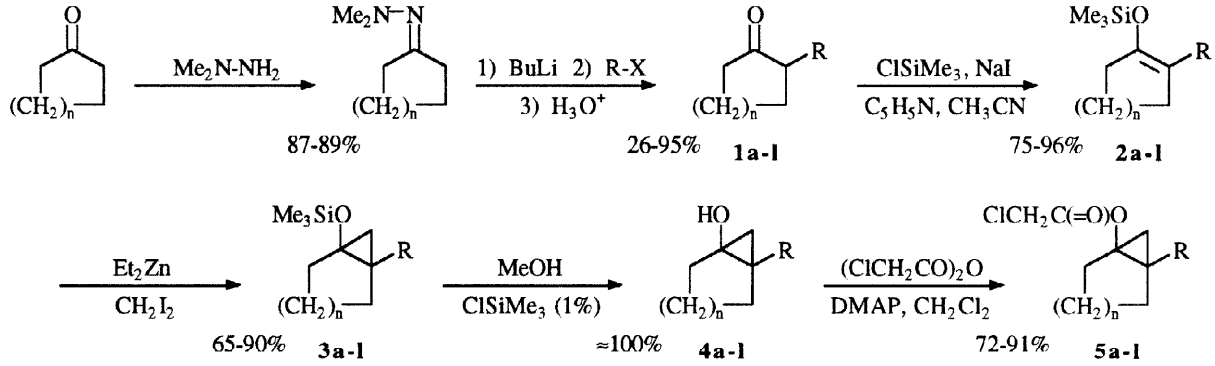
functionnalities and the appropriate chain length to avoid further tedious chemical transformations on this moiety.

Herein is reported an examination of the scope of this synthetic method with respect to the size of the bicycloalkane core and to the chain length and the functionality of the substituent.

The bicyclo[n.1.0]alkan-1-yl chloroacetates **5a-l** were prepared from 2-substituted cycloalkanones **1a-l** as shown in Scheme 1.

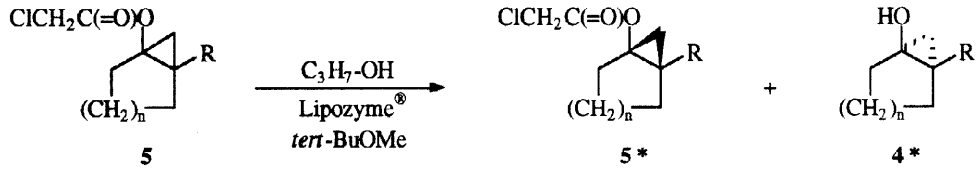


a n = 1 R = $(CH_2)_3$-CH_3
b n = 1 R = $(CH_2)_2$-CH=CH_3
c n = 1 R = $(CH_2)_3$-CH_2Cl
d n = 1 R = $(CH_2)_5$-CH_3
e n = 1 R = $(CH_2)_3$-OCH_2Ph
f n = 1 R = $(CH_2)_4$-OCH_2Ph
g n = 1 R = $(CH_2)_5$-OCH_2Ph
h n = 2 R = $(CH_2)_5$-CH_3
i n = 2 R = $(CH_2)_9$-CH_3
j n = 2 R = $(CH_2)_3$-OCH_2Ph
k n = 2 R = $(CH_2)_4$-OCH_2Ph
l n = 3 R = $(CH_2)_5$-CH_3

Scheme 1. Preparation of 1-(chloroacetoxy)bicyclo[n.1.0]alkanes **5a-l**

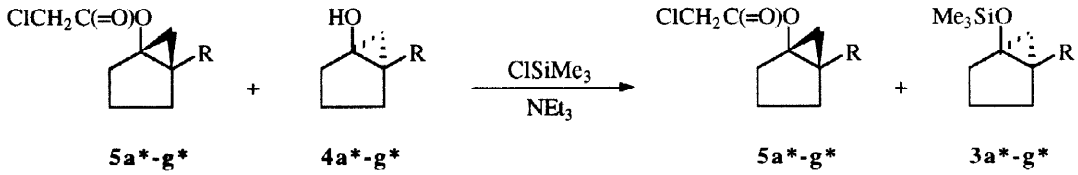
The α-substituted cycloalkanones **1a-l** were obtained by addition of various alkylating agents to the lithium derivatives [16] of cyclopentanone, cyclohexanone and cycloheptanone dimethylhydrazone.[17] Hydrolysis of the alkylated hydrazone to obtain the corresponding α-substituted cycloalkanone was made using an aqueous solution of potassium monophosphate and phosphorus acid.[18] The α-substituted silyl enol ethers **2a-l**, synthetized by reaction of the 2-substituted cycloalkanones **1a-l** with chlorotrimethylsilane, sodium iodide and pyridine in acetonitrile,[19,20] were cyclopropanated by a diethylzinc-methylene iodide mixture [21] to give the corresponding 1-(trimethylsilyloxy)bicyclo[n.1.0]alkanes **3a-l**. The beneficial influence of oxygen in the cyclopropanating reaction should be emphasized.[22] When the reaction was run under argon, low reaction rates and low yields of cyclopropanated products were generally observed and in some cases no cyclopropanation has occurred.[23,24] Treatment of the trimethylsilylethers **3a-l** by methanol acidified by addition of $ClSiMe_3$ (1 mole %) gave cleanly the bicycloalkan-1-ols **4a-l** which are isolated [25] after addition of NEt_3 (1 mole %) [26] and esterified with chloroacetic anhydride in the presence of 4-dimethylaminopyridine. Chloroacetates **5a-l** [27] were caracterized by their ^1H and ^{13}C NMR, IR and mass spectra.

Transesterifications of chloroacetates **5a-l** by 1-propanol were run in *tert*-butyl methyl ether at 36°C in the presence of Lipozyme® [28] which was found to be an appropriate lipase to catalyze the transesterification of bicyclo[4.1.0]heptan-1-yl chloroacetates. [15] Generally, reactions were stopped after about 50% conversion by removing the enzyme by filtration.



In the case of the bicycloheptanes and the bicyclooctane the separation of the unreacted chloroacetate **5*** (n = 2, 3) and the bicycloalkanol **4*** (n = 2, 3) was made by chromatography on neutral alumina (Activity III). (On silica gel, transformation of the bicycloalkanol into 2-methylcycloalkanone occurs).

Generally, bicyclohexanols **4*** (n = 1) are not recovered after chromatography under usual conditions (on silica gel, alumina or Florisil®) because they are air-sensitive.[29] After transesterification of the bicyclohexanes **5a-g** the mixtures of optically active products were treated under argon with chlorotrimethylsilane in the presence of triethylamine in ether, then the silyloxybicyclohexane **3*** was easily separated from the chloroacetate **5*** by chromatography on Florisil® (silyloxycyclopropanes were partly decomposed on silica gel or alumina).



In Table I are collected our results and those concerning other (chloroacetoxy)bicycloheptanes previously reported.[15] Generally no transesterification of the isomeric (chloroacetoxy)bicycloalkanes synthetized from the minor less substituted silyl enol ethers were observed. The remaining optically active chloroacetates **5*** were always isolated mixed with their regioisomers and the bicycloalkanols **4*** or the silyl ethers **3*** were obtained in pure form. Enantiomeric purities of the remaining chloroacetates **5*** and those of optically active bicycloalkanols **4*** or the corresponding trimethylsilylethers **3*** were determined after transformation into 2-substituted 2-methylcycloalkanones **6** (vide infra).

The reaction rate of the transesterification catalyzed by the lipase of *Mucor miehei* was dependent on the starting chloroacetate ring size. In the conditions used in this work (see experimental part) about 50% conversion was reached after 8 hours for the cyclopentanic and the cyclohexanic compounds **5a-5k** and 36% conversion only was observed after 48 hours in the case of the cycloheptanic compound **5l**.[31]

In the cases studied, moderate to excellent ee's were found for the remaining chloroacetates **5*** and for the bicycloalkanols **4*** or the silylethers **3***. Enantioselectivity of the reaction appears generally better for the cyclopentanic compounds **5a-5g** (enantiomeric ratio E between 40 and 420) than for the cyclohexanic compounds **5h-5k** (E between 14 and 20). For the much slower reacting cycloheptanic chloroacetate **5l** the enantiomeric ratio (E = 19) was closed to that calculated for the cyclohexanic homolog **5h** (E = 18) which bears the same substituent.

For a same size of the bicycloalkane the enantioselectivity of the reaction is chain length dependent. In the case of the cyclohexanic compounds it appears that the enantiomeric ratio E increases from the unsubstituted chloroacetate (**5**, n = 2, R = H, E = 22) to the compound substituted with a butyl chain (**5**, n = 2, R = C_4H_9, E = 38) then the E value decreases when the substituent is longer (**5h** : E = 18; **5i** : E = 14). The same decrease of the E value was observed with cyclopentanic compounds when the alkyl chain increases from butyl (**5a** : E = 420) to

Table I. Transesterification of bicyclo[n.1.0]alkan-1-yl chloroacetates **5** by 1-propanol in the presence of Lipozyme® (Lipase from *Mucor miehei*)[a]

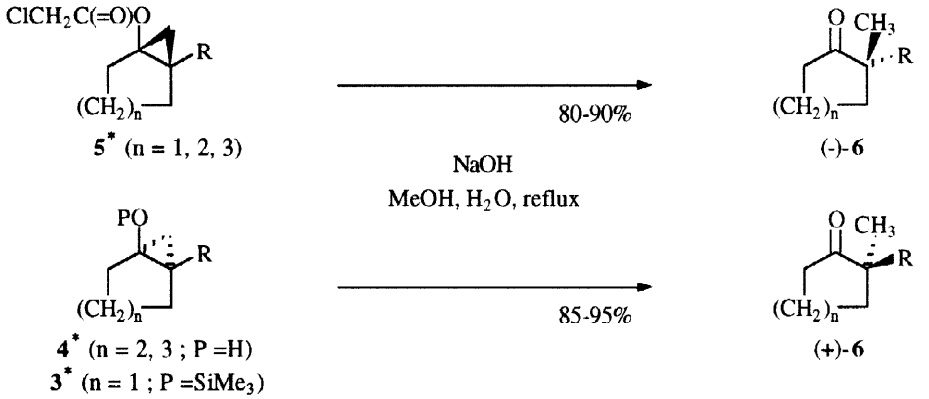
Substrate **5**				Remaining Chloroacetate **5***			Product (see text) **4*** (P = H) or **3*** (P = $SiMe_3$)				
n	R		c[d]	Yield (%)	$[\alpha]_D^{20}$ [e]	ee_S(%)	P	Yield (%)	$[\alpha]_D^{20}$ [e]	ee_P(%)	E[d]
1	$(CH_2)_3$-CH_3	**5a**	0.50	47	+14.2° (0.5)	97	$SiMe_3$	42	+0.7° (0.5)	98	420
1	$(CH_2)_2$-CH=CH_2	**5b**	0.53	46	+11.6° (1)	97	$SiMe_3$	38	+1.3° (1)	86	55
1	$(CH_2)_3$-CH_2Cl	**5c**	0.49	37	+9.3° (2)	93	$SiMe_3$	29	+1.8° (1)	94	110
1	$(CH_2)_5$-CH_3	**5d**	0.46	39	+7.7° (1)	81	$SiMe_3$	41	+0.9° (1)	97	165
1	$(CH_2)_3$-OCH_2Ph	**5e**	0.51	36	+6.4° (1)	91	$SiMe_3$	42	+2.3° (1.5)	87	46
1	$(CH_2)_4$-OCH_2Ph	**5f**	0.53	50	+10.2° (2)	95	$SiMe_3$	49	+2.1° (1)	85	45
1	$(CH_2)_5$-OCH_2Ph	**5g**	0.51	48	+6.7° (1)	90	$SiMe_3$	40	+2.0° (1)	86	40
2[c]	H		0.51		+10.4° (1)	84	H		+5.7° (1)	79	22
2[c]	CH_3		0.57		+30.2° (1)	95	H		-18.5° (1)	72	22
2[c]	C_2H_5		0.53		+18.5° (1)	91	H		-10.5° (1)	80	28
2[c]	$(CH_2)_3$-CH_3		0.51		+18.5° (1)	90	H		-11.6° (1)	86	38
2[c]	$(CH_2)_5$-CH_3	**5h**	0.56		+13.0° (1)	86	H		-8.0° (1)	66	13(18)[f]
2	$(CH_2)_9$-CH_3	**5i**	0.54	49	+12.6° (1.3)	86	H	43	-6.4° (0.9)	74	14
2	$(CH_2)_3$-OCH_2Ph	**5j**	0.54	52	+12.5° (1.5)	88	H	42	-11.1° (1)	75	20
2	$(CH_2)_4$-OCH_2Ph	**5k**	0.55	54	+14.2° (1.4)	85	H	41	-9.1° (1.3)	70	15
3[b]	$(CH_2)_5$-CH_3	**5l**	0.38	76	-1.3 (0.9)	51	H	28	-3.7 (0.8)	84	19

a) Unless otherwise noted the reaction time was about 8 hours.
b) 48 hours reaction time.
c) From reference 15.
d) conversion (c) and E calculated from ee_S and ee_P according to ref. 30.
e) In parenthesis is indicated the concentration in THF.
f) Using the conditions of this work.

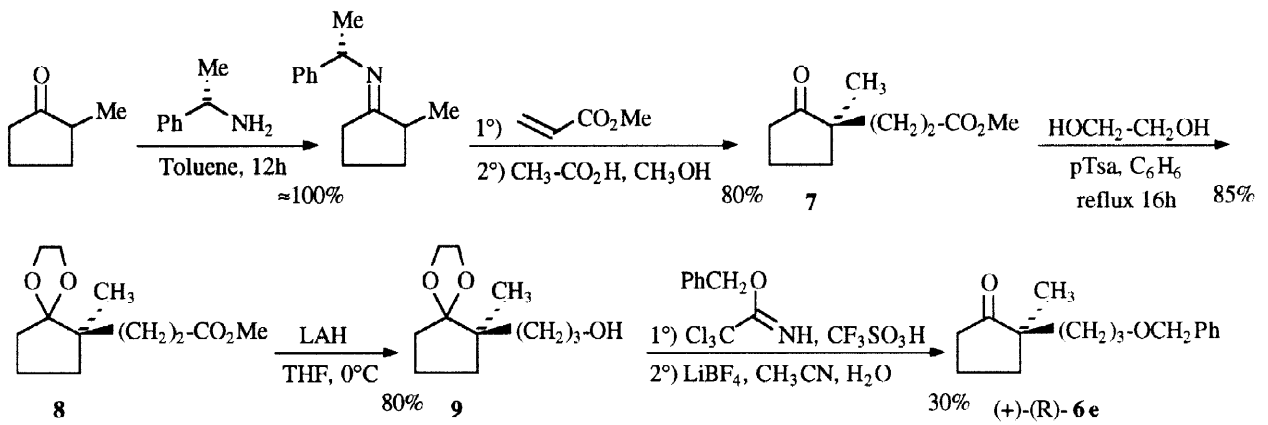
hexyl (**5d** : E = 165) and with the cyclopentanic and the cyclohexanic chloroacetates when the ω-benzyloxyalkyl chain length increases (compare E values calculated for the reactions of **5e**, **5f** and **5g** in one part and those of **5j** and **5k** in another part). It is also noteworthy that the presence of a carbon-carbon double bond or an heteroatom at the end of a butyl chain decreases the enantioselectivity of the reaction (compare the E values calculated for the reactions of **5b** and **5c** to that of **5a**).

Treatment of optically active chloroacetates **5***, bicycloalkanols **4*** and trimethylsilyl ethers **3*** with 2 equivalents of sodium hydroxide in refluxing hydromethanolic solutions led to the enantiomerically enriched 2-substituted 2-methylcycloalkanones **6a-6l** (yields ≥ 80%). At this point the two isomeric α,α'-disubstituted cycloalkanones which were always present in the reaction mixture obtained from a chloroacetate were generally separated from the cycloalkanone **6** during purification by silica gel column chromatography. The ee's of the ketones **6e**, **6g** and **6j** were measured by ^1H NMR spectroscopy in the presence of $Eu(hfc)_3$. For all the other

ketones ee's were determined by gas chromatography on a chiral column (Lipodex E). From the chloroacetoxybicycloalkanes **5*** levorotatory cycloalkanones were obtained and dextrorotatory compounds were isolated from the bicycloalkanols **4*** or the trimethylsilyl ethers **3***.



A sample of the cyclopentanone **6e** enriched in the R-configurated isomer was synthetized starting from the known (R)-ketoester **7** [3] which was easily obtained by reaction of methyl acrylate with the imine resulting from the reaction of 2-methylcyclopentanone with (S)-1-phenylethylamine. After formation of a dioxolane protecting group, the ester function was reduced,[32] then the hydroxyl group was transformed into a benzyloxy group [33] and the ketone was deprotected (Scheme 2).

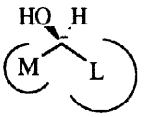


Scheme 2. Synthesis of cyclopentanone **6e** of known configuration

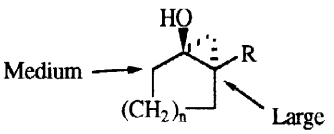
This (R)-cyclopentanone **6e** shows the same positive specific rotation in THF and the same retention time in gas chromatography on a Lipodex E column than the main isomer isolated after treatment in basic medium of the trimethylsilyl ether **3e*** which was obtained from the bicyclohexanol formed in the Lipozyme®-catalyzed transesterification of **5e**. So the transesterification of **5e** has occurred mainly on the (1S, 5R) enantiomer. The same enantioselectivity was observed in the Lipozyme®-catalyzed transesterification of the chloroacetoxybicyclo[4.1.0]heptanes **5** with R = H or C_4H_9 [15] and was postulated in all the other cases. The homogeneousness of the specific rotation sign of silyloxybicycloalkanes **3a*-3g*** (dextrorotatory) in one part, of bicycloalkanols **4h*-4l*** (levorotatory) in another part and of all the cycloalkanones **6** obtained from the more reactive chloroacetoxybicycloalkane enantiomers were in agreement with such an assumption.

An empirical rule predicts which enantiomer of secondary alcohols reacts faster with the lipase from *Mucor miehei*.[34] When the hydroxyl group points up and forward out of the plane defined by the chiral carbon

center, the large and the medium substituents, the favored enantiomer bears the large substituent on the right.



Generally in the transesterification of secondary alcohol esters it is the enantiomer with the same configuration that reacts faster. To our knowledge this empirical rule was not extended to tertiary alcohols or their derivatives because few examples of enzyme-catalyzed reactions of such compounds were reported in the literature.[35] In the case of the bicyclo[n.1.0]alkan-1ol derivatives it appears that the fast reacting enantiomer presents the same caracteristics than above, if we consider that the polysubstituted C_{n+2} cyclopropanic carbon atom is the larger substituent and the C_2 methylene group the medium substituent.



In conclusion this method allows the selective preparation of the two enantiomers of α-methylcycloalkanones of various size α-substituted by various substituents.

Experimental Section

General Methods. ^1H and ^{13}C NMR spectra were recorded on a Brucker AC-200 or on a AC-250 instrument. Chemical shifts are expressed relative to tetramethylsilane. Abbreviations are as follows : s, singlet ; d, doublet ; dd, doublet of doublet ; t, triplet ; tt, triplet of triplet ; m, multiplet. Infrared spectra were recorded on a Perkin-Elmer 682 spectrometer. Mass spectra were determined on a GC-Mass spectrometer Nermag R10-10 (capillary column: CPSIL 5, 25 m) at an ionizing voltage of 70 eV. Column chromatography was carried out with 70-230 mesh silica gel, 100-200 mesh neutral alumina or 100-200 mesh Florisil. TLC was performed on 0.25-mm silica gel (Merk 60 F_{254}). Dry solvents were obtained as follows : diethyl ether was distilled over $LiAlH_4$, THF was distilled over sodium-benzophenone radical-anion and pentane was distilled over P_2O_5. Triethylamine and pyridine were purified by distillation over CaH_2 and chlorotrimethylsilane by distillation over quinoline under argon. Other reagents were distilled before use. The dimethylhydrazones were prepared according to a literature procedure [17] and the ω-benzyloxy-1-bromoalkanes were synthetized (1°- $MeSO_2Cl$, NEt_3, CH_2Cl_2. 2°- LiBr, acetone) [36] from ω-benzyloxy-1-alkanols.[37] The sequence to prepare the chloroacetate **5h** and the spectroscopic properties of the compound **5h** and the intermediates were previously reported.[15] A 25 meters capillary column Lipodex E was used for the ee's measurements (flow carrier: helium).

Preparation of 2-butylcyclopentanone ***1a****. Representative Procedure.* To a solution of 1.26 g of cyclopentanone dimethylhydrazone (10 mmol) in 20 mL of dry THF under argon was added 6.56 mL of a 1.6 M solution of n-BuLi (10.5 mmol) in hexane. After 1h at -30°C the mixture was allowed to warm to 0°C and 1.07 mL of 1-bromobutane (10 mmol) was added. After 2h at 25°C, 1.4 g of KH_2PO_4 (10 mmol) and 1.65 g of H_3PO_3 (20 mmol) were added, followed by 10 mL of water. This mixture was left overnight at 25°C. Water was added and the reaction mixture was extracted several times using ethyl ether. The combined organic phases were dried (Na_2SO_4) and the solvents were evapored. The product was purified by silica gel column chromatography (pentane/ethyl ether : 80/20) to give 1.12 g (82%) of 2-butylcyclopentanone.[38]

Cycloalkanones **1b - 1l** were prepared following the same procedure.

2-(But-3-ényl)cyclopentanone ***1b***: From cyclopentanone dimethylhydrazone and 4-bromo-1-butene: 1.04 g,

75% .[39]

2-(4-Chlorobutyl)cyclopentanone ***1c***: From cyclopentanone dimethylhydrazone and 1-chloro-4-iodobutane: 0.454 g, 26%; IR (neat) 2940, 2860, 1785, 1450 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.55 (t, J = 6.6 Hz, 2H), 2.40-2.21 (m, 3H), 2.09-1.93 (m, 2H), 1.68-1.49 (m, 4H), 1.38-1.19 (m, 4H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 219.9, 48.3, 44.2, 37.4, 31.9, 28.9, 28.3, 24.2, 20.1; EI-MS (m/z) 176 (M^+, 0.8), 174 (M^+, 1.7), 97(5), 84 (100), 83 (27), 55 (27).

2-Hexylcyclopentanone ***1d***: From cyclopentanone dimethylhydrazone and 1-bromohexane: 1.38 g, 82%.[40]

2-(3-Benzyloxypropyl)cyclopentanone ***1e***: From cyclopentanone dimethylhydrazone and 3-benzyloxy-1-bromopropane: 2.10 g, 91%; IR (neat) 2940, 2860, 1740, 1460, 1100 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.40-7.20 (m, 5H), 4.50 (s, 2H), 3.48 (t, J = 6.3 Hz, 2H), 2.40-1.90 (m, 5H), 1.90-1.20 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 221.9, 138.4, 128.2, 127.5, 127.4, 72.7, 70.1, 48.8, 37.9, 29.4, 27.6, 26.3, 20.6; EI-MS (m/z) 232 (M^+, 2.3), 125 (4), 107 (6), 97 (31), 91 (100), 84 (17), 77 (4), 55 (10).

2-(4-Benzyloxybutyl)cyclopentanone ***1f***: From cyclopentanone dimethylhydrazone and 4-benzyloxy-1-bromobutane: 2.10 g, 87%; IR (neat) 2940, 2860, 1740, 1460, 1100 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.40-7.20 (m, 5H), 4.50 (s, 2H), 3.48 (t, J = 6.4 Hz, 2H), 2.40-1.90 (m, 5H), 1.90-1.20 (m, 8H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 220.6, 138.2, 127.9, 127.1, 127.0, 72.4, 69.7, 48.6, 37.6, 29.3, 29.1, 29.05, 23.8, 20.3; EI-MS (m/z) 246 (M^+, 3), 139 (2), 111 (3), 107 (5), 97 (45), 91 (100), 84 (14), 77 (4), 55 (12).

2-(5-Benzyloxypentyl)cyclopentanone ***1g***: From cyclopentanone dimethylhydrazone and 5-benzyloxy-1-bromopentane: 1.92 g, 74%; IR (neat) 2930, 2860, 1740, 1455, 1100 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.42-7.29 (m, 5H), 4.50 (s, 2H), 3.48 (t, J = 6.4 Hz, 2H), 2.36-1.88 (m, 5H), 1.87-1.57 (m, 4H), 1.57-1.17 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 220.0, 128.2, 127.6, 126.8, 126.7, 72.1, 69.6, 48.3, 37.4, 29.0, 28.9, 26.7, 25.6, 20.1, 19.9; EI-MS (m/z) 260 (M^+, 4), 107 (14), 97 (23), 91 (100), 84 (19), 83 (6), 77 (4), 55 (9).

2-Decylcyclohexanone ***1i***: From cyclohexanone dimethylhydrazone and 1-bromodecane: 2.14 g, 90%; IR (neat) 2930, 2860, 1715, 1455 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.45-2.18 (m, 3H), 2.18-1.90 (m, 2H), 1.90-1.50 (m, 4H), 1.45-1.05 (m, 18H), 0.85 (t, J = 6.4 Hz, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 213.3, 50.6, 41.8, 33.7, 31.8, 29.7, 29.5, 29.4, 29.3, 29.2, 27.9, 27.1, 24.7, 22.5, 22.2, 13.9; EI-MS (m/z) 238 (M^+, 7), 195 (3), 99 (79), 98 (100), 97 (25), 85 (4), 71 (6), 57 (11), 55 (22), 43 (20).

2-(3-Benzyloxypropyl)cyclohexanone ***1j***: From cyclohexanone dimethylhydrazone and 3-benzyloxy-1-bromopropane: 2.21 g, 90%; IR (neat) 2940, 2860, 1715, 1455, 1100 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.40-7.20 (m, 5H), 4.50 (s, 2H), 3.48 (t, J = 6.5 Hz, 2H), 2.49-2.20 (m, 3H), 2.20-1.95 (m, 2H), 1.95-1.75 (m, 2H), 1.75-1.50 (m, 4H), 1.50-1.22 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 213.0, 138.4, 128.1, 127.4, 127.3, 72.6, 70.2, 50.3, 41.8, 33.8, 27.9, 25.9, 24.7; EI-MS (m/z) 246 (M^+, 5), 155 (14), 139 (19), 111 (27), 107 (5), 98 (17), 97 (11), 91 (100), 77 (10), 55 (46).

2-(4-Benzyloxybutyl)cyclohexanone ***1k***: From cyclohexanone dimethylhydrazone and 4-benzyloxy-1-bromobutane: 2.47 g, 95% .[41]

2-Hexylcycloheptanone ***1l***: From cycloheptanone dimethylhydrazone and 1-bromohexane: 1.63 g, 83% .[42]

2-Substituted 1-(trimethylsilyloxy)cycloalkenes **2a-2l** were prepared from the 2-substituted cycloalkanones **1a-1l** using chlorotrimethylsilane, sodium iodide and pyridine in acetonitrile.[19] In some cases the product has been purified by distillation, in the other cases the crude product was used in the next step.

2-Butyl-1-(trimethylsilyloxy)cyclopentene ***2a***: 1.74 g, 82%; IR (neat) 2960, 2840, 1690, 1455, 1350, 1260, 950, 750 cm^{-1}; ^1H NMR (250 MHz, C_6D_6) δ 2.40-2.15 (m, 6H), 1.82-1.65 (m, 2H), 1.57-1.22 (m, 4H), 1.03-0.95 (m, 3H), 0.16 (s, 9H); EI-MS (m/z) 212 (M^+, 5), 195 (6), 183 (61), 155 (34), 73 (100).

2-(3-Butenyl)-1-(trimethylsilyloxy)cyclopentene ***2b***: 1.68 g, 80%; IR (neat) 2960, 2840, 1690, 1650, 1455, 1350, 1260, 950, 750 cm^{-1}; ^1H NMR (250 MHz, C_6D_6) δ 5.98-5.75 (m, 1H), 5.19-4.93 (m, 2H), 2.38-2.06

(m, 8H), 1.93-1.58 (m, 2H), 0.15 (s, 9H); EI-MS (m/z) 210 (M^+, 11), 169 (6), 155 (33), 73 (100).

2-(4-Chlorobutyl)-1-(trimethylsilyloxy)cyclopentene **2c**: 1.85 g, 75%; IR (neat) 2960, 2840, 1690, 1455, 1350, 1260, 950, 750 cm^{-1}; ^1H NMR (200 MHz, C_6D_6) δ 3.20 (t, J = 6.6 Hz, 2H), 2.36-1.98 (m, 6H), 1.80-1.64 (m, 2H), 1.64-1.28 (m, 4H), 0.15 (s, 9H); EI-MS (m/z) 248 (M^+, 3), 246 (M^+, 8), 169 (60), 73 (100).

2-Hexyl-1-(trimethylsilyloxy)cyclopentene **2d**: 2.09 g, 87% .[40]

2-(3-Benzyloxypropyl)-1-(trimethylsilyloxy)cyclopentene **2e**: 2.52 g, 83%; bp 130°C/0.04 mmHg; IR (neat) 2960, 2840, 1685, 1460, 1360, 1255, 1100, 950, 750 cm^{-1}; ^1H NMR (200 MHz, C_6D_6) δ 7.40-7.04 (m, 5H), 4.37 (s, 2H), 3.40 (t, J = 6.4 Hz, 2H), 2.40-2.14 (m, 6H), 1.91-1.52 (m, 4H), 0.16 (s, 9H); EI-MS (m/z) 304 (M^+, 2), 169 (5), 107 (2), 91 (49), 89 (2), 73 (100).

2-(4-Benzyloxybutyl)-1-(trimethylsilyloxy)cyclopentene **2f**: 2.45 g, 77%; bp 145°C/0.04 mmHg; IR (neat) 2940, 2860, 1690, 1460, 1360, 1255, 1100, 950, 750 cm^{-1}; ^1H NMR (200 MHz, C_6D_6) δ 7.37-7.05 (m, 5H), 4.37 (s, 2H), 3.39 (t, J = 6.1 Hz, 2H), 2.45-2.05 (m, 6H), 1.82-1.46 (m, 6H), 0.16 (s, 9H); EI-MS (m/z) 318 (M^+, 7), 211 (2), 183 (4), 107 (2), 91 (74), 89 (2), 77 (5), 73 (100).

2-(5-Benzyloxypentyl)-1-(trimethylsilyloxy)cyclopentene **2g**: 2.66 g, 80%; IR (neat) 2940, 2860, 1680, 1455, 1360, 1250, 1100, 950, 750 cm^{-1}; ^1H NMR (200 MHz, C_6D_6) δ 7.42-7.04 (m, 5H), 4.35 (s, 2H), 3.34 (t, J = 6.4 Hz, 2H), 2.42-2.11 (m, 6H), 1.85-1.58 (m, 4H), 1.52-1.39 (m, 4H), 0.16 (s, 9H); EI-MS (m/z) 332 (M^+, 8), 225 (4), 107 (2), 91 (82), 89 (3), 77 (5), 73 (100).

2-Decyl-1-(trimethylsilyloxy)cyclohexene **2i**: 2.33 g, 75%; bp 140°C/0.06 mmHg; IR (neat) 2940, 2865, 1680, 1450, 1355, 950, 750 cm^{-1}; ^1H NMR (200 MHz, C_6D_6) δ 2.27 (t, J = 7.3 Hz, 2H), 2.12-1.94 (m, 4H), 1.65-1.18 (m, 20H), 0.92 (t, J = 6.3 Hz, 3H), 0.16 (s, 9H); EI-MS (m/z) 310 (M^+, 18), 295 (4), 267 (2), 197 (1), 183 (100), 169 (13), 75 (17),73 (72).

2-(3-Benzyloxypropyl)-1-(trimethylsilyloxy)cyclohexene **2j**: 2.73 g, 88%; bp 142°C/0.06 mmHg; IR (neat) 2940, 2860, 1680, 1455, 1360, 1255, 1100, 950, 750 cm^{-1}; ^1H NMR (250 MHz, C_6D_6) δ 7.45-7.02 (m, 5H), 4.41 (s, 2H), 3.45 (t, J = 6.5 Hz, 2H), 2.32 (t, J = 6.5 Hz, 2H), 2.07-1.92 (m, 4H), 1.83 (tt, J = 6.5, 6.5 Hz, 2H), 1.59-1.38 (m, 4H), 0.19 (s, 9H); EI-MS (m/z) 318 (M^+, 6), 203 (4), 183 (60), 169 (8), 107 (3), 91 (80), 77 (5), 73 (100).

2-(4-Benzyloxybutyl)-1-(trimethylsilyloxy)cyclohexene **2k**: 3.19 g, 96%; bp 155°C/0.03 mmHg; IR (neat) 2940, 2860, 1680, 1460, 1360, 1255, 1100, 950, 750 cm^{-1}; ^1H NMR (200 MHz, C_6D_6) δ 7.39-7.04 (m, 5H), 4.39 (s, 2H), 3.43 (t, J = 6.5 Hz, 2H), 2.25 (t, J = 6.4 Hz, 2H), 2.08-1.88 (m, 4H), 1.82-1.27 (m, 8H), 0.19 (s, 9H); EI-MS (m/z) 332 (M^+, 10), 225 (2), 197 (2), 183 (53), 169 (9), 107 (3), 91 (76), 77 (7), 73 (100).

2-Hexyl-1-(trimethylsilyloxy)cycloheptene **2l**: 2.14 g, 80%; bp 130°C/0.06 mmHg; IR (neat) 2940, 2860, 1685, 1450, 1345, 1255, 950, 750 cm^{-1}; ^1H NMR (200 MHz, C_6D_6) δ 2.44-2.34 (m, 2H), 2.31 (t, J = 7.3 Hz, 2H), 2.19-2.10 (m, 2H), 1.80-1.25 (m, 14H), 1.01 (t, J = 6.4 Hz, 3H), 0.28 (s, 9H); EI-MS (m/z) 268 (M^+, 9), 253 (2), 225 (2), 197 (51), 183 (7), 73 (100).

Preparation of 5-butyl-1-(trimethylsilyloxy)bicyclo[3.1.0]hexane **3a**. *Representative Procedure.* In a two necked flask equipped with a magnetic stirrer, were placed 2.12 g of silyl enol ether **2a** (10 mmol). After removal of air by a stream of argon, 11 mL of 1M solution of Et_2Zn (11 mmol) in hexane were then added at 25°C. After the white fumes had disappeared, 886 µL of diiodomethane (11 mmol) were added dropwise. An exothermic reaction occurred after a short induction period. This mixture was left stirring 15 min at 25°C then the two necked flask was equipped with a calcium chloride guard. A white precipitate appeared and after two hours the mixture was diluted with 20 mL of ethyl ether and ammonia was bubbled into the solution maintained at 0°C. Zinc salt-ammonia complexes were removed by filtration through Celite®. The filtrate was concentrated, and the product was purified by silica gel column chromatography (pentane/ethyl ether : 98/2) to give 1.69 g (75%) of silyloxybicyclohexane **3a**: IR (neat) 2940, 2860, 1450, 1350, 1250, 950, 750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.06-1.81 (m, 2H), 1.69-1.15 (m, 10H), 1.03-0.75 (m, 3H), 0.60 (d, J = 5.3 Hz, 1H), 0.39 (dd, J =

5.3, 1.2 Hz, 1H), 0.14 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 67.2, 34.5, 31.3, 31.1, 30.9, 30.4, 23.0, 20.1, 19.0, 14.2, 1.0; EI-MS (m/z) 226 (M^+, 0.9), 211 (1), 183 (2), 169 (91), 73 (100).

(n+2)-Substituted 1-(trimethylsilyloxy)bicyclo[n.1.0]alkanes **3b-3l** were prepared following the same procedure.

5-(3-Butenyl)-1-(trimethylsilyloxy)bicyclo[3.1.0]hexane ***3b***: 1.68 g, 75%; IR (neat) 2940, 2860, 1650, 1450, 1350, 1250, 950, 750 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.00-5.80 (m, 1H), 5.09-4.88 (m, 2H), 2.31-2.04 (m, 2H), 2.03-1.80 (m, 2H), 1.69-1.48 (m, 4H), 1.46-1.30 (m, 1H),1.12-0.84 (m, 1H), 0.62 (dd, J = 5.5, 1.1 Hz, 1H), 0.41 (dd, J = 5.5, 1.5 Hz, 1H), 0.14 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 139.2, 113.7, 67.0, 34.4, 32.4, 31.4, 31.1, 30.4, 20.0, 19.0, 0.9; EI-MS (m/z) 244 (M^+, 1.3), 183 (5), 169 (31), 73 (100).

5-(4-Chlorobutyl)-1-(trimethylsilyloxy)bicyclo[3.1.0]hexane ***3c***: 1.69 g, 65%; IR (neat) 2960, 2840, 1440, 1370, 1230, 950, 750 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.56 (t, J = 6.8 Hz, 2H), 2.04-1.75 (m, 4H), 1.62-1.42 (m, 6H), 1.42-1.20 (m, 2H), 0.62 (d, J = 5.4 Hz, 1H), 0.38 (d, J = 5.4 Hz, 1H), 0.14 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 139.2, 113.7, 67.0, 34.4, 32.4, 31.4, 31.1, 30.4, 20.0, 19.0, 0.9; EI-MS (m/z) 262 (M^+, 0.3), 260 (M^+, 0.8), 169 (72), 73 (100).

5-Hexyl-1-(trimethylsilyloxy)bicyclo[3.1.0]hexane ***3d***: 2.28 g, 90%; IR (neat) 2940, 2860, 1450, 1350, 1250, 950, 750 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.04-1.80 (m, 2H), 1.67-1.12 (m, 14H), 0.89 (t, J = 6.8 Hz, 3H), 0.60 (d, J = 5.3 Hz, 1H), 0.39 (d, J = 5.3 Hz, 1H), 0.14 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 66.8, 34.4, 33.6, 31.7, 30.9, 29.5, 29.1, 27.9, 23.5, 22.1, 19.7, 13.9, 0.8; EI-MS (m/z) 254 (M^+, 6), 239 (4), 225 (2), 211 (2), 197 (2), 183 (21), 169 (12), 89 (2), 73 (100).

5-(3-Benzyloxypropyl)-1-(trimethylsilyloxy)bicyclo[3.1.0]hexane ***3e***: 2.51 g, 79%; IR (neat) 2940, 2860, 1460, 1360, 1260, 1100, 950, 750 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.43-7.23 (m, 5H), 4.52 (s, 2H), 3.52 (t, J = 6.6 Hz, 2H), 2.06-0.90 (m, 10H), 0.61 (d, J = 5.4 Hz, 1H), 0.39 (dd, J = 5.4, 1.4 Hz, 1H), 0.14 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 138.7, 128.2, 127.5, 127.3, 72.7, 70.6, 67.1, 34.4, 30.9, 30.4, 28.2, 28.0, 20.0, 18.9, 1.0; EI-MS (m/z) 229 (M^+-$OSiMe_3$, 2), 183 (1), 169 (47), 107 (2), 91 (76), 77 (6), 73 (100).

5-(4-Benzyloxybutyl)-1-(trimethylsilyloxy)bicyclo[3.1.0]hexane ***3f***: 2.55 g, 77%; IR (neat) 2940, 2860, 1460, 1360, 1260, 1100, 950, 750 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.45-7.24 (m, 5H), 4.52 (s, 2H), 3.49 (t, J = 6.5 Hz, 2H), 2.05-1.77 (m, 2H), 1.77-1.15 (m, 8H), 1.10-0.80 (m, 2H), 0.61 (d, J = 5.5 Hz, 1H), 0.39 (dd, J = 5.5, 1.3 Hz, 1H), 0.14 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 138.7, 128.2, 127.5, 127.3, 72.8, 70.5, 67.1, 34.4, 31.3, 31.0, 30.7, 29.9, 24.7, 20.1, 19.0, 1.0; EI-MS (m/z) 332 (M^+, 0.7), 241 (31), 183 (2), 169 (99), 107 (2), 91 (76), 77 (6), 73 (100).

5-(5-Benzyloxypentyl)-1-(trimethylsilyloxy)bicyclo[3.1.0]hexane ***3g***: 2.87 g, 83%; IR (neat) 2940, 2860, 1460, 1360, 1260, 1100, 950, 750 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.44-7.23 (m, 5H), 4.54 (s, 2H), 3.52 (t, J = 6.4 Hz, 2H), 2.09-1.86 (m, 2H), 1.79-1.18 (m, 10H), 1.11-0.86 (m, 2H), 0.65 (d, J = 5.4 Hz, 1H), 0.39 (dd, J = 5.4, 0.7 Hz, 1H), 0.19 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 138.6, 128.2, 127.4, 127.3, 72.7, 70.4, 67.1, 34.4, 31.4, 30.9, 30.7, 29.7, 27.9, 26.4, 20.0, 18.9, 0.9.

6-Decyl-1-(trimethylsilyloxy)bicyclo[4.1.0]heptane ***3i***: 2.82 g, 87%; IR (neat) 2940, 2860, 1460, 1350, 1250, 950, 750 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.16-1.97 (m, 2H), 1.97-0.96 (m, 24H), 0.88 (t, J = 6.4 Hz, 3H), 0.44 (d, J = 5.3 Hz, 1H), 0.39 (d, J = 5.3 Hz, 1H), 0.14 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 60.9, 34.9, 33.6, 31.9, 30.2, 30.1, 29.7, 29.6, 29.5, 29.4, 26.5, 25.3, 23.3, 22.7, 22.3, 22.1, 14.1, 1.3; EI-MS (m/z) 324 (M^+, 4), 309 (2), 197 (7), 183 (100), 169 (4), 73 (65).

6-(3-Benzyloxypropyl)-1-(trimethylsilyloxy)bicyclo[4.1.0]heptane ***3j***: 2.99 g, 90%; IR (neat) 2940, 2860, 1455, 1360, 1250, 1100, 950, 750 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.47-7.22 (m, 5H), 4.54 (s, 2H), 3.52 (t, J = 6.5 Hz, 2H), 2.19-2.03 (m, 2H), 2.01-1.59 (m, 4H), 1.59-1.39 (m, 2H), 1.39-1.07 (m, 4H), 0.49 (d, J = 5.4 Hz, 1H), 0.45 (d, J = 5.4 Hz, 1H), 0.19 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 138.7, 128.1, 127.4, 127.2, 72.6, 70.7, 60.7, 33.3, 31.4, 29.9, 26.8, 24.6, 23.3, 22.2, 22.0, 1.2; EI-MS (m/z) 332 (M^+, 16), 241

(5), 197 (17), 183 (10), 169 (16), 151 (42), 107 (11), 91 (100), 77 (4), 73 (73).

6-(4-Benzyloxybutyl)-1-(trimethylsilyloxy)bicyclo[4.1.0]heptane ***3k***: 2.77 g, 80%; IR (neat) 2940, 2860, 1460, 1360, 1250, 1100, 950, 750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.45-7.22 (m, 5H), 4.52 (s, 2H), 3.49 (t, J = 6.5 Hz, 2H), 2.17-2.00 (m, 2H), 1.79-0.80 (m, 12H), 0.45 (d, J = 6.1 Hz, 1H), 0.41 (d, J = 6.1 Hz, 1H), 0.13 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 138.7, 128.3, 127.6, 127.4, 72.8, 70.6, 60.8, 34.7, 33.4, 30.1, 30.0, 25.0, 23.3, 23.1, 22.2, 22.0, 1.3; EI-MS (m/z) 346 (M^+, 1.3), 197 (2), 183 (59), 107 (3), 91 (72), 89 (2), 77 (7), 73 (100).

7-Hexyl-1-(trimethylsilyloxy)bicyclo[5.1.0]octane ***3l***: 2.54 g, 90%; IR (neat) 2940, 2860, 1460, 1350, 1260, 950, 750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.36-2.13 (m, 1H), 2.13-1.92 (m, 1H), 1.92-1.04 (m, 18H), 0.89 (t, J = 6.5 Hz, 3H), 0.56 (d, J = 5.3 Hz, 1H), 0.41 (d, J = 5.3 Hz, 1H), 0.13 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 64.7, 39.4, 39.2, 34.3, 31.9, 31.8, 31.0, 29.8, 29.6, 28.8, 27.7, 26.2, 23.8, 14.0, 1.1; EI-MS (m/z) 282 (M^+, 4), 267 (3), 253 (2), 239 (15), 225 (1), 211 (4), 197 (38), 73 (100).

Preparation of Racemic 5-butyl-1-(chloroacetoxy)bicyclo[3.1.0]hexane ***5a****. Representative Procedure.* To a solution of 1.42 g of silyloxycyclopropane **3a** (6.3 mmol) in 10 mL of dichloromethane, maintained under argon, were added 6.3 mL of dry methanol and 8 µL of $ClSiMe_3$ (63 µmol). After 15 min at 25°C, TLC analysis showed that the reaction was over. After addition of 9 µL of triethylamine (63 µmol), the solvents were evaporated under reduced pressure. The flask containing the crude 5-butyl-1-bicyclo[3.1.0]hexanol **4a** was refilled with argon, and cooled at -30°C. Then a solution of 1.5 g of DMAP (12.3 mmol) in 9 mL of CH_2Cl_2 and a solution of 2.7 g of chloroacetic anhydride (15.8 mmol) in 9 mL of CH_2Cl_2 were added. The mixture was allowed to warm to 25°C, the reaction mixture becoming brown. After 2h at 25°C, 5g of Celite® were added and CH_2Cl_2 was evaporated. The residue was taken up with 40 mL of ethyl ether and filtrated through Celite®. The filtrate was concentrated, and the product was purified by silica gel column chromatography (pentane/ether : 90/10) to give 1.06 g (73%) of chloroacetate **5a**: IR (neat) 2940, 2860, 1775, 1750, 1460 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.04 (s, 2H), 2.32-2.20 (m, 1H), 2.11-1.92 (m, 1H), 1.82-1.04 (m, 10H), 0.98 (d, J = 6.4 Hz, 1H), 0.91 (t, J = 6.8 Hz, 3H), 0.59 (d, J = 6.4 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 167.5, 70.8, 40.9, 31.6, 31.5, 30.5, 30.3, 30.0, 22.7, 20.0, 18.7, 14.0; EI-MS (m/z) 230 (M^+, 0.07), 95 (5), 93 (10), 79 (18), 77 (2), 51 (8), 49 (4), 41 (12).

Chloroacetates **5b-5l** were prepared following the same procedure.

5-(3-Butenyl)-1-(chloroacetoxy)bicyclo[3.1.0]hexane ***5b***: 1.08 g, 75%; IR (neat) 2940, 2860, 1775, 1750, 1650, 1460 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.00-5.72 (m, 1H), 5.13-4.90 (m, 2H), 4.04 (s, 2H), 2.34-1.90 (m, 4H), 1.82-1.55 (m, 4H), 1.46-1.07 (m, 2H), 1.03 (d, J = 6.4 Hz, 1H), 0.62 (d, J = 6.4 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 167.5, 138.7, 114.4, 70.7, 40.9, 32.1, 31.5, 31.4, 30.4, 30.3, 20.0, 18.5; EI-MS (m/z) 95 (33), 93 (70), 79 (22), 77 (51), 55 (82), 51 (16), 49 (26), 41 (100).

1-(Chloroacetoxy)-5-(4-chlorobutyl)bicyclo[3.1.0]hexane ***5c***: 1.52 g, 91%; IR (neat) 2940, 2860, 1775, 1750, 1460 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.02 (s, 2H), 3.52 (t, J = 6.5 Hz, 2H), 2.32-2.11 (m, 1H), 2.10-1.97 (m, 1H), 1.97-1.42 (m, 7H), 1.41-1.02 (m, 3H), 0.97 (d, J = 6.3 Hz, 1H), 0.55 (d, J = 6.3 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 167.5, 76.4, 70.6, 44.9, 40.8, 32.4, 31.2, 30.2, 29.6, 25.0, 20.0, 18.4.

1-(Chloroacetoxy)-5-hexylbicyclo[3.1.0]hexane ***5d***: 1.30 g, 80%; IR (neat) 2940, 2860, 1775, 1750, 1460 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.03 (s, 2H), 2.31-2.14 (m, 1H), 2.09-1.86 (m, 1H), 1.81-0.99 (m, 14H), 0.98 (d, J = 6.2 Hz, 1H), 0.88 (t, J = 6.1 Hz, 3H), 0.58 (dd, J = 6.2, 1.3 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 167.6, 70.9, 40.9, 31.9, 31.8, 30.5, 30.4, 29.7, 29.4, 27.8, 22.6, 20.1, 18.5, 14.0; EI-MS (m/z) 95 (5), 93 (10), 79 (8), 77 (17), 51 (2), 49 (4); Anal. calcd for $C_{14}H_{23}O_2Cl$: C, 64.98; H, 8.96; Cl, 13.70, found: C, 65.15; H, 9.08; Cl, 13.61.

5-(3-Benzyloxypropyl)-1-(chloroacetoxy)bicyclo[3.1.0]hexane ***5e***: 1.51 g, 72%; IR (neat) 2940, 2860, 1770, 1750, 1455, 1100 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.39-7.24 (m, 5H), 4.51 (s, 2H), 4.02 (s, 2H),

3.50 (t, J = 6.4 Hz, 2H), 2.31-2.16 (m, 1H), 2.09-1.93 (m, 1H), 1.87-1.56 (m, 6H), 1.46-1.05 (m, 2H), 0.93 (d, J = 6.3 Hz, 1H), 0.62 (dd, J = 6.3, 1.2 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 167.3, 138.3, 128.0, 127.3, 127.2, 72.4, 70.5, 69.9, 40.9, 31.0, 30.2, 30.1, 28.3, 26.7, 19.8, 18.1; EI-MS (m/z) 233 (2), 231 (6), 155 (28), 107 (3), 95 (5), 93 (9), 91 (100), 79 (7), 77 (13), 51 (2), 49 (3); Anal. calcd for $C_{18}H_{23}O_3Cl$: C, 66.97; H, 7.18; Cl, 10.98, found: C, 66.74; H, 7.23; Cl, 10.20.

5-(4-Benzyloxybutyl)-1-(chloroacetoxy)bicyclo[3.1.0]hexane ***5f***: 1.74 g, 82%; IR (neat) 2940, 2860, 1775, 1750, 1460, 1100 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.45-7.24 (m, 5H), 4.52 (s, 2H), 4.03 (s, 2H), 3.48 (t, J = 6.3 Hz, 2H), 2.25-2.15 (m, 1H), 2.15-1.85 (m, 1H), 1.85-1.04 (m, 10H), 0.99 (d, J = 6.4 Hz, 1H), 0.61 (dd, J = 6.4, 1.4 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 167.3, 138.3, 128.0, 127.3, 127.1, 72.5, 70.4, 70.0, 40.6, 33.5, 31.3, 30.2, 30.1, 29.5, 24.3, 19.8, 18.1; EI-MS (m/z) 245 (5), 151 (9), 107 (5), 95 (3), 93 (7), 91 (100), 79 (10), 77 (30), 51 (1), 49 (4); Anal. calcd for $C_{19}H_{25}O_3Cl$: C, 67.75; H, 7.78; Cl, 10.22, found: C, 67.58; H, 7.31; Cl, 10.60.

5-(5-Benzyloxypentyl)-1-(chloroacetoxy)bicyclo[3.1.0]hexane ***5g***: 1.61 g, 73%; IR (neat) 2940, 2860, 1775, 1750, 1460, 1100 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.45-7.24 (m, 5H), 4.51 (s, 2H), 4.02 (s, 2H), 3.48 (t, J = 6.4 Hz, 2H), 2.35-2.12 (m, 1H), 2.12-1.88 (m, 1H), 1.88-1.05 (m, 12H), 0.98 (d, J = 6.2 Hz, 1H), 0.59 (d, J = 6.2 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 167.4, 138.5, 128.1, 127.4, 127.3, 72.7, 70.6, 70.2, 40.8, 31.8, 30.5, 30.4, 30.2, 29.6, 27.5, 26.2, 19.9, 18.3; EI-MS (m/z) 261 (5), 259 (16), 183 (21), 107 (4), 95 (4), 93 (9), 91 (100), 79 (8), 77 (29), 51 (1), 49 (3); Anal. calcd for $C_{20}H_{27}O_3Cl$: C, 68.46; H, 7.76; Cl, 10.10, found: C, 69.25; H, 7.84; Cl, 9.93.

1-(Chloroacetoxy)-6-decylbicyclo[4.1.0]heptane ***5i***: 1.55 g, 75%; IR (neat) 2940, 2860, 1770, 1750, 1455 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.00 (s, 2H), 2.25-2.10 (m, 1H), 2.10-1.88 (m, 1H), 1.80-1.02 (m, 24H), 0.89 (t, J = 6.6 Hz, 3H), 0.70 (d, J = 6.3 Hz, 1H), 0.65 (d, J = 6.3 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 167.2, 65.3, 41.0, 34.9, 31.8, 29.9, 29.8, 29.6, 29.3, 29.2, 27.5, 26.3, 25.9, 22.6, 21.9, 21.8, 21.2, 21.0, 14.1; EI-MS (m/z) 189 (1), 187 (2), 124 (3), 121 (22), 111 (100), 108 (80), 95 (15), 94 (9), 93 (35), 79 (11), 77 (25), 51 (1), 49 (2); Anal. calcd for $C_{19}H_{33}O_2Cl$: C, 69.61; H, 10.02; Cl, 10.69, found: C, 66.38; H, 10.11; Cl, 10.78.

6-(3-Benzyloxypropyl)-1-(chloroacetoxy)bicyclo[4.1.0]heptane ***5j***: 1.93 g, 91%; IR (neat) 2940, 2860, 1770, 1750, 1450, 1100 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.38-7.22 (m, 5H), 4.51 (s, 2H), 3.96 (s, 2H), 3.49 (t, J = 6.5 Hz, 2H), 2.33-2.10 (m, 1H), 2.08-1.87 (m, 1H), 1.87-1.05 (m, 10H), 0.73 (d, J = 6.8 Hz, 1H), 0.68 (d, J = 6.8 Hz, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 167.3, 138.5, 128.3, 127.6, 127.5, 72.8, 70.3, 65.2, 41.0, 34.4, 29.7, 29.0, 26.6, 25.5, 21.9, 21.8, 21.1; EI-MS (m/z) 245 (3), 151 (21), 107 (4), 95 (4), 93 (9), 91 (100), 79 (10), 77 (18), 51 (2), 49 (5).

6-(4-Benzyloxybutyl)-1-(chloroacetoxy)bicyclo[4.1.0]heptane ***5k***: 1.72 g, 78%; IR (neat) 2940, 2860, 1770, 1750, 1450, 1100 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.41-7.22 (m, 5H), 4.51 (s, 2H), 3.98 (s, 2H), 3.47 (t, J = 6.3 Hz, 2H), 2.28-2.09 (m, 1H), 2.05-1.83 (m, 1H), 1.75-1.05 (m, 12H), 0.72 (d, J = 6.5 Hz, 1H), 0.67 (d, J = 6.5 Hz, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 167.2, 138.6, 128.2, 127.5, 127.4, 72.8, 70.3, 65.2, 40.9, 34.7, 29.8, 29.7, 29.1, 25.8, 23.0, 22.0, 21.8, 21.1; EI-MS (m/z) 107 (4), 95 (7), 93 (16), 91 (100), 79 (8), 77 (20), 51 (2), 49 (4); Anal. calcd for $C_{20}H_{27}O_3Cl$: C, 68.46; H, 7.76; Cl, 10.10, found: C, 68.01; H, 7.85; Cl, 10.28.

1-(Chloroacetoxy)-7-hexylbicyclo[5.1.0]octane ***5l***: 1.44 g, 80%; IR (neat) 2940, 2860, 1770, 1750, 1460 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.02 (s, 2H), 2.59-2.42 (m, 1H), 2.21-2.03 (m, 1H), 1.90-1.06 (m, 18H), 1.00-0.85 (m, 4H), 0.77 (d, J = 6.4 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 166.8, 69.3, 41.1, 34.6, 33.5, 31.7, 31.6, 31.5, 30.6, 20.4, 28.8, 27.1, 26.7, 25.8, 25.6, 13.9; EI-MS (m/z) 203 (0.7), 201 (1.5), 122 (21), 95 (13), 93 (30), 85 (3), 79 (8), 77 (19), 51 (7), 49 (18), 41 (100); Anal. calcd for $C_{16}H_{27}O_2Cl$: C, 66.01; H, 9.49; Cl, 13.34, found: C, 65.72; H, 9.47; Cl, 13.37.

Enzymatic Transesterification of 5-butyl-1-(chloroacetoxy)bicyclo[3.1.0]hexane ***5a. Representative Procedure.*** In a flask equipped with a magnetic stirrer, were placed under argon 100 mg of the chloroacetate **5a** (0.43 mmol), and 500 mg of Lipozyme®. To the mixture were added 3 mL of *tert*-BuOMe and 886 µL of dry 1-propanol (11.8 mmol) both previously purged of air by bubbling of argon. After 8h at 36°C, the reaction mixture was filtered under argon, and the solid was washed with air-free *tert*-BuOMe . After concentration under reduced pressure, the flask containing the residue was refilled with argon, 5 mL of ethyl ether were added and the mixture was cooled at -20°C. Then 243 µL of triethylamine (1.7 mmol) and 221 µL of chlorotrimethylsilane (1.7 mmol) were added. After 18h at 25°C, the reaction mixture was concentrated and the reaction products were separated by Florisil® column chromatography (pentane/ethyl ether : 90/10) to give 20 mg (42%) of silyloxycyclopropane **3a*** and 23 mg (47%) of chloroacetate **5a***.

Transesterifications of the chloroacetates **5b-5g** were made following the same procedure. Specific rotation of these optically active chloroacetates **5*** and silyloxybicycloalkanes **3*** are reported in Table 1.

Enzymatic Transesterification of 1-(chloroacetoxy)-6-decylbicyclo[4.1.0]heptane ***5i.*** *Representative Procedure.* 52.6 mg of Chloroacetate **5i** (0.16 mmol) were dissolved in 0.7 mL of *tert*-BuOMe in a flask equipped with a magnetic stirrer. To this solution were added 210 mg of Lipozyme® and 330 µL of dry 1-propanol (4.4 mmol). After 8h at 36°C, the reaction mixture was filtered and the solid was washed with *tert*-BuOMe. After concentration under reduced pressure, the reaction products were separated by column chromatography on neutral alumina activity III (pentane/ethyl ether : 90/10) to give 26 mg (49%) of chloroacetate **5i*** and 17.4 mg (43%) of 6-decylbicyclo[4.1.0]heptan-1-ol **4i***: IR (neat) 3420, 3060, 2930, 2860, 1460 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.22-2.07 (m, 1H), 1.79-1.68 (m, 2H), 1.60-1.02 (m, 24H), 0.88 (t, J = 6.6 Hz, 3H), 0.45 (s, 2H).

Transesterifications of the chloroacetates **5j-5l** were made following the same procedure. Specific rotation of these optically active chloroacetates **5*** and bicycloalkanols **4*** are reported in Table 1.

6-(3-Benzyloxypropyl)bicyclo[4.1.0]heptan-1-ol ***4j***: IR (neat) 3400, 3090, 3060, 3030, 2940, 2860, 1460, 1100 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.43-7.21 (m, 5H), 4.52 (s, 2H), 3.49 (t, J = 6.6 Hz, 2H), 2.24-2.09 (m, 1H), 1.85-1.04 (m, 12H), 0.47 (s, 2H).

6-(4-Benzyloxybutyl)bicyclo[4.1.0]heptan-1-ol ***4k***: IR (neat) 3420, 3090, 3060, 3030, 2940, 2860, 1450, 1100 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.43-7.26 (m, 5H), 4.51 (s, 2H), 3.49 (t, J = 6.2 Hz, 2H), 2.23-2.10 (m, 1H), 1.98-1.08 (m, 14H), 0.47 (s, 2H).

7-Hexylbicyclo[5.1.0]octan-1-ol ***4l***: IR (neat) 3420, 3060, 2920, 2860, 1450 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.31 (dd, J = 6.6, 14.4 Hz, 1H), 1.95-1.78 (m, 1H), 1.78-1.10 (m, 19H), 0.89 (t, J = 6.8 Hz, 3H), 0.59 (d, J = 6.1 Hz, 1H), 0.46 (d, J = 6.1 Hz, 1H).

Rearrangement of chloroacetate ***5a**** *and silyloxybicyclohexane* ***3**** *into 2-butyl-2-methylcyclopentanone* ***6a.*** *Representative Procedure.* 23 mg of optically active chloroacetate **5a*** (0.1mmol) were dissolved in 200 µL of methanol and 100 µL of 2N NaOH solution (0.2 mmol) were added. This mixture was stirred 4h at 60°C. The product was extracted with ethyl ether, and the organic solution was washed with brine and dried (Na_2SO_4). After concentration the crude product was purified by column chromatography on silica gel (pentane/ethyl ether : 90/10) to give 12.3 mg (80%) of 2-butyl-2-methylcyclopentanone **(-)-6a**: IR (neat) 2960, 2840, 1750, 1460 cm^{-1} ; ^1H NMR (250 MHz, $CDCl_3$) δ 2.42-2.13 (m, 2H), 2.02-1.64 (m, 4H), 1.52-1.09 (m, 6H), 0.99 (s, 3H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 222.9, 47.7, 36.4, 35.6, 29.7, 26.5, 23.3, 21.8, 18.7, 14.0; EI-MS (m/z) 154 (M^+, 29), 111 (17), 98 (100), 97 (11), 55 (55), 43 (25), 41 (41); Anal. calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76, found: C, 78.18; H, 11.73; $[\alpha]_D^{20}$ = -39° (c = 1.9, THF, ee = 97%). Rearrangement of silyloxycyclopropane **3a*** made using the same procedure gave mainly the enantiomer **(+)-6a** (yield 85%): $[\alpha]_D^{20}$ = +47° (c = 0.8, THF, ee = 98%). Measurements of the ee's of **6a** were made by GC: 80°C,

0.75 bar: **(-)-(*R*)**, T_R = 23.32 min; (+)-(*S*), T_R = 26.51 min.

Rearrangements of 6b*-6l*, 3b*-3g* and **4h*-4l*** were made following the same procedure.

*2-(3-Butenyl)-2-methylcyclopentanone **6b***: IR (neat) 2960, 2840, 1750, 1650, 1460 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.89-5.67 (m, 1H), 5.09-4.88 (m, 2H), 2.63-2.41 (m, 2H), 2.19-1.64 (m, 6H), 1.52-1.48 (m, 2H), 1.02 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 223.4, 128.5, 114.5, 48.1, 37.7, 35.7, 35.6, 28.6, 21.7, 18.7; Anal. calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59; O, 10.51, found: C, 79.11; H, 10.51; O, 10.47. From **5b*** was obtained **(-)-6b** (Yield 85%): $[\alpha]_D^{20}$ = -36.8° (c = 0.8, THF, ee = 97%) and from **3b*** the compound **(+)-6b** (Yield 92%): $[\alpha]_D^{20}$ = +32.5° (c = 0.8, THF ee = 86%). The 2-(3-butenyl)-2-methylcyclopentanone **6b** was transformed by hydrogenation (1 bar, Pd-C 10%, EtOH) into 2-butyl-2-methylcyclopentanone **6a** for the measurement of the ee's (vide supra).

*2-(4-Chlorobutyl)-2-methylcyclopentanone **6c***: IR (neat) 2960, 2840, 1750, 1460 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.54 (t, J = 6.7 Hz, 2H), 2.49-2.12 (m, 2H), 1.99-1.64 (m, 5H), 1.61-1.22 (m, 5H), 1.01 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 228.4, 48.2, 44.8, 37.6, 35.8, 35.5, 32.9, 21.8, 21.7, 18.7; Anal. calcd for $C_{10}H_{17}ClO$: C, 63.65; H, 9.08; Cl, 18.79; O, 8.48, found: C, 63.82; H, 9.15; Cl, 18.78; O, 8.61. From **5c*** was obtained **(-)-6c** (Yield 88%): $[\alpha]_D^{20}$ = -36.1° (c = 1.2, THF, ee = 93%) and from **3c*** the compound **(+)-6c** (Yield 90%): $[\alpha]_D^{20}$ = +33.6° (c = 0.5, THF, ee = 94%). Measurements of the ee's of **6c** were made by GC: 100°C, 0.8 bar: **(-)-(*S*)**, T_R = 93.7 min; **(+)-(*R*)**, T_R = 126.9 min.

*2-Hexyl-2-methylcyclopentanone **6d***: IR (neat) 2960, 2840, 1750, 1460 cm-^{1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.40-2.10 (m, 2H), 2.00-1.61 (m, 4H), 1.48-1.07 (m, 10H), 0.98 (s, 3H), 0.87 (t, J = 6.7 Hz, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 224.6, 48.3, 37.7, 36.7, 35.6, 31.7, 29.8, 24.2, 22.6, 21.8, 18.7, 14.1; EI-MS (m/z) 182 (M^+, 1.9), 98 (100), 97 (11), 71 (3), 57 (11), 55 (29); Anal. calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16; O, 8.78, found: C, 79.27; H, 12.19; O, 8.81. From **5d*** was obtained **(-)-6d** (Yield 86%): $[\alpha]_D^{20}$ = -26.0° (c = 0.5, THF, ee = 81%) and from **3d*** the compound **(+)-6d** (Yield 90%): $[\alpha]_D^{20}$ = +32.7° (c = 1, THF ee = 97%). Measurements of the ee's of **6d** were made by GC: 90°C, 0.75 bar: **(-)-(*R*)**, T_R = 45.8 min; **(+)-(*S*)**, T_R = 49.5 min.

*2-(3-Benzyloxypropyl)-2-methylcyclopentanone **6e***: IR (neat) 2940, 2860, 1740, 1460, 1100 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.42-7.14 (m, 5H), 4.49 (s, 2H), 3.46 (t, J = 6.7 Hz, 2H), 2.40-2.12 (m, 2H), 1.98-1.37 (m, 8H), 1.01 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 222.6, 128.1, 127.8, 127.1, 127.0, 72.3, 70.1, 47.4, 37.1, 35.2, 32.6, 24.3, 21.3, 18.2; EI-MS (m/z) 139 (7), 111 (1), 107 (7), 98 (35), 97 (11), 91 (100), 77 (6), 55 (14); Anal. calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00, found: C, 78.17; H, 8.92. From **5e*** was obtained **(-)-6e** (Yield 87%): $[\alpha]_D^{20}$ = -29.8° (c = 1, THF, ee = 91%) and from **3e*** the compound **(+)-6e** (Yield 92%): $[\alpha]_D^{20}$ = +24.8° (c = 1.7, THF ee = 87%). Measurements of the ee's of **6e** were made by ^1H NMR in the presence of $Eu(hfc)_3$: the methyl singulets (δ 1.01 ppm) were shifted to 2.56 [**(-)-(*S*)**] and 2.58 ppm [**(+)-(*R*)**].

*2-(4-Benzyloxybutyl)-2-methylcyclopentanone **6f***: IR (neat) 2940, 2860, 1740, 1460, 1105 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.42-7.20 (m, 5H), 4.50 (s, 2H), 3.46 (t, J = 6.4 Hz, 2H), 2.39-2.11 (m, 2H), 1.99-1.15 (m, 10H), 0.99 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 223.5, 138.4, 128.2, 127.5, 127.3, 72.7, 69.9, 48.1, 37.5, 36.3, 35.4, 30.1, 21.6, 20.8, 18.5; EI-MS (m/z) 260 (M^+, 0.8), 153 (2), 111 (6), 107(9), 98 (38), 97 (9), 91 (100), 77 (6), 55 (15); Anal. calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29, found: C, 78.11; H, 9.11. From **5f*** was obtained **(-)-6f** (Yield 85%): $[\alpha]_D^{20}$ = -37.0° (c = 1, THF, ee = 95%) and from **3f*** the compound **(+)-6f** (Yield 92%): $[\alpha]_D^{20}$ = +28.3° (c = 1, THF, ee = 85%). Measurements of the ee's of **6f** were made by GC: 160°C, 0.75 bar: **(-)-(*R*)**, T_R = 202.3 min; **(+)-(*S*)**, T_R = 206.7 min.

*2-(5-Benzyloxypentyl)-2-methylcyclopentanone **6g***: IR (neat) 2940, 2860, 1740, 1460, 1105 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.40-7.19 (m, 5H), 4.48 (s, 2H), 3.46 (t, J = 6.4 Hz, 2H), 2.38-2.05 (m, 2H), 1.98-1.07 (m, 12H), 0.98 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 223.0, 138.3, 127.9, 127.2, 127.0, 72.4, 69.9, 47.8, 37.2, 36.2, 35.2, 29.3, 26.4, 23.7, 21.4, 18.3; EI-MS (m/z) 274 (M^+, 2), 153 (2), 111 (16), 107 (15), 98 (90), 97 (11), 91 (100), 77 (4), 55 (11); Anal. calcd for $C_{18}H_{26}O_2$: C, 78.83; H, 8.76, found: C, 79.08; H, 8.48.

From **5g*** was obtained **(-)-6g** (Yield 86%): $[\alpha]_D^{20}$ = -25.2° (c = 1.6, THF, ee = 90%) and from **3g*** the compound **(+)-6g** (Yield 91%): $[\alpha]_D^{20}$ = +22.6° (c = 1, THF, ee = 86%). Measurements of the ee's of **6g** were made by ^{1}H NMR in the presence of Eu(hfc)$_3$: the methyl singulets (δ 0.98 ppm) were shifted to 2.60 [(-)-(***R***)] and 2.68 ppm [(+)-(***S***)].

*2-Decyl-2-methylcyclohexanone **6i***: IR (neat) 2940, 2860, 1715, 1455 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.49-2.25 (m, 2H), 2.02-1.59 (m, 6H), 1.49-1.16 (m, 18H), 1.12 (s, 3H), 0.89 (t, J = 6.7 Hz, 3H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 216.3, 48.6, 39.5, 38.8, 37.5, 31.9, 30.3, 29.6, 29.5, 29.4, 29.3, 27.5, 23.7, 22.7, 22.5, 21.0, 14.1; EI-MS (m/z) 252 (M^+, 0.3), 113 (36), 112 (100), 111 (7), 85 (3), 71 (4), 69 (23), 57 (14), 55 (12), 43 (43); HRMS, calcd for $C_{17}H_{32}O$: 252.2453, found: 252.2456. From **5i*** was obtained **(-)-6i** (Yield 85%): $[\alpha]_D^{20}$ = -31.0° (c = 0.7, THF, ee = 74%) and from **4i*** the compound **(+)-6i** (Yield 90%): $[\alpha]_D^{20}$ = +35.0° (c = 0.6, THF, ee = 85%). Measurements of the ee's of **6i** were made by GC: 130°C, 0.75 bar: (-)-(***R***), T_R = 220.6 min; (+)-(***S***), T_R = 227.5 min.

*2-(3-Benzyloxypropyl)-2-methylcyclohexanone **6j***: IR (neat) 2940, 2860, 1715, 1460, 1100 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.42-7.20 (m, 5H), 4.50 (s, 2H), 3.46 (t, J = 6.0 Hz, 2H), 2.53-2.39 (m, 2H), 2.04-1.25 (m, 10H), 1.06 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 215.9, 138.4, 127.5, 128.3, 127.4, 72.7, 70.5, 48.2, 39.2, 38.6, 33.9, 27.4, 24.1, 22.4, 20.9; EI-MS (m/z) 260 (M^+, 0.4), 153 (17), 112 (34), 111 (6), 107 (6), 91 (100), 77 (4), 55 (12); Anal. calcd for $C_{17}H_{24}O_2$: C, 78.46; H, 9.23, found: C, 78.25; H, 8.97. From **5j*** was obtained **(-)-6j** (Yield 88%): $[\alpha]_D^{20}$ = -38.6° (c = 1, THF, ee = 90%) and from **4j*** the compound **(+)-6j** (Yield 90%): $[\alpha]_D^{20}$ = +36.3° (c = 1, THF, ee = 86%). Measurements of the ee's of **6j** were made by ^{1}H NMR in the presence of Eu(hfc)$_3$: the methyl singulets (δ 1.06 ppm) were shifted to 2.63 [(-)-(***S***)] and 2.65 ppm [(+)-(***R***)].

*2-(4-Benzyloxybutyl)-2-methylcyclohexanone **6k***: IR (neat) 2940, 2860, 1715, 1450, 1100 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.32-7.15 (m, 5H), 4.51 (s, 2H), 3.46 (t, J = 6.3 Hz, 2H), 2.21-2.07 (m, 2H), 1.68-1.06 (m, 12H), 1.01 (s, 3H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 215.9, 138.5, 128.2, 127.6, 127.4, 72.8, 70.1, 48.5, 39.2, 38.7, 37.3, 30.3, 27.4, 22.5, 20.9, 20.4; EI-MS (m/z) 274 (M^+, 1.1), 167 (2.1), 112 (100), 111 (8), 107 (6), 91 (95), 77 (4), 55 (55) ; Anal. calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55, found: C, 79.02; H, 9.75. From **5k*** was obtained **(-)-6k** (Yield 88%): $[\alpha]_D^{20}$ = -31.0° (c = 1.4, THF, ee = 85%) and from **4k*** the compound **(+)-6k** (Yield 91%): $[\alpha]_D^{20}$ = +24.0° (c = 0.9, THF, ee = 70%). Measurements of the ee's of **6k** were made by GC: 165°C, 0.75 bar: (-)-(***S***), T_R = 199.2 min; (+)-(***R***), T_R = 201.9 min.

*2-Hexyl-2-methylcycloheptanone **6l***: IR (neat) 2940, 2860, 1710, 1455 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.79-2.49 (m, 1H), 2.42-2.25 (m, 1H), 1.92-1.13 (m, 18H), 1.03 (s, 3H), 0.87 (t, J = 6.2 Hz, 3H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 217.9, 66.7, 50.9, 40.2, 37.7, 30.7, 29.9, 28.4, 26.6, 24.4, 23.9, 22.5, 21.4, 14.0; EI-MS (m/z) 139 (1.3), 126 (100), 125 (3), 111 (8), 97 (27), 83 (16), 69 (44), 57 (23), 55 (83), 43 (23); Anal. calcd for $C_{14}H_{26}O$: C, 79.94; H, 12.46; O, 7.61, found: C, 79.41; H, 12.21; O, 7.86. From **5l*** was obtained **(-)-6l** (Yield 82%): $[\alpha]_D^{20}$ = -20.7 (c = 2.8, THF, ee = 51%) and from **4l*** the compound **(+)-6l** (Yield 86%): $[\alpha]_D^{20}$ = +33.0 (c = 0.8, THF, ee = 87%). Measurements of the ee's of **6l** were made by GC: 100°C, 0.75 bar: (-)-(***R***), T_R = 111.5 min; (+)-(***S***), T_R = 116.7 min.

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25. Handling of the bicycloalkanols was made under argon. This precaution is particularly important in the case of bicyclo[3.1.0]hexan-1-ols which are air sensitive.[29]
26. Careful neutralisation of the reaction mixture before evaporation of methanol gave a more reliable method to obtain the bicycloalkanol free of α-methylketone resulting from cyclopropanic bond cleavage which is easier in acid or basic medium.
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