

Supporting Information

Table A. ^1H NMR data for the six hydrogenation products. Values of $J_{\text{calc.}}$ are from Table 4.

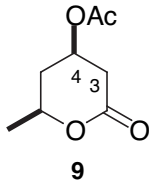
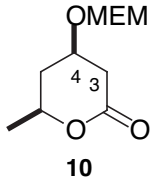
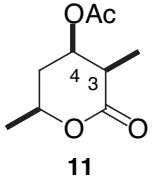
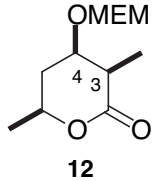
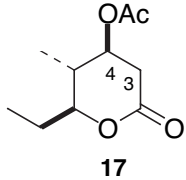
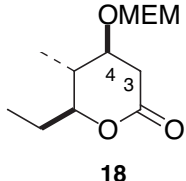
	Ring proton: δ , mult.	J found (J calc.)	Side chain protons
	3α : 2.92, ddd 3β : 2.57, dd 4α : 5.21, dq 5α : 2.39, ddd 5β : 1.62, ddd 6α : 4.39, ddq	3α - 4α : 6.2 (5.8) 3β - 4α : 6.6 (9.4) 4α - 5α : 6.2 (5.0) 4α - 5β : 8.6 (10.3) 5α - 6α : 2.9 (2.6) 5β - 6α : 11.7 (11.4)	3α - 3β : 17.2 3α - 5α : 0.9 δ 2.07 (s, 3 H, OAc); δ 1.43 (d, 3 H, C(6)-CH ₃)
	3α : 2.88, ddd 3β : 2.54, dd 4α : 4.14, ddt 5α : 2.33, dddd 5β : 1.59, ddd 6α : 4.33, ddq	3α - 4α : 6.2 3β - 4α : 7.7 4α - 5α : 5.5 4α - 5β : 9.2 5α - 6α : 2.9 5β - 6α : 11.5	3α - 3β : 17.1 3α - 5α : 1.3 δ 4.80 (d, 1 H) and 4.78 (d, 1 H), J_{AB} 7.3, OCH ₂ O; δ 3.71 (m, 2 H) and δ 3.55 (m, 2 H), OCH ₂ CH ₂ O; δ 3.39 (s, 3 H, OCH ₃); δ 1.41 (d, 3 H, C(6)-CH ₃)
	3α : 2.78, dq 4α : 5.29, ddd 5α : 2.51, ddd 5β : 1.63, ddd 6α : 4.42, ddq	3α - 4α : 4.7 (2.5) 4α - 5α : 8.5 (7.2) 4α - 5β : 3.7 (3.6) 5α - 6α : 4.0 (4.2) 5β - 6α : 11.6 (10.6)	5α - 5β : 15.3 δ 2.06 (s, 3 H, OAc); δ 1.40 (d, 3 H, C(6)-CH ₃); δ 1.22 (d, 3 H, C(3)-CH ₃)
	3α : 2.71, dq 4α : 4.19, dt 5α : 2.31, ddd 5β : 1.76, ddd 6α : 4.38, ddq	3α - 4α : 4.6 4α - 5α : 7.6 4α - 5β : 4.0 5α - 6α : 4.2 5β - 6α : 11.1	5α - 5β : 14.8 δ 4.78 (d, 1 H) and 4.68 (d, 1 H), J_{AB} 7.3, OCH ₂ O; δ 3.71 (m, 2 H) and δ 3.55 (t, 2 H, J 4.6); δ 3.39 (s, 3 H, OCH ₃); all these H in MEMO; δ 1.39 (d, 3 H, C(6)-CH ₃); δ 1.28 (d, 3 H, C(3)-CH ₃)
	3α : 2.92, dd 3β : 2.56, dd 4α : 4.88, q 5β : \approx 1.86, obsc. 6α : 3.87, ddd	3α - 4α : 5.8 (4.3) 3β - 4α : 6.2 (6.4) 4α - 5β : \approx 7 (5.8) 5β - 6α : 10.3 (10.0) 6α -CH ₂ : 7.5 and 3.1	3α - 3β : 17.1 δ 2.08 (s, 3 H, OAc); $\delta \approx$ 1.86 (m, 1 H, obsc.) and δ 1.64 (septet, 1 H), C(6)-CH ₂ ; δ 1.05 (d, 3 H, C(5)-CH ₃); δ 1.04 (t, 3 H, Et)
	3α : 2.87, dd 3β : 2.61, dd 4α : \approx 3.72, obsc. 5β : \approx 1.81, obsc. 6α : 3.81, ddd	3α - 4α : 5.5 3β - 4α : 6.4 4α - 5β : obscured 5β - 6α : 10.3 6α -CH ₂ : 7.3 and 2.9	3α - 3β : 16.8 δ 4.79 (d, 1 H) and 4.74 (d, 1 H), J_{AB} 7.3; $\delta \approx$ 3.72 (2 H, obsc.) and δ 3.56 (m, 2 H); δ 3.40 (s, 3 H, OCH ₃); $\delta \approx$ 1.84 (1 H, obsc.) and δ 1.62 (1 H, septet), C(6)-CH ₂ ; δ 1.06 (d, 3 H, C(5)-CH ₃); δ 1.03 (t, 3 H, Et)

Table B. Energies^a and dihedral angles calculated for the most stable conformers of the unsaturated lactones **3**, **5** and **14**.

	Con- former	MM3* energy	QM energy	Dihedral angles ^a (degrees)					
				τ_1	τ_2	τ_3	τ_4	τ_5	τ_6
3-01	0.00	0.00		-12.2	2.9	29.7	-53.7	49.7	-16.1
3-02	0.19	1.47		7.4	-1.0	-26.1	46.7	-45.2	17.6
3-03	0.75	0.10		-14.1	7.3	25.4	-52.0	50.3	-16.9
3-04	0.95	1.82		13.5	-3.0	-28.1	49.2	-43.7	12.0
5-01	0.00	0.00		12.1	-4.5	-27.6	52.4	-50.0	17.1
5-02	0.19	1.57		-9.9	2.4	26.7	-48.0	45.6	-16.2
5-03	0.77	0.14		-12.2	5.8	25.7	-51.1	49.7	-17.6
5-04	0.93	2.19		14.6	-3.2	-29.1	50.2	-43.9	11.1
14-01	0.00	0.00		-9.5	-1.0	30.1	-49.2	44.5	-14.3
14-02	0.67	0.61		-11.5	-0.5	31.2	-50.4	44.2	-12.4
14-03	1.18	1.90		-9.4	2.8	25.2	-46.6	45.5	-16.8
14-04	1.86	2.54		-8.6	2.7	26.0	-48.4	48.3	-18.9
14-05	2.17	1.11		7.2	-3.2	-24.0	48.9	-51.3	21.8
14-06	2.36	0.14		7.6	-5.9	-21.3	46.5	-50.9	22.5

^a In kcal/mol. ^b The dihedral angles are defined as $\tau_1 = \text{O}(1)\text{-C}(2)\text{-C}(3)\text{-C}(4)$, etc.; the signs correspond to the enantiomers drawn in Scheme 1.

Table C. Selected conformers of δ -lactones **9**, **11** and **17** found by MM and QM techniques.^{a,b}

Ring type	MM2*	MM3*	MMFF	QM	Dihedral angles ^c (degrees) $\tau_1 / \tau_2 / \tau_3 / \tau_4 / \tau_5 / \tau_6$	
	$\Delta E/\text{OAc}/\text{Et}$	$\Delta E/\text{OAc}/\text{Et}$	$\Delta E/\text{OAc}/\text{Et}$	$\Delta E/\text{OAc}/\text{Et}$		
9	³ S ₁		2.6/160		-36.9/63.5/-37.3/-13.5/44.5/-17.5	
	⁶ S ₂	2.4/163	2.5/177		-58.3/22.5/29.8/-58.6/28.9/25.4	
	B _{3,6}			1.4/82	44.5/-53.9/12.1/40.2/-55.7/11.2	
	B _{3,6}	0.0/173		0.1/159	1.5/162	45.9/-40.5/-7.2/53.3/-53.5/3.1
	⁵ C ₂ - ⁵ H ₄	0.5/165	0.0/154	0.0/159	0.0/159	-25.8/45.0/-59.4/54.8/-37.3/22.3
	⁵ C ₂ - ⁵ H ₄	1.6/168	1.8/153	1.4/158	2.5/158	32.3/-45.6/52.1/-43.6/30.1/-24.6
11	² C ₅		1.1/157	1.4/155	37.6/-49.9/53.0/-41.3/29.4/-28.1	
	⁴ E	1.5/167	0.0/150		36.4/-60.7/56.5/-28.1/1.1/-5.1	
	⁵ C ₂	1.7/163	0.0/86	0.9/157	1.0/156	-29.7/47.3/-59.6/53.0/-38.0/26.1
	B _{3,6} - ¹ S ₃				0.0/159	45.0/-53.8/11.9/40.5/-55.4/10.4
	B _{3,6} - ² S ₆	0.0/173	1.4/155	0.0/158		58.9/-38.2/16.4/58.6/-41.5/-16.1
17	² S ₆	1.9/-59/-178			45.4/-19.8/-31.5/64.5/-42.3/-12.4	
	³ S ₁	2.8/84/174		2.2/85/176	-39.0/65.4/-38.1/-13.0/44.7/-17.0	
	² C ₅	2.1/84/168	1.9/150/171	0.8/156/169	2.2/156/172	30.3/-41.5/50.5/-47.6/38.4/-29.5
	⁴ E	2.0/164/170				28.0/-53.6/55.6/-33.8/6.4/-3.0
	⁵ C ₂ - ⁵ H ₄	1.1/80/179	0.0/94/178	0.2/85/180	0.0/83/180	-24.8/43.2/-57.9/55.5/-40.8/24.3
	⁶ S ₂	1.7/162/172		2.2/77/173		-52.6/23.9/27.5/-57.9/31.6/22.4
	¹ S ₃	0.2/166/176		0.8/155/179	0.1/161/174	40.2/-57.4/20.1/33.2/-56.5/17.1
	B _{3,6} - ² S ₆	0.0/79/-177		0.0/81/-178	0.8/81/-177	44.9/-29.8/-20.6/60.9/-51.1/-2.5

^a Only the lowest energy conformer is listed for each ring type; QM refers to HF/6-31G^{*}. ^b The headings $\Delta E/OAc/Et$ refer to relative energy in kcal/mol, then orientations of the acetate and ethyl groups are given as the dihedral angles C(3)-C(4)-O-C(=O) and C(5)-C(6)-CH₂-CH₃, respectively. ^c The lactone ring dihedral angles are defined as $\tau_1=O(1)-C(2)-C(3)-C(4)$, etc. and refer to the QM conformer when this is available, otherwise to the MM2* (for **9** ³S₁ to the MMFF) conformer.

Experimental

Compound **1** (commercially available) was prepared (75%) as described⁶⁴ but using EtOH instead of EtOAc to obtain a higher solubility. Compounds **2**^{4b}, **5**^{4b} and **13**^{4a} were previously prepared. Catalytic hydrogenations are described below.

The stereochemical purities of the hydrogenation products were determined by fused silica capillary column GLC using DB-225, SE-52 and Carbowax 20 M columns mounted in a Hewlett-Packard 5830 A gas chromatograph (FID detector, electronic integration) using H₂ as carrier gas. To find the retention times of the minute amounts of minor isomers formed we used reference mixtures. Compounds **1**, **2** and **13** were reduced with ammonia borane to give β -hydroxy lactones as previously described for **1**.¹¹ This reduction method gave rather low stereoselectivities (66, 44 and 81% respectively) and is thus useful for making reference mixtures containing all possible stereoisomers. The mixtures of isomeric β -hydroxy lactones were converted to acetates and MEM ethers and these were analyzed by GLC. All diastereomers separated well, even the four isomers obtained from **2** (in the product ratios 30:44:8:18). NMR spectra of the crude product mixtures were compatible with the high stereochemical purities found by GLC.

Separations on silica gel were performed using Kieselgel 60 (Merck, 70-230 mesh). ¹H NMR spectra were recorded at 270 MHz on a JEOL GSX 270 spectrometer or at 400 MHz on a Varian Mercury spectrometer. ¹³C NMR spectra were recorded at 100 MHz using a Varian Mercury spectrometer. The NMR solvent was CDCl₃; tetramethylsilane was used as internal reference. Coupling constants (*J*) are given in Hz. HR-FAB mass spectra were measured using a JEOL JMS SX/SX102A instrument (direct inlet).

X-ray structural data were downloaded from the CSD database⁶⁵ and dihedral angles were then extracted using the Windows-based program DIAMOND⁶⁶.

Computational work. Conformations of the saturated lactones **9**, **11**, and **17** and unsaturated lactones **3**, **5**, and **14** were found by exploring the conformational space using a Monte Carlo Multiple Minimum (MCMM) search in which new structures were generated by random changes

in torsional angles, followed by an energy minimization using the truncated Newton conjugate-gradient method.⁶⁷ The MM3* force field of Macromodel 7.0⁶⁷ was used in the MCMM search of the lactones **3**, **5**, and **14**. The obtained conformers were used as starting geometries for HF/6-31G* ab initio geometry optimizations performed in the MacSpartan Pro⁶⁸ program. The results are presented in Table B.

The MM2*, MM3* and MMFF force fields of Macromodel 7.0 were employed in three separate MCMM searches of each of the saturated lactones **9**, **11**, and **17**. Conformers with a relative energy exceeding +3.0 kcal/mol were discarded. For each compound the three sets of low energy conformers were used as starting geometries for HF/6-31G* optimizations performed in the Jaguar program.⁶⁹ Duplicates were removed and the energy exclusion limit was again applied. This led to the results in Table C.

Conformations reported in Table 3 were generally obtained by QM optimization of input structures obtained by axial or equatorial substitution in ring types ⁴H₅, B_{3,6}, ¹S₃-B_{3,6} and ²S₆-B_{3,6}. The ab initio HF/6-31G* optimizations were performed with the MacSpartan Pro program using default settings and the convergence criterion keyword TOLG=0.00001.

The other ab initio HF/6-31G* optimizations, i.e. torsional drivers (Figures 4 and 5), were performed with the Jaguar 4.2 program using default settings and the ultrafine grid accuracy. Transition states were verified to have a hessian yielding a single imaginary frequency and the transition vibrational mode was animated and visually inspected.

Boltzmann-averaged coupling constants were calculated using the extended Karplus equation⁷⁰ implemented in Macromodel 7.0.

Computational results

Compound **3**

Conformer	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
30001	-608.2405261	0.000
30002	-608.2381783	1.473
30003	-608.2403616	0.103
30004	-608.2376250	1.820

Compound **5**

Conformer	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
50001	-647.2799215	0.000
50002	-647.2774195	1.570
50003	-647.2796942	0.143

50004 -647.2764320 2.190

Compound 14

Conformer	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
140001	-686.3078038	0.000
140002	-686.3068384	0.606
140003	-686.3047808	1.897
140004	-686.3037522	2.542
140005	-686.306033	1.111
140006	-686.307577	0.142

Compound 9

hartrees	kcal/mol	ring type	tau-6
-609.424118	1.37	B _{3,6}	11.2
-609.423992	1.45	B _{3,6}	3.1
-609.426305	0.00	⁵ C ₂ - ⁵ H ₄	22.3
-609.425591	0.45	⁵ C ₂ - ⁵ H ₄	21.1
-609.422269	2.53	² C ₅ - ⁴ H ₅	-24.6
-609.422150	2.61	² C ₅ - ⁴ H ₅	-23.9

Compound 11

hartrees	kcal/mol	ring type	tau-6
-648.457557	1.40	² C ₅	-28.1
-648.458197	1.00	⁵ C ₂	26.1
-648.457490	1.44	⁵ C ₂	23.9
-648.459784	0.00	B _{3,6}	10.4

Compound 17

hartrees	kcal/mol	ring type	tau-6
-687.489820	2.17	² C ₅	-29.5
-687.489446	2.41	² C ₅	-29.9
-687.493281	0.00	⁵ C ₂ - ⁵ H ₄	24.3
-687.492610	0.42	⁵ C ₂ - ⁵ H ₄	20.1
-687.493062	0.14	¹ S ₃	17.1
-687.492717	0.35	¹ S ₃	15.7
-687.491174	1.32	¹ S ₃	13.1
-687.489238	2.54	¹ S ₃	16.7
-687.489369	2.45	¹ S ₃	18.8
-687.492047	0.77	B _{3,6} - ² S ₆	-2.5
-687.491080	1.38	B _{3,6} - ² S ₆	-5.3

δ -Valerolactone

	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
⁴ H ₅ - ² C ₅	-343.7366456	0.000
B _{3,6}	-343.7347981	1.159

TS-1	-343.7335737	1.928
TS-2	-343.7318793	2.991

δ -Valerolactone, locked (“ideal”) conformations

ring type	locked torsions	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
${}^4\text{H}_5$	6-1-2-3	-343.7359326	0.447
$\text{B}_{3,6}$	6-1-2-3, 3-4-5-6	-343.7345989	1.284
${}^4\text{E}$	5-6-1-2, 6-1-2-3	-343.7340462	1.631
E_5	6-1-2-3, 1-2-3-4	-343.7352873	0.852
skew	4-5-6-2	-343.7333903	2.043
skew	1-2-3-5, 4-5-6-2	-343.7328895	2.357
skew	1-2-3-5	-343.7328876	2.358
skew	5-6-1-3	-343.7340497	1.629
skew	5-6-1-3, 2-3-4-6	-343.7283413	5.211
skew	2-3-4-6	-343.7355192	0.707
skew	3-4-5-1	-343.7342311	1.515
skew	3-4-5-1, 6-1-2-4	-343.7323632	2.687
skew	6-1-2-4	-343.7364384	0.130 (3-5 on the same side)
${}^1\text{C}_4$	2-3-5-6	-343.7352006	0.907
${}^2\text{C}_5$	3-4-6-1	-343.7364609	0.116
${}^3\text{C}_6$	1-2-4-5	-343.7343126	1.464

δ -Valerolactone derivatives (cf. Table 5)

3-methyl

ring type	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
${}^2\text{C}_5$	-382.7721626	0.000
$\text{B}_{3,6}$	-382.7710526	0.697
${}^4\text{H}_5$ - ${}^2\text{C}_5$	-382.7698223	1.469

6-methyl

ring type	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
${}^4\text{H}_5$ - ${}^2\text{C}_5$	-382.7769748	0.000
$\text{B}_{3,6}$	-382.7751446	1.148
${}^4\text{H}_5$ - ${}^2\text{C}_5$	-382.7742587	1.704

cis-3,6-dimethyl

ring type	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
${}^2\text{C}_5$	-421.8097981	0.983
${}^4\text{H}_5$ - ${}^2\text{C}_5$	-421.8101597	0.756
$\text{B}_{3,6}$	-421.8113649	0.000

3-tert-butyl

ring type	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
$\text{B}_{3,6}$ - ${}^2\text{S}_6$	-499.8661435	0.00
${}^2\text{C}_5$	-499.8659386	0.13

3-methoxy

ring type	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
2C_5	-457.6104439	0.00
4H_5 - 2C_5	-457.6101708	0.17
$B_{3,6}$ (4exo)	-457.6095431	0.57
$B_{3,6}$ (4endo)	-457.6090714	0.86

4-methoxy

ring type	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
2C_5	-457.6153987	0.00
2C_5	-457.6148084	0.37
4H_5 - 2C_5	-457.6141055	0.81
4H_5 - 2C_5	-457.6140350	0.86
2S_6	-457.6126329	1.74
2S_6	-457.6125271	1.80
$B_{3,6}$	-457.6115179	2.44
$B_{3,6}$	-457.6110939	2.70

5-methoxy

ring type	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
4H_5	-457.6132887	0.00
4H_5	-457.6129319	0.22
4H_5 - 2C_5	-457.6131965	0.06
4H_5 - 2C_5	-457.6127181	0.36
$B_{3,6}$ - 1S_3	-457.6122490	0.65
$B_{3,6}$ - 1S_3	-457.6109796	1.45
1S_3	-457.6100049	2.06
1S_3	-457.6103495	1.84

Model compound 20

ring type	6-31g* (hartrees)	Δ 6-31G* (kcal/mol)
1S_3 - $B_{3,6}$	-649.5628382	0.00
4H_5 (ax OMe)	-649.5619369	0.57
4H_5 (ax OMe)	-649.5617185	0.70
5H_4 (eq OMe)	-649.5610818	1.10

4-Acetoxy-6-methyl-1-oxa-3-cyclohexen-2-one (3) was prepared as described for **5**^{4b} using acetyl chloride and *N*-ethyl-diisopropylamine and was obtained as an oil; yield >95%; ¹H NMR: δ 5.92 (dd, 1 H, *J* 2.2 and 1.0, H-3), 4.63 (ddq, 1 H, *J* 11.2, 4.2, 6.4, H-6), 2.64 (ddd, 1 H, *J* 17.6, 11.2, 2.2, H-5 β), 2.49 (ddd, 1 H, *J* 17.6, 4.2, 1.0, H-5 α), 2.24 (s, 3 H, OAc), 1.47 (d, 3 H, *J* 6.4, CHCH₃).

6-methyl-4-[(2-methoxyethoxy)methoxy]-1-oxa-3-cyclohexen-2-one (4) . The tetrabutylammonium salt of **1** (4 mmol) was extracted from water (60 mL) into dichloromethane (3 x 150 mL). After concentration and drying (Na_2SO_4), anhydrous K_2CO_3 (40 mmol) and MEMCl (6 mmol) were added to the solution (15 mL) of the tetrabutylammonium salt and the compounds were allowed to react for 15 min. The mixture was filtered, the solvent evaporated and the residue partitioned between Et_2O and dilute aqueous NaHCO_3 . After three additional extractions with Et_2O the extracts were combined and the solvent was evaporated. Dichloromethane was added. After drying (Na_2SO_4) and concentration, **4** was obtained in a purity of *ca.* 90%; the major contaminant was 2-methoxyethanol. The crude product was purified on a silica gel column to give **4** in a 73% yield; ^1H NMR: δ 5.33 (1 H, three equal intensity resonances with spacings *ca.* 0.6 and 1.0 Hz, H-3), 5.20 (1 H, *J* 6.4, OCH_2O), 5.17 (1 H, *J* 6.4, OCH_2O), 4.55 (ddq, 1 H, *J* 11.2, 4.6, 6.3, H-6), 3.79 (m, 2 H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.56 (m, 2 H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.39 (s, 3 H, OCH_3), 2.47 (ddd, 1 H, *J* 17.2, 11.2, 1.3, H-5 β), 2.36 (dd, 1 H, *J* 17.2, 4.4, H-5 α), 1.44 (d, 3 H, *J* 6.3, CHCH_3).

3,6-dimethyl-4-[(2-methoxyethoxy)methoxy]-1-oxa-3-cyclohexen-2-one (6). A solution of **2** (1 mmol) in acetonitrile (5 mL) was added to a stirred suspension of sodium hydride (1.45 mmol, freed from stabilizing mineral oil) in acetonitrile (3 mL). Hydrogen was evolved and a light gray precipitate was formed. A solution of MEM-Cl (1.2 mmol) in acetonitrile was added. After 25 min the reaction mixture was acidified with acetic acid (1 mmol) and the solvent evaporated. The residue was partitioned between Et_2O (30 mL) and saturated aq. NaHCO_3 (10 mmol). The Et_2O phase was separated, the solvent was evaporated and dichloromethane added. Drying (Na_2SO_4), evaporation of the solvent and purification on silica gel gave **6** in a 62% yield. ^1H NMR: δ 5.18 (s, 2 H, OCH_2O), 4.47 (ddq, 1 H, *J* 11.7, 4.0, 6.2, H-6), 3.79 (m, 2 H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.55 (m, 2 H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.38 (s, 3 H, OCH_3), 2.69 (ddq, 1 H, *J* 17.2, 4.0, 1.1, H-5 α), 2.52 (ddd, 1 H, *J* 17.2, 11.7, 2.2, H-5 β), 1.82 (dd, 3 H, *J* 2.2, 1.1, C(3)- CH_3), 1.44 (d, 3 H, *J* 6.2, CHCH_3).

cis-4-Acetoxy-6-methyl-1-oxacyclohexan-2-one (9) and **trans-4-Acetoxy-6-methyl-1-oxacyclohexan-2-one** were prepared as a mixture of *cis* and *trans* isomers from a mixture of the corresponding alcohols¹¹ (*cis-7/trans-7*, *ca.* 3:1). **Cis acetate (9)**: ^1H NMR data are given in Table A. ^{13}C NMR: δ 170.1, 169.7, 73.0, 66.0, 36.2, 35.6, 21.1, 21.0. **Trans acetate**: ^1H NMR: δ 5.25 (dq, 1 H, *J* 5.2, 3.6, H-4), 4.72 (ddq, 1 H, *J* 11.3, 2.9, 6.4, H-6), 2.78 (dd, 1 H, *J* 18.2, 5.2, H-3),

2.70 (ddd, 1 H, J 18.0, 3.5, 1.7, H-3), *ca.* 2.10 (1 H, partly obscured by OAc, H-5- α), 2.08 (s, 3 H, OAc), 1.78 (ddd, 1 H, J 14.8, 11.4, 3.4, H-5- β), 1.42 (d, 3 H, J 6.7, C(6)-CH₃). ¹³C NMR: δ 170.0, 169.1, 72.6, 65.7, 35.1, 34.5, 21.3, 21.0. The 90 MHz ¹H NMR data in the literature⁷² show moderate agreement with ours.

trans-4-Acetoxy-6-ethyl-5-methyl-1-oxa-3-cyclohexen-2-one (14) was prepared in the same way as **3** and was obtained as an oil; yield >95%; ¹H NMR: δ 5.93 (d, 1 H, J 1.3, H-3), 4.12 (q, 1 H, J 6.4, H-6), 2.69 (d of pentet, 1 H, J 1.3, 7.0, H-5), 2.25 (s, 3 H, OAc), 1.81 (dq, 2 H, J 6.1 and 7.4, CH₂CH₃) 1.19 (d, 3 H, J 7.1, C(5)-CH₃) 1.05 (t, 3 H, J 7.4, CH₂CH₃).

trans-6-ethyl-5-methyl-4-[(2-methoxyethoxy)methoxy]-1-oxa-3-cyclohexen-2-one (15) was prepared by the method used for **4**. The crude product was purified on a silica gel column to give **15** in a 94% yield; ¹H NMR: δ 5.28 (s, 1 H, H-3), 5.18 (s, 2 H, OCH₂O), 4.04 (q, 1 H, J 6.4, H-6), 3.80-3.76 (m, 2 H, OCH₂CH₂O), 3.59-3.54 (m, 2 H, OCH₂CH₂O), 3.39 (s, 3 H, OCH₃), 2.51 (pentet, 1 H, J 7.1, H-5), 1.76 (pentet-like, 2 H, J 7.1, CH₂CH₃), 1.21 (d, 3 H, J 7.0, C(5)-CH₃), 1.04 (t, 3 H, J 7.4, CH₂CH₃).

Hydrogenation of 1, 2 and 13. All catalytic hydrogenations were run at 20-22 °C. Conditions in hydrogenations using W2 Raney-Ni: for **1**, EtOH, 5 atm H₂, 3 days; for **2**, THF, 30 atm H₂, 2 days; for **13**, EtOAc, 5 atm H₂, 17 h. For hydrogenations of **1, 2 and 13** using PtO₂ (Adams' catalyst): 5 atm H₂, EtOAc, Parr apparatus, 20 h.

Hydrogenation of enol acetates and enol MEM ethers. Diethyl ether was used as solvent; 20-22 °C; catalysts were 10% Pd/C (Fluka, batch number 258624785; 0.04-0.09 equiv. Pd for the enol acetates and 0.09-0.32 equiv. for the enol MEM ethers; see also next paragraph) or 5 % Rh/C (Merck-Schuchardt, batch number 1175926). For **5** and **6** a 5 atm pressure was applied (Parr apparatus); the other enol acetates and enol MEM ethers were reduced at 1 atm pressure. The reaction mixtures obtained from the enol acetates contained acetic acid which was removed by washing first with a minimum amount of conc. aq. NaHCO₃ and then with a little brine. After drying (Na₂SO₄), filtration and concentration the product mixtures were analysed by GLC and ¹H NMR spectroscopy. All stereoselectivities are presented in Table 1. The saturated acetates or MEM ethers were separated from the hydrogenolysis products using silica gel columns and were thus obtained in >95 % purity (¹H and ¹³C NMR) as colorless oils.

The hydrogenation of **3** (305 mg) in Et₂O (30 mL) was carried out using 10% Pd/C from another supplier (80 mg, Merck, batch no. 34627). After filtration and evaporation of the solvent the crude product was carefully analyzed by ¹H and ¹³C NMR at 400 and 100 MHz respectively. The ratio of *cis*-**9** to *trans*-**9** was >99/<1. The yield of the byproduct formed by hydrogenolysis was ca. 20-22%, which is less than with the other catalyst.

cis-4-Acetoxy-6-methyl-1-oxacyclohexan-2-one (9), 40% yield; indistinguishable (¹H NMR, GLC) from the acetate prepared by acetylation of **7** (*cis*). ¹H NMR data are given in Table A. ¹³C NMR data are presented above.

cis-4-[(2-Methoxyethoxy)methoxy]-6-methyl-1-oxacyclohexan-2-one (10), 81% yield; indistinguishable (¹H NMR, GLC) from the MEM ether prepared from **7**. ¹H NMR data are given in Table A.

all-cis-4-Acetoxy-3,6-dimethyl-1-oxacyclohexan-2-one (11), 40% yield; ¹H NMR data are given in Table A; ¹³C NMR: δ 173.3, 170.4, 71.8, 69.7, 37.6, 37.5, 20.9, 20.8, 11.0. FAB MS: *m/z* 187 (M+H⁺), 127 (M+H⁺-HOAc); HR-FAB MS: *m/z* 187.0965; calc. for C₉H₁₅O₄: 187.0971.

all-cis-4-[(2-Methoxyethoxy)methoxy]-3,6-dimethyl-1-oxacyclohexan-2-one (12), 88% yield; ¹H NMR data are given in Table A; ¹³C NMR (CDCl₃, two signals coincide): δ 174.0, 94.1, 72.2, 71.7, 67.3, 59.1, 39.0, 36.8, 21.2, 11.5; ¹³C NMR in acetone-d₆: δ 174.0, 94.8, 73.5, 72.5, 72.3, 67.9, 58.8, 39.3, 38.0, 21.3, 11.9. FAB MS: *m/z* 255 (M+Na⁺), 233 (M+H⁺), 218 (M+H⁺-CH₃), 217; HR-FAB MS: *m/z* 233.1404; calc. for C₁₁H₂₁O₅: 233.1389.

r-4-Acetoxy-c-6-ethyl-t-5-methyl-1-oxacyclohexan-2-one (17), 48% yield; ¹H NMR data are given in Table A; ¹³C NMR: δ 170.3, 169.9, 82.8, 71.8, 38.0, 35.4, 25.7, 21.0, 14.2, 8.8. FAB MS: *m/z* 201 (M+H⁺), 141 (M+H⁺-HOAc); HR-FAB MS: *m/z* 201.1128; calc. for C₁₀H₁₇O₄: 201.1127.

c-6-Ethyl-r-4-[(2-methoxyethoxy)methoxy]-t-5-methyl-1-oxacyclohexan-2-one (18), 95% yield; ¹H NMR data are given in Table A; ¹³C NMR: δ 169.9, 93.6, 82.1, 74.5, 70.6, 66.3, 58.0, 37.9, 35.3, 24.8, 13.4, 7.8. FAB MS: *m/z* 269 (M+Na⁺), 247 (M+H⁺), 141 (M+H⁺-HOCH₂OCH₂CH₂OCH₃); HR-FAB MS: *m/z* 247.1533; calc. for C₁₂H₂₃O₅: 247.1546.

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