Synthesis and Properties of 4,4,9,9-Tetramethyl-1-oxa-cycloundecane-5,6,7,8-tetrone and 5,5,10,10-Tetramethyl-1-oxa-cyclotridecane-6,7,8,9-tetrone

Rolf Gleiter,* Uwe Ackermann, Thomas Oeser, and Hermann Irngartinger

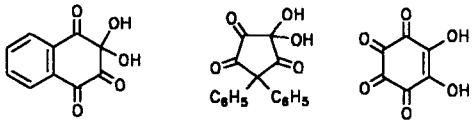
Dedicated to Professor Richard Neidlein on the occasion of his 65th birthday

Abstract: The synthesis of 4,4,9,9-tetramethyl-1-oxa-cycloundecane-5,6,7,8-tetrone (**9**) and 5,5,10,10-tetramethyl-1-oxa-cyclotridecane-6,7,8,9-tetrone (**10**) has been achieved in a multistep procedure. The key steps in this synthesis were the ring closure of **23** and **24** to **25** and **26**, respectively, and the oxidation of the triple bond with $RuO_2/NaIO_4$ to the dihydroxydiketones **31** and **32**. Compound **9** is the first cyclic tetraketone for which an intramolecular donor–acceptor stabilization has been found. A strong transannular interaction between the ether oxygen and the C_4O_4 unit in **9** was detected by X-ray studies on single crystals of **9**. The transannular distance is 2.7–2.8 Å. Further evidence for a strong transannular interaction was obtained from the comparison of the reduction potential and the first band in the UV/Vis spectrum with the corresponding values from other open-chain tetraketones. These findings were substantiated by PE investigations on **9**. The crystal structures of the dihydroxydiketones **31a** and **32a** showed that, in the case of the eleven-membered ring (**31a**), there are also short transannular distances between the ether oxygen and the C_2O_2 moiety (2.5 Å and 2.9 Å). In the case of the thirteen-membered ring (**32a**), no transannular interactions were found in the solid state.

Keywords
biomineralization · calcite · crystal morphology · glycoproteins · polysaccharides

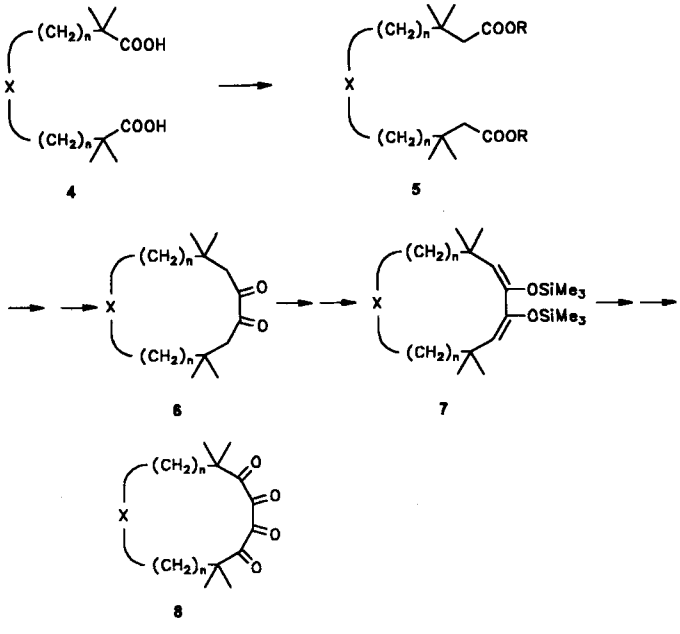
Introduction

The tri-[1] tetra-[2], and pentaketones[3] are known members of the family of vicinal polyketones. They are of interest with respect to their reactivity towards nucleophiles, their photochemistry, and as acceptor groups for forming complexes with donors.[4, 5] Cyclic vicinal polyketones of medium-sized rings are of interest in so far as the dihedral angles between the CO groups are defined and a study of the properties as a function of the ring size is thus possible. There are several procedures available for the preparation of cyclic vicinal triketones,[4] but only one method has been published for the synthesis of cyclic vicinal tetraketones.[6, 7] Other cyclic tetraketones described in the literature were either hydrates, such as **1** and **2**,[8] or were conjugated with strong electron-donor fragments, such as in rhodizonic acid (**3**).[9]



1 **2** **3**

The key steps of a recently described synthesis of cyclic vicinal tetraketones,[10] summarized in Scheme 1, are the Arndt–Eistert procedure for chain elongation (**4** → **5**), the acyloin condensation (**5** → **6**), and the Rubottom oxidation of the bis(silyl) ethers of type **7**. This protocol has a number of shortcomings. The step from the diacid **4** to the homologous diester **5** failed when X was a nucleophilic atom such as O or N,[10] due to faster intramolecular rearrangment of the neopentyl fragment in an SN′ reaction. Furthermore the bis(enol ether)s such as **7** could be obtained only for ring sizes larger than eleven.[10]



Scheme 1. Key steps to synthesize cyclic tetraketones.

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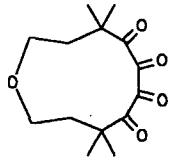
In this paper we report a new reaction pathway that overcomes the above-mentioned limitations. We report the synthesis of 4,4,9,9-tetramethyloxacycloundecane-5,6,7,8-tetrone (**9**) and its congener 5,5,10,10-tetramethyloxacyclotridecane-6,7,8,9-tetrone (**10**).



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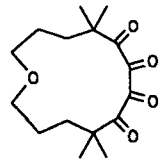

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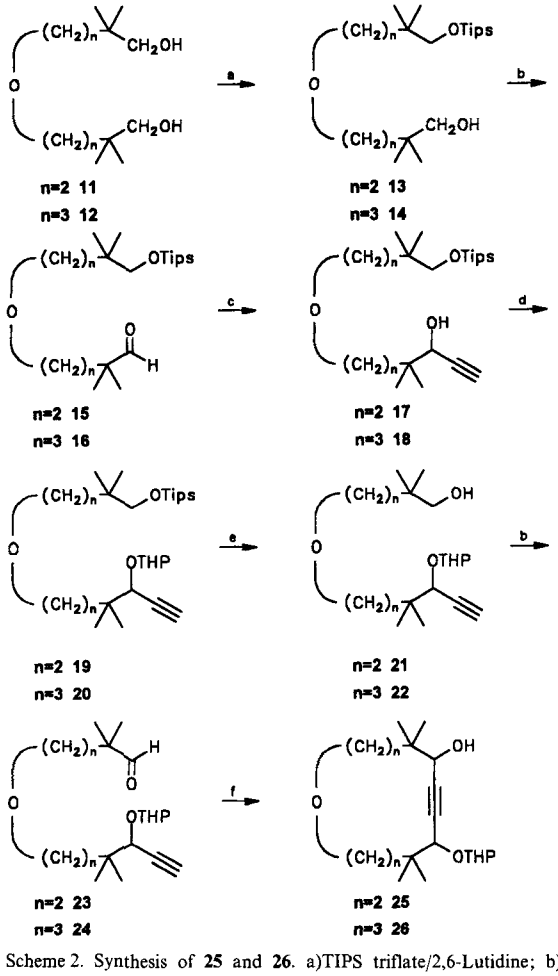
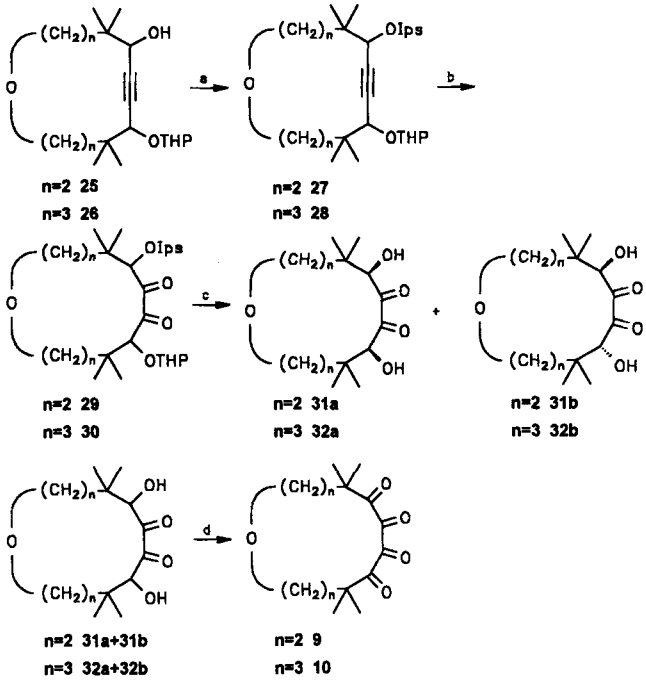
Results and Discussion

Synthesis: We started our synthesis with the diols **11** and **12**, prepared by conventional methods as described recently.[10] The diols were treated with one mole of triisopropylsilyl trifluoromethanesulfonate (TIPS triflate)[11] in a dilute solution to give the monoprotected alcohols **13** and **14**, respectively (Scheme 2). The oxidation of the alcohol function with pyridinium chlorochromate (PCC)[12] gave the corresponding monoaldehydes **15** and **16** in good yields. A C_2 unit was introduced by reaction of **15** and **16** with the dilithium salt of acetylene (Li_2C_2) to yield the ynols **17** and **18**, respectively. Protection of the secondary alcohol group with dihydropyran (DHP)[13] in presence of pyridinium *p*-toluenesulfonate (PPTS) and removal of the TIPS protecting group at the primary alcohol with tetrabutylammonium fluoride (nBu$_4$NF)[14] yielded **21** and **22**. Oxidation of the primary alcohol function with PCC yielded the aldehydes **23** and **24**. The ring closure[15] of **23** and **24** was achieved by deprotonation in situ with lithium bis(trimethylsilyl)amide (LBTSA). This yielded the eleven- and thirteen-membered rings **25** and **26** in excellent yields.

The OH function in **25** and **26** was protected by reaction with isopropyldimethylsilyl chloride (IPS-Cl)[16] to yield **27** and **28**. The triple bond could then be oxidized with RuO_2/$NaIO_4$[17] in excellent yields to afford the yellow diketones **29** and **30**. Deprotection with ion exchange resins (Bio-Rad)[18] and oxidation of the dioldiones **31** and **32** with NBS[19] yielded the desired tetraketones **9** and **10** (Scheme 3). Both compounds are red; **9** is



Scheme 2. Synthesis of **25** and **26**. a)TIPS triflate/2,6-Lutidine; b)PCC/AOX; c)Li_2C_2/THF; d)DHP/PPTS; e)NBu$_4$F; f)LBTSA.



Scheme 3. Synthesis of **9** and **10**. a)IPS-Cl/2,6-lutidine; b)RuO_2/$NaIO_4$; c)Bio-Rad; d)NBS/CCl_4.

crystalline while **10** is an oily liquid. The synthetic protocol presented in Schemes 2 and 3 is superior to that used earlier,[6, 7, 10] since all steps afforded yields of between 60 and 90%, all reactions were fast, and there were no problems with intramolecular rearrangements due to SN′ reactions.

Crystal Structures of 31a, 32a, and 9: We were able to grow single crystals of **31a**, **32a**, and **9**. The molecular structures are shown in Figures 1–3. Our motivation for investigating the molecular structure of **31** and **32** was twofold: 1) we wanted to investigate conformational differences between the eleven- and thirteen-membered rings and 2) we were interested in the configurations of the diastereoisomers **31a/b** and of **32a/b**. In the oxidation of **7** with *m*-chloroperbenzoic acid (*m*-CPBA (Rubottom reaction,[7, 20] Scheme 1) the ratio of the two diastereomers **32a** and **b** was found to depend strongly on the solvent used.[10] We ascribed this to the fact that two different reaction mechanisms were operating: In methylene chloride, we assume that the monoepoxide rearranges before the second double bond is oxidized. For steric reasons this rearrangement yields mainly the

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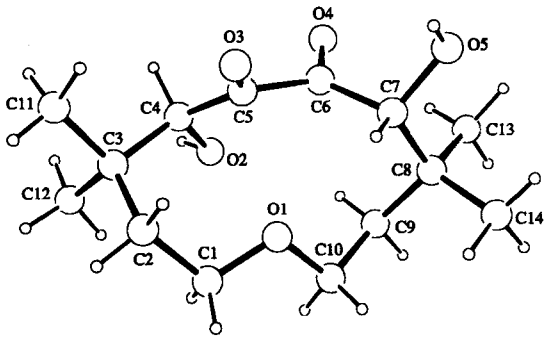


Fig. 1. Crystal structure of **31a**.

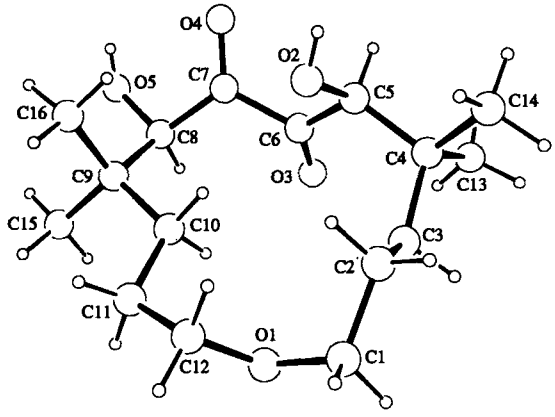


Fig. 2. Crystal structure of **32a** (only one of two independent molecules is shown).

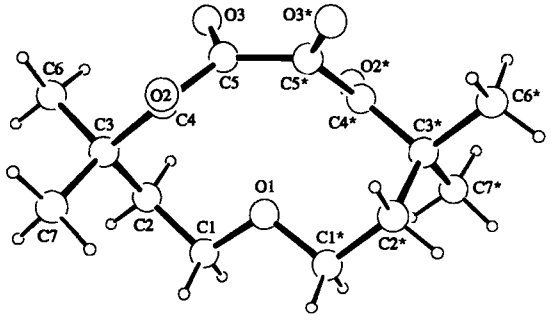


Fig. 3. Crystal structure of **9**.

"*syn*" isomer **32a** ((*R*,*S*) configuration at the secondary alcohol functions). In ether the bisepoxide is relatively stable (an intermediate bisepoxide can be isolated) and rearranges to the "*anti*" isomer **32b** ((*R*,*R*) or (*S*,*S*) configuration at the secondary alcohol functions).[10]

In the crystal structure of **32a** (Fig. 2) the asymmetric unit contains two independent molecules **32a** and **32a'**, which have very similar conformations. Our investigations showed a pronounced difference between **31a** and **32a**: in **31a** the distances between the ether oxygen O1 and the carbon atoms C5 and C6 of the C_2O_2 unit are shorter than the sum of the van der Waals radii of C and O (3.1 Å) (Table 1); in **32a** the corresponding distances are longer than 4.6 Å. We ascribe the short distance in **31a** to a donor–acceptor interaction between the ether oxygen and the C_2O_2 acceptor group. This interpretation is supported by cyclovoltammetric studies on **31** and **32**. The recorded half-wave potential of **31a** and **31b** is 160–200 mV higher than that

Table 1. Selected geometrical parameters (distances in Å, torsional angles in °) of **31a** and **32a**. The numbering refers to that shown in Figures 1 and 2.

	31a		**32a**	**32a'**
C4–C5	1.511(3)	C5–C6	1.525(3)	1.519(2)
C5–C6	1.530(2)	C6–C7	1.537(3)	1.535(2)
C6–C7	1.534(3)	C7–C8	1.515(2)	1.514(2)
O3–C5	1.210(2)	O3–C6	1.206(2)	1.208(2)
O4–C6	1.215(2)	O4–C7	1.208(3)	1.211(3)
O1···C5	2.574(2)	O1···C6	4.615(2)	4.548(2)
O1···C6	2.913(2)	O1···C7	5.291(2)	5.234(2)
O3-C5-C6-O4	−114.4(2)	O3-C6-C7-O4	−130.7(2)	130.6(2)

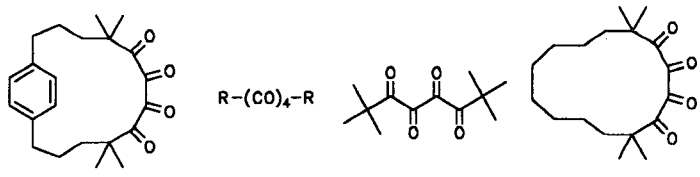
of **32a** and **32b**, respectively (Table 3, see below). There is no signifigant change in the bond lengths in the C_2O_4 unit between **31a** and **32a**. The only difference is in the torsional angle between the (CO) units, which is 114° for **31a** and 131° for **32a** (Table 1). Between the hydroxyl group O5–H22 and the keto oxygen atom O4 in **32a** and **32a'** there is an intramolecular hydrogen bond (O4···O5 = 2.640(2), O4'···O5' = 2.637(2), O4···H22 = 2.22(2), O4'···H22' = 2.15(3) Å). The second hydroxyl group O2–H20 forms an intermolecular hydrogen bond to an ether oxygen atom of a neighboring molecule [O2···O1* $(1-x, 0.5+y, 1.5-z)$ = 2.809(2) Å; O2'···O1*' $(2-x, -0.5+y, 1.5-z)$ = 2.748(2) Å].

In the crystal, compound **9** has a twofold rotational axis of symmetry. Like **31a**, **9** has relatively short transannular distances of 2.703(2) and 2.794(2) Å between the ether oxygen atom and the carbonyl carbon atoms of the C_4O_4 moiety (see Table 2).

Table 2. Selected geometrical parameters (distances in Å, torsional angles in °) of **9**, **33**, and **34**.

	9	**33** [7]	**34a** [21a]	**34b** [21b]
O2–C4	1.210(2)	1.203(5)	1.221(3)	1.218
		1.206(5)	1.220(3)	
O3–C5	1.202(2)	1.208(5)	1.194(4)	1.196
		1.201(5)	1.200(4)	
C3–C4	1.519(2)	1.522(6)	1.465(3)	1.463
		1.527(6)	1.465(3)	
C4–C5	1.529(2)	1.541(6)	1.522(4)	1.541
		1.543(6)	1.512(4)	
C5–C5*	1.534(2)	1.541(6)	1.552(4)	1.523
O1···C4	2.703(2)			
O1···C5	2.794(2)			
O2-C4-C5-O3	−130.2(2)	−141.2(4)	144.6	144.1
		−145.4(4)	128.4	
O3-C5-C5*-O3*	107.1(2)	−132.7(4)	−24.2	128.5

In the tetrone moieties of cyclic compounds **9** and **33**, which have aliphatic substituents, the C–C bond lengths are equal within the accuracy of measurement. The O=C–C=O torsion angles are of the same order of magnitude in both compounds



33 **34a: R=Ph** **34b: R=Mes** **35** **36**

(Table 2). The C–C bond lengths in the tetrone units of the open-chain analogues **34a** and **34b**, which have aromatic substituents, are slightly different to those in **9** and **33**, as a result of the different torsion angles and of substituent effects (Table 2).[21]

Reduction Potentials, UV/Vis Spectra, and PE Spectra: We compared the reduction potentials (Table 3) and first two bands in the UV/Vis spectra (Table 4) of **9** and **10** with those of the tetraketones **33**, **35**, and **36**, which also have alkyl groups adjacent to the $(CO)_4$ moiety. A pronounced difference was found

Table 3. Half-wave reduction potentials of the tetraketones **9**, **10**, **33**, **35**, and **36**, and the dihydroxydiketones **31a**, **31b**, **32a**, and **32b**.

	$E_{1/2}$ [mV]		$E_{1/2}$ [mV]
9	−810	**31a**	−1180
10	−660	**31b**	−1240
33	−685	**32a**	−1020
35	−630	**32b**	−1008
36	−630		

Table 4. First bands of the UV/Vis Spectra of **9**, **10**, **33**, **35**, and **36** (wavelength λ in nm, the extinction coefficient ε in $L mol^{-1} cm^{-1}$).

	$\lambda_1(\varepsilon)$	$\lambda_2(\varepsilon)$
9	400 (27)	362 (64)
10	512 (25)	380 (132)
33	507 (59)	402 (42)
35	525 (85)	386 (76)
36	533 (87)	385 (87)

between the value of the first half-wave potential of **9** and those values recorded for the other compounds. We ascribe this to a through-space interaction in **9** between the lone pair at the ether oxygen and the lowest unoccupied π^* orbital (LUMO) of the C_4O_4 moiety. This interaction destabilizes the lowest π^* MO and stabilizes the n orbital. As a result the reduction potential is higher. The destabilization of the LUMO in **9** is also confirmed by a blue shift of the first two bands in the UV/Vis spectra as compared to the bands recorded for **10**, **33**, **35**, and **36**. Owing to the low intensity of the first bands, it is safe to assign these bands to $\pi^* \leftarrow$n transitions localized at the C_4O_4 moiety. To check our conclusions further we recorded the He(I) photoelectron (PE) spectrum of **9** (Fig. 4). It shows three peaks below 10.5 eV. The peak areas are in a ratio of 1:1:2. To assign these peaks to individual ionization processes we compared the PE

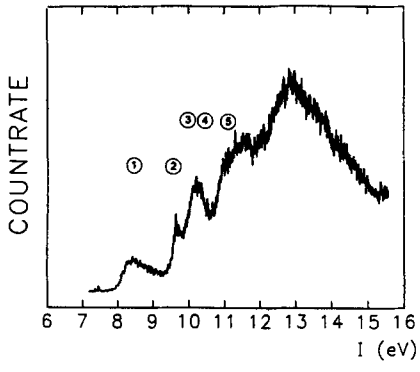


Fig. 4. PE spectrum of **9**.

spectum of **9** with that of **35**[25] and tetrahydropyran (Fig. 5).[23] The bands at 8.5, 9.6, and 10.3 eV in the PE spectrum of **9** can thus be assigned to ionizations from various combinations of lone pairs at the oxygen atoms of the carbonyl

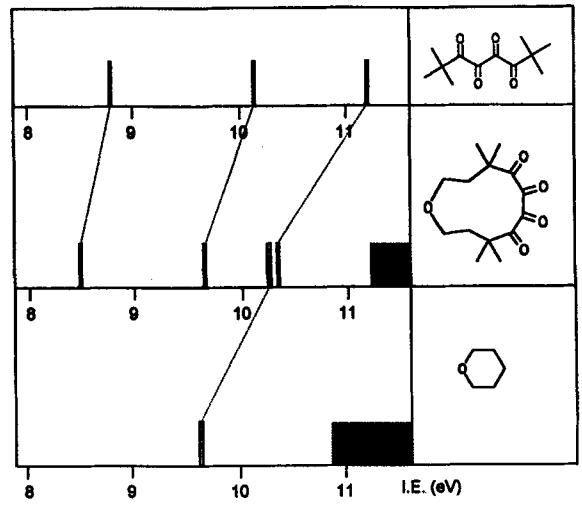


Fig. 5. Correlation between the first bands in the PE spectra of **9**, **35**, and tetrahydropyran.

groups.[23] Furthermore, the third peak (bands 3,4; Fig. 4) can be assigned to two transitions, one from the 2p lone pair at the ether oxygen and one from the lone pairs at the carbonyl oxygens. The larger area below the third peak is consistent with this assignment. The areas below the first two peaks indicate that they each correspond to one transition.

To check these qualitative assignments further we carried out semiempirical MO calculations on **9** by the MINDO/3[24] method assuming that the first vertical ionization energies ($I_{v,j}$) are equal to the negative value of the calculated orbital energies ε_j (Koopmans' approximation[22]) (Table 5). The agreement between experiment and calculation is rather good. For the calculations we adopted the geometrical parameters derived from the X-ray investigations.

Table 5. Comparison between the recorded vertical ionization energies ($I_{v,j}$) of **9** and calculated orbital energies ε_j (all values in eV).

Band	$I_{v,j}$	Assignment	$-\varepsilon_j$
1	8.5	n_1	8.24
2	9.66	n_2	9.71
3	10.2	2p	10.75
4	10.3	n_3	10.73

In Figure 5 it can also be seen that the ionization energy from the 2p orbital at the ether oxygen in **9** is considerably greater than that from the lone pair of the ether oxygen in tetrahydropyran.[25] Assuming that the latter is a good model for an unperturbed ether oxygen in **9**, we ascribe the high-energy shift to the above-mentioned interaction between the LUMO of the C_4O_4 moiety and the ether oxygen.

It is noteworthy that the first absorption band of **9** is 0.74 eV higher in energy than that of **35**, whereas the HOMO of **9** is 0.3 eV higher in energy. This can be rationalized by a very strong shift of the LUMO of **9** towards higher orbital energy, shown by the reduction potentials listed in Table 3.

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Experimental Procedure

General: All melting points are uncorrected. NMR spectra were measured on a Bruker AS200 (^{1}H NMR at 200 MHz and ^{13}C NMR at 50.23 MHz), Bruker AS300 (^{1}H NMR at 300 MHz and ^{13}C NMR at 75 MHz) with either the solvent or Me_4Si as internal standard (δ, J/Hz). Owing to the THP protecting group in **19–30** there are two diastereomers for each of these compounds. This affects the number of ^{13}C and ^{1}H resonances in the NMR spectra of these compounds. The resulting second set of proton resonances of the propargylic and acetal protons, and, in some cases, of the proton bound to the triple bond and of the OH group are assigned to Ha, Hb, Hc, and Hd, respectively. The ratio of the two diastereomers ranges from 1:1 to 3:1. The mass spectra refer to data from a Vacuum Generators ZAB instrument (EI, 100 eV). IR spectra were recorded with Perkin Elmer 580 B and Beckmann 4200 instruments. UV absorption spectra were recorded with a Varian Cary 17D spectrometer. The He(I) photoelectron spectrum was recorded with a PS18 spectrometer of Perkin Elmer (Beaconsfield, England) at 109 °C. For the calibration we used Ar and Xe. A resolution of 25 meV of the $^2P_{3/2}$ Ar line was obtained. The buffer solution used in the cases of **25–28** was a 1 M aqueous solution prepared from equal parts of H_3PO_4 and NaH_2PO_4. The elemental analyses were carried out at Mikroanalytisches Laboratorium der Chemischen Institute der Universität Heidelberg (Germany).

X-ray analysis: The crystallographic data of **9**, **31a**, and **32a** are listed in Table 6. The data were collected on an automatic diffractometer (CAD4, Enraf-Nonius, $Mo_{K\alpha}$ radiation, graphite monochromator, $\omega-2\theta$ scan); Lorentz and polarization corrections were applied. The structures were solved by direct methods (MULTAN [26]) and refined by full-matrix least-squares procedures on F^2 with anisotropic thermal parameters for the carbon and oxygen atoms. The hydrogen atoms were refined isotropically. The atomic coordinates are given as supplementary material [28]. The MolEN program system [27] was used.

Table 6. Crystallographic and refinement parameters of **9**, **31a**, and **32a** [28].

Compound	**9**	**31a**	**32a**
empirical formula	$C_{14}H_{20}O_5$	$C_{14}H_{24}O_5$	$C_{16}H_{28}O_5$
M_r [g mol^{-1}]	268.3	272.3	300.4
solvent	Et_2O/CH_2Cl_2	Et_2O	Et_2O/pentane
crystal size [mm]	0.45 × 0.4 × 0.35	0.45 × 0.35 × 0.15	0.3 × 0.4 × 0.5
crystal color	red	yellow	light yellow
crystal shape	pyramid	prism	prism
space group	*Pbcn*	$P\bar{1}$	$P2_1/c$
a [Å]	11.364(1)	7.541(1)	20.474(3)
b [Å]	11.282(1)	9.629(1)	10.374(1)
c [Å]	10.903(1)	10.454(2)	16.649(2)
α [°]	90	102.84(1)	90
β [°]	90	90.41(1)	110.40(1)
γ [°]	90	97.01(1)	90
V [Å^3]	1397.9(4)	734.1(4)	3314(2)
D_{calcd} [Mg m^3]	1.28	1.23	1.20
Z	4	2	8
$F(000)$	576	296	1312
T [K]	293	293	293
$h_{min} - h_{max}$	0–15	0–9	0–27
$k_{min} - k_{max}$	0–14	−12–12	0–13
$l_{min} - l_{max}$	0–14	−13–13	−21–21
$(\sin\theta/\lambda)_{max}$ [Å^{-1}]	0.66	0.66	0.66
μ [mm^{-1}]	0.09	0.09	0.08
refl. collected	1677	3768	8150
refl. unique	1677	3503	7936
refl. observed [$I > 2.5\sigma(I)$]	1015	2237	4145
R_{int}	–	0.019	0.016
variables	127	268	603
$(\Delta/\sigma)_{max}$	<0.01	0.01	0.03
R	0.044	0.046	0.044
R_w	0.048	0.058	0.048
S (Gof)	1.94	2.29	1.88
$(\Delta\rho)_{max}$ [e Å^{-3}]	0.16	0.28	0.17
$(\Delta\rho)_{min}$ [e Å^{-3}]	−0.21	−0.20	−0.05

Cyclic voltammetry: The electrochemical measurements on **9**, **10**, **33**, **35**, and **36** were performed with the HEKA potentiostat system PG28 in a 0.1 M solution of $(n\text{Bu})_4NPF_6$ in CH_2Cl_2. A METROHM disk electrode was used as the working electrode (r = 0.3 an). The potential of ferrocene/ferrocene$^+$ was measured at 480 mV with an error of ±5 mV.

4-(4-Triisopropylsiloxy-3,3-dimethylbutoxy)-2,2-dimethylbutan-1-ol (13): Triisopropylsilyl triflate (8.75 mL, 32.6 mmol) dissolved in methylene chloride (400 mL) was added (under argon atmosphere) over 2 h to a solution of the diol **11** (22 g, 58.7 mmol) and 2,6-lutidine (5.85 mL) in methylene chloride (500 mL). After being stirred overnight the reaction mixture was concentrated to a volume of approximately 200 mL and then twice washed with buffer solution. The combined aqueous phases were extracted twice with diethyl ether. The organic phases were combined and dried over $MgSO_4$. Flash chromatography over silica gel with cyclohexane/ethyl acetate yielded 8.5 g (70%) of **13**. Excess **11** was eluted with ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.51–3.39 (m; 4H), 3.32 (s; 2H), 3.23 (s; 2H), 1.58–1.49 (m; 4H), 1.11–0.93 (m; 21H), 0.87 (s; 6H), 0.86 (s; 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 72.38 (t), 71.33 (t), 68.27 (t), 67.44 (t), 39.69 (t), 38.14 (t), 34.97 (s), 34.94 (s), 25.08 (q), 24.39 (q), 18.03 (q), 17.70 (q), 12.33 (d), 12.00 (d), 11.61 (d). $C_{21}H_{46}O_3Si$ (374.5): calcd C 67.32, H 12.37; found C 67.49, H 12.24.

5-(5-Triisopropylsiloxy-4,4-dimethylpentyloxy)-2,2-dimethylpentan-1-ol (14): The same procedure as described for the preparation of **13** yielded 9.17 g (70%) of **14** as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.39–3.35 (m; 4H), 3.33 (s; 2H), 3.29 (s; 2H), 1.86 (br s; 1H), 1.57–1.47 (m; 4H), 1.29–1.16 (m; 4H), 1.07–1.03 (m; 21H), 0.86 (s; 6H), 0.84 (s; 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 72.03 (CH_2), 71.61 (CH_2), 71.45 (CH_2), 35.42 (C), 34.91 (C), 34.82 (CH_2), 34.64 (CH_2), 24.35 (CH_2), 24.17 (CH_2), 24.10 (CH_3), 23.96 (CH_3), 18.07 (CH_3), 17.71 (CH_3), 12.30 (CH), 12.01(CH). $C_{23}H_{50}O_3Si$ (402.5): calcd C 68.59, H 12.51; found C 68.74, H 12.52.

4-(4-Triisopropylsiloxy-3,3-dimethylbutoxy)-2,2-dimethylbutanal (15): To a solution of **13** (2.4 g, 6.4 mmol) in methylene chloride was added a mixture of pyridinium chlorochromate (2.52 g) and of Alox (neutral, 2.52 g). The mixture was stirred at RT until the reaction had stopped (monitored by TLC). The dark brown solution was filtered through silica gel with ether as solvent. The resulting dark brown solution was allowed to stand for three days at RT. After removal of the ether, the product was purified by flash chromatography on silica gel with cyclohexane/ethyl acetate 20:1 as eluent. The reaction yielded 1.78–2.02 g (75–85%) of **15**. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.42 (s; 1H), 3.48–3.33 (m; 4H), 3.32 (s; 2H), 1.76 (t, ^3J = 6.3 Hz; 2H), 1.50 (t, ^3J = 6.5 Hz; 2H), 1.13–0.98 (m; 27H), 0.88–0.81 (m; 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.28 (CH), 72.42 (CH_2), 68.12 (CH_2), 66.66 (CH_2), 44.54 (C), 38.05 (CH_2), 37.94 (CH_2), 34.93 (C), 24.37 (CH_3), 21.56 (CH_3), 18.04 (CH_3), 12.00 (CH); $C_{21}H_{44}O_3Si$ (372.5): calcd C 67.68; H 11.90; found C 67.44, H 11.70.

5-(5-Triisopropylsiloxy-4,4-dimethylpentyloxy)-2,2-dimethylpentanal (16): The same procedure as described for the preparation of **15** yielded 1.92–2.17 g (75–85%) of **16** as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.44 (s; 1H), 3.39–3.32 (m; 6H), 1.67–1.45 (m; 6H), 1.26–1.19 (m; 2H), 1.07–0.84 (m; 33H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.12 (C), 72.08 (CH_2), 71.94 (CH_2), 70.68 (CH_2), 45.5 (C), 35.4 (C), 34.94 (CH_2), 33.68 (CH_2), 24.87 (CH_2), 24.53 (CH_2), 24.27 (CH_3), 22.44 (CH_3), 17.94 (CH_3), 11.91 (CH); $C_{23}H_{48}O_3Si$ (400.5): calcd C 68.94, H 12.07; found C 69.21, H 11.98.

6-(4-Triisopropylsiloxy-3,3-dimethylbutoxy)-4,4-dimethylhex-1-yn-3-ol (17): THF (8 mL) was cooled to −45 °C under argon atmosphere, and *n*-butyllithium (1.6 M in hexane, 6 mL) was added. Acetylene was bubbled through the solution. The rising temperature and formation of a white precipitate indicated that reaction had begun. Acetylene continued to be bubbled through for about 4 h, and the temperature was maintained at −50 °C. The reaction mixture was then cooled to −78 °C, and the aldehyde **15** (1.49 g, 4 mmol) dissolved in THF (5 mL) was added. The cooling bath was removed, and the reaction was allowed to warm up to 0 °C. The homogenous mixture was then hydrolized with buffer solution (10 mL). Ether (10 mL) was added, and the phases were separated. The aqueous phase was extracted three times with ether. The organic phases were combined and dried over $MgSO_4$. Subsequent flash chromatography (cyclohexane/ethyl acetate 10:1) yielded 1.37–1.45 g (86–91%) of **17**. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.43 (d, ^3J = 7.7 Hz; 1H), 4.02 (dd, ^4J = 2.2 Hz, ^4J = 7.7 Hz; 1H), 3.57–3.43 (m; 4H), 3.31 (s; 2H), 2.38 (d, ^4J = 2.2 Hz; 1H), 2.05–1.88 (m; 1H), 1.56 (t, ^3J = 7.8 Hz; 2H), 1.44–1.32 (m; 1H), 1.09–1.00 (m; 27H), 0.85 (s; 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 83.82 (C), 73.16 (CH), 72.41 (CH_2), 69.95 (CH), 68.24 (CH_2), 67.09 (CH_2), 38.31 (CH_2), 38.09 (C), 38.04 (CH_2), 34.97 (CH_2), 25.23 (CH_3), 24.55 (CH_3), 24.35 (CH_3), 23.92 (CH_3), 18.11 (CH_3), 12.01 (CH); $C_{23}H_{46}O_3Si$ (398.7): calcd C 69.29, H 11.63; found C 69.28, H 11.43.

7-(5-Triisopropylsiloxy-4,4-dimethylpentyloxy)-4,4-dimethylhept-1-yne-3-ol (18): The same procedure as described for the preparation of **17** yielded 1.38–1.59 g (81–93%) of **18**. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.09 (d, ^4J = 2.1 Hz; 1H), 3.40–3.35 (m; 4H), 3.34 (s; 2H), 2.43 (d, ^4J = 2.1 Hz; 1H), 1.71–1.42 (m; 6H), 1.40–1.13 (m; 2H), 1.09–1.01 (m; 21H), 0.97 (s; 3H), 0.95 (s; 3H), 0.84 (s; 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 83.50 (C), 73.93 (CH), 72.05 (CH_2), 71.99 (CH_2), 71.52 (CH_2), 70.03 (CH), 37.94 (C), 35.42 (C), 34.87 (CH_2), 34.31 (CH_2), 26.92 (CH_2), 25.01 (CH_2), 24.36 (CH_3), 24.10 (CH_3), 22.55 (CH_3), 22.31 (CH_3), 18.07 (CH_3), 12.03 (CH); $C_{25}H_{50}O_3Si$ (426.5): calcd C 70.36, H 11.81; found C 70.30, H 11.83.

6-(4-Triisopropylsiloxy-3,3-dimethylbutoxy)-4,4-dimethyl-3-tetrahydropyran-2-yloxyhex-1-yne (19): Alcohol **17** (713 mg, 1.79 mmol), 3,4-dihydro-2*H*-pyran

(270 mg, 3.22 mmol), and pyridinium *p*-toluenesulfonate (50 mg, 0.18 mmol) were dissolved in methylene chloride (4 mL). The mixture was stirred overnight and then worked up by adding ether (10 mL) and buffer solution (10 mL). The aqueous layer was separated and extracted once with ether. The organic phases were combined and dried over $MgSO_4$. The product was purified by flash chromatography on silica gel with cyclohexane/ethyl acetate 10:1 yielding 737–806 mg (85–93%) of **19**. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.01–5.00 (m; Ha), 4.65 (s; Ha') (Ha + Ha' = 1H), 4.07 (d, ^4J = 2.1 Hz; Hb), 3.86 (d, ^4J = 2.2 Hz; Hb') (Hb + Hb' = 1H), 3.75–3.43 (m; 6H), 3.32 (s; 2H), 2.38 (d, ^4J = 2.1 Hz; Hc), 2.33 (d, ^4J = 2.1 Hz; Hc') (Hc + Hc' = 1H), 1.80–1.50 (m; 10H), 1.10–0.91 (m; 27H), 0.86 (s; 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 100.73 (CH), 94.82 (CH), 82.62 (C), 81.08 (C), 76.69 (CH), 74.60 (CH), 73.47(CH), 72.77 (CH), 72.51 (CH_2), 67.95 (CH_2), 67.90 (CH_2), 67.54 (CH_2), 62.25 (CH_2), 61.85 (CH_2), 38.31 (CH_2), 37.81 (C), 37.70 (CH_2), 37.49 (CH_2), 36.85 (C), 35.00 (C), 30.36 (CH_2), 30.32 (CH_2), 25.55 (CH_2), 25.46 (CH_2), 24.41 (CH_3), 23.59 (CH_3), 23.57 (CH_3), 23.20 (CH_3), 23.15 (CH_3), 19.02 (CH_2), 18.06 (CH_3), 12.03 (CH); $C_{28}H_{54}O_4Si$ (482.8): calcd C 69.65, H 11.27; found C 69.54, H 11.30.

7-(5-Triisopropylsiloxy-4,4-dimethylpentyloxy)-4,4-dimethyl-3-tetrahydropyran-2-yloxyhept-1-yne (20): The same procedure as described for the preparation of **19** yielded 766–866 mg (84–95%) of **20**. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.01 (t, ^3J = 3.9 Hz; Ha), 4.67 (t, ^3J = 3.2 Hz; Ha) (Ha + Ha' = 1H), 4.12–3.34 (m; 9H), 2.40 (d, ^4J = 2.1 Hz; Hc), 2.34 (d, ^4J = 2.1 Hz; Hc') (Hc + Hc' = 1H) 1.84–1.50 (m; 12H), 1.38–1.21 (m; 2H), 1.09–1.02 (m; 21H), 1.00 (s; 3H), 0.96 (s; 3H), 0.85 (s; 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 100.70 (CH), 94.92 (CH), 82.74 (C), 81.33 (C), 76.45 (CH), 74.42 (CH), 73.39 (CH), 72.58 (CH), 72.07 (CH_2), 71.88 (CH_2), 71.67 (CH_2), 71.58 (CH_2), 62.32 (CH_2), 61.90 (CH_2), 38.32 (C), 37.34 (C), 34.95 (CH_2), 34.63 (CH_2), 34.37 (CH_2), 30.40 (CH_2), 30.33 (CH_2), 26.92 (CH_2), 25.57 (CH_2), 25.46 (CH_2), 24.45 (CH_2), 24.34 (CH_2), 24.11 (CH_3), 24.04 (CH_3), 23.16 (CH_3), 23.10 (CH_3), 19.09 (CH_2), 18.06 (CH_3), 18.02 (CH_2), 12.05 (CH); $C_{30}H_{58}O_4Si$ (510.9): calcd C 70.53, H 11.44; found C 70.77, H 11.55.

6-(4-Hydroxy-3,3-dimethylbutoxy)-4,4-dimethyl-3-tetrahydropyran-2-yloxyhex-1-yne (21): To a solution of **19** (672 mg, 1.39 mmol) in THF (3.6 mL) was added NBu_4F (1M in THF, 1.44 mL). The reaction was stirred until **19** was consumed (ca. 3 h). Then buffer solution (5 mL) and ether (10 mL) were added, and the phases separated. The aqueous phase was extracted three times with ether. The combined organic phases were dried over $MgSO_4$, and the product was isolated by flash chromatography on silica gel, with cyclohexane/ethyl acetate (4:1) as eluent, yielding 418–431 mg (92–95%) of **21**. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.99–4.97 (m; Ha), 4.65–4.63 (m; Ha') (Ha + Ha' = 1H), 4.07 (d, ^4J = 2.0 Hz; Hb), 4.03–4.00 (m; Hd'), 3.83 (d, ^4J = 2.1 Hz; Hb'), 3.77–3.69 (m; Hd) (Hb + Hb' = 1H, Hd + Hd' = 1H), 3.53–3.42 (m; 6H), 3.24 (s; 1H), 3.22 (s; 1H), 2.40 (d, ^4J = 2.1Hz; Hc'), 2.35 (d, ^4J = 2.1Hz; Hc) (Hc + Hc' = 1H), 1.82–1.49 (m; 10H), 1.01 (s; 3H), 0.96 (s; 3H), 0.86 (s; 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 100.76 (CH), 94.91 (CH), 82.36 (C), 80.88 (C), 76.56 (CH), 74.79 (CH), 73.72 (CH), 72.59 (CH), 71.35 (CH_2), 67.95 (CH_2), 67.58 (CH_2), 67.53 (CH_2), 62.23 (CH_2), 61.95 (CH_2), 39.58 (CH_2), 39.54 (CH_2), 37.76 (C), 37.55 (CH_2), 37.30 (CH_2), 36.78 (C), 34.95 (C), 30.34 (CH_2), 30.21 (CH_2), 25.49 (CH_2), 25.41 (CH_2), 25.08 (CH_3), 25.03 (CH_3), 23.74 (CH_3), 23.67 (CH_3), 23.42 (CH_3), 23.22 (CH_3), 19.07 (CH_2), 18.95 (CH_2); $C_{19}H_{34}O_4$ (326.5): calcd C 69.90, H 10.50; found C 69.70, H 10.57.

7-(5-Hydroxy-4,4-dimethylpentyloxy)-4,4-dimethyl-3-tetrahydropyran-2-yloxyhept-1-yne (22): The same procedure as described for the preparation of **21** yielded 446–470 mg (90–95%) of **22**. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.01 (m; Ha), 4.67 (s; Ha') (Ha + Ha' = 1H), 4.12 (d, ^4J = 2.1 Hz; Hb), 3.88 (d, ^4J = 2.1 Hz; Hb) (Hb + Hb' = 1H), 3.78–3.65 (m; 1H), 3.50–3.40 (m; 1H), 3.41–3.36 (m; 4H), 3.31 (s; 2H), 2.40 (d, ^4J = 2.1 Hz; Hc), 2.35 (d, ^4J = 2.1 Hz; Hc') (Hc + Hc' = 1H), 2.2–2.05 (broad; 1H), 1.84–1.50 (m; 12H), 1.38–1.21 (m; 2H), 1.00 (s; 3H), 0.06 (s; 3H), 0.86 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 100.65 (CH), 94.81 (CH), 82.59 (C), 81.16 (C), 74.50 (CH), 73.45 (CH), 72.50 (CH), 71.71 (CH_2), 71.63 (CH_2), 71.51 (CH_2), 71.30 (CH_2), 62.23 (CH_2), 61.84 (CH_2), 38.24 (C), 37.26 (C), 34.83 (CH_2), 34.60 (CH_2), 34.47 (CH_2), 34.19 (CH_2), 30.30 (CH_2), 30.22 (CH_2), 26.83 (CH_2), 25.46 (CH_2), 25.35 (CH_2), 24.12 (CH_2), 24.10 (CH_2), 23.90 (CH_3), 23.07 (CH_3), 23.01 (CH_3), 22.72 (CH_3), 22.64 (CH_3), 19.00 (CH_2), 18.94 (CH_2); $C_{21}H_{38}O_4$ (354.5): calcd C 71.15, H 10.80; found C 70.93, H 10.79.

4-(4-Tetrahydropyran-2-yloxy-3,3-dimethyl-hex-5-ynyloxy)-2,2-dimethylbutanal (23): To a solution of **21** (326 mg, 1 mmol) in methylene chloride (3.5 mL) was added a mixture of pyridinium chlorochromate (347 mg) and Alox (neutral, 347 mg). The mixture was stirred at RT until the reaction had stopped (monitored by TLC). The dark brown solution was filtered through silica gel with ether as solvent. After removal of the ether, the product was purified by flash chromatography on silica gel with cyclohexane/ethyl acetate 5:1 as eluent. The reaction yielded 268–298 mg (83–92%) of **23**. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.42 (s;1H), 4.99 (t, ^3J = 2.8 Hz; Ha), 4.65 (t, ^3J = 3.3 Hz; Ha) (Ha + Ha' = 1H), 4.07 (d, ^4J = 2.1 Hz; Hb), 3.75 (d, ^4J = 2.9 Hz; Hb') (Hb + Hb' = 1H), 3.72–3.71 (m; 1H), 3.52–3.48 (m; 1H), 3.45–3.30 (m; 4H), 2.40 (d, ^4J = 2.1 Hz; Hc'), 2.35 (d, ^4J = 2.0 Hz; Hc) (Hc' + Hc = 1H), 1.89–1.52 (m; 10H), 1.16–0.90 (m; 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.26 (CH), 100.72 (CH), 94.83 (CH), 82.5 (C), 81.01 (C), 76.61 (CH), 74.71 (CH), 73.58 (CH), 72.61 (CH), 67.83 (CH_2), 66.80 (CH_2), 66.75 (CH_2), 62.28 (CH_2), 61.90 (CH_2), 44.54 (C), 37.90 (CH_2), 37.88 (CH_2), 37.76 (C), 37.48 (CH_2), 37.23 (CH_2), 36.7 (C), 30.35 (CH_2), 30.29 (CH_2), 25.52 (CH_2), 25.43 (CH_2), 23.82 (CH_3), 23.65 (CH_3), 23.61 (CH_3), 23.29 (CH_3), 23.17 (CH_3), 21.61 (CH_3), 21.51 (CH_3), 19.03 (CH_2); $C_{19}H_{32}O_4$ (324.5): calcd C 70.33, H 9.94; found C 70.35, H 10.06.

5-(5-Tetrahydropyran-2-yl-oxy-4,4-dimethyl-hept-6-ynyloxy)-2,2-dimethylpentanal (24): The same procedure as described for the preparation of **23** yielded 281–330 mg (80–94%) of **24**. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.43 (s; 1H), 5.01 (m; Ha), 4.66 (m; Ha') (Ha + Ha' = 1H), 4.11 (d, ^4J = 2.1 Hz; Hb), 3.86 (s; Hb') (Hb + Hb' = 1H), 3.79–3.72 (m; 1H), 3.53–3.41 (m; 1H), 3.38–3.34 (m; 4H), 2.40 (d, ^4J = 2.1 Hz; Hc'), 2.35 (d, ^4J = 2.1 Hz; Hc) (Hc + Hc' = 1H), 1.80–1.39 (m; 14H), 1.03 (s; 3H), 0.98 (s; 6H), 0.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.20 (CH), 100.98 (CH), 94.86 (CH), 81.24 (C), 74.50 (CH), 73.45 (CH), 72.55 (CH), 71.69 (CH_2), 70.90 (CH_2), 70.74 (CH_2), 62.30 (CH_2), 61.90 (CH_2), 45.50 (C), 41.78 (C), 37.32 (C), 36.92 (CH_2), 34.57 (CH_2), 33.61 (CH_2), 30.35 (CH_3), 25.51 (CH_3), 25.40 (CH_2), 25.27 (CH_2), 24.94 (CH_2), 24.61 (CH_3), 24.19 (CH_3), 23.14 (CH_3), 23.06 (CH_3), 22.68 (CH_3), 21.26 (CH_3), 19.05 (CH_2); $C_{21}H_{36}O_4$ (352.2): calcd C 71.14, H 10.80; found C 71.04, H 10.56.

4,4,9,9-Tetramethyl-8(tetrahydropyran-2-yloxy)-1-oxacycloundec-6-yn-5-ol (25): A solution of **23** (217 mg, 0.67 mmol) in THF (400 mL) was added slowly during 4–5 h to a solution of lithium bis(trimethylsilyl)amide (350 mg, 2.1 mmol) in THF (60 mL). Then ethanol (10 mL) was added, and the reaction mixture concentrated to a volume of 30 mL. Buffer solution (20 mL) and ether (30 mL) were added. The phases were separated, and the aqueous layer extracted three times with ether. The organic layers were combined and dried over $MgSO_4$. The product was purified by flash chromatography on silica gel with cyclohexane/ethyl acetate (4:1) as eluent yielding 151–184 mg (70–85%) of **25**. ^{1}H NMR (300 MHz, C_6D_6): δ = 5.29 (t, ^3J = 3.4 Hz; 1H), 4.31 (s; Ha), 4.19 (2s, ^3J = 2.4 Hz; Ha') (Ha + Ha' = 1H), 3.90 (t, ^3J = 8.4 Hz; 1H), 3.76–3.08 (m; 6H), 2.23–2.13 (m; 1H), 1.72–0.87 (m; 21H); ^{13}C NMR (75 MHz, C_6D_6): δ = 95.35 (CH), 95.22 (CH), 88.63 (C), 87.88 (C), 84.56 (C), 84.11 (C), 72.90 (CH), 72.66 (CH), 70.27 (CH), 67.53 (CH_2), 67.15 (CH_2), 65.91 (CH_2), 65.48 (CH_2), 61.85 (CH_2), 39.74 (C), 39.44 (C), 38.74 (C), 38.56 (C), 38.01 (CH_2), 37.81 (CH_2), 37.41 (CH_2), 34.95 (CH_2), 30.96 (CH_2), 30.80 (CH_2), 28.98 (CH_3), 28.53 (CH_3), 27.58 (CH_3), 27.45 (CH_3), 25.95 (CH_3), 25.88 (CH_2), 23.85 (CH_3), 19.61 (CH_2), 19.55 (CH_2); $C_{19}H_{32}O_4$ (324.5): calcd C 70.33, H 9.94; found C 70.48, H 9.82.

5,5,10,10-Tetramethyl-9-(tetrahydropyran-2-yloxy)-1-oxacyclotridec-7-yn-6-ol (26): A solution of **24** (232 mg, 0.67 mmol) in THF (240 mL) was slowly added over 4–5 h to a solution of lithium bis(trimethylsilyl)amide (350 mg, 2.1 mmol) in THF (60 mL). Then ethanol (10 mL) was added, and the reaction mixture concentrated to a volume of 30 mL. Buffer solution (20 mL) and ether (30 mL) were added. The phases were separated, and the aqueous layer was extracted three times with ether. The organic layers were combined and dried over $MgSO_4$. The product was purified by flash chromatography on silica gel with cyclohexane/ethyl acetate 4:1 as eluent, yielding 195–225 mg (83–96%) of **26**; ^{1}H NMR (300 MHz, C_6D_6): δ = 5.35 (s; 1H), 4.51–4.05 (m; 2H), 3.75–3.62 (m; 1H), 3.48–3.44 (m; 1H), 3.36–3.22 (m; 4H), 1.93–0.90 (m; 26H); ^{13}C NMR (75 MHz, C_6D_6): δ = 101.89 (CH), 95.02 (CH), 87.67 (C), 86.43 (C), 86.26 (C), 83.80 (C), 73.44 (CH), 72.99 (CH), 71.20 (CH), 70.93 (CH), 70.76 (CH_2), 70.69 (CH_2), 70.66 (CH_2), 70.52 (CH_2), 70.42 (CH_2), 61.65 (CH_2), 38.98 (C), 38.93 (C), 38.85 (C), 38.49 (C), 38.39 (C), 36.26 (CH_2), 35.91 (CH_2), 35.48 (CH_2), 35.41 (CH_2), 35.03 (CH_2), 30.76 (CH_2), 28.10 (CH_2), 25.91 (CH_2), 25.29 (CH_2), 24.95 (CH_3), 24.80 (CH_3), 24.21 (CH_2), 24.17 (CH_2), 24.06 (CH_2), 23.59 (CH_3), 23.24 (CH_3), 23.10 (CH_3), 22.65 (CH_3), 22.55 (CH_3), 22.19 (CH_3), 22.12 (CH_3), 19.52 (CH_2), 19.35 (CH_2); $C_{21}H_{36}O_4$ (352.5): calcd C 71.14, H 10.80; found C 70.91, H 10.58.

4,4,9,9-Tetramethyl-8-(tetrahydropyran-2-yloxy)-5-isopropyldimethylsiloxy-1-oxacycloundec-6-yne (27): To a solution of **25** (486 mg, 1.5 mmol) and 2,6-lutidine (1 mL) in methylene chloride (3 mL) was added (under argon atmosphere) isopropyldimethylsilyl chloride (240 mg, 1.5 mmol). After the mixture had been stirred overnight, a white precipitate formed. Buffer solution (10 mL) with ether (20 mL) were added. The aqueous phase was twice extracted with diethyl ether. The organic phases were combined and dried over $MgSO_4$. Flash chromatography over silica gel with ether/pentane 1:10 yielded 578–616 mg (91–97%) of **27**; ^{1}H NMR (300 MHz, C_6D_6): δ = 5.36–5.33 (m; Ha), 4.7–4.68 (m; Ha') (Ha + Ha' = 1H), 4.39–3.21 (m; 8H), 2.05–1.88 (m; 1H), 1.78–0.85 (m; 27H), 0.35–0.05 (m; 7H); ^{13}C NMR (75 MHz, C_6D_6): δ = 100.39 (CH), 100.28 (CH), 95.36 (CH), 95.15 (CH), 87.54 (C), 87.40 (C), 84.17 (C), 83.94 (C), 76.44 (CH), 76.05 (CH), 72.90 (CH), 72.53 (CH), 70.99 (CH), 70.84 (CH), 67.46 (CH_2), 67.41 (CH_2), 67.29 (CH_2), 67.13 (CH_2), 62.09 (CH_2), 62.01 (CH_2), 61.96 (CH_2), 61.84 (CH_2), 39.96 (C), 38.88 (C), 38.23 (CH_2), 37.71 (CH_2), 37.51 (CH_2), 37.40 (CH_2), 36.91 (CH_2), 30.95 (CH_2), 30.88 (CH_2), 30.84 (CH_2), 30.61 (CH_2), 28.38 (CH_3), 28.11 (CH_3), 27.90 (CH_3), 27.86 (CH_3), 27.63 (CH_3), 27.46 (CH_3), 27.22 (CH_3), 26.76 (CH_3), 26.36 (CH_3), 26.21 (CH_3), 26.06 (CH_2), 25.94 (CH_2), 25.86 (CH_3), 25.56 (CH_3), 19.76 (CH_2), 19.64 (CH_2), 19.11 (CH_2), 17.20 (CH_3), 17.13 (CH_3), 15.33 (CH_3), −3.17 (CH_3), −3.31 (CH), −3.32 (CH), −3.95 (CH_3), −4.00 (CH_3), −4.02 (CH_3); $C_{24}H_{44}O_4Si$ (424.7): calcd C 67.87, H 10.44; found C 67.75, H 10.53.

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5,5,10,10-Tetramethyl-9-(tetrahydropyran-2-yloxy)-6-isopropyldimethylsiloxy-1-oxacyclotridec-7-yne (28): The same procedure as described for the preparation of **27** yielded 630–657 mg (93–97%) of **28**; ^{1}H NMR (300 MHz, C_6D_6): δ = 5.31 (s; 1H), 4.46 (d, ^5J = 1.2 Hz; 1H), 4.15 (d, ^5J = 1.2 Hz; 1H), 3.81–3.73 (m; 1H), 3.46–3.37 (m; 1H), 3.36–3.28 (m; 4H), 1.92–0.87 (m; 26H), 0.29–0.13 (m; 13H); ^{13}C NMR (75 MHz, C_6D_6): δ = 100.35 (CH), 95.54 (CH), 87.39 (C), 84.02 (C), 77.22 (CH), 73.52 (CH), 71.84 (CH), 70.45 (CH_2), 70.38 (CH_2), 61.98 (CH_2), 39.58 (C), 39.30 (C), 38.48 (C), 35.91 (CH_2), 35.06 (CH_2), 34.87 (CH_2), 30.93 (CH_2), 30.37 (CH_2), 25.95 (CH_2), 25.08 (CH_3), 24.96 (CH_3), 24.32 (CH_2), 24.12 (CH_2), 23.14 (CH_3), 22.51 (CH_3), 22.47 (CH_3), 22.24 (CH_3), 19.75 (CH_2), 17.18 (CH_3), 16.92 (CH_3), 15.30 (CH), −3.50 (CH_3), −4.29 (CH_3), −4.35 (CH_3); $C_{26}H_{48}O_4Si$ (452.8): calcd C 68.97, H 10.68; found C 69.04, H 10.61.

4,4,9,9-Tetramethyl-8-(tetrahydropyran-2-yloxy)-5-isopropyldimethylsiloxy-1-oxacycloundecane-6,7-dione (29): To a solution of **27** (127 mg, 0.3 mmol) in carbon tetrachloride (1.4 mL) was added acetonitrile (1.4 mL), water (2.1 mL), and sodium periodate (250 mg). The mixture was stirred vigorously until two clear phases resulted. After that 1 mg of $RuO_2 \cdot H_2O$ was added, and the vigorous stirring was continued. The mixture immediately turned black, and a white precipitate was formed. The reaction was complete within 30–60 min (monitored by TLC) and worked up by adding water (7.5 mL). The phases were separated, and the aqueous phase was extracted with methylene chloride (3 × 10 mL). The organic layers were combined, dried with $MgSO_4$, and then concentrated slightly. The black organic phase was filtered through Celite with methylene chloride as eluent. After removal of the solvent the product was purified by flash chromatography on silica gel with ether/pentane 1:20 as eluent, yielding 116–131 mg (85–96%) of **29** as a yellow oil. ^{1}H NMR (300 MHz, C_6D_6): δ = 5.16 (s; Ha), 4.94 (s; Ha') (Ha + Ha' = 1H), 4.91–4.40 (m; 2H), 3.84–3.79 (m; 1H), 3.42–3.25 (m; 2H), 3.07–2.81 (m; 3H), 1.78–0.85 (m; 28H), 0.29–0.13 (m; 7H); ^{13}C NMR (75 MHz, C_6D_6): δ = 203.6 (C), 203.33 (C), 196.91 (C), 196.56 (C), 101.29 (CH), 98.13 (CH), 81.35 (CH), 76.66 (CH), 75.52 (CH), 73.80 (CH), 86.00 (CH_2), 67.71 (CH_2), 76.58 (CH_2), 67.39 (CH_2), 64.83 (CH_2), 63.70 (CH_2), 61.82 (CH_2), 39.76 (CH_2), 39.33 (CH_2), 38.71 (C), 38.07 (C), 37.10 (C), 37.03 (C), 36.35 (C), 31.52 (CH_2), 31.41 (CH_2), 30.05 (CH_2), 29.78 (CH_3), 28.05 (CH_3), 26.56 (CH_3), 25.69 (CH_2), 21.52 (CH_2), 19.63 (CH_3), 17.29 (CH_3), 17.26 (CH_3), 17.20 (CH_3), 17.16 (CH_3), 15.46 (CH_3), 15.37 (CH_3), −3.28 (CH), −3.53 (CH), −3.87 (CH), −4.06 (CH_3), −4.11 (CH_3); $C_{24}H_{44}O_6Si$ (456.7): calcd C 63.12, H 9.71; found C 62.89, H 9.46.

5,5,10,10-Tetramethyl-9-(tetrahydropyran-2-yloxy)-6-isopropyldimethylsiloxy-1-oxacyclotridecane-7,8-dione (30): The same procedure as described for the preparation of **29** yielded 126–137 mg (87–95%) of **30**. ^{1}H NMR (300 MHz, C_6D_6): δ = 5.46 (m; Ha), 5.21 (m; Ha') (Ha + Ha' = 1H), 4.96–4.44 (m; 2H), 3.84–3.72 (m; 1H), 3.35–2.99 (m; 5H), 2.19–0.72 (m; 33H), 0.28–0.00 (m; 6H); ^{13}C NMR (75 MHz, C_6D_6): δ = 202.8 (C), 200.55 (C), 200.36 (C), 199.76 (C), 199.30 (C), 199.13 (C), 198.15 (C), 102.21 (CH), 101.46 (CH), 97.37 (CH), 82.42 (CH), 79.05 (CH), 77.33 (CH), 76.42 (CH), 70.92 (CH_2), 70.86 (CH_2), 70.84 (CH_2), 70.23 (CH_2), 69.87 (CH_2), 69.80 (CH_2), 69.47 (CH_2), 65.84 (CH_2), 64.55 (CH_2), 62.85 (CH_2), 61.99 (CH_2), 39.68 (C), 39.47 (C), 39.33 (C), 39.04 (C), 38.98 (C), 38.83 (C), 38.67 (C), 36.59 (CH_2), 35.51 (CH_2), 35.25 (CH_2), 34.91 (CH_2), 33.90 (CH_2), 31.45 (CH_2), 30.91 (CH_2), 30.86 (CH_2), 30.61 (CH_2), 25.62 (CH_2), 25.52 (CH_2), 25.37 (CH_3), 25.05 (CH_3), 24.98 (CH_3), 24.39 (CH_2), 24.13 (CH_2), 23.97 (CH_2), 23.85 (CH_2), 23.72 (CH_2), 22.00 (CH_3), 21.92 (CH_3), 21.09 (CH_3), 20.55 (CH_3), 19.97 (CH_2), 19.88 (CH_2), 19.64 (CH_2), 17.39 (CH_3), 17.29 (CH_3), 17.22 (CH_3), 17.18 (CH_3), 17.16 (CH_3), 17.08 (CH_3), 15.51 (CH), 15.23 (CH), 15.14 (CH), −3,.66 (CH_3), −3.75 (CH_3), −3.87 (CH_3), −4.09 (CH_3), −4.17 (CH_3); $C_{26}H_{48}O_6Si$ (484.7): calcd C 64.42, H 9.98; found C 64.68, H 9.93.

***syn/anti*-4,4,9,9-Tetramethyl-1-oxacycloundecane-5,8-dihydroxy-6,7-dione (31)**: The ion exchange resin AG 500 W-X2 from Bio-Rad in methanol (2.5 mL) was added to a solution of **29** (456 mg, 1 mmol) in methanol (5 mL). The suspension was stirred until **29** was no longer detected by TLC (ca. 4 h). The ion-exchange resin was then removed by filtration. Methanol was removed in vacuo, and the products were isolated by flash chromatography (silica gel; ether/pentane 1:1). The diastereomeric products were obtained in a 1:1 ratio. The overall yield was 225–242 mg (83–89%). *syn* isomer **31a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.26 (d, ^3J = 7.5 Hz; 2H), 3.68 (d, ^3J = 7.5 Hz; 2H), 3.43–3.33 (m; 4H), 1.94–1.85 (m; 2H), 1.48–1.23 (m; 2H), 1.09 (s; 6H), 1.05 (s; 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.24 (C), 80.80 (CH), 67.76 (CH_2), 37.43 (C), 35.93 (CH_2), 25.68 (CH_3), 25.40 (CH_3); IR (KBr): $\tilde{\nu}$ [cm^{-1}] = 3548 (vs), 3470 (vs), 2961 (m), 2944 (m), 2886 (m), 1710 (vs), 1699 (vs), 1478 (w), 1387 (w), 1108 (vs), 1066 (m), 710 (w); UV (CH_2Cl_2): λ_{max} [nm] (log ε) = 232 (2.88), 414 (1.35); $C_{14}H_{24}O_5$(272.3): calcd C 61.74, H 8.88; found C 61.77, H 8.95. *anti* isomer **31b**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.62 (d, J = 8.6 Hz, 2H), 3.35–3.23 (m; 4H), 2.82 (d, J = 8.7 Hz; 4H), 2.01–1.90 (m; 2H), 1.46–1.41 (m; 2H), 1.17 (s; 6H), 0.91 (s; 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.15 (C), 76.91 (CH), 67.89 (CH_2), 37.41 (C), 36.30 (CH_2), 29.16 (CH_3), 18.97 (CH_3); IR (KBr): $\tilde{\nu}$ [cm^{-1}] = 3500 (vs), 2982 (s), 2968 (m), 2938 (m), 2911 (s), 2871 (s), 2857 (s), 1707 (vs), 1124 (vs), 1063 (s), 763 (m); UV (CH_2Cl_2): λ_{max} [nm] (log ε) = 234 (2.96), 406 (1.29); $C_{14}H_{24}O_5$(272.3): calcd C 61.74, H 8.88; found C 61.94, H, 8.92.

5,5,10,10-Tetramethyl-6,9-dihydroxy-7,8-dioxo-1-oxacyclotridecane (32): The same procedure as described for the preparation of **31** yielded 255–270 mg (85–90%) of **32** [10].

4,4,9,9-Tetramethyl-1-oxacycloundecane-5,6,7,8-tetrone (9): To a solution of **31** (68 mg, 0.25 mmol) in CCl_4 (10 mL) was added *N*-bromosuccinimide (98 mg, 0.55 mmol). The mixture was heated to reflux until succinimide precipitated (ca. 2 h). Succinimide was filtered off in a frit under argon, and the red solution was then concentrated. The resulting red crystals of **9** were washed with ether (2 × 5 mL). The ether was evaporated, and the residue heated under vacuum (0.01 torr) in a kugelrohr apparatus, where additonal **9** was obtained. The overall yield was 40–45 mg (59–67%) of **9**. M.p. 136–137 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.46 (t, J = 5.5 Hz; 4H), 1.94 (t, J = 5.5 Hz; 4H), 1.29 (s; 12H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 203.48 (C), 191.48 (C), 68.27 (CH2), 44.53 (C), 38.35 (CH2), 24.03 (CH3). IR (KBr): $\tilde{\nu}$ [cm^{-1}] = 2975 (s), 2936 (m), 2903 (m), 2873 (m), 1733 (vs), 1720 (vs), 1476 (m), 1363 (m), 1339 (w), 1097 (vs), 1037 (m); UV (CH_2Cl_2): λ_{max} [nm] (log ε) = 460 (1.44), 362 (1.8), 294 (2.53), 226 (3.08); HRMS: m/z = 268.1312 (calcd for $C_{14}H_{20}O_5$: m/z = 268.1310).

5,5,10,10-Tetramethyl-1-oxacyclotridecane-6,7,8,9-tetrone (10): The same procedure as described for the preparation of **9** yielded 54–63 mg (74–85%) of **10** [10].

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