A Synthesis of α-Methylene-γ-lactones Fused to Medium and Large Rings by Intramolecular Cyclization of Formylated Allyl Halides[1)]

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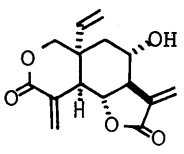
Carbocyclic rings fused to an α-methylene-γ-lactone unit were synthesized from ω-formylated β-ethoxycarbonylallyl halides (4a—g) through intramolecular cyclization by the use of a low-valent chromium reagent, prepared from $CrCl_3$ and $LiAlH_4$, in *N,N*-dimethylformamide. α-Methylene-γ-lactones fused to medium (eight-membered) or large (twelve- and fourteen-membered) ring system (5a, c and d) were synthesized by this method in good to fairly good yields. However, the formylated allyl halide (4b), expected to afford a ten-membered carbocyclic ring system, gave dilactones fused to a twenty-membered ring unit even under a high dilution reaction condition.

Keywords formylated allyl halide; intramolecular; cyclization; α-methylene; γ-lactone; medium carbocyclic ring; large carbocyclic ring; low valence; chromium reagent

The naturally occurring terpenes include a variety of carbocyclic structures, often with the α-methylene-γ-lactone unit fused to six-, seven-, ten-, and fourteen-membered carbocyclic rings, such as vernolepine (**1**),[2)] elephantopin (**2**)[3)] and kericembrenolide A (**3**).[4)] The α-methylene-γ-lactone structural unit has been assigned a central role in the mechanism of action of these physiologically active compounds.[5)] Many methods are now available for introduction of the exo-methylene unit into a γ-lactone ring,[6)] but a more direct strategy would seem advantageous. Some synthetic methods to germacranolides and cembranolides using intramolecular cyclization reactions of ω-formylated allyl bromide or allylstannane derivatives without an alkoxycarbonyl group at the β position were recently reported by Shibuya *et al.*[7)] and Marshall *et al.*[8)] They needed several additional steps in order to introduce the α-methylene-γ-lactone unit into the ten- and fourteen-membered ring systems initially formed by the above cyclization reaction.

There are many reports on the synthesis of α-methylene-γ-lactones by intermolecular reaction of α-bromomethylacrylate and aldehyde by the use of zinc dust,[9)] low-valent chromium reagent,[10)] tin metal,[11)] tin chloride[12)] or nickel reagent.[13)]



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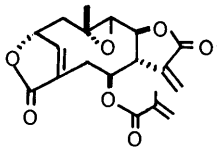

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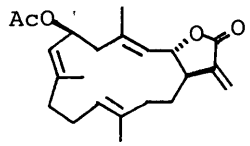

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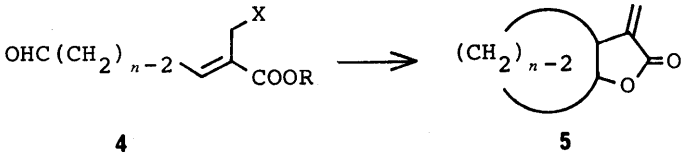
Chart 1



4 **5**

Chart 2

We previously reported the intramolecular cyclization of formylated β-ethoxycarbonylallylsilanes (**4**; X = $SiMe_3$, $n=5$ and 6) giving excellent yields of α-methylene-γ-lactones fused to five- and six-membered carbocyclic rings.[14)] This method was applied to the synthesis of α-methylene-γ-lactones fused to medium or large carbocyclic rings, but gave less satisfactory results.[15)]

Some reports have appeared on the intramolecular cyclization of formylated β-alkoxycarbonylallyl bromides (**4**; X = Br) using chromium(II) reagent[10)] or zinc dust,[16)] affording the respective α-methylene-γ-lactones fused to a six- or seven-membered carbocyclic ring. However, there is no report about the synthesis of α-methylene-γ-lactones fused to medium- or large-sized carbocyclic rings using intramolecular cyclization of β-alkoxycarbonylallyl halides. Okuda *et al.*[10)] reported an intramolecular cyclization of methyl 2-bromomethyl-7-formyl-hept-2(*Z*)-enoate by use of a low-valent chromium reagent ($CrCl_3$–$LiAlH_4$) giving an α-methylene-γ-lactone fused to a six membered carbocyclic ring.

We wish to report a further application of this method for the synthesis of medium and large (8-, 10-, 12- and 14-membered) carbocyclic rings fused to an α-methylene-γ-lactone unit by intramolecular cyclization of formylated β-methoxycarbonylallyl halides (**4**: X = Br or Cl).

Synthesis of the Formylated Allyl Bromides (4a—d) The formylated allyl halides (**4a—d**) were synthesized from ω-tetrahydropyranyloxy alkanols (**6**)[14)] *via* seven steps by a procedure similar to that reported by Semmelhack and Wu.[16)] The yields are summarized in Table II. The Swern oxidation[17)] of the alkanols (**6**), derived from glycols,[18)] gave aldehydes (**8**). The aldehydes were treated with the dilithium salt of methyl 3-hydroxypropionate[19)] to give a

TABLE I. Intramolecular Cyclization of Formylated Allyl Halide or Allylsilane (**4**) into α-Methylene-γ-lactones Fused to an *n*-Membered Carbocyclic Ring System (**5**)

Entry	X in **4**	*n*	Reagent
1	Br	6	$CrCl_3$–$LiAlH_4$[8)]
2	Br	7	Zn dust[14)]
3	Me_3Si	5, 6	$TiCl_4$[12)]

mixture of diastereoisomers of the diols (**9**), which were treated with *p*-toluenesulfonyl chloride (1.2 mol eq), giving the sulfonate esters (**10**) in good yields. Elimination of *p*-toluenesulfonic acid by the use of 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) in ether afforded allylic alcohols (**11**). Bromination of the allylic alcohols (**11**) with *N*-bromosuccinimide (NBS) and methyl sulfide in dichloromethane proceeded with stereospecific allylic rearrangement to the *Z* configuration of the double bond[16,20,21] (in the proton nuclear magnetic resonance (^{1}H-NMR) spectra, olefinic proton signals appeared at about δ 6.9) and spontaneous removal of the tetrahydropyranyl (THP) protecting group afforded allyl bromides (**13a—d**) in good yields. Allyl chloride (**13g**) was also obtained from allyl alcohol (**11c**) by the use of *N*-chlorosuccinimide (NCS) and methyl sulfide. The Swern oxidation of the allyl halides afforded formylated allyl halides (**4a—d**) in good yields. When the Swern oxidation of the allyl bromide (**13b**) was carried out above -60 °C after addition of triethylamine, the allyl chloride (**4f**) was considerably obtained instead of the allyl bromide (**4b**),[22] as shown in Table III.

Intramolecular Cyclization of the Formylated Allyl Halides (4a—e and g) Okuda *et al.*[10] reported the intramolecular cyclization of ethyl 2-bromomethyl-7-formyl

Table II. Synthesis of Formylated Allyl Halides (**4**)

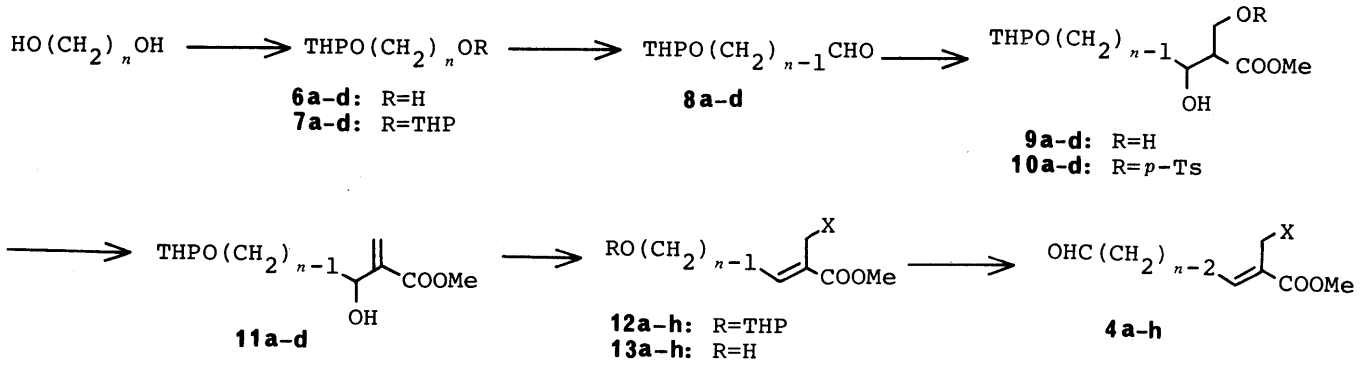
Mono-ol	*n*	Product yield (%)					
		8	**9**	**10**	**11**	**13**	**4**
6a	8	91	61	60	88	62	79
6b	10	Quant	79	84	Quant	79	94
6c	12	Quant	81	80	88	43[a]	70
6g	12					74	86
6d	14	Quant	79	77	90	76	82

a) When the protecting group of **12** was removed, the starting material (**12**) was recovered in 27% yield.

Table III. Swern Oxidation of the Allyl Bromide (**13b**)

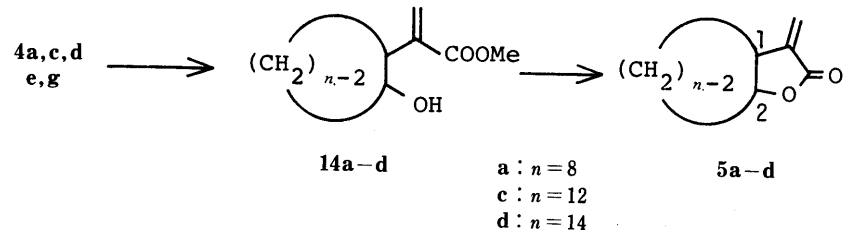
Entry	Reaction condition		Product yield (%)	
	Temp (°C)[a]	Time (min)[a]	**4b**	**4f**
1	-60— -40[b]	60	36	36
2	-60— r.t.[b]	20	48	12
3	-60	30	94	0

a) After addition of triethylamine. *b*) The temperature was gradually allowed to rise from -60 °C to the indicated temperature. r.t., room temperature.



4—**13**: **a**, **e**, $n=8$; **b**, **f**, $n=10$; **c**, **g**, $n=12$; **d**, **h**, $n=14$; **4**, **12**, **13**: **a**—**d**, X=Br; **e**—**h**, X=Cl

Chart 3



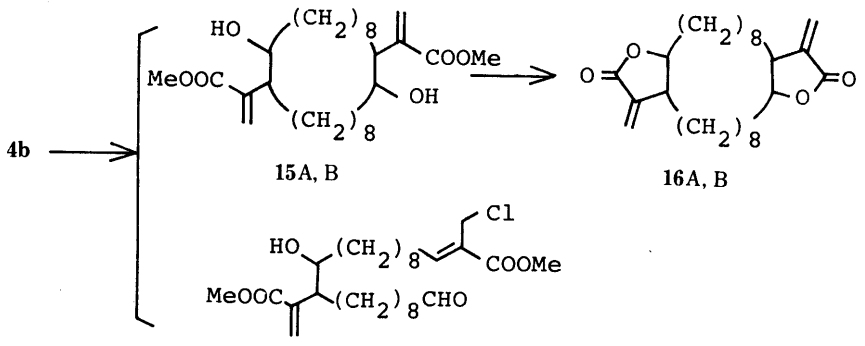


Chart 4

heptanoate in tetrahydrofuran (THF) by using 5 eq of chromium(II) reagent prepared from chromium(III) chloride and lithium aluminum hydride (2:1), giving the *cis*-fused lactone (**5**: $n=6$) in 55% yield.

The cyclization reactions of the formylated allyl bromides (**4a—d**) were examined by the method described above. The reaction proceeded more smoothly and clearly in *N,N*-dimethylformamide (DMF) than THF. The allyl halides (**4a—g**) were treated with 5 eq of chromium(II) reagent in anhydrous DMF at room temperature, giving the γ-hydroxyl esters (**14, 15**) or γ-lactones (**5, 16**).

Formylated allyl bromide (**4d**) in DMF (0.02 M concentration) was treated with chromium(II) reagent for 1 h to give the γ-hydroxy ester (**14d**) as an oil in 59% yield. The γ-hydroxy ester (**14d**) was treated with *p*-toluenesulfonic acid at reflux temperature in benzene to give the lactone (**5d**) as colorless crystals, mp 68—70 °C, in 78% yield. The lactone (**5d**) showed a characteristic absorption band at 1765 cm^{-1} in its infrared (IR) spectrum and two doublet signals assigned to exocyclic olefinic protons at δ 5.48 (d, $J=3.0$ Hz) and 6.18 (d, $J=3.0$ Hz) in its ^{1}H-NMR spectrum, indicating the presence of an α-methylene-γ-lactone moiety. Double resonance experiments with the lactone (**5d**) as shown in Table V confirmed that the C-1 methine proton [δ 2.97 (1H, qt, $J=7.3$, 3.0 Hz)] was coupled to the C-2 methine proton [δ 4.51 (1H, td, $J=7.3$, 5.1 Hz)] and

TABLE IV. Cyclization Reaction of Formylated Allylhalides (**4**) by Means of Chromium (II) Reagent in DMF[a]

Entry	Substrate (n, X)	Reaction conditions		Products (yield, %)	
		Conc. (mol/l)	Time (h)	Halide	Cyclic compd.
1	**4a** (8, Br)	0.002	44	**4e** (75)	
2		0.005	7	**4e** (78)	
3		0.005	45	**4e** (8)	**5a** (24)
4	**4e** (8, Cl)	0.005	24	**4e** (32)	**5a** (19)
5	**4b** (10, Br)	0.002	27	**4f** (20)	**17** (11)
6		0.02	3		**15** (64)[b]
7	**4c** (12, Br)	0.005	19	**4g** (24)	**14c** (72)
8	**4g** (12, Cl)	0.005	19	**4g** (5)	**14c** (24), **5c** (31)
9	**4d** (14, Br)	0.003	21	**4h** (95)	
10		0.02	1		**14d** (59)

a) All reactions were carried out at room temperature under an argon atmosphere. *b*) The yield is calculated as a mixture of stereoisomers (**15A** and **B**).

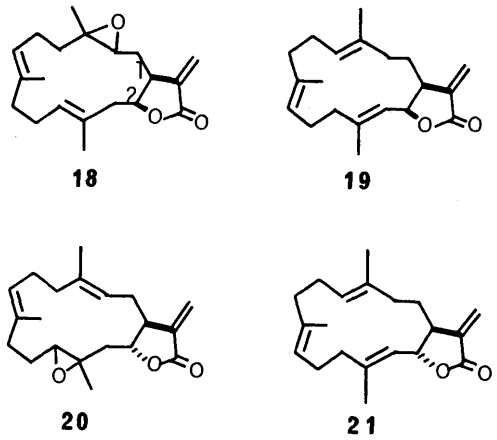


Chart 5

TABLE V. ^{1}H-NMR Data for the Lactones (**5a**, **c**, **d** and **16A**, **B**) and Double Resonance Experimental Results at 500 MHz in $CDCl_3$

Lactone	Chemical shift δ (ppm) (J=Hz)						Coupling constant J_{1-2}
	Exocyclic CH_2		C-2H	C-1H	C-3H		
5a	6.25	5.54	4,72	3.01			
	(d, 3.0)	(d, 3.0)	(ddd, 10.5, 8.0, 1.5)	(ddt, 10.5, 8.0, 3.0)			8.0 Hz
	s	s	(br d, 10.0)	irr			
	—	—	irr	m			
5c	6.15	5.48	4.54	2.96	1.76		
	(d, 2.5)	(d, 2.5)	(q, 6.5)	(ddt, 12.0, 6.5, 2.5)	(dq, 13.0, 6.5)		6.5 Hz
	—	—	(t, 6.5)	—	irr		
	s	s	(t, 6.5)	irr	—		
	—	—	irr	m	(dt, 13.0, 6.5)		
5d	6.18	5.48	4.51	2.97	1.68	1.38	
	(d, 3.0)	(d, 3.0)	(td, 7.3, 5.1)	(qt, 7.3, 3.0)	m	m	7.3 Hz
	—	—	(dd, 7.3, 5.1)	—	irr		
	—	—	(t, 7.3)	—		irr	
	s	s	(dd, 7.3, 5.7)	irr	—	—	
	—	—	irr	(tt, 7.3, 3.0)	—		
	—	irr	—	(qd, 7.3, 3.0)	—	—	
	irr	—	—	(qd, 7.3, 3.0)			
16A	6.205	5.495	4.55	3.00			
	(d, 2.0)	(d, 2.0)	(m)	(m)			
	6.200	5.480					
	(d, 2.0)	(d, 2.0)					
	s, s	s, s	(br d, 8.0)	irr			
	—	—	irr	m			
16B	6.205	5.508	4.49	2.94			
	(d, 2.5)	(d, *ca.* 1.0)	(m)	(m)			
	s	s	(br d, 8.0)	irr			
	—	—	irr	m			

irr: double resonance irradiation. —: no change in splitting pattern.

exocyclic methylene protons. The coupling constants between the protons adjacent to the ring fusion in **5d** ($J_{1,2}$ = 7.3 Hz) more closely resembled the corresponding values reported for *cis*-fused cembranolides [(**18**)[23] ($J_{1,2}$ = 7.0 Hz), (**19**)[24] ($J_{1,2}$ = 7.5 Hz)] than for *trans*-fused cembranolides [lobophytolide (**20**)[25] ($J_{1,2}$ = 5 Hz), (**21**)[23] ($J_{1,2}$ = 3.5 Hz)]. The α-methylene-γ-lactone fused to a fourteen membered carbocyclic ring (**5d**) was thus tentatively assigned the *cis* ring fusion.

Intramolecular cyclization of the formylated allyl bromide (**4c**) by means of chromium(II) reagent gave a hydroxyl ester (**14c**) in 72% yield together with the formylated allyl chloride (**4g**) in 24% yield. The hydroxy ester (**14c**) was treated with *p*-toluenesulfonic acid to afford an α-methylene-γ-lactone fused to twelve-membered carbocyclic ring (**5c**), mp 53—54 °C, as colorless needles in 78% yield. The structure of the γ-lactone (**5c**) was supported by its mass spectrum (MS) (*m/z* 236, M^+), IR (1760, 1660 cm^{-1}) and ^{1}H-NMR [δ 2.96 (ddt, *J* = 12.0, 6.5, 2.5 Hz, 1-H), 4.54 (q, *J* = 6.5 Hz, 2-H), 5.48 and 6.15 (each 1H, d, *J* = 2.5 Hz, 16-H)] spectra. However, the configuration of the ring fusion could not be clearly determined from the coupling constants between protons adjacent to the ring fusion ($J_{1,2}$ = 6.5 Hz). When the formylated allyl chloride (**4g**) was used for the cyclization reaction instead of the allyl bromide (**4c**), the hydroxy ester (**14c**) and the lactone (**5c**) were obtained in 24% and 31% yields, respectively.

Reaction of the formylated allyl bromide (**4a**) (0.005 M concentration) with chromium(II) reagent for 7 h gave the allyl chloride (**4e**) in 78% yield. The same reaction carried out for 45 h gave a 24% yield of the γ-lactone (**5a**) and an 8% yield of the allyl chloride (**4e**). Treatment of the formylated allyl chloride (**4e**) with chromium(II) reagent for 24 h afforded the γ-lactone (**5a**) and the allyl chloride (**4e**) in 19% and 32% yields, respectively. The structure of the lactone (**5a**) was supported by its MS (*m/z* 180, M^+), IR (1770, 1660 cm^{-1}) and ^{1}H-NMR [δ 3.01 (ddt, *J* = 10.5, 8.0, 3.0 Hz; 1-H), 4.72 (ddd, *J* = 10.5, 8.0, 1.5 Hz; 2-H), 5.54 and 6.25 (d, *J* = 3.0 Hz, exocyclic CH_2)] spectra. However, the configuration of the lactone fusion could not be determined.

The formylated allyl bromide (**4b**) at 0.02 M concentration was treated with chromium(II) reagent for 1 h to afford the hydroxy esters (**15A**) and (**15B**) as oil in 29% and 35% yields, respectively. These hydroxy esters (**15A** and **B**) were expected to have dimeric structures from their mass spectral data (**15A**: 416 ($M^+ - 2MeOH$), 391, 280, 279; **14B**: 480 (M^+), 416, 321, 284, 256). Lactonization of these hydroxy esters was performed by the use of *p*-toluenesulfonic acid giving the lactones (**16A**: mp 120—121 °C; and **16B**: oil). The lactone (**16A**) was determined to be a dimer having two α-methylene-γ-lactone moieties and a twenty-membered carbocyclic ring system by means of its high-resolution mass ($C_{26}H_{40}O_4$: M^+ 416.2923), IR (1765, 1660 cm^{-1}) and ^{1}H-NMR [δ 5.480 and 5.495 (each d, *J* = 2.0 Hz), 6.200 and 6.205 (each d, *J* = 2.0 Hz)] spectra. The spectral data of the lactone (**16B**) [MS *m/z*: 284, 279, 223, 205, 149; IR 1770, 1660 cm^{-1}; ^{1}H-NMR δ 5.508 (d, *J* = 1.0 Hz), 6.205 (d, *J* = 2.5 Hz)] also suggested the dimeric structure **16B**. The configuration of the ring fusion has not yet been established. The cyclization reaction of the allyl bromide (**4b**) was carried out at 0.002 M concentration giving the allyl chloride (**4f**) in 20% yield and the aldehyde (**17**) in 11% yield. The aldehyde was tentatively determined to be the acyclic dimer (**17**) from its spectral data.

Conclusion

The results of the cyclization reaction of ω-formylated allyl halides (**4a**—**e** and **g**) by the use of chromium(II) reagent in DMF are summarized in Table IV. Intramolecular cyclization to large (twelve- and fourteen-membered) ring systems gave good yield and stereoselectivity. The reaction failed to give the expected ten-membered ring system but formed dimeric lactones having a twenty-membered carbocyclic ring system even at a very low concentration (0.002 M). The rate of the reaction depended on the concentration of the reagent or substrate. The cyclization reaction of the formylated allyl bromides at a low concentration (0.002 M) or for a short reaction time gave mainly the allyl chlorides (**4e**—**h**). The bromine atom of the allyl bromides (**4a**—**d**) was easily displaced by a chlorine atom under these reaction conditions.

Further synthetic applications and the limitations of this method are currently being investigated in our laboratory.

Experimental

All melting points were measured with a Yanaco hot-stage micro melting point apparatus and are uncorrected. ^{1}H-NMR spectra were recorded on a JEOL FX-100 (100 MHz) or on a GSX-500 (500 MHz) spectrometer. All NMR spectra were recorded in $CDCl_3$ and are reported in parts per million (ppm) relative to tetramethylsilane (TMS) (δ = 0.0), or $CHCl_3$ (δ = 7.26) unless otherwise noted. IR spectra were run on a Hitachi 215 spectrophotometer. Ultraviolet (UV) spectra were obtained on a Hitachi 200-10 spectrophotometer using ethanol as a solvent. MS were recorded at 70 eV on a D-300 (low resolution) or on a Hitachi M-80 (high resolution) spectrometer using a direct inlet system. Fuji-Davison Silica gel BW-127ZH (100—270 mesh) containing 2% fluorescence indicator F_{254} was used for column chromatography with a quartz column. Preparative thin-layer chromatography (TLC) was carried out using Merck Silica gel HF_{254}.

8-Tetrahydropyranyloxyoctanol (6a) 1,8-Octanediol (22.0 g, 0.15 mol) was dissolved in THF (200 ml) followed by addition of CH_2Cl_2 (100 ml). 2,3-Dihydropyran (15.1 ml, 0.17 mol) and pyridinium *p*-toluenesulfonate (PPTS) (4.0 g, 0.015 mol) were added to this solution. The mixture was stirred for 4 h, and then washed with water and brine, and dried over anhydrous Na_2SO_4. Concentration gave a residue that was washed with CH_2Cl_2 on a filter paper with suction. The starting diol (820 mg) was obtained on the filter paper. The filtrate was subjected to column chromatography, affording 1,8-bistetrahydropyranyloxyoctane (**7a**) (11.4 g, 24.3%) as an oil, the title compound (**6a**) (19.1 g, 55.5%) as an oil and the starting diol (4.70 g) as a colorless solid from the 20% EtOAc/hexane, 40% EtOAc/hexane and EtOAc eluates, respectively. Data for **6a**: IR (neat) cm^{-1}: 3450, 1120. ^{1}H-NMR δ: 1.04—2.00 (18H, m), 3.24—4.00 (7H, m), 4.55 (1H, br s). MS *m/z* (relative intensity): 230 (M^+, <1), 229 (2), 101 (20), 85 (100). High-resolution MS Calcd for $C_{13}H_{26}O_3$ (M^+) *m/z*: 230.1880. Found *m/z*: 230.1861. Data for **7a**: IR (neat) cm^{-1}: 1120. ^{1}H-NMR δ: 1.00—2.00 (24H, m), 3.00—4.04 (8H, m), 4.55 (2H, br s). MS *m/z* (relative intensity): 314 (M^+, <1), 101 (15), 85 (100). High-resolution MS Calcd for $C_{18}H_{34}O_4$ (M^+) *m/z*: 314.2455. Found *m/z*: 314.2465.

10-Tetrahydropyranyloxydecanol (6b) 1,10-Decanediol (15.5 g, 90 mmol) was treated with dihydropyran (8.1 ml, 90 mmol) and PPTS (2.4 g, 9.0 mmol) in THF (170 ml) and CH_2Cl_2 (65 ml) for 4 h. Work-up as above afforded **6b** (12.6 g, 55.0%), 1,10-bistetrahydropyranyloxydecane (**7b**) (3.7 g, 12.0%) and the starting diol (5.6 g). Data for **6b**: Oil, IR (neat) cm^{-1}: 3400, 1120. ^{1}H-NMR δ: 1.00—2.00 (23H, m), 3.20—4.00 (6H, m), 4.55 (1H, br s). MS *m/z* (relative intensity): 258 (M^+, 0.1), 257 (1), 240 (0.4), 173 (0.5), 101 (20), 85 (100). High-resolution MS Calcd for $C_{15}H_{30}O_3$ (M^+) *m/z*: 258.2192. Found *m/z*: 258.2169. Data for **7b**: Oil, IR (neat) cm^{-1}: 1120. ^{1}H-NMR δ: 1.00—2.00 (28H, m), 3.20—4.00 (8H, m), 4.55 (2H, br s). MS *m/z* (relative intensity): 342 (M^+, 0.7), 341 (0.4), 257 (12), 101 (19), 85 (100). High-resolution MS Calcd for $C_{20}H_{38}O_4$ (M^+) *m/z*: 342.2767. Found *m/z*: 342.2761.

12-Tetrahydropyranyloxydodecanol (6c) 1,12-Dodecanediol (20.2 g, 0.1 mol) was treated with dihydropyran (10 ml, 0.11 mol) and PPTS (2.7 g, 0.01 mol) in THF (400 ml) and CH_2Cl_2 (100 ml) for 5 h. Work-up as above afforded **6c** (15.2 g, 53.0%), 1,12-bistetrahydropyranyloxydodecane (**7c**) (9.8 g, 26.4%) and the starting diol (3.3 g). Data for **6c**: Oil, IR (neat) cm^{-1}: 3420, 1120. ^{1}H-NMR δ: 1.04—1.96 (27H, m), 3.24—4.00 (6H, m), 4.55 (1H, br s). MS *m/z* (relative intensity): 286 (M^+, 0.3), 285 (1.4), 268 (0.3), 201 (1), 101 (31), 85 (100). High-resolution MS Calcd for $C_{17}H_{34}O_3$ (M^+) *m/z*: 286.2506. Found *m/z*: 286.2477. Data for **7c**: IR (neat) cm^{-1}: 1120. ^{1}H-NMR δ: 1.00—1.96 (32H, m), 3.20—4.00 (8H, m), 4.55 (2H, br s). MS *m/z* (relative intensity): 370 (M^+, 0.6), 285 (12), 101 (22), 85 (100). High-resolution MS Calcd for $C_{22}H_{42}O_4$ (M^+) *m/z*: 370.3080. Found *m/z*: 370.3080.

14-Tetrahydropyranyloxytetradecanol (6d) 1,14-Tetradecane diol[18] (2.5 g, 11 mmol) was treated with dihydropyrane (1.0 ml, 11 mmol) and PPTS (296 mg, 1.1 mmol) in THF (65 ml) and CH_2Cl_2 (65 ml) for 5 h. Work-up as described above afforded **6d** (1.7 g, 50.3%), 1,14-bistetrahydropyranyloxytetradecane (**7d**) (503 mg, 11.5%) and the starting diol (955 mg). Data for **6d**: Oil, IR (neat) cm^{-1}: 3400, 1120. ^{1}H-NMR δ: 1.00—1.96 (31H, m), 3.22—4.00 (6H, m), 4.55 (1H, br s). MS *m/z* (relative intensity): 314 (M^+, 0.8), 313 (2), 229 (4), 101 (35), 85 (100). High-resolution MS Calcd for $C_{19}H_{38}O_3$ (M^+) *m/z*: 314.2819. Found *m/z*: 314.2815. Data for **7d**: Oil, IR (neat) cm^{-1}: 1120. ^{1}H-NMR δ: 1.00—1.96 (36H, m), 3.22—4.14 (8H, m), 4.55 (2H, br s). MS *m/z* (relative intensity): 398 (M^+, 0.6), 397 (0.3), 313 (8), 101 (25), 85 (100). High-resolution MS Calcd for $C_{24}H_{46}O_4$ (M^+) *m/z*: 398.3392. Found *m/z*: 398.3370.

Formation of the Aldehyde (8) by the Swern Oxidation of the Alcohol (6); General Procedure Dimethyl sulfoxide (DMSO) (2.2 eq) was added to a solution of oxalyl chloride (1.3 eq) in dry CH_2Cl_2 at −60 °C. The mixture was stirred for 2 min and the alcohol (**6**) was added; stirring was continued for an additional 5 min. Triethylamine (5 eq) was added and the reaction mixture was stirred at −60—−30 °C for 1 h. Water was then added and the aqueous layer was reextracted with additional CH_2Cl_2. The organic layers were combined, washed with brine, and dried (anhydrous Na_2SO_4). The solvent was removed *in vacuo* to give the crude aldehyde, which was purified by column chromatography (10% EtOAc/hexane) to give the pure aldehyde.

Preparation of 8-Tetrahydropyranyloxyoctanal (8a) Reaction of **6a** (5.75 g, 25 mmol) by the general procedure described above afforded **8a** (5.10 g, 90.6%) as an oil. IR (neat) cm^{-1}: 1735, 1120. ^{1}H-NMR δ: 1.08—2.00 (16H, m), 2.2 (2H, td, J=7, 2 Hz), 3.20—4.00 (4H, m), 4.55 (1H, br s), 9.73 (1H, t, J=2 Hz, CHO). MS *m/z* (relative intensity): 228 (M^+, 0.2), 227 (1), 109 (15), 101 (20), 85 (100). High-resolution MS Calcd for $C_{13}H_{24}O_3$ (M^+) *m/z*: 228.1723. Found *m/z*: 228.1716.

Preparation of 10-Tetrahydropyranyloxydecanal (8b) Reaction of **6b** (3.1 g, 12 mmol) by the general procedure described above afforded **8b** (quant.) as an oil: IR (neat) cm^{-1}: 1730, 1120. ^{1}H-NMR δ: 1.04—1.96 (20H, m), 2.22 (2H, td, J=7, 2 Hz), 3.20—4.00 (4H, m), 4.55 (1H, br s), 9.72 (1H, t, J=2 Hz, CHO). MS *m/z* (relative intensity): 256 (M^+, 1), 255 (2), 101 (26), 85 (100). High resolution MS Calcd for $C_{15}H_{28}O_3$ (M^+) *m/z*: 256.2037. Found *m/z*: 256.2055.

Preparation of 12-Tetrahydropyranyloxydodecanal (8c) Reaction of **6c** (5.7 g, 20 mmol) by the general procedure described above afforded **8c** (quant.) as an oil. IR (neat) cm^{-1}: 1735, 1120. ^{1}H-NMR δ: 1.04—1.92 (24H, m), 2.41 (2H, td, J=7, 2 Hz), 3.20—4.00 (4H, m), 4.55 (1H, br s), 9.73 (1H, t, J=2 Hz, CHO). MS *m/z* (relative intensity): 284 (M^+, 2), 283 (3), 101 (33), 85 (100). High-resolution MS Calcd for $C_{17}H_{32}O_3$ (M^+) *m/z*: 284.2349. Found *m/z*: 284.2345.

14-Tetrahydropyranyloxytetradecanal (8d) Reaction of **6d** (942 mg, 3 mmol) by the general procedure described above afforded **8d** (quant.) as an oil: IR (neat) cm^{-1}: 1735, 1120. ^{1}H-NMR δ: 1.00—1.96 (28H, m), 2.41 (2H, td, J=7, 2 Hz), 3.20—4.00 (4H, m), 4.55 (1H, br s), 9.72 (1H, t, J=2 Hz, CHO). MS *m/z* (relative intensity): 312 (M^+, 0.5), 311 (0.7), 227 (1), 101 (24), 85 (100). High-resolution MS Calcd for $C_{19}H_{36}O_3$ (M^+) *m/z*: 312.2663. Found *m/z*: 312.2665.

Reaction of the Aldehyde (8) with Methyl β-Hydroxylpropionate; General Procedure Methyl β-hydroxypropionate (1.2 eq) was treated with 2.2 eq of lithium diisopropylamide (LDA) [prepared from diisopropylamine and 1.5 M *n*-BuLi hexane solution] in THF (40—100 ml) at −78 °C for 40 min. A THF (4—10 ml) solution of the aldehyde (**8**) (4—10 mmol) was added to the resulting mixture. After stirring of the reaction mixture for an additional 10 min, saturated NH_4Cl solution was added. The whole was extracted with ether, and the extracts were washed with brine, dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was subjected to column chromatography using 50% EtOAc/hexane. The first eluate gave the starting aldehyde (**8**), and the second gave the adduct (**9**).

Methyl 3-Hydroxy-2-hydroxymethyl-10-tetrahydropyranyloxydecanoate (9a) Reaction of methyl β-hydroxypropionate (1.25 g, 12 mmol) and **8a** (2.56 g, 10 mmol) by the general procedure described above afforded diol (**9a**) (2.0 g, 61%) as an oil together with the starting aldehyde (895 mg, 39%). Data for **9a**: IR (neat) cm^{-1}: 3450, 1740, 1120. ^{1}H-NMR δ: 1.04—2.00 (18H, m), 2.44—2.76 (1H, m), 2.76—3.08 (2H, OH), 3.20—4.24 (7H, m), 3.74, 3.75 (3H, s, OMe), 4.54 (1H, br s). MS *m/z* (relative intensity): 331 (M^+-1, <1), 314 ($M-18$, <1), 229 (1), 133 (17), 104 (29), 85 (100).

Methyl 3-Hydroxy-2-hydroxymethyl-12-tetrahydropyranyloxydodecanoate (9b) Reaction of β-hydroxypropionate (1.25 g, 12 mmol) and **8b** (2.56 g, 10 mmol) by the general procedure described above afforded **9b** (2.80 g, 79%) as an oil. IR (neat) cm^{-1}: 3450, 1740, 1120. ^{1}H-NMR δ: 1.04—1.88 (22H, m), 2.44—2.76 (1H, m), 3.00 (2H, OH), 3.24—4.16 (7H, m), 3.72, 3.74 (3H, s), 4.56 (1H, br s). MS *m/z* (relative intensity): 360 (M^+, <1), 359 (<1), 257 (2), 245 (2), 228 (2), 133 (8), 104 (12), 85 (100). High-resolution MS Calcd for $C_{19}H_{36}O_6$ (M^+) *m/z*: 360.2509. Found *m/z*: 360.2495.

Methyl 3-Hydroxy-2-hydroxymethyl-14-tetrahydropyranyloxytetradecanoate (9c) Reaction of methyl β-hydroxypropionate (0.5 g, 4.8 mmol) and **8c** (1.1 g, 4.8 mmol) by the general procedure described above afforded diol (**9c**) (1.3 g, 81%) as an oil together with the starting aldehyde (470 mg, 19%). Data for **9c**: IR (neat) cm^{-1}: 3400, 1740, 1120. ^{1}H-NMR δ: 1.00—1.92 (26H, m), 2.20—3.04 (3H, m), 3.74 (3H, s, OMe), 3.20—4.22 (7H, m), 4.54 (1H, br s). MS *m/z* (relative intensity): 387 (M^+-1, trace), 315 (0.02), 305 (0.05), 201 (3), 133 (17), 104 (25), 85 (100).

Methyl 3-Hydroxy-2-hydroxymethyl-16-tetrahydropyranyloxyhexadecanoate (9d) Reaction of methyl β-hydroxypropionate (705 mg, 6.8 mmol) and **8d** (1.76 g, 5.6 mmol) by the general procedure described above afforded the diol (**9d**) as an oil (1.85 g, 79%) together with the starting aldehyde (364 mg, 21%). Data for **9d**: IR (neat) cm^{-1}: 3400, 1730, 1120. ^{1}H-NMR δ: 1.04—1.92 (30H, m), 2.48—2.76 (1H, m), 2.85 (2H, OH), 3.24—4.20 (7H, m), 3.70, 3.74 (3H, s, OMe), 4.54 (1H, br s). MS *m/z* (relative intensity): 415 (M^+-1, <1), 229 (3), 133 (14), 104 (19), 85 (100).

***p*-Toluenesulfonylation of the Adduct (9); General Procedure** *p*-Toluenesulfonyl chloride (1.2—3.0 eq) was added to a pyridine solution of the diol (**9**). The solution was stirred for 3—6 h at room temperature, diluted with ether, washed with water and brine, and then dried. After evaporation of the solvent *in vacuo*, the residue was purified on a silica gel column using 50% EtOAc/hexane.

The *p*-Toluenesulfonate (10a) Reaction of **9a** (675 mg, 2.0 mmol) with *p*-toluenesulfonyl chloride (1.1 g, 6.0 mmol) in pyridine (20 ml) by the general procedure as described above afforded **10a** (900 mg, 93%) together with the starting diol (40 mg, 6%). Data for **10a**: IR (neat) cm^{-1}: 3500, 1745, 1605, 1370, 1180, 1120. ^{1}H-NMR δ: 1.00—1.96 (19H, m), 2.45 (3H, s), 2.60—2.94 (1H, m), 3.20—4.00 (5H, m), 3.78, 3.79 (3H, s), 4.20—4.40 (2H, m), 4.55 (1H, br s), 7.32, 7.76 (each 2H, d, J=8 Hz, aromatic H). MS *m/z* (relative intensity): 279 (0.1), 84 (75), 55 (100).

The *p*-Toluenesulfonate (10b) Reaction of **9b** (1.50 g, 4.2 mmol) with *p*-toluenesulfonyl chloride (960 mg, 50.3 mmol) in pyridine (6 ml) by the general procedure as described above afforded **10b** (1.82 g, 84.4%) as an oil. IR (neat) cm^{-1}: 3500, 1740, 1600, 1370, 1180, 1120. ^{1}H-NMR δ: 1.00—1.96 (23H, m), 2.44 (3H, s), 2.64—2.94 (1H, m), 3.20—4.00 (5H, m), 3.66, 3.68 (3H, s), 4.24—4.40 (2H, m), 4.56 (1H, br s), 7.32, 7.76 (each 2H, d, J=8 Hz, aromatic H). MS *m/z* (relative intensity): 344 (0.2), 330 (0.4), 312 (0.3), 157 (9), 141 (5), 115 (10), 91 (21), 84 (77), 55 (100).

The *p*-Toluenesulfonate (10c) Reaction of **9c** (3.50 g, 9.0 mmol) with *p*-toluenesulfonyl chloride (2.60 g, 13.5 mmol) in pyridine (50 ml) by the general procedure as described above afforded **10c** (3.90 g, 79.9%) as an oil together with the starting diol (713 mg, 20.4%). Data for **10c**: IR (neat) cm^{-1}: 3500, 1745, 1610, 1370, 1180, 1120. ^{1}H-NMR δ: 1.00—1.96 (27H, m), 2.45 (3H, s), 2.56—2.94 (1H, m), 3.20—4.00 (5H, m), 3.66, 3.67 (3H, s, OMe), 4.20—4.40 (2H, m), 4.55 (1H, br s), 7.32, 7.75 (each 2H, d, J=8 Hz, aromatic H). MS *m/z* (relative intensity): 458 (0.8), 236 (2.9), 172 (56), 155 (21), 115 (100), 91 (48), 87 (70).

The *p*-Toluenesulfonate (10d) Reaction of **9d** (2.50 g, 6.0 mmol) with *p*-toluenesulfonyl chloride (1.50 g, 7.8 mmol) in pyridine (10 ml) by the general procedure as described above afforded **10d** (2.60 g, 76.6%) together with the starting diol (215 mg, 8.6%) as an oil. Data for **10d**: IR (neat) cm^{-1}: 3500, 1740, 1605, 1370, 1180, 1120. ^{1}H-NMR δ: 1.08—1.96 (31H, m), 2.45 (3H, s), 2.60—2.94 (1H, m), 3.24—4.00 (5H, m), 3.77, 3.78 (3H, s, OMe), 4.20—4.40 (2H, m), 4.55 (1H, br s), 7.32, 7.76 (each 2H, d, J=8 Hz, aromatic H). MS *m/z* (relative intensity): 258 (22), 155 (46), 103 (88), 91 (100).

Conversion of the *p*-Toluenesulfonate (10) into the α,β-Unsaturated Ester

(11); General Procedure An ethereal solution of *p*-toluenesulfonate (**10**) was treated with 1.2 eq of DBU. The resulting mixture was stirred at room temperature for 1 h. After addition of water, it was extracted with ether. The extracts were washed with brine and dried over $MgSO_4$. Removal of the solvent gave a crude product, which was purified by column chromatography using 20% EtOAc/hexane as an eluent.

Methyl 3-Hydroxy-2-methylene-10-tetrahydropyranyloxydecanoate (11a) The *p*-toluenesulfonate (**10a**) (822 mg, 1.69 mmol) was treated with DBU (0.3 ml, 2.0 mmol) in ether (17 ml) by the general procedure to afford **11a** (465 mg, 87.5%) as an oil. IR (neat) cm^{-1}: 3470, 1725, 1640, 1120. ^{1}H-NMR δ: 1.04—1.92 (18H, m), 2.44—2.68 (1H, OH), 3.20—4.00 (4H, m), 3.77 (3H, s), 4.24—4.48 (1H, m), 4.55 (1H, br s), 5.77 (1H, t, J=1 Hz), 6.20 (1H, d, J=1 Hz). MS m/z (relative intensity): 313 (M^+-1, 0.1), 299 (1.1), 163 (3), 135 (9), 115 (95), 85 (100).

Methyl 3-Hydroxy-2-methylene-12-tetrahydropyranyloxydodecanoate (11b) The *p*-toluenesulfonate (**10b**) (1.88 g, 3.7 mmol) was treated with DBU (0.68 ml, 4.5 mmol) in ether (25 ml) by the general procedure to afford **11b** (1.28 g, quant.) as an oil. IR (neat) cm^{-1}: 3450, 1720, 1640, 1120. ^{1}H-NMR δ: 1.08—1.88 (22H, m), 2.58 (1H, d, J=6 Hz, OH), 3.24—3.96 (4H, m), 3.76 (3H, s, OMe), 4.36 (1H, q, J=6 Hz), 4.54 (1H, br s), 5.76 (1H, t, J=1 Hz), 6.18 (1H, d, J=1 Hz). MS m/z (relative intensity): 341 (M^+-1, 0.1), 327 (1), 310 (2), 163 (5), 115 (46), 85 (100).

Methyl 3-Hydroxy-2-methylene-14-tetrahydropyranyloxytetradecanoate (11c) The *p*-toluenesulfonate (**10c**) (930 mg, 1.7 mmol) was treated with DBU (0.47 ml, 3.4 mmol) in ether (10 ml) by the general procedure to afford **11c** (556 mg, 88.2%) as an oil. IR (neat) cm^{-1}: 3450, 1720, 1635, 1120. ^{1}H-NMR δ: 1.04—1.92 (26H, m), 2.67 (1H, d, J=7 Hz, OH), 3.20—4.00 (4H, m), 3.76 (3H, s, OMe), 4.36 (1H, q, J=7 Hz), 4.55 (1H, br s), 5.76 (1H, t, J=1 Hz), 6.19 (1H, d, J=1 Hz). MS m/z (relative intensity): 355 (M^+ − Me, 3), 338 (14), 320 (6), 115 (43), 85 (100).

Methyl 3-Hydroxy-2-methylene-16-tetrahydropyranyloxyhexadecanoate (11d) The *p*-toluenesulfonate (**10d**) (2.6 g, 4.6 mmol) was treated with DBU (0.82 ml, 5.5 mmol) in ether (25 ml) by the general procedure to afford **11d** (1.40 g, 78.5%) as an oil. IR (neat) cm^{-1}: 3400, 1720, 1635, 1120. ^{1}H-NMR δ: 1.12—1.86 (30H, m), 2.60 (1H, d, J=7 Hz, OH), 3.24—4.00 (4H, m), 3.77 (3H, s, OMe), 4.36 (1H, m), 4.56 (1H, br s), 5.76 (1H, t, J=1 Hz), 6.20 (1H, d, J=1 Hz). MS m/z (relative intensity): 366 (0.2), 348 (0.2), 115 (100).

Bromination of the α,β-Unsaturated Esters (11); General Procedure Dimethyl sulfide (1.2 eq) was added to a CH_2Cl_2 solution of NBS (1.0 eq) at 0 °C. The mixture was stirred for 10 min, and then a CH_2Cl_2 solution of an alcohol (**11**) was added. The reaction mixture was stirred for 20 h, and extracted with ether. The extract was washed with water, brine and dried. Evaporation of the solvent gave a crude oil, which was chromatographed on a silica gel column. The first eluate with 20% EtOAc/hexane gave the bromide (**12**), the second with 30% EtOAc/hexane gave the starting alcohol (**11**), and the third with 40% EtOAc/hexane gave the bromo alcohol (**13**).

Bromination of the Alcohol (11a) Reaction of **11a** (965 mg, 3.1 mmol) with a mixture of NBS (965 mg, 3.1 mmol) and dimethyl sulfide (0.27 ml, 3.7 mmol) in CH_2Cl_2 (20 ml) as described in the general procedure afforded the bromide (**12a**) (853 mg, 73.0%) as an oil, the starting alcohol (84 mg, 8.7%) and methyl 2-bromomethyl-10-hydroxy-2(*Z*)-octenoate (**13a**) (77 mg, 8.4%) as an oil. Data for **12a**: UV λ_{max} nm (ε): 216 (10990). IR (neat) cm^{-1}: 1730, 1650, 1120. ^{1}H-NMR δ: 1.16—1.92 (16H, m), 2.28 (2H, q, J=7 Hz), 3.24—4.00 (4H, m), 3.79 (3H, s, OMe), 4.21 (2H, s), 4.54 (1H, br s), 6.95 (1H, t, J=7 Hz). MS m/z (relative intensity): 378, 376 (M^+, 0.1), 377, 375 (M^+-1, 0.3), 347 (0.05), 346 (0.1), 345 (0.2), 344 (0.1), 343 (0.2), 213 (5), 163 (5), 135 (11), 101 (17), 85 (100). Data for **13a**: UV λ_{max} nm (ε): 217 (10440). IR (neat) cm^{-1}: 3370, 1720, 1645. ^{1}H-NMR δ: 1.12—1.76 (11H, m), 2.29 (2H, q, J=7 Hz), 3.63 (2H, t, J=6 Hz), 3.79 (3H, s, OMe), 4.22 (2H, s), 6.95 (1H, t, J=8 Hz). MS m/z (relative intensity): 262, 260 (M^+ − MeOH, 2), 213 (M^+ − Br, 56), 181 (68), 163 (39), 135 (84), 107 (41), 93 (72), 79 (63), 67 (78), 55 (92), 41 (100).

Bromination of the Alcohol (11b) Reaction of **11b** (1.20 g, 3.5 mmol) with a mixture of NBS (694 mg, 3.9 mmol) and dimethyl sulfide (0.31 ml, 4.2 mmol) in CH_2Cl_2 (24 ml) as described in the general procedure afforded the bromide (**12b**) (1.08 g, 76.0%) as an oil, the starting alcohol (48 mg) and methyl 2-bromomethyl-12-hydroxy-2(*Z*)-dodecenoate (**13b**) (101 mg, 9.6%). Data for **12b**: UV λ_{max} nm (ε): 215 (11980). IR (neat) cm^{-1}: 1720, 1640, 1120. ^{1}H-NMR δ: 1.16—2.00 (20H, m), 2.16—2.40 (2H, q, J=7 Hz), 3.24—4.08 (4H, m), 3.79 (3H, s, OMe), 4.21 (2H, s), 4.54 (1H, br s), 6.94 (1H, t, J=7 Hz). MS m/z (relative intensity): 405, 403 (M^+-1, 0.2), 325 (M^+ − Br, 16), 324 (14), 163 (8), 101 (25), 85 (100). Data for **13b**: UV λ_{max} nm (ε): 217 (11770). IR (neat) cm^{-1}: 3350, 1720, 1640. ^{1}H-NMR δ: 1.20—1.72 (15H, m), 2.28 (2H, q, J=8 Hz), 3.63 (2H, t, J=7 Hz), 3.79 (3H, s, OMe), 4.22 (2H, s), 6.96 (1H, t, J=8 Hz). MS m/z (relative intensity): 292, 290 (M^+ − MeOH, 0.5), 241 (M^+ − Br, 37), 209 (M^+ − Br − MeOH, 31), 163 (47), 145 (12), 121 (26), 107 (33), 95 (65), 81 (81), 67 (67), 55 (95), 41 (100).

Bromination of the Alcohol (11c) Reaction of **11c** (2.6 g, 7.2 mmol) with a mixture of NBS (1.5 g, 8.7 mmol) and dimethyl sulfide (0.69 ml, 9.4 mmol) in CH_2Cl_2 (110 ml) as described above afforded the bromide (**12c**) (1.70 g, 55.1%), the starting alcohol (355 mg, 13.4%) and methyl 2-bromomethyl-14-hydroxy-2(*Z*)-tetradecenoate (**13c**) (547 mg, 21.8%). Data for **12c**: UV λ_{max} nm (ε): 215 (8850). IR (neat) cm^{-1}: 1730, 1650, 1120. ^{1}H-NMR δ: 1.00—1.92 (24H, m), 2.28 (2H, q, J=7 Hz), 3.16—4.08 (4H, m), 3.78 (3H, s, OMe), 4.21 (2H, s), 4.54 (1H, br s), 6.95 (1H, t, J=7 Hz). MS m/z (relative intensity): 434, 432 (M^+, 0.1), 433, 431 (M^+-1, 3, 4), 353 (M^+ − Br, 0.1), 352 (0.1), 269 (3), 191 (3), 101 (20), 85 (100). High-resolution MS Calcd for $C_{21}H_{37}O_4Br$ (M^+) m/z: 432.1873. Found m/z: 432.1851. Data for **13c**: UV λ_{max} nm (ε): 217 (10350). IR (neat) cm^{-1}: 3370, 1725, 1645. ^{1}H-NMR δ: 1.04—1.72 (19H, m), 2.29 (2H, q, J=7 Hz), 3.63 (2H, t, J=7 Hz), 3.79 (3H, s, OMe), 4.21 (2H, s), 6.96 (1H, t, J=7 Hz). MS m/z (relative intensity): 350, 348 (M^+, 1), 320 (15), 318 (18), 269 (M^+ − Br, 65), 237 (38), 219 (10), 191 (23), 149 (11), 135 (21), 121 (25), 109 (51), 95 (62), 81 (70), 55 (100). High-resolution MS Calcd for $C_{16}H_{29}O_3Br$ (M^+) m/z: 348.1299. Found m/z: 348.1308.

Bromination of the Alcohol (11d) Reaction of **11d** (1.44 g, 3.6 mmol) with a mixture of NBS (765 mg, 4.3 mmol) and dimethyl sulfide (0.31 ml, 4.3 mmol) in CH_2Cl_2 (40 ml) as described above afforded the bromide (**12d**) (1.20 g, 70.3%) as an oil and methyl 2-bromomethyl-16-hydroxy-2(*Z*)-hexadecenoate (**13d**) as an oil. Data for **12d**: UV λ_{max} nm (ε): 217 (11210). IR (neat) cm^{-1}: 1720, 1640, 1120. ^{1}H-NMR δ: 1.04—1.92 (28H, m), 2.28 (2H, m), 3.20—4.00 (4H, m), 3.79 (3H, s, OMe), 4.21 (2H, s), 4.55 (1H, br s), 6.96 (1H, t, J=8 Hz). MS m/z (relative intensity): 462, 460 (M^+, 0.8), 461, 459 (M^+-1, 1.2), 381 (M^+ − Br, 20), 297 (1), 101 (31), 85 (100). Data for **13d**: UV λ_{max} nm (ε): 218 (11000). IR (neat) cm^{-1}: 3350, 1730, 1645. ^{1}H-NMR δ: 1.16—1.72 (23H, m), 2.28 (2H, q, J=8 Hz), 3.63 (2H, t, J=7 Hz), 3.79 (3H, s, OMe), 4.21 (2H, s), 6.96 (1H, t, J=8 Hz). MS m/z (relative intensity): 378, 376 (M^+, 0.1), 360, 358 (M^+-H_2O, 0.1), 348, 346 (M^+ − MeOH, 0.1), 297 (M^+ − Br, 79), 265 (M^+ − Br − H_2O, 52), 247 (9), 149 (12), 123 (21), 109 (32), 95 (59), 81 (70), 69 (60), 55 (100).

Chlorination of the Alcohol (11c) Dimethyl sulfide (0.08 ml, 1.1 mmol) was added to a solution of NCS (130 mg, 1.0 mmol) in CH_2Cl_2 (3 ml) at 0 °C. The mixture was stirred for 10 min, then a CH_2Cl_2 solution of the alcohol (**11c**) (320 mg, 0.9 mmol) was added. The reaction mixture was stirred at room temperature for an additional 3 h and extracted with ether. The extracts were washed with brine and dried ($MgSO_4$). Evaporation of the solvent gave the crude chloride, which was subjected to column chromatography with 20% EtOAc/hexane. The first eluate gave the chloride (**12g**) (260 mg, 77.7%) as an oil, the second gave the starting alcohol (19 mg) and the third gave methyl 2-chloromethyl-14-hydroxy-2(*Z*)-tetradecenoate (**13g**) (24 mg, 7.9%) as an oil. Data for **12g**: UV λ_{max} nm (ε): 216 (10840). IR (neat) cm^{-1}: 1725, 1650, 1120, 780. ^{1}H-NMR δ: 1.04—1.92 (24H, m), 2.31 (2H, q, J=8 Hz), 3.22—4.00 (4H, m), 3.79 (3H, s, OMe), 4.31 (2H, s), 4.55 (1H, br s), 6.95 (1H, t, J=8 Hz). MS m/z (relative intensity): 389, 387 (M^+-1, 0.1, 0.3), 353 (M^+ − Cl, 0.9), 191 (2), 121 (3), 101 (24), 85 (100). Data for **13g**: UV λ_{max} nm (ε): 217 (11100). IR (neat) cm^{-1}: 3350, 1725, 1645, 780. ^{1}H-NMR δ: 1.00—1.72 (19H, m), 2.31 (2H, q, J=8 Hz), 3.63 (2H, t, J=7 Hz), 3.79 (3H, s, OMe), 4.31 (2H, s), 6.98 (1H, t, J=7 Hz). MS m/z (relative intensity): 306, 304 (M^+, 0.6, 1.8), 269 (M^+ − Cl, 21), 236 (25), 219 (5), 191 (16), 149 (8), 135 (33), 109 (35), 95 (50), 81 (59), 67 (46), 55 (100). High-resolution MS Calcd for $C_{16}H_{29}O_3Cl$ (M^+) m/z: 304.1804. Found m/z: 304.1816.

Removal of the THP Protecting Group; General Procedure An ethanol solution of a THP-ether (**12**) and PPTS (0.1 eq) was heated at 50—60 °C for 2.5—3 h. After evaporation of the solvent, the residue was extracted with ether. The extracts were washed with brine, dried ($MgSO_4$), and then concentrated. The residue was chromatographed on a silica gel column. Elution with 20% EtOAc/hexane gave the starting material (**12**) and with 50% EtOAc/hexane gave the alcohol (**13**).

Methyl 2-Bromomethyl-10-hydroxy-2(*Z*)-decenoate (**13a**): Treatment of **12a** (173 mg, 0.46 mmol) with PPTS (16 mg, 0.06 mmol) in ethanol (6 ml) afforded **13a** (97 mg, 72.3%) together with **12a** (18 mg, 10.5%).

Methyl 2-Bromomethyl-12-hydroxy-2(*Z*)-dodecenoate (**13b**): Treatment of **12b** (81 mg, 0.2 mmol) with PPTS (6 mg, 0.02 mmol) in ethanol (3 ml) afforded **13b** (59 mg, 92.0%) together with **12b** (5 mg, 6.0%).

Methyl 2-Bromomethyl-14-hydroxy-2(*Z*)-tetradecenoate (**13c**): Treatment of **12c** (1.70 g, 3.9 mmol) with PPTS (105 mg, 0.39 mmol) in eth-

anol (40 ml) afforded **13c** (523 mg, 38.4%) together with **12c** (456 mg, 26.9%).

Methyl 2-Bromomethyl-16-hydroxy-2(*Z*)-hexadecenoate (**13d**): Treatment of **12d** (1.20 g, 2.6 mmol) was treated with PPTS (81 mg, 0.3 mmol) in ethanol (30 ml) afforded **13d** (758 mg, 77.2%) together with **12d** (134 mg, 11.2%).

Methyl 2-Chloromethyl-14-hydroxy-2(*Z*)-tetradecenoate (**13g**): Treatment of **12g** (220 mg, 0.56 mmol) was treated with PPTS (16 mg, 0.06 mmol) afforded **13g** (160 mg, 94.1%) together with **12g** (7 mg, 3.4%).

The Swern Oxidation of the Halogenated Alcohol (13); General Procedure DMSO (2.2 eq) was added to a solution of oxalyl chloride (1.3 eq) in dry CH_2Cl_2 at −60 °C. The mixture was stirred for 2 min and the alcohol (**13**) was added; stirring was continued for an additional 5 min. Triethylamine (5 eq) was added and the reaction mixture was kept at −60 °C with stirring for 1 h. Water was then added and the aqueous layer was reextracted with additional CH_2Cl_2. The organic layers were combined, washed with brine, and dried (anhydrous Na_2SO_4). The solvent was removed *in vacuo* to give the crude aldehyde, which was purified by column chromatography (10% EtOAc/hexane) to give the pure aldehyde.

Preparation of Methyl 2-Bromomethyl-9-formyl-2(*Z*)-nonenoate (4a) Oxidation of **13a** (97 mg) by the general procedure described above gave **4a** (76 mg, 79.0%) as an oil. UV λ_{max} nm (ε): 215 (11380). IR (neat) cm^{-1}: 2730, 1730, 1645. ^{1}H-NMR δ: 1.16—1.80 (8H, m), 2.29 (2H, q, *J*=7 Hz), 2.43 (2H, td, *J*=7, 2 Hz), 3.79 (3H, s, OMe), 4.21 (2H, s), 6.93 (1H, t, *J*=7 Hz), 9.72 (1H, t, *J*=2 Hz, CHO). MS *m/z* (relative intensity): 261, 259 (M^+ − MeO, 3), 260, 258 (M^+ − MeOH, 8), 211 (M^+ − Br, 71), 197 (M^+ − Br − MeOH, 86), 161 (21), 133 (75), 107 (41), 91 (44), 81 (61), 67 (73), 55 (68), 41 (100).

Preparation of Methyl 2-Bromomethyl-11-formyl-2(*Z*)-undecenoate (4b) Oxidation of **13b** (161 mg, 0.5 mmol) by the general procedure described above gave **4b** (150 mg, 94.0%) as an oil. UV λ_{max} nm (ε): 215 (10070). IR (neat) cm^{-1}: 2730, 1720, 1645. ^{1}H-NMR δ: 1.08—1.80 (12H, m), 2.28 (2H, q, *J*=7 Hz), 2.42 (2H, td, *J*=7, 2 Hz), 3.79 (3H, s, OMe), 4.21 (2H, s), 6.95 (1H, t, *J*=7 Hz), 9.72 (1H, t, *J*=2 Hz, CHO). MS *m/z* (relative intensity): 289, 287 (M^+ − MeO, 1), 288, 286 (M^+ − MeOH, 4), 239 (M^+ − Br, 71), 207 (M^+ − Br − MeOH, 69), 189 (12), 161 (37), 121 (15), 109 (29), 93 (56), 81 (80), 67 (77), 55 (79), 41 (100).

Preparation of Methyl 2-Bromomethyl-13-formyl-2(*Z*)-tridecenoate (4c) Oxidation of **13c** (473 mg, 1.4 mmol) by the general procedure described above gave **4c** (340 mg, 70.1%) as an oil. UV λ_{max} nm (ε): 215 (10950). IR (neat) cm^{-1}: 2730, 1730, 1640. ^{1}H-NMR δ: 1.08—1.80 (16H, m), 2.29 (2H, q, *J*=7 Hz), 2.42 (2H, td, *J*=7, 1.5 Hz), 3.79 (3H, s, OMe), 4.21 (2H, s), 6.95 (1H, t, *J*=7 Hz), 9.72 (1H, t, *J*=1.5 Hz, CHO). MS *m/z* (relative intensity): 316, 314 (M^+ − MeOH, 2.5), 305, 303 ($M^+ - C_2H_3O$, 4), 267 (M^+ − Br, 78), 235 (M^+ − Br − MeOH, 64), 207 (15), 189 (14), 121 (40), 95 (74), 81 (90), 79 (76), 65 (80), 41 (100).

Preparation of Methyl 2-Bromomethyl-15-formyl-2(*Z*)-pentadecenoate (4d) Oxidation of **13d** (102 mg, 0.27 mmol) by the general procedure described above gave **4d** (83 mg, 81.6%) as an oil. UV λ_{max} nm (ε): 215 (11970). IR (neat) cm^{-1}: 2720, 1730, 1720, 1640. ^{1}H-NMR δ: 1.16—1.80 (20H, m), 2.28 (2H, q, *J*=8 Hz), 2.41 (2H, td, *J*=7, 2 Hz), 3.80 (3H, s, OMe), 4.22 (2H, s), 6.96 (1H, t, *J*=8 Hz), 9.72 (1H, t, *J*=2 Hz, CHO). MS *m/z* (relative intensity): 344, 342 (M^+ − MeOH, 1), 333, 331 ($M^+ - C_2H_3O$, 2), 295 (M^+ − Br, 56), 263 (M^+ − Br − MeOH, 47), 235 (12), 191 (3), 149 (8), 135 (17), 121 (17), 109 (34), 95 (62), 81 (74), 67 (64), 55 (85), 41 (100).

Preparation of Methyl 2-Chloromethyl-13-formyl-2(*Z*)-tridecenoate (4g) Oxidation of **13g** (131 mg, 0.43 mmol) by the general procedure described above gave **4g** (112 mg, 85.7%) as an oil. UV λ_{max} nm (ε): 215 (12500). IR (neat) cm^{-1}: 2710, 1720, 1640, 780. ^{1}H-NMR δ: 1.10—1.80 (16H, m), 2.30 (2H, q, *J*=7 Hz), 2.38 (2H, td, *J*=7, 2 Hz), 3.78 (3H, s, OMe), 4.31 (2H, s), 6.97 (1H, t, *J*=8 Hz), 9.72 (1H, t, *J*=2 Hz, CHO). MS *m/z* (relative intensity): 304, 302 (M^+, 0.2, 0.6), 272, 270 (M^+ − MeOH, 3.9, 11), 267 (M^+ − Cl, 8.3), 235 (M^+ − Cl − MeOH, 16), 207 (5), 189 (4), 163 (6), 135 (25), 95 (47), 81 (61), 77 (61), 55 (74), 41 (100). High-resolution MS Calcd for $C_{16}H_{27}O_3Cl$ (M^+) *m/z*: 302.1647. Found *m/z*: 302.1638.

Intramolecular Cyclization of the Formylated Allyl Halide (4); General Procedure Preparation of low-valent chromium reagent: A suspension of 5 eq of anhydrous chromium(III) chloride (Nakarai Chemical Ltd.) in dry THF (0.37 M solution) was treated with 2.5 eq of $LiAlH_4$ at 0 °C under an argon atmosphere. The resulting charcoal-gray mixture was stirred for 10 min and at room temperature for 20 min. The THF was removed by a stream of argon, and the residue was dissolved in dry DMF. Cyclization method: To the resulting dark green solution was added a DMF solution of a formylated allyl halide (**4**), and the mixture was stirred at room temperature. The reaction mixture was poured into ice-cold water, and extracted with ether three times. The extracts were washed with brine and dried ($MgSO_4$). Evaporation of the solvent *in vacuo* gave a crude oil, which was subjected to column chromatography.

Cyclization of the Formylated Allyl Bromide (4a) i) At 0.005 M Concentration for a Short Time: A DMF (4 ml) solution of the allyl bromide (**4a**) (57 mg, 0.2 mmol) was added to a DMF solution (36 ml) of the low-valent chromium reagent prepared from anhydrous $CrCl_3$ (158 mg, 1.0 mmol) and $LiAlH_4$ (19 mg, 0.5 mmol) by the general procedure. The reaction mixture was stirred for 7 h, and worked up as described in the general procedure above. The crude product was chromatographed on silica gel with 35% EtOAc/hexane to afford methyl 2-chloromethyl-9-formyl-2(*Z*)-nonenoate (**4e**) (38.6 mg, 78.2%) as an oil. UV λ_{max} nm (ε): 215 (11970). IR (neat) cm^{-1}: 2720, 1720, 1645, 780. ^{1}H-NMR δ: 1.12—1.80 (8H, m), 2.32 (2H, q, *J*=7 Hz), 2.43 (2H, td, *J*=7, 2 Hz), 3.79 (3H, s, OMe), 4.31 (2H, s), 6.96 (1H, t, *J*=8 Hz), 9.72 (1H, t, *J*=2 Hz, CHO). MS *m/z* (relative intensity): 217, 215 (M^+ − MeO, 3.9, 13), 216, 214 (M^+ − MeOH, 13, 39), 211 (M^+ − Cl, 7.8), 179 (M^+ − MeOH − Cl, 54), 150 (18), 133 (58), 107 (45), 81 (63), 67 (70), 55 (85), 41 (100).

ii) At 0.005 M Concentration for a Long Reaction Time: A DMF solution of the allyl bromide (**4a**) (54 mg, 0.19 mmol in 38 ml) was treated with 5 eq of the low-valent chromium reagent for 45 h, and worked up as described above. Separation of the crude product (49 mg) by preparative TLC using 30% EtOAc/hexane afforded the lactone (**5a**) (oil; 8.3 mg, 24.3%) and the allyl chloride (**4e**) (4.3 mg, 8.0%). Data for **6a**: IR (neat) cm^{-1}: 1770, 1660. ^{1}H-NMR δ: 0.72—2.12 (12H, m), 3.00 (1H, m), 4.70 (1H, m), 5.52 (1H, d, *J*=3 Hz), 6.22 (1H, d, *J*=3 Hz). MS *m/z* (relative intensity): 180 (M^+, 97), 151 (35), 124 (32), 109 (41), 96 (53), 84 (70), 67 (65), 54 (100). High-resolution MS Calcd for $C_{11}H_{16}O_2$ (M^+) *m/z*: 180.1149. Found *m/z*: 180.1157.

iii) At 0.002 M Concentration: The allyl bromide (**4a**) (52 mg, 0.18 mmol) was treated with 5 eq of the low-valent chromium reagent in DMF (94 ml) for 44 h. Work-up gave the allyl chloride (**4e**) (33.5 mg, 75.4%).

Cyclization of the Formylated Allyl Chloride (4e) Treatment of **4e** (37 mg, 0.15 mmol) with the low-valent chromium reagent prepared from $CrCl_3$ (101 mg, 0.64 mmol) and $LiAlH_4$ (12 mg, 0.32 mmol) in DMF (28 ml) for 24 h followed by preparative TLC using 35% EtOAc/hexane afforded the lactone (**5a**) (5.1 mg, 18.9%) and the starting chloride (**4e**) (11.8 mg, 31.9%).

Cyclization of the Formylated Allyl Bromide (4b) i) At 0.02 M Concentration: Treatment of **4b** (96 mg, 0.30 mmol) with the low-valent chromium reagent, prepared from $CrCl_3$ (238 mg, 1.50 mmol) and $LiAlH_4$ (28 mg, 0.75 mmol), in DMF (14 ml) for 1 h followed by separation by column chromatography using 30% EtOAc/hexane afforded the hydroxy esters (**15A**; 21.2 mg, 29.4% and **15B**; 25.1 mg, 34.8%) as an oil. Data for **15A**: IR (neat) cm^{-1}: 3450, 1720, 1625. ^{1}H-NMR δ: 1.04—1.80 (16H, m), 2.44—2.88 (4H, m), 3.68 (2H, br s), 3.76 (6H, s, OMe), 5.61 and 6.29 (each 2H, s, vinyl-H). MS *m/z* (relative intensity): 416 (trace), 398 (trace), 392 (trace), 391 (0.02), 390 (trace), 280 (3), 279 (20), 167 (46), 149 (100). Data for **15B**: IR (neat) cm^{-1}: 3450, 1720, 1625. ^{1}H-NMR δ: 1.00—1.84 (16H, m), 2.20—2.84 (4H, m), 3.64 (2H, br s), 3.76 (6H, s, OMe), 5.58 and 6.28 (each 2H, s, vinyl-H). MS *m/z* (relative intensity): 480 (M^+, 0.05), 461 (1), 430 (1), 416 (3), 398 (2), 321 (5), 284 (10), 256 (18), 208 (17), 55 (100).

ii) At 0.002 M Concentration: The allyl bromide (**4b**; 80 mg, 0.25 mmol) was treated with the low-valent chromium reagent (1.25 mmol) in DMF (125 ml) for 27 h by the procedure described above. The crude product was subjected to preparative TLC using 25% EtOAc/hexane to give the allyl chloride (**4f**) (13.6 mg, 19.8%) as an oil and the dimer (**17**) (13.7 mg, 10.6%) as an oil. Data for **4f**: UV λ_{max} nm (ε): 215 (11760). IR (neat) cm^{-1}: 1730, 1650, 785. ^{1}H-NMR δ: 1.12—1.80 (12H, m), 2.31 (2H, t, *J*=7 Hz), 2.42 (2H, td, *J*=7, 1.5 Hz), 3.78 (3H, s, OMe), 4.31 (2H, s), 6.97 (1H, t, *J*=7 Hz), 9.72 (1H, t, *J*=1.5 Hz, CHO). MS *m/z* (relative intensity): 276, 274 (M^+, 1, 3), 244, 242 (M^+ − MeOH, 10, 27), 239 (M^+ − Cl, 9), 207 (M^+ − Cl − MeOH, 21), 206 (12), 178 (7), 161 (19), 135 (33), 93 (45), 67 (70), 55 (76), 41 (100). High-resolution MS Calcd for $C_{14}H_{23}O_3Cl$ (M^+) *m/z*: 274.1334. Found *m/z*: 274.1339. Data for **17**: IR (neat) cm^{-1}: 3450, 1725, 1650, 1630, 780. ^{1}H-NMR δ: 1.04—1.88 (28H, m), 2.12—2.72 (5H, m), 3.55—3.72 (1H, m), 3.77 (3H, s, OMe), 3.78 (3H, s, OMe), 4.31 (2H, s, CH_2Cl), 5.55 and 6.26 (each 1H, s, d, *J*=1 Hz, =CH_2), 6.95 (1H, t, *J*=7 Hz, =CH−), 9.71 (1H, t, *J*=1.5 Hz, CHO). MS *m/z* (relative intensity): 462 (M^+ − Cl − OH, 4), 416 (6), 321 (14), 208 (15), 115 (58), 81 (71), 55 (100), 41 (99).

Cyclization of the Formylated Allyl Bromide (4c) The allyl bromide (**4c**) (75 mg, 0.2 mmol) was treated with the low-valent chromium reagent prepared from $CrCl_3$ (158 mg, 1.0 mmol) and $LiAlH_4$ (23 mg, 0.6 mmol) in

DMF (37 ml) for 19 h as outlined in the general procedure. The resulting crude product was subjected to column chromatography using 20% EtOAc/hexane to give the allyl chloride (**4g**) (14.4 mg, 24%) and the hydroxy ester (**14c**) (39 mg, 72%) as an oil. Data for **14c**: IR (neat) cm^{-1}: 3450, 1720, 1635. ^{1}H-NMR δ: 1.00—1.84 (20H, m), 2.78—2.97 (2H, m), 3.52—3.80 (1H, m), 3.77 (3H, s, OMe), 5.66 and 6.28 (each 1H, s, d, J= 1 Hz, $=CH_2$). MS m/z (relative intensity): 268 (M^+, 2), 236 ($M^+ - MeOH$, 86), 208 (12), 193 (5), 152 (17), 124 (38), 109 (35), 95 (75), 82 (75), 67 (58), 55 (75), 41 (100). High-resolution MS Calcd for $C_{16}H_{28}O_3$ (M^+) m/z: 268.2037. Found m/z: 268.2036.

Cyclization of the Allyl Chloride (4g) The allyl chloride (**4g**) (82 mg, 0.27 mmol) was treated with 5 eq of the low-valent chromium reagent in DMF (54 ml) for 19 h as described above. The crude product was chromatographed on a silica gel column using 10% EtOAc/hexane to give the lactone (**5c**) (19.8 mg, 31.0%) as colorless crystals, the starting material (**4g**) (4.1 mg, 5.0%) and the hydroxy ester (**14c**) (17.3 mg, 23.9%). Data for pure **5c**: colorless needles, mp 53—54 °C, UV λ_{max} nm (ε): 208 (10810). IR (neat) cm^{-1}: 1760, 1660. ^{1}H-NMR δ: 1.10—1.92 (20H, m), 2.95 (1H, m, $W_{1/2}$= 14 Hz), 4.52 (1H, q, J=6.5 Hz), 5.46 and 6.13 (each 1H, d, J=2.5 Hz, $=CH_2$). MS m/z (relative intensity): 236 (M^+, 26), 207 (19), 193 (5), 152 (15), 124 (42), 109 (33), 96 (65), 82 (81), 67 (72), 41 (100). High-resolution MS Calcd for $C_{15}H_{24}O_2$ (M^+) m/z: 236.1775. Found m/z: 236.1778. *Anal.* Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24. Found: C, 76.12; H, 10.27.

Cyclization of the Allyl Bromide (4d) i) At 0.02 M Concentration: The allyl bromide (**4d**) (47 mg, 0.125 mmol) was treated with the low-valent chromium reagent prepared from $CrCl_3$ (99 mg, 0.63 mmol) and $LiAlH_4$ (12 mg, 0.31 mmol) in DMF (6 ml) for 1 h as outlined in the general procedure. The crude product was purified by column chromatography using 30% EtOAc/hexane to give hydroxy ester (**14d**) (21.9 mg, 59.2%) as an oil. IR (neat) cm^{-1}: 3450, 1720, 1630. ^{1}H-NMR δ: 1.00—1.80 (24H, m), 2.48 (1H, OH), 2.84 (1H, m, $W_{1/2}$=14 Hz), 3.64 (1H, br s), 3.76 (3H, s, OMe), 5.64 and 6.32 (each 1H, t, d, J=1 Hz, $=CH_2$). MS m/z (relative intensity): 296 (M^+, 3), 278 ($M^+ - H_2O$, 0.6), 264 ($M^+ - MeOH$, 100), 236 (11), 166 (20), 152 (23), 124 (37), 110 (31), 109 (31), 96 (60), 95 (60), 82 (66), 67 (43), 55 (60), 41 (57). High-resolution MS Calcd for $C_{18}H_{32}O_3$ (M^+) m/z: 296.2350. Found m/z: 296.2353.

ii) At 0.003 M Concentration: Treatment of **4d** (70 mg, 0.019 mmol) in DMF (63 ml) with the chromium reagent for 21 h followed by usual work-up afforded the allyl chloride (**4h**) (59.5 mg, 95%) as an oil. IR (neat) cm^{-1}: 2720, 1715, 1640, 1270, 770. ^{1}H-NMR δ: 1.20—1.80 (20H, m), 2.27 (2H, t, J=7 Hz), 2.41 (2H, dd, J=7, 2 Hz), 3.78 (3H, s), 4.32 (2H, s, CH_2Cl), 6.98 (1H, t, J=8 Hz), 9.72 (1H, t, J=2 Hz, CHO).

Lactonization of the Hydroxy Ester (14); General Procedure The hydroxy ester (**14**) and 0.1—0.2 eq of *p*-toluenesulfonic acid in benzene was heated to reflux. After removal of the solvent, the residue was chromatographed on a silica gel column.

The Dilactone (16A) The hydroxy ester (**15A**) (20 mg, 0.041 mmol) and *p*-toluenesulfonic acid (2 mg) were refluxed in benzene (4 ml) for 0.5 h. The reaction mixture was purified by column chromatography using 20% EtOAc/hexane to give the dilactone (**16A**) (17.0 mg, 98.2%) as colorless crystals, mp 120—122 °C. IR (KBr) cm^{-1}: 1765, 1660. ^{1}H-NMR δ: 1.04—1.84 (32H, m), 2.98 (2H, m, $W_{1/2}$=16 Hz), 4.50 (2H, m, $W_{1/2}$=16 Hz), 5.47 and 6.18 (each 1H, each t, d, J=2 Hz, $=CH_2$). MS m/z (relative intensity): 416 (M^+, 19), 399 (17), 398 ($M^+ - H_2O$, 58), 380 (12), 370 (13), 352 (3), 303 (6), 275 (7), 247 (6), 205 (5), 163 (21), 95 (63), 81 (81), 67 (91), 55 (100). High-resolution MS Calcd for $C_{26}H_{40}O_4$ (M^+) m/z: 416.2923. Found m/z: 416.2915.

The Dilactone (16B) The hydroxy ester (**15B**) (20 mg, 0.041 mmol) and *p*-toluenesulfonic acid (2 mg) were refluxed in benzene (4 ml) for 0.5 h. The reaction mixture was purified by column chromatography using 20% EtOAc/hexane to give the dilactone (**16B**) (14.9 mg, 86.1%) as an oil. IR (neat) cm^{-1}: 1770, 1660. ^{1}H-NMR δ: 1.04—1.76 (32H, m), 2.94 (2H, br s, $W_{1/2}$=16 Hz), 4.47 (2H, br s, $W_{1/2}$=12 Hz), 5.49 and 6.18 (each 2H, each t, d, J=3, 4 Hz, $=CH_2$). MS m/z (relative intensity): 284 (0.5), 279 (0.2), 256 (2), 224 (1), 223 (7), 213 (1), 206 (1), 205 (6), 150 (9), 149 (100), 57 (16).

The Lactone (5c) The hydroxy ester (**14c**) (19.5 mg, 0.073 mmol) and *p*-toluenesulfonic acid (3 mg) were heated to reflux in benzene (2 ml) for 15 min. The crude product was purified by column chromatography using 30% EtOAc/hexane to give the lactone (**5c**) (13.2 mg, 76.6%) as colorless needles, mp 53—54 °C.

The Lactone (5d) Treatment of the hydroxy ester (**14d**) (76 mg, 0.257 mmol) with *p*-toluenesulfonic acid (8 mg) in benzene (4 ml) for 15 min followed by column chromatography using 10% EtOAc/hexane as described in the general procedure afforded the lactone (**5d**) (53.1 mg, 78.1%) as colorless crystals, mp 68—70 °C. UV λ_{max} nm (ε): 210 (9540). IR (KBr) cm^{-1}: 1765, 1660. ^{1}H-NMR: 1.10—1.70 (24H, m), 2.97 (1H, m, $W_{1/2}$= 16 Hz), 4.48 (1H, m, $W_{1/2}$=12 Hz), 5.46, 6.15 (each 1H, d, J=3.0 Hz, $=CH_2$). MS m/z (relative intensity): 264 (M^+, 82), 235 ($M^+ - CHO$, 28), 152 (36), 124 (70), 110 (55), 109 (27), 96 (99), 82 (100), 67 (70), 55 (86), 41 (100). High-resolution MS Calcd for $C_{17}H_{28}O_2$ (M^+) m/z: 264.2087. Found m/z: 264.2072.

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