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OLEFIN METATHESIS REACTIONS OF SOME AROMATIC DIENES WITH *ORTHO*- AND *META*-DISUBSTITUTION. FORMATION OF 10-, 12-, 14-, AND 17-MEMBERED CYCLIC COMPOUNDS AND ISOMERIZATION OF AN ALLYLIC ALCOHOL

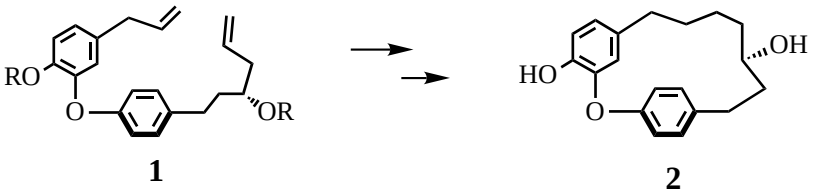
Katsuyuki Nakashima, Rika Ito, Masakazu Sono, and Motoo Tori*

Faculty of Pharmaceutical Sciences, Tokuhsima Bunri University,
Yamashiro cho, Tokushima, 770-8514, Japan

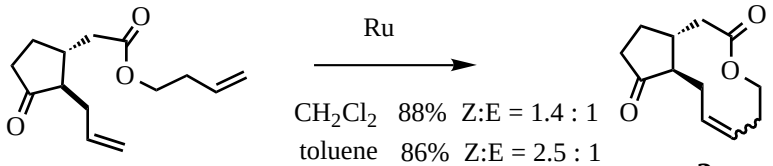
Abstract—Some aromatic dienes with *ortho*- and *meta*-disubstitution have been subjected to olefin metathesis reactions. Compounds having allylphenyl groups substituted at their *ortho* positions successfully cyclized into 12-, 14-, and 17-membered alkenes in moderate to good yields, while compounds having the same groups substituted at their *meta* positions and those having vinylphenyl groups substituted at their *ortho* positions afforded mainly polymers. *o*-Allylphenyl 5-hexenyl ether produced 10-membered cyclooxadecadiene in 7.5% yield.

Ring closing metathesis (RCM) has emerged as a powerful tool for the synthesis of medium and large ring compounds.[1-7] Although considerable amounts of examples have been reported, it is not easy to find out the specific positions for favorable cyclization reactions to form medium and large rings.[8] The different positions for cyclizations lead to different yields (sometimes disappointingly poor).[8] A number of large ring heterocycles have successfully been synthesized using the RCM reaction as a key step.[1-7] There are some examples to construct 10-membered rings, lactone (**3**) fused with a cyclopentanone (eq. 2),[9] a part of marine polyether (**4**) (eq. 3),[10] lactone (**5**) (eq. 4),[11] oxasilacycle (**6**) (eq. 5),[12] oxazacycle (**7**) (eq. 6),[13] oxacycle (**8**) (eq. 7),[14] and dioxacycle (**9**) (eq. 8)[14] in 3-88% yield. We have encountered that diene (**10**) did not afford the desirable cyclodecene at all with catalyst (**11**).[15] However, the diene (**24**) has successfully cyclized to a 10-membered cyclic ether (**25**) in spite of poor yield (7.5%). Thus, carbocycles seem to be more difficult to be formed by RCM reactions than heterocycles, presumably because of the absence of interaction between the catalyst and hetero atoms as discussed by Fürstner.[4,14] Synthesis of cyclic diarylheptanoids[16] such as **2**, which has a hetero atom in its 15-membered ring, may be accomplished by the RCM reaction (eq. 1) of diene (**1**). Therefore, we have tested whether the *ortho*- and *meta*-disubstituted dienes cyclize into medium and large rings by RCM reactions and found that compounds having allylphenyl groups substituted at their *ortho* positions successfully cyclized into 12-, 14-, and 17-membered alkenes in 52-79% yields, while compounds having the same groups substituted at

their *meta* positions and those having vinylphenyl groups substituted at their *ortho* positions afforded mainly polymers. We now report the details of these successful and unsuccessful reactions.



1 **2** (eq. 1)



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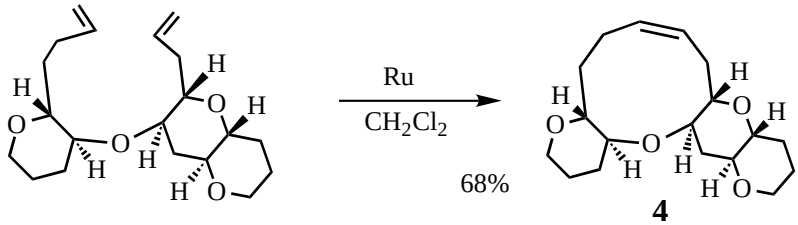
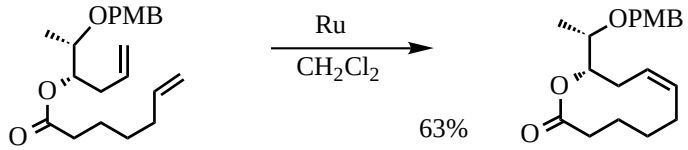
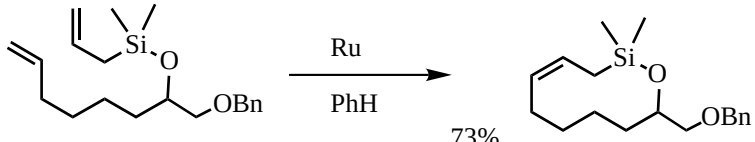


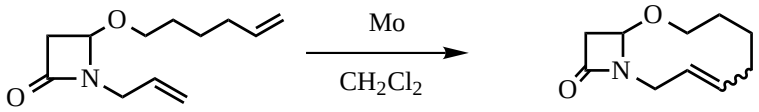
4 (eq. 3)



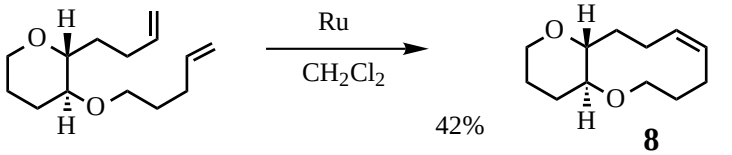
5 (Z : E = 12 : 1) (eq. 4)



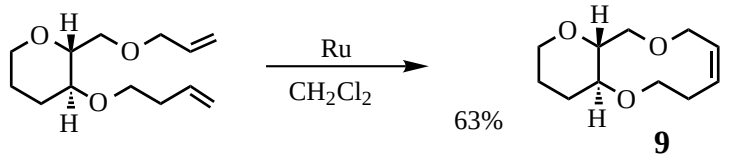
6 (eq. 5)



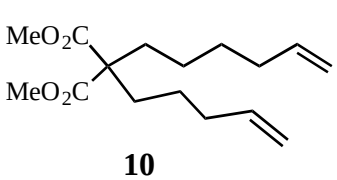
7 (eq. 6)



8 (eq. 7)



9 (eq. 8)



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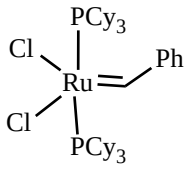

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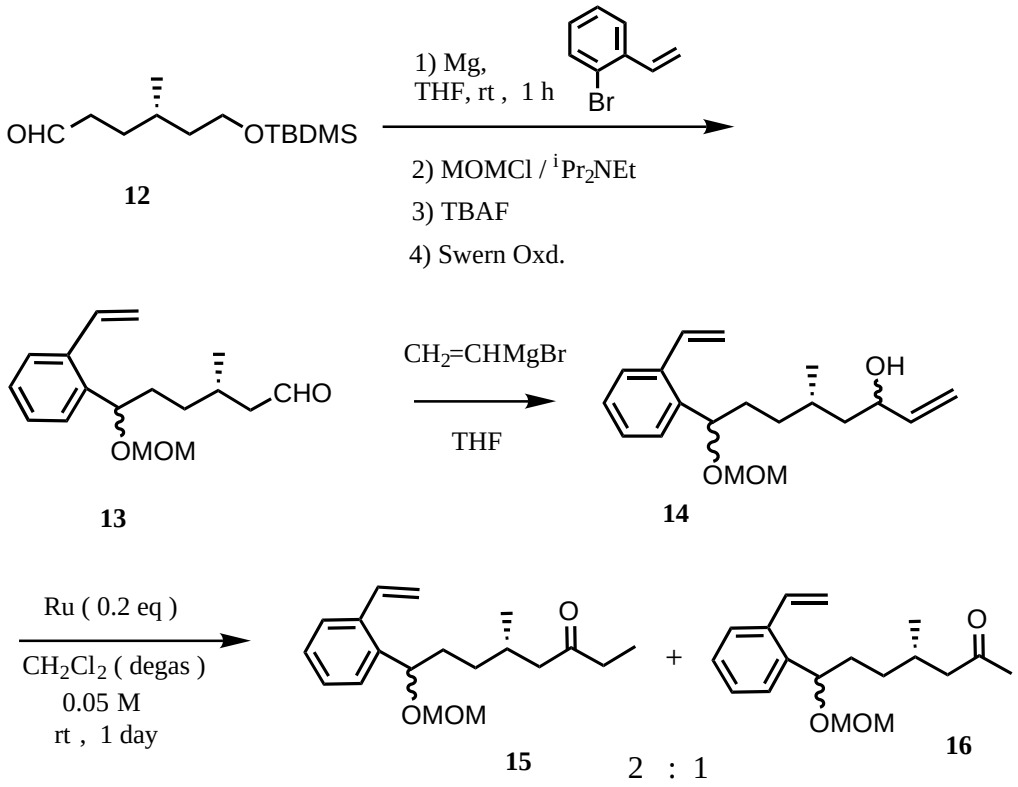
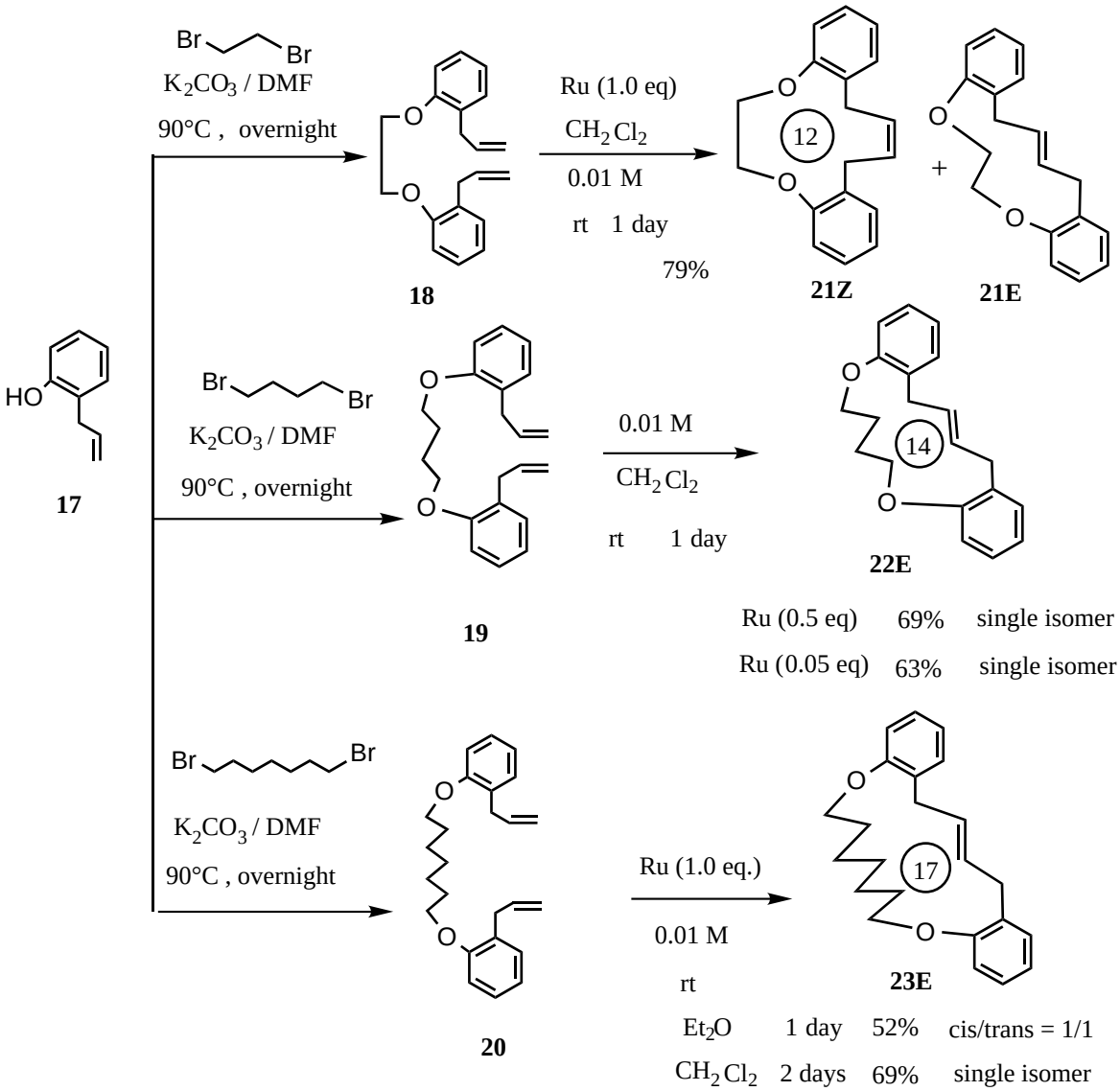
ortho-Bromostyrene was used for a Grignard reagent to add aldehyde (**12**),[17] which was prepared from (*S*)-(-)-citronellol by silylation and ozonolysis. The resulting alcohol was protected, deprotected, and oxidized to aldehyde (**13**), a mixture of diastereoisomers. Aldehyde (**13**) was treated with vinylmagnesium bromide to yield alcohol (**14**). When alcohol (**14**) was treated with Grubbs' Ru catalyst (**11**), a 2:1 mixture of ketones (**15**) and (**16**) was obtained in 68% yield. Ketone (**15**) was produced by isomerization of the double bond in **14**, which did not cyclize into a 10-membered ring. This kind of isomerization has also been reported in the case of Schrock's Mo catalyst.[18] Ketone (**16**) was one carbon degraded product.[19] Although compound (**14**) was an *ortho*-substituted benzene, cyclization was not induced, presumably due to slow reaction between the vinyl group and the ruthenium catalyst.[20-23] The corresponding acetate was also tried to cyclize under the similar conditions, but only the polymerization was observed. Polymerization was also observed for the acetates of allyl or butenyl substituted compounds, prepared from **13** with allyl- and butenylmagnesium bromide followed by acetylation.



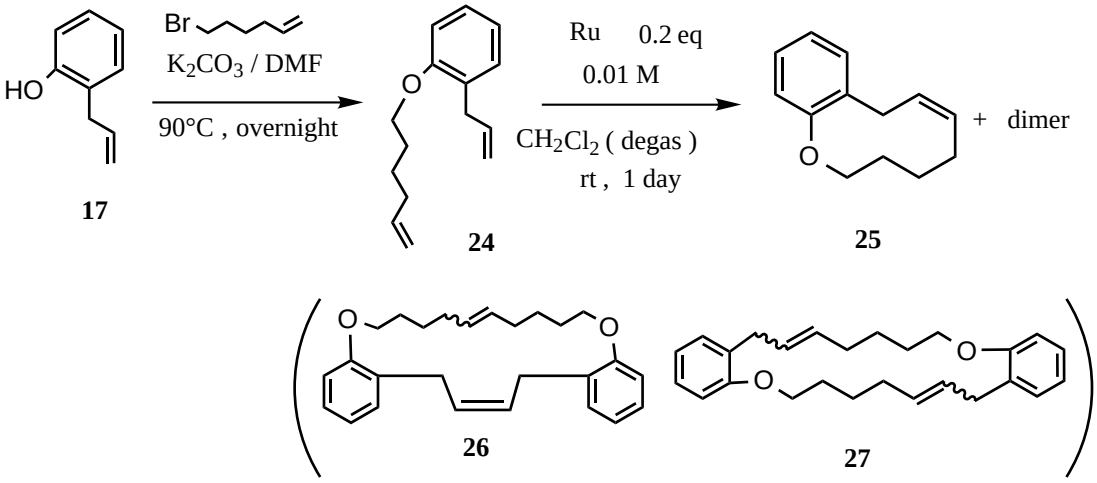
We next prepared symmetrically disubstituted ethers (**18**), (**19**), and (**20**) from *ortho*-allylphenol (**17**) by the reaction with corresponding dibromides under the basic conditions. In each case the RCM reaction occurred to form 12-, 14-, and 17-membered alkenes in 52-79% yield as an *E/Z* mixture or a single isomer depending on the reaction conditions. The crude reaction product from **18** showed two kinds of olefinic signals at δ_H 5.38 and 5.48, suggesting the presence of the *E/Z* isomers. Therefore, the mixture

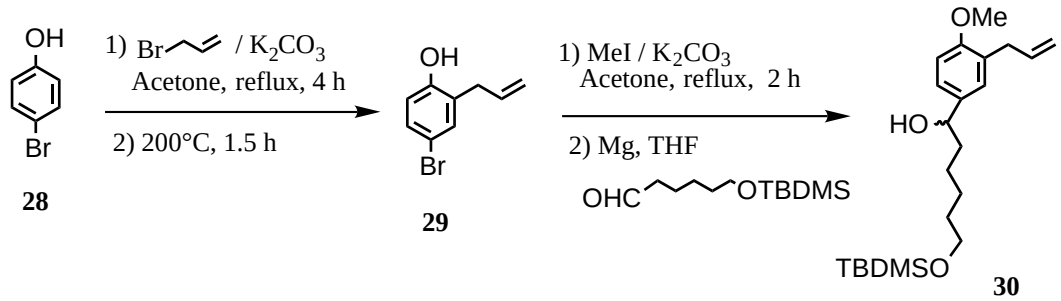
was separated by $AgNO_3$-impregnated silica gel column chromatography to afford **21E** (43%) and **21Z** (36%), respectively. The *E/Z* was assigned by the ^{13}C NMR chemical shifts. Compound (**21E**) showed the signal for the allylic (benzylic) carbon at δ_C 36.0, while **21Z** at δ_C 29.2, indicating each geometry.[24] Thus, in the case of **22E**, the geometry must be *E*, because the allylic methylene appeared at δ_C 34.3.[24] When diene (**20**) was treated with Ru catalyst in ether, *ca.* 1:1 mixture of *E/Z* isomers (**23**) was obtained. However, in CH_2Cl_2, almost the *E* isomer (**23E**) was produced, with a trace amount of *Z* isomer, which was not characterized.

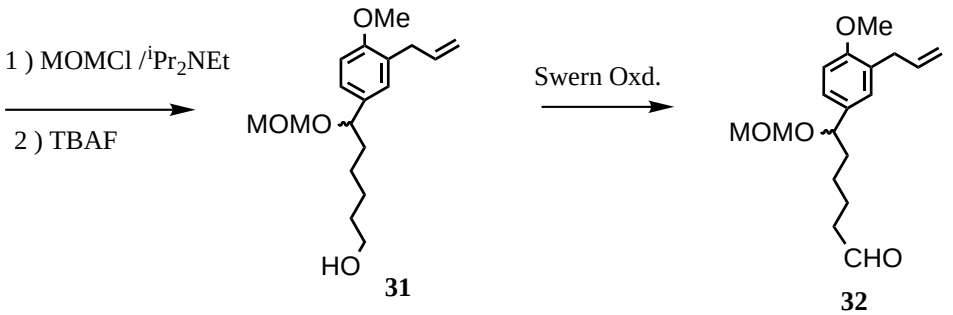


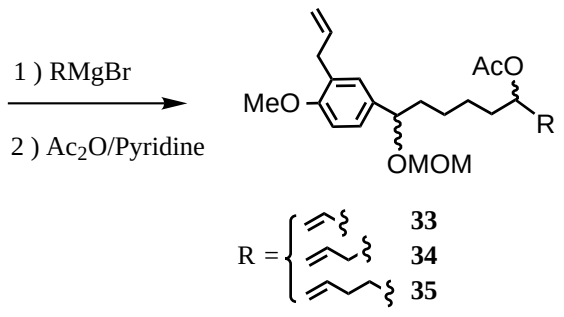
The hexenyl ether (**24**) could also afford 10-membered ether (**25**) albeit in the poor yield (7.5%), together with 19% of the olefins, which seem to be **26** and/or **27**. The geometry of **25** should be *Z*, because the olefinic protons at δ_H 5.48 and 5.22 exhibited a *vicinal* coupling with *J*=10 Hz.

In our successful examples described above suggest that the role of oxygen function may be very important for the cyclization.[4,14] The MOM and acetate groups probably have the interaction with the catalyst and thus did not work favorably to cyclize.[25,26]









The Claisen rearrangement reaction of allyl ether derived from **28** afforded phenol (**29**), whose methyl ether yielded alcohol (**30**) by the Grignard reaction with 6-*tert*-butyldimethylsilyloxyhexanal. Protection with MOM ether, deprotection of silyl ether, and Swern oxidation afforded aldehyde (**32**). Three kinds of Grignard reagents were used for making dienes (**33**), (**34**), and (**35**), mixtures of diastereoisomers, all of which failed to cyclize by Ru reagent (**11**), but afforded polymers reacted at both ends of olefins.

These results show that styryl ends are least reactive because the reaction of a styryl group with the Ru catalyst is not favored due to the formation of styrene itself.[1-7] The Ar-allylic ends were even more reactive than alkylvinyl or allylic substituents.[27,28] The double bond of the butenyl group may not be enough far away from the acetate group, which caused the reversed effect to cyclize into large rings.[25,26] We may avoid the oxygen functionality close to the reaction site.[14] Only compounds having allylphenyl groups substituted at their *ortho* positions had successfully cyclized, while unfortunately compounds having the same groups substituted at their *meta* positions did not yield the desired carbocycles. However, the difference in the reactivity is not fully explained and we are currently engaged in preparing various types of substrate dienes for RCM reactions.

EXPERIMENTAL

General. The IR spectra were measured on a Jasco FTIR 500 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL ECP-400, a Varian Unity 200, or a Varian Gemini 200 spectrometer. The solvent used for NMR spectra was $CDCl_3$ unless otherwise stated. MS spectra were measured on a JEOL AX-500 spectrometer. Silica gel BW-127ZH (100-230 mesh, Fuji silycia) was used for column chromatography, and silica gel $60F_{254}$ plate (0.25mm, Merck) were used for TLC.

Preparation of aldehyde (**13**). A solution of 2-vinylphenylmagnesium bromide prepared from Mg (106 mg, 4.32 mmol) and 2-bromostyrene (876 mg, 4.78 mmol) in dry THF (37 mL) was added to a solution of aldehyde (**12**, 920 mg, 3.77 mmol) in dry THF (14 mL) at 0°C under Ar. The reaction mixture was stirred for 1 h at rt. Usual work-up afforded the alcohol (1.0 g). A solution of the alcohol (1.0 g, 3.0 mmol) in CH_2Cl_2 (15 mL) was treated with *N*,*N*-diisopropylethylamine (1.04 mL, 6.0 mmol) and MOMCl (0.34 mL, 4.5 mmol) at 0 °C. The reaction mixture was stirred at rt overnight. Water was added at 0°C and the mixture was extracted with CH_2Cl_2. The organic layer was washed with 0.2 M HCl, saturated $NaHCO_3$ solution, and with brine. Evaporation of the solvent after drying ($MgSO_4$) afforded a residue (1.0 g). The residue (500 mg) was dissolved in dry THF (2 mL) and tetrabutylammonium fluoride (TBAF) (1.0 M, 2 mL, 2.0 mmol) was added at 0°C. The mixture was stirred at rt for 4 h. Water was added at 0°C and the mixture was extracted with ether. The organic layer was washed with brine, dried ($MgSO_4$), and was evaporated to afford a residue, which was purified by silica gel column chromatography (elution with Hexane-AcOEt gradient; 30-50%) to yield alcohol (353 mg). The alcohol (353 mg, 1.27

mmol) was treated with oxalyl chloride (0.13 mL, 1.49 mmol) and DMSO (0.1 mL, 1.41 mmol) in CH_2Cl_2 (7 mL) at -45°C. In 15 min Et_3N (0.9 mL, 6.46 mmol) was added, and the mixture was stirred at 0°C for 15 min. Water was added, and the mixture was extracted with CH_2Cl_2. The organic layer was washed with brine, dried ($MgSO_4$), and evaporated to afford a residue, which was purified by silica gel column chromatography (elution with hexane-AcOEt gradient; 10-20%) to yield aldehyde (**13**, 319 mg, 31% from **12**); oil; IR (FT) 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.94 (3H, d, *J* = 6.6), 1.2-1.8 (4H, m), 2.05 (1H, m), 2.25 (1H, dt, *J* =7.8, 2.2), 2.38 (1H, m), 3.36 (3H, s), 4.49 (1H, d, *J* = 6.6), 4.53 (1H, d, *J* = 6.6), 4.88 (1H, t, *J* = 6.6), 5.31 (1H, dt, *J* = 11, 1.0), 5.60 (1H, d, *J* = 18), 7.07 (1H, dd, *J* = 18, 11), 7.2 (2H, m), 7.4 (2H, m), 9.73 (1H, dd, *J* = 4.4, 1.8); ^{13}C NMR (50 MHz, $CDCl_3$): δ 19.4 (CH_3), 19.6 (CH_3), 27.6 (CH), 27.7 (CH), 32.7 (CH_2), 34.4 (CH_2), 50.4 (CH_2), 50.6 (CH_2), 55.2 (CH_3), 74.2 (CH), 74.3 (CH), 93.9 (CH_2), 94.0 (CH_2), 116.0 (CH_2), 125.9 (CH), 126.3 (CH), 127.2 (CH), 127.6 (CH), 134.0 (CH), 134.1 (CH), 136.3 (C), 136.4 (C), 138.9 (C), 139.1 (C), 202.1 (CH); MS (EI) *m/z* 276 (M^+), 244, 231, 203, 177 (base), 147, 129, 117, 103; EI-HRMS Found *m/z* 276.1721. $C_{17}H_{24}O_3$ requires 276.1725.

Preparation of alcohol (**14**). A solution of aldehyde (**13**) (100 mg, 0.36 mmol) in dry THF (6.0 mL) was treated with vinylmagnesium bromide (1.04 M, 0.55 mL, 0.57 mmol) at -78°C under Ar. The temperature was raised to 0°C during 3 h. Usual work-up afforded a residue, which was purified by silica gel column chromatography (elution with hexane-AcOEt gradient; 0-50%) to yield alcohol (**14**) (56.0 mg, 51%); oil; IR (FT) 3400 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.89 (3H, d, *J* = 6.6), 1.1-1.9 (9H, m), 3.36 (3H, s), 4.48 (1H, d, *J* = 7.0), 4.53 (1H, d, *J* = 7.0), 4.88 (1H, t, *J* = 7.2), 5.07 (1H, dd, *J* = 15, 4.8), 5.19 (1H , br d, *J* = 17), 5.30 (1H, dd, *J* = 11, 1.6), 5.60 (1H, dd, *J* = 17, 1.4), 5.82 (1H, m), 7.09 (1H, ddd, *J* = 17, 11, 3.4), 7.25 (2H, m), 7.43 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$): δ 19.2 (CH_3), 19.8 (CH_3), 29.0 (CH), 29.2 (CH), 32.8 (CH_2), 32.9 (CH_2), 33.6 (CH_2), 34.5 (CH_2), 44.2 (CH_2), 44.3 (CH_2), 55.6 (CH_3), 70.8 (CH), 71.4 (CH), 74.9 (CH), 94.2 (CH_2), 114.0 (CH_2), 114.7 (CH_2), 116.3 (CH_2), 126.1 (CH), 126.5 (CH), 127.4 (CH), 127.9 (CH), 134.4 (CH), 136.3 (C), 138.9 (CH), 141.5 (CH), 141.8 (CH); MS (CI-NH_3) *m/z* 322 $(M+NH_4)^+$, 272, 260, 225 (base), 197, 177, 147, 132, 117; CI-HRMS (NH_3) Found *m/z* 322.2379 $(M+NH_4)^+$. $C_{19}H_{32}NO_3$ requires 322.2382.

Reaction of alcohol (**14**) *with Ru.* Ru catalyst (**11**, 37 mg, 0.045 mmol) was added to a solution of alcohol (**14**, 56 mg, 0.18 mmol) in degassed CH_2Cl_2 (3.6 mL) under Ar. The mixture was stirred at rt overnight, and was filtered through silica gel (230 - 400 mesh) with CH_2Cl_2. The solvent was removed *in vacuo* to afford ketone (**15**, 38 mg, 68%) as a main product; oil; IR (FT) 1710 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.86 (3H, d, *J* = 6.4), 0.87 (3H, d, *J* = 6.6), 1.02 (3H, t, *J* = 6.6), 2.09 (3H, s), 2.10 (3H, s), 3.36 (3H, s), 4.48 (1H, d, *J* = 6.8), 4.52 (1H, d, *J* = 6.8), 4.86 (1H, t, *J* = 5.4), 5.30 (1H, d, *J* = 11), 5.60 (1H, d, *J* = 17), 7.08 (1H dd, *J* = 17, 11), 7.27 (2H, m), 7.44 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$): δ 7.6 (CH_3), 19.6 (CH_3), 19.8 (CH_3), 29.1 (CH), 33.0 (CH_2), 34.7 (CH_2), 36.4 (CH_2), 49.5 (CH_2), 49.7 (CH_2), 55.6 (CH_3), 74.7 (CH), 94.2 (CH_2), 116.3 (CH_2), 126.2 (CH), 126.7 (CH), 127.5 (CH), 127.9 (CH), 134.3

(CH), 136.7 (C), 139.3 (C), 139.4 (C), 211.5 (C); GC-MS (CI-NH_3, 18.1 min for **16**) *m/z* 308 $(M+NH_4)^+$, 282, 258, 246, 229, 211 (base), 177, 147, 131, 117; GC-MS (CI-NH_3, 18.6 min for **15**) *m/z* 322 $(M+NH_4)^+$, 272, 260, 249, 225 (base), 177, 147, 132, 115; GC-HRMS (CI-NH_3, 18.1 min for **16**) Found *m/z* 308.2231 $(M+NH_4)^+$. $C_{18}H_{30}NO_3$ requires 308.2226; GC-HRMS (CI-NH_3, 18.6 min for **15**) Found *m/z* 322.2377 $(M+NH_4)^+$. $C_{19}H_{32}NO_3$ requires 322.2382.

Preparation of ether (**18**). A solution of dibromoethane (0.25 mL, 2.9 mmol) in MeCN (10 mL) was treated with K_2CO_3 (2.06 g, 14.9 mmol), *o*-allylphenol (**17**) (1.0 g, 7.46 mmol) and DMF (5 mL). The mixture was heated under reflux overnight. Water was added, and the mixture was extracted with Et_2O. The organic layer was washed with 1 M NaOH solution, water and brine. Evaporation of the solvent after drying ($MgSO_4$) afforded ether (**18**, 222 mg, 26%); oil; IR (FT) 1640, 1600, 1490, 1450 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 3.39 (4H, d, *J* = 6.5), 4.35 (4H, s), 5.03 (2H, br d, *J* = 17), 5.05 (2H, br d, *J* = 9.6), 5.99 (2H, ddt, *J* = 17, 9.6, 6.5), 6.91 (4H, t, *J* = 8.7), 7.15 (4H, m); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 34.4 (CH_2), 66.9 (CH_2), 111.6 (CH), 115.4 (CH_2), 121.0 (CH), 127.3 (CH), 129.1 (C), 129.9 (CH), 136.9 (CH), 156.3 (C); MS (EI) *m/z* 294 (M^+, base), 252, 173, 161, 145, 133, 119, 91; HRMS (EI) Found *m/z* 294.1604. $C_{20}H_{22}O_2$ required 294.1620.

Preparation of ether (**19**). A solution of 1,4-dibromobutane (0.30 mL, 2.98 mmol) in DMF (10 mL) was similarly treated with K_2CO_3 (2.06 g, 14.9 mmol) and *o*-allylphenol (**17**, 1.0 g, 7.46 mmol) to yield ether (**19**, 806 mg, 84%); oil; IR (FT) 1640, 1600, 1500, 1450 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.00 (4H, br s), 3.40 (4H, d, *J* = 6.5), 4.02 (4H, br s), 5.03 (2H, br d, *J* = 17), 5.08 (2H, br d, *J* = 11), 6.00 (2H, ddt, *J* = 17, 11, 6.5), 6.84 (4H, t, *J* = 8.2), 7.14 (4H, m); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 26.3 (CH_2), 34.5 (CH_2), 67.4 (CH_2), 111.1 (CH), 115.3 (CH_2), 120.4 (CH), 127.2 (CH), 128.7 (C), 129.8 (CH), 137.0 (CH), 156.6 (C); MS (EI) *m/z* 322 (M^+), 293, 280, 189 (base), 173, 161, 147, 133, 119, 107; HRMS (EI) Found *m/z* 322.1912. $C_{22}H_{26}O_2$ required 322.1933.

Preparation of ether (**20**). A solution of 1,7-dibromoheptane (0.63 mL, 3.69 mmol) in DMF (5 mL) was similarly treated with K_2CO_3 (2.05 g, 14.8 mmol) and *o*-allylphenol (**17**, 1.0 g, 7.45 mmol) to yield ether (**20**, 982 mg, 73%); oil; IR (FT) 1640, 1600, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.3-1.6 (6H, m), 1.7-1.9 (4H, m), 3.39 (4H, d, *J* = 6.2), 3.96 (4H, t, *J* = 6.2), 5.03 (2H, br d, *J* = 18), 5.07 (2H, br d, *J* = 10), 6.00 (2H, ddt, *J* = 18, 10, 6.2), 6.90 (4H, m), 7.15 (4H, m); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.6 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 34.4 (CH_2), 67.6 (CH_2), 111.1 (CH), 115.2 (CH_2), 120.2 (CH), 127.2 (CH), 128.6 (C), 129.6 (CH), 137.0 (CH), 156.6 (C); MS (EI) *m/z* 364 (M^+), 349, 322, 308, 231, 201, 173, 159, 147, 133, 119, 107; HRMS (EI) Found *m/z* 364.2381. $C_{25}H_{32}O_2$ required 364.2403

Reaction of ether (**18**) *with Ru.* Ru catalyst (156 mg, 0.19 mmol) in degassed CH_2Cl_2 (15 mL) was added to a solution of ether (**18**, 57 mg, 0.19 mmol) in degassed CH_2Cl_2 (4.0 mL) under Ar. The mixture

was stirred at rt overnight, and was filtered through silica gel (230 - 400 mesh) with CH_2Cl_2. The solvent was removed *in vacuo* to afford a residue, which was purified by silica gel column chromatography (elution with benzene-AcOEt gradient; 0-10%) to afford ether (**21E**, 22 mg, 43%) and its isomer (**21Z**, 19 mg, 36%); **21E**: oil; IR (FT) 1600, 1580, 1490, 1450 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 3.33 (4H, br s), 4.29 (4H, s), 5.48 (2H, br s), 6.87 (4H, t, *J* = 9.2), 7.15 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.0 (CH_2), 67.2 (CH_2), 113.2 (CH), 130 (CH), 127.4 (CH), 129.4 (CH), 130.7 (CH), 130.9 (C), 157.7 (C); MS (EI) *m/z* 266 (M^+, base), 237, 223, 202, 159, 131, 115; HRMS (EI) Found *m/z* 266.1299. $C_{18}H_{18}O_2$ requires 266.1306. **21Z**: oil; 1600, 1590, 1500, 1400 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 3.60 (4H, d, *J*=5.5), 4.23 (4H, s), 5.38 (2H, t, *J*=5.5), 6.97 (4H, t, *J*=8.7), 7.20 (4H, m); ^{13}C NMR (50 MHz, $CDCl_3$): δ 29.2 (CH_2), 69.3 (CH_2), 116.2 (CH), 122.4 (CH), 127.3 (CH), 128.2 (CH), 129.4 (CH), 130.6 (C), 157.0 (C); MS (EI) *m/z* 266 $(M)^+$ (base), 237, 223, 202, 178, 159, 131, 107; HRMS (EI) Found *m/z* 266.1313. $C_{18}H_{18}O_2$ requires 266.1307.

Reaction of ether (**19**) *with Ru.* A solution of ether (**19**, 125 mg, 0.19 mmol) was treated with Ru catalyst (160 mg, 0.19 mmol) in degassed CH_2Cl_2 (39 mL) under Ar to yield ether (**22E**, 51 mg, 69%); oil; IR (FT) 1600, 1500, 1450 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.96 (4H, m), 3.33 (4H, d, *J* = 3.5), 3.95 (4H, br t, *J* = 6.5), 5.46 (2H, m), 6.88 (4H, t, *J* = 8.7), 7.10 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.2 (CH_2), 34.3 (CH_2), 68.3 (CH_2), 114.2 (CH), 121.1 (CH), 127.5 (CH), 129.4 (CH), 130.5 (C), 131.0 (CH), 157.8 (C); MS (EI) *m/z* 294 (M^+, base), 279, 265, 251, 237, 202, 187, 159, 131, 115, 107; HRMS (EI) Found *m/z* 294.1588. $C_{20}H_{22}O_2$ requires 294.1620.

Reaction of ether (**20**) *with Ru.* A solution of ether (**20**, 50 mg, 0.14 mmol) was treated with Ru catalyst (115 mg, 0.14 mmol) in degassed CH_2Cl_2 (14 mL) under Ar to yield ether (**23E**, 32 mg, 69%); oil; IR (FT) 1600, 1500, 1450 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.5-1.8 (6H, m), 1.8-1.9 (4H, m), 3.29 (4H, d, *J* = 5.0), 3.98 (4H, t, *J* = 6.2), 5.67 (2H, m), 6.85 (4H, t, *J* = 8.3), 7.10 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.0 (CH_2), 27.9 (CH_2), 29.0 (CH_2), 34.7 (CH_2), 67.8 (CH_2), 111.8 (CH), 120.4 (CH), 127.2 (CH), 129.1 (CH), 129.7 (C), 130.2 (CH), 157.2 (C); MS (EI) *m/z* 336 (M^+, base), 321, 307, 279, 265, 229, 201, 187, 159, 131, 115, 107; HRMS (EI) Found *m/z* 336.2084. $C_{23}H_{28}O_2$ requires 336.2089.

Preparation of ether (**24**). A solution of 6-bromo-1-hexene (0.4 mL, 2.99 mmol) in DMF (10 mL) was treated with K_2CO_3 (2.06 g, 14.9 mmol) and *o*-allylphenol (**17**, 1.0 g, 7.45 mmol) at 90°C overnight. Water was added, and the mixture was extracted with Et_2O. The organic layer was washed with 1M NaOH solution, water, and with brine. Evaporation of the solvent after drying ($MgSO_4$) afforded a residue, which was purified by silica gel column chromatography (elution with hexane-AcOEt gradient; 0-20%) to yield ether (**24**, 619 mg, 96%); oil; IR (FT) 1640, 1600, 1500, 1450 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.5-1.7 (2H, m), 1.7-1.9 (2H, m), 2.15 (2H, q, *J* =8.5), 3.40 (2H, d, *J* = 6.4), 3.96 (2H, t, *J* = 6.4), 5.00 (4H, m), 5.83 (1H, ddt, *J* = 17, 11, 6.4), 6.00 (1H, ddt, *J* = 17, 9.4, 6.4), 6.85 (2H, m), 7.14 (2H,

d, *J* = 8.2); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 25.4 (CH_2), 28.8 (CH_2), 33.4 (CH_2), 34.5 (CH_2), 67.6 (CH_2), 111.1 (CH), 114.6 (CH_2), 115.2 (CH_2), 1220.3 (CH), 127.2 (CH), 128.7 (C), 129.7 (CH), 137.1 (CH), 138.5 (CH), 156.7 (C); MS (EI) *m/z* 216 (M^+, base), 134, 119, 78, 67; HRMS (EI) Found *m/z* 216.1530. $C_{15}H_{20}O$ requires 216.1514.

Reaction of ether (**24**) *with Ru.* A solution of ether (**24**, 98 mg, 0.45 mmol) was treated with Ru catalyst (180 mg, 0.22 mmol) in degassed CH_2Cl_2 (45 mL) under Ar to afford a residue, which was purified by 5% $AgNO_3$ - silica gel column chromatography (elution with hexane-AcOEt gradient; 0-20%) to yield a monomer (**25**, 6.4 mg, 5%) and a dimer (16 mg, 19%); **25**: oil; IR (FT) 1600, 1500, 1450 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.5-1.8 (4H, m), 2.55 (2H, dd, *J* = 12, 8.2), 3.30 (2H, d, *J* = 8.5), 4.27 (2H, m), 5.22 (1H, dt, *J* = 10, 8.2), 5.48 (1H, dt, *J* = 10, 8.5), 6.90 (2H, m), 7.14 (2H, d, *J* = 7.4); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 26.0 (CH_2), 26.5 (CH_2), 28.5 (CH_2), 29.4 (CH_2), 72.7 (CH_2), 115.7 (CH), 121.6 (CH), 127.2 (CH), 128.3 (CH), 129.6 (CH), 129.8 (CH), 130.3 (C), 132.7 (C); MS (EI) *m/z* 188 (M^+), 159, 145, 131, 120, 107 (base), 79; HRMS (EI) Found *m/z* 188.1225. $C_{13}H_{16}O$ requires 188.1201.

Preparation of phenol (**29**). A solution of 4-bromophenol (**28**, 5.0 g, 28.9 mmol) in acetone (50 mL) was added to K_2CO_3 (8.0 g, 57.8 mmol) and allyl bromide (3.8 mL, 43.3 mmol) and was heated under reflux for 4 h. Water was added, and the solvent was removed *in vacuo.* The mixture was extracted with Et_2O. The organic layer was washed with brine. Evaporation of the solvent after drying ($MgSO_4$) afforded ether (6.7 g). The ether (1.5 g, 7.04 mmol) was heated at 200°C for 1.5 h. The mixture was purified by silica gel column chromatography (elution with hexane-AcOEt gradient, 6 - 9%) to yield phenol (**29**, 1.3 g, 83%); oil; IR (FT) 3400 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.36 (2H, d, *J* = 6.2), 5.15 (1H, br d, *J* = 9.2), 5.16 (1H, br d, *J* = 18), 5.98 (1H, ddt, *J* = 18, 9.2, 6.2), 6.69 (1H, d, *J* = 9.2), 7.22 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 33.8 (CH_2), 112.3 (C), 116.3 (CH_2), 116.9 (CH), 128.3 (C), 129.8 (CH), 132.5 (CH), 135.3 (CH), 152.6 (C); MS *m/z* 214 $(M+2)^+$, 212 (M^+, base), 199, 187, 174, 162, 134, 105; HRMS Found *m/z* 211.9831. C_9H_9OBr requires 211.9837.

Preparation of alcohol (**30**). To a solution of phenol (**29**, 1.3 g, 5.87 mmol) in acetone (20 mL), K_2CO_3 (1.6 g, 11.7 mmol) and methyl iodide (0.7 mL, 11.7 mmol) was added. The mixture was heated under reflux for 2 h. Water was added, and the solvent was removed *in vacuo*. The mixture was extracted with Et_2O. The organic layer was washed with brine. Evaporation of the solvent after drying ($MgSO_4$) afforded bromo ether (1.1 g). A solution of Grignard reagent prepared from Mg (116 mg, 4.78 mmol) and bromo ether (1.1 g, 4.78 mmol) in dry THF (35 mL) was added to a solution of 6-*tert*-butyldimethylsilyloxyhexanal (1.0 g, 4.35 mmol) in THF (10 mL) at 0°C. The mixture was stirred at rt overnight. Usual work-up afforded a residue, which was purified by silica gel column chromatography (elution with hexane-AcOEt gradient; 7-10%) to yield alcohol (**30**, 0.7 g, 46%); oil; IR (FT) 3370 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.02 (6H, s), 0.88 (9H, s), 1.2-1.8 (8H, m), 3.36 (3H, s), 3.36 (1H, br d, *J* =6.0), 3.58 (2H, t, *J* =6.0),

3.81 (3H, s), 4.47 (1H, d, *J* = 6.6), 4.52 (1H, d, *J* = 6.6), 5.04 (2H, m), 5.99 (1H, ddt, *J* = 18, 9.2, 7.6), 6.80 (1H, d, *J* = 8.2) , 7.10 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ -5.67 ($CH_3\times2$), 17.9 (C), 25.3 (CH_2), 25.4 (CH_2), 25.6 ($CH_3\times3$), 32.4 (CH_2), 33.9 (CH_2), 37.6 (CH_2), 55.0 ($CH_3\times2$), 62.8 (CH_2), 77.4 (CH), 93.5 (CH_2), 109.7 (CH), 115.1 (CH_2), 125.6 (CH), 128.1 (CH), 133.7 (C), 136.4 (CH), 136.6 (C), 156.5 (C); MS (CI-CH_4) *m/z* 421 $(M+1)^+$, 389, 377, 361 (base), 335, 303, 229, 161; CI-HRMS (CH_4) Found *m/z* 421.2766 $(M+1)^+$. $C_{24}H_{41}O_4Si$ requires 421.2774.

Preparation of alcohol (**31**). A solution of alcohol (**30**, 750 mg, 1.98 mmol) in CH_2Cl_2 (15 mL) was treated with MOMCl (0.23 mL, 2.97 mmol) and *N*,*N*-diisopropylethylamine (0.69 mL, 3.96 mmol) at 0°C under Ar and was stirred at rt overnight. Water was added and the mixture was extracted with CH_2Cl_2, and the organic layer was washed with 0.2 M HCl, saturated $NaHCO_3$ solution, and with brine. Evaporation of the solvent after drying ($MgSO_4$) afforded to a residue (959 mg), which was directly dissolved in dry THF (3.5 mL) and the mixture was treated with TBAF (1.0 M, 3.4 mL, 3.40 mmol) at 0°C. The mixture was stirred at rt for 5 h. Water was added and the mixture was extracted with Et_2O. The organic layer was washed with brine, dried ($MgSO_4$), and was evaporated to afford a residue, which was purified by silica gel column chromatography (elution with hexane-AcOEt gradient; 50-80%) to yield alcohol (**31**, 449 mg, 73%); oil; IR (FT) 3430 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.3-1.9 (10H, m), 3.36 (3H, s), 3.37 (2H, d, *J* = 5.0), 3.62 (2H, t, *J* = 6.6), 3.82 (3H, s), 4.48 (1H, d, *J* = 6.8), 4.52 (1H, d, *J* = 6.8), 5.04 (2H, m), 5.99 (1H, ddt, *J* = 18, 9.6, 6.6), 6.81 (1H, d, *J* = 8.4), 7.06 (1H, d, *J* = 2.2), 7.12 (1H, dd, *J* = 8.4, 2.2); ^{13}C NMR (50 MHz, $CDCl_3$) δ 25.4 (CH_2), 25.6 (CH_2), 32.5 (CH_2), 34.1 (CH_2), 37.7 (CH_2), 55.3 ($CH_3\times2$), 62.6 (CH_2), 77.5 (CH), 93.7 (CH_2), 110.0 (CH), 115.3 (CH_2), 125.8 (CH), 128.4 (CH), 133.8 (C), 136.8 (CH), 156.7 (C); MS *m/z* 308 (M^+), 287, 275, 247, 221 (base), 189, 161; HRMS Found *m/z* 308.1969. $C_{18}H_{28}O_4$ requires 308.1988.

Preparation of aldehyde (**32**). The alcohol (**31**, 449 mg, 1.45 mmol) was treated with oxalyl chloride (0.14 mL, 1.60 mmol) and DMSO (1.3 mL, 18.4 mmol) in CH_2Cl_2 (10 mL) at -45°C. In 15 min Et_3N (1.02 mL, 7.3 mmol) was added, and the mixture was stirred at 0°C for 15 min. Water was added, and the mixture was extracted with CH_2Cl_2. The organic layer was washed with brine, dried ($MgSO_4$), and evaporated to afford a residue, which was purified by silica gel column chromatography (elution with hexane-AcOEt gradient; 10-50%) to yield aldehyde (**32**, 369 mg, 83%); oil; IR (FT) 1720 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.2-2.0 (7H, m), 2.40 (2H, td, *J* = 7.2, 1.8), 3.35 (3H, s), 3.37 (2H, d, *J* = 5.8), 3.82 (3H, s), 4.47 (1H, d, *J* = 6.6), 4.51 (1H, d, *J* = 6.6), 5.04 (2H, m), 5.99 (1H, ddt, *J* = 18, 9.6, 6.6), 6.80 (1H, d, *J* = 8.4), 7.06 (1H, d, *J* = 2.2), 7.11 (1H, dd, *J* = 8.4, 2.2), 9.74 (1H, t, *J* = 1.8); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.8 (CH_2), 25.4 (CH_2), 34.1 (CH_2), 37.5 (CH_2), 43.6 (CH_2), 55.3 ($CH_3\times2$), 77.3 (CH), 93.7 (CH_2), 110.0 (CH), 115.3 (CH_2), 125.7 (CH_2), 128.2 (CH_2), 128.5 (C), 133.5 (C), 136.7 (CH), 156.7 (C), 202.5 (CH); MS *m/z* 306 (M^+), 245, 221 (base), 201, 191, 161; HRMS Found *m/z* 306.1840. $C_{18}H_{26}O_4$ requires 306.1831.

Preparation of acetate (**33**). A solution of the aldehyde (**32**, 84 mg, 0.26 mmol) in dry THF (3.0 mL) was treated with vinylmagnesium bromide (1.0 M, 0.4 mL, 0.4 mmol) at -40°C under Ar. The temperature was gradually raised to rt during overnight. Usual work-up afforded a residue (17 mg), which was directly treated with pyridine (1.0 mL) and acetic anhydride (0.5 mL). The mixture was stirred at rt for 8 h. MeOH was added and was evaporated *in vacuo* to afford a residue, which was extracted with Et_2O. The organic layer was washed with 10% $CuSO_4$ solution, saturated $NaHCO_3$ solution, and with brine. Evaporation of the solvent after drying ($MgSO_4$) afforded acetate (**33**, 19 mg, 25%); oil; IR (FT) 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.2-1.9 (9H, m), 2.04 (3H, s), 3.35 (3H, s), 3.36 (2H, br d, *J* = 5.6), 3.82 (3H, s), 4.45 (1H, m), 4.47 (1H, d, *J* = 7.2), 4.52 (1H, d, *J* = 7.2), 5.03 (2H, m), 5.20 (2H, m), 5.75 (1H, ddd, *J* = 16, 10, 6.2), 5.99 (1H, ddt, *J* = 18, 9.6, 6.6), 6.80 (1H, d, *J* = 8.4), 7.06 (1H, d, *J* = 2.0), 7.11 (1H, dd, *J* = 8.4, 2.0); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.2 (CH_3), 24.9 (CH_2), 25.8 (CH_2), 34.0 (CH_2), 34.2 (CH_2), 37.7 (CH_2), 55.4 ($CH_3\times2$), 74.7 (CH), 77.6 (CH), 93.8 (CH_2), 110.0 (CH), 115.4 (CH_2), 116.5 (CH_2), 125.8 (CH), 128.4 (CH), 128.4 (C), 133.8 (C), 136.5 (CH), 136.9 (CH), 156.7 (C); MS *m/z* 376 (M^+), 315, 255, 221 (base), 161; HRMS Found *m/z* 376.2249. $C_{22}H_{32}O_5$ requires 376.2249.

Preparation of acetate (**34**). A solution of aldehyde (**32**, 30 mg, 0.10 mmol) in dry Et_2O (3.0 mL) was similarly treated with allylmagnesium bromide (1.0 M, 0.14 mL, 0.14 mmol) as before and acetylation afterwards to give acetate (**34**, 22 mg, 52%); oil; IR (FT) 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.2-2.0 (8H, m), 2.01 (3H, s), 2.27 (2H, m), 3.36 (3H, s), 3.37 (2H, br d, *J* = 5.6), 3.81 (3H, s), 4.45 (1H, m), 4.47 (1H, d, *J* = 6.8), 4.51 (1H, d, *J* = 6.8), 4.88 (1H, quint, *J* = 6.2), 5.04 (4H, m), 5.72 (1H, m), 5.99 (1H, ddd, *J* = 18, 9.4, 6.2), 6.80 (1H, d, *J* = 8.4), 7.06 (1H, d, *J* = 2.4), 7.11 (1H, dd, *J* = 8.4, 2.4); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.1 (CH_3), 25.1 (CH_2), 25.8 (CH_2), 33.4 (CH_2), 34.2 (CH_2), 34.2 (CH_2), 37.7 (CH_2), 38.5 (CH_2), 55.4 ($CH_3\times2$), 73.2 (CH), 77.6 (CH), 93.8 (CH_2), 110.0 (CH), 115.4 (CH_2), 117.6 (CH_2), 125.9 (CH), 128.4 (CH), 128.6 (C), 133.8 (CH), 133.8 (C), 136.9 (CH), 156 (C); MS *m/z* 390 (M^+), 329, 269, 245, 221 (base), 187, 175, 161; HRMS Found *m/z* 390.2400. $C_{23}H_{34}O_5$ requires 390.2406.

Preparation of acetate (**35**). A solution of aldehyde (**32**, 50 mg, 0.16 mmol) in dry THF (3.0 mL) was similarly treated with a solution of the Grignard reagent prepared from Mg (12 mg , 0.48 mmol) and 4-bromo-1-butene (67 mg, 0.49 mmol) in dry THF (3.0 mL). The resulting alcohol was acetylated to give acetate (**35**, 16 mg, 20%); oil; IR (FT) 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.2-1.9 (12H, m), 2.02 (3H, s), 3.36 (3H, s), 3.37 (2H, br d, *J* = 5.8), 3.81 (3H, s), 4.45 (1H, m), 4.47 (1H, d, *J* = 6.6), 4.51 (1H, d, *J* = 6.6), 4.86 (1H, quint, *J* = 6.0), 5.20 (4H, m), 5.79 (1H, ddt, *J* = 17, 10, 6.4), 5.99 (1H, ddt, *J* = 18, 9.4, 6.4), 6.80 (1H, d, *J* = 8.4), 7.06 (1H, d, *J* = 2.2), 7.11 (1H, dd, *J* = 8.4, 2.2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 21.1 (CH_3), 25.0 (CH_2), 25.9 (CH_2), 29.5 (CH_2), 33.1 (CH_2), 33.9 (CH_2), 34.2 (CH_2), 37.7 (CH_2), 55.4 ($CH_3\times2$), 73.7 (CH), 77.6 (CH), 93.8 (CH_2), 110.0 (CH), 114.8 (CH_2), 115.4 (CH_2), 125.9 (CH), 128.4 (CH), 128.4 (C), 133.8 (C), 136.9 (CH), 137.9 (CH); MS *m/z* 404 (M^+), 343, 283, 221, 166 (base); HRMS Found *m/z* 404.2580. $C_{24}H_{36}O_5$ requires 404.2563.

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