DABCO-Catalyzed Coupling of Aldehydes with Activated Double Bonds. 4.[1] Stereoselective Synthesis of Trisubstituted Olefins and Terpenoid Building Blocks via 2-(Hydroxyalkyl)-2-propenoic Esters

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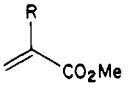
A variety of 2-(hydroxyalkyl)-2-propenoic esters **16a–g** has been prepared in high yield by DABCO-catalyzed coupling of aldehydes **14a–g** with methyl acrylate. The product esters **16a–g** are useful building blocks in syntheses which undergo regioselective and *Z*-selective S_N2' reactions with *N*-bromosuccinimide/dimethyl sulfide and *N*-chlorosuccinimide/dimethyl sulfide to furnish (*Z*)-2-(bromomethyl)-2-alkenoic esters **17a–g** and (*Z*)-2-(chloromethyl)-2-alkenoic esters **18b,c,d**, respectively. Similarly, the derived allylic acetates **21g,h** and also allylic bromide **17g** react with lithium triethylhydridoborate via mechanism S_N2' to give (*E*)-2-methyl-2-alkenoic esters **22g,h** and, respectively, 2-methylenealkanoic esters **20g**. Methyl (*Z*)-6,6-(ethylenedioxy)-2-methyl-2-heptenoate (**22h**) has been prepared as an intermediate en route to the norsesquiterpenoid ketone **23**. The allylic bromides **17d,e,f** also furnish (*Z*)-6-methyl-5-[(trimethylsilyl)methyl]-4-heptene-1,6-diol (**19a**), (*Z*)-2-methyl-3-[(trimethylsilyl)methyl]-3-octene-2,7-diol (**19e**), and (*Z*)-7-methyl-6-[(trimethylsilyl)methyl]-5-octene-1,2,7-triol (**19f**), which are terpenoid building blocks.

In recent years numerous methods have been developed for preparing α-functionalized acrylic esters **1** in response to a number of synthetic challenges, e.g., the naturally occurring α-methylene-γ-butyrolactones.[2] Among the precursors **2–13** of **1**, many are masked acrylic esters of the



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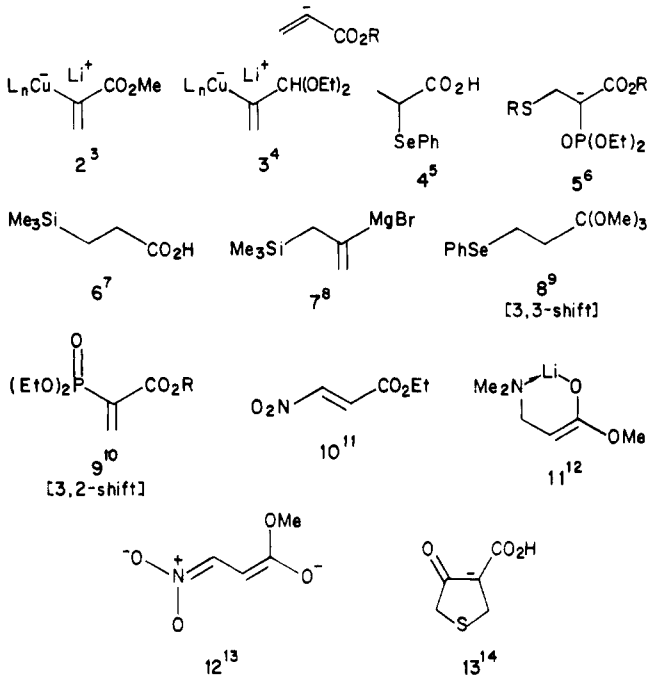
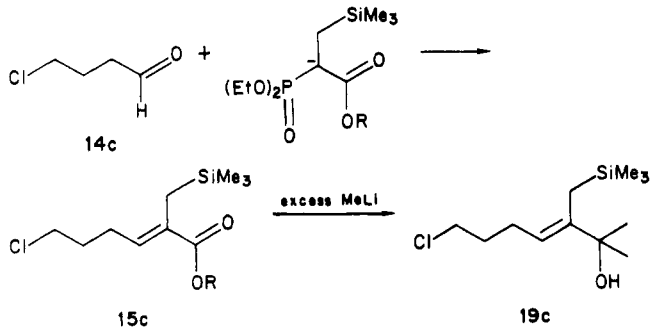
d^2 variety as shown in Scheme I. However, with more complex target molecules there are drawbacks in generating carbanionic intermediates under strongly basic conditions. Other precursors of **1** contain activating groups that must be removed subsequently.

In context with a number of ongoing synthetic efforts, we required a simple and efficient route to terpenoid building blocks such as **19c** (see Scheme II). Compound **19c** is an acid-sensitive, trisubstituted olefin with *Z* configuration. The three substituents attached to the olefinic carbons contain different functionalities and also introduce some steric crowding. The other terminus of **19c** contains a further functionality, i.e., Cl. From previous experience we knew that **19c** could be prepared from **15c** with an excess of methyllithium.[15a] Thus the synthetic problem amounted to preparing a range of functionalized acrylic esters **15** stereoselectively. We here describe two routes to **15** and **19**, namely, (i) the Horner–Wittig reaction using aldehydes **14a,b,c** and (ii) the α-functionalization of acrylic esters with aldehydes **14a–g** followed by brominative allylic rearrangement and silylation. The second approach has

Scheme I. d^2 Acrylic Ester Equivalents



Scheme II



(1) Part 3: Hoffmann, H. M. R.; Rabe, J. *Helv. Chim. Acta* **1984**, *67*, 413.
(2) Review: Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94.
(3) Marino, J. P.; Linderman, R. J. *J. Org. Chem.* **1981**, *46*, 3696.
(4) Marino, J. P.; Farina, J. S. *J. Org. Chem.* **1976**, *41*, 3213. Marino, J. P.; Floyd, D. M. *Tetrahedron Lett.* **1979**, 675. See also: Goldberg, O.; Dreiding, A. S. *Helv. Chim. Acta* **1976**, *59*, 1904.
(5) Petragnani, N.; Ferraz, H. M. C. *Synthesis* **1978**, 476.
(6) Semmelhack, M. F.; Tomesch, J. C.; Czarny, M.; Boettger, S. *J. Org. Chem.* **1978**, *43*, 1259.
(7) Fleming, I.; Goldhill, J. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1493.
(8) Nishiyama, H.; Yokoyama, H.; Narimatsu, S.; Itoh, K. *Tetrahedron Lett.* **1982**, *23*, 1267.
(9) Raucher, S.; Hwang, K. J.; Macdonald, J. E. *Tetrahedron Lett.* **1979**, *33*, 3057.
(10) Corbet, J. P.; Benezra, C. *Tetrahedron Lett.* **1979**, *41*, 4003.
(11) Patterson, J. W.; McMurry, J. E. *J. Chem. Soc. D* **1971**, 488.
(12) Yu, L. C.; Helquist, P. *J. Org. Chem.* **1981**, *46*, 4536.
(13) Seebach, D.; Henning, R.; Mukhopadhyay, T. *Chem. Ber.* **1982**, *115*, 1705.
(14) Baraldi, P. G.; Guarneri, M.; Pollini, G. P.; Simoni, D.; Barco, A.; Benetti, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2501.
(15) (a) Hoffmann, H. M. R.; Henning, R. *Helv. Chim. Acta* **1983**, *66*, 828. (b) Henning, R.; Hoffmann, H. M. R. *Tetrahedron Lett.* **1982**, *23*, 2305.

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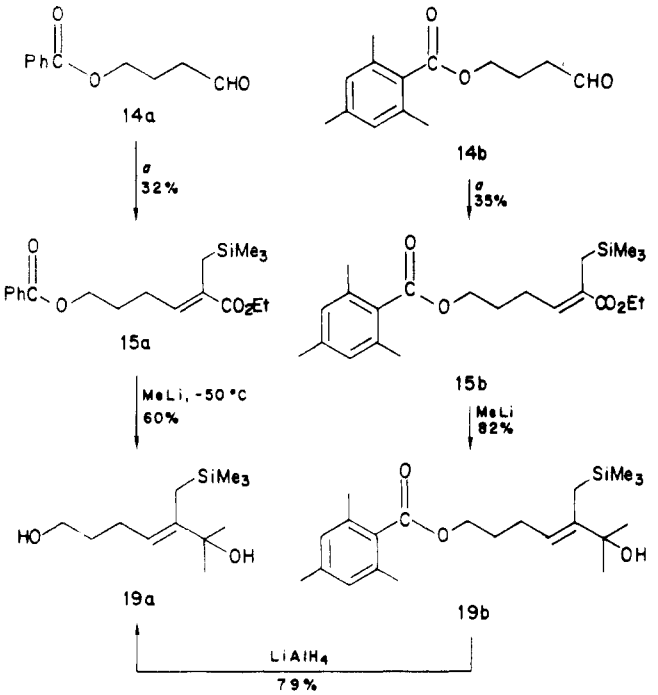
Scheme III. Horner-Wittig Route to Functionalized Acrylic Esters 15a,b and Conversion into 19a



[a] The aldehyde was added to 0 °C to the Horner reagent prepared by (i) $(EtO)_2P(O)CH_2CO_2Et$ + NaH in 1,2-dimethoxyethane; (ii) Me_3SiCH_2I, 70 °C, 4 h; (iii) NaH, 0 °C → room temperature, then 0 °C (and (iv) addition of **14a** or **14b**, 0 °C → room temperature, 16 h).

proved to be simpler and could be applied to other syntheses.

Horner–Wittig Reaction.[16] This reaction was carried out several times in one pot as follows (see Scheme III).

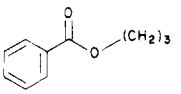
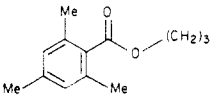
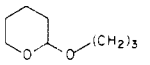
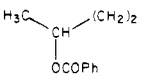
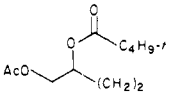
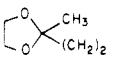
(i) Ethyl(diethoxyphosphinyl)acetate $[(EtO)_2P(O)CH_2CO_2Et]$ was deprotonated with sodium hydride, (ii) the resulting anion was alkylated with (iodomethyl)trimethylsilane (Me_3SiCH_2I), a reasonably good S_N2 alkylating agent, (iii) the resulting phosphono ester was deprotonated again with sodium hydride, and (iv) aldehydes **14a,b** were olefinated with the phosphonate anion.

Aldehyde **14a** gave (*Z*)-olefin **15a** in 32% yield and a minor amount of (*E*)-olefin (*Z*:*E* = 4:1), which was detected by ^1H NMR and removed by chromatography. The final conversion of **15a** into **19a** proceeded in 60% yield, which compares with a more favorable yield of 90% for converting **15c** into **19c**.[15a]

As a test for the resistance of the benzyloxy group in **14a** to the basic conditions of the Horner–Wittig reaction, we studied the 2,4,6-trimethylbenzoyl derivative **14b**. As expected the transformation of **14b** into the desired (*Z*)-acrylic ester **15b** was feasible (35% yield), but the *E*-configurated olefin was again formed (Z:E ~ 3:1), i.e., the Horner–Wittig reaction in its simple form is not stereocontrolled.[16] In this instance, **15b** and its *E* isomer could not be easily separated by column chromatography, because the difference in polarity was less. Addition of methyllithium to **15b** and its *E* isomer at −50 °C gave **19b** in 82% yield. The removal of the protecting group in **19b** was not possible with an excess of methyllithium as in **15a** but required an additional step with $LiAlH_4$ (**19b** → **19a**). Thus we had obtained the desired olefin **19a** from aldehyde **14a** in 19% overall yield and from aldehyde **14b** in 23% overall yield.

Since these experiments were reproduced several times without an improvement in yield, it is clear that there are at least two drawbacks of the Horner–Wittig route: (i) Under the basic conditions of the reaction, butyraldehydes, which are functionalized at C4, react less readily than simple butanal and are more prone to decomposition. (ii) The reaction is not stereocontrolled. A second approach to **19** is described below.

Table I. 2-(Hydroxyalkyl)-2-propenoic Esters 16 via DABCO-Catalyzed Coupling of Aldehydes 14 with Methyl Acrylate

	14 and 16 R	reacn time, days	yield, %
a		7	95
b		7	87
c	$Cl(CH_2)_3$	7	60
d		7	87
e		8	92
f		7	89
g	$CH_3(CH_2)_2$	7	85
h		10	63

α-Functionalization of Acrylic Esters and Stereoselective Allylic Rearrangement to (*Z*)-2-(Halomethyl)-2-alkenoic Esters. The protected 4-hydroxybutanals **14a,b** and other aldehydes can be coupled efficiently with methyl acrylate in the presence of DABCO (1,4-diazabicyclo[2.2.2]octane) to give, without loss of material, a variety of 2-(hydroxyalkyl)-2-propenoic esters (Table I). Structurally more simple aliphatic aldehydes, and also aromatic and heteroaromatic aldehydes, have been coupled with methyl acrylate in similar fashion and in similar yield.[1,17] The reaction is remarkably clean. After evaporation of the excess of methyl acrylate no polymeric material has been detected.

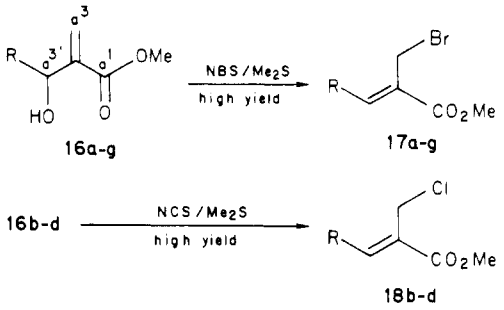
The resulting 3-hydroxy-2-methylenealkanoic esters **16** offer three electrophilic sites for further bond formation: i.e., they are $a^1a^3a^{3'}$ components, using the Seebach nomenclature,[18] and they are therefore valuable intermediates in synthesis. As an illustration, the seven esters **16a–g** have been submitted to brominative allylic rearrangement with

(16) Reviews: (a) Boutagy, J.; Thomas, R. *Chem. Rev.* **1974**, *74*, 87. (b) Wadsworth, W. S. *Org. React. (N.Y.)* **1977**, *25*, 73. Recent stereoselective approaches: Cornish, C. A.; Warren, S. *Tetrahedron Lett.* **1983**, *24*, 2603. Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405. Note that a *Z*/*E* differentiation is easier for disubstituted olefins (greater diastereomeric differences) than for trisubstituted olefins.

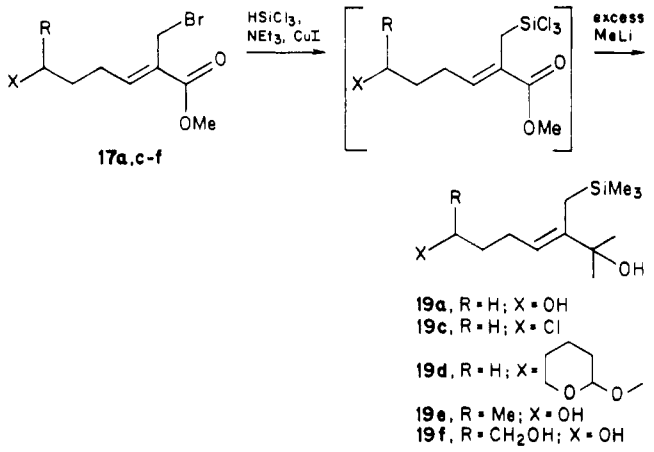
(17) Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 795. Rabe, J.; Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 796 and references cited therein. Hoffmann, H. M. R.; Poly, W.; Grundke, C., unpublished work.

(18) Seebach, D.; Knochel, P. *Helv. Chim. Acta* **1984**, *67*, 261.

Scheme IV. Regioselective and *Z* Selective Allylic Rearrangement of 2-(Hydroxyalkyl)-2-propenoic Esters 16 to (*Z*)-2-(Halomethyl)-2-alkenoic Esters 17 and 18



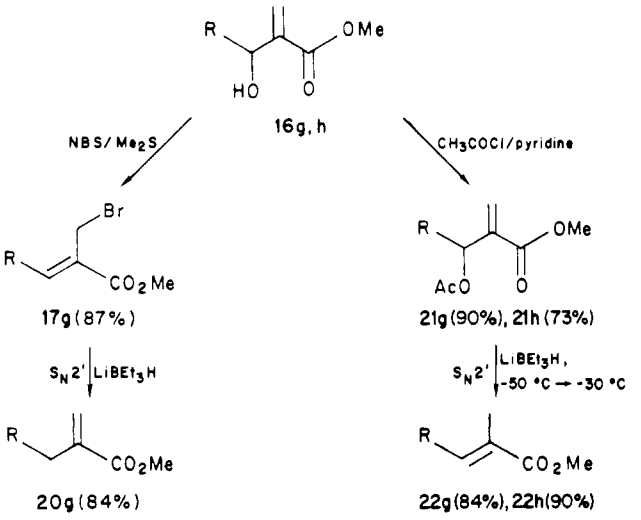
Scheme V. A New Route to Functionalized Allylsilanes 19



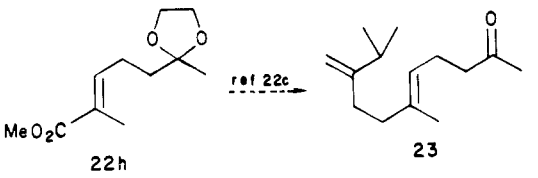
N-bromosuccinimide/dimethyl sulfide[1,17,19] to give, with clean allylic transposition[20,21] and *Z* selectivity, (*Z*)-2-(bromomethyl)-2-alkenoic esters **17a–g** (Scheme IV). No *E* isomers of **17a–g** were detected in the ^1H NMR spectrum. The 2-(hydroxyalkyl)-2-propenoic esters **16b,c,d** were also allowed to react with *N*-chlorosuccinimide/dimethyl sulfide to afford (*Z*)-2-(chloromethyl)-2-alkenoic esters **18b,c,d** in high yield. Again, chlorination proceeded regioselectively, i.e., via an S_N2' reaction, and *Z* selectively. Apparently, the allylic rearrangement has a considerable thermodynamic driving force, because 2-(hydroxyalkyl)-acrylic esters **16a–g**, apart from being reactive secondary allylic alcohols, are also good Michael acceptors (a^1a^3 components). The resulting allylic bromides **17a–g** are trisubstituted olefins with sharply differing and therefore useful functionalities.

The transformation of **17** into the desired allylsilanes **19** was not trivial and required the replacement of an allylic bromine by a trimethylsilyl group in a direct S_N2 reaction. The transformation was accomplished by (a) treatment of **17** with $HSiCl_3$, NEt_3, and CuI[8] to introduce the trichlorosilyl anion and (b) quenching the intermediate allyltrichlorosilane with 8 equiv of methyllithium to give, in a highly convergent step, the desired allylsilanes **19** (Scheme V). Although this one-pot reaction was not optimized and proceeded in only 42% yield, the overall yield for the sequence aldehydes **14a,e → 16a,e → 17a,e → 19a,e** amounted to 37% as compared with 19–23% yield for the conventional phosphonate anion reaction (see Scheme III). The new route to **19** is stereocontrolled,

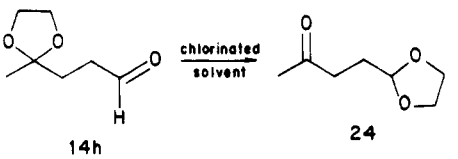
Scheme VI



Scheme VII



Scheme VIII



proceeds under mild conditions, tolerates a great deal of further functionalization (cf. preparation of **19f**), and uses simple starting materials that are coupled in the first step without recourse to esoteric activating groups and organometallic conditions.

Stereoselective Conversion of 2-(Hydroxyalkyl)-2-propenoic Esters into 2-Methylenealkanoic Esters and (*Z*)-2-Methyl-2-alkenoic Esters. The propensity of 2-(hydroxyalkyl)-2-propenoic esters toward stereoselective S_N2' reactions allows other synthetic transformations in high yields (Scheme VI). Thus, with lithium triethylhydridoborate $LiBEt_3H$, which is a powerful nucleophile toward saturated carbon, the allylic bromide **17g** has been smoothly converted into **20g**. The sequence butanal **14g → 16g → 17g → 20g** corresponding to an α-alkylation of acrylic ester by an *n*-butyl group proceeds in 64% overall yield. α-Alkylated acrylic esters such as **20g** cannot be obtained directly from acrylic ester and the alkyl halide, i.e., *n*-butyl halide, because the DABCO catalyst is deactivated by quaternization.

To further illustrate the synthetic utility of DABCO-catalyzed couplings we chose the C_{14} terpenoid ketone **23** as a target (Scheme VII). **23** is a constituent of *Costus* root oil and presumably is a metabolite of the irones, olfactory components of the violet.[22a] A general difficulty in the synthesis of terpenes such as **23** is the stereoselective construction of a precursor with the correct *E* configuration of the C-5–C-6 double bond. **23** and **22h** are also a γ,δ-

(19) Cf. also: Ameer, F.; Drewes, S. E.; Emslie N. D.; Kaye, P. T.; Mann, R. L. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2293.
(20) Magid, R. M. *Tetrahedron* **1980**, *36*, 1901.
(21) Katz, H. E.; Starnes, W. H., Jr. *J. Org. Chem.* **1984**, *49*, 2758 and references cited therein.

(22) (a) Maurer, B.; Ohloff, G. *Helv. Chim. Acta* **1977**, *60*, 2191. (b) Dubs, P.; Schenk, H. P. *Helv. Chim. Acta* **1978**, *61*, 984. (c) Morizur, J. P.; Tortajada, J. *Bull. Soc. Chim. Fr.* **1983**, 175. See also: Rohela, L. C.; Anand, C. *Indian J. Chem. Sect. B* **1978**, *16B*, 1121.

unsaturated carbonyl compounds, a stereocontrolled synthesis of which is usually attempted by the Claisen rearrangement,[23] by the Wittig reaction and its variants[16] and by acetylene chemistry.[24] In the first synthesis of **23** the central double bond was constructed by a Carroll reaction, i.e., a modified Claisen rearrangement, and the *E*:*Z* ratio amounted to 2:1.[22a] The second synthesis (via a Wittig reaction) gave *E*:*Z* = 1.5:1[22b] and the third synthesis (via a Norrish I photochemical cleavage of 1-methyl-2-cyclopentanone-1-carboxylic acid ester) gave *E*:*Z* = 1.7:1.[22c]

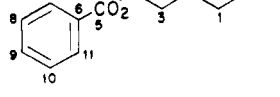
The coupling of protected levulinic aldehyde **14h** with methyl acrylate in the presence of DABCO gave **16h** in 63% yield. Under these conditions the sensitive aldehyde **14h** did not rearrange to the corresponding acetal ketone **24** (Scheme VIII), as it does in faintly acidic solvents. A standard acetylation of **16g,h** afforded the allylic acetates **21g,h**, which were reduced with $LiBEt_3H$ to give the (*E*)-2-methyl-2-alkenoic esters **22g,h** stereoselectively and with clean allylic rearrangement (Scheme VI). The methoxycarbonyl group was not attacked. Since the transformation of **22h** into **23** has already been described,[22c] the preparation of **22h** completes an *E* selective synthesis of **23**.

Conclusions and Summary. Trisubstituted alkenes with the carboxyl group trans to the chain R as in **17** and **18** are now readily available. **17** and **18** and their precursor **16** bear functionality that is valuable for further elaboration to complex molecules. For example, nucleophilic substitutions (S_N2 and S_N2') have been carried out. An adjustment of the oxidation level (conversion of ester into alcohol, aldehyde) is equally feasible. Further functionality has been introduced via the appendage of the aldehyde component **14**. Compounds **17** are versatile intermediates, for example, for the synthesis of terpenoids and as $a^1a^3a^{3'}$ components for the preparation of α-methylene-γ-butyrolactones.[2]

Experimental Section

^1H NMR spectra were recorded on a Bruker WH 90 spectrometer and ^{13}C NMR spectra on a WP 80 Bruker spectrometer. ^{13}C NMR shifts are listed along the sequence of numbering the carbon atoms.

Preparation of Functionalized Aldehydes 14a–h. 3-Formylpropyl Benzoate (14a). (a) 4-Hydroxybutyl Benzoate (25). 1,4-Butanediol (90 g, 1 mol) and pyridine (87 g, 1.1 mol) were dissolved in $CHCl_3$ (150 mL) and cooled to 0 °C. Benzoyl



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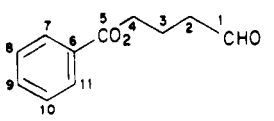
chloride (115 mL, 1 mol) in $CHCl_3$ (80 mL) was dropped in slowly, the resulting solution being stirred overnight, diluted with ether (400 mL), and washed with water (3 × 100 mL) and aqueous $NaHCO_3$ (2 × 100 mL). The organic phase was dried ($MgSO_4$), and the solvent was removed to leave an oil, which was distilled in vacuo, giving **25** (78.5 g, 41%): IR ($CHCl_3$) 3620 (w, OH), 3450 (br, OH), 3000 (w), 2950 (m), 1715 (s, C=O), 1600 (w, Ar), 1580 (Ar), 1450 (m), 1380 (w), 1315 (m), 1280 (s), 1180 (m), 1120 (m), 1070, 1025 (m) cm^{-1}; mass spectrum (10 eV, 25 °C), *m*/*z* (relative intensity) 194 (M^+, 2), 166 (2), 123 (46), 122 (15), 105 (100), 77 (67), 71 (17), 51 (25), 42 (30); 90-MHz ^1H NMR ($CDCl_3$) δ 1.55–2.00 (m, 4 H, 2 CH_2), 3.7 (t, *J* = 6 Hz, 2 H, CH_2O), 4.33 (t, *J* = 6.5 Hz, 2 H, CH_2OC=O), 4.40 (s, 1 H, OH), 7.30–7.60 (m, 3 H, Ar H), 7.95–8.1 (dd, 2 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 64.97 (t, C-1), 25.32 (t, C-2), 29.11 (t, C-3), 62.28 (t, C-4), 166.87 (s, C-5), 130.34 (s, C-6), 132.97, 129.52, 128.40 (d, C-7–C-11).

(**b**) Pyridinium chlorochromate (68 g, 0.32 mol, 1.2 equiv) in absolute CH_2Cl_2 (200 mL) was stirred vigorously in a three-necked flask (1 L) which was fitted with a stirrer and reflux condenser and kept under nitrogen. **25** (50 g, 0.26 mol, 1 equiv) in CH_2Cl_2



14a

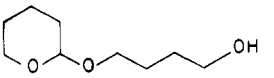
(50 mL) was added rapidly. The solution turned black quickly and started to boil. After being stirred for 2 h, the solid was allowed to settle, and the supernatant solution was decanted. The tar-like residue was extracted with ether (4 × 200 mL), the brown, combined organic phase was pressed through a column of silica gel (40 cm, ϕ = 3 cm), and the solvent was removed to leave **14a** (42 g, 85%): IR ($CHCl_3$) 3000 (w), 2960 (w), 1710 (vs, CO_2R, CHO), 1595 (w), 1575 (w), 1445 (m), 1410 (w), 1270 (s, C–O), 1110 (s), 700 (s) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 2.13 (m, *J* = 7 Hz, *J* = 6 Hz, 2 H, CH_2CH_2CHO), 2.65 (dt, *J* = 7 Hz, *J* = 1.5 Hz, 2 H, CH_2CHO), 4.36 (t, *J* = 6 Hz, 2 H, $COOCH_2CH_2$), 7.47 and 8.03 (m, 3 H and 2 H, Ar), 9.82 (t, *J* = 1.5 Hz, 1 H, CHO); ^{13}C NMR ($CDCl_3$) δ 201.46 (s, C-1), 40.41 (dt, C-2), 21.57 (t, C-3), 64.12 (t, C-4), 166.35 (s, C-5), 130.31 (s, C-6), 133.06, 129.58, 128.49 (d, C-7–C-11); mass spectrum (70 eV) *m*/*z* (relative intensity) 192 (M^+, 0), 164 (11, M – CO), 123 (45), 122 (34), 106 (13), 105 (100), 77 (92), 51 (50), 50 (33).

3-Formylpropyl 2,4,6-Trimethylbenzoate (14b). (a) 4-Hydroxybutyl 2,4,6-Trimethylbenzoate (26). 1,4-Butanediol (150 g, 1.67 mol) was dissolved in $CHCl_3$ (150 mL) and pyridine (80 mL), and 2,4,6-trimethylbenzoyl chloride (67 g, 0.37 mol) in $CHCl_3$ (100 mL) was dropped in at 0 °C. The solution was stirred overnight, diluted with ether (500 mL), and shaken with a solution (4 × 200 mL) of aqueous sodium chloride. The aqueous phase was extracted with ether (2 × 100 mL), the combined organic phase was dried ($MgSO_4$), and the solvent was removed to leave an oil, which was subjected to fractional distillation in vacuo, giving **26** (65.5 g, 75%): IR ($CHCl_3$) 3620 (w, OH), 3450 (br w, OH), 3000 (w), 2950 (m), 2880 (w), 1715 (vs, C=O), 1610 (m), 1560 (w), 1445 (m), 1380 (m), 1270 (s, C–O), 1170 (s), 1080 (s), 1035 (m), 850 (m) cm^{-1}; 60-MHz ^1H NMR ($CDCl_3$) δ 1.62–1.91 (m, 4 H, 2 CH_2), 2.31 (s, 9 H, 3 CH_3), 2.93 (s, 1 H, OH), 3.64 (t, *J* = 6 Hz, 2 H, CH_2OH), 4.36 (t, *J* = 6 Hz, 2 H, CH_2OC=O), 6.90 (s, 2 H Ar H); mass spectrum (10 eV), *m*/*z* (relative intensity) 236 (M^+, 19), 200 (4), 198 (4), 164 (9), 163 (6), 147 (56), 46 (100), 119 (16), 91 (6).

(**b**) The oxidation was carried out as described for the preparation of **14a**. **26** (23.6 g, 0.1 mol) was treated with pyridinium chlorochromate (26 g, 0.12 mol) in CH_2Cl_2 (200 mL), and the product was purified by chromatography to give **14b** (18.5 g, 79%): IR ($CHCl_3$) 3010 (w), 2960 (w), 2920 (w), 1720 (vs CO_2R, CHO), 1610 (m), 1580 (w), 1440 (w), 1380 (w), 1270 (s, C–O), 1170 (s), 1080 (s), 850 (m) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.9–2.2 (m, 2 H, $CH_2CH_2CH_2$), 2.29 (s, 9 H, 3 CH_3), 2.4–2.7 (dt, *J* = 1 Hz, *J* = 7 Hz, 2 H, CH_2CHO), 4.33 (t, *J* = 7 Hz, 2 H, CH_2O), 6.85 (s, 2 H, Ar H), 9.78 (t, *J* = 1 Hz, 1 H, CHO); mass spectrum (10 eV), *m*/*z* (relative intensity) 234 (M^+, 12), 206 (5), 164 (14), 147 (85), 146 (100), 119 (21), 91 (12), 71 (49).

4-Chlorobutanal (14c) was prepared as described.[15a]

4-(Tetrahydropyranyloxy)butanal (14d). (**a**) Dihydropyran (23 g, 0.27 mol) was added to a well-stirred solution of 1,4-butanediol (37 g, 0.41 mol) containing a few drops of hydrochloric acid. The temperature rose to ca. 40 °C. After 3 h ether (40 mL)



27

was added, and the mixture was shaken thoroughly with 50 mL of 10% aqueous KOH. The aqueous phase was reextracted with

(23) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227. Bennett, G. B. *Synthesis* **1977**, 589. Rhoads, S. J.; Raulins, N. R. *Org. React. (N.Y.)* **1975**, *22*, 1.

(24) (a) Marfat, A.; McGuirk, P. R.; Helquist, P. *J. Org. Chem.* **1979**, *44*, 3888 and references cited therein. (b) Baker, R.; Billington, D. C.; Ekanayake, N. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1387. (c) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841.

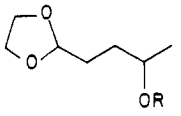
(25) Büchi, G.; Wüest, H. *J. Org. Chem.* **1969**, *34*, 1122.

(26) Oku, A.; Harada, T.; Kita, K. *Tetrahedron Lett.* **1982**, *23*, 681.

ether (50 mL), and the combined organic phase was dried ($MgSO_4$). After removal of the solvent the residue was fractionally distilled to give **27** (20 g, 42%): IR (CCl_4) 3640 (m, OH), 3460 (m, OH), 1120 (s, C–O), 1035 (s, C–O), 1025 (s), 905 (m), 870 (m) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.3–1.9 (m, 10 H, 5 CH_2), 2.95 (br s, 1 H, OH), 3.3–3.9 (m, 6 H, 3 OCH_2), 4.6 (br s, 1 H, OCHO).

(b) 27 (39 g, 0.224 mol) in CH_2Cl_2 (60 mL) was added quickly to a suspension of pyridinium chlorochromate (75 g, 0.35 mol) in absolute CH_2Cl_2 (450 mL) containing anhydrous sodium acetate (5.4 g). The mixture quickly turned black, and after 1.5 h it was diluted with absolute ether (450 mL). The supernatant solution was decanted from the tarry residue, which was washed with ether (3 × 150 mL). The combined organic phase was filtered through basic alumina (activity II–III), and the solvent was removed to give **14d** (32 g, 82%): IR (CCl_4) 2800 (w), 2720 (w), 1730 (s, C=O), 1035 (s, C–O), 1020 (s, C–O) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.3–2.2 (m, 8 H, 4 CH_2), 2.50 (t, J = 7.5 Hz, 2 H, CH_2C=O), 3.2–4.1 (m, 4 H, 2 CH_2O), 4.53 (br s, 1 H, OCHO), 9.73 (t, J = 1.5 Hz, 1 H, CHO).

3-Formyl-1-methylpropyl Benzoate (14e). (a) 2-(3-Hydroxybutyl)-1,3-dioxolane (28). 2-(2-Bromoethyl)-1,3-dioxolane (147 g, 0.8 mol) in tetrahydrofuran (400 mL) was slowly dropped into a flame-dried flask containing magnesium turnings (19 g, 0.78 mol) and a catalytic amount of iodine (*Caution*: the reaction may start suddenly). At a temperature of 25 °C inside

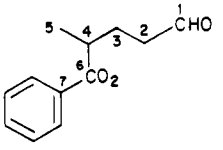


28, R = H
29, R = C(O)Ph

the flask, the rest of the solution of the alkyl bromide was dropped in and then acetaldehyde (45 mL, 0.8 mol) added. The mixture was stirred for a further 3 h. It was poured into 400 mL of a 10% solution of aqueous NH_4Cl and extracted continuously for 16 h with ether. The ether was distilled off, and the residue was fractionally distilled giving **28** (43 g, 36%): IR ($CHCl_3$) 3620 (w, OH), 3500 (br w, OH), 2960 (s), 2930 (m), 2880 (s), 1450 (w), 1400 (w), 1370 (m), 1215 (m), 1140 (s, C–O), 1030 (m), 970 (m), 940 (w), 925 (w) cm^{-1}; 90-MHz ^1H NMR (Me_2SO-d_6) δ 1.03 (d, J = 6 Hz, 3 H, CH_3), 1.25–1.74 (m, 4 H, CH_2CH_2), 3.47–3.81 (m, J = 6 Hz, 1 H, CH_3CHOH), 3.71–3.90 (m, 4 H, OCH_2CH_2O), 4.38 (d, J = 5 Hz, 1 H, OH), 4.76 (t, J = 5 Hz, 1 H, OCHO); mass spectrum (70 eV), m/z (relative intensity) 146 (M^+, 3), 105 (1), 73 (100), 45 (42).

(b) Benzoic Ester 29. Alcohol **28** (8.8 g, 60 mmol) and absolute pyridine (20 mL) were dissolved in absolute $CHCl_3$ (8 mL) and 4-(dimethylamino)pyridine (0.8 g, 6 mmol) was added. Benzoyl chloride (12.8 g, 90 mmol) in $CHCl_3$ (12 mL) was slowly added at 0 °C. The solution was stirred for 15 h, poured onto ice–water, and extracted with ether (100 mL). The ether layer was washed with 50 mL of aqueous $NaHCO_3$, then with 0.5 N hydrochloric acid, and saturated aqueous NaCl solution and dried ($MgSO_4$). After evaporation of the solvent, **29** (13 g, 86%) was obtained cleanly: IR ($CHCl_3$) 2980 (w), 2890 (w), 1790 (w), 1710 (vs, C=O), 1600 (w), 1585 (w), 1450 (m), 1315 (m), 1280 (s, C–O), 1110 (m), 710 (s) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.36 (d, J = 6.5 Hz, 3 H, CH_3), 2.78–2.86 (m, 4 H, CH_2CH_2), 4.66–5.09 (m, 4 H, OCH_2CH_2O), 5.85–5.97 (dt, 1 H, OCHO), 6.10–6.34 (m, J = 6.5 Hz, CHOCO), 7.25–7.70 (m, 3 H, Ar H), 7.99–8.23 (m, 2 H, Ar H); mass spectrum (10 eV), m/z (relative intensity) 250 (M^+, 1), 198 (1), 185 (1), 147 (6), 105 (28), 77 (25), 74 (100).

(c) 29 (13 g, 52 mmol) was refluxed with 0.5 N hydrochloric acid (40 mL) for 0.5 h. After cooling, the emulsion was extracted with CH_2Cl_2 (4 × 40 mL). The combined organic phase was

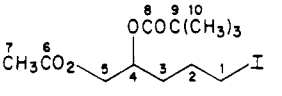


14e

washed with aqueous $NaHCO_3$ (40 mL) and a saturated solution of NaCl. After removal of the solvent this operation was repeated twice giving **14e** (10 g, 93%): IR ($CHCl_3$) 3020 (w), 2970 (w), 1790 (w), 1715 (vs, C=O), 1600 (w), 1585 (w), 1450 (w), 1315 (m), 1275 (s, C–O), 1110 (m), 1090 (w), 1070 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.36 (d, J = 6 Hz, 3 H, CH_3), 1.91–2.15 (m, J = 1 Hz, J = 7 Hz, 2 H, CH_2CH_2CHO), 2.51–2.66 (dt, J = 1 Hz, J = 7 Hz, 2 H, CH_2CHO), 5.20 (m, J = 6 Hz, 1 H, CHOCO), 7.31–7.65 (m, 3 H, Ar H), 7.95–8.18 (m, 2 H, Ar H), 8.69 (t, J = 1 Hz, CHO); ^{13}C NMR ($CDCl_3$) δ 201.10 (d, C-1), 39.83 (dt (allylic coupling), C-2), 28.29 (t, C-3), 70.73 (d, C-4), 19.93 (q, C-5), 165.84 (s, C-6), 130.52 (s, C-7) [129.52, 128.40, 132.90 (d, Ar C)]; mass spectrum (70 eV), m/z (relative intensity) 206 (M^+, 0), 178 (5), 161 (1), 123 (47), 105 (100), 77 (73), 55 (18), 51 (29).

Aldehyde 14f. (a) Tetrahydrofurfuryl Acetate (30). Tetrahydrofurfuryl alcohol (102 g, 1 mol) and pyridine (150 mL) in $CHCl_3$ (150 mL) were cooled to 0 °C, and acetyl chloride (78 mL, 1.1 mol) was slowly stirred in under N_2. The solution was stirred for 2 h at room temperature and poured into ice–water (1 L). The organic phase was separated, and the aqueous phase was washed with $CHCl_3$ (100 mL). The combined organic phase was washed with 10% aqueous hydrochloric acid and dried ($MgSO_4$). On distillation [80 °C (water pump)] **30** (110 g, 86%) was isolated: IR ($CHCl_3$) 3000 (w), 2980 (w), 2940 (w), 1735 (vs, C=O), 1370 (m), 1230 (s, C–O), 1090 (m), 1040 (m) cm^{-1}; 60-MHz ^1H NMR ($CDCl_3$) δ 1.85–2.05 (m, 4 H, CH_2CH_2), 2.10 (s, 3 H, CH_3C=O), 3.75–4.24 (m, 5 H, 2 CH_2O and HCO).

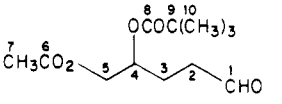
(b) Iodo Diester 31. 30 (72 g, 0.5 mol) was stirred with a solution of dried NaI (90 g, 0.6 mol) in absolute acetonitrile (400 mL) containing a spatula tip of copper powder, the reaction mixture being kept under nitrogen. Trimethylacetyl chloride



31

(60 g, 0.5 mol) in absolute acetonitrile (100 mL) was slowly dropped in at 0 °C, and the mixture was stirred for 24 h at room temperature. After addition of water (1.5 L) the product settled and was separated. The acetonitrile–water mixture was extracted with pentane (4 × 150 mL), and the pentane phase was combined with the product layer. The resulting organic layer was shaken with a dilute solution of aqueous $NaHSO_3$ and dried ($MgSO_4$). The solvent was evaporated, and the remaining ester **30** was removed with an oil pump at 40 °C, giving **31** (130 g, 73%). The product was sufficiently clean for the following reaction: IR ($CHCl_3$) 2990 (m), 1810 (w), 1730 (vs, C=O), 1480 (m), 1460 (w), 1400 (w), 1370 (m), 1280 (m), 1230 (s, C–O), 1160 (s, C–O), 1040 (m), 1010 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.20 (s, 9 H, CMe_3), 1.6–1.9 (m, 4 H, CH_2CH_2), 2.05 (s, 3 H, CH_3C=O), 3.20 (t, J = 6 Hz, 2 H, CH_2I), 3.90–4.33 (AB part of an ABX system, 2 H, CH_2O), 5.00–5.20 (X part of an ABX system, 1 H, HCO); ^{13}C NMR ($CDCl_3$) δ 5.72 (t, C-1), 31.59 (t, C-2), 28.93 (t, C-3), 69.85 (d, C-4), 64.71 (t, C-5), 170.23 (s, C-6), 20.60 (q, C-7), 177.56 (s, C-8), 38.71 (s, C-9), 27.05 (q, C-10); mass spectrum (10 eV), m/z (relative intensity) 357 (M^+, 0), 255 (3), 254 (1), 229 (3), 212 (5), 195 (5), 169 (6), 127 (16), 85 (34), 71 (14), 67 (27), 57 (100).

(c) Absolute dimethyl sulfoxide (150 mL) and dried $NaHCO_3$ (15 g) were heated to 80–90 °C under nitrogen in a preheated oil bath. **31** (15 g, 42 mmol) was added quickly. The mixture was



14f

stirred for 10 min and poured onto ice (100 g). The resulting mixture was diluted with water (200 mL) and extracted with ether (3 × 100 mL). The ether layer was washed with aqueous NaCl and dried ($MgSO_4$), and the solvent was removed. After chromatography on silica gel (2:1 light petroleum/ether), aldehyde **14f** (3–4 g, 30–40%) was isolated: IR ($CHCl_3$) 2980 (s), 2940 (m), 2870 (w), 1730 (br vs, C=O), 1480 (m), 1460 (m), 1400 (m), 1370 (s, C–O), 1280 (s, C–O), 1155 (vs) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.20 (s, 9 H, CMe_3), 1.90–2.10 (m, 2 H, CH_2CHO), 2.05 (s, 3 H, CH_3C=O), 2.30–2.45 (m, 2 H, CH_2CH_2CHO), 3.95–4.35 (AB part of an ABX system, 2 H, CH_2O), 5.00–5.20 (X part of an ABX

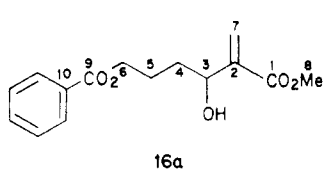
system, 1 H, HCO), 8.76 (t, J = 1 Hz, 1 H, CHO); ^{13}C NMR ($CDCl_3$) δ 200.58 (d, C-1), 39.47 (dt, C-2), 23.32 (t, C-3), 70.47 (d, C-4), 64.67 (t, C-5), 173.99 (s, C-6), 20.47 (q, C-7), 177.53 (s, C-8), 38.50 (s, C-9), 27.08 (q, C-10); mass spectrum (70 eV), m/z (relative intensity) 244 (M^+, 0), 159 (1), 143 (3), 117 (2), 114 (3), 85 (30), 57 (100), 43 (50).

4,4-(Ethylenedioxy)pentanal (14h).[27] Pyridinium chlorochromate (23 g, 0.107 mol) and anhydrous sodium acetate (4 g, 0.05 mol) were suspended in absolute CH_2Cl_2 (200 mL). 4,4-(Ethylenedioxy)-1-pentanol (11.5 g, 0.78 mol) in CH_2Cl_2 (50 mL) was added at once. The solution, which turned black rapidly, was stirred for 1.5 h and decanted from the tarry residue, which was extracted with ether (3 × 150 mL). The combined organic phase was sucked through a column of basic alumina (activity II–III), and the solvent was removed to leave acid-sensitive **14h** (9.5 g, 84%), which was used directly for the next reaction: 60-MHz ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 3 H, CH_3), 1.67–2.20 (m, 4 H, CH_2CH_2CHO), 3.50 (s, 4 H, OCH_2CH_2O), 9.43 (s, 1 H, CHO).

Horner–Wittig Reactions. 6-(Benzoyloxy)-2-[(trimethylsilyl)methyl]-2-hexenoic Acid, Ethyl Ester (15a). Ethyl (diethoxyphosphinyl)acetate (11.2 g, 9.9 mL, 50 mmol) in absolute 1,2-dimethoxyethane (DME) (15 mL) was dropped (at 0 °C and under N_2) in 75% NaH (1.76 g, 55 mmol) and stirred for 0.5 h. (Iodomethyl)trimethylsilane (12 g, 56 mmol) in DME (20 mL) was added, and the mixture was heated to 70 °C for 3 h. After the mixture was cooled to 0 °C, NaH (55 mmol) was added again in portions, and the strongly foaming solution was stirred for 2 h. **14a** (9 g, 50 mmol) in DME (20 mL) was added at 0 °C, and the resulting mixture was allowed to reach room temperature overnight. It was poured into ice–water and extracted with pentane (3 × 150 mL). The organic phase was dried ($MgSO_4$), and the solvent was removed to leave crude **15a**, which was purified by chromatography on alumina (Brockmann activity II–III, 4:1 eluent pentane/ethyl acetate): yield, 5.3 g (31%); IR ($CHCl_3$) 2940 (m), 1700 (vs, C=O), 1630 (w), 1595 (w), 1575 (w), 1440 (m), 1360 (w), 1310 (m), 1270 (vs, C–O), 1240 (s, Si–C), 1170 (m), 1110 (s), 1060 (m), 1020 (m), 845 (s, Si–C) cm^{-1}; 90-MHz ^{1}H NMR (Me_4Si was added afterwards) ($CDCl_3$) δ −0.01 (s, 9 H, Me_3Si), 1.29 (t, J = 7 Hz, 3 H, $CO_2CH_2CH_3$), 1.82 (s, 2 H, CH_2Si), 1.9–2.4 (m, 4 H, CH_2), 4.16 (q, J = 7 Hz, 2 H, OCH_2CH_3), 4.35 (t, J = 6 Hz, 2 H, $PhCOOCH_2$), 6.64 (t, J = 7 Hz, 1 H, HC=C), 7.4–7.6 (m, 3 H, Ar), 7.95–8.1 (dd, 2 H, Ar); mass spectrum (10 eV), m/z (relative intensity) 348 (M^+, 1), 333 (4), 271 (3), 227 (3), 216 (12), 195 (33), 157 (27), 150 (29), 105 (100), 85 (55), 77 (89), 73 (75).

6-[(2,4,6-Trimethylbenzoyl)oxy]-2-[(trimethylsilyl)methyl]-2-hexenoic Acid, Ethyl Ester (15b). 14b (11.7 g, 50 mmol) was subjected to the Horner–Wittig sequence as described for **14a**, giving 6.8 g (35%) of **15b** (Z:E = 3:1): IR ($CHCl_3$) 2940 (m), 2910 (m), 1710 (vs, C=O), 1600 (m), 1570 (w), 1260 (s, C–O), 1160 (m), 1080 (m), 845 (m, Si–C) cm^{-1}; 90-MHz ^{1}H NMR (Me_4Si was added afterwards; chemical shifts in square brackets refer to minor E isomer) δ 0.00 (s, 9 H, $SiMe_3$), 1.30 (t, J = 7 Hz, 3 H, CH_3CH_2) [1.27 (t, J = 7 Hz, 3 H, CH_3CH_2)], 1.72–1.95 (m, 2 H, $CH_2CH_2CH_2$), 1.79 (s, 2 H, CH_2Si), 2.15–2.4 (m, 2 H, CH_2CH=C), 2.3 (s, 9 H, 3 CH_3), 4.29 (q, J = 7 Hz, 2 H, OCH_2CH_3) [4.28 (q, J = 7 Hz, 2 H, OCH_2CH_3)], 4.34 (t, J = 7 Hz, 2 H, CH_2OC=O) [5.69 (t, J = 6.5 Hz, 1 H, HC=C)], 6.61 (t, J = 6.5 Hz, 1 H, HC=C), 6.95 (s, 2 H, Ar H); mass spectrum (70 eV), m/z (relative intensity) 390 (M^+, 1) 375 (1), 227 (2), 221 (3), 185 (15), 154 (11), 147 (100), 146 (43), 119 (26), 91 (24), 73 (46).

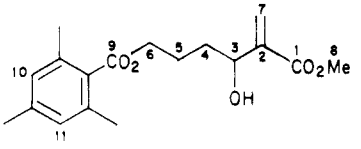
6-(Benzoyloxy)-3-hydroxy-2-methylenehexanoic Acid, Methyl Ester (16a). Aldehyde **14a** (0.1 mol, 19.2 g) was mixed with methyl acrylate (0.15 mol, 13 g, 14 mL), and DABCO (1,4-diazabicyclo[2.2.2]octane) (1.6 g, 0.015 mol) was dissolved in the resulting solution. The mixture was allowed to stand at room



16a

temperature until **14a** had disappeared (ca. 7 days). The excess of the methyl acrylate was removed on a Rotavap, and the residue was taken up in diethyl ether (100 mL) and washed with 10% hydrochloric acid (50 mL). The ether phase was washed with water and dried ($MgSO_4$), and the solvent was removed to leave 26.4 g (95%) of spectroscopically pure **16a**: IR ($CHCl_3$) 3500 (br w, OH), 3010 (w), 2970 (w), 1700 (vs, C=O), 1620 (w, C=C), 1595 (w), 1575 (w), 1440 (m), 1430 (m), 1310 (s), 1270 (s, C–O), 1150 (m), 1110 (s, C–O), 1090 (m), 1060 (m), 1020 (m), 950 (m), 810 (w), cm^{-1}; 90-MHz ^{1}H NMR ($CDCl_3$) δ 1.68–2.02 (m, 4 H, CH_2CH_2), 2.90 (br s, 1 H, OH), 3.76 (s, 3 H, CH_3O), 4.25–4.55 (m, 3 H, OCH and OCH_2), 5.84 (t, J = 1 Hz, 1 H, HC=C), 6.24 (s, 1 H, HC=C), 7.32–7.60 (m, 3 H, Ar H), 7.98–8.12 (dd, J = 7 Hz, J = 1.5 Hz, 2 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 166.35 (s, C-1), 142.61 (s, C-2), 69.70 (d, C-3), 32.32 (t, C-4), 24.62 (t, C-5), 64.40 (t, C-6), 124.37 (t, C-7), 51.28 (q, C-8), 166.17 (s, C-9), 129.91 (s, C-10) [132.43, 129.07, 127.88 (d, Ar C)]; mass spectrum (10 eV), m/z (relative intensity) 278 (M^+, 0), 180 (1), 156 (11), 124 (15), 123 (33), 122 (31), 115 (27), 105 (100), 83 (30), 77 (53), 51 (20); mass spectrum, m/z 156.0787 (M^+ calcd for $C_8H_{12}O_3$, m/z 156.0787).

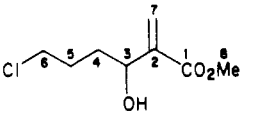
6-[(2,4,6-Trimethylbenzoyl)oxy]-3-hydroxy-2-methylenehexanoic Acid, Methyl Ester (16b). Aldehyde **14b** (17 g, 0.073 mol), methyl acrylate (20 mL, 0.22 mol), and DABCO (3 g, 0.026 mol) were allowed to react at room temperature until **14b** had disappeared. The remaining methyl acrylate was evaporated,



16b

the residue was taken up in ether (100 mL), the catalyst was washed out with 10% aqueous hydrochloric acid, the organic phase was washed with water and dried ($MgSO_4$), and the solvent was removed to leave spectroscopically pure **16b** (20 g, 87%): IR ($CHCl_3$) 3500 (br, OH), 2950 (w), 1690–1720 (vs, C=O), 1620 (w, C=C), 1600 (w), 1430 (w), 1260 (m), 1160 (m), 1075 (m) cm^{-1}; 90-MHz ^{1}H NMR ($CDCl_3$) δ 1.8–2.9 (m, 4 H, 2 CH_2), 2.2 (s, 9 H, 3 CH_3), 3.8 (s, 3 H, CH_3O), 4.2–4.6 (m, 3 H, HCO and CH_2O), 5.9 (s, 1 H, HC=C), 6.3 (s, 1 H, HC=C), 6.9 (s, 2 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 166.72 (s, C-1), 143.12 (s, C-2), 70.06 (d, C-3), 32.96 (t, C-4), 25.08 (t, C-5), 64.82 (t, C-6), 124.58 (t, C-7), 51.67 (q, C-8), 170.23 (s, C-9), 128.40 (d, C-10, C-11), 139.12, 135.03, 131.22 (s, Ar), 19.72, 19.72, 20.99 (q, CH_3Ph).

6-Chloro-3-hydroxy-2-methylenehexanoic Acid, Methyl Ester (16c). 4-Chlorobutanal[15a] (**14c**) (21.5 g, 0.2 mol) was mixed at 0 °C with methyl acrylate (0.3 mol, 25.8 g, 27 mL), and DABCO (2.25 g, 0.02 mol) was added with dissolution. The reaction



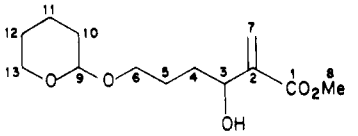
16c

mixture was stirred for 7 days at 0 °C, a white crystalline solid being slowly precipitated. After completion of the reaction the excess of the acrylic ester was evaporated in vacuo, and the residue was taken up in ether (150 mL). The organic phase was washed with 2 N hydrochloric acid (3 × 50 mL) and water and dried ($MgSO_4$). After evaporation of the solvent the remaining acrylic ester was removed on an oil pump to leave a colorless, oily liquid (22.6–24 g, 59–63%), which was uniform by ^{1}H and ^{13}C NMR: IR ($CHCl_3$) 3500 (br, OH), 2980 (m), 1710 (vs, C=O), 1630 (w, C=C), 1440 (s), 1305 (w), 1200 (w), 1160 (m), 1140 (m), 1075 (m), 965 (w), 820 (w) cm^{-1}; 60-MHz ^{1}H NMR ($CDCl_3$) δ 1.6–2.2 (m, 4 H, 2 CH_2), 3.5–3.7 (t, J = 6.5 Hz, 2 H, CH_2Cl), 3.8 (s, 3 H, OCH_3), 4.3–4.6 (m, 2 H, CHOH), 5.9 (t, J = 1 Hz, 1 H, HC=C), 6.3 (s, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 166.90 (s, C-1), 142.88 (s, C-2), 70.12 (d, C-3), 33.59 (t, C-4), 28.99 (t, C-5), 44.95 (t, C-6), 124.94 (t, C-7), 51.92 (q, C-8); mass spectrum (10 eV), m/z (relative intensity) 192/194 (M^+, 0), 157/159 (2, M − Cl), 137 (5), 135 (5), 105 (99), 98 (13), 87 (16), 83 (100), 79 (17), 55 (37).

6-(Tetrahydropyranyloxy)-3-hydroxy-2-methylenehexanoic Acid, Methyl Ester (16d). 14d (17.2 g, 0.1 mol) was

(27) Cf.: Bulat, J. A.; Liu, H. J. *Can. J. Chem.* **1976**, *54*, 3869.

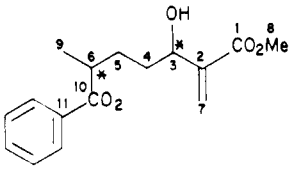
mixed with methyl acrylate (17.2 g, 18 mL, 0.2 mol) and DABCO (1.2 g, 0.01 mol) was added with dissolution. The reaction was



16d

monitored by GC and discontinued as soon as the aldehyde peak had disappeared. The excess of the acrylic ester was removed in vacuo, and the residue was taken up in ether (100 mL). The ether phase was washed several times with water for removing DABCO and dried ($MgSO_4$). The ether was evaporated on a Rotavap, and the remaining solvent was removed with an oil pump to leave **16d** (22.5 g, 87%): IR ($CHCl_3$) 3400 (br w, OH), 3000 (m), 2950 (s), 2870 (m), 1710 (vs, C=O), 1630 (w, C=C), 1440 (m), 1155 (m), 1135 (m), 1120 (m, C–O), 1075 (m), 1020 (s, C–O) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.1–1.7 (m, 10 H, 5 CH_2), 3.0–3.7 (m, 4 H, 2 CH_2O), 3.53 (s, 3 H, CH_3O), 4.2–4.5 (m, 2 H, CHOH), 5.65 (t, J = 1 Hz, 1 H, CH=C), 6.04 (br s, 1 H, CH=C); ^{13}C NMR ($CDCl_3$) δ 166.84 (s, C-1), 143.58 (s, C-2), 70.10 (d, C-3), 33.56 (t, C-4), 26.02 (t, C-5), 62.06 (t, C-6), 124.37 (t, C-7), 51.67 (q, C-8), 98.72 (d, C-9), 30.71 (t, C-10), 19.54 (t, C-11), 25.56 (t, C-12), 67.43 (t, C-13); mass spectrum, (70 eV), m/z (relative intensity) 258 (M^+, 0), 199 (4), 185 (2), 162 (36), 125 (35), 115 (16), 85 (100), 83 (20).

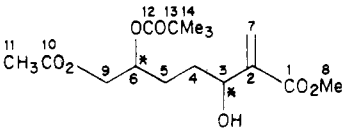
6-(Benzoyloxy)-3-hydroxy-2-methyleneheptanoic Acid, Methyl Ester (16e). **14e** (10 g, 0.048 mol), methyl acrylate (6.2 g, 6.5 mL, 0.072 mol), and DABCO (2 g, 0.018 mol) were allowed to react as usual, and the reaction mixture was worked up as



16e

described for **16c** to give **16e** (13.1 g, 92%): IR ($CHCl_3$) 3500 (br w, OH), 2970 (w), 2940 (w), 1705 (vs), 1620 (w), 1595 (w), 1575 (w), 1440 (m), 1430 (m), 1305 (m), 1280 (s), 1110 (m), 1060 (w), 1020 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.35 (d, J = 6 Hz, 3 H, CH_3), 1.66–1.91 (m, 4 H, CH_2CH_2), 2.9 (br s, 1 H, OH), 3.71 and 3.74 (s, 3 H, OCH_3), 4.45 (br t, 1 H, CHOH), 5.06–5.33 (m, 1 H, HCOCO), 5.83 (t, J = 1 Hz, 1 H, HC=C), 6.22 (br s, 1 H, HC=C), 7.30–7.59 (m, 3 H , Ar H), 7.96–8.14 (m, 2 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 166.14 (s, C-1), 143.18 (s, C-2) [70.27, 70.12 (d, C-3)] [32.29, 32.20, 32.08 (t, C-4, C-5)] [71.70, 71.30 (d, C-6)], 124.64 (t, C-7), 51.64 (q, C-8) [20.05, 19.99 (q, C-9)], 166.72 (s, C-10), 130.79 (s, C-11) [132.76, 129.49, 128.31 (d, Ar C)]; mass spectrum (70 eV), m/z (relative intensity) 292 (M^+, 0), 206 (1), 178 (10), 177 (9), 170 (19), 138 (15), 128 (13), 123 (54), 115 (33), 105 (100), 83 (18), 77 (33), 73 (17).

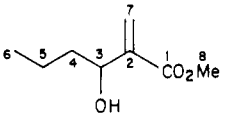
7-Acetoxy-6-(trimethylacetoxy)-3-hydroxy-2-methyleneheptanoic Acid, Methyl Ester (16f). **14f** (10 g, 0.041 mol) and methyl acrylate (20 mL, 0.2 mol) with DABCO (2 g, 0.017 mol) were allowed to stand at room temperature until the reaction was complete. The excess methyl acrylate was evaporated, the residue



16f

was taken up in ether (100 mL), and the catalyst was washed out with 10% aqueous hydrochloric acid. The organic phase was dried ($MgSO_4$), and the solvent was removed to leave **16f** (12.2 g, 89%): IR ($CHCl_3$) 3500 (br s, OH), 2980 (m), 2970 (m), 2870 (w), 1725 (vs, C=O), 1630 (w, C=C), 1480 (m), 1440 (m), 1400 (w), 1370 (m), 1290 (s, C–O), 1160 (s, C–O), 1040 (m), 960 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (s, 9 H, CMe_3), 1.61–1.80 (m, 4 H, CH_2CH_2), 2.05 (s, 3 H, CH_3C=O), 3.79 (s, 3 H, CH_3O), 4.06–4.21 (m, 3 H, CH_2O, OH), 4.36–4.49 (m, 1 H, CHOH), 5.05–5.25 (m, 1 H, CHOC=O), 5.83 (t, J = 1 Hz, 1 H, HC=C), 6.25 (s, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 166.63 (s, C-1), 143.27 (s, C-2), 71.18, 70.73 (d, C-3), 31.93, 31.62 (t, C-4), 26.44 (t, C-5), 69.97, 69.70 (d, C-6), 124.52 (t, C-7), 51.71 (q, C-8), 65.09, 65.00 (t, C-9), 170.51 (s, C-10), 20.54 (q, C-11), 177.81 (s, C-12), 38.80 (s, C-13), 27.08 (q, C-14); mass spectrum (10 eV), m/z (relative intensity) 330 (M^+, 0), 215 (3), 197 (3), 196 (4), 168 (5), 155 (30), 137 (14), 136 (12), 123 (21), 115 (24), 114 (17), 85 (20), 83 (15), 71 (19), 57 (100), 43 (60).

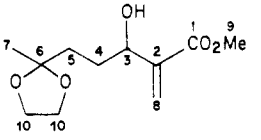
3-Hydroxy-2-methylenehexanoic Acid, Methyl Ester (16g). Butanal (**14g**) (14.5 g, 0.2 mol), methyl acrylate (27 mL, 0.3 mol), and DABCO (3.5 g, 0.03 mol) were mixed, and the reaction was monitored by GC. After the aldehyde had disappeared, the excess



16g

of acrylic ester was evaporated, and the residue was taken up in ether (200 mL). The organic phase was washed with 10% aqueous HCl (2 × 50 mL) and water (2 × 50 mL) and dried ($MgSO_4$). The solvent was removed first on a Rotavap and then with an oil pump to leave **16g** (27 g, 85%): IR ($CHCl_3$) 3600 (w), 3500 (w), 2980 (w), 2940 (s), 2100 (m), 2850 (w), 1700 (vs, C=O), 1620 (m, C=C), 1430 (s), 1325 (m), 1285 (w), 1150 (m), 1100 (m), 1060 (w), 1020 (w), 960 (m) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 0.92 (t, J = 7 Hz, 3 H, CH_3), 1.2–1.75 (m, 4 H, CH_2CH_2), 2.72 (br d, J = 6.5 Hz, 1 H, OH), 3.78 (s, 3 H, OCH_3), 4.43 (q, J = 7 Hz, 1 H, CHOH), 5.80 (t, J = 1 Hz, 1 H, HC=C), 6.22 (d, J = 1 Hz, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 167.20 (s, C-1), 143.82 (s, C-2), 70.42 (d, C-3), 38.89 (t, C-4), 19.08 (t, C-5), 13.93 (q, C-6), 124.40 (t, C-7), 51.80 (q, C-8); mass spectrum (70 eV), m/z (relative intensity) 158 (M^+, 0), 141 (6), 127 (5), 126 (8), 125 (6), 115 (99), 109 (15), 98 (12), 87 (16), 83 (100), 55 (20).

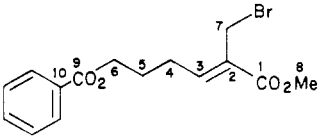
6,6-(Ethylenedioxy)-3-hydroxy-2-methyleneheptanoic Acid, Methyl Ester (16h). **14h** (9.5 g, 65 mmol), methyl acrylate (8.8 g, 102 mmol), and DABCO (2.5 g, 22 mmol) were allowed to react until the aldehyde **14h** had disappeared. The reaction



16h

mixture was worked up as usual (cf. **16c**) to give oily **16h** (9.5 g, 63%): IR ($CHCl_3$) 3450 (br w, OH), 2980 (w), 2950 (w), 2880 (w), 1710 (vs, C=O), 1625 (w, C=C), 1440 (m), 1350 (m), 850 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.33 (s, 3 H, CH_3), 1.79 (m, 4 H, CH_2CH_2), 3.78 (s, 3 H, OCH_3), 3.96 (s, 4 H, OCH_2CH_2O), 4.46 (br s, 1 H, OH), 5.87 (t, J = 1 Hz, 1 H, HC=C), 6.26 (s, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 166.81 (s, C-1), 143.70 (s, C-2), 70.00 (d, C-3), 34.92 (t, C-4), 30.90 (t, C-5), 109.95 (d, C-6), 23.81 (q, C-7), 124.31 (t, C-8), 51.71 (q, C-9), 64.61 (t, C-10); mass spectrum (70 eV), m/z (relative intensity) 230 (M^+, 0), 215 (3), 141 (6), 140 (11), 137 (8), 113 (17), 112 (16), 87 (100), 85 (14), 73 (10), 43 (51); mass spectrum, m/z 215.0919 [M^+ calcd for $C_{10}H_{15}O_5$ (M – CH_3), m/z 215.0919].

6-(Benzoyloxy)-2-(bromomethyl)-2-hexenoic Acid, Methyl Ester (17a). Dimethyl sulfide (1.55 g, 2 mL, 25 mmol) in dry CH_2Cl_2 (15 mL) was dropped into a solution of *N*-bromosuccinimide (NBS) (4 g, 23 mmol) in dry CH_2Cl_2 (50 mL) cooled at 0 °C. The white complex of NBS and Me_2S was precipitated. After

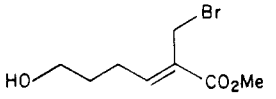


17a

the mixture was stirred for 10 min at 0 °C, a solution of **16a** (5.8 g, 21 mmol) in CH_2Cl_2 (20 mL) was added dropwise; the mixture

was stirred for 24 h at room temperature, diluted with light petroleum (50 mL), and poured into ice–water–NaCl (100 mL). The organic phase was separated and washed with a saturated NaCl solution (2 × 50 mL). The combined aqueous phase was reextracted with ether (2 × 50 mL), and the combined organic phase was dried ($MgSO_4$). The solvent was evaporated, and the sulfur compounds were removed on an oil pump. Chromatography on silica gel using ether/dichloromethane (1:1) as eluent gave **17a** (6.6 g, 92%): IR ($CHCl_3$) 3010 (w), 2960 (w), 1720 (vs, C=O), 1640 (w, C=C), 1600 (w), 1580 (w), 1450 (m) 1440 (m), 1310 (m), 1250 (vs, C–O), 1160 (m), 1120 (s, C–O), 1070 (m), 1030 (m) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.85–2.15 (m, 2 H, $CH_2CH_2CH_2$), 2.36–2.61 (q, J = 7 Hz, 2 H, CH_2CH=C), 3.76 (s, 3 H, OCH_3), 4.23 (s, 2 H, CH_2Br), 4.38 (t, J = 6 Hz, 2 H, CH_2O), 7.02 (t, J = 7 Hz, 1 H, HC=C), 7.32–7.60 (m, 3 H, Ar H), 7.98–8.12 (dd, J = 7 Hz, J = 1.5 Hz, 2 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 165.66 (s, C-1), 130.19 (s, C-2), 146.82 (d, C-3), 27.35 (t, C-4), 25.74 (t, C-5), 64.09 (t, C-6), 24.08 (t, C-7), 52.09 (q, C-8), 166.23 (s, C-9), 129.98 (s, C-10) [132.94, 129.52, 128.37 (d, Ar C)]; mass spectrum, (70 eV), m/z (relative intensity) 340/342 (M^+, 0), 261 (1), 260 (4), 230 (1), 229 (1), 140 (3), 139 (11), 138 (4), 137 (9), 125 (7), 123 (6), 122 (9), 112 (10), 105 (100), 81 (8), 79 (27), 77 (55).

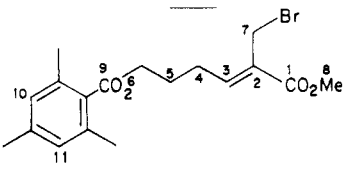
(*Z*)-6-Hydroxy-2-(bromomethyl)-2-hexanoic Acid, Methyl Ester (17aα). **17d** (1.6 g, 5 mmol) was stirred in 3 N methanolic hydrobromic acid (20 mL) at room temperature and purified by chromatography (cf. **18aα**) to give **17aα** (0.8 g, 67%): IR ($CHCl_3$)



17aα

3500 (br w, OH), 3000 (w), 2950 (m), 2870 (w), 1715 (vs, C=O), 1640 (w, C=C), 1440 (m), 1270 (w), 1160 (w), 1030 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.63–1.94 (m, 2 H, $CH_2CH_2CH_2$), 2.25–2.63 (m, 2 H, CH_2C=C), 3.75 (t, 2 H, J = 6 Hz, CH_2OH), 3.8 (s, 3 H, OCH_3), 4.23 (s, 2 H, CH_2Br), 6.99 (t, J = 7 Hz, 1 H, HC=C); mass spectrum (70 eV), m/z (relative intensity) 236/238 (M^+, 0), 157 (57, M – Br), 125 (86), 79 (100), 71 (74), 55 (85).

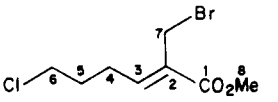
(*Z*)-6-[(2,4,6-Trimethylbenzoyl)oxy]-2-(bromomethyl)-2-hexenoic Acid, Methyl Ester (17b). *N*-Bromosuccinimide (4.1 g, 23 mmol) in dry CH_2Cl_2 (40 mL) was added under N_2 at 0 °C to dimethyl sulfide (1.55 g, 2 mL, 25 mmol) in CH_2Cl_2 (30 mL).



17b

After the mixture was stirred for 10 min, **16b** (6.4 g, 20 mmol) in CH_2Cl_2 (20 mL) was added; the resulting mixture was stirred for 16 h and worked up as usual to give, after chromatography on silica gel (1:1 eluent ether/light petroleum) **17b** (6.5 g, 89%): IR ($CHCl_3$) 2980 (m), 1720 (vs, C=O), 1640 (w, C=C), 1610 (m), 1440 (m), 1270 (s, C–O), 1170 (s), 1090 (s), 850 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 2.25 (s, 9 H, 3 CH_3), 1.8–2.6 (m, 4 H, CH_2CH_2), 3.75 (s, 3 H, OCH_3), 4.19 (s, 2 H, CH_2Br), 4.25–4.42 (t, J = 7 Hz, 2 H, CH_2O), 6.82 (s, 2 H, Ar H), 6.87–7.05 (t, J = 7 Hz, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 165.60 (s, C-1), 130.22 (s, C-2), 146.36 (d, C-3), 27.35 (t, C-4), 25.59 (t, C-5), 63.88 (t, C-6), 23.90 (t, C-7), 52.01 (q, C-8), 169.72 (s, C-9), 128.43 (d, C-10, C-11) [139.21, 135.03, 130.94 (s, Ar C)] [19.78, 21.02 (q, CH_3Ph)]; mass spectrum (70 eV), m/z (relative intensity) 382/384 (M^+, 1), 312 (2), 304 (3), 303 (13), 253 (4), 251 (4), 164 (5), 163 (8), 142 (100), 141 (60), 119 (13).

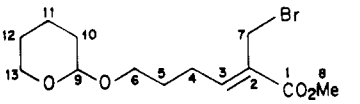
(*Z*)-6-Chloro-2-(bromomethyl)-2-hexenoic Acid, Methyl Ester (17c). Dimethyl sulfide (4.6 g, 75 mmol) in dry CH_2Cl_2 (50 mL) was dropped into a solution of NBS (12.3 g, 70 mmol) in dry CH_2Cl_2 (150 mL) cooled to 0 °C, to give a white precipitate. After the mixture was stirred for 10 min at 0 °C, a solution of **16c** (11 g, 58 mmol) in CH_2Cl_2 (50 mL) was dropped in. The reaction mixture was stirred for 24 h at room temperature, diluted with light petroleum (100 mL), and poured into ice–water–NaCl



17c

(200 mL). The organic phase was separated and washed with saturated NaCl solution (100 mL). The aqueous phase was reextracted with ether (2 × 100 mL), and the combined organic phase was dried ($MgSO_4$). The solvent was evaporated, and the sulfur compounds were removed with an oil pump. Chromatography on silica gel (1:1 eluent ether/CH_2Cl_2) gave **17c** (12.9 g, 87%): IR ($CHCl_3$) 2975 (m), 1715 (vs, C=O), 1645 (w, C=C), 1440 (s), 1390 (s), 1370 (s, C–O), 1195 (m), 1170 (m, C–O), 1100 (w), 1050 (w), 870 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.85–2.15 (dq, J = 6 Hz, 2 H, CH_2), 2.35–2.6 (dq, J = 7 Hz, 2 H, CH_2), 3.59 (t, J = 6 Hz, 2 H, CH_2Cl), 3.8 (s, 3 H, OCH_3), 4.25 (s, 2 H, CH_2Br), 6.92 (t, J = 7 Hz, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 165.66 (s, C-1), 130.58 (s, C-2), 145.88 (d, C-3), 30.87 (t, C-4), 26.01 (t, C-5), 44.13 (t, C-6), 20.08 (t, C-7), 52.13 (q, C-8); mass spectrum (70 eV), m/z (relative intensity) 254/256 (M^+, 0), 222/224 (3), 176 (10), 174 (29), 139 (17), 107 (67), 89 (24), 79 (100).

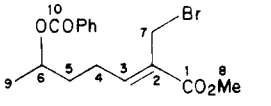
(*Z*)-6-(Tetrahydropyranyloxy)-2-(bromomethyl)-2-hexenoic Acid, Methyl Ester (17d). Dimethyl sulfide (3.7 g, 4.7 mL, 60 mmol) in CH_2Cl_2 (20 mL) was dropped at 0 °C and under N_2 into a solution of NBS (10 g, 55 mmol) in CH_2Cl_2 (80 mL). After



17d

10 min **16d** (12.9 g, 50 mmol) in CH_2Cl_2 (50 mL) was dropped in, and the resulting mixture was stirred overnight at room temperature to give, after the usual isolation procedure, **17d** (15.1 g, 94%): IR ($CHCl_3$) 3000 (w), 2950 (s), 2880 (w), 1715 (s, C=O), 1640 (w, C=C), 1440 (m), 1270 (m), 1160 (m), 1125 (m), 1060 (m), 1030 (s, C–O), 980 (w), 900 (w), 870 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.39–1.95 (m, 6 H, CH_2 in THP), 2.21–2.48 (m, 4 H, 2 CH_2), 3.35–3.95 (m, 4 H, 2 CH_2O), 3.81 (s, 3 H, CH_3O), 4.27 (s, 2 H, CH_2Br), 4.51–4.65 (br s, 1 H, OCHO), 7.03 (t, J = 7 Hz, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 165.78 (s, C-1), 129.58 (s, C-2), 147.82 (d, C-3), 28.34 (t, C-4), 25.87 (t, C-5), 62.16 (t, C-6), 24.26 (t, C-7), 51.98 (q, C-8), 98.74 (d, C-9), 30.71 (t, C-10), 19.57 (t, C-11), 25.53 (t, C-12), 66.40 (t, C-13); mass spectrum (10 eV), m/z (relative intensity) 320/322 (M^+, 0), 221 (2), 219 (2), 165 (10), 163 (10), 157 (13), 125 (23), 85 (100), 84 (51), 83 (32), 79 (29), 71 (44), 55 (75).

(*Z*)-6-(Benzoyloxy)-2-(bromomethyl)-2-heptenoic Acid, Methyl Ester (17e). **16e** (5.8 g, 20 mmol) was rearranged with NBS (4.1 g, 23 mmol) and dimethyl sulfide (1.55 g, 2 mL, 25 mmol) as usual. Chromatography on silica gel (2:1 eluent ether/CH_2Cl_2)

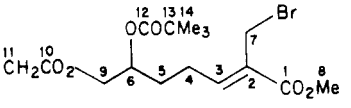


17e

gave oily **17e** (6.4 g, 89%): IR ($CHCl_3$) 2970 (w), 2940 (w), 1710 (vs, C=O), 1635 (w), 1590 (w), 1450 (m), 1435 (m), 1305 (m), 1270 (s), 1150 (m), 1105 (m), 1060 (w), 1020 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.4 (d, J = 6 Hz, 3 H, CH_3CH), 1.79–2.06 (m, 2 H, CH_2CH), 2.26–2.59 (q, 2 H, CH_2CH=), 3.76 (s, 3 H, OCH_3), 4.19 (s, 2 H, CH_2Br), 5.03–5.40 (m, 1 H, CHOC=O), 6.95 (t, J = 7.5 Hz, 1 H, HC=C), 7.32–7.60 (m, 3 H, Ar H), 7.98–8.11 (m, 2 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 165.60 (s, C-1), 130.13 (s, C-2), 147.12 (d, C-3), 34.35 (t, C-4), 25.11 (t, C-5), 70.85 (d, C-6), 24.08 (t, C-7), 51.95 (q, C-8), 20.02 (q, C-9), 165.84 (s, C-10), 128.92 (s, C-11) [132.85, 129.52, 128.34 (d, Ar C)]; mass spectrum, (10 eV), m/z (relative intensity) 354/356 (M^+, 0), 276 (2), 275 (15, M – Br), 153 (31), 123 (7), 121 (9), 105 (100), 100 (13), 93 (25), 79 (4), 77 (28); mass spectrum, m/z 275.1284 (M^+ calcd for $C_{16}H_{19}O_4$, m/z 275.1283).

(*Z*)-7-Acetoxy-6-(trimethylacetoxy)-2-(bromomethyl)-2-heptenoic Acid, Methyl Ester (17f). **16f** (9.2 g, 30 mmol) was treated with NBS (5.9 g, 33 mmol) and dimethyl sulfide (2.8 mL,

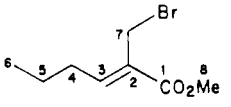
36 mmol) as described (cf. **16c**). Work up by chromatography



17f

gave **17f** (10.5 g, 90%): IR ($CHCl_3$) 3020 (w), 2980 (w), 1730 (br vs, C=O), 1640 (w, C=C), 1480 (w), 1440 (w), 1370 (m), 1280 (m), 1220 (s, C–O), 1160 (s, C–O), 1050 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.21 (s, 9 H, CMe_3), 1.68–1.95 (m, 2 H, CH_2), 2.05 (s, 3 H, CH_3C=O), 2.21–2.49 (m, 2 H, CH_2CH=C), 3.80 (s, 3 H, CH_3O), 4.19 (s, 2 H, CH_2Br), 4.02–4.23 (m, 2 H, CH_2O), 5.01–5.16 (m, 1 H, HCO), 6.95 (t, J = 7 Hz, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 165.63 (s, C-1), 130.16 (s, C-2), 146.39 (d, C-3), 29.32 (t, C-4), 25.66 (t, C-5), 70.52 (d, C-6), 23.87 (t, C-7), 52.07 (q, C-8), 64.58 (t, C-9), 170.29 (s, C-10), 20.57 (q, C-11), 177.65 (s, C-12), 38.83 (s, C-13), 27.08 (q, C-14); mass spectrum (70 eV), m/z (relative intensity) 392 (M^+, 0), 313 (9, M – Br), 253 (20), 229 (5), 211 (28), 169 (9), 151 (18), 137 (15), 119 (26), 93 (13), 91 (33), 85 (21), 81 (8), 79 (12), 71 (18), 57 (100), 43 (43); mass spectrum, m/z 313.1648 (M^+ calcd for $C_{16}H_{25}O_6$, m/z 313.1651).

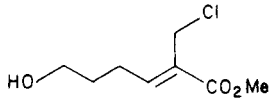
2-(Bromomethyl)-2-hexenoic Acid, Methyl Ester (17g). 16g (15.8 g, 0.1 mol) was allowed to react with NBS (19.6 g, 0.11 mol) and dimethyl sulfide (9.3 mL, 0.12 mol), giving, after chromatography, **17g** (19.1 g, 87%): IR ($CHCl_3$) 2960 (m), 2930 (w), 2880



17g

(w), 1710 (s, C=O), 1640 (w), 1440 (m), 1290 (s), 1160 (s), cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 0.96 (t, J = 7 Hz, 3 H, CH_3), 1.35–1.76 (m, 2 H, CH_3CH_2), 2.28 (q, J = 7.5 Hz, 2 H, CH_2CH=C), 3.79 (s, 3 H, OCH_3), 4.22 (s, 2 H, CH_2Br), 6.98 (t, J = 7.5 Hz, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 165.90 (s, C-1), 129.58 (s, C-2), 148.12 (d, C-3), 30.87 (t, C-4), 21.57 (t, C-5), 13.93 (q, C-6), 24.32 (t, C-7), 52.01 (q, C-8); mass spectrum (10 eV), m/z (relative intensity) 220/222 (M^+, 6), 142 (10), 141 (96), 140 (8), 125 (11), 109 (100), 81 (87), 79 (26), 67 (13), 59 (14), 53 (20); mass spectrum, m/z 220.0098 (M^+ calcd for $C_8H_{13}BrO_2$, m/z 220.0099).

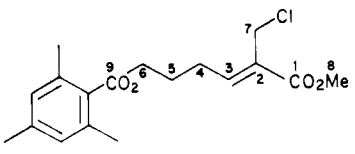
(*Z*)-6-Hydroxy-2-(chloromethyl)-2-hexenoic Acid, Methyl Ester (18aα). 18d (1.4 g, 5 mmol) was stirred for 12 h in 3 N methanolic hydrogen chloride (20 mL), poured into water (150 mL), and neutralized with aqueous K_2CO_3. The mixture was



18aα

extracted with ether (3 × 40 mL), the organic phase was dried ($MgSO_4$), and the solvent was evaporated to give, after chromatography on silica gel (1:1 eluent ether/acetone), **18aα** (0.67 g, 70%): IR ($CHCl_3$) 3600 (w, OH), 3500 (br w, OH), 3000 (w), 2950 (m), 2880 (w), 1715 (s, C=O), 1645 (w, C=C), 1435 (m), 1280 (br m), 1195 (m), 1180 (m), 1120 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.61–1.93 (m, 2 H, CH_2CH_2O), 2.28–2.60 (m, 2 H, CH_2CH=C), 3.69 (t, J = 6 Hz, 2 H, CH_2O), 3.80 (s, 3 H, CH_3O), 4.36 (s, 2 H, CH_2Cl), 7.02 (t, J = 7.5 Hz, 1 H, CH=C); mass spectrum (70 eV), m/z (relative intensity) 192 (M^+, 1), 157 (36, M – Cl), 125 (100), 111 (29), 97 (25), 79 (81), 67 (52).

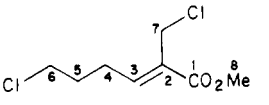
(*Z*)-6-[(2,4,6-Trimethylbenzoyl)oxy]-2-(chloromethyl)-2-hexenoic Acid, Methyl Ester (18b). 16b (1.6 g, 5 mmol) was allowed to react with *N*-chlorosuccinimide (0.8 g, 6 mmol) and



18b

dimethyl sulfide (0.55 mL, 7 mmol) (cf. preparation of **18c,d**) to give, after chromatography, **18b** (1.5 g, 89%): IR ($CHCl_3$) 2980 (m), 1710 (vs, C=O), 1650 (w, C=C), 1610 (m), 1435 (m), 1380 (w), 1270 (s, C–O), 1170 (s), 1090 (s), 850 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.8–2.7 (m, 4 H, CH_2CH_2), 2.3 (s, 9 H, 3 CH_3), 3.8 (s, 3 H, OCH_3), 4.25–4.5 (m, 4 H, OCH_2, CH_2Cl), 6.9 (s, 2 H, Ar H), 6.9–7.2 (t, J = 7 Hz, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 165.81 (s, C-1), 130.01 (s, C-2), 146.79 (d, C-3), 27.65 (t, C-4), 25.59 (t, C-5), 63.91 (t, C-6), 36.98 (t, C-7), 51.98 (q, C-8) [139.27, 135.01, 131.04 (s, Ar C), 128.49 (d, Ar C)], 19.81, 21.02 (q, CH_3Ph)]; mass spectrum (10 eV), m/z (relative intensity) 338/340 (M^+, 1), 271 (1), 154 (8), 153 (9), 148 (11), 147 (95), 146 (100), 119 (30), 117 (13), 115 (12), 103 (10), 91 (24).

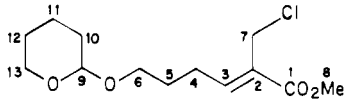
(*Z*)-6-Chloro-2-(chloromethyl)-2-hexenoic Acid, Methyl Ester (18c). Dimethyl sulfide (10.5 g, 12.5 mL, 0.17 mol) in CH_2Cl_2 (20 mL) was dropped into a solution of *N*-chlorosuccinimide (20 g, 0.15 mol) in dry CH_2Cl_2 (200 mL), which was kept at 0 °C. A white precipitate was formed. After complete addition,



18c

the mixture was stirred for a further 10 min, and **16c** (19.3 g, 0.1 mol) in dry CH_2Cl_2 (30 mL) was dropped in. After 12 h the precipitate had dissolved. The reaction mixture was diluted with light petroleum (100 mL) and washed with aqueous NaCl (3 × 100 mL). The aqueous phase was washed with ether (50 mL), and the combined organic phase was dried ($MgSO_4$). The solvent was evaporated, and the sulfur compounds formed were removed by using an oil pump for several hours. Flash chromatography on silica gel (1:1 eluent ether/CH_2Cl_2) gave **18c** (18.8 g, 89%): IR ($CHCl_3$) 2980 (m), 1710 (vs, C=O), 1640 (w, C=C), 1440 (s), 1390 (s), 1370 (s, C–O), 1190 (m), 1170 (m, C–O), 1050 (w) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.9–2.15 (dq, J = 6 Hz, 2 H, CH_2), 2.4–2.65 (dq, J = 7 Hz, 2 H, CH_2), 3.8 (t, J = 6 Hz, 2 H, CH_2Cl), 3.8 (s, 3 H, OCH_3), 4.35 (s, 2 H, CH_2Cl), 6.95 (t, J = 7 Hz, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 165.93 (s, C-1), 130.46 (s, C-2), 146.30 (d, C-3), 31.14 (t, C-4), 26.05 (t, C-5), 44.10 (t, C-6), 37.07 (t, C-7), 52.16 (q, C-8); mass spectrum (10 eV), m/z (relative intensity) 211 (M^+, 0), 181 (9), 179 (14), 175 (10), 139 (22), 138 (20), 137 (64), 107 (48), 79 (100).

(*Z*)-6-(Tetrahydropyranyloxy)-2-(chloromethyl)-2-hexenoic Acid, Methyl Ester (18d). Dimethyl sulfide (1.55 g, 1.95 mL, 25 mmol) in CH_2Cl_2 (10 mL) was dropped slowly into a solution of NCS (3.1 g, 23 mmol) in absolute CH_2Cl_2 (40 mL), which was kept at 0 °C and under N_2. After the mixture was



18d

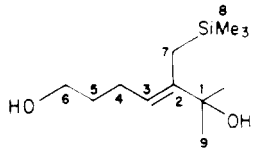
stirred for 10 min, **16d** (5.2 g, 20 mmol) in CH_2Cl_2 (15 mL) was dropped in, and the ice bath was removed. After 18 h pentane (50 mL) was added, and the reaction mixture was washed with a concentrated solution of aqueous NaCl (2 × 50 mL) and with water (50 mL). The aqueous phase was reextracted with ether (50 mL), and the combined organic phase was dried ($MgSO_4$). After evaporation of the solvent, the remaining sulfur compounds were removed with an oil pump. Chromatography on basic Al_2O_3 (activity II–III; 1:1 eluent ether/light petroleum) gave **18d** (4.6 g, 83%): IR ($CHCl_3$) 3000 (m), 2950 (s), 2870 (m), 1710 (vs, C=O), 1645 (w, C=C), 1445 (m), 1275 (s), 1135 (s), 1070 (s), 1030 (vs, C–O) cm^{-1}; 60-MHz ^1H NMR ($CDCl_3$) δ 1.4–2.0 (m, 6 H, CH_2 in THP), 2.2–2.8 (m, 4 H, 2 CH_2), 3.4–4.0 (m, 4 H, 2 CH_2O), 3.80 (s, 3 H, CH_3O), 4.4 (s, 2 H, CH_2Cl), 4.6 (br s, 1 H, OCHO), 7.15 (t, J = 7 Hz, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 166.02 (s, C-1), 129.46 (s, C-2), 148.12 (d, C-3), 28.59 (t, C-4), 25.84 (t, C-5), 62.22 (t, C-6), 37.17 (t, C-7), 51.98 (q, C-8), 98.84 (d, C-9), 30.74 (t, C-10), 19.60 (t, C-11), 25.56 (t, C-12), 66.40 (t, C-13); mass spectrum (10 eV) m/z (relative intensity) 276 (M^+, 0.3), 241 (2, M – Cl), 213 (1.3), 157 (8), 125 (7), 85 (100), 79 (20).

(*Z*)-6-Methyl-5-[(trimethylsilyl)methyl]-4-heptene-1,6-diol (19a). (a) From 17a. 17a (3.4 g, 10 mmol) and trichlorosilane

(1.5 g, 1.15 mL, 11 mmol) were dissolved in ether (10 mL) and dropped under N_2 at 0 °C into a suspension of triethylamine (1.1 g, 1.6 mL, 11 mmol) and CuI (0.1 g, 0.5 mmol) in ether (5 mL). The mixture was stirred at 0 °C for 1.5 h and then at room temperature for 2.5 h.[8] After the mixture was cooled to −50 °C a 1.6 M solution of methyllithium (50 mL, 80 mmol) was dropped in slowly, and then the solution was stirred for 1 h at 0 °C and poured into ice-cold 10% aqueous NH_4Cl (100 mL). The product was extracted with ether (3 × 50 mL), the ether phase was dried ($MgSO_4$), and the solvent was removed to leave an oily residue, which was taken up in pentane (100 mL). The product was precipitated at −20 °C overnight, colorless crystals of **19a** (0.97 g, 42%) being formed.

(b) From 15a. 15a (3.2 g, 9 mmol) in ether (10 mL) was cooled to −50 °C, and methyllithium (25 mL of a 1.6 M solution, 40 mmol) was slowly dropped in under N_2. After the addition was completed the reaction mixture was slowly warmed to 0 °C, stirred for 1 h, and poured onto aqueous NH_4Cl (10% solution, 50 mL). The mixture was extracted with ether (3 × 40 mL), and the ether layer was washed with water and dried ($MgSO_4$). After removal of the solvent the residue was taken up in pentane (100 mL) and allowed to stand overnight at −20 °C to give white crystals of **19a** (1.3 g, 62%).

(c) From 19b. 19b (0.9 g, 2.6 mmol) in ether (5 mL) was slowly dropped into a suspension of $LiAlH_4$ (140 mg, 3.6 mmol, 1.5 equiv) in absolute ether (10 mL), the mixture being kept at 0 °C under N_2. After 4 h at room temperature the reaction solution was



19a

hydrolyzed by careful addition of 1 N NaOH (40 mL). The product was extracted with ether (3 × 40 mL), the ether phase was dried ($MgSO_4$), and the solvent was removed to leave a residue, which was taken up in pentane (50 mL). The product precipitated overnight at −20 °C to give white crystals of **19a** (0.47 g, 79%): IR (KBr) 3360 (s, OH), 3250 (s, OH), 2980 (m), 2970 (m), 2950 (m), 2940 (m), 1400 (w), 1345 (w), 1240 (s, Si–C), 1165 (m), 1060 (m), 960 (w), 840 (s, Si–C) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$, standard benzene) δ 0.6 (s, 9 H, $SiMe_3$), 1.33 (s, 6 H, 2 CH_3), 1.65 (s, 2 H, CH_2Si), 1.5–2.1 (m, 4 H, 2 CH_2), 3.62 (t, J = 7 Hz, 2 H, OCH_2), 5.3 (t, J = 6.5, 1 H, CH=C); ^{13}C NMR ($CDCl_3$) δ 73.12 (s, C-1), 144.43 (s, C-2), 119.01 (d, C-3), 25.02 (t, C-4), 32.38 (t, C-5), 61.98 (t, C-6), 17.45 (t, C-7), −0.06 (q, C-8), 29.47 (q, C-9); mass spectrum (10 eV), m/z (relative intensity) 230 (M^+, 0), 216 (6), 185 (5), 157 (11), 145 (8), 125 (96), 107 (45), 81 (43), 79 (46), 75 (78), 73 (100), 67 (52). Anal. Calcd for $C_{12}H_{26}O_2Si$: C, 62.61; H, 11.3. Found: C, 62.87; H, 11.26.

Allylic Alcohol 19b. 15b (1.95 g, 5 mmol) was dissolved in ether (3 mL), and methyllithium (7 mL of a 1.6 M solution, 11 mmol) was slowly added at −30 °C under N_2. After 20 min at −30 °C, the solution was stirred for 0.5 h at room temperature, poured onto ice–water, and extracted with ether (3 × 20 mL). The organic phase was dried ($MgSO_4$) and the solvent evaporated. The residue was purified by chromatography (Brockmann activity II–III, 5:1 eluent pentane/ethyl acetate) to give 1.55 g (82%) of **19b**: IR ($CHCl_3$) 3600 (w, OH), 3500 (br w, OH), 2940 (m), 2910 (m), 1710 (s, C=O), 1600 (w), 1380 (w), 1260 (s), 1160 (m), 1080 (m) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$, afterwards addition of Me_4Si) δ 0.03 (s, 9 H, $SiMe_3$), 1.33 (s, 6 H, 2 CH_3), 1.63 (s, 2 H, CH_2Si), 1.55–2.05 (m, 4 H, CH_2CH_2), 2.28 (m, 9 H, CH_3Ph), 4.32 (t, J = 7 Hz, 2 H, CH_2OC=C), 5.31 (t, J = 7 Hz, 1 H, HC=C), 6.85 (s, 2 H, Ar H); mass spectrum (70 eV), m/z (relative intensity) 376 (M^+, 0), 221 (3), 213 (2), 194 (5), 181 (7), 147 (100), 119 (24), 107 (22), 91 (25), 73 (58).

(Z)-7-Chloro-2-methyl-3-[(trimethylsilyl)methyl]-3-hepten-2-ol (19c).[15a] A mixture of **17c** (7.6 g, 30 mmol) and trichlorosilane (4.5 g, 3.4 mL, 33 mmol) was dropped into a solution of triethylamine (3.34 g, 4.6 mL, 33 mmol) and CuI (0.3 g, 1.5 mmol) in absolute ether (15 mL), kept at 0 °C. The heterogeneous mixture was stirred for 1.5 h at 0 °C and then for 2.5 h at room temperature and cooled to −55 °C. An ethereal solution of methyllithium (110 mL of a 1.65 M solution, 182 mmol) was slowly added. After complete addition the mixture was allowed to reach 0 °C and poured into NH_4Cl–ice–water (150 mL of a 10% solution). The aqueous layer was washed with ether (2 × 100 mL), and the combined organic phase was dried ($MgSO_4$). After evaporation of the solvent, chromatography on basic alumina (Brockmann activity II–III, 10:1 eluent light petroleum/ethyl acetate) gave **19c** as a light yellow oil (4.1 g, 55%), which was kept at −20 °C: IR (CCl_4) 3625 (m, OH), 3500 (br, OH), 1250 (s, Si–C), 1170 (s, C–O), 852 (s) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$, benzene standard) δ −0.02 (s, 9 H, Me_3Si), 1.22 (s, 6 H, 2 CH_3), 1.23 (br s, 1 H, OH), 1.56 (br s, 2 H, CH_2Si), 1.59–2.13 (m, 4 H, 2 CH_2), 3.41 (t, J = 6.5 Hz, 2 H, CH_2Cl), 5.15 (t, J = 6.5 Hz, 1 H, HC=C).

(Z)-7-(Tetrahydropyranyloxy)-3-[(trimethylsilyl)methyl]-2-methyl-3-hepten-2-ol (19d). Triethylamine (1.1 g, 1.6 mL, 11 mmol) and CuI (0.1 g, 0.5 mmol) were stirred in absolute ether (5 mL) under nitrogen. Allyl chloride **18d** (2.76 g, 10 mmol) and trichlorosilane (1.5 g, 1.15 mL, 11 mmol) in ether (8 mL) were slowly dropped in at 0 °C. The mixture was stirred for 1.5 h at 0 °C and 2.5 h at room temperature. The mixture was cooled to −50 °C and methyllithium in ether (38 mL of a 1.6 M solution, 60 mmol) was dropped in. The solution was allowed to reach 0 °C and worked up as for **19c**, giving **19d** (0.8 g, 25%) after chromatography: IR ($CHCl_3$) 3000 (m), 2950 (s), 2870 (m), 1250 (m, Si–C), 1135 (w), 1120 (m, C–O), 1070 (m), 1030 (s), 900 (w), 850 (br m) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$, Me_4Si was added afterwards) δ 0.05 (s, 9 H, $SiMe_3$), 1.38 (s, 6 H, 2 CH_3), 1.69 (s, 2 H, CH_2Si), 1.55–1.81 (m, 10 H, 5 CH_2), 3.35–4.05 (m, 4 H, 2 CH_2O), 4.65 (br s, 1 H, OCHO), 5.46 (t, J = 7 Hz, 1 H, HC=C); mass spectrum (70 eV), m/z (relative intensity) 314 (M^+, 0), 296 (0.4), 212 (1), 197 (1), 194 (1), 173 (2), 139 (3), 125 (8), 107 (13), 85 (100), 73 (61), 67 (23).

(Z)-2-Methyl-3-[(trimethylsilyl)methyl]-3-octene-2,7-diol (19e). 17e (3.55 g, 10 mmol) and trichlorosilane (1.65 g, 1.26 mL, 12 mmol) in ether (8 mL) were dropped at 0 °C into a suspension of triethylamine (1.21 g, 1.8 mL, 12 mmol) and CuI (100 mg, 0.5 mmol) in ether (5 mL). After being stirred for 1.5 h at 0 °C and 2.5 h at room temperature, the white reaction solution was cooled to −78 °C, and methyllithium (50 mL of a 1.6 M solution, 80 mmol) was slowly added. After complete addition, the mixture was stirred for 1 h at 0 °C and then hydrolyzed with an ice-cold solution of 10% NH_4Cl (75 mL). The product was extracted with ether (3 × 30 mL), the organic phase was dried ($MgSO_4$), and the solvent was evaporated, finally, with an oil pump. The residue was taken up in pentane (50 mL) and the product was frozen out at −78 °C, giving **19e** (1.1 g, 45%): IR ($CHCl_3$) 3600 (w), 3000 (w), 2960 (m), 2920 (w), 1460 (w), 1440 (w), 1380 (w), 1360 (w), 1250 (m), 850 (s) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$, benzene standard) δ 0.025 (s, 9 H, $SiMe_3$), 1.19 (d, J = 6 Hz, 3 H, CH_3CH), 1.31 (s, 6 H, 2 CH_3), 1.56 (s, 2 H, CH_2Si), 1.5–2.15 (m, 4 H, CH_2CH_2), 3.65–3.90 (m, 1 H, $CHOH$), 5.30 (t, J = 7 Hz, 1 H, HC=C); mass spectrum (10 eV), m/z (relative intensity) 244 (M^+, 0), 226 (5), 139 (77), 121 (35), 93 (31), 81 (25), 79 (32), 75 (71), 73 (100), 43 (44).

(Z)-7-Methyl-6-[(trimethylsilyl)methyl]-5-octene-1,2,7-triol (19f). Triethylamine (1.6 g, 11 mmol) and CuI (100 mg, 0.5 mmol) were stirred in absolute ether (5 mL) under nitrogen and cooled to 0 °C. The resulting white suspension was dropped into a solution of allylic bromide **17f** (3.9 g, 10 mmol) and trichlorosilane (1.15 mL, 11 mmol) in ether (10 mL). After being stirred for 1.5 h at 0 °C and for 2.5 h at room temperature,[8] the solution was cooled to −50 °C, and methyllithium (62.5 mL of a 1.6 M solution, 100 mmol) was dropped in slowly. The solution was stirred for 0.5 h at 0 °C and poured into an ice-cooled solution of 10% NH_4Cl. The organic phase was separated and the aqueous phase was extracted with ether (2 × 50 mL). The combined organic phase was washed with water (50 mL) and dried ($MgSO_4$), and the solvent was removed, finally, on an oil pump. After addition of pentane (100 mL) and cooling overnight to −20 °C, triol **19f** (1.1 g, 42%) was precipitated as a thick yellow oil: IR ($CHCl_3$) 3600 (w, OH), 3400 (br w, OH), 3000 (w), 2940 (m), 1240 (m, Si–C), 850 (m) cm^{-1}; 90-MHz ^1H NMR (Me_2SO-d_6, Me_4Si added afterwards) δ 0.01 (s, 9 H, $SiMe_3$), 1.25 (s, 6 H, CMe_2), 1.64 (s, 2 H, CH_2Si), 1.70–2.50 (m, 4 H, CH_2CH_2), 3.38 (q, J = 5 Hz, 2 H, CH_2OH), 4.29 (s, 1 H, OH), 4.36–4.54 (m, 3 H, CHOH, CH_2OH), 5.23 (t, J = 7 Hz, 1 H, HC=C); mass spectrum (10 eV), m/z

(relative intensity) 260 (M^+, 0), 245 (1), 242 (1), 229 (4), 227 (4), 171 (6), 155 (47), 121 (16), 119 (15), 109 (23), 107 (23), 95 (29), 93 (39), 91 (21), 87 (26), 81 (21), 79 (31), 75 (69), 73 (100), 67 (35), 59 (22).

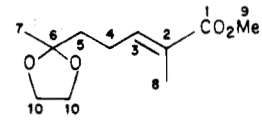
2-Methylenehexanoic Acid, Methyl Ester (20g). 17g (1.1 g, 5 mmol) in tetrahydrofuran (1 mL) was cooled to −25 °C, and a solution (5.5 mL) of 1 M $LiBEt_3H$ [Super-Hydride (Aldrich)] in THF was dropped in. The solution was stirred for 2 h and poured into ice–water (50 mL). After extraction with pentane (3 × 30 mL) the organic phase was dried ($MgSO_4$), and the solvent was evaporated. Distillation of the residue at 90 °C gave **20g** (0.6 g, 85%): IR ($CHCl_3$) 2960 (m), 1715 (vs, C=O), 1630 (w, C=C), 1440 (m), 1160 (s) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 0.9 (t, J = 6.5 Hz, 3 H, CH_3), 1.32–1.5 (m, 4 H, CH_2CH_2), 2.30 (t, J = 7 Hz, 2 H, CH_2C=C), 3.74 (s, 3 H, OCH_3), 4.51 (t, J = 1.5 Hz, 1 H, HC=C), 6.13 (br s, 1 H, HC=C); mass spectrum (10 eV), m/z (relative intensity) 142 (M^+, 21), 127 (27), 111 (35), 101 (100), 95 (22), 88 (40), 81 (23), 69 (49), 55 (60).

3-Acetoxy-2-methylenehexanoic Acid, Methyl Ester (21g). Acetyl chloride (1 g, 0.93 mL, 13 mmol) was slowly dropped into a solution of **16g** (1.58 g, 10 mmol) and pyridine (10 mL) in CH_2Cl_2 (5 mL), kept at 0 °C and under nitrogen. After being stirred for 4 h, the solution was poured onto ice–water and extracted with ether (3 × 40 mL). The organic phase was dried, and the solvent was evaporated, leaving **21g** (1.8 g, 90%): IR ($CHCl_3$) 2960 (m), 1750 (br vs, C=O), 1640 (w, C=C), 1440 (m), 1370 (m), 1160 (m), 1110 (m) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 0.9 (t, J = 7 Hz, 3 H, CH_3CH_2), 1.25–1.75 (m, 4 H, CH_2CH_2), 2.06 (s, 3 H, CH_3C=O), 3.77 (s, 3 H, OCH_3), 5.62 (t, J = 7 Hz, 1 H, HCO), 5.76 (t, J = 1 Hz, 1 H, HC=C), 6.27 (br s, 1 H, HC=C); mass spectrum (10 eV) m/z (relative intensity) 200 (M^+, 0), 157 (54), 140 (19), 125 (81), 115 (76), 109 (21), 83 (40), 81 (30), 71 (18), 43 (100).

3-Acetoxy-6,6-(ethylenedioxy)-2-methyleneheptanoic Acid, Methyl Ester (21h). Acetyl chloride (1.1 mL, 15 mmol) was dropped into a solution of **16h** (2.1 g, 9 mmol) in pyridine (8 mL), kept at 0 °C under nitrogen, and stirred for 3 h. The reaction solution was poured onto ice–water (30 mL) and extracted with ether (3 × 30 mL). The ether phase was washed with ice–water (3 × 20 mL) and dried ($MgSO_4$). After evaporation of the solvent any remaining pyridine was removed with an oil pump to give **21h** (1.8 g, 73%): IR ($CHCl_3$) 2980 (m), 2960 (m), 2880 (w), 1730 (vs, C=O), 1630 (w, C=C), 1440 (m), 1380 (m), 1250 (s, C-O) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.30 (s, 3 H, CH_3), 1.75 (m, 4 H, CH_2CH_2), 2.09 (s, 3 H, CH_3C=O), 3.79 (s, 3 H, OCH_3), 3.93 (s, 4 H, OCH_2CH_2O), 5.65 (t, J = 7 Hz, 1 H, CHO), 5.78 (t, J = 1 Hz, 1 H, HC=C), 6.31 (s, 1 H, HC=C); mass spectrum (70 eV), m/z (relative intensity) 272 (M^+, 0), 257 (3), 197 (7), 137 (8), 87 (100), 43 (30).

(*E*)-2-Methyl-2-hexenoic Acid, Methyl Ester (22g). 21g (1 g, 5 mmol) in absolute THF (1 mL) was cooled to −30 °C, and a solution (5.5 mL) of 1 M $LiBEt_3H$ in THF was dropped in. After 2 h the reaction solution was poured into water, and the product was extracted with ether (3 × 40 mL). The organic phase was dried ($MgSO_4$), and the solvent was evaporated, leaving a residue, which was distilled at 100 °C, (water pump vacuum). The yield was 0.6 g (84%) of **22g**: IR ($CHCl_3$) 2960 (m), 1710 (vs, C=O), 1650 (w), 1440 (m), 1330 (w), 1280 (s), 1150 (m), 1100 (m) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 0.91 (t, J = 7 Hz, 3 H, CH_3CH_2), 1.33–1.57 (m, 2 H, CH_2), 1.82 (t, J = 1.5 Hz, 3 H, CH_3C=C), 2.01–2.29 (q, J = 7 Hz, 2 H, CH_2C=C), 3.72 (s, 3 H, OCH_3), 6.77 (dt, J = 7 Hz, J = 1.5 Hz, 1 H, HC=C); mass spectrum (70 eV), m/z (relative intensity) 142 (M^+, 61), 127 (28), 111 (48), 101 (62), 95 (32), 88 (51), 83 (38), 55 (100).

6,6-(Ethylenedioxy)-2-methyl-2-heptenoic Acid, Methyl Ester (22h). 21h (1.3 g, 5 mmol) in absolute THF (2 mL) was cooled to −50 °C, and a solution (5.5 mL) of 1 M $LiBEt_3H$ in THF was slowly added. After 1 h at −50 °C the solution was poured



22h

into a solution (20 mL) of ice-cold 10% NH_4Cl, and the product was extracted with pentane (3 × 20 mL). After evaporation of the solvent the product was purified by Kugelrohr distillation, yielding 0.92 g (90%) of **22h**: IR ($CHCl_3$) 2950 (w), 1710 (s, C=O), 1645 (w, C=C), 1440 (m), 1380 (m) cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.32 (s, 3 H, CH_3), 1.78 (m, 2 H, CH_2CH_2C=C), 1.86 (t, J = 1 Hz, 3 H, CH_3C=C), 2.29 (m, 2 H, CH_2C=C), 3.70 (s, 3 H, OCH_3), 3.95 (s, 4 H, OCH_2CH_2O), 6.77 (dt, J = 8 Hz, J = 1 Hz, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 168.56 (s, C-1), 127.58 (s, C-2), 142.18 (d, C-3), 37.77 (t, C-4), 23.41 (t, C-5), 109.53 (s, C-6), 23.90 (q, C-7), 12.27 (qm, C-8), 51.55 (q, C-9), 64.76 (t, C-10); mass spectrum (70 eV), m/z (relative intensity) 214 (M^+, 1), 199 (7, M − CH_3), 113 (5), 87 (100), 79 (10), 69 (8), 43 (29).

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Registry No. **14a**, 22927-31-7; **14b**, 87102-03-2; **14c**, 6139-84-0; **14d**, 54911-85-2; **14e**, 87050-29-1; **14f**, 87114-19-0; **14g**, 123-72-8; **14h**, 24108-29-0; (*Z*)-**15a**, 87050-34-8; (*E*)-**15a**, 97592-19-3; (*Z*)-**15b**, 97592-03-5; (*E*)-**15b**, 97592-18-2; **16a**, 87050-30-4; **16b**, 87102-06-5; **16c**, 87102-08-7; **16d**, 87102-05-4; **16e**, 87050-31-5; **16f**, 87102-07-6; **16g**, 18020-64-9; **16h**, 87050-26-8; (*Z*)-**17a**, 87050-32-6; **17a**α, 97592-04-6; **17b**, 97592-05-7; **17c**, 97592-06-8; **17d**, 97592-07-9; **17e**, 87050-33-7; **17f**, 97592-08-0; (*Z*)-**17g**, 87050-38-2; **18a**α, 97592-09-1; **18b**, 97592-10-4; **18c**, 97592-11-5; **18d**, 97592-12-6; **19a**, 87050-35-9; **19b**, 97592-13-7; **19c**, 82010-24-0; **19d**, 97592-14-8; **19e**, 87050-36-0; **19f**, 97592-15-9; **20g**, 3070-68-6; **21g**, 87050-27-9; **21h**, 87050-28-0; **22g**, 16493-96-2; **22h**, 34312-78-2; **25**, 32651-37-9; **26**, 97592-16-0; **27**, 51326-51-3; **28**, 79131-60-5; **29**, 97592-17-1; **30**, 1608-67-9; **31**, 82131-14-4; DABCO, 280-57-9; 1,4-butanediol, 110-63-4; benzoyl chloride, 98-88-4; 2,4,6-trimethylbenzoyl chloride, 938-18-1; 2-(2-bromoethyl)-1,3-dioxolane, 18742-02-4; 4-(dimethylamino)-pyridine, 1122-58-3; tetrahydrofurfuryl alcohol, 97-99-4; trimethylacetyl chloride, 3282-30-2; 4,4-(ethylenedioxy)-1-pentanol, 29021-98-5; ethyl (diethoxyphosphinyl)acetate, 867-13-0; (iodomethyl)(trimethyl)silane, 4206-67-1; methyl acrylate, 96-33-3; dimethyl(2,5-dioxo-1-pyrrolidinyl)sulfonium bromide, 39149-95-6; dimethyl(2,5-dioxo-1-pyrrolidinyl)sulfonium chloride, 39095-38-0.