# Allylic Mono- and Di-hydroxylation of Isolated Double Bonds with Selenium Dioxide–*tert*-Butyl Hydroperoxide. NMR Characterization of Long-chain Enols, Allylic and Saturated 1,4-Diols, and Enones

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Selenium dioxide with *tert*-butyl hydroperoxide as re-oxidant was used in the allylic hydroxylation of isolated double bonds in straight-chain hydrocarbons. This was shown for mono-unsaturated fatty acids, esters and alcohols. Either allylic position was hydroxylated individually or both positions reacted to give dihydroxy isomers, affording numerous novel hydroxy compounds. Yields of monohydroxy compounds in which the OH group is between the double bond and C-1 were usually higher than those in which the OH group is between the double bond and the methyl terminus. Monohydroxy products were used as starting material in subsequent allylic hydroxylation reactions to increase the yield of dihydroxy product, although this reaction is slow. Coinciding with the known mechanism, *cis* double bonds of starting materials isomerized nearly quantitatively to *trans* double bonds in the products while *trans* double bonds did not isomerize. Resonance differences of the olefinic carbons in $^{13}C$ NMR of the unsaturated monohydroxy compounds show on which side of the double bond the hydroxy group is located. The magnitude of these differences depends on the nature of the group at C-1 and the distance of the double bond from C-1. Corresponding saturated hydroxy fatty acids were synthesized with the hydrazine–air system. $^{13}C$ NMR of the saturated compounds showed that the dihydroxy products were *erythro/threo* diastereoisomers. With this assignment, $^1H$ NMR of the unsaturated allylic dihydroxy compounds may be used to distinguish these diastereoisomers. The olefinic protons of the *erthryo* dihydroxy diastereoisomer resonate downfield from those in the *threo* form. The *threo* diastereoisomers are formed in higher yields than their *erythro* counterparts. Compounds with allylic keto group (enones) analogous to the monohydroxy products arose as side products. The $^{13}C$ NMR spectra of these enones are discussed.

Selenium dioxide has for several decades been the preferred reagent for accomplishing allylic hydroxylations.[1] The introduction of *tert*-butyl hydroperoxide (TBHP) as re-oxidant for colloidal selenium formed during the reaction[2] enhanced the applicability of this reaction.[1] However, $SeO_2$ has been almost exclusively used for introducing a hydroxy group only at one specific site in the substrate molecule. In early studies on oxidation with $SeO_2$, Guillemonat[3] selected non-3-ene and non-4-ene among other substrates. A mixture of nonenols resulted and no crystalline material could be obtained. The mechanism was elucidated by Sharpless and coworkers.[4] Few studies exist in which reactions of olefins such as oleic acid [octadec-9(*Z*)-enoic acid] and methyl oleate with $SeO_2$ were evaluated.[5] One group[5a,b] indicated the formation of allylic dihydroxy acids. Individual products were not isolated or fully characterized. These studies were carried out without TBHP. Acetylenes, however, mainly underwent dihydroxylation with the $SeO_2$–TBHP system.[6a] Minor, almost trace, amounts of dihydroxy products were found in other reactions of olefins with $SeO_2$–TBHP.[6b] In any case, allylic dihydroxylation of olefins is a rare reaction.[6a] Other reports on the syntheses or occurrence of allylic hydroxy compounds exist.[7] To our knowledge, the reaction of $SeO_2$ with isolated double bonds in long, unsubstituted, linear hydrocarbons and its potential for allylic dihydroxylation ($\alpha,\alpha'$-dihydroxylation) has not been systematically investigated.

. The recent microbial synthesis of 7,10-dihydroxyoctadec-8-(*E*)-enoic acid from oleic acid by the strains *Pseudomonas* PR3[8a] and 42A2,[8b] which involves double allylic hydroxylation with shift of the double bond, provided an incentive to seek chemical means for obtaining the allylic dihydroxy functionality. To possibly achieve allylic dihydroxylation in only one step[9] and without shift of the double bond, we studied oleic acid and other compounds with long unsubstituted and monosaturated hydrocarbon chains for their susceptibility to allylic mono- and di-hydroxylation with $SeO_2$.

Compounds with chiral centres in 1,4-position[10] have received attention due to their value in organic synthesis. Allylic dihydroxylation with $SeO_2$ in the presence of TBHP could provide access to similar unsaturated (and saturated) 1,4-diols. It is conceivable that additional materials may be found for the $SeO_2$–TBHP system (or only $SeO_2$) such as ligands (in analogy to those used in osmium-based asymmetric dihydroxylations of double bonds which afford vicinal diols[11]) to enhance enantio- or diastereo-selectivity or in the form of coreagents for increasing the yields of 1,4-diols.

Recently, we reported on the hydroxy fatty acids arising from the reaction of oleic acid with the $SeO_2$–TBHP system.[12] We extend this method here to similar alkenes and discuss some interesting aspects of product characterization by NMR spectroscopy.

## Results and Discussion

Isolated double bonds in long, linear alkenes with functional groups at C-1 can be hydroxylated with the $SeO_2$–TBHP system to give four fractions of hydroxy compounds which are separable by high-performance liquid chromatography (HPLC). Two of these are products of allylic monohydroxylation. The remaining pair are the *erythro* and *threo* diastereoisomers from allylic dihydroxylation. In the following text, the allylic positions nearer to and further from the functional group at C-1 are referred to as position I and position II, respectively. Corresponding saturated hydroxy products were

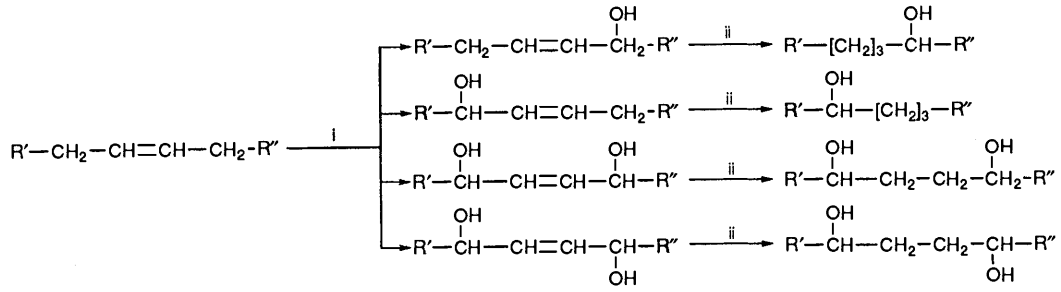

Fig. 1 Reaction procedure and hydroxy products; *reagents and conditions*: i, $SeO_2$–TBHP; ii, $N_2H_4$–air

**Table 1** Yields of monohydroxy and dihydroxy compounds in the reaction of isolated double bonds in long, straight-chain hydrocarbons with $SeO_2$–TBHP

| | Yield (%) | | | |
|---|---|---|---|---|
| | Monohydroxy[b] | | Dihydroxy | |
| Starting material[a] | I[c] | II[c] | *erythro* | *threo* |
| 16,Δ9*Z*,$CO_2H$ | 20 | 16 | 4 | 7 |
| 18,Δ6*Z*,$CO_2H$[d] | — | 21 | — | — |
| 18,Δ9*Z*,$CO_2H$ | 24 | 15 | 5 | 7 |
| 18,Δ9*E*,$CO_2H$ | 17 | 10 | 4 | 3 |
| 18,Δ11*Z*,$CO_2H$ | 26 | 15 | 3 | 5 |
| 18,Δ11*E*,$CO_2H$ | 21 | 14 | 3 | 4 |
| 20,Δ11*Z*,$CO_2H$ | 36 | 22 | 4 | 6 |
| 22,Δ13*Z*,$CO_2H$ | 38 | 14 | 5 | 8 |
| 16,Δ9*Z*,$CO_2CH_3$ | 13 | 15 | 2 | 2 |
| 18,Δ6*Z*,$CO_2CH_3$[d] | — | 25 | — | — |
| 18,Δ9*Z*,$CO_2CH_3$ | 25 | 15 | 2 | 2 |
| 18,Δ9*E*,$CO_2CH_3$ | 20 | 20 | 2 | 3 |
| 18,Δ11*Z*,$CO_2CH_3$ | 20 | 18 | 4 | 6 |
| 20,Δ11*Z*,$CO_2CH_3$ | 31 | 24 | 3 | 3 |
| 22,Δ13*Z*,$CO_2CH_3$ | 36 | 15 | 5 | 5 |
| 18,Δ6*Z*,OH | 30 | 30 | 2 | 3 |
| 18,Δ9*Z*,OH | 37 | 16 | 2 | 4 |
| 18,Δ11*Z*,OH | 23 | 14 | 4 | 5 |
| 20,Δ11*Z*,OH | 31 | 15 | 2 | 3 |
| 22,Δ13*Z*,OH | 33 | 10 | 2 | 4 |

[a] The starting materials are coded as in the following example: octadec-9(*Z*)-enoic acid is 18,Δ9*Z*, $CO_2H$. First the number of carbon atoms in the chain is given, followed by location and geometry of the double bond and finally by the functional groups at C-1. [b] Yields of the monohydroxy products were determined by a combination of gravimetry and GC-MS of HPLC fractions. In fractions containing both monohydroxy products, the relative amounts of each compound were determined by comparing peak intensities of the major fragments (*e.g.* *m*/*z* 241 for silylated 8-hydroxyoctadec-9(*E*)-enoic acid and *m*/*z* 343 for silylated 11-hydroxyoctadec-9(*E*)-enoic acid) and relating them to the weight of the fraction. Yields determined after HPLC by this method are considerably lower than from GC-MS of the crude reaction mixtures. [c] Position of hydroxy group. [d] No position I monohydroxy and dihydroxy compounds were obtained due to lactonization (see text).

**Table 2** Melting points of *trans*-mono-enoic allylic monohydroxy compounds and $^{13}C$ NMR signals (solvent: $CDCl_3$) of their olefinic carbon atoms

| Compound[a] | M.p./°C | $\delta_C$[b] |
|---|---|---|
| 16,Δ9,$CO_2H$,8-OH | 40.5 | 132.73 (9), 132.36 (10) |
| 16,Δ9,$CO_2H$,11-OH | 39.5 | 132.96 (10), 132.07 (9) |
| 18,Δ6,$CO_2H$,8-OH | 54–55 | 133.42 (7), 131.22 (6) |
| 18,Δ9,$CO_2H$,8-OH | 54–55 | 132.82 (9), 132.36 (10) |
| 18,Δ9,$CO_2H$,11-OH | 43–44 | 133.05 (10), 132.05 (9) |
| 18,Δ11,$CO_2H$,10-OH | 50–50.5 | 132.88 (11), 132.27 (12) |
| 18,Δ11,$CO_2H$,13-OH | 48.5 | 132.92 (12), 132.18 (11) |
| 20,Δ11,$CO_2H$,10-OH | 59–61 | 132.75 (11), 132.30 (12) |
| 20,Δ11,$CO_2H$,13-OH | 54.5 | 132.92 (12), 132.18 (11) |
| 22,Δ13,$CO_2H$,12-OH | 65–66 | 132.74 (13), 132.23 (14) |
| 22,Δ13,$CO_2H$,15-OH | 68.70 | 132.89 (14), 132.24 (13) |
| 16,Δ9,$CO_2CH_3$,8-OH | liq.[c] | 132.95 (9), 132.21 (10) |
| 16,Δ9,$CO_2CH_3$,11-OH | liq. | 133.09 (10), 131.87 (9) |
| 18,Δ6,$CO_2CH_3$,8-OH | liq. | 133.58 (7), 131.21 (6) |
| 18,Δ9,$CO_2CH_3$,8-OH | liq. | 132.72 (9), 132.05 (10) |
| 18,Δ9,$CO_2CH_3$,11-OH | liq. | 133.07 (10), 131.78 (9) |
| 18,Δ11,$CO_2CH_3$,10-OH | liq. | 132.98 (11), 132.09 (12) |
| 18,Δ11,$CO_2CH_3$,13-OH | liq. | 133.01 (12), 132.08 (11) |
| 20,Δ11,$CO_2CH_3$,10-OH | 29.5–31 | 132.90 (11), 132.05 (12) |
| 20,Δ11,$CO_2CH_3$,13-OH | 28.5–30 | 133.01 (12), 131.96 (11) |
| 22,Δ13,$CO_2CH_3$,12-OH | 35–36 | 132.95 (13), 132.15 (14) |
| 22,Δ13,$CO_2CH_3$,15-OH | 38 | 133.03 (14), 132.11 (13) |
| 18,Δ6,OH,5-OH | 52–52.5 | 132.80 (6), 132.42 (7) |
| 18,Δ6,OH,8-OH | 52–52.5 | 133.30 (7), 131.65 (6) |
| 18,Δ9,OH,8-OH | 66–67 | 132.95 (9), 132.21 (10) |
| 18,Δ9,OH,11-OH | 65 | 133.07 (10), 132.03 (9) |
| 18,Δ11,OH,10-OH | 47.5–48 | 132.97 (11), 132.18 (12) |
| 18,Δ11,OH,13-OH | 46–47 | 133.01 (12), 133.12 (11) |
| 20,Δ11,OH,10-OH | 53.5–54 | 132.99 (11), 132.18 (12) |
| 20,Δ11,OH,13-OH | 57 | 133.05 (12), 132.03 (11) |
| 22,Δ13,OH,12-OH | 61–62 | 132.99 (13), 132.23 (14) |

[a] The compounds are coded as in Table 1. However, here the location of the hydroxy group is also indicated. [b] The number in parentheses indicates the carbon atom assigned to the signal. [c] Liquid at room temperature.

obtained by hydrogenation with the hydrazine–air system (diimide reduction). Fig. 1 schematically depicts the hydroxy products synthesized in the present work, most of which are novel compounds. Side products, *e.g.* compounds containing keto groups, were obtained in small amounts.

Mono-unsaturated compounds with chain lengths of $C_{16}$, $C_{18}$, $C_{20}$ and $C_{22}$ were used in the present study. Functionalities at C-1 were carboxyl, methyl ester, and hydroxy groups. The crude reaction mixture was analysed by thin-layer chromatography (TLC) and gas chromatography-mass spectrometry (GC-MS) to determine conversion (> 80%, typically over 90% conversion) with the $SeO_2$–TBHP system in $CH_2Cl_2$ after 24 h under ambient conditions. Yields of the hydroxy products are reported in Table 1. Tables 2–7 contain data for characterizing the products.

The combined yields of hydroxy compounds (Table 1) generally increase with increasing chain length for acids and esters. This results from an increase in the yield of monohydroxy compounds while the yield of dihydroxy products remains relatively constant. Usually a slight to moderate excess of the *threo* diastereoisomer of the allylic dihydroxy compounds is formed in comparison to the *erythro* form. The position I monohydroxy product is usually formed in higher yields than the position II monohydroxy compound. Higher yields were reported[2] on the side of the longer hydrocarbon chain when using alkenes with a double bond close to one end of the molecule. In the present work, perhaps the greater proximity to the functional group at C-1 facilitates intermediate[4] formation at the reaction site close to C-1 due to coiling or bending of the substrate molecule. This effect may also influence the higher yields of position I product found at greater chain lengths. The

**Table 3** Melting points and selected $^{13}C$ NMR signals (solvent: $CDCl_3$) of *trans*-mono-enoic allylic dihydroxy acids and esters and *trans*-mono-enoic triols

| Compound[a] | M.p./°C | $\delta_C$ Olefinic[b] | $\delta_C$ OH-bearing[b] |
|---|---|---|---|
| 16,Δ9,$CO_2$H,*e*-8,11-diOH | 77.5–80 | 133.45 133.27, | 72.05, 71.96 |
| 16,Δ9,$CO_2$H,*t*-8,11-diOH | 64–64.5 | 133.85, 133.72 | 72.39, 72.28 |
| 18,Δ9,$CO_2$H,*e*-8,11-diOH | 85 | 133.72, 133.52 | 72.34, 72.26 |
| 18,Δ9,$CO_2$H,*t*-8,11-diOH | 62 | 133.67, 133.49 | 72.31, 72.23 |
| 18,Δ11,$CO_2$H,*e*-10,13-diOH[c] | 87 | 133.07, 133.02 | 71.70, 71.67 |
| 18,Δ11,$CO_2$H,*t*-10,13-diOH | 64.5 | 133.85, 133.79 | 72.54, 72.49 |
| 20,Δ11,$CO_2$H,*e*-10,13-diOH[c] | 87–88 | 133.37, 133.29 | 72.00, 71.97 |
| 20,Δ11,$CO_2$H,*t*-10,13-diOH[c] | 72 | 133.71, 133.66 | 72.22, 72.18 |
| 22,Δ13,$CO_2$H,*e*-12,15-diOH[c] | 92.5–93 | 133.18[d] | 71.86[d] |
| 22,Δ13,$CO_2$H,*t*-12,15-diOH[c] | 75 | 133.73[d] | 72.25[d] |
| 16,Δ9,$CO_2CH_3$,*e*-8,11-diOH | 39.5–40 | 133.58, 133.38 | 72.14, 72.09 |
| 16,Δ9,$CO_2CH_3$,*t*-8,11-diOH | liq.[e] | 133.86, 133.67 | 72.42, 72.38 |
| 18,Δ9,$CO_2CH_3$,*e*-8,11-diOH | 52–55 | 133.70, 133.46 | 72.26[d] |
| 18,Δ9,$CO_2CH_3$,*t*-8,11-diOH | liq. | 133.87, 133.67 | 72.41, 72.37 |
| 18,Δ11,$CO_2CH_3$,*e*-10,13-diOH | 49.5–51 | 133.60, 133.52 | 72.24[d] |
| 18,Δ11,$CO_2CH_3$,*t*-10,13-diOH | liq. | 133.81, 133.75 | 72.43[d] |
| 20,Δ11,$CO_2CH_3$,*e*-10,13-diOH | 51–54 | 133.61, 133.52 | 72.24[d] |
| 20,Δ11,$CO_2CH_3$,*t*-10,13-diOH | 41–42 | 133.84, 133.77 | 72.43[d] |
| 22,Δ13,$CO_2CH_3$,*e*-12,15-diOH | 58–58.5 | 133.55[d] | 72.24[d] |
| 22,Δ13,$CO_2CH_3$,*t*-12,15-diOH | 51 | 133.82[d] | 72.44[d] |
| 18,Δ6,OH,*e*-5,8-diOH[c] | 87–88 | 133.54, 133.18 | 71.96, 71.78 |
| 18,Δ6,OH,*t*-5,8-diOH | 41–42 | 133.89, 133.61 | 72.36, 72.05 |
| 18,Δ9,OH,*e*-8,11-diOH | 86–87 | 133.23, 133.12 | 71.78, 71.75 |
| 18,Δ9,OH,*t*-8,11-diOH | 38–39.5 | 133.85, 133.74 | 72.43[d] |
| 18,Δ11,OH,*e*-10,13-diOH[c] | 82.5–83 | 133.34, 133.28 | 71.91[d] |
| 18,Δ11,OH,*e*-10,13-diOH | 37–40 | 133.95, 133.92 | 72.45[d] |
| 20,Δ11,OH,*e*-10,13-diOH | 87 | 133.18, 133.13 | 71.77 |
| 20,Δ11,OH,*t*-10,13-diOH | 69–70 | 133.82, 133.80 | 72.30[d] |
| 22,Δ13,OH,*e*-12,15-diOH | 93 | 133.17[d] | 71.80[d] |
| 22,Δ13,OH,*t*-12,15-diOH | 64–64.5 | 133.87[d] | 72.32[d] |

[a] The compounds are coded as in the preceding Tables. *erythro* and *threo* are abbreviated *e* and *t*, respectively. [b] The $^{13}C$ signals of the olefinic and hydroxy-bearing carbons of the dihydroxy compounds could not be assigned. [c] NMR spectrum obtained with $CD_3OD$ as cosolvent. [d] One signal. [e] Liquid at room temperature.

**Table 4** Melting points and $^{13}C$ NMR signals (solvent: $CDCl_3$) of saturated monohydroxy fatty acids and saturated diols

| Compound[a] | M.p./°C | $\delta_C$[b] OH-bearing | Neighbouring |
|---|---|---|---|
| 16,$CO_2$H,8-OH | 71.5–72 | 72.02 (8) | 37.48 (9), 37.32 (7) |
| 18,$CO_2$H,8-OH | 71 | 72.00 (8) | 37.52 (9) 37.35 (7) |
| 18,$CO_2$H,10-OH | 72 | 71.79 (10) | 37.22 (11) 37.17 (9) |
| 18,$CO_2$H,11-OH | 71–2 | 72.10 (11) | 37.44 (12), 37.40 (10) |
| 18,$CO_2$H,13-OH | 71 | 72.13 (13) | 37.41 (12, 14)[c] |
| 20,$CO_2$H,10-OH | 81 | 72.08 (10) | 37.48 (11) 37.41 (9) |
| 20,$CO_2$H,13-OH | 80 | 72.12 (13) | 37.46 (12, 14)[c] |
| 22,$CO_2$H,12-OH | 76 | 72.12 (12) | 37.46 (11, 13)[c] |
| 22,$CO_2$H,15-OH[d] | 80.5–81 | 71.79 (15) | 37.12 (14, 16)[c] |
| 18;1,5-diOH[e] | 63 | 71.90 (5) | 37.56 (6), 37.02 (4) |
| 18;1,8-diOH[d] | 65 | 71.81 (8) | 37.34 (9), 37.23 (7) |
| 18;1,10-diOH | 64–64.5 | 72.01 (10) | 37.49 (11), 37.45 (9) |
| 18;1,11-diOH | 72–73 | 72.01 (11) | 37.50 (10, 12)[c] |
| 18;1,13-diOH | 62.5–63 | 72.02 (13) | 37.47 (14), 37.45 (12) |
| 20;1,10-diOH | 68–70 | 71.87 (10) | 37.33 (11), 37.29 (9) |
| 22;1,1,13-diOH | 78–79 | 72.02 (13) | 37.48 (12, 14)[c] |

[a] The compounds are coded as in the preceding Tables. However, the double bond has been omitted. [b] The number in parentheses indicates the carbon atom assigned to the signal. [c] One signal. [d] NMR spectrum obtained with $CD_3OD$ as cosolvent. [e] Saturated diols are coded as follows: First the number of carbon atoms in the chain is given and then the location of the hydroxy groups. Thus 18;1,8-diOH is octadecane-1,8-diol.

greater number of carbon atoms between C-1 and the double bond may facilitate coiling or bending as mentioned above.

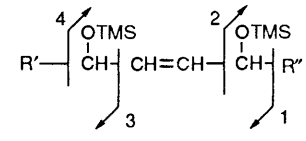


**Fig. 2** EIMS cleavage pattern for silylated allylic dihydroxy compounds. R′ contains the methyl terminus and R″ contains the trimethylsilyl ester group. This cleavage pattern is also valid for the hydrogenated products. It can also be applied to the monohydroxy compounds (see text).

Rules on preferred directions for $SeO_2$-based allylic hydroxylations were already developed by Guillemonat.[3c]

The saturated hydroxy products in Tables 4 and 5 were obtained by diimide reduction with the hydrazine–air system.[13] The hydrogenated compounds were obtained in 60–95% yields.

*Mass Spectrometry.*—The unsaturated products as trimethylsilyl derivatives (trimethylsilyl ether trimethylsilyl esters of the hydroxy acids) were analysed by GC-MS. The cleavage pattern for the silylated dihydroxy products is depicted in Fig. 2, where R′ is the hydrocarbon terminus and R″ contains the functional group at C-1. The silylated dihydroxy compounds cause a typical pattern of six fragments formed by cleavages 1, 2, 3 and 4 in Fig. 2 and liberation of TMSOH from the ions formed by cleavages 1 and 4. This pattern also holds for saturated dihydroxy compounds. The two dihydroxy isomers are indistinguishable by GC-MS under the conditions used here.

The most intense fragments for the silylated monohydroxy products arise from cleavage 1 in Fig. 2 when the OH group is in position I and from cleavage 4 when the OH group is in position II. This coincides with previous studies,[14] which also showed

**Table 5** Melting points and $^{13}C$ NMR signals (solvents: $CDCl_3$–$CD_3OD$ cosolvents for acids and triols, $CDCl_3$ for esters) of saturated dihydroxy acids and esters and saturated triols

| Compound[a] | M.p./°C | $\delta_C$[b] OH-bearing C<br>C adjacent to C–OH |
|---|---|---|
| 16,$CO_2H$,*e*-8,11-diOH | 95–96 | 71.62 (11), 71.46 (8)<br>37.12 (12), 36.96 (7), 32.82/31.81[e] (9,10) |
| 16,$CO_2H$,*t*-8,11-diOH | 71.5–74 | 72.21 (11), 72.04 (8)<br>37.53 (12), 37.39 (7), 33.91[c] (9,10) |
| 18,$CO_2H$,*e*-8,11-diOH | 99 | 71.41 (11), 71.29 (8)<br>36.98 (12), 36.83 (7), 32.68 (9,10)[c] |
| 18,$CO_2H$,*t*-8,11-diOH | 84 | 71.90 (11), 71.77 (8)<br>37.38 (12), 37.33 (7), 33.65 (9,10)[c] |
| 18,$CO_2H$,*e*-10,13-diOH | 101–104 | 71.70 (13), 71.60 (10)[d]<br>37.18 (9, 14), 32.90 (11, 12) |
| 18,$CO_2H$,*t*-10,13-diOH | 87–88 | 71.88 (13), 71.84 (10)[d]<br>37.32 (9, 14), 33.93 (11, 12) |
| 20,$CO_2H$,*e*-10,13-diOH | 97–98 | 71.63 (13), 71.54 (10)<br>37.18 (14), 37.11 (9), 32.83 (11,12)[c] |
| 20,$CO_2H$,*t*-10,13-diOH | 81 | 72.24 (13), 72.11 (10)<br>37.65 (14), 37.57 (9), 33.96/33.81[e] (11,12)[c] |
| 22,$CO_2H$,*e*-12,15-diOH | 109.5 | 71.48 (12, 15)[c]<br>37.03 (11, 16),[c] 32.70 (13, 14)[c] |
| 22,$CO_2H$,*t*-12,15-diOH | 83 | 72.11 (12, 15)[c]<br>37.56 (16), 37.51 (11), 33.93/33.88[e] (13,14)[c] |
| 16,$CO_2CH_3$,*e*-8,11-diOH | 64–65 | 71.96 (11), 71.85 (8)<br>37.51 (12), 37.40 (7), 33.32/33.26[e] (9,10)[c] |
| 16,$CO_2CH_3$,*t*-8,11-diOH | 55 | 72.32 (11), 72.20 (8)<br>37.75 (12), 37.65 (7), 33.99/33.94[e] (9,10)[c] |
| 18,$CO_2CH_3$,*e*-8,11-diOH | 79–81 | 71.87 (11), 71.74 (8)<br>37.43 (12), 37.28 (7), 33.13/33.07[e] (9,10)[c] |
| 18,$CO_2CH_3$,*t*-8,11-diOH | 60–62 | 72.28 (11), 72.16 (8)<br>37.78 (12), 37.64 (7), 34.09/34.04[e] (9,10)[c] |
| 18,$CO_2CH_3$,*e*-10,13-diOH | 75–77 | 71.95 (13), 71.91 (10)<br>37.53 (9,14),[c] 33.33 (11,12)[c] |
| 18,$CO_2CH_3$,*t*-10,13-diOH | 69 | 72.28 (13), 72.24 (10)<br>37.77 (9,14),[c] 34.03 (11,12)[c] |
| 20,$CO_2CH_3$,*e*-10,13-diOH | 75–76 | 71.86 (13), 71.81 (10)<br>37.46 (14), 37.42 (9), 33.15 (11,12)[c] |
| 20,$CO_2CH_3$,*t*-10,13-diOH | 71–71.5 | 72.29 (13), 72.24 (10)<br>37.78 (14), 37.73 (9), 34.05 (11,12)[c] |
| 22,$CO_2CH_3$,*e*-12,15-diOH | 102–103 | 71.95 (12,15)[c]<br>37.57 (11,16),[c] 33.33 (13,14)[c] |
| 22,$CO_2CH_3$,*t*-12,15-diOH | 81 | 72.28 (12,15)[c]<br>37.80 (11,16),[c] 34.03 (13,14)[c] |
| 18,OH,*e*-5,8-diOH | 96 | 71.52 (8), 71.22 (5)<br>37.12 (9), 36.51 (4), 32.84/32.78 (6,7) |
| 18,OH,*t*-5,8-diOH | 79 | 72.22 (8), 71.89 (5)<br>37.70 (9), 37.05 (4), 34.16/34.02 (6,7) |
| 18,OH,*e*-8,11-diOH | 97 | 71.45 (11), 71.38 (8)<br>37.03 (12), 36.93 (7), 32.70 (9,10) |
| 18,OH,*t*-8,11-diOH | 72 | 72.18 (11), 72.09 (8)<br>37.66 (12), 37.55 (7), 33.99/33.95 (9,10) |
| 18,OH,*e*-10,13-diOH | 97 | 71.61 (11), 71.57 (8)<br>37.16 (9,14),[c] 32.85 (11,12)[c] |
| 18,OH,*t*-10,13-diOH | 71 | 72.31 (11), 72.28 (8)<br>37.74 (9,14),[c] 34.00 (11,12)[c] |
| 20,OH,*e*-10,13-diOH | 101–102 | 71.36 (10,13)[c]<br>36.92 (14), 36.88 (9), 32.58 (11,12)[c] |
| 20,OH,*t*-10,13-diOH | 73.5–74.5 | 71.99 (13), 71.96 (10)<br>37.46 (14), 37.43 (9), 33.78 (11,12)[c] |
| 22,OH,*e*-12,15-diOH | 102–103 | 71.74 (12,15)[c]<br>37.35 (16,11),[c] 33.02 (13,14)[c] |
| 22,OH*t*-12,15-diOH | 81 | 72.12 (12,15)[c]<br>37.58 (16,11),[c] 33.91 (13,14)[c] |

[a] The compounds are coded as in the preceding Tables. [b] The number in parentheses indicates the carbon atom assigned to the signal. [c] One signal. [d] The signals of the carbons of the *erythro* and *threo* diastereoisomers are closer here due to a higher concentration of cosolvent $CD_3OD$. [e] These signals may be assignable to either C-2 or C-13 and C-14. They are close in these compounds and were not distinguished. C-13 and C-14, however, give rise to only one one signal.

that the silylated enol functionality can rearrange. This rearrangement does not affect the critical *m/z*. The silylated saturated hydroxy acids have two diagnostic peaks, either a combination of cleavages 1 and 2 for saturated position I compounds or a combination of cleavages 3 and 4 for saturated position II compounds.

**Table 6** Selected $^1$H NMR signals (solvent: $CDCl_3$) of allylic dihydroxy compounds

| Compound[a] | $\delta_H$ CH=CH | $\delta_H$ $H_2$-2 (t) |
|---|---|---|
| 18,Δ9,$CO_2$H,*e*-8,11-diOH | 5.68 | 2.33 |
| 18,Δ9,$CO_2$H,*t*-8,11-diOH | 5.66 | 2.33 |
| 18,Δ11,$CO_2$H,*e*-10,13-diOH[b] | 5.58 | 2.22 |
| 18,Δ11,$CO_2$H,*t*-10,13-diOH | 5.59 | 2.29 |
| 18,Δ9,$CO_2CH_3$,*e*-8,11-diOH | 5.68 | 2.29 |
| 18,Δ9,$CO_2CH_3$,*t*-8,11-diOH | 5.64 | 2.28 |
| 18,Δ11,$CO_2CH_3$,*e*-10,13-diOH | 5.68 | 2.28 |
| 18,Δ11,$CO_2CH_3$,*t*-10,13-diOH | 5.64 | 2.28 |
| 18,Δ6,OH,*e*-5,8-diOH[b] | 5.61 | 3.57 |
| 18,Δ6,OH,*t*-5,8-diOH | 5.60 | 3.58 |
| 18,Δ9,OH,*e*-8,11-diOH[b] | 5.57 | 3.51 |
| 18,Δ9,OH,*t*-8,11-diOH | 5.64 | 3.61 |
| 18,Δ11,OH,*e*-10,13-diOH[b] | 5.62 | 3.55 |
| 18,Δ11,OH,*t*-10,13-diOH | 5.59 | 3.58 |

[a] The compounds are coded as in the preceding Tables. [b] NMR spectrum obtained with $CD_3OD$ as cosolvent.

**Table 7** Melting points and $^{13}$C NMR signals (solvent: $CDCl_3$) of enones obtained as side products in allylic hydroxylations

| Compound[a] | M.p./°C | $\delta_C$[b] Olefinic carbons C adjacent to C=O |
|---|---|---|
| 18,Δ9,$CO_2$H,8-oxo | 48.5 | 147.52 (10), 130.22 (9) 39.89 (7) |
| 18,Δ9,$CO_2$H,11-oxo | 47.5–48.5 | 147.16 (9), 130.32 (10) 40.14 (12) |
| 18,Δ9,OH,8-oxo | 30–33 | 147.40 (10), 130.23 (9) 39.99 (7) |
| 18,Δ9,OH,11-oxo | sws[c] | 147.23 (9), 130.27 (10) 40.09 (12) |

[a] Compounds are coded as in the preceding tables. [b] The number in parentheses indicates the carbon atom assigned to the signal. [c] Soft white solid at room temperature. No melting point determined.

Cleavage patterns of this kind were also discussed for 7,10-dihydroxyoctadec-8(*E*)-enoic acid,[8a] 7,10-dihydroxyoctadecanoic acid,[15] and other oxygenated fatty acid derivatives.[16]

*Isomerization of* cis *Double Bonds. Retention of* trans *Configuration.*—All major products formed in the reactions have the *trans* configuration regardless of the geometry of the double bond in the starting material. The effect of *cis* to *trans* isomerization but not *vice versa* coincides with the mechanism for allylic hydroxylation with $SeO_2$.[4]

The FTIR spectra of the products exhibited a medium to strong absorption at 960–970 $cm^{-1}$, which is typical for *trans* double bonds. The *trans* configuration was confirmed by the coupling constants of the olefinic protons of the monohydroxy products which were in the region of $J$ = 15 to 15.5 Hz.

For the unsaturated dihydroxy compounds, a simulation of the olefinic proton signals confirmed the *trans* assignment. The key to this assignment are two small resonances in the outlying parts of the peak region of the olefinic protons (see Fig. 3). For *trans* configuration, the separation of these two small peaks would be about 32 Hz and for *cis* configuration it would be about 22 Hz or less. The present allylic dihydroxy compounds show differences of 32–33 Hz, coinciding with *trans* configuration.

*Characterization of the Monohydroxy Products.*—Table 2 contains the melting points and $^{13}$C NMR signals of the olefinic

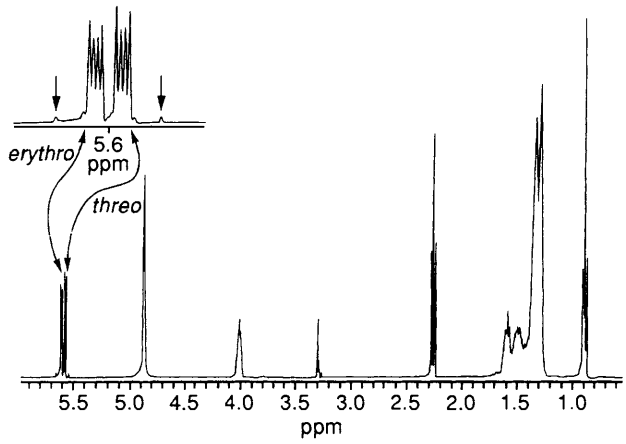


**Fig. 3** $^1$H NMR spectrum (in $CD_3OD$) of a prepared mixture of *erythro*/*threo* diastereoisomers of 8,11-dihydroxyoctadec-9(*E*)-enoic acid. The resonances of the olefinic protons in the *erythro* form are shifted downfield by approximately 0.05 ppm compared to the *threo* diastereoisomer. The arrows pointing downward highlight the small peaks whose separation by about 32 Hz in the pure diastereoisomers indicates *trans* configuration.

carbons of the monohydroxy products. The olefinic carbons in $^{13}$C NMR were assigned their signals by 2D heteronuclear correlation with $^1$H NMR. In the $^1$H NMR, the olefinic carbon adjacent to the hydroxy-bearing carbon causes a doublet of doublet of triplets in the range of 5.3–5.5 ppm. The 2D correlation assigns the olefinic carbon shifted downfield in the $^{13}$C NMR to these resonances. The reverse assignments made by other authors[14] for allylic hydroxy fatty esters without the aid of 2D correlation are thus incorrect.

Furthermore, the $^{13}$C NMR data reported for an alleged 10-hydroxyoctadec-8(*Z*)-enoic acid[17] is inconsistent with the present data. The signal of an 'allylic' carbon at 123.75 ppm in combination with mass spectral data and the melting point (the product is liquid at room temperature) makes another structure such as 10-hydroxyoctadec-7(*Z*)-enoic acid likely. The reported $^1$H NMR is also inconsistent with the suggested structure (*i.e.*, the signal at 2.55 ppm).

The $^{13}$C resonance differences of the olefinic carbons in position II monohydroxy compounds groups are greater than those in position I compounds. For example, the differences for 8-hydroxyoctadec-9(*E*)-enoic acid and 11-hydroxyoctadec-9(*E*)-enoic acid are about 0.5 and 1.0 ppm, respectively. With increasing distance of the double bond from C-1, this effect diminishes. For example, the differences are 2.2 ppm for 8-hydroxyoctadec-6(*E*)-enoic acid and 0.64 ppm for 15-hydroxydocos-13(*E*)-enoic acid. This may be expected due to the reduced effect of the group at C-1. The decrease in the $^{13}$C resonance differences of the olefinic carbons for position II OH groups is presumably a rational function. Such a relationship for position I OH groups is not apparent from the present data. The reason is presumably that a hydroxy group in position I blocks the influence of the functionality at C-1. When the OH is in position II, both functional groups influence the double bond.

This effect makes it possible to distinguish two monohydroxy compounds with the OH group in allylic positions on opposite sides of the double bond only by the differences of the $^{13}$C olefinic carbon signals. This effect was also found for homoallylic (two carbons away from the olefinic carbon) and bis homoallylic (three carbons away from the olefinic carbon) hydroxy substitution in fatty acid methyl esters with *cis* double bonds.[18] Other authors obtained allylic hydroxymethyl (branched homoallylic position of the OH group) fatty

compounds by ene reaction.[19] Here the separation of the olefinic carbons was greater for position I compounds. In unsubstituted, unsaturated fatty compounds, steric and electric field effects were invoked to account for the difference in $^{13}C$ shifts of the olefinic carbons.[20a,b] Other authors developed shift parameters for numerous fatty acid methyl esters with double and triple bonds in various positions.[20c] These authors also showed that the position of double bonds in unsubstituted fatty acids can be determined from the shift difference of the olefinic carbons.[20d] Other papers deal with these and other aspects of NMR characterization of unsaturated fatty acids and esters[20e-h] and $^{13}C$ NMR of hydroxy, oxo, and acetoxy stearates.[20h]

The $^{13}C$ NMR shift differences of the olefinic carbons in position II monohydroxy compounds are stronger when the functionality at C-1 is a methyl ester. The more polar hydroxy and carboxyl groups at C-1 have nearly identical effects, which demonstrates the effect of different functional groups at C-1 along a chain of numerous carbon atoms.

erythro/threo *Dihydroxy Diastereoisomers.*—GC-MS analyses of HPLC fractions showed that two dihydroxy products were present. The EI mass spectra of the trimethylsilylated derivatives and FTIR were indistinguishable. These products, however, possess different physical properties. The dihydroxy compound which eluted first in HPLC regularly showed the higher melting point.

The $^{13}C$ NMR of the saturated dihydroxy diastereoisomers can easily be distinguished. The signals of the hydroxy-bearing carbons and all α carbon atoms are shifted upfield in the higher-melting allylic dihydroxy compounds and downfield in the lower-melting isomers. The comparison of the shifts in Table 5 with the $^{13}C$ NMR of methyl *erythro*- and *threo*-9,10-dihydroxyoctadecanoate,[21] where the methylene carbons were shifted upfield for the *erythro* diastereoisomer and downfield for its *threo* congener,* permits the assignments of *erythro* to the higher-melting compound and *threo* to the lower-melting isomer. Correspondingly, the $^{13}C$ shifts of the C-8 and C-11 carbons of the *erythro* isomer of methyl 9,10-dihydroxyoctadecanoate were observed upfield from those of the *threo* diastereoisomer.[21] For the present 1,4-diols, the *erythro/threo* shift of the discussed $^{13}C$ NMR signals is about equal for the hydroxy-bearing and α carbons in the 'outer' positions (about 0.5 ppm) while the α carbons in the 'inner' positions (C-2 and C-3 for the 1,4-diol moiety) show stronger shifts (about 1 ppm). The shifts in 1,2-diols like the 9,10-dihydroxyoctadecanoates are stronger for the α carbons than for the hydroxylated carbons. Other cases of distinguishing *erythro/threo* isomers by $^{13}C$ NMR were reported.[22]

The assignments of the *erythro* configuration (absolute configurations *R,S* and *S,R*) and *threo* configuration (*R,R* and *S,S*) are confirmed by the melting points as discussed above. The *erythro* and *threo* forms of 9,10-dihydroxyoctadecanoic acid possess melting points of 132 °C and 95 °C, respectively.[23] Furthermore, the lower melting points of the *threo* diastereoisomers coincide with the absolute configuration of *R,R* found for microbially produced 7,10-dihydroxyoctadec-8(*E*)-enoic acid.[15] This compound has a melting point of 64 °C,[8a] close to that of *threo*-8,11-dihydroxyoctadec-9(*E*)-enoic acid

With the *erythro* and *threo* assignments made above, the NMR spectra of the unsaturated allylic dihydroxy compounds were evaluated in order to establish regular differences for these *erythro/threo* diastereoisomers.

The $^{13}C$ NMR of the allylic dihydroxy compounds show effects similar to those of the saturated dihydroxy compounds. The $^{13}C$ resonances of the olefinic and hydroxy-bearing carbons in the *threo* diastereoisomers regularly appear downfield of the *erythro* diastereoisomers (Table 3). The $^{13}C$ signals of the olefinic carbons for dihydroxy compounds could not be assigned. However, the difference between these signals decreased with increasing distance from C-1 and at a chain length of 22 carbon atoms one signal is observed. The hydroxy-bearing carbons mostly exhibit only one signal.

For distinguishing the $^1H$ NMR of the allylic dihydroxy compounds, it is convenient to choose the signals of the two C-2 protons (which cause a triplet at around 2.30 ppm) as a standard for comparing differences in the olefinic proton shifts. These peaks were chosen because they appear in all spectra uninfluenced by other resonances and to account for slightly varying cosolvent concentrations which can cause some resonance shifts. The values of selected olefinic and C-2 protons are given in Table 6.

Distinguishing *erythro/threo* diastereoisomers of unsaturated allylic dihydroxy compounds is thus possible by $^1H$ NMR. Previously, $^1H$ NMR was applied only in distinguishing the *erythro/threo* isomers of saturated long-chain compounds with vicinal hydroxy groups.[24] The above observations are verified by the $^1H$ NMR of microbially produced 7,10-dihydroxyoctadec-8(*E*)-enoic acid. Here the difference between the resonances of the protons at C-2 and the olefinic protons was 3.31 ppm (5.63 − 2.32)[8a] and 3.3 ppm (5.6 − 2.3)[8b] in $CDCl_3$ which indicates a *threo* diastereoisomer. Thus NMR provides another confirmation of the configuration of this compound. Furthermore, the effect is sufficiently large and regular to eliminate the preparation of derivatives for NMR studies.

The $^1H$ NMR resonances of the olefinic protons appear as a strong doublet of doublets consisting of an inner and an outer pair besides the two much weaker outlying peaks used for determining the geometry of the double bond as discussed above. The separation of the outer pair is 5–6 Hz while that of the inner pair is 1.7–2.1 Hz. Comparing the $^1H$ NMR of the two diastereoisomers shows that consistently the separation of the peaks is greater for the *threo* compounds than for the corresponding *erythro* compounds.

A similar result holds for the protons attached to the hydroxy-bearing carbon atoms which resonate at about 4.1–4.0 ppm. The broad multiplet caused by these protons contains two stronger inner resonances. The separation of these two peaks is 5–6 Hz for the *threo* and 3–4 Hz for the *erythro* diastereoisomers. These signals are, however, less suitable for distinguishing the two diasterisomers because they are often not well-resolved and degenerate into one broad peak or show more resonances.

*Saturated Compounds.*—Hydrogenated compounds were characterized by the same methods as their unsaturated precursors (Tables 4 and 5). The saturated dihydroxy compounds were used in the assignment of *erythro* and *threo* configurations. The $^{13}C$ NMR characterization of the saturated monohydroxy compounds coincides with that reported for the corresponding methyl esters.[25]

*Hydroxylation of the Monohydroxy Products.*—The monohydroxy products can be used for increasing the yield of dihydroxy compounds under the present reaction conditions. When using a monohydroxy substrate, extended reaction times are required and yields are low. The yields of dihydroxy compounds do not exceed approximately 15% regardless of the starting material, *i.e.* unsubstituted fatty compound or enol.

*Side Products with Allylic Keto Groups (Enones).* GC-MS analyses showed that side products arise during the allylic

* In ref. 21, the $^{13}C$ signal of C-8 and C-11 was at 31.3 ppm for methyl *erythro*- and 33.7 ppm for methyl *threo*-9,10-dihydroxyoctadecanoate.

hydroxylation of isolated double bonds. The yields of these compounds are low compared to the hydroxy products.

The most prominent side products resulted from 'over-oxidation', *i.e.* compounds with keto groups in position I or position II. The enones were formed in yields about one-tenth or less of the corresponding hydroxy compounds (combined yields of enones < 5%). Generally, lower amounts of enones were obtained with increasing chain length, coinciding with the higher amounts of hydroxy compounds. A few enones with chain lengths of 18 carbon atoms were selected for characterization in the same manner as the hydroxy compounds. Table 7 contains some analytical data for these enones.

The coupling constants of the olefinic protons in the enones were slightly below 16 ppm, confirming *trans* configuration. The allylic position of the oxo groups was ascertained by IR (carbonyl absorption around 1675 $cm^{-1}$).

Two of the enones in Table 7 [8-oxooctadec-9(*E*)-enoic acid and 11-oxooctadec-9(*E*)-enoic acid] were reported previously[26] without $^{13}C$ NMR characterization. Other enones of this kind rarely were characterized in earlier literature. Besides the compounds mentioned above, other exceptions are 9-oxooctadec-10(*E*)-enoic acid and 10-oxooctadec-8(*E*)-enoic acid[24] as well as 6-oxooctadec-4(*E*)-enoic acid, methyl 6-oxooctadec-4(*E*)-enoate, and methyl 6-oxodocos-4(*E*)-enoate.[27] The shift differences in $^{13}C$ NMR (in $CDCl_3$) of the olefinic carbons of these compounds are as follows: 9-oxooctadec-10(*E*)-enoic acid 17.2 ppm; 10-oxooctadec-8(*E*)-enoic acid 16.6 ppm; 6-oxooctadec-4(*E*)-enoic acid 12.9 ppm; methyl 6-oxooctadec-4(*E*)-enoate and methyl 6-oxodocos-4(*E*)-enoate both 13.3 ppm.

The data of these compounds and the present enones are consistent with regard to the effects discussed for hydroxy compounds. The effects of the functional group at C-1 on the olefinic carbons (methyl esters cause a greater difference in the shifts than the corresponding acids) are observed. Position I and II compounds can be distinguished by the shift differences of the olefinic carbons. The shift differences are greater for position I compounds than for position II compounds. This is the reverse of the effect in the allylic monohydroxy compounds. The carbons α to the carbonyl group apparently are another possibility for discerning position I and II compounds. The shift of these carbons is slightly downfield for the position II compounds. This coincides with literature values for 9-oxooctadec-10(*E*)-enoic acid and 10-oxooctadec-8(*E*)-enoic acid, which are 40.0 and 40.2 ppm, respectively.[26]

*Other Side Products.*—Although the formation of *trans* double bonds is favoured, there is some indication that hydroxylated products with *cis* double bonds exist. GC-MS studies of the hydroxy products revealed a weak peak preceding the major peak caused by the *trans* isomer. Both peaks show identical major fragments in MS. This observation can only be explained by the existence of *cis*/*trans* isomers. The ratio of *trans*:*cis*, however, in the products often exceeded 100:1 (yields < 1%). These compounds were not isolated due to their low amounts.

Rearrangement of the double bond during the hydroxylation is another side reaction. Analogues of the main products in which the double bond had been shifted one position in the chain in either of the two directions were obtained in small amounts (yields approximately 1%). This was verified by GC-MS in which peaks deviating by 14 ($=CH_2$) mass units from the theoretical values were observed. These compounds were also not purified due to separation difficulties.

The substrates with 18 carbon atoms in the chain and the double bond at C-6 only give one hydroxylated product. This is the product with the OH in position II. Hydroxylation of position I leads to spontaneous lactonization. HPLC fractions containing such a δ-lactone, which is liquid at room temperature, were identified by GC-MS and IR (carbonyl absorption at 1730 $cm^{-1}$).

Besides these minor constituents, slight amounts of other, unidentified products were formed.

*Conclusions.*—The reaction of isolated double bonds with $SeO_2$ in the presence of TBHP gave two allylic monohydroxy products and *erythro*/*threo* diastereoisomers of allylic dihydroxy products. Position I monohydroxy compounds and *threo* diastereoisomers are the preferred products of mono- and di-hydroxylation, respectively. Corresponding enones were formed as side products. The position of the OH group in the monohydroxy products could be determined by $^{13}C$ NMR.* These spectra also showed differences depending on the distance of the double bond from C-1 and the functional group at C-1. The allylic dihydroxy products were discernible by $^1H$ and $^{13}C$ NMR. The enone products were also distinguishable by $^{13}C$ NMR.

*Supplementary Publication.*—A supplementary publication accompanies this paper and contains the characterization data of the products described in the paper by EI-MS, of the trimethylsilylated samples, HR-FAB-MS, FTIR, $^1H$ and $^{13}C$ NMR. Copies of all $^{13}C$ NMR spectra, 2D heteronuclear correlation and some $^1H$ NMR spectra are provided.†

## Experimental

All fatty acids, esters and alcohols were obtained from Nu Chek Prep, Inc. and were of > 99% purity. Selenium dioxide (99.8%) and 90% TBHP solution containing 5% water and 5% *tert*-butyl alcohol were purchased from Aldrich Chemical Co. Hydrazine hydrate solution (64% hydrazine in water) was obtained from Eastman or Aldrich. Solvents were acquired from EM Science. Silylations were carried out at ambient temperature by adding a Supelco Sylon BTZ mixture to the sample.

NMR spectra were recorded with $CDCl_3$ as solvent on a Bruker WM-300 spectrometer operating at 300 MHz ($^1H$ NMR) and 75.5 MHz ($^{13}C$ NMR) or on a Bruker ARX-400 spectrometer operating at 400 and 100 MHz, respectively. In some cases (allylic dihydroxy compounds; noted in the appropriate Tables) $CD_3OD$ was added to enhance solubility. GC-MS analyses were conducted on a Hewlett-Packard 5890/5970 GC-MS system with electron ionization (EI). FTIR spectra of solids were recorded on a Mattson Polaris spectrometer as KBr pellets or with KBr as matrix in diffuse reflectance. FTIR spectra of liquids were obtained as film on NaCl plates. Melting points (uncorrected) were determined on an Electrothermal 9300 or a Fisher-Johns apparatus.

The GC-MS conditions were described previously as were equipment and conditions of normal-phase HPLC.[12]

*General Procedure for the Mono- and Dihydroxylation.*[12]—A synthesis with oleic as starting material is described. The amounts of $SeO_2$ and TBHP solution were calculated accordingly when using 10 g of the other starting materials. In a

* Differences in the shifts of olefinic carbons for determining position I and II compounds hold not only for hydroxy and keto groups but apparently also for hydroperoxides. In ref. 26, the shift difference of the olefinic carbons was 8.8 ppm for 9-hydroperoxyoctadec-10(*E*)-enoic acid and 7.9 ppm for 10-hydroperoxyoctadec-8(*E*)-enoic acid. Although the functional groups are not at the same carbons, they are sufficiently remote from C-1 for the effect to be validated.

† For details of the supplementary publications scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1994, issue 1. [Supp. Pub. No. 57009 145pp.]

flask equipped with a reflux condenser, $SeO_2$ (3.83 g; 34.5 mmol), TBHP solution (15 $cm^3$) and dichloromethane (40 $cm^3$) were mixed at room temperature and stirred for 0.5 h. Then oleic acid (10 g, 35.4 mmol) was added, and the reaction mixture was stirred for 24 h at room temperature. After this time, TLC (70:30:1 hexane–ethyl acetate–acetic acid, spots visualized with iodine vapour, spraying with 50% $H_2SO_4$, and baking at 120 °C for 5 min) showed that most of the substrate had reacted. The reaction was worked-up by removing the $CH_2Cl_2$, adding water immediately, and extracting into toluene. (**CAUTION**: Water must be added immediately, because the concentrated residue may form harmful fumes. Presumably, the vapours are volatile organoselenium compounds that form without solvent in the presence of air by exothermic reaction. Such vapours have been observed within 15 min following removal of $CH_2Cl_2$. As an alternative procedure, add water to the reaction mixture without removing $CH_2Cl_2$, and then proceed with extracting as described above.) The organic phase was washed ($H_2O$ ×3; brine ×3), dried ($Na_2SO_4$), filtered, and evaporated. The products were dried *in vacuo* in a desiccator. The dried reaction mixture was subjected to several HPLC purifications. The first HPLC run was conducted with a 90:10:1 hexane–ethyl acetate–acetic acid ($C_6H_{14}$–EtOAc–AcOH) system, the second one with an 80:20:1 $C_6H_{14}$–EtOAc–AcOH system and the third and final run with a 92:8 $CH_2Cl_2$–MeOH system. Even when using the $C_6H_{14}$–EtOAc–AcOH system, the column was washed with methanol to remove the unseparated dihydroxy products. When using lesser amounts (< 5 g) of material, the first HPLC run was omitted. The first HPLC run separated starting material, keto acids, and other side products as well as significant amounts of monohydroxy products. The second HPLC run separated residual monohydroxy products and other side products. The third HPLC run purified the dihydroxy acids which were obtained as two fractions (*erythro*/*threo* isomers). The two monohydroxy products often coeluted in the HPLC runs mentioned above. However, they could be separated from a concentrate by repeating the HPLC purification on a smaller scale (≤1 g) with an 80:20:1 $C_6H_{14}$–EtOAc–AcOH system. The products were obtained either as white solids or colourless liquids.

*Hydroxylation of Monohydroxy Products.*—$SeO_2$ (230 mg, 2.07 mmol), TBHP (0.9 $cm^3$) and $CH_2Cl_2$ (5 $cm^3$) were mixed as described above. After 0.5 h stirring at room temperature, 11-hydroxyoxooctadec-9(*E*)-enoic acid (600 mg, 2 mmol) (obtained by hydroxylation of oleic acid) was added. The reaction was monitored by TLC as described above. After 96 h, the reaction was terminated and worked-up as described above. Yields of the *erythro* and *threo* compounds were 51 (8%) and 49 (8%) mg, respectively.

*Hydrogenation Reactions.*—In a typical reaction, 100 mg of substrate was placed in a three-necked flask equipped with an air inlet and a reflux condenser and dissolved in 20 $cm^3$ of ethanol. Then 3 $cm^3$ hydrazine hydrate was added. A gentle stream of air was bubbled through the solution, which was heated at 60 °C for 48 h. The reaction was acidified to pH 2 with conc. HCl and diluted to a volume of about 200 $cm^3$. A white precipitate formed during this procedure. The mixture was stored overnight at 2–5 °C in a refrigerator. The white precipitate was isolated by filtration and washed with water until pH was neutral. The products obtained by this work-up did not require further purification.

*Methylations.*—As a more rapid procedure for obtaining methyl esters, the hydroxy acids were also methylated by a standard method with diazomethane as methylating agent. These esters were identical to those obtained from reactions with the corresponding methyl esters as starting materials.

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