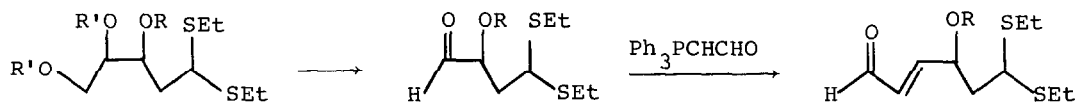




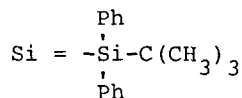
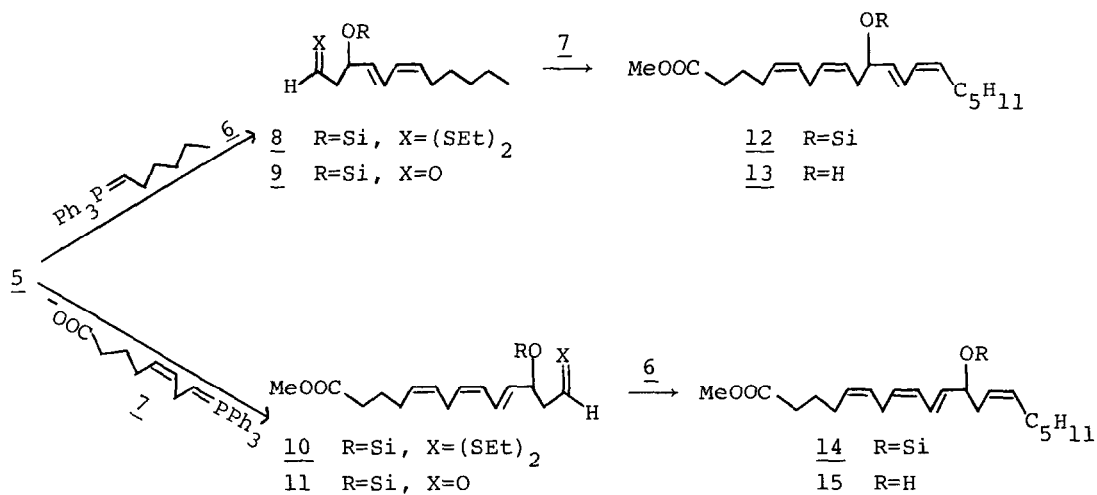
esters, using arabinose as the chiral starting material. In contrast to most carbohydrates, it is readily available in both D and L form.



- 1 R'R'=CMe<sub>2</sub>, R=H  
2 R'R'=CMe<sub>2</sub>, R=Si  
3 R'=H, R=Si

4 R=Si

5 R=Si



The synthesis of the D-2-deoxypentose dithioacetal 1 has been described by Wong and Gray<sup>6</sup> and allows for its large-scale easy preparation from arabinose. Transformation to its t-butyldiphenylsilyl ether 2<sup>7</sup>,  $[\alpha]_D^{20} + 13.7^\circ$  (CHCl<sub>3</sub>), using the method of Hannessian and co-workers<sup>8</sup>, followed by hydrolysis with trifluoroacetic acid/tetrahydrofuran (THF)/water (1:2:1, 3.5 mL per 1 mmol of 2, 20-25°, 6 h) gave diol 3<sup>7</sup>,  $[\alpha]_D^{20} + 24.7^\circ$  (CHCl<sub>3</sub>), which was obtained in 78% yield after flash chromatography (EtOAc-petroleum ether, 1:4). Treatment of 3 with 3.5 eq of sodium periodate in THF-acetone-water (2:1:2.5, 7 mL per 1 mmol of 3) at 20° for 15-20 min. gave aldehyde 4<sup>7</sup> as an oil in 72% yield. Reaction of 4 with formylmethylenetriphenylphosphorane in dry benzene at 70° for 6 h gave  $\alpha,\beta$ -unsaturated aldehyde 5, which was obtained in 79% yield after purification<sup>9</sup>. In contrast to aldehyde 4, 9 and 11, 5 was quite stable and could be stored at 0-10° for weeks. This material corresponds to fragment B in 11(S) and 12(S)-HETE.

Coupling of 5 with dianion 7<sup>3</sup> gave, after methylation with dimethyl

sulfate *in situ*, ester 10<sup>7</sup> in 75% yield after chromatography. Hydrolysis of the dithioacetal function<sup>10</sup> provided unstable aldehyde 11<sup>11</sup> in 61% yield after rapid chromatography purification. It was immediately treated with hexyl-triphenylphosphorane to give 14 in 42% yield. Although both 14Z and 14E isomers were obtained, they could not easily be separated at this stage. Hydrolysis of the silyl ether function with 1.9 eq of  $n\text{-Bu}_4\text{NF}\cdot 3\text{H}_2\text{O}$  in THF at 45° for 4 h gave a mixture of the 14Z (major) and 14E (minor) isomer of 12(S)-HETE methyl ester, which were easily separated by flash chromatography<sup>12</sup>.

Further purification by HPLC (7.5% EtOAc in hexane, Microporasil) gave pure 15<sup>13</sup>,  $[\alpha]_D^{22} + 1.3^\circ$  (c 0.3 in  $\text{CHCl}_3$ ),  $[\alpha]_D^{25} + 1.5^\circ$  (c 0.2 in  $\text{CHCl}_3$ )<sup>5</sup>. An attempt was made to determine enantiomeric purity by forming the Mosher ester<sup>15</sup> of 15, and comparing it to the one derived from d,l-12-HETE methyl ester kindly provided by Dr. Julian Adams. Unfortunately, the diastereomeric Mosher esters derived from racemic 15 appeared as a single peak on HPLC using two different systems. Proton n.m.r. of the Mosher ester of 15 was consistent with the formation of one diastereomer only. The overall yield of 15, based on crystalline arabinose dithioacetal<sup>6</sup>, was 5.7%

For the synthesis of 11(S)-HETE methyl ester, a very similar sequence was used:  $\alpha,\beta$ -unsaturated aldehyde 5 was first treated with 6 to provide 8 in 58% yield<sup>14</sup>. Condensation of highly unstable aldehyde 9, which was obtained after removal of the dithioacetal function of 8 as described above, with 7 gave, after methylation *in situ*, ester 12 and its olefinic isomers in 52% yield. Hydrolysis of the silyl ether function of 12 and its isomers with  $n\text{-Bu}_4\text{NF}\cdot 3\text{H}_2\text{O}$  in THF gave a mixture of 13 and isomers, which was easily separated by chromatography<sup>12</sup>. After further purification by HPLC (7.5% AcOEt in hexane, Microporasil), pure 11(S)-HETE methyl ester 13 was obtained in 3.2% overall yield, based on crystalline arabinose dithioacetal. It was in all respects identical to 13 previously prepared<sup>4b</sup>.

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7. All compounds were characterized by 200 MHz  $^1\text{H}$  n.m.r. and mass spectra.
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11.  $^1\text{H}$  n.m.r. 200 MHz ( $\text{CDCl}_3$ )  $\delta$ : 1.09 (s, 9H,  $\text{CMe}_3$ ), 1.64 (t of d, 2H,  $\text{C}_3\text{-H}$ ), 2.27 (t, 2H,  $\text{C}_2\text{-H}$ ), 2.51 (t of d, 2H,  $\text{C}_{13}\text{-H}$ ), 2.72 (t, 2H,  $\text{C}_7\text{-H}$ ), 3.60 (s,  $\text{OCH}_3$ ), 4.67 (q,  $\text{C}_{12}\text{-H}$ ), 5.10-5.40 (m, 3H,  $\text{C}_{5,6,8}\text{-H}$ ), 5.60 (q,  $\text{C}_{11}\text{-H}$ ), 5.80 (t,  $\text{C}_9\text{-H}$ ), 6.22 (q,  $\text{C}_{10}\text{-H}$ ), 7.36 (m, 6H, p,m-Ar-H), 7.62 (m, 4H, o-Ar-H), 9.66 (t, CHO); IR ( $\text{CHCl}_3$ ):  $1715\text{ cm}^{-1}$  (C=O),  $1725\text{ cm}^{-1}$  (O-C=O); MS (m/e 70eV): 504 ( $\text{M}^+$ ), 473 ( $\text{M}^+ - \text{OCH}_3$ ), 447 ( $\text{M}^+ - \text{CMe}_3$ ), 225 (447-222,  $\text{Ph}_2\text{Si}=\text{O}-\text{CH}=\text{CH}_2$ ), 199 (225 -  $\text{HC}\equiv\text{CH}$ ).
12. Silica gel (Kieselgel 60  $\text{HF}_{254}$  from BDH), petroleum ether-EtOAc 10:1.
13.  $^1\text{H}$  n.m.r. 200 MHz ( $\text{CDCl}_3$ )  $\delta$ : 0.88 (br.t, 3H,  $\text{C}_{20}\text{-H}$ ), 1.31 (m, 6H,  $\text{C}_{17,18,19}\text{-H}$ ), 1.69 (m, 2H,  $\text{C}_3\text{-H}$ ), 1.80 (d, OH), 2.08 (m, 2H,  $\text{C}_{16}\text{-H}$ , 2H,  $\text{C}_{2,4}\text{-H}$ ), 2.34 (br.t, 2H,  $\text{C}_{13}\text{-H}$ , 2H,  $\text{C}_{2,4}\text{-H}$ ), 2.94 (br.t, 2H,  $\text{C}_7\text{-H}$ ), 3.66 (s,  $\text{OCH}_3$ ), 4.24 (br.m,  $\text{C}_{12}\text{-H}$ ), 5.30-5.50 (m, 4H,  $\text{C}_{5,6,8,14}\text{-H}$ ), 5.50-5.60 (m,  $\text{C}_{15}\text{-H}$ ), 5.70 (d of d,  $\text{C}_{11}\text{-H}$ ), 5.95 (br.t,  $\text{C}_9\text{-H}$ ), 6.55 (d of d,  $\text{C}_{10}\text{-H}$ ); MS (m/e 70eV): 316 ( $\text{M}^+ - \text{H}_2\text{O}$ ), 303 ( $\text{M}^+ - \text{OCH}_3$ ), 223 ( $\text{M}^+ - \text{CH}_2\text{CH}=\text{CH}(\text{CH}_2)_4\text{CH}_3$ ), 141 ( $\text{M}^+ - 223$ , loss of  $\text{MeO}_2\text{C}(\text{CH}_2)_3\text{CH}=\text{CHCH}_2\text{CH}=\text{CH}=\text{CH}$ ), 191 (223 -  $\text{CH}_4\text{O}$ ), 107 (191-84).
14.  $^1\text{H}$  n.m.r. 200 MHz ( $\text{CDCl}_3$ )  $\delta$ : 0.88 (t, 3H,  $(\text{CH}_2)_3\text{CH}_3$ ), 1.09 (s, 9H,  $\text{CMe}_3$ ), 1.12 (t, 3H,  $\text{SCH}_2\text{CH}_3$ ), 1.15 (t, 3H,  $\text{SCH}_2\text{CH}_3$ ), 1.27 (m, 6H,  $\text{CH}_2(\text{CH}_2)_3\text{CH}_3$ ), 1.68-2.12 (m, 4H,  $\text{SCH}_2\text{CH}_3$ , 1H,  $\text{CH}=\text{CHCH}_2\text{CH}_2$ ), 2.29 (q of d, 1H,  $\text{CH}=\text{CHCH}_2\text{CH}_2$ ), 2.51 (m, 2H,  $\text{CH}_2\text{CHS}$ ), 3.79 (t, CHS), 4.17 (q, CHOSi), 5.34 (m,  $\text{CH}=\text{CHCH}_2$ ), 5.50 (q,  $\text{CH}=\text{CHCHOSi}$ ), 5.79 (t,  $\text{CH}=\text{CHCH}_2$ ), 6.09 (q,  $\text{CH}=\text{CHCHOSi}$ ), 7.34 (m, 6H, p,m-Ar-H), 7.66 (t of t, 4H, o-Ar-H); MS (m/e, 70eV): 540 ( $\text{M}^+$ ), 483 ( $\text{M}^+ - \text{CMe}_3$ ), 421 ( $\text{M}^+ - \text{CMe}_3 - \text{HSEt}$ ), 417 ( $\text{M}^+ - \text{CH}=\text{CHCH}=\text{CH}(\text{CH}_2)_4\text{CH}_3$ ), 360 (483 -  $\text{CH}=\text{CHCH}=\text{CH}(\text{CH}_2)_4\text{CH}_3$ ), 199 ( $\text{O}=\text{SiHPh}_2$ );  $[\alpha]_{\text{D}}^{20} = -27^\circ$  (c 2.10 in  $\text{CHCl}_3$ ).
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