Tetrahedron, Vol. 37, Supplement No. 1, pp. 263 to 267, 1981
Printed in Great Britain.

0040-4020/81/Suppl. 1-0263-05 $02.00/0
Pergamon Press Ltd.

PHENYLSELENYLATION OF ARACHIDONIC ACID AS A ROUTE TO INTERMEDIATES FOR LEUKOTRIENE SYNTHESIS

ISOMERIZATION OF CONJUGATED DIENES DURING SELENOXIDE ELIMINATION

JACK E. BALDWIN*, NEVILLE V. REED, and ERIC J. THOMAS
The Dyson Perrins Laboratory, South Parks Road, Oxford OX1 3QY, England

(*Received in UK* 28 *August* 1980)

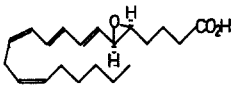
Abstract—Methyl (5*SR*, 6*SR*)-5-hydroxy-6-phenylselenyleicosa-*cis*,*cis*,*cis*-8,11,14-trienoate (**8**), available in two steps from arachidonic acid, undergoes oxidative deselenylation to give selectively either methyl (5*SR*)-5-hydroxyeicosa-*trans*,*trans*,*cis*,*cis*-6,8,11,14-tetraenoate (**5**) or its *cis*-8 isomer (**6**), depending upon the reaction conditions.

Recently there has been considerable interest in a series of metabolites derived from arachidonic acid called leukotrienes.[1] In particular, the epoxide leukotriene A **1**, has been implicated in the biosynthesis of several "slow reacting substances" (SRS's),[2-4] important agonists in asthma and other forms of hypersensitivity,[5] and the methyl ester of epoxide **1** has been used as an intermediate in chemical syntheses of leukotrienes C **2**,[4-6] and D **3**.[7] Several total syntheses of epoxide **1** have been reported,[4,6,8] and a conversion of arachidonic acid into epoxide **1**, *via* hydroperoxide **4**, has been described.[9] Because of our interest in oxidation of arachidonic acid, we decided to develop a chemical conversion of arachidonic acid into compounds of the leukotriene type. We wish to report some of our early results in this field, namely stereoselective syntheses of (±)-methyl 5-hydroxyeicosa-*trans*,*trans*,*cis*,*cis*-6,8,11,14-tetraenoate **5** and its 8-*cis* isomer **6**.

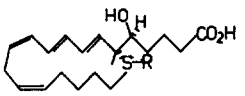
RESULTS AND DISCUSSION

The formation of 5- and 6-membered lactones by intramolecular phenylselenolactonization of unsaturated carboxylic acids is known to be an efficient reaction.[10] We therefore decided to study phenylselenolactonization of arachidonic acid as a method of functionalizing selectively the 5,6-double-bond.

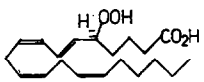
Treatment of arachidonic acid with phenylselenenyl chloride in dichloromethane at −78° proceeded smoothly and gave lactone **7**, isolated as an oil, and purified by chromatography on silica. The structure shown, which was consistent with all the spectroscopic data, was assigned by analogy with the literature assuming a *trans* addition across the originally *cis* double-bond. The completely selective functionalization of the 5,6-double bond is in accordance with the recently reported iodolactonization of arachidonic acid.[11] The lactone **7** was then hydrolysed using



(1)

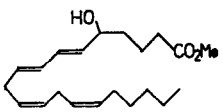


(2) R = $-CH_2-CH(CONHCH_2CO_2H)-NHCOCH_2CH_2CH(NH_2)CO_2H$

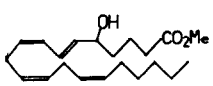


(4)

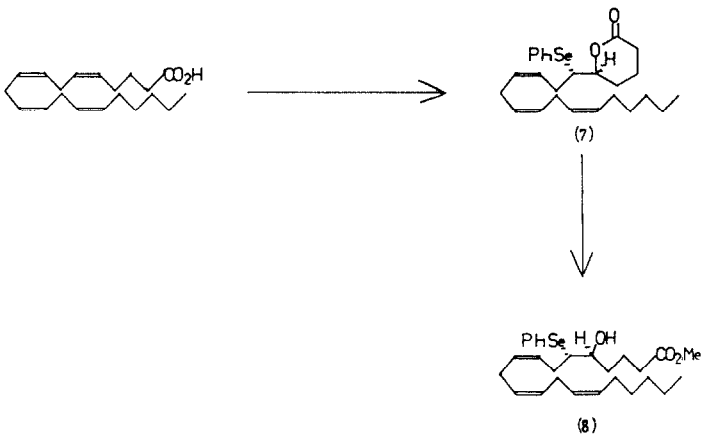
(3) R = $-CH_2-CH(CONHCH_2CO_2H)-NH_2$



(5)



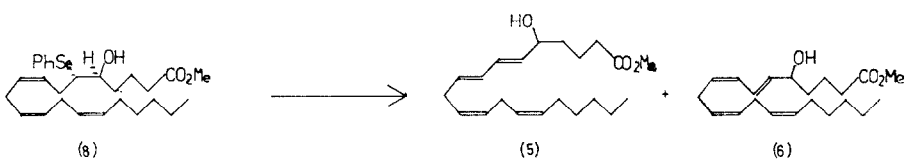
(6)



lithium hydroxide in tetrahydrofuran–water, and the free acid immediately esterified using diazomethane to give ester **8** (80%), also an oil.

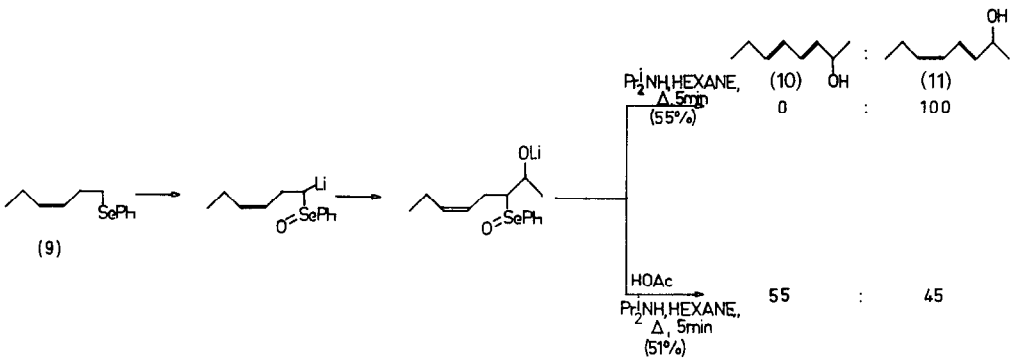
Oxidative removal of the phenylselenyl moiety from ester **8** was studied using several sets of conditions, and the results are summarized in Scheme 1.[12,13] For example treatment of ester **8** with excess sodium periodate in buffered ($NaHCO_3$) aqueous methanol at 25° for 24 hr. gave an oil which showed two closely moving spots on tlc (CH_2Cl_2-EtOAc 9:1, R_f's 0.37, 0.32). These two products were separated by column chromatography, and were identified as the hydroxy-*trans,trans*-eicosatetraenoate **5**, 60%, R_f 0.32, and its *cis*-8 isomer **6**, 15%, R_f 0.37. Similar results were obtained using excess hydrogen peroxide in aqueous methanol sodium bicarbonate, and with one equivalent of *m*-chloroperoxybenzoic acid in tetrahydrofuran at −78°, followed by addition to aqueous acetic acid and treatment with di-isopropylamine in refluxing hexane.

The structures of the products were established rigorously by spectroscopic methods. For the major product, the slower moving on tlc, ^{1}H NMR spin decoupling (300 MHz) showed the presence of two conjugated *trans* double-bonds, coupling constants of 15 Hz being observed across each double-bond. The position of the OH group was established by the mass spectral fragmentation of the t-butyldimethylsilyl ether, and was shown to be adjacent to the conjugated diene by spin-decoupling. Since ^{1}H NMR showed a total of four double-bonds, and two methylene groups each flanked by two double-bonds, the whole structure was effectively established. The *cis* geometry was assigned to the isolated double-bonds, since they had not been involved in any of the chemical transformations from arachidonic acid, and was supported by the presence of a band in the IR spectrum at 720 cm^{-1}. Isolated *cis* double-bonds are not usually affected by selenoxide elimination.[14] The minor product was similarly rigorously identified. In this case



REACTION CONDITIONS	(5) : (6)	TOTAL YIELD %
$NaIO_4$, MeOH, H_2O, $NaHCO_3$, 25°, 24h	85 : 15	75
H_2O_2, MeOH, H_2O, $NaHCO_3$, 25° 24h	85 : 15	70
MCPBA, THF, -78°; H_2O, AcOH, 0°; Pr^i_2NH, HEXANE, REFLUX	90 : 10	60
H_2O_2, THF, H_2O, KOH, 25°, 18h, CH_2N_2, Et_2O	20 : 80	60

Scheme 1.



Scheme 2.

^{1}H NMR indicated the presence of a *trans* double-bond (J 15 Hz) adjacent to the OH group, and conjugated with a *cis* double-bond (J 10.5 Hz). The *cis,trans* conjugated diene unit was also supported by IR bands at 980 and 950 cm^{-1}.[15] After our work on these compounds was complete, a synthesis of the *cis,trans*-diene **6** was reported.[16] The spectroscopic data reported for compound **6** are entirely in agreement with our own.

Therefore under these standard conditions, the oxidative elimination of the phenylselenyl moiety from hydroxyselenide **8** has been accompanied by geometrical isomerization of the *cis*-8 double-bond, which is not directly involved in the selenoxide elimination itself. No such isomerisations have been reported in recent papers, or in recent reviews, of selenoxide eliminations.[12] However we have observed a second example in a simpler system. Thus sequential treatment of *cis*-hex-3-en-1-yl phenyl selenide **9** with *m*-chloroperoxybenzoic acid, lithium di-isopropylamide, and acetaldehyde at −78°, followed by addition of the reaction mixture to aqueous acetic acid at 0°, and heating under reflux in hexane containing di-isopropylamine (Scheme 2), gave a mixture containing *trans,trans*-octa-3,5-dien-2-ol **10** and *trans,cis*-octa-3,5-dien-2-ol **11** in which the *trans,trans*-isomer **10** was the major component, **10**:**11** = 55:45.[17]

The cause of these isomerizations was not immediately apparent. However in the second example, if the aqueous acetic acid quench was omitted, and the basic solution from the selenoxide reaction with acetaldehyde, added directly to refluxing hexane containing di-isopropylamine, no isomerization was observed, and the *trans,cis*-isomer **11** was the only product isolated (55% after chromatography). Thus isomerization had not occurred under these strongly basic conditions (Scheme 2). To check this point, the long-chain hydroxyselenide **8** was treated with excess hydrogen peroxide in the presence of four equivalents of potassium hydroxide. Under these conditions, after re-esterification with diazomethane, a mixture of elimination products was obtained, in which the 8-*cis* isomer **6**, was the major component, **5**:**6** = 20:80 (Scheme 1).

Therefore the hydroxyselenide **8** can be used to prepare either the *trans,trans*-conjugated alcohol **5**, or its 8-*cis* isomer **6**. Oxidative elimination under neutral conditions ($NaHCO_3$), leads to the *trans,trans*-isomer **5** predominantly (60% isolated yield), whereas addition of base (KOH) reduces isomerization, and leads to the selective formation of the *trans,cis*-isomer **6**.

The details of the mechanism of this isomerization were not studied. However treatment of a mixture of hydroxyselenide **8** and the *trans,cis*-octa-3,5-dien-2-ol **11** with sodium periodate in buffered aqueous methanol, caused isomerization of the octadienol to its *trans,trans*-isomer **10**, 80% isomerization. Little isomerization was observed if hydroxyselenide **8** was omitted from this mixture. Possibly the side-product of the selenoxide elimination, phenyl selenenic acid is reversibly adding to the diene unit before being trapped by excess oxidant or amine, and so is responsible for the isomerization. Sulphoxide elimination is known to be reversible, but attempts to show that selenoxide elimination was reversible using D-labelling were not conclusive.[13b] However this point was not studied further.

Studies are in progress to assess the utility of the methyl 5-hydroxyeicosatetraenoates (**5** and **6**) as intermediates for leukotriene synthesis.

EXPERIMENTAL

NMR spectra (300 MHz) were obtained using a Bruker WH 300 spectrometer. UV spectra were measured on a Perkin–Elmer 555 spectrometer, and the IR spectra on a Perkin–Elmer 297 spectrometer. Hopkins and Williams silica gel MFC without binder was used for column chromatography and analytical tlc was on Merck $H_{254/366}$ silica gel. Solvents were purified and dried using standard procedures. Se-containing compounds exhibited the characteristic isotopic family in their mass spectra [^{74}Se(1), ^{76}Se(10), ^{77}Se(9), ^{78}Se(27), ^{80}Se(57), ^{82}Se(11)] but only peaks due to most abundant isotope (^{80}Se) are reported. Low resolution mass spectra were obtained using chemical ionisation techniques (methane as reagent gas), and accurate mass data obtained using field ionization, both measured on a VG micromass ZAB 1F spectrometer.

Phenylselenolactonization of arachidonic acid

Penylselenenyl chloride (3.29 g, 17.2 mmol) was added to a stirred soln of arachidonic acid (5 g, 16.4 mmol) in anhyd CH_2Cl_2 (30 ml) under dry N_2 at −78°. After the red solid had dissolved, the soln was concentrated *in vacuo*, and the oily residue chromatographed on silica (250 g) being eluted with CH_2Cl_2, to give the *lactone* **7** (5.178 g), a colourless oil homogeneous by tlc, R_f (CH_2Cl_2) 0.4; ν_{max} 3010, 2960, 2940, 2860, 1740, 1600, 1580, 1235, 745, and 700 cm^{-1}, δ ($CDCl_3$) 0.89 (3 H, t, J = 5.8 Hz, CH_2CH_3), 1.3 (6 H, m, 3 × CH_2), 1.72–2.1 (6 H, m, 3 × CH_2), 2.35–2.9 (8 H, m, 4 × CH_2), 3.28

(1 H, m, CHSePh), 4.49 (1 H, m, CHO), 6.3–6.59 (6 H, m, vinyl H), 7.29 (3 H, m, aromatic H), and 7.59 (2 H, m, aromatic H); *m/z* 461 [(M + H)$^+$, 45%] and 303 [(*M* + H)$^+$ + PhSeH, 100%]. (Found: *m/z* 460.1883 $C_{26}H_{36}O_2Se$ requires: M$^+$ 460.1880).

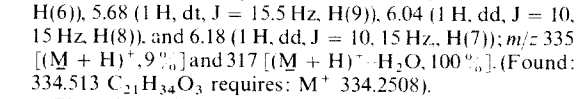
Methyl(5SR, 6SR)-5-*Hydroxy*-6-*phenylselenyleicosa*-cis,cis,cis-8,11,14-*trienoate* (**8**)

Lithium hydroxide (25 ml of an 0.1 N aqueous soln) was added to **7** (1 g, 2.17 mmol) in aqueous THF (25 ml, 1:1), and the soln stirred at 25° for 1 hr. Acidification then extraction into CH_2Cl_2 (2 × 20 ml), was followed by immediate treatment of the CH_2Cl_2 extracts with ethereal diazomethane. Drying ($MgSO_4$) and concentration *in vacuo* gave an oil which was chromatographed on silica to give *methyl* (5*SR*, 6*SR*) 5-*hydroxy*-6-*phenylselenyleicosa*-cis,cis,cis-8,11,14-*trienoate* **8** (860 mg), a colourless oil, homogeneous by tlc, R_f (CH_2Cl_2) 0.24, ν_{max} 3500, 3020, 2960, 2930, 2860, 1740, 1580, 1200, 745, and 700 cm^{-1}, δ ($CDCl_3$) 0.89 (3 H, t, J = 6 Hz, CH_2CH_3), 1.2–1.44 (6 H, m, 3 × CH_2), 1.55–1.88 (4 H, m, 2 × CH_2), 2.06 (2 H, m, CH_2), 2.23–2.48 (4 H, m, one exch. with D_2O, OH), 2.59 (1 H, m), 2.79 (4 H, m, 2 × CH_2), 3.17 (1 H, m, CHOH), 3.55–3.69 (4 H, m, CH_3 + CH), 5.26–5.57 (6 H, m, vinylic H), 7.27 (3 H, m, aromatic H), and 7.57 (2 H, m, aromatic H); *m/z* 493 [M + H)$^+$, 7%] and 317 [(M + H)$^+$–PhSeH, 100%]. (Found: *m/z* 492.2141 $C_{27}H_{40}O_3Se$ requires: M$^+$ 492.2142).

Oxidative elimination of phenylselenium from hydroxyselenide (**8**)

(a) *Using sodium periodate-sodium bicarbonate.* $NaHCO_3$ (252 mg, 3 mmol) in water (5 ml) was added to **8** (0.4 g, 0.81 mmol) in MeOH (40 ml) at 0°, and sodium periodate (0.52 g, 2.43 mmol) in water (7 ml) added dropwise. The mixture was stirred at 25° for 24 hr before being diluted with ether (20 ml), and water (20 ml), and the organic layer separated, washed with water (2 × 20 ml), brine (2 × 20 ml), and dried ($MgSO_4$). Concentration *in vacuo* gave an oil which was shown by tlc to consist of two major components (CH_2Cl_2–EtOAc, 9:1). These two compounds were separated by chromatography on silica. The first product off the column was identified as (±)-*methyl* 5-*hydroxyeicosa*-trans,cis-,cis,cis-6,8,11,14-*tetraenoate* **6** (50 mg) a colourless oil homogeneous by tlc, R_f 0.37, ν_{max} (CS_2) 3600, 3010, 2950, 2920, 2850, 1740, 1200, 980, 950 and 720 cm^{-1}, λ_{max} (MeOH) 232 nm (ε 29, 600), δ ($CDCl_3$) 0.89 (3 H, t, J = 6.5 Hz, CH_2CH_3), 1.33 (6 H,, m, 3 × CH_2), 1.51–1.83 (5 H, m, 2 × CH_2 + OH), 2.05 (2 H, m, CH_2), 2.36 (2 H, t, J = 6.25 Hz, CH_2), 2.83 (2 H, t, J = 5 Hz, CH_2), 2.96 (2 H, t, J = 5 Hz, CH_2), 3.68 (3 H, s, OCH_3), 4.19 (1 H, m, CHOH), 5.4 (5 H, m, vinylic H), 5.7 (1 H, dd, J = 6, 15 Hz, H (6)), 6.0 (1 H, m, H(8)), and 6.53 (1 H, dd, J = 10.5, 15 Hz, H(7)); *m/z* 334 ((M + 1)$^+$, 9%), 317 (M + H)$^+$–H_2O, 100%), 303 (M + H)$^+$–CH_3OH, 17%) (Found: *m/z* 334.2505. $C_{21}H_{34}O_3$ requires: M$^+$ 334.2508). The second product off the column was identified as (±)-*methyl* 5-*hydroxyeicosa*-trans,trans,cis,cis-6,8,11,14,-*tetraenoate* **5** (150 mg), a colourless oil, homogeneous by tlc, R_f 0.32, ν_{max} (CS_2) 3600, 3010, 2950, 2920, 2850, 1740, 1200, 985, and 720 cm^{-1}, λ_{max} (MeOH) 230 nm (ε 28, 400), δ ($CDCl_3$) 0.91 (3 H, t, J = 6.25 Hz, CH_2CH_3), 1.31 (6 H, m, 3 × CH_2), 1.46–1.8 (5 H, m, 2 × CH_2 + OH), 2.06 (2 H, m, CH_2), 2.36 (2 H, m, CH_2), 2.78 (2 H, t, J = 5 Hz, CH_2), 2.95 (2 H, t, J = 5 Hz, CH_2), 3.68 (3 H, s, OCH_3), 4.13 (1 H, m, H(5)), 5.4 (4 H, m, vinylic H), 5.6 (1 H, dd, J = 7.5, 15 Hz, H(6)), 5.68 (1 H, dt, J = 15.5 Hz, H(9)), 6.04 (1 H, dd, J = 10, 15 Hz, H(8)), and 6.18 (1 H, dd, J = 10, 15 Hz,, H(7)); *m/z* 335 [(M + H)$^+$, 9%] and 317 [(M + H)$^+$–H_2O, 100%]. (Found: 334.513 $C_{21}H_{34}O_3$ requires: M$^+$ 334.2508).

The t-butyldimethyl silyl ether were prepared by the method of Corey and Ventateswarln, and showed the characteristic cleavage product in the mass spectrum at 245



corresponding to the $Me_3C—Si(Me)_2—O—CH(CH_2)_3CO_2Me$ fragement.[18]

(b) *Using hydrogen peroxide–sodium bicarbonate.* $NaHCO_3$ (84 mg, 1 mmol) in water (3 ml) was added to **8** (44 mg, 0.089 mmol) in MeOH (10 ml) and 30% H_2O_2 (1 cm^3, 11.4 mmol) added dropwise. The reaction was stirred at room temp for 18 hr, then worked up in the normal way to yield a similar mixture of **6** 4 mg, and **5** 17 mg.

(c) *Using* m-*chloroperoxybenzoic acid–diisopropylamine.* m-Chloroperoxybenzoic acid (18.6 mg, 0.108 mmol) in THF (1 ml) was added to **8** (50 mg, 0.108 mmol) in THF (5 ml) at −78° under anhyd N_2. The mixture was stirred for 60 min, then warmed to 0°. AcOH (0.05 ml) and water (0.05 ml) added, and the resulting suspension added to diisopropylamine (21.8 mg, 0.216 mmol) in hexane (10 ml) at reflux.

After 5 min, the reaction was cooled, then worked up in the normal way to give **6** 3 mg. and **5** 20 mg.

(d) *Using hydrogen peroxide–potassium hydroxide.* KOH (24 mg, 0.43 mmol) was added to a stirred soln of **8** (50 mg, 0.108 mmol) in THF-water (5 ml, 10:1), followed by 30% H_2O_2 (5 ml, 15 mmol). The mixture was stirred at 25° for 18 hr, water (10 ml) added, and the mixture acidified to pH 5 using 0.1 N HCl, and extracted into ether (3 × 30 ml). The ether extract was treated with excess diazomethane, dried ($MgSO_4$), and concentrated *in vacuo* to give an oil. Column chromatography on silica (5 g), eluting with CH_2Cl_2–EtOAc (9:1) gave the 8-*cis*-eicosatetraenoate **6** (18 mg) and the 8-*trans*-isomer **5** (4.5 mg).

cis-*Hex*-3-*en*-1-*yl phenyl selenide* (**9**). Methanesulphonyl chloride (1.26 g, 11 mmol) was added dropwise over a period of 20 min to a soln of *cis*-hex-3-en-1-ol (1 g, 10 mmol) in pyridine (40 ml). The mixture was allowed to warm to room temp, stirred for 6 hr, then diluted with ether (30 ml) and water (50 ml). The organic layer was separated, washed with water (3 × 50 ml), 0.5 N aq. HCl (3 × 50 ml), sat $NaHCO_3$aq (3 × 50 ml), and brine (3 × 50 ml), then dried ($MgSO_4$). Concentration *in vacuo* gave an oil which was chromatographed on silica (20 g) to give *cis*-hex-3-en-1-yl mesylate, a colourless oil, homogeneous by tlc, R_f 0.58 (CH_2Cl_2), ν_{max} 1340, 1170, and 740 cm^{-1}, δ ($CDCl_3$) (60 MHz) 1.0 (3 H, t, J = 6 Hz, CH_2CH_3), 1.7–2.8 (4 H, m, 2 × CH_2), 2.95 (3 H, s, SO_2CH_3), 4.25 (2 H, t, J = 5 H_2, $CH_2OSO_2CH_3$), and 5.0–5.8 (2 H, m, vinylic H).

cis-Hex-3-en-1-yl mesylate (892 mg) in EtOH (50 ml) was added to a colourless soln of sodium phenylselenide (prepared by the addition of sodium borohydride (84.8 mg, 2.23 mmol) to a stirred soln of diphenyl diselenide (634 mg, 2.03 mmol) in anhyd EtOH (40 ml) under N_2) under a dry N_2 atmosphere, and the mixture stirred for 18 hr. Dilution with ether (30 ml) and water (50 ml), gave an organic phase which was separated, washed with water (3 × 40 ml), brine (3 × 40 ml), and dried ($MgSO_4$). Concentration *in vacuo* and distillation gave a yellow oil identified as cis-*hex*-3-*en*-1-*yl phenyl selenide* **9** (854 mg), b.p. 134–136°/0.5 mm Hg, ν_{max} 1590 and 740 cm^{-1}, δ ($CDCl_3$) 1.0 (3 H_1 t, J = 6 Hz, CH_2CH_3), 2.05 (2 H, m, CH_2), 2.55 (2 H, m, CH_2), 2.93 (2 H, t, J = 8 Hz, CH_2SePh), 5.3–5.55 (2 H, m, vinylic H), 7.2 (3 H, m, aromatic H), and 7.53 (2 H, m, aromatic H); *m/z* 240 (M$^+$, 27%) and 158 (M$^+$ + H-PhSe, 50%).

Preparation of octa-3,5-*dien*-2-*ols* (**10** *and* **11**) *from* cis-*hex*-3-*en*-1-*yl phenyl selenide* (**9**).

(a) *Under standard conditions.*[17] m-Chloroperoxybenzoic acid (180.5 mg, 1.04 mmol) in THF (1 ml) was added to a soln of *cis*-hex-3-en-1-yl phenyl selenide (250 mg, 1.04 mmol) in THF at −78° under anhyd N_2. After 45 min, a soln of lithium di-isopropylamide in THF (2.3 ml of a 1 N soln) was added, the mixture stirred for 5 min, and a soln of freshly distilled acetaldehyde (48.5 mg, 1.1 mmol) in THF (1 ml) added. Stirring was continued for 30 min, the soln warmed to 0°, AcOH (0.2 ml) and water (0.2 ml) in THF (1 ml) added, and then the mixture added to di-isopropylamine (0.15 ml, 1.05 mmol) in hexane (10 ml) at reflux. The mixture was heated under reflux for 5 min, cooled, diluted with 5% Na_2CO_3aq (50 ml), washed with 0.1 N HClaq (3 × 30 ml), $NaHCO_3$aq (3 × 30 ml), and brine (3 × 30 ml), and then

dried ($MgSO_4$). Concentration *in vacuo* gave an oil, which was chromatographed on silica (10 g), being eluted with CH_2Cl_2, to give a mixture of *trans,trans-* and *trans,cis*-octa-3,5-dien-2-ols **10** and **11** (65 mg). These components could not be separated by chromatography. However comparison with the pure materials (see below) showed the ratio to be **10**:**11** = 55:45.

(b) *Omitting acetic acid step.* The procedure described in (a) above was repeated except that the addition of aqueous AcOH was omitted. Work-up as described above gave a colourless oil which was purified by column chromatography and identified as trans,cis-*octa*-3,5-*dien*-2-*ol* **11** (73 mg), R_f 0.22 (CH_2Cl_2)) λ_{max} 3400 (broad), 1640, 990, 950, and 740 cm^{-1}, ($CDCl_3$) 1.0 (3 H, t, J = 6.25 Hz, $CH_2C\underline{H}_3$), 1.27 (3 H, d, J = 6.25 Hz, $CHOHC\underline{H}_3$), 1.9 (1 H, s, exch. with D_2O, OH), 2.03–2.1 (2 H, m, $C\underline{H}_2CH_3$), 4.3 (1 H, m, $C\underline{H}OH$), 5.4 (1 H, m, H(6)), 5.68 (1 H, t, J = 15 Hz, H(3)), 5.93 (1 H, dd, J = 10.5, 12 Hz, H(5)), and 6.45 (1 H, dd, J = 10.5, 15 Hz, H(4)), λ_{max} (MeOH) 233 nm (ε 27, 240). (Found *m/z*: M^+ 126.1048, $C_8H_{14}O$ requires $\underline{M}^+$ 126.1048).

(c) *Oxidative elimination of phenylselenium from hydroxyselenide* (**8**) *in the presence of* trans,cis-*octa*-3,5 *dien*-2-*ol* (**11**). The oxidation procedure of **8** using sodium periodate-sodium hydrogen carbonate was repeated but in the presence of *trans,cis*-octa-3,5-dien-2-ol (10 mg). Normal work up procedure was used except for chromatography with CH_2Cl_2 only as solvent. Oxidative removal of the phenylselenyl group had occurred to give a mixture (as above), but the recovered dienol had isomerised (80%) and was identified as trans,trans-*octa*-3,5- *dien*-2-*ol* (6 mg), R_f 0.22 (CH_2Cl_2), ν_{max} 3400, 1650, 990, δ ($CDCl_3$) 1.0 (3 H, t, J = 6.25 Hz, $CH_2C\underline{H}_3$), 1.25 (3 H, d, J = 6.25 Hz, $CHOHC\underline{H}_3$), 1.9 (1 H, s exch. D_2O, OH), (2.05–2.15 (2 H, m, $C\underline{H}_2CH_3$), 4.38 (1 H, m, $C\underline{H}OH$), 5.66 (1 H, dd, H_3), 5.76 (1 H, m, H_6), 6.0 (1 H, t, H5), 6.18 (1 H, dd, H4), λ_{max} (MeOH) 231 nm (ε 25, 350). (Found: *m/z*: M^+ 126.1048, $C_8H_{14}O$, required: H^+ 126.1048).

Acknowledgements—We thank the SRC and Glaxo Group Research Ltd., for a CASE Award (to N.V.R.) and Dr. W. Leimgruber (Hofmann La Roche, Nutley, U.S.A.) for a generous gift of arachidonic acid. We also thank Dr. R. F. Newton for helpful discussion, Lady Richards and Mrs. McGuiness for ^1H NMR spectra, Dr. R. T. Aplin for mass spectra, and finally the SRC for a research grant for the purchase of a ZAB 1F spectrometer and associated data systems.

REFERENCES

[1]B. Samuelsson, P. Borgeat, S. Hammarström and R. C. Murphy, *Prostaglandins* **17**, 785 (1979).
[2]P. Borgeat and B. Samuelsson, *Proc. Natl. Acad. Sci. U.S.A.* **76**, 3213, 2148 (1979); P. Borgeat and B. Samuelsson, *J. Biol. Chem.* **254**, 2643 (1979).
[3]R. C. Murphy, S. Hammarström and B. Samuelsson, *Proc. Natl. Acad. Sci. U.S.A.* **76**, 4275 (1979).
[4]E. J. Corey, D. A. Clark, G. Goto, A. Marfat, C. Mioskowski, B. Sammuelsson and S. Hammarström, *J. Am. Chem. Soc.* **102**, 1436 (1980).
[5]K. F. Austen, *J. Immunol.* **121**, 793 (1978); C. W. J. Parker, *J. Allergy Clin. Immunol.* **63**, 1 (1979); R. P. Orange and K. F. Austen, *Adv. Immunol.* **10**, 105 (1969).
[6]K. Rokach, Y. Girard, Y. Guindon, J. G. Atkinson, M. Larue, R. N. Young, P. Masson and G. Holme, *Tetrahedron Letters* 1485 (1980).
[7]E. J. Corey, D. A. Clark, A. Marfat and G. Goto, *Ibid*, 3143 (1980).
[8]E. J. Corey, Y. Arai and C. Mioskowski, *J. Am. Chem. Soc.* **101**, 6748 (1979); J. G. Gleason, D. B. Bryan, and C. M. Kinzig, *Tetrahedron Letters* 1129 (1980).
[9]E. J. Corey, A. E. Barton and D. A. Clark, *J. Am. Chem. Soc.* **102**, 4278 (1980).
[10]K. C. Nicolaou and Z. Lysenko, *Ibid.* **99**, 3185 (1977); D. L. J. Clive and G. Chittattu, *J. Chem. Soc.* Chem. Commun. 484 (1977); K. Nicolaou, S. Sietz, W. Sipio, and J. Blount, *J. Am. Chem. Soc.* **101**, 3884 (1979).
[11]E. J. Corey, H. Niwa and J. R. Falck, *Ibid.* **101**, 1586 (1979).
[12]D. L. J. Clive, *Tetrahedron* **34**, 1049 (1978); H. J. Reich, *Accounts Chem. Res.* **12**, 22 (1979).
[13a]T. Hori and K. B. Sharples, *J. Org. Chem.* **43**, 1689 (1978); [b]H. J. Reich, S. Wollowitz, J. E. Trend, F. Chow, D. F. Wendelborn, *Ibid.* p. 1697.
[14]K. B. Sharpless, K. F. Lauer and A. Y. Teranishi, *J. Am. Chem. Soc.* **95**, 6137 (1973).
[15]E. Truscheit and K. Eiter, *Liebigs Ann.*, **658**, 65 (1962); L. K. Montgomery, K. Schueller and P. D. Bartlett, *J. Am. Chem. Soc.* **86**, 622 (1964).
[16]E. J. Corey, J. O. Allright, A. E. Barton and S.-i. Hashimoto, *Ibid.* **102**, 1435 (1980).
[17]H. J. Reich, S. K. Shah and F. Chow, *Ibid.* **101**, 6648 (1979).
[18]N. A. Porter, J. Logan, V. Kontoyiannidou, *J. Org. Chem.* **44**, 3177 (1979).