Convergent Syntheses of 9-Deoxy-12-phenylthioprostanoids and 9-Deoxy-$\Delta^{8(12)}$-PGD$_1$ Derivatives

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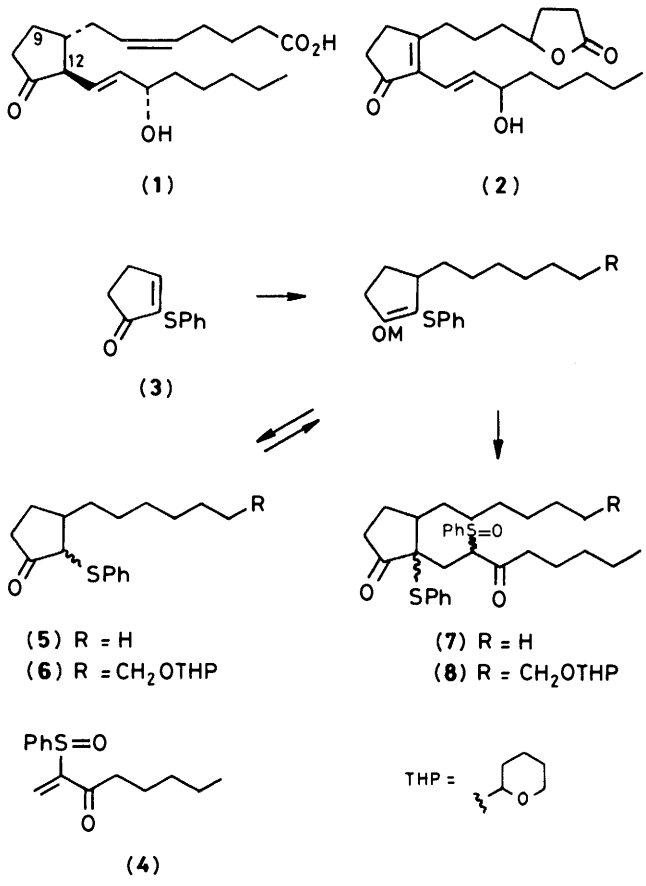
Conjugate additions of organolithium or organomagnesium compounds, mediated by copper(I), to 2-phenylthiocyclopent-2-enone, and of enolates of the initial adducts to 2-phenylsulphinyloct-1-en-3-one, provided convergent constructions of the prostanoid framework. Stereospecific introduction of the Δ^{13} double bond by sulphoxide elimination, the elimination of benzenesulphenic acid from 12β-phenylsulphinylprostanoids at room temperature, and the chemoselective reduction of 11-oxo-13-en-15-ones to 11-oxo-13-en-15-ols, provided 9-deoxy-12-phenylthioprostaglandin D$_1$ analogues and 9-deoxy-$\Delta^{8(12)}$-prostaglandin D$_1$ derivatives. The conjugate additions, and the propensity for ether formation during the Meerwein–Ponndorf–Verley reduction of the 13-en-15-ones, were influenced by the presence of remote oxygen substitutents in the incipient α-side-chain.

The synthesis of 9-deoxyprostanoids,[1-4] stimulated by their varied biological activity, has received impetus from the recent discovery that 9-deoxyprostaglandin D$_2$ (9-deoxy-PGD$_2$) (**1**) exceeds PGD$_2$ in activity as a potent inhibitor of blood platelet aggregation.[1] This potency is markedly diminished in PGD$_1$ (5,6-dihydro-PGD$_2$), and in the Δ^{12} isomers to which these compounds readily isomerize, and the possibility of such rearrangement under physiological conditions reduces their potential therapeutic utility. The presence of a 12-substituent, or further unsaturation, would prevent isomerization, and this suggests that 9-deoxy-12-phenylthioprostanoids, *e.g.* (**28**) and the enone (**34**), could manifest interesting biological profiles, despite the absence of unsaturation at C-5. This paper describes their convergent syntheses by simple procedures which involve the consecutive introduction of the prostanoid side-chains into 2-phenylthiocyclopentenone. Prostanoids bearing other substituents at C-12,[3,5] and the enone (**2**),[4] have been synthesized previously by less direct methods.

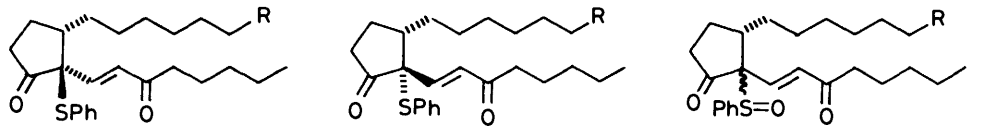
In initial experiments hexyl cuprate was used for conjugate addition to 2-phenylthiocyclopentenone. The prostanoid analogues so derived were themselves of potential interest for biological evaluation since functionality at C-1 is not a prerequisite for physiological activity.[6] Sequential addition of 2-phenylthiocyclopentenone (**3**)[7] (1 equiv.) and 2-phenylsulphinyloct-1-en-3-one (**4**)[3] (1.1 equiv.) at −25 °C to the cuprate generated by treatment of hexyl-lithium (1.1 equiv.) with dimethyl sulphide–copper(I) bromide[8] gave a mixture of diastereoisomeric adducts (**7**). The crude mixture was thermolysed in boiling toluene containing trimethyl phosphite to give, after chromatography, 12β-phenylthio-1-nor-12α-prost-13-ene-11,15-dione (**9**) (36%) together with its 12α-isomer (**14**) (16%).† The stereospecificity of the sulphoxide elimination to generate the (*E*)-Δ^{13}-15-ones, which has been demonstrated in related systems,[3] was confirmed by n.m.r. spectral evidence. When greater molar proportions of hexyl cuprate and oxo-alkenyl sulphoxide (**4**) were used, increasingly complex mixtures of products and reduced yields of compounds (**9**) and (**14**) were obtained. These yields could possibly have been improved by use of hexylcopper–tributylphosphine complexes,[9] but to achieve these ends we settled instead for a two-step procedure which took advantage



of the influence of the phenylthio group in directing the regiospecificity of enolization. The adduct (**5**) from the reaction of hexyl cuprate (2 equiv.) or hexylmagnesium bromide [2 equiv., catalysed by copper(I) chloride] to 2-phenylthiocyclopentenone (**3**) was isolated in 95% yield, as a mixture of diastereoisomers, and then treated in sequence with butyllithium and 2-phenylsulphinyloct-1-en-3-one (**4**) (1.2 equiv.) in tetrahydrofuran (THF) at −78 °C. Thermolysis of the crude products (**7**) gave the compounds (**9**) and (**14**) in 57 and 29% yield respectively.

In extending these reactions in order to synthesize pro-

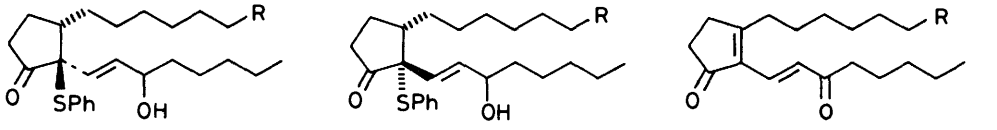
† These compounds, and those related to them, were racemic modifications. Only one enantiomer is depicted in each case, and the α,β convention is used to describe stereochemistry in relation to an arbitrarily assigned α-configuration of the alkyl side-chains in compounds (**5**) and (**6**).



(9) R = H
(10) R = CH_2OTHP
(11) R = CH_2OH
(12) R = CO_2H
(13) R = CO_2Me

(14) R = H
(15) R = CH_2OTHP
(16) R = CH_2OH
(17) R = CO_2H
(18) R = CO_2Me

(19) R = H, 12β-PhSO
(20) R = CH_2OH, 12β-PhSO
(21) R = H, 12α-PhSO
(22) R = CH_2OH, 12α-PhSO



(23) R = H, 15α-OH
(24) R = H, 15β-OH
(25) R = CO_2Me, 15α-OH
(26) R = CO_2Me, 15β-OH

(27) R = H, 15α- and 15β-
(28) R = CO_2Me, 15α-OH
(29) R = CO_2Me, 15β-OH

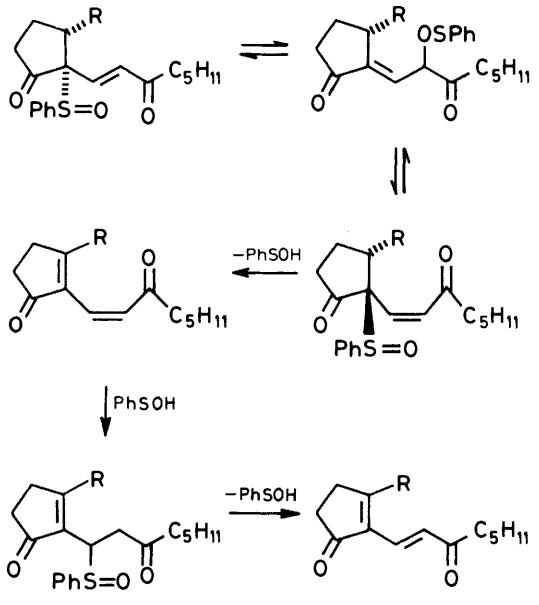
(30) R = H
(31) R = CH_2OH
(32) R = CO_2Me

stanoids functionalized at C-1 (prostaglandin numbering), it was found that the presence of a remote tetrahydropyranyloxy group influenced their efficiency and stereochemical outcome. The copper-catalysed addition of 7-(tetrahydropyran-2-yloxy)-heptylmagnesium bromide (1 equiv.) to 2-phenylthiocyclopent-2-enone (**3**) in boiling THF gave the adduct (**6**) (41%), which was isolated as a mixture of diastereoisomers. Self-coupling of the organomagnesium compound occurred under these conditions, but use of excess of Grignard reagent further complicated a difficult chromatographic separation and diminished the yield of the adduct (**6**). The sodium enolate of this adduct, on treatment with the oxo-alkenyl sulphoxide (**4**) at −78 °C in THF, followed by thermolysis of the crude products (**8**), gave the diastereoisomeric enones (**10**) (13%) and (**15**) (32%) after chromatographic separation. The lithium enolate of (**6**) was even less effective (see Experimental section). However, when the magnesium enolate, made by copper-catalysed addition of the Grignard reagent to 2-phenylsulphinylcyclopent-2-enone (**3**) as before, was quenched with the oxo-alkenyl sulphoxide (**4**), and the crude products thermolysed in boiling toluene, the enones (**10**) and (**15**) were obtained in 25 and 32% yield respectively, from (**3**). Complexation of the tetrahydropyranyloxy group with the metal cations clearly inhibits both of the consecutive conjugate additions, and influenced the diastereoselectivity of reactions of the enolate anions. Organocopper conjugate additions were not used to introduce the functionalized α-side-chain, since lithium 7-lithioheptanoate, formed by treatment of 7-bromoheptanoic acid with sodium naphthalenide,[10] gave complex mixtures on treatment in sequence with dimethyl sulphide–copper(I) bromide and 2-phenylthiocyclopent-2-enone (**3**), whilst 1-lithio-7-(t-butyldimethylsilyloxy)heptane rapidly underwent self-coupling.

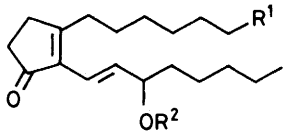
The orientations of the 12-phenylthio substituents in the isomers (**9**) and (**14**), and in (**10**) and (**15**), were revealed during their conversion into the diene-diones (**30**) and (**31**). Oxidation of the 12β-isomer (**9**) to the sulphoxide (**19**) with *m*-chloroperbenzoic acid (MCPBA) at 0 °C, followed by warming the mixture to 20 °C, was attended by elimination of benzenesulphenic acid to give 1-norprosta-8(12),13-diene-11,15-dione (**30**) in 90% yield. Oxidation of the 12α-isomer (**14**) gave the diene-dione (**30**) in only 12% yield (together with a mixture of other unidentified products) only after the intermediate sulphoxide (**21**) was thermolysed in boiling benzene for 90 min. Similar treatment of the 1-hydroxy compounds (**11**) and (**16**) gave, *via* the sulphoxides (**20**) and (**22**), the diene-dione (**31**), in 79% yield from (**11**), and 24% yield from (**16**). The sulphoxides (**19**) and (**21**) were detectable (t.l.c.), but neither could be isolated by rapid chromatography, during which they decomposed, the isomer (**19**) mainly to the diene-dione (**30**), and the isomer (**21**) to give a mixture of products.

Allocation of configuration at C-12 followed from the known preference of sulphoxides to undergo thermal *syn*-elimination to give olefins.[11] The particularly easy elimination in these cases is undoubtedly a consequence of the location of the phenylsulphinyl group adjacent to one keto group and vinologous to another (*cf.* ref. 12). The influence of the vinologous ketone in facilitating this elimination was illustrated in the following manner. The adduct (**5**), a mixture of inseparable diastereoisomers in the ratio 3:1 (according to n.m.r. spectroscopy), was oxidised to the corresponding sulphoxides (89%) with MCPBA. These, in contrast to the case for the sulphoxides (**19**) and (**20**), were stable at room temperature, but in boiling toluene containing trimethyl phosphite gave 3-hexylcyclopent-2-enone (92%). Epimerization of the phenylsulphinyl group must have occurred to account for the high yield.

The elimination of benzenesulphenic acid from the sulphoxide (**21**) to give (**30**) may involve either an uncommon *trans*-elimination *via* radical intermediates,[11,13] facilitated in this case by the location of the phenylsulphinyl group at an 'activated' position, or inversion at C-12 *via* a sulphoxide–sulphenate rearrangement,[14] followed by isomerization of the Δ^{13} double bond, mediated by addition–elimination of benzenesulphenic acid (Scheme): additions of sulphenic acids to α,β-unsaturated carbonyl compounds,[15] and stereospecific elimination of sulphenic acids from β-arylsulphinyl ketones to give (*E*)-conjugated olefins, have been documented.[16] Other reaction



Scheme.



(33) $R^1 = R^2 = H$
(34) $R^1 = CO_2Me, R^2 = H$
(35) $R^1 = CO_2Me, R^2 = Pr^i$
(36) $R^1 = CO_2Pr^i, R^2 = H$
(37) $R^1 = CO_2Pr^i, R^2 = Pr^i$
(38) $R^1 = CH_2OH, R^2 = H$
(39) $R^1 = CH_2OH, R^2 = Pr^i$

pathways are available to the intermediates formed in both of these postulated mechanisms, which would account reasonably for the mixture of products obtained from the sulphoxide (**21**).

Oxidation of the hydroxy compounds (**11**) and (**16**) with pyridinium dichromate (PDC)[17] in dimethylformamide (DMF) gave the acids (**12**) and (**17**), which were converted into the esters (**13**) and (**18**) with diazomethane. Oxidation of the 12β-phenylthio ene-dione (**13**) with MCPBA at 0 °C was attended by spontaneous elimination of benzenesulphenic acid to give the diene-dione (**32**) (86%). The unsaturated dioxo ester (**32**) could not be obtained *via* oxidation of the hydroxy-compound (**31**) with PDC because the derived acid rapidly decomposed.

Reduction of the 12β-phenylthio ene-diones (**9**) and (**13**) with sodium cyanoborohydride[18] proceeded chemoselectively to give the 9-deoxy-12β-phenylthio-PGD_1 analogues (**23**) and (**24**) (80%), and (**25**) and (**26**) (97%) respectively. These allylic alcohols, isomeric at C-15, were separated by chromatography; configurations at C-15 were assigned only on the basis of their relative chromatographic mobility,[2] and are therefore tentative. Reduction of the 12α-phenylthio ene-diones (**14**) and (**18**) with sodium cyanoborohydride were less chemoselective, the allylic alcohols (**27**) (58%), and (**28**) and (**29**) (60%) being formed together with diastereoisomeric 11,15-diols. The 9-deoxy-12α-phenylthio-PGD_1 analogues (**28**) and (**29**), isomeric at C-15, were separated by careful chromatography, but the mixture (**27**) could not be separated into its components.

The chemoselectivity of reduction of the 12β-phenylthio compounds extended to the unsaturated compounds (**30**) and (**32**), which furnished respectively the prostanoids (**33**) (40%) and (**34**) (48%) on treatment with sodium cyanoborohydride. The yield of the allylic alcohol (**33**) was improved to 60% on reduction of the diene-dione (**30**) with aluminium isopropoxide,[4,19] but use of this reagent with the unsaturated dioxo ester (**32**) led to complications. The expected ester interchange was accompanied by an unusual reductive etherification at C-15, so that a mixture of the four compounds (**34**)—(**37**) was obtained. Ether formation has been observed rarely in other cases, such as in the reduction of diarylketones with aluminium isopropoxide.[20] In the present cases the 1-ester function clearly facilitates ether formation at C-15, and the probable role of intramolecular participation by an oxygen function at C-1 in this process was substantiated by the observation that reduction of the 1-hydroxy compound (**31**) with aluminium isopropoxide also gave rise to the 15-isopropyl ether (**39**) (23%) together with the 15-hydroxy compound (**38**) (23%). The mechanism of this participation remains obscure, but the phenomenon is a matter for consideration when prostanoid Δ^{13}-15-ones are reduced by the Meerwein–Ponndorf–Verley method.[19,21]

The compounds (**23**), (**24**), (**25**), (**27**), and (**34**) were weak inhibitors of collagen-induced blood platelet aggregation, in which test the allylic ether (**35**) was a potent inhibitor at a concentration of 8.4 μg/ml.

Experimental

I.r. spectra were determined with a Perkin-Elmer 157G spectrophotometer for chloroform solutions, u.v. spectra with a Perkin-Elmer 559 spectrophotometer for ethanol solutions, and mass spectra with a Kratos MS25 or MS80 spectrometer. Proton n.m.r. spectra were determined at 220 MHz with a Perkin-Elmer R34 spectrometer, and refer to deuteriochloroform solutions with tetramethylsilane as internal standard. Column chromatography was performed with Merck 7736 60H silica gel, and eluants were solvent mixtures which are indicated later within parentheses. Ether refers to diethyl ether, and light petroleum to the fraction boiling between 40 and 60 °C.

3-Hexyl-2-phenylthiocyclopentanone (**5**).—(*a*) Hexyl-lithium (5.9 g, 64 mmol) in hexane (100 ml) was added to a stirred solution of dimethyl sulphide–copper(I) bromide[8] (6.75 g, 32 mmol) in a mixture of dry THF (150 ml) and freshly distilled dimethyl sulphide (40 ml) at 0 °C under nitrogen. After 15 min, a solution of 2-phenylthiocyclopent-2-enone (**3**)[7] (6.25 g, 32 mmol) in dry THF (10 ml) was added, and the mixture was stirred at 0 °C for a further 45 min before being poured onto saturated aqueous ammonium chloride (50 ml). Work-up with ether afforded an oil, which was chromatographed [ether–light petroleum (1:19)] to give the oily *product* (**5**) (8.56 g, 94%) as a mixture of diastereoisomers in the ratio 3:1, $\nu_{max.}$ 1 738 cm^{-1} (C=O); δ 7.55—7.25 (5 H, m, C_6H_5), 3.57 (0.25 H, d, *J* 5 Hz, C*H*SPh), and 3.04 (0.75 H, d, *J* 7 Hz, C*H*SPh); *m/z* 276 (M^+) (Found: C, 73.6; H, 8.7; S, 11.7. $C_{17}H_{24}OS$ requires C, 73.9; H, 8.7; S, 11.6%).

(*b*) A solution of 2-phenylthiocyclopent-2-enone (**3**) (1.0 g, 5.25 mmol) in dry THF (2 ml) was added under nitrogen to a stirred solution of hexylmagnesium bromide [prepared from hexyl bromide (1.49 g, 7.88 mmol)] in dry THF (20 ml) containing copper(I) chloride (8 mg, 1 mol%)]. The mixture was boiled for 30 min, during which catalytic amounts of copper(I) chloride (8 mg) were added at ten minute intervals, and the mixture was then poured onto saturated aqueous ammonium chloride and then worked up with ether. Chromatography of the residue after evaporation [ether–light petroleum (1:9)] gave the product (**5**) (1.389, 95%), identical with that obtained above.

2-Phenylthio-3-[7-(tetrahydropyran-2-yloxy)heptyl]cyclopentanone (**6**).—Treatment of 2-phenylthiocyclopent-2-enone (**3**) (670 mg, 3.53 mmol) with 7-(tetrahydropyran-2-yloxy)heptylmagnesium bromide [prepared from the corresponding bromide[22] (1.02 g, 3.66 mmol)] in the manner described under procedure (*b*) above gave, after chromatography [ether–light petroleum (1:4)], the *product* (**6**) (560 mg, 41%) as an oil, $\nu_{max.}$ 1 744 cm^{-1} (C=O); δ 7.60—7.26 (5 H, m, C_6H_5), 4.60 (1 H, m, OCHO), 3.97—3.04 (5 H, m, 2 × OCH_2 and CHSPh), and 2.50—1.03 (23 H, m); *m/z* 390 (M^+) (Found: C, 72.7; H, 8.1; S, 12.7. $C_{23}H_{34}O_3S$ requires C, 72.6; H, 8.1; S, 12.9%).

3-Hexyl-2-phenylsulphinylcyclopentanone.—A solution of 3-hexyl-2-phenylthiocyclopentanone (**5**) (500 mg, 1.8 mmol) in dichloromethane (5 ml) at 0 °C was treated with a solution of MCPBA (314 mg, 1.8 mmol) in dichloromethane (2 ml). After 30 min at 0 °C and a further 45 min at room temperature the mixture was worked up with dichloromethane to give an oil. Chromatography [ether–light petroleum (7:3)] gave the *title product* (473 mg, 89%), $\nu_{max.}$ 1 745 (C=O) and 1 035 cm^{-1} (S=O); δ 7.67—7.25 (5 H, m, C_6H_5) and 3.24 and 2.92 (1 H, 2 d, *CH*SOPh in diastereoisomers); *m/z* 292 (M^+) (Found: C, 69.9; H, 8.2; S, 10.8. $C_{17}H_{24}O_2S$ requires C, 69.9; H, 8.2; S, 11.0%).

A solution of this sulphoxide (529 mg, 1.8 mmol) in toluene (15 ml) containing trimethyl phosphite (446 mg, 3.6 mmol) was boiled under nitrogen for 30 min. Evaporation of the solvent and chromatography of the residue [ether–light petroleum (3:7)] gave 3-hexylcyclopent-2-enone (277 mg, 92%), $\nu_{max.}$ 1 710 (C=O), 1 680 (C=C), and 1 610 cm^{-1}; δ 5.94 (1 H, s, vinyl proton), 2.55 (2 H, m, CH_2CO), and 2.45—2.30 (4 H, m, allylic protons).

Preparation of the Adducts (**9**), (**10**), (**14**), *and* (**15**).—(*a*) Butyllithium (2.2 g, 34 mmol) in hexane (21 ml) was added dropwise to a stirred solution of 3-hexyl-2-phenylthiocyclopentanone (**5**) (9.0 g, 32 mmol) in dry THF (250 ml), maintained at −25 °C under nitrogen. After 20 min the mixture was cooled to −78 °C, and a solution of 2-phenylsulphinyloct-1-en-3-one (**4**)[3] (9.9 g, 39.6 mmol) in dry THF (10 ml) was added dropwise. The mixture was stirred for 15 min, and allowed to warm during 30 min to −25 °C, before being poured onto saturated aqueous ammonium chloride. Work-up with ether afforded an oil, which was dissolved in toluene (200 ml) containing trimethyl phosphite (7.93 g, 64 mmol). After the solution had been boiled for 30 min under nitrogen, the solvent was evaporated and the residue was chromatographed (light petroleum) to give, first, 12β-*phenylthio-1-nor-12α-prost-13-ene-11,15-dione* (**9**) (7.53 g, 57%) as an oil, $\nu_{max.}$ 1 730 (C=O), 1 670 (C=C–C=O), and 1 612 cm^{-1}; δ 7.45—7.20 (5 H, m, C_6H_5), 6.72 (1 H, d, *J* 16 Hz, HC=C–C=O), and 6.14 (1 H, d, *J* 16 Hz, C=CH–C=O); *m/z* 400 (M^+) (Found: C, 75.15; H, 8.85; S, 7.9. $C_{25}H_{36}O_2S$ requires C, 75.0; H, 9.0; S, 8.0%), and then 12α-*phenylthio-1-norprost-13-ene-11,15-dione* (**14**) (3.86 g, 29%), $\nu_{max.}$ 1 730 (C=O), 1 670 (C=C–C=O), and 1 612 cm^{-1}; δ 7.45—7.20 (5 H, m, C_6H_5), 6.78 (1 H, d, *J* 15 Hz, HC=C–C=O), and 6.16 (1 H, d, *J* 15 Hz, C=CH–C=O); *m/z* 400 (M^+) (Found: C, 74.9; H, 9.1; S, 8.05%).

(*b*) Hexyl-lithium (254 mg, 2.8 mmol) in hexane (2.3 ml) was added to a stirred solution of dimethyl sulphide–copper(I) bromide (230 mg, 1.1 mmol) in a mixture of dry THF (20 ml) and dimethyl sulphide (3 ml) maintained at 0 °C under nitrogen. A solution of 2-phenylthiocyclopent-2-enone (**3**) (500 mg, 2.6 mmol) in dry THF was added and the mixture was stirred for 15 min before being cooled to −25 °C. A solution of 2-phenylsulphinyloct-1-en-3-one (**4**) (715 mg, 2.9 mmol) in dry THF was added, and the mixture was stirred at −25 °C before being poured onto saturated aqueous ammonium chloride. Work-up with ether gave an oil which was dissolved in toluene (40 ml) containing trimethyl phosphite (744 mg, 6 mmol), and the solution was boiled under nitrogen for 40 min. Evaporation of the solvent and chromatography (light petroleum) of the residue gave the 12β-isomer (**9**) (382 mg, 36%), a mixed fraction (44 mg, 4%), and then the 12α-isomer (**14**) (174 mg, 16%).

(*c*) Treatment of compound (**6**) (118 mg, 0.30 mmol) in the manner described under (*a*) gave 12β-*phenylthio-1-(tetrahydropyran-2-yloxy-12α-prost-13-ene-11,15-dione* (**10**) (14 mg, 9%), $\nu_{max.}$ 1 726 (C=O), 1 690, 1 670, and 1 615 cm^{-1} (C=C–C=O); δ 7.44—7.10 (5 H, m, C_6H_5), 6.70 (1 H, d, *J* 16 Hz, HC=C–C=O), 6.13 (1 H, d, *J* 16 Hz, C=CH–C=O), 4.56 (1 H, m, OCHO), 3.95—3.25 (4 H, m, 2 × OCH_2), 2.62—0.96 (31 H, m), and 0.86 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/z* 514 (M^+) (Found: C, 72.5; H, 9.15; S, 6.1. $C_{31}H_{46}O_4S$ requires C, 72.4; H, 8.95; S, 6.25%), and the 12α-*phenylthio isomer* (**15**) (38 mg, 25%), $\nu_{max.}$ 1 726 (C=O), 1 690, 1 670, and 1 615 cm^{-1} (C=C–C=O); δ 7.42—7.10 (5 H, m, C_6H_5), 6.82 (1 H, d, *J* 16 Hz, HC=C–C=O), 6.17 (1 H, d, *J* 16 Hz, C=CH–C=O), 4.58 (1 H, m, OCHO), 3.94—3.25 (4 H, m, 2 × OCH_2), 2.75 (1 H, m), 2.40 (2 H, t, *J* 7 Hz, $COCH_2$), 2.33—1.00 (28 H, m), and 0.86 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/z* 514 (M^+) (Found: C, 72.2; H, 9.15; S, 6.25%).

(*d*) Reaction of the sodium enolate of compound (**6**) [prepared by treatment of (**6**) (1.30 g, 3.33 mmol) in dry THF (13 ml) with sodium hydride (50% dispersion in oil; 169 mg, 3.52 mmol) at 0 °C for 1 h under nitrogen] with 2-phenylsulphinyloct-1-en-3-one (**4**) (1.03 g, 4.12 mmol) in dry THF, followed by thermolysis as described under (*a*) above, gave the 12β-phenylthio isomer (**10**) (220 mg, 13%), and the 12α-phenylthio isomer (**15**) (580 mg, 34%).

(*e*) A solution of 1-bromo-7-(tetrahydropyran-2-yloxy)-heptane (13.4 g, 48 mmol) in dry THF (30 ml) was added dropwise during 1 h to a stirred suspension of magnesium turnings (1.34 g, 55.8 mg-atom) and iodine (1 crystal) in dry THF (50 ml), maintained under argon. After being stirred for 1.5 h at 50 °C the solution was cooled to room temperature, and copper(I) chloride (48 mg, 1 mol %) was added, followed by a solution of 2-phenylthiocyclopent-2-enone (**3**) (8.3 g, 43.7 mmol) in dry THF (30 ml). The mixture was boiled for 30 min, during which further portions (48 mg) of copper(I) chloride were added at 10 min intervals, and the mixture was then cooled to −78 °C. A solution of 2-phenylsulphinyloct-1-en-3-one (**4**) (12 g, 48 mmol) in dry THF (30 ml) was added dropwise during 10 min, and the mixture was allowed to warm slowly, during 30 min, to 0 °C before being poured onto saturated aqueous ammonium chloride (100 ml). Work-up with ether afforded an oil which was thermolysed in boiling toluene (150 ml) containing trimethyl phosphite (1.03 g, 84 mmol) to give, after manipulation as before, the 12β-phenylthio isomer (**10**) (5.6 g, 25%) and the 12α-phenylthio isomer (**15**) (7.2 g, 32%).

1-Hydroxy-12β-phenylthio-12α-prost-13-ene-11,15-dione (**11**) *and its 12α-Phenylthio Isomer* (**16**).—(*a*) Hydrolysis of the tetrahydropyranyl ether (**10**) (1.12 g) in a mixture of methanol (50 ml) and dil. hydrochloric acid (20 ml) overnight at room temperature, and work-up with ether, gave, after chromatography [ether–light petroleum (1:1)] the *title product* (**11**) (0.92 g, 98%), $\nu_{max.}$ 3 440 (OH), 1 723 (C=O), and 1 688 and 1 610 cm^{-1} (C=C–C=O); δ 7.40—7.05 (5 H, m, C_6H_5), 6.72 (1 H, d, *J* 16 Hz, HC=C–C=O), 6.12 (1 H, d, *J* 16 Hz, C=CH–C=O), 3.64 (2 H, t, *J* 7 Hz, OCH_2), and 2.54—0.95 (26 H, m); *m/z* 430 (M^+) (Found: C, 72.4; H, 8.95; S, 7.5. $C_{26}H_{38}O_3S$ requires C, 72.55; H, 8.85; S, 7.45%).

(*b*) Hydrolysis of the tetrahydropyranyl ether (**15**) (1.48 g) in the above manner gave 1-*hydroxy-12α-phenylthioprost-13-ene-11,15-dione* (**16**) (1.12 g, 91%), $\nu_{max.}$ 3 444 (OH), 1 725 (C=O), and 1 690 and 1 615 cm^{-1} (C=C–C=O); δ 7.44—7.22 (5 H, m, C_6H_5), 6.80 (1 H, d, *J* 16 Hz, HC=C–C=O), 6.16 (1 H, d, *J* 16 Hz, C=CH–C=O), 3.63 (2 H, t, *J* 7 Hz, OCH_2), 2.75 (1 H, m), 2.39 (2 H, t, *J* 7 Hz, $COCH_2$), 2.35—1.12 (23 H, m), and 0.86 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/z* 430 (M^+) (Found: C, 72.4; H, 9.0; S, 7.55%).

11,15-*Dioxo*-12β-*phenylthio*-12α-*prost*-13-*en*-1-*oic Acid* (**12**), *its* 12α-*Phenylthio Isomer* (**17**), *and their Methyl Esters* (**13**) *and* (**18**).—(*a*) A solution of pyridinium dichromate[17] (19.0 g, 28.7 mmol) in DMF (20 ml) was added to a stirred solution of the alcohol (**11**) (2.0 g, 4.65 mmol) in DMF (5 ml). After 24 h at room temperature, dilution with water and the usual work-up with ether gave an oil which was chromatographed [ethyl acetate–light petroleum (1:1)] to afford the *acid* (**12**) (1.6 g, 78%), $\nu_{max.}$ 3 500 and 3 030 (CO_2H), 1 720 (C=O), 1 700 (CO_2H), and 1 690 and 1 610 cm^{-1} (C=C–C=O); δ 7.55—7.10 (5 H, m, C_6H_5), 6.72 (1 H, d, *J* 16 Hz, HC=C–C=O); 6.13 (1 H, d, *J* 16 Hz, C=CH–C=O), 2.65—2.00 (6 H, m, 2 × $COCH_2$ and CH_2CO_2H), 1.95—1.00 (19 H, m), and 0.87 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/z* 444 (M^+) (Found: C, 70.1; H, 8.2; S, 7.25. $C_{26}H_{36}O_4S$ requires C, 70.25; H, 8.1; S, 7.2%).

(*b*) Oxidation of the alcohol (**16**) (480 mg) in the above manner gave 11,15-*dioxo*-12α-*phenylthioprost*-13-*en*-1-*oic acid* (**17**) (363 mg, 73%), $\nu_{max.}$ 3 400 (CO_2H), 1 725 (C=O) and (CO_2H), and 1 667 and 1 610 cm^{-1} (C=C–C=O); δ 7.50—7.16 (5 H, m, C_6H_5), 6.81 (1 H, d, *J* 16 Hz, HC=C–C=O), 6.18 (1 H, d, *J* 16 Hz, C=CH–C=O), 2.75 (1 H, m), 2.46—2.08 (6 H, m, 2 × $COCH_2$ and CH_2CO_2H), 2.06—1.04 (18 H, m), and 0.86 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/z* 444 (M^+) (Found: C, 70.4; H, 8.05; S, 7.0%).

(*c*) Treatment of a solution of 11,15-dioxo-12β-phenylthio-12α-prost-13-en-1-oic acid (**12**) (1.30 g, 2.93 mmol) in ether (10 ml) with diazomethane (123 mg, 2.93 mmol) in ether (10 ml) for 15 min at 0 °C, evaporation of the solvent, and chromatography of the residue [ethyl acetate–light petroleum (1:1)], gave the *methyl ester* (**13**) (1.10 g, 82%), $\nu_{max.}$ 1 722 (C=O and CO_2Me), 1 686, 1 662, and 1 608 cm^{-1} (C=C–C=O); δ 7.55—7.06 (5 H, m, C_6H_5), 6.72 (1 H, d, *J* 16 Hz, HC=C–C=O), 6.13 (1 H, d, *J* 16 Hz, C=CH–C=O), 3.65 (3 H, s, CO_2Me), 2.65—2.10 (6 H, m, 2 × $COCH_2$ and CH_2CO_2Me), 2.05—1.00 (19 H, m), and 0.86 (3 H, t, CH_2CH_3); *m/z* 458 (M^+) (Found: C, 70.5; H, 8.4; S, 6.9. $C_{27}H_{38}O_4S$ requires C, 70.75; H, 8.3; S, 7.0%).

(*d*) Treatment of the acid (**17**) (1.54 g) with diazomethane in the manner described above gave *methyl* 11,15-*dioxo*-12α-*phenylthioprost*-13-*en*-1-*oate* (**18**) (1.48 g, 93%), $\nu_{max.}$ 1 725 (C=O and CO_2Me), 1 690, 1 670, and 1 615 cm^{-1} (C=C–C=O); δ 7.44—7.22 (5 H, m, C_6H_5), 6.79 (1 H, d, *J* 16 Hz, HC=C–C=O), 6.16 (1 H, d, *J* 16 Hz, C=CH–C=O), 3.65 (3 H, s, CO_2CH_3), 2.75 (1 H, m), 2.44—2.12 (6 H, m, 2 × $COCH_2$ and CH_2CO_2Me), 2.10—1.04 (18 H, m), and 0.86 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/z* 458 (M^+) (Found: C, 70.6; H, 8.5; S, 7.0%).

1-*Norprosta*-8(12),13-*diene*-11,15-*dione* (**30**) *and its Analogues* (**31**) *and* (**32**).—(*a*) A solution of MCPBA (474 mg, 2.7 mmol) in dichloromethane (3 ml) and t-butyl alcohol (3 ml) was added to a stirred solution of 12β-phenylthio-1-nor-12α-prost-13-ene-11,15-dione (**9**) (1 g, 2.5 mmol) in dichloromethane (5 ml) at 0 °C. After 2 h, more MCPBA (120 mg, 0.7 mmol) was added, followed by another portion (120 mg) after a further 2 h. The mixture was allowed to warm to room temperature, and then worked up with dichloromethane in the usual way to give, after chromatography [ether–light petroleum (1:19)], the *title product* (**30**) (658 mg, 90%), $\nu_{max.}$ 1 709, 1 695, 1 619, and 1 582 cm^{-1}; $\lambda_{max.}$ 275 nm (ε 17 100); δ 7.36 (2 H, AB system, *J* 15 Hz, vinyl protons) and 2.68—2.30 (8 H, m, 2 × CH_2CO and 4 allylic protons) (Found: M^+ 290.2247. $C_{19}H_{30}O_2$ requires *M*, 290.2245).

(*b*) MCPBA (99 mg, 0.6 mmol) was added to a solution of 12α-phenylthio-1-norprost-13-ene-11,15-dione (**14**) (200 mg, 0.5 mmol) in dichloromethane (4 ml) at 0 °C. After 30 min, the mixture was allowed to warm to room temperature, and stirred for a further hour before being worked up with dichloromethane in the usual way. The oily product, which contained none of the diene-dione (**30**) (t.l.c.), was dissolved in benzene (10 ml) and the solution was boiled under nitrogen for 90 min. Evaporation of the solvent and chromatography [ether–light petroleum (1:19)] gave 1-norprosta-8(12),13-diene-11,15-dione (**30**) (22 mg, 12%), identical with the sample prepared above.

(*c*) Oxidation of 1-hydroxy-12β-phenylthio-12α-prost-13-ene-11,15-dione (**11**) (210 mg) with MCPBA in the manner described under (*a*) above, followed by chromatography [ether–light petroleum (1:1)], gave 1-*hydroxyprosta*-8(12),13-*dien*-11,15-*dione* (**31**) (123 mg, 79%), $\nu_{max.}$ 3 610 and 3 462 (OH), 1 700, 1 685, 1 610, and 1 575 cm^{-1}; $\lambda_{max.}$ 279 nm (ε 15 300); δ 7.37 (2 H, AB system, *J* 16 Hz, vinyl protons), 3.63 (2 H, t, *J* 7 Hz, OCH_2), 2.75—2.44 (9 H, m, 2 × $COCH_2$ and OH and 4 allylic protons), 1.75—1.20 (16 H, m), and 0.88 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/z* 320 (M^+) (Found: C, 74.85; H, 9.85. $C_{20}H_{32}O_3$ requires C, 75.0; H, 10.0%).

(*d*) Oxidation of 1-hydroxy-12α-phenylthioprost-13-ene-11,15-dione (**16**) (380 mg) with MCPBA in the manner described under (*b*) above, followed by chromatography [ether–light petroleum (1:1)], gave 1-hydroxyprosta-8(12),13-diene-11,15-dione (**31**) (41 mg, 14%).

(*e*) Oxidation of methyl 11,15-dioxo-12β-phenylthio-12α-prost-13-en-1-oate (**13**) (600 mg) with MCPBA in the manner described under (*a*) above gave, after chromatography [ethyl acetate–light petroleum (3:7)], *methyl* 11,15-*dioxoprosta*-8(12),13-*dien*-1-*oate* (**32**) (394 mg, 86%), $\nu_{max.}$ 1 731 (CO_2Me), 1 714, 1 695, 1 614, and 1 575 cm^{-1}; $\lambda_{max.}$ 220 (ε 5 860) and 277 nm (18 740); δ 7.37 (2 H, AB system, *J* 16 Hz, vinyl protons), 3.65 (3 H, s, CO_2CH_3), 2.75—2.38 (8 H, m, 2 × $COCH_2$ and 4 allylic protons), 2.31 (2 H, t, *J* 7 Hz, CH_2CO_2Me), 1.78—1.12 (14 H, m), and 0.87 (3 H, m, CH_2CH_3); *m/z* 348 (M^+) (Found: C, 71.9; H, 9.4. $C_{21}H_{32}O_4$ requires C, 72.4; H, 9.2%).

Reductions with Sodium Cyanoborohydride.—(*a*) The following procedure was typical. A stirred solution of sodium cyanoborohydride (175 mg, 2.8 mmol) and 12β-phenylthio-1-nor-12α-prost-13-ene-11,15-dione (**9**) (1 g, 2.5 mmol) in THF (20 ml) was adjusted to pH 4 by dropwise addition of dil. hydrochloric acid. After 2 h, more sodium cyanoborohydride (87 mg, 1.4 mmol) was added, the solution was adjusted to pH 4, and the mixture was stirred for a further 2 h. The solvent was evaporated, and the residue was partitioned between ether and saturated aqueous sodium chloride. Work-up with ether afforded an oil, which was chromatographed [ether–light petroleum (1:9)] to give 15β-*hydroxy*-12β-*phenylthio*-1-*nor*-12α-*prost*-13-*en*-11-*one* (**24**) (451 mg, 44%), $\nu_{max.}$ 3 600 and 3 450 (OH) and 1 740 cm^{-1} (C=O); δ 7.55—7.22 (5 H, m, C_6H_5), 5.57 (2 H, m, vinyl protons), and 6.02 (1 H, m, C*H*OH); *m/z* 384 ($M^+ - H_2O$) (Found: C, 74.6; H, 9.7; S, 8.1. $C_{25}H_{38}O_2S$ requires C, 74.6; H, 9.45; S, 8.0%), and 15α-*hydroxy*-12β-*phenylthio*-1-*nor*-12α-*prost*-13-*en*-11-*one* (**23**) (370 mg, 36%), $\nu_{max.}$ 3 600 and 3 450 (OH) and 1 740 cm^{-1} (C=O); δ 7.55—7.22 (5 H, m, C_6H_5), 5.62 (2 H, m, vinyl protons, and 4.03 (1 H, m, C*H*OH); *m/z* 402 (M^+) (Found: C, 74.7; H, 9.7; S, 7.7%).

(*b*) Reduction of compound (**13**) (510 mg) and chromatography [ethyl acetate–light petroleum (1:4)] of the product gave *methyl* 15β-*hydroxy*-11-*oxo*-12β-*phenylthio*-12α-*prost*-13-*en*-1-*oate* (**26**) (279 mg, 55%), $\nu_{max.}$ 3 590 and 3 480 (OH) and 1 724 cm^{-1} (C=O); δ 7.58—7.22 (5 H, m, C_6H_5), 5.59 (2 H, m, vinyl protons), 3.99 (1 H, m, C*H*OH), 3.66 (3 H, s, CO_2CH_3), 2.30 (4 H, t, *J* 7 Hz, 2 × $COCH_2$), 2.07—1.04 (22 H, m), and 0.86 (3 H, t, *J* 7 Hz, CH_2CH_3) (Found: C, 70.2; H, 8.75; S, 7.0. $C_{27}H_{40}O_4S$ requires C, 70.45; H, 8.7; S, 6.95%), and *methyl* 15α-*hydroxy*-11-*oxo*-12β-*phenylthio*-12α-*prost*-13-*en*-1-*oate* (**25**) (215 mg, 42%), $\nu_{max.}$ 3 580 and 3 444 (OH) and 1 724 cm^{-1} (C=O); δ 7.65—7.14 (5 H, m, C_6H_5), 5.61 (2 H, m, vinyl protons), 4.00 (1 H, m, C*H*OH), 3.65 (3 H, s, CO_2CH_3), 2.30 (4 H, t, *J* 7 Hz, 2 × $COCH_2$), 2.05—1.00 (22 H, m), and 0.86 (3 H, m, CH_2CH_3) (Found: C, 70.15; H, 8.8; S, 7.05%).

(*c*) Reduction of compound (**14**) (1.0 g) and chromatography [ether–light petroleum (1:9)] of the product gave 15-*hydroxy*-12α-*phenylthio*-1-*norprost*-13-*en*-11-*one* (**27**) (593 mg, 58%) (a mixture of 15-epimers), $\nu_{max.}$ 3 605 and 3 450 (OH) and 1 730 cm^{-1} (C=O); δ 7.40—7.10 (5 H, m, C_6H_5), 5.64 (2 H, m, vinyl protons), and 3.91 (1 H, m, C*H*OH); *m/z* 402 (M^+) (Found: C, 74.5; H, 9.6; S, 7.8. $C_{25}H_{38}O_2S$ requires C, 74.6; H, 9.45; S, 8.0%), together with a mixture of 11,15-diols (218 mg).

(*d*) Reduction of compound (**18**) (400 mg) and chromatography [ethyl acetate–light petroleum (1:9)] of the product gave a mixture of 11-oxo-15-ols (**28**) and (**29**) (241 mg, 60%) together with a mixture of 11,15-diols (112 mg, 28%). A portion (114 mg) of the mixture of 11-oxo-15-ols was re-chromatographed [ethyl acetate–dichloromethane (2:8)] to give *methyl* 15β-*hydroxy*-11-*oxo*-12α-*phenylthioprost*-13-*en*-1-*oate* (**29**) (38 mg), $\nu_{max.}$ 3 410 (OH) and 1 723 cm^{-1} (C=O); δ 7.55—7.19 (5 H, m, C_6H_5), 5.74 (2 H, m, vinyl protons), 4.05 (1 H, m, C*H*OH), 3.67 (3 H, s, CO_2CH_3), 2.73 (1 H, m), 2.31 (2 H, t, *J* 7 Hz, $COCH_2$), 2.25—1.12 (23 H, m), and 0.87 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/z* 460 (M^+) (Found: C, 70.7; H, 8.55; S, 6.85. $C_{27}H_{40}O_4S$ requires C, 70.45; H, 8.7; S, 6.95%), and *methyl* 15α-*hydroxy*-11-*oxo*-12α-*phenylthioprost*-13-*en*-1-*oate* (**28**) (41 mg), $\nu_{max.}$ 3 410 (OH) and 1 722 cm^{-1} (C=O); δ 7.52—7.20 (5 H, m, C_6H_5), 5.73 (2 H, m, vinyl protons), 4.04 (1 H, m, C*H*OH), 3.67 (3 H, s, CO_2CH_3), 2.74 (1 H, m), 2.31 (2 H, t, *J* 7 Hz, $COCH_2$), 2.25—1.12 (23 H, m), and 0.89 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/z* 460 (M^+) (Found: C, 70.2; H, 8.9; S, 7.2%).

(*e*) Reduction of the diene-dione (**30**) (1.0 g), followed by chromatography [ether–light petroleum (2:3)] of the product gave 15-*hydroxy*-1-*norprosta*-8(12),13-*diene*-11-*one* (**33**) (427 mg, 42%), $\nu_{max.}$ 3 590 and 3 420 (OH) and 1 690 and 1 596 cm^{-1} (C=C–C=O); $\lambda_{max.}$ 265 nm (ε 10 730); δ 6.68 (1 H, dd, *J* 6.6, *J* 16.5 Hz, HC=C*H*–CHOH), 6.14 (1 H, d, *J'* 16.5 Hz, *H*C=CH–CHOH), 4.07 (1 H, q, *J* 6 Hz, C*H*OH), 2.64 (1 H, br s, OH), and 2.45—2.20 (6 H, m, CH_2CO and 4 allylic protons); *m/z* 292 (M^+) (Found: C, 77.8; H, 10.9. $C_{19}H_{32}O_2S$ requires C, 78.1; H, 11.0%).

(*f*) Reduction of the diene-dione (**32**) (250 mg), followed by chromatography [ethyl acetate–light petroleum (1:4)] of the product gave *methyl* 15-*hydroxy*-11-*oxoprosta*-8(12),13-*diene*-1-*oate* (**34**) (121 mg, 48%), $\nu_{max.}$ 3 590 and 3 440 (OH), 1 720 (CO_2Me), and 1 680 cm^{-1} (C=O); $\lambda_{max.}$ 224 (ε 12 600) and 266 nm (8 490); δ 6.83 (1 H, dd, *J* 16, *J'* 16 Hz, HC=C*H*–CHOH), 6.28 (1 H, d, *J* 16 Hz, *H*C=CH–CHOH), 4.19 (1 H, q, *J* 6 Hz, C*H*OH), 3.66 (3 H, s, CO_2CH_3), 2.65—1.91 (9 H, m, OH, 2 × $COCH_2$, and 4 allylic protons), 1.76—0.97 (16 H, m), and 0.86 (3 H, m, CH_2CH_3); *m/z* 332 ($M^+ - H_2O$) (Found: C, 72.3; H, 9.8. $C_{21}H_{34}O_4$ requires C, 72.0; H, 9.7%).

Reductions with Aluminium Isopropoxide.—(*a*) The following procedure was typical. A mixture of aluminium turnings (135 mg, 5 mg-atom), mercury(II) chloride (15 mg), tetrachloromethane (3 ml), and dry isopropyl alcohol (50 ml) was boiled under nitrogen until the aluminium had dissolved (about 1 h). A solution of 1-norprosta-8(12),13-diene-11,15-dione (**30**) (290 mg, 1 mmol) in dry isopropyl alcohol (20 ml) was added, and the mixture was boiled gently. Isopropyl alcohol, which distilled slowly from the mixture, was collected during 90 min, and the residual reaction mixture was then cooled and diluted with ethyl acetate and 10% aqueous tartaric acid. The non-aqueous phase was separated, and the aqueous phase was extracted with ethyl acetate. The combined extracts were dried and evaporated to give an oil which was chromatographed [ether–light petroleum (2:3)] to furnish 15-hydroxy-1-norprosta-8(12),13-dien-11-one (**33**) (180 mg, 62%), identical with the sample prepared above.

(*b*) Reduction of methyl 11,15-dioxoprosta-8(12),13-dien-1-oate (**32**) (374 mg), followed by chromatography [ethyl acetate–light petroleum (4:6)] of the product gave, in order of elution, *isopropyl* 15-*isopropoxy*-11-*oxoprosta*-8(12),13-*dien*-1-*oate* (**37**) (94 mg, 21%), ν_{max} 1 712 (CO_2Pr^i), 1 684 (C=O), and 1 586 cm^{-1}; $\lambda_{max.}$ 223 (ε 11 640) and 262 nm (7 070); δ 6.67 (1 H, dd, *J* 16, *J'* 6 Hz, HC=C*H*–CHOH), 6.21 (1 H, d, *J* 16 Hz, *H*C=CH–CHOH), 5.00 (1 H, CO_2CHMe_2), 3.83 (1 H, q, *J* 7 Hz, C*H*OPr^i), 3.64 (1 H, m, OC*H*Me$_2$), 2.65—2.18 (8 H, m, 2 × $COCH_2$ and 4 allylic protons), 1.75—1.03 (28 H, m), and 0.86 (3 H, m, CH_2CH_3) (Found: M^+, 420.3247. $C_{24}H_{44}O_4$ requires *M*, 420.3239); *methyl* 15-*isopropoxy*-11-*oxoprosta*-8(12),13-*dien*-1-*oate* (**35**) (95 mg, 24%), $\nu_{max.}$ 1 720 (CO_2Me) and 1 680 and 1 586 cm^{-1} (C=C–C=O); $\lambda_{max.}$ 224 (ε 12 310), and 262 nm (7 780); δ 6.65 (1 H, dd, *J* 16, *J'* 7 Hz, HC=C*H*–CHOH), 6.19 (1 H, d, *J* 16 Hz, *H*C=CH–CHOH), 3.82 (1 H, q, *J* 7 Hz, C*H*OPr^i), 3.64 (3 H, s, CO_2CH_3), 3.62 (1 H, m, OC*H*Me$_2$), 2.66—2.17 (8 H, m, 2 × $COCH_2$ and 4 allylic protons), 1.74—1.04 (22 H, m), and 0.86 (3 H, CH_2CH_3) (Found: M^+, 392.2924. $C_{24}H_{40}O_4$ requires *M*, 392.2926); *isopropyl* 15-*hydroxy*-11-*oxoprosta*-8(12),13-*dien*-1-*oate* (**36**) (54 mg, 14%), $\nu_{max.}$ 3 592 and 3 454 (OH), 1 720 (CO_2Pr^i), and 1 685 and 1 592 cm^{-1} (C=C–C=O); $\lambda_{max.}$ 223 (ε 15 680) and 265 nm (8 510); δ 6.82 (1 H, dd, *J* 16, *J'* 6 Hz, HC=C*H*–CHOH), 6.27 (1 H, d, *J* 16 Hz, *H*C=CH=CHOH), 5.00 (1 H, m, CO_2CHMe_2), 4.18 (1 H, q, *J* 6 Hz, C*H*OH), 2.58—2.33 (6 H, m, $COCH_2$ and 4 allylic protons), 2.25 (2 H, t, *J* 7 Hz, $CH_2CO_2Pr^i$), 1.96 (1 H, br s, OH), 1.70—1.18 (22 H, m), and 0.87 (3 H, m, CH_2CH_3); *m/z* 378 (M^+) (Found: C, 72.8; H, 9.95. $C_{23}H_{38}O_4$ requires C, 73.0; H, 10.05%); and methyl 15-hydroxy-11-oxoprosta-8(12),13-dien-1-oate (**34**) (45 mg, 12%), identical with the sample prepared previously.

(*c*) Reduction of 1-hydroxyprosta-8(12),13-diene-11,15-dione (**31**) (120 mg), followed by chromatography [ether–light petroleum (1:1)] of the product, gave 1-*hydroxy*-15-*isopropoxyprosta*-8(12),13-*dien*-11-*one* (**39**) (31 mg, 23%), $\nu_{max.}$ 3 604 and 3 445 (OH) and 1 686 and 1 590 cm^{-1} (C=C–C=O); $\lambda_{max.}$ 225 (ε 12 620) and 263 nm (9 080); δ 6.66 (1 H, dd, *J* 16, *J'* 6 Hz, HC=C*H*–CHOPr^i), 6.23 (1 H, d, *J* 16 Hz, *H*C=CH–CHOPr^i), 3.84 (1 H, q, *J* 6 Hz C*H*OPr^i), 3.63 (2 H, t, *J* 6 Hz, OCH_2), 3.60 (1 H, m, OC*H*Me$_2$), 2.60—2.34 (6 H, m, $COCH_2$ and 4 allylic protons), 1.93 (1 H, br s, OH), 1.68—1.00 (24 H, m), and 0.87 (3 H, m, CH_2CH_3); *m/z* 364 (M^+) (Found: C, 75.7; H, 11.0. $C_{23}H_{40}O_3$ requires C, 75.8; H, 11.0%), and 1,15-*dihydroxyprosta*-8(12),13-*dien*-11-*one* (**38**) (33 mg, 28%), $\nu_{max.}$ 3 595 and 3 430 (OH) and 1 684 and 1 590 cm^{-1} (C=C–C=O); $\lambda_{max.}$ 225 (ε 14 480) and 266 nm (8 290); δ 6.81 (1 H, dd, *J* 16, *J'* 6 Hz, HC=C*H*–CHOH), 6.23 (1 H, d, *J* 16 Hz, *H*C=CH–CHOH), 4.19 (1 H, q, *J* 6 Hz, C*H*OH), 3.63 (2 H, t, *J* 6 Hz, OCH_2), 2.60—2.24 (8 H, m, 2 × OH, $COCH_2$, and 4 allylic protons), 1.68—1.12 (18 H, m), and 0.86 (3 H, m, CH_2CH_3); *m/z* 322 (M^+) (Found: C, 74.4; H, 10.8. $C_{20}H_{34}O_3$ requires C, 74.55; H, 10.55%).

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