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BF_3-MEDIATED REACTION OF A SULPHONE WITH ALDEHYDES. A METHOD FOR STEREOSPECIFIC CONSTRUCTION OF PROSTAGLANDIN ω-CHAIN

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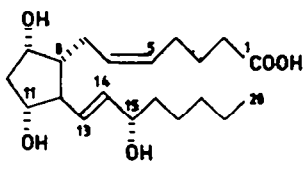
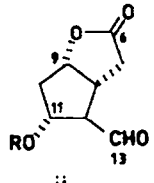
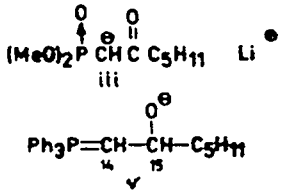
Abstract: A new method for stereospecific construction of the allylic alcohol moiety of prostaglandins, based on application of optically active α-hydroxy aldehydes, is described. In the presence of $BF_3.Et_2O$, lithiated sulphones 1 prepared from Corey aldehyde, and carbonyl compounds 2 give the corresponding adducts 3 in moderate to excellent yields, while in the absence of the Lewis acid either no products or only their traces were formed. The addition products 3, in the form of benzoates, mesylates or free alcohols, were subjected to reductive elimination by means of sodium amalgam to give the alkenes 4. Compounds 4d and 4f were transformed into racemic and natural $PGF_{2\alpha}$, respectively, in line with the known method.

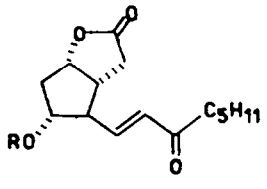
Interest in the synthesis of prostaglandins /1/ has given rise to a number of methodological approaches to stereospecific construction of different fragments of their structure, among others, of an allylic alcohol unit in an aliphatic chain. The classical Corey strategy /2/ aimed at synthesis of $PGF_{2\alpha}$ (i) which with some tactical modifications still appears to be most versatile and best suited for technical scale, involves phosphorus-mediated alkenylation reactions. Condensation of the lactone-aldehyde ii with oxo-phosphonate iii affords α,β-unsaturated ketone iv with E configuration of the double bond (Chart 1). Completion of the formation of the prostaglandin ω chain (C_{13}-C_{20}) requires selective, stereospecific reduction of the keto group in intermediate iv /3/. An alternative direct preparation of chiral allylic alcohol vi by condensation of aldehyde ii with β-oxido phosphonium ylide v has been found to be markedly less effective /4/. Since the corresponding betaine vii collapses with selective loss of the oxygen atom originating in the aldehyde to give 13,14-ene /5/, the low yield of the whole process (35%) can be attributed to instability of the reactants. In fact, aldehyde ii (R=tetrahydropyran-2-yl) is not stable enough to be isolated.

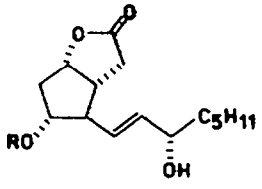
Chart 1

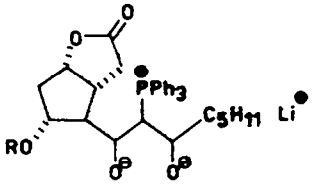








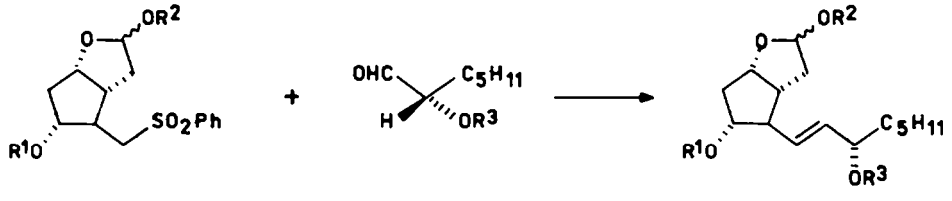




R=protecting group

Considering the stability of synthons ii and v one can conclude that the reversal of their polarity by placing the oxo-group at C_{14} (prostaglandin numbering) and generatng an anion at C_{13} would be advantageous. Obviously, α-hydroxy aldehydes are readily available stable compounds. On the other hand, introduction on C_{13} of an anion-stabilizing group instead of the oxo-function would allow to avoid elimination of the substituent at C_{11}, which notoriously creates difficulties in handling aldehyde ii and the unsaturated ketone iv. The purpose of this work was to develop a methodology for stereospecific construction of allylic alcohols, utilizing derivatives of α-hydroxy aldehydes, and to apply such methodology to prostaglandin synthesis /6/. The accessibility of sulphones viii drew our attention to Julia alkenylation /7,8/. It was thought that combining of sulphone viii with the derivative of hydroxy aldehyde ix would give intermediate x which could be transfered to $PGF_{2\alpha}$(i) according to the known procedure /9/ (Scheme 1; R^1, R^2, R^3- protecting groups). However, there was no precedent for the reaction of sterically hindered sulphones with aldehydes, and it was unclear whether under the conditions of alkenylation the configuration of the hydroxy aldehyde derivative could be retained.

Scheme 1



viii ix x

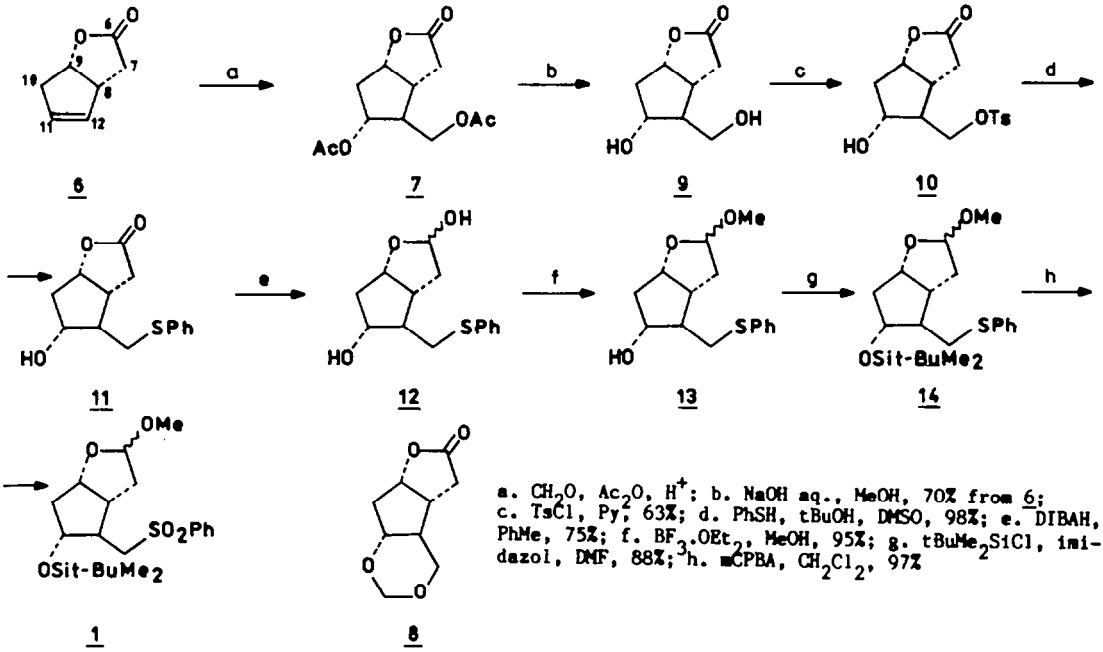
Results and Discussion

In practical realization of Scheme 1, the following protective groups were chosen: R^1=SitBuMe$_2$, R^2=Me, R^3=SitBuMe$_2$ or SitBuPh$_2$. The structure of corresponding starting material and intermediates are given in Chart 2.

Synthesis of sulphone 1

Sulphone 1 was synthesized from the readily available /10/ racemic, unsaturated lactone 6, as shown in Scheme 2. The Scheme has to be supplemented by the following comments.

Scheme 2



6 7 9 10 11 12 13 14 1 8

a. CH_2O, Ac_2O, H^+; b. NaOH aq., MeOH, 70% from 6; c. TsCl, Py, 63%; d. PhSH, tBuOH, DMSO, 98%; e. DIBAH, PhMe, 75%; f. BF_3.OEt_2, MeOH, 95%; g. $tBuMe_2SiCl$, imidazol, DMF, 88%; h. mCPBA, CH_2Cl_2, 97%

The Prince reaction /11/ was carried out in a sealed vessel to prevent evaporation of formaldehyde. The product, diacetate 7, contaminated with ca 5% of acetal /12/ 8, was isolated by distillation under reduced pressure.

Reduction of the lactone 11 led to a mixture of epimeric lactols 12 at ca 1:1 ratio. After protection of the lactol group and other transformations indicated in the Scheme, the corresponding epimers of intermediate 1 were resolved by chromatography and found to be stable during several weeks of storage.

Addition of sulphone 1 to aldehydes

Treatment of sulphone 1 in a tetrahydrofuran (THF) solution with one equivalent of butyllithium in hexane, and subsequently with one equivalent of racemic 2-(t-butyldimethylsilyloxy)heptanal (2d) in THF (Chart 2), at -78°C, afforded only minute amounts of adduct 3d (<10%). Under the same conditions, benzaldehyde provided the addition product 3b in an appreciable yield (75%), but hexanal did not enter into the reaction at all. Extensive varying of the reaction conditions, solvents, temperature, use of an excess of the aldehyde, use of lithiumdiisopropyl amide for generation of the anion etc., failed to improve the yields of adducts 3d and 3a, respectively.

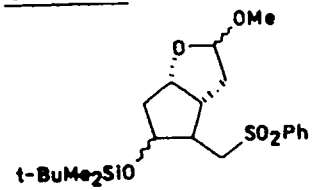
Kocieński and co-authors /13/ have reported that easily enolysable aldehydes, such as hexanal gave higher yields of adducts with MgBr derivatives of sulphones as compared with their Li derivatives. However, this methodology did not help in solving our problem. More recently it has been discovered that alkylcuprates /14/, alkynyl- /15/ and alkyllithium /16/ derivatives are compatible, at low temperatures, with Lewis acids, such as boron trifluoride or aluminum trichloride. The resulting "ate" complexes exhibit /14a,17/ anhanced activity in nucleophilic addition and nucleophilic substitution /18/. It appeared of interest to examine the behaviour of lithiated sulphone 1 towards carbonyl compounds in the presence of Lewis acids, although there is a clear difference in the structure between this compound and the previously investigated organometallics. Pursuing along this line, we found that treatment of the sulphone 1 in THF solution, at -78°C, with - successively - one equivalent of butyllithium, one equivalent of $BF_3.Et_2O$, and one equivalent of aldehyde 2d afforded the addition product 3d in a 90% yield. The addition of sulphone 1 to the glyceraldehyde derivative 2c (Chart 2) was similarly effective; hexanal (2a) afforded the product 3a in a 40% yield. Under conditions of BF_3-mediated reaction, lithium sulphone 1 formed adducts not only with aldehydes, but also with methyl ketones, as exemplified by heptan-2-one (2e) (adduct 3e, 99% yield, 30% conversion). It should be mentioned that benzaldehyde and sulphone 1, in the presence of BF_3 - Et_2O gave the adduct 3b in higher yield (89%) and within a much shorter reaction time than under conditions of the conventional procedure (Table 1).

Table 1

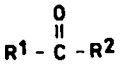
Entry	Aldehyde	$BF_3.Et_2O$	Adduct (% yield)[a]	Procedure	Olefine (% yield)[a]
1	2a	+	3a (40)	A	4a (70)
2	2b	-	3b (75)	B	4b (53)
3	2b	+	3b (89)		
4	2b	+	not isolated	C	4b (84)[b]
5	2c	+	3c (87)	B	4c (52)
6	2c	+	not isolated	C	4c (75)[b]
7	2d	+	3d (90)	A	4d (70)
8	2d	+	3d (90)	B	4d (67)
9	2d	+	not isolated	C	4d (76)[b]
10	2e	+	3e (30)	A	4e (62)
11	2f	+	3f	C	4f (88)[b]

Procedures: A - reduction of purified hydroxy sulphone 3; B - mesylation or benzoylation of purified hydroxy sulphone 3 followed by reduction; C - alkylation, mesylation (benzoylation) and reduction in one pot.
a) isolated yield, b) overall yield

Chart 2

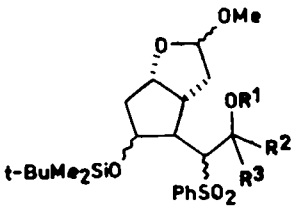


1



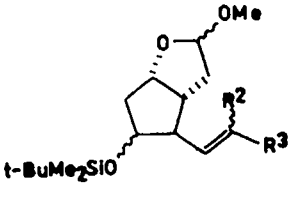
2

a R^1=H R^2=C_5H_{11}
b R^1=H R^2=C_6H_5
c R^1=H R^2=A
d R^1=H R^2=CH-C_5H_{11} (rac), OSiMe$_2$tBu
e R^1=Me R^2=C_6H_{13}
f R^1=H R^2=CH-C_5H_{11} (2S), OSiPh$_2$tBu



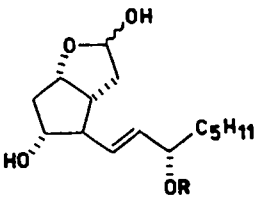
3

a R^1=H R^2=H R^3=C_5H_{11}
b R^1=H R^2=H R^3=C_6H_5
c R^1=H R^2=H R^3=A
d R^1=H R^2=H R^3=CH=C_5H_{11} (rac), OSiMe$_2$tBu
e R^1=H R^2=Me R^3=C_6H_{13}
f R^1=H R^2=H R^3=CH-C_5H_{11} (2S), OSiPh$_2$tBu
g R^1=SO_2Me R^2=H R^3=CH-C_5H_{11} (rac), OSiMe$_2$tBu
h R^1=COPh R^2=H R^3=C_6H_5
i R^1=COPh R^2=H R^3=A
j R^1=SO_2Me R^2=H R^3=CH-C_5H_{11} (rac), OSiMe$_2$tBu
k R^1=SO_2Me R^2=H R^3=CH-C_5H_{11} (2S), OSiPh$_2$tBu



4

a R^2=H R^3=C_5H_{11}
b R^2=H R^3=C_6H_5
c R^2=H R^3=A
d R^2=H R^3=CH-C_5H_{11} (rac), OSiMe$_2$tBu
e R^2=Me R^3=C_6H_{13}
f R^2=H R^3=CH-C_5H_{11} (2S), OSiPh$_2$tBu

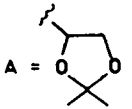


5

a R=SiMe$_2$tBu
b R=SiPh$_2$tBu

$Ph_3P{=}CHCH_2CH_2CH_2CO_2^-$

15



The order of addition of the carbonyl compound and $BF_3.Et_2O$ to the lithiated sulphone has no detectable effect on the reaction course, providing that both components are added within a short time (15 min). The adducts 3a - 3i were obtained in the form of complex mixtures of diastereoisomers. No attempt was made to determine their ratios.

Having on hand the hydroxy sulphones, we could approach the second step of sulphone-based alkenylation, i.e. reductive elimination. Sulphonyl carbinols 3a, 3c, 3d were esterified with benzoyl chloride or methanesulphonyl chloride prior to their reduction. Reductions were carried out with 6% sodium amalgam in methanol /7/ or with a mixture of methanol and THF, in the presence of phosphate buffer /19/. Intermediates 3a and 3e were transformed into the corresponding alkenes 4a and 4e, respectively, without preliminary esterification. However, generally the reduction of free hydroxy-benzenesulphonyl derivatives affords alkenes accompanied by alcohols formed by substitution of the benzenesulphonyl group by a hydrogen atom. The yields of alkenes 4 are compiled in Table 1.

The steps involved in the alkenylation sequence were conveniently combined in a one-pot procedure (see Experimental) which allowed an increase in the yields of the final products (Table 1).

It is well documented that Julia alkenylation furnishes trans alkenes exclusively or predominantly /7b,20/ (some exceptions involving relatively high proportion of the cis isomer have been reported /21/). The ^1H NMR (400 MHz) spectra of styrene derivative 4b indicated that two compounds (epimers at C_6) are present in a ca 1:1 ratio, both with trans configuration of the double bond (δ 6.4963 and 6.4366 ppm, doublets, J=15.8 Hz; δ 6.0545 and 5.9737 ppm, doublet of doublets, J=15.8 Hz, J=1.6 Hz). The cis isomers could not be detected.

In case of the other alkenes (4a,c,d,e,f) the ^1H NMR spectra did not permit assignment of configurations, owning to complexity of vinylic protons signals of the mixtures of diastereoisomers.

Completion of the prostaglandin synthesis

A mixture of isomers 4d was subjected to acid hydrolysis /9/ and the product, without isolation, was treated with the ylide 15 (Chart 2) prepared from (4-carboxybutyl)triphenylphosphonium bromide. After chromatography, $PGF_{2\alpha}$ and 15-epi $PGF_{2\alpha}$ were obtained in a ca 1:1 ratio. No other compounds could be detected in the reaction mixture. Formation of two isomers only, differing in the configuration of the hydroxy group at C_{15} indicated that reductive elimination applied to intermediate 4d proceeds with high trans-selectivity.

For the synthesis of optically active $PGF_{2\alpha}$, optically active , epimeric at C_6 sulphones 1 were prepared from optically active lactone 6. The reaction of optically active 1 with (S) 2-(t-butyldiphenylsilyloxy)heptanal /22/ (2f) in the presence of $BF_3.Et_2O$ afforded the addition product which without isolation was subjected to mesylation, followed by reductive elimination. The elimination product 4f showing the expected spectroscopic properties was hydrolyzed and the resulting product 5 was treated with ylide 15. 15-t-Butyldiphenylsilyl $PGF_{2\alpha}$ was obtained, and after deprotection with tetrabutylammonium fluoride in THF - furnished $PGF_{2\alpha}$ in 52% yield from 1. Specific rotation of the final product 1 $[\alpha]_D^{14}$ +23° (c=1.4, THF) was identical with that of the commercial product ($[\alpha]_D^{14}$+23°, c=1, THF).

Preparation of natural $PGF_{2\alpha}$ from optically active sulphone 1 and aldehyde 2f indicates that under the applied conditions of Julia alkenylation there was no racemization of the hydroxy aldehyde derivative 2f.

Experimental

M. ps were determined on a Kofler hot-stage apparatus. The spectra were recorded using the following instruments: IR, Beckmann 4240 or Unicam SP 200 spectrophotometers (unless otherwise stated, $CHCl_3$ solutions); ^1H NMR, Varian EM 360, Bruker 270 and Bruker 400 spectrometers (in $CDCl_3$ solutions); mass - LKB 2091 spectrometer (at 15 eV ionization potential unless otherwise stated); high-resolution mass - Varian 731 spectrometer. Chemical shifts were reported in δ units, downfield from Me_4Si. Column chromatography was performed on silica gel, Merck, and TLC - on silica gel G, Merck. Organic solvents were dried over anh. Na_2SO_4 and solvents were removed under reduced pressure using a rotary evaporator. Microanalyses were performed at our analytical laboratory.

4β-Hydroxymethyl-5α-hydroxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan-2-one (9)

A sealed ampoule equipped with a Rotaflo stopcock containing: lactone 6 (24.8 g, 0.2 mol), Ac_2O (15 mL), glacial acetic acid (100 mL), paraformaldehyde (17 g), and conc. sulphuric acid (4 mL) was heated at 70-80°C for 20 h or at 60-65°C for 40 h. The reaction was monitored by TLC (acetone-hexane, 1:1). After cooling, the reaction mixture was diluted with AcOEt (400 mL) and the resulting solution was treated with 10% aq KOH (at 0 to 5°C) to pH 6. The aqueous layer was separated and extracted with AcOEt (2x50 mL). The combined organic solutions were dried ($MgSO_4$), the solvent was evaporated, and the residue was distilled at 150-180°C/0.01 mm Hg. The crude diacetate 7 (41 g, 80%) was obtained in the form of a colourless or yellowish liquid. This product was contaminated with ca 5% of acetal 8.

To a solution of diacetate 7 (41 g) in MeOH (150 mL), 25% aqueous NaOH (50 mL) was added and the mixture was set aside at room temperature for 20 h. Then it was acidified with conc. hydrochloric acid to pH 1 (ca 30 mL). The solvent was evaporated under reduced pressure and the organic material was taken up in acetone. The acetone solution was dried (Na_2SO_4) and the solvent was removed to give diol 9 as yellow oil (24 g, 70% yield). This product was used for the further step without additional purification. A sample was chromatographed on a SiO_2 column (230-400 mesh, acetone-heptane, 2:1) to give acetal 8, mp 150-153°C, ν_{max} ($CHCl_3$), 1760 (C=O) cm^{-1} and diol 9, mp 117-118°C (lit. /1,2,4/ mp 117.5-118.5°C).

4β-(p-Toluenesulphoxymethyl)-5α-hydroxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan-2-one (10)

To a stirred solution of dihydroxy lactone 9 (2.03 g, 11.8 mmoles) in pyridine (8 mL), tosyl chloride (2.25 g, 11.8 mmoles) was added at -20°C. The mixture was set aside at -18°C for two days, whereupon it was diluted with $CHCl_3$ (50 mL) and washed with 3% hydrochloric acid, water, saturated aqueous $NaHCO_3$ and brine. After drying, the solvent was evaporated under reduced pressure and the residue was chromatographed on a SiO_2 column (30 g, 230-400 mesh, $CHCl_3$-AcOEt 1:1) to give monotosylate 10 (2.4 g, 63%) in the form of colourless crystals. A sample was recrystallized from $CHCl_3$-AcOEt, mp 122-123°C; ν_{max} (nujol) 1760 (C=O), 1180 (SO_2O) cm^{-1}; δ_H(ppm) 7.8 (d, 2H, J=8.5 Hz) and 7.4 (d, 2H, J=8.5 Hz, arom.H), 4.85 (m, 1H, C_{6a}-H), 4.0 (m, 3H, C_5-H and CH_2-OSO_2), 2.4 (s, 3H, CH_3-C_6H_4). Mass spec. m/e 326 (M+). (Found: C, 55.11; H, 5.54. Calcd. for $C_{15}H_{18}SO_6$: C, 55.21; H, 5.56%).

4β-(Thiophenoxymethyl)-5α-hydroxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan-2-one (11)

To a solution of thiophenol (800 mg, 7.5 mmole) in DMSO (6 mL), stirred under argon at room temperature, t-BuOK (900 mg, 6.2 mmole) was added, followed by a solution of tosylate 10 (2 g, 6.2 mmole) in DMSO (6 mL). The reaction mixture was stirred for 30 min., whereupon it was diluted with $CHCl_3$ (60 mL) and washed with water. The usual work-up and chromatography of the crude product on SiO_2 column (25 g, 230-400 mesh, elution: hexane-$CHCl_3$-AcOEt, 1:1:1) gave the sulphide 11 (1.58 g, 98%) in crystalline form. A sample was recrystallized from Et_2O-hexane, mp 62-63°C; ν_{max} ($CHCl_3$) 3420 (OH), 1750 (C=O), 1200 (C-O-C) cm^{-1}; δ_H (ppm) 7.4 (m, 5H, aromat. H), 5.05 (m, 1H, C_{6a}-H), 4.2 (m, 1H, C_5-H), 3.3-1.9 (m, 8H) (Found: C, 63.52; H, 5.95; S, 12.4. Calcd. for $C_{14}H_{16}O_3S$: C, 63.61; H, 6.10; S, 12.13%). Optically active 11, $[\alpha]_D^{15}$ -35.2° (c=2.8 $CHCl_3$).

4β-(Thiophenoxymethyl)-2ξ,5α-dihydroxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan (12)

To a solution of lactone 11 (258 mg, 2 mmol) in CH_2Cl_2 (10 mL), stirred under argon at -78°C, a 2.2 M solution of diisobutylaluminum hydride in toluene (6.5 mL, 8 mmol) was added dropwise. Stirring at -78°C was continued for 30 min, and MeOH (5 mL) was carefully added, followed by SiO_2 (3 g). The mixture was evaporated under reduced pressure. The residue was transferred to a SiO_2 column (45 g, 230-400 mesh). Elution with a mixture of $CHCl_3$-AcOEt-MeOH 50:50:1 gave lactol 12 (400 mg, 75%) as a colorless oil. A sample was rechromatographed and dried under high vacuum; ν_{max} ($CHCl_3$) 3360 (OH) cm^{-1}; (Found: C, 62.95; H, 6.67; S, 12.21. Calcd. for $C_{14}H_{18}O_3S$: C, 63.13; H, 6.81; S, 12.04%).

4β-(Thiophenoxymethyl)-5α-hydroxy-2ξ-methoxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan 13

To a stirred solution of lactol 12 (538 mg, 2 mmol) in MeOH (16 mL) BF_3.Et_2O (0.2 mL) was added at -20°C. After 2 hrs the reaction was quenched by addition of a few drops of triethylamine. The work-up and filtration of the crude product through a SiO_2 column (2 g, 230-400 mesh, $CHCl_3$) gave methyl-lactol 13 (570 mg, 95%) as a thick oil. A sample was rechromatographed and dried in high vacuum; ν_{max} 3370 (OH) cm^{-1}; (Found: C, 64.39; H, 7.10; S, 11.55. Calcd. for $C_{15}H_{20}O_3S$: C, 64.25; H, 7.19; S, 11.44%).

4β-(Thiophenoxymethyl)-5α-(t-butyldimethylsilyloxy)-2ξ-methoxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan (14)

To a stirred solution of alcohol 13 (570 mg, 2 mmol) in DMF (1.6 mL), imidazole (340 mg, 5 mmol) and t-butylchlorodimethylsilane (370 mg, 3 mmol) were added. The mixture was kept at 40°C for 10 min. The work-up and chromatography of the crude product on SiO_2 (5 g, 230-400 mesh, $CHCl_3$) gave the derivative 14 (710 mg, 88%); ν_{max} no characteristic absorption; δ_H (ppm) 7.3 (m, 5H, aromat. H), 5.1 (m, 1H, C_2-H), 4.5 (m, 1H, C_{6a}-H), 4.0 (m, 1H, C_5-H), 3.3 (2s, 3H, OCH_3), 0.9 (s, 9H, CH_3CSi). (Found: C, 63.80; H, 8.80; S, 8.31. Calcd. for $C_{21}H_{34}OSSi$: C, 63.91; H, 8.68; S, 8.12%).

4β-(Benzenesulphonylmethyl)-5α-(t-butyldimethylsilyloxy)-2ξ-methoxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan (1)

To a stirred solution of sulphide 14 (1.1 g, 2.7 mmol) in CH_2Cl_2 (50 mL) m-chloroperbenzoic acid (80%, 1.4 g, 6.5 mmol) in CH_2Cl_2 (30 mL) was added at -78°C. The mixture was allowed to warm to 0°C during 30 min, maintained at this temperature for 2 hrs, whereupon it was diluted with $CHCl_3$ (50 mL) and washed with a saturated sodium thiosulphate solution, a saturated $NaHCO_3$ solution and brine. Conventional isolation gave sulphones 1 (1.12 g, 97%). A sample was crystallized from Et₂O-hexane, mp 69-70°C; ν max ($CHCl_3$) 1315, 1150 and 840 cm^{-1}; δ_H 8.05 and 7.75 (m, 5H, aromat. H), 5.13 (m, 1H, C_{6a}-H), 4.55 (m, 1H, C_5-H), 3.87 (m, 1H, C_5-H), 3.34 (2s, 3H, O-CH_3), 0.9 (s, 9H, $SiCCH_3$); (Found: C, 59.24; H, 7.85; S, 7.80. Calcd. for $C_{21}H_{34}O_5SSi$: C, 59.12; H, 8.03; S, 7.52%).

A general procedure for addition of sulphone 1 to a carbonyl compound 2 in the presence of $BF_3.Et_2O$

To a solution of sulphone 1 (427 mg, 1 mmol) in THF (5 mL), stirred under argon at -78°C, n-butyllithium (1.4 M in hexane, 0.7 mL, 1 mmol) was added, followed after 10 min by addition of BF_3Et_2O (0.12 mL, 1 mmol) and, after further 5 min, of a carbonyl compound 2. The mixture was allowed to warm to -18°C during 1.5 h and this temperature was maintained for 16 h. Saturated NH_4Cl (0.5 mL) was added, the mixture was diluted with water (20 mL) and the product was extracted with CH_2Cl_2. The crude product was purified on a SiO_2 column.

a. Carbonyl compound: rac. 2-(t-butyldimethylsilyloxy)heptanal (2d)

Crude product: 990 mg; chromatography; SiO_2, 0.06-0.08 mm, 20 g. Product: 4β-[(1'ξ-benzenesulphonyl)-2'ξ-hydroxy-3'ξ-(t-butyldimethylsilyloxy)-1'-octyl]-5α-(t-butyldimethylsilyloxy)-2ξ-methoxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan (3d), (600 mg, 90% yield); ν max 3500 (OH), 1300, 1130 (SO_2Ph), 1250 (tBuMe₂Si), 1040-1090 (C-O, Si-O) cm^{-1}; δ_H (ppm, 60 MHz) 8.1-7.3 (m, 5H, aromat. H), 5.1 (m, 1H, C_2-H), 4.8-3.6 (m, 4H, O-CH_2), 3.30 and 3.32 (2s, 3H, O-CH_3), 2.9 (m, 1H, C_1-H), 0.74 (s, 9H, CH_3CSi). High resolution e.i.m.s. M⁺, ($C_{34}H_{62}O_5SSi_2$) requires 670.3754; found 670.3755; M⁺-C_4H_9 ($C_{30}H_{53}O_5SSi$) requires 613.3051; found 613.3063.

b. Carbonyl compound: hexanal (2a)

Crude product: 520 mg; chromatography; SiO_2, 0.06-0.08 mm, 15 g, $CHCl_3$. Product: 4β-[1'ξ-(benzenesulphonyl)-2'ξ-hydroxy-1'-heptyl]-5α-(t-butyldimethylsilyloxy)-2ξ-methoxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan (3a), 216 mg, 40% yield); ν max (film) 3450 (OH), 1300 (SO_2), 1250 ($SiCH_3$), 1140, 1050, 830 cm^{-1}; δ_H (ppm, 60 MHz) 7.95-7.25 (m, 5H, aromat. H), 5.0 (m, 1H, C_2-H), 4.4 (m, 1H, C_{6a}-H), 4.5-3.1 (m, 5H, CH-O, CH), 3.27 (s. 3H, O-CH_3), 2.9 (m, 1H, C_1-H), 2.5-2.0 (m, 4H, CH_2), 0.5 (m, 1H, CH_2, CH_2), 0.75 (s, 9H, $SiOCCH_3$), 0.0 (s, 6H, $SiCH_3$); high resolution e.i.m.s. no molecular ion ($C_{27}H_{46}O_6SSi$), M⁺-C_4H_9 ($C_{23}H_{37}O_6SSi$) requires 469.2080; found 469.2036; M⁺-C_4H_9-CH_3OH ($C_{22}H_{33}O_5SSi$) requires 437.1818; found 437.1832; M⁺-C_4H_9-CH_3OH-$C_6H_5S(O)OH$ ($C_{16}H_{27}O_3Si$), requires 295.1729; found 295.1730.

c. Carbonyl compound: benzaldehyde (2b)

Crude product: 650 mg; chromatography: SiO_2, 230-400 mesh, 15 g, hexane-AcOEt, 3:1. Product: 5α-(t-butyldimethylsilyloxy)-2ξ-methoxy-4β-[ethyl-2(1'-benzenesulphonyl)-2'ξ-hydroxy-2'-phenyl]-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan (3b), (475 mg, 89% yield); ν max ($CHCl_3$) 3500 (OH), 1600 (C=C), 1340 and 1150 (SO_2), 1100 (C-O-C) cm^{-1}; δ_H (ppm, 60 MHz) 8.2-7.1 (m, 10H, aromat. H), 5.2-5.0 (m, 1H, C_2-H), 4.25-3.95 (m, 1H, C_5-H), 3.21 (s, 3H, O-CH_3), 2.7-1.0 (m, 9H, C_2-, C_{3a}-, C_4-, C_6-, C_{6a}-, C_1- and C_2-H), 0.85 (s, 9H, CH_3CSi), 0.0 (s, 6H, CH_3Si).

d. Carbonyl compound: O,O'-isopropylidene D-glyceraldehyde (2c)

Crude product: 565 mg; chromatography: SiO_2, 230-400 mesh, 5 g, hexane-AcOEt, 3:1. Product: 4β-[butyl-(1'ξ-benzenesulphonyl-2'ξ-hydroxy-3',4'-isopropylidendioxy)]-5α-(t-butyldimethylsilyloxy)-2ξ-methoxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan (3c), (484 mg, 87% yield); ν max ($CHCl_3$) 3500 (OH), 1350, 1150 (SO_2), 1100 (C-O-C) cm^{-1}; δ_H (ppm, 400 MHz) 8.1-7.85 (m, 2H) and 7.80-7.40 (m, 3H, aromat. H), 5.30-4.95 (m, 1H, C_2-H), 4.85-3.45 (m, 7H, C_5-, C_1-, C_2-, C_3-, C_4-H and OH), 3.30 (s, 3H, O-CH_3), 2.95-1.45 (m, 7H, C_3-, C_{3a}-, C_4-, C_6- and C_{6a}-H), 1.25 (s, 6H, $C(CH_3)_3$), 0.9 (s, 9H, $SiOCCH_3$), 0.0 (s, 6H, $SiCH_3$).

e. Carbonyl compound: octan-2-one (2e)

Crude product: 520 mg; chromatography: SiO_2, 0.06-0.08 mm, 6 g, $CHCl_3$. Product: 4β-[1'-(benzenesulphonyl)-2'ξ-hydroxy-2'-methyl-1'-octyl]-5α-(t-butyldimethylsilyloxy)-2ξ-methoxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan (2e), (170 mg, 30% yield); ν max ($CHCl_3$) 3500 (OH), 1300 and 1125 (SO_2), 1100, 1050 (C-O-C) cm^{-1}; δ_H (ppm, 400 MHz) 8.00-7.31 (m, 5H, aromat. H), 5.10 (m, 1H, C_2-H), 4.41 (m, 1H, C_{6a}-H), 4.11 (m, 1H, C_4-H), 3.32 and 3.30 (2s, 3H, O-CH_3), 2.85 (m, 1H, C_1-H), 1.61 and 1.63 (2s, 3H, OCH_3), 0.74 (s, 9H, $SiOCCH_3$), 0.0 (s, 6H, $SiCH_3$); e.i.m.s.: 554 M⁺ ($C_{29}H_{50}O_6SSi$), 497 M⁺-t-Bu, 411 M⁺-t-Bu-C_6H_{13}.

Addition of sulphone 1 to benzaldehyde in the absence of $BF_3.Et_2O$

To a solution of sulphone 1 (427 mg, 1 mmol) in THF (2.5 mL), stirred under argon at -78°C n-butyllithium (1.4 M in hexane, 0.7 mL, 1 mmol) and, after 15 min, benzaldehyde (106 mg, 1 mmol) were added. The mixture was stirred at - 78°C for 3 h and left aside at room temperature for 12 h. The work-up with a saturated NH_4Cl solution and CH_2Cl_2 gave the crude product (650 mg) which was purified on a SiO_2 column. Compound 3b (399 mg, 75% yield) was obtained, identical with a sample described above (cf . experiment with the use of $BF_3.Et_2O$).

4β-[3'(S)-(t-Butyldimethylsilyloxy)-1'-octen-1'-yl]-5α-(t-butyldimethylsilyloxy)-2(S)-methoxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan (4d)

To a solution of hydroxy sulphone 3d (671 mg, 1 mmol) in pyridine (15 mL), stirred at -10°C, methanesulphonyl chloride (0.3 mL, 4 mmol) was added and the mixture was left aside at 5°C for 16 h, whereupon it was evaporated. The residue was diluted with toluene (10 mL), washed with 3% hydrochloric acid, brine, saturated $NaHCO_3$, and evaporated. The crude material (700 mg) was filtered through a SiO_2 column (0.06-0.08 mm, toluene-AcOEt, 98:2) to give methanesulphonate 4j (600 mg, 80%).

To a mixture of a latter compound, powdered anhydrous Na_2HPO_4 (660 mg) and MeOH (7 mL), stirred under argon at -10°C, sodium amalgam (6%, 2.2 g) was added in portions during 30 min. The mixture was allowed to warm to room temperature and a saturated NH_4Cl solution was added. The product was isolated with toluene and purified on a SiO_2 column (10 g, 0.04-0.06 mm, toluene-AcOEt, 98:2) to give alkene 4d (344 mg, 67% yield from 3d); ν_{max} ($CHCl_3$) 1655, 1250, 1120, 1100, 1050, 835 and 720 cm^{-1}; δ_H (ppm, 400 MHz) 5.55 (m, 2H, vinyl H), 5.15 (m, 1H, C_2-H), 4.8-3.5 (m, 3H, O-CH), 3.38 and 3.35 (2s, 3H, $O-CH_3$), 2.8-1.8 (m, 6H, CH_2, CH), 1.6-0.5 (m, 11H, CH_2, CH_3), 0.9 (s, 18H, t-Bu), 0.0 (s, 12H, $SiCH_3$); (Calcd. for $C_{28}H_{56}O_4Si$ (512.9): C, 65.56; H, 11.01, found: C, 65.72; H, 11.28%).

4β-(1'-Hepten-1'-yl)-5α-(t-butyldimethylsilyloxy)-2(S)-methoxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan (4a)

Hydroxy sulphones 3a (540 mg) were dissolved in MeOH (5 mL) and treated with sodium amalgam (6%, 3 g) during 3 h at room temperature. The solution was decanted from the remaining amalgam, whereupon it was diluted with water and the product was isolated with benzene. The crude material was filtered through a SiO_2 column (10 g, $CHCl_3$) to give the alkene 4a (270 mg, 70%). A sample was distilled at 160°C/0.1 mm Hg; ν_{max} ($CHCl_3$) 1100 (C-O, Si-O) cm^{-1}; δ_H (ppm, 60 MHz) 5.5 (m, 2H, C_1- and C_2-H), 5.2 (m, 1H, C_2-H), 3.25 (br.s, 3H, $O-CH_3$), 2.8-1.8 (m, 6H, CH_2, CH), 1.6-0.5 (m, 9H, $CH-CH_3$), 0.9 (s, 9H, $SiCCH_3$), 0.0 (s, 6H, $SiCH_3$); high resolution e.i.m.s.: M$^+$, $C_{21}H_{40}O_3Si$ requires 368.2747; found 368.2747; M$^+$ - CH_3OH-tBu, $C_{16}H_{27}O_2Si$ requires 279.1780; found 279.1781; M$^+$ - CH_3OH-tBuMe$_2$SiOH, $C_{14}H_{21}O$ requires 205.1592; found 205.1591.

5α-(t-Butyldimethylsilyloxy)-4β-(ethen-2'-phenyl)-2(S)-methoxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan (4b)

A solution of hydroxy sulphones 3b (533 mg, 1 mmol) in THF (3 mL), containing 1,10-phenantroline (1 mg), stirred under argon at -78°C, was treated with n-butyllithium until persistence of dark-red colour (1.5 M in hexane, ca 0.7 mL). After 15 min benzoyl chloride (0.13 mL, 1.1 mmol) was added, the mixture was allowed to warm to room temperature, and stirring was continued for 3 h. Then 3-dimethylamino-1-propylamine (0.1 mL) was added, the mixture was diluted with water, the product (0.9 g) was isolated with CH_2Cl_2 and it was chromatographed on a SiO_2 column (15 g, 230-400 mesh, hexane-AcOEt, 5:1) to give the benzoyl derivative 3h (0.7 g).

To a mixture of the latter compounds (3h), THF (6 mL) and sodium amalgam (6%, 1.0 g), stirred under argon at -20°C, MeOH was added. After 3 h a saturated NH_4Cl solution was added, the product (400 mg) was isolated with CH_2Cl_2 and filtered through a SiO_2 column (10 g, 230-400 mesh, hexane-AcOEt, 50:1) to give alkene 4b (178 mg, 53% yield); ν_{max} 1640, 1610 (aromat., C=C), 1100 (C-O-C) cm^{-1}; δ_H (ppm, 400 MHz) 7.4-7.2 (m, 5H, aromat. H), 6.4963 and 6.4366 (2d, 1H, $J_{1',2'}$=15.8 Hz, $C_{2'}$-H), 6.0545 and 5.9737 (2q, 1H, $J_{1',2'}$=15.8 Hz, $J_{1',4}$=1.6 Hz, $C_{1'}$-H), 5.0-5.2 (m, 1H, C_2-H), 4.7-4.3 (m, 1H, C_{6a}-H), 4.1-3.6 (m, 1H, C_5-H), 3.3771 and 3.3308 (2s, 3H, $O-CH_3$), 2.8-1.6 (m, 6H, C_3-, C_{3a}-, C_4- and C_{6a}-H), 0.8506 (s, 9H, $SiCCH_3$), 0.0130 and 0.0099 (2s, 6H, $SiCH_3$); mass spec. m/z: 374 (M$^+$), 342 (M$^+$ - CH$_3$OH), 317 (M$^+$ - C_4H_9), 285 (M$^+$ - $CH_3OH-C_4H_9$), 259 (M$^+$ - SiMe$_2$tBu); high resolution e.i.m.s. M$^+$, $C_{22}H_{39}O_3Si$ requires 374.2277; found 374.2275.

5α-(t-Butyldimethylsilyloxy)-4β-(3',4'-isopropylidenedioxybut-1'-ene)-2(S)-methoxy-3,3aβ,4,5,6,6aβ-hexahydro-2H-cyclopenta[b]furan (4c)

The preparation was carried out according to the above described procedure starting from hydroxy sulphones 3c (557 mg, 1 mmol). The crude product of benzoylation (1 g) was purified by chromatography using hexane-AcOEt, 3:1, for elution to give the derivative 3i. The crude product of reduction was chromatographed using hexane-AcOEt, 10:1, to give alkene 4c (207 mg, 52% yield); ν_{max} 1645 (C=C) and 1100 (C-O-C) cm^{-1}; δ_H (ppm) 5.8-5.3 (m, 2H, C_1- and C_2-H), 5.15-4.95 (m, 1H, $C_{1'}$-H), 4.6-4.3 (m, 2H, C_{6a}- and C_2-H), 4.15-3.95 (m, 1H, C_5-H), 3.8-3.55 (m, 2H, $C_{4'}$-H), 3.339 and 3.3084 (2s, 3H, $O-CH_3$), 2.6-1.7 (m, 6H, C_3-, C_{3a}-, C_4- and C_6-H), 1.4127 and 1.3873 (2s, 6H, $C(CH_3)_2$), 0.8830 and 0.8499 (2s, 9H, $SiCCH_3$), 0.0234 and 0.0037 (2s, 6H, $SiCH_3$); high resolution e.i.m.s. (MAT 711, 70 eV, resolution 13000) no molecular ion, M$^+$ - CH_3, $C_{20}H_{35}SiO_5$ requires 383.2253; found 383.2255, M$^+$ - CH_3O, $C_{20}H_{35}SiO_4$ requires 367.2304; found 367.2303, M$^+$ - C_4H_9, $C_{17}H_{29}O_5Si$ requires 341.1783; found 341.1785.

4β-(2'-Methyl-1'-octen-1'-yl)-5α-(t-butyldimethylsilyloxy)-2β-methoxy-3,3aβ,4,5,6,6aβ-hexahydro-2H--cyclopenta[b]furan (4e)

To a solution of hydroxy sulphones 3e (81 mg, 0.15 mmol) in MeOH (1 mL), stirred under argon at room temperature, sodium amalgam (6%, 200 mg) was added. The mixture was stirred for 8h, then sodium amalgam (200 mg) was added once more and stirring was continued for 6 h. The solution was decanted from the remaining amalgam, diluted with hexane (30 mL) and washed with a saturated NH_4Cl solution and brine. The product (42 mg) isolated in the usual way was chromatographed on a SiO_2 column (0.06--0.08 mm, 1 g, toluene-hexane, 4:1) to give alkene 4e (36 mg, 62% yield); ν_{max} ($CHCl_3$) 1450 (C=C), 1260, 1170, 1150, 1060 (C-O, Si-O) cm-1; δ_H (ppm, 270 MHz) 5.07 (m, 1H, C_2-H), 4.8 (m, 1H, C_1-H), 4.41 (m, 1H, C_6-H), 3.69 (m, 1H, C_5-H), 3.33 and 3.29 (2s, 3H, O-CH_3), 1.68 (m, 3H, C_{21}-CH_3), 0.83 (s, 9H, $SiCCH_3$), 0.0 (s, 6H, $SiCH_3$); e.i.m.s.: M$^+$, $C_{23}H_{44}O_3Si$ requires 396.3060; found 396.3060.

Preparation of alkenes from sulphone 1 and aldehydes; one-pot procedure

a. Compound 4b

The operations were performed according to the general procedure until the addition of benzaldehyde. The reaction mixture was stirred for 3 h at -78°C, treated with a solution of methanesulphonyl chloride (115 mg, 1 mmol) in THF (0.5 mL), and set aside at 0°C for 12 h. Subsequently addition was made of: THF (3 mL), sodium amalgam (6%, 1.0 g), powdered anhydrous Na_2HPO_4 (0.5 g) and -after cooling of the mixture to -20°C - MeOH (2 mL). The resulting mixture was stirred at -20°C for 3 h, whereupon the product was isolated in the usual way and purified by chromatography. Compound 4b (314 mg, 84% yield), identical with the specimen described above was obtained.

b. Compound 4c

The use of 0,0'-isopropylidene D-glyceraldehyde (2c) in the above described procedure afforded compound 4c (299 mg, 75% yield) identical with the specimen described above.

c. Compound 4d

To a solution of sulphones 3d (427 mg, 1 mmol) in THF (2 mL), stirred under argon at -78°C, n-butyllithium (1.5 M in hexane, 0.67 mL, 1 mmol) was added, followed (after 10 min) by $BF_3.Et_2O$ (0.12 mL, 1 mmol) and (after further 5 min) by rac. 2-(t-butyldimethylsilyloxy)heptanal (2d) (250 mg, 1 mmol). The mixture was stirred at -78°C for 2 h, allowed to warm to -20°C, treated with methanesulphonyl chloride (0.1 mL, 1.3 mmol) in THF (0.5 mL) and set aside at 0°C for 12 h. Subsequently addition was made of: THF (2 mL), sodium amalgam (6%, 1.0 g), anhydrous Na_2HPO_4 (0.5 g) and MeOH (2 mL). The resulting mixture was stirred at room temperature for 2 h. The work-up with a saturated NH_4Cl solution and benzene, and chromatographic purification of the crude product gave alkene 4d (390 mg, 76% yield) identical with the specimen described above.

Rac. $PGF_{2\alpha}$ and rac 15-epi $PGF_{2\alpha}$

A solution of protected acetal 4d (197 mg, 0.4 mmol) in a mixture of CH_3CN - water (2:1, 20 mL), containing hydrochloric acid (0.6 mmol), was stirred at room temperature for 16 h, whereupon the product was isolated with toluene. The crude material (62 mg) was purified on a SiO_2 column (0.06-0.08 mm, 3 g, toluene-$CHCl_3$-MeOH, 10:5:1) to give dihydroxy acetal 5a (35 mg, 90% yield); ν_{max} 3350 (OH), 1650 (C=C) and 1100-1000 (C-O) cm^{-1}; δ_H (ppm) 5.55 (m, 2H, vinylic H), 5.28 (m, 1H, C_2-H), 4.42 (m, 1H, C_{6a}-H), 3.95 (m, 2H, O-CH).

To a solution of (4-carboxybutyl)triphenylphosphonium bromide (443 mg, 1 mmol) in DMSO (1 mL) dimsyl sodium in DMSO (1.7 M, 1.2 mL, 2 mmol) was added. After the occurence of a dark-red colour, acetal 5 (97 mg, 0.36 mmol) in DMSO (1 mL) was added. The mixture was stirred at room temperature for 1 h and at 50°C for 1 h. Water (5 mL) was added, the mixture was acidified with 3% hydrochloric acid, and the product was isolated with AcOEt. The crude material (0.5 g) was chromatographed on a SiO_2 column (0.06-0.08 mm, toluene-$CHCl_3$-MeOH, 7:5:2) to give nonpolar fractions which were not identified, then 15-epi $PGF_{2\alpha}$ (30 mg, 24% yield) and $PGF_{2\alpha}$ (28 mg, 22% yield), both being identical (TLC, NMR, e.i.m.s.) with authentic samples.

Opt. active $PGF_{2\alpha}$

To a solution of optically active sulphone 1 (98 mg, 0.23 mmol) in THF (0.5 mL), stirred under argon at - 78°C, addition was made of n-butyllithium (1.4 M in hexane, 0.175 mL, 0.25 mmol), after 5 min - of BF_3Et_2O (0.031 mL, 0.25 mmol) and after further 10 min - of aldehyde 2f ($[\alpha]_D^{13}$-6.0°, c=2.8, benzene) (85 mg, 0.23 mmol) in THF (1 mL). The mixture was allowed to warm to -30°C and this temperature was maintained for 2 h; subsequently THF (5 mL), few drops of a saturated NH_4Cl solution and triethylamine (0.2 mL) were added. The solvent was evaporated under reduced pressure. To the residue toluene (2 mL) was added, evaporation was repeated and the residue was dried for 6 h (0.1 mm Hg)

The residue (200 mg) was dissolved in pyridine (0.5 mL), the solution was cooled to -20°C and methanesulphonyl chloride (0.031 mL, 0.4 mmol) was added. The mixture was allowed to warm to room temperature and set aside for 15 h, whereupon it was diluted with $CHCl_3$ (10 mL) and washed with a saturated $NaHCO_3$ solution, 3% hydrochloric acid and water. The solvent was evaporated and the residue was dried under vacuum to give crude mesylate 3g (200 mg).

To a solution of the latter compound (116 mg) in THF-MeOH (3:1, 1.6 mL), stirred under argon at -20°C, sodium amalgam (6%, 370 mg) was added. The mixture was allowed to warm to room temperature and stirring was continued for 3 h. The solution was decanted from the residue and the latter was washed with THF. The combined solutions were evaporated, and the residue (90 mg) was filtered

through a SiO_2 column (2 g, toluene) to give unsaturated product 4f (75 mg, 88% yield from 1) $\nu_{max}^{(CHCl_3)}$ 1650, 1260, 1130, 1100, 1055, 840 and 780 cm^{-1}; δ_H (ppm) 8.1-7.4 (m, 10H, aromat. H), 5.5 (m, 2H, vinyl H), 5.1 (m, 1H, C_2-H), 4.8-3.4 (m, 4H, O-CH_2), 3.25 (2s, 3H, O-CH_3), 2.7-1.0 (m, 17H, CH, CH_2 and CH_3), 0.9 (s, 18 H, t-Bu).

To a solution of the above described product (75 mg) in MeCN (7 mL) 0.3 N hydrochloric acid (1 mL) was added. The mixture was stirred for 2 h, powdered K_2CO_3 (0.5 g) was added and stirring was continued for 20 min. The solution was decanted from the precipitate which was washed with AcOEt. The combined solutions were dried over Na_2SO_4 and evaporated. The residue (75 mg) was chromatographed on a SiO_2 column (2 g, AcOEt-toluene 1:1) to give hydroxy lactol 5b (46 mg, 77% yield).

To a solution of (4-carboxybutyl)triphenylphosphonium bromide (159 mg, 0.36 mmol) in THF (1.5 mL), stirred under argon at room temperature, tBuOK (81 mg, 0.72 mmol) in THF (1.5 mL) was added. To the resulting orange-red mixture, a solution of hydroxy lactol 5b (46 mg, 0.09 mmol) in THF (0.5 mL) was added. The mixture was stirred for 30 min, whereupon a saturated NH_4Cl solution was added (0.5 mL), followed by 80% acetic acid (0.5 mL) and THF (20 mL). The solution was dried ($MgSO_4$), the solvent was evaporated and the residue was filtered through a SiO_2 column (0.04-0.06 mm, 1 g, toluene-AcOEt, 4:1) to give crude 15-(t-butyldiphenylsilyl) $PGF_{2\alpha}$ (60 mg).

A mixture of the crude silyl derivative (60 mg), anhydrous tetrabutylammonium fluoride (54 mg, 0.2 mmol) and THF (0.5 mL) was stirred under argon for 2 days, whereupon ice (ca 1 g) and 3% hydrochloric acid were added. The product was isolated with $CHCl_3$ and the crude material (80 mg) was chromatographed on a SiO_2 column (0.04-0.06 mm, 3 g, toluene-$CHCl_3$-MeOH, 5:5:1) to give $PGF_{2\alpha}$ (24 mg, 0.07 mmol) identical in all respects (^1H NMR, IR, e.i.m.s., TLC) with the commercial product; $[\alpha]_D^{14}$ +23° (c=1.4, THF). The commercial product (Chinoin), described $[\alpha]_D^{20}$ +26 to 28° (c=1, THF), determined $[\alpha]_D$ +23° (c=1, THF).

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