SYNTHETIC ANALOGUES OF 15,15-ACETALS OF PROSTAGLANDIN $F_{2\alpha}$ AND E_2

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Within a systematic study of substituent changes in the ω-chain of prostaglandins, Král and coworkers[1] demonstrated that substitution of the 15-hydroxy group (PG numbering) by a 15,15-acetal group gives rise to an entirely opposite biological response, i.e. increase in the progesteron level (luteotropic effect). This effect is made use of in practice to reduce early embryonal mortality of cattle.

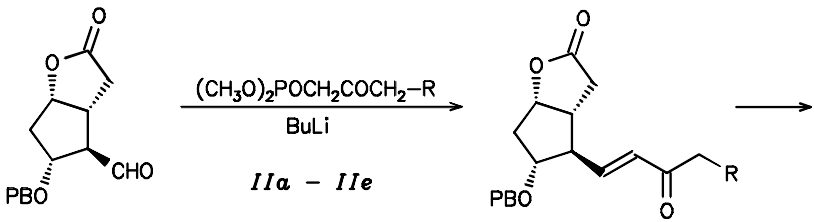
Two series of 15,15-ethyleneacetals of PG $F_{2\alpha}$ and PG E_2 modified both in the α- and ω-chains were prepared with a view to find more stable and efficient analogues of this type. The synthesis of the analogues starting from the easily available (±)-[(3aα,4α,5β,6aα)]-5-(1,1′-biphenylyl-4-carbonyloxy)-4-formylhexahydro-2*H*-cyclopenta[*b*]furan-2-one, the so-called Corey aldehyde *I*, was based on conventional procedures[2,3], some of which were modified to achieve the optimum yields (Scheme 1).

The Corey aldehyde *I* was reacted with the ylides, generated in situ from the corresponding phosphonates *IIa – IIe* on treatment with a base, to obtain the enones *IIIa – IIIe*. The enones were converted to the desired *p*-phenylbenzoates of the 15,15-acetals *IVa – IVe* (Table I) by action of 1,2-ethanediol in the presence of a catalytic amount of *p*-toluenesulfonic acid; the yields of this step were good. The protecting *p*-phenylbenzoyl group was subsequently removed by reesterification with methanol, catalyzed with anhydrous potassium carbonate, to obtain the 11-hydroxy-15,15-acetals *Va – Ve* (Table II), which were converted to the *tert*-butyldimethylsilyl ethers *VIa – VIe* (Table III) by using *tert*-butyldimethylsilyl chloride and imidazole in dimethylformamide[4]. Reduction of the lactone grouping with diisobutylaluminium hydride in toluene at −70 to −78 °C gave the lactols *VIIa – VIIe* (Table IV) in nearly quantitative yields. By reaction with ylides obtained from the phosphonium salts *VIIIk – VIIIq* using potassium *tert*-butoxide or anhydrous potassium carbonate, the lactols were transformed into protected derivatives of 15,15-acetals of prostaglandin $F_{2\alpha}$ *IX* involving a furan, thiophene or benzene ring in the α-chain (Table V). Removal of the protecting *tert*-butyldimethylsilyl group by using tetrabutylammonium fluoride in tetrahydrofuran gave the analogues of 15,15-acetals of PG $F_{2\alpha}$ *XI* (Table VII). The feasibility was examined of direct transformation of the protected lactone *IVe* to the lactol *VII* (R^1 = H), which, reacted with the corresponding

ylides in similar conditions[2], afforded the analogues of 15,15-acetals of PG $F_{2\alpha}$ *XI* in good yields. In both cases, the 1,2-disubstituted ethylene derivatives *Xk – Xq*, which were formed by recombination of the reactive part of the ylides[5], were isolated from the reaction mixture in relatively low amounts (5 to 15%) in both cases.

Several protected 11-*tert*-butyldimethylsilyl analogues of 15,15-acetals of PG $F_{2\alpha}$ were deliberately selected, the HO group in position 9 was oxidized with the complex of *N*-chlorosuccinimide with thioanisole[6] in dichloromethane (Table VI), and the analogues of 15,15-acetal of PG E_2 *XIII* (Table VIII) were prepared by deprotection of the *tert*-butyldimethylsilyl group.

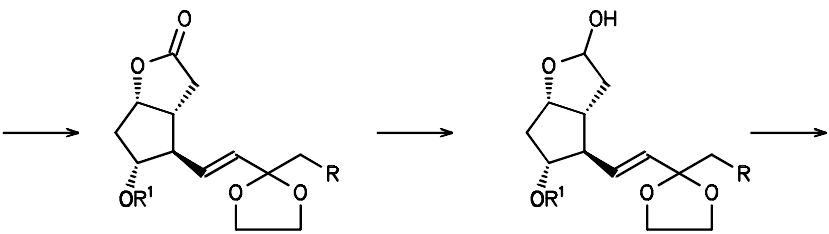
The spectral data (IR, ^{1}H NMR, MS) of the substances synthesized are consistent with the suggested structures. Processed spectral characteristics in a tabular form can be obtained from the authors on request.



I

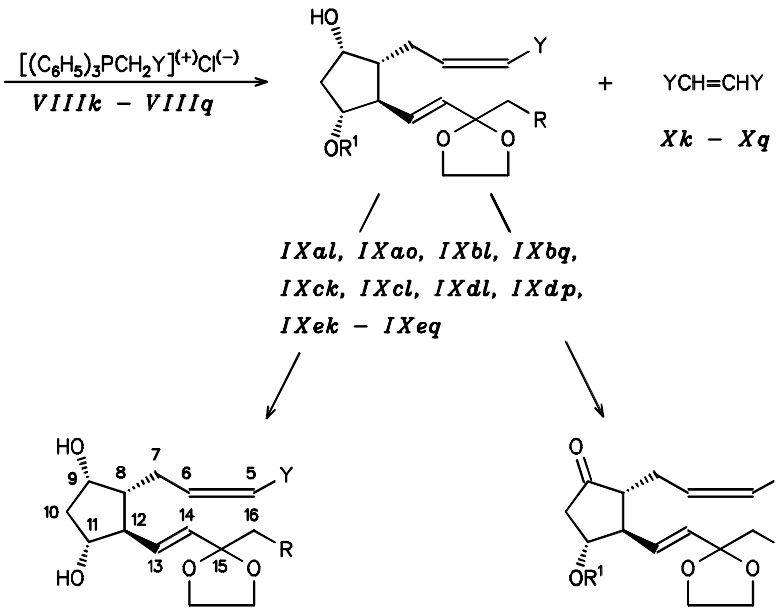
I, PB = 4-C_6H_5–C_6H_4CO–

IIIa – IIIe



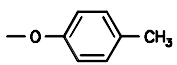
IVa – IVe, R^1 = PB
Va – Ve, R^1 = H
VIa – VIe, R^1 = TBDMS

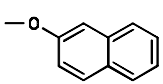
VIIa – VIIe, R^1 = TBDMS

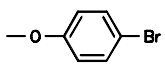


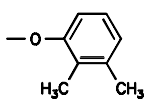
XIal, XIao, XIbl, XIbq, XIck, XIcl, XIdl, XIdp, XIek – XIeq

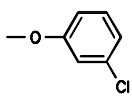
XIIdl, XIIek, XIIel, XIIeo, R^1 = TBDMS
XIIIdl, XIIIek, XIIIel, XIIIeo, R^1 = H

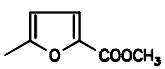
a, R = 

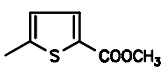
b, R = 

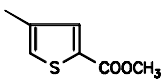
c, R = 

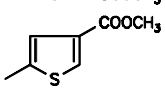
d, R = 

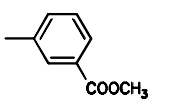
e, R = 

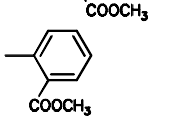
k, Y = 

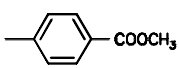
l, Y = 

m, Y = 

n, Y = 

o, Y = 

p, Y = 

q, Y = 

SCHEME 1

TABLE I
Yields and physico-chemical characteristics of the acetals *IVa – IVd*

Compound	Yield, % m.p.[a], °C	Formula (M.w.)	Calculated/Found		
			% C	% H	% Br
IVa	87	$C_{33}H_{32}O_7$	73.32	5.97	
	99 – 101	(540.6)	73.16	5.84	
IVb	84	$C_{36}H_{32}O_7$	74.98	5.59	
	126 – 127	(576.6)	75.16	5.64	
IVc	84	$C_{32}H_{29}BrO_7$	63.48	4.83	13.20
	99 – 101	(605.5)	63.60	4.88	12.90
IVd	84	$C_{34}H_{34}O_7$	73.63	6.18	
	113 – 115	(554.6)	73.64	6.23	

[a] Crystallized from a toluene–heptane mixture.

TABLE II
Yields and physico-chemical characteristics of the hydroxyacetals *Va – Ve*

Compound	Yield, % m.p.[a], °C	Formula (M.w.)	Calculated/Found		
			% C	% H	% hal.
Va	99	$C_{20}H_{24}O_6$	66.65	6.71	
	117 – 118	(360.4)	66.65	6.83	
Vb	98	$C_{23}H_{24}O_6$	69.68	6.10	
	139 – 140	(396.4)	70.06	6.16	
Vc	90	$C_{19}H_{21}BrO_6$	53.66	4.98	18.79
	87 – 89	(425.3)	53.82	5.26	18.03
Vd	95	$C_{21}H_{26}O_6$	67.36	7.00	
	132 – 134	(374.4)	67.35	7.02	
Ve	97	$C_{19}H_{21}ClO_6$	59.93	5.56	9.31
	99.5 – 100.5	(380.8)	60.05	5.60	9.50

[a] Crystallized from a benzene–heptane mixture.

TABLE III
Yields and physico-chemical characteristics of the lactones *VIa – VIe*

Compound	Yield, % m.p.[a], °C	Formula (M.w.)	Calculated/Found		
			% C	% H	% hal.
VIa	93	$C_{26}H_{38}O_6Si$	65.79	8.07	
	90 – 91[a]	(474.7)	65.98	8.27	
VIb	96	$C_{29}H_{38}O_6Si$	68.20	7.50	
	101 – 102[a]	(510.7)	68.10	7.58	
VIc	94	$C_{25}H_{35}BrO_6Si$	55.65	6.54	14.81
	62 – 64[a]	(539.5)	55.70	6.82	14.51
VId	93	$C_{27}H_{40}O_6Si$	66.36	8.25	
	93 – 94[a]	(488.7)	66.49	8.36	
VIe	94	$C_{25}H_{35}ClO_6Si$	60.65	7.13	7.16
	89 – 91[b]	(495.1)	60.91	7.30	7.33

[a] Crystallized from a diethyl ether–hexane mixture; [b] crystallized from a diethyl ether–heptane mixture, a different modification, m.p. 67 – 68 °C, was also obtained by crystallization from this mixture.

TABLE IV
Yields and physico-chemical characteristics of the lactols *VIIa – VIIe*

Compound	Yield, % m.p.[a], °C	Formula (M.w.)	Calculated/Found		
			% C	% H	% hal.
VIIa	98	$C_{26}H_{40}O_6Si$	65.51	8.46	
	82 – 83	(476.7)	65.32	8.38	
VIIb	99	$C_{29}H_{40}O_6Si$	67.94	7.86	
	93 – 95	(512.7)	68.20	7.95	
VIIc	97	$C_{25}H_{37}BrO_6Si$	55.45	6.89	14.75
	oil	(541.6)	55.18	6.62	14.52
VIId	98	$C_{27}H_{42}O_6Si$	66.09	8.63	
	79 – 82	(490.7)	65.88	8.61	
VIIe	96	$C_{25}H_{37}ClO_6Si$	60.41	7.50	7.13
	69 – 71	(497.1)	60.16	7.31	7.23

[a] Crystallized from a diethyl ether–heptane mixture.

TABLE V
Yields and physico-chemical characteristics of the prostaglandin $F_{2\alpha}$ protected derivatives *IX*

Compound	Procedure/ Yield, %	Formula (M.w.)	Calculated/Found			
			% C	% H	% hal.	% S
IXck	*A*/98	$C_{32}H_{43}BrO_8Si$	57.91	6.53	12.04	
		(663.7)	57.72	6.53	11.84	
IXek	*A*/94	$C_{32}H_{43}ClO_8Si$	62.07	7.00	5.73	
	B/90	(619.2)	61.85	6.84	6.05	
IXal	*A*/77	$C_{33}H_{46}O_7SSi$	64.46	7.54		5.21
		(614.9)	64.18	7.28		5.10
IXbl	*A*/90	$C_{36}H_{46}O_7SSi$	66.43	7.12		4.93
		(650.9)	66.13	7.39		4.80
IXcl	*A*/89	$C_{32}H_{43}BrO_7SSi$	56.54	6.38	11.76	4.72
		(679.7)	56.32	6.21	11.54	4.69
IXdl	*A*/90	$C_{34}H_{48}O_7SSi$	64.94	7.69		5.10
		(628.9)	64.72	7.45		4.93
IXel	*A*/94	$C_{32}H_{43}ClO_7SSi$	60.50	6.82	5.58	5.05
	B/91	(635.3)	60.24	6.56	5.72	5.08
IXem	*A*/85	$C_{32}H_{43}ClO_7SSi$	60.50	6.82	5.58	5.05
	B/90	(635.3)	60.22	6.58	5.88	4.88
IXen	*A*/80	$C_{32}H_{43}ClO_7SSi$	60.50	6.82	5.82	5.05
	B/81	(635.3)	60.32	6.61	5.82	4.92
IXao	*A*/83	$C_{35}H_{48}O_7Si$	64.46	7.54		
		(614.9)	64.17	7.94		
IXeo	*A*/87	$C_{34}H_{45}ClO_7Si$	64.90	7.21	5.63	
	B/58	(629.3)	64.65	7.12	5.91	
IXdp	*A*/83	$C_{36}H_{50}O_7Si$	69.42	8.09		
		(622.9)	69.15	7.84		
IXep	*A*/85	$C_{34}H_{45}ClO_7Si$	64.90	7.21	5.63	
	B/ 9	(629.3)	64.11	7.15	5.82	
IXbq	*A*/55	$C_{38}H_{48}O_7Si$	70.78	7.50		
		(644.9)	70.59	7.28		
IXeq	*A*/58	$C_{34}H_{45}ClO_7Si$	64.90	7.21	5.63	
	B/65	(629.3)	64.61	6.99	5.41	

EXPERIMENTAL

The temperature data have not been corrected. The melting points were determined on a Boetius block. The ^{1}H NMR spectra were measured with a Bruker 400 apparatus in deuteriochloroform and tetramethylsilane was used as the internal standard. The values of chemical shifts are given in the δ units (ppm). The IR spectra were measured with a Perkin–Elmer 325 apparatus in chloroform.

Starting Substances

(±)-[(3aα,4α,5β,6aα)]-5-(1,1′-Biphenylyl-4-carbonyloxy)-4-formylhexahydro-2*H*-cyclopenta[*b*]furan--2-one (*I*) (the Corey aldehyde) and (±)-[(3aα,4α,5β,6aα)]-4-[(*E*)-3,3-ethylenedioxy-4-(3-chlorophenoxy)-1-butenyl]hexahydro-5-hydroxy-2*H*-cyclopenta[*b*]furan-2-ol (*VIIe*, R^1 = H) were obtained from Spolana, a.s., Neratovice (The Czech Republic). Dimethyl [3-(substituted aryloxy)-2-oxopropyl]phosphonates *IIa – IIe* were prepared from the corresponding substituted aryloxyacetates with the lithium salt of dimethyl methylphosphonate by the conventional procedure[7]. The phosphonium salts *VIIIk*, *VIIIl* (ref.[8]), *VIIIn* (m.p. 212 – 217 °C), *VIIIm* (210 – 216 °C) and *VIIIp* (190 – 196 °C) were prepared following ref.[8].

(±)-[(3aα,4α,5β,6aα)]-5-(1,1′-Biphenylyl-4-carbonyloxy)hexahydro-4-[(*E*)-4-(4-methylphenoxy)-3-oxo-1-butenyl]-2*H*-cyclopenta[*b*]furan-2-one (*IIIa*)

A 2.2 M solution of butyllithium in hexane (2.5 ml, 5.5 mmol) was added dropwise to a stirred solution of phosphonate *IIa* (1.56 g, 5.74 mmol) in 1,2-dimethoxyethane (20 ml) at −70 to −78 °C. After heating the mixture to −10 °C, the Corey aldehyde *I* (1.83 g, 5.23 mmol) in 1,2-dimethoxyethane

TABLE VI
Yields and physico-chemical characteristics of the prostaglandin E_2 protected derivatives *XII*

Compound	Yield, %	Formula (M.w.)	Calculated/Found			
			% C	% H	% hal.	% S
XIIek	75	$C_{32}H_{41}ClO_8Si$	62.27	6.70	5.74	
		(617.2)	62.02	6.46	6.02	
XIIdl	75	$C_{34}H_{46}O_7SSi$	65.14	7.40		5.11
		(626.9)	65.18	7.21		4.82
XIIel	74	$C_{32}H_{41}ClO_7SSi$	60.69	6.53	5.60	5.06
		(633.3)	60.39	6.28	5.75	5.35
XIIeo	76	$C_{34}H_{43}ClO_7Si$	65.11	6.91	5.65	
		(627.2)	64.83	6.68	5.92	

TABLE VII
Yields and physico-chemical characteristics of the prostaglandin $F_{2\alpha}$ analogues *XI*

Compound	Yield, %	Formula (M.w.)	Calculated/Found			
			% C	% H	% hal.	% S
XIck	91	$C_{26}H_{29}BrO_8$	56.84	5.32	14.54	
		(549.4)	56.58	5.13	14.34	
XIek	88	$C_{26}H_{29}ClO_8$	61.84	5.79	7.02	
		(505.0)	61.65	5.65	7.12	
XIal	86	$C_{27}H_{32}O_7S$	64.78	6.44		6.40
		(500.6)	64.58	6.21		6.33
XIbl	99	$C_{30}H_{32}O_7S$	67.15	6.01		5.97
		(536.6)	66.97	5.78		5.95
XIcl	84	$C_{26}H_{29}BrO_7S$	55.23	5.17	14.13	5.67
		(565.5)	54.95	4.98	14.07	5.58
XIdl	97	$C_{26}H_{34}O_7S$	65.35	6.66		6.23
		(514.6)	65.33	6.66		6.27
XIel	94	$C_{26}H_{29}ClO_7S$	59.94	5.61	6.80	6.15
		(521.0)	59.65	5.45	6.89	6.08
XIem	93	$C_{26}H_{29}ClO_7S$	59.94	5.61	6.80	6.15
		(521.0)	59.72	5.51	6.65	6.11
XIen	96	$C_{26}H_{29}ClO_7S$	59.94	5.61	6.80	6.15
		(521.0)	59.85	5.55	6.73	6.10
XIao	84	$C_{29}H_{34}O_7$	70.43	6.93		
		(494.6)	70.23	6.75		
XIeo	97	$C_{28}H_{31}ClO_7$	65.30	6.07	6.88	
		(515.0)	65.03	5.89	6.65	
XIdp	92	$C_{30}H_{36}O_7$	70.85	7.13		
		(508.6	70.64	6.99		
XIep	92	$C_{28}H_{31}ClO_7$	65.30	6.07	6.88	
		(515.0)	65.22	5.98	6.75	
XIbq	98	$C_{32}H_{34}O_7$	72.44	6.46		
		(530.6)	72.37	6.35		
XIeq	86	$C_{28}H_{31}ClO_7$	65.30	6.07	6.88	
		(515.0)	65.21	6.02	6.76	

(45 ml) was added. The system was stirred at −10 °C for 1 h and subsequently at room temperature for 2 h. The mixture was decomposed by adding saturated ammonium chloride solution (10 ml) and water (10 ml), and extracted with ethyl acetate (3 × 10 ml). The combined organic layers were washed with a saturated solution of sodium hydrogen carbonate (2 × 10 ml) and dried with anhydrous magnesium sulfate. The solvent was evaporated off and the product was crystallized from a mixture of ethyl acetate and heptane. The enone *IIIa* was obtained (1.85 g, 71%); m.p. 151 – 153 °C. For $C_{31}H_{28}O_6$ (496.6) calculated: 74.98% C, 5.68% H; found: 75.01% C, 5.70% H.

The enone *IIIc* (48%), m.p. 139 – 140 °C, was obtained likewise. For $C_{30}H_{25}BrO_6$ (561.4) calculated: 64.18% C, 4.49% H, 14.23% Br; found: 64.42% C, 4.71% H, 14.00% Br.

(±)-[(3aα,4α,5β,6aα)]-5-(1,1′-Biphenylyl-4-carbonyloxy)hexahydro-4-[(*E*)-3,3-ethylenedioxy-4-(4-methylphenoxy)-1-butenyl]-2*H*-cyclopenta[*b*]furan-2-one (*IVa*)

A mixture of the enone *IIIa* (1.1 g, 2.2 mmol), 1,2-dihydroxyethane (2 ml), a catalytic amount of remelted *p*-toluenesulfonic acid, and toluene (50 ml) was heated to boil under a Fridrichs azeotropic condenser; the emerging reaction water was removed constantly. In 2.5 h the reaction mixture was washed with water (2 × 15 ml), saturated sodium hydrogen carbonate solution (2 × 15 ml), and water (15 ml), and dried with anhydrous magnesium sulfate. The solvent was removed by evaporation, and 0.74 g of the product (62%) was obtained by crystallization from a toluene–heptane mixture. Another fraction was isolated from the mother liquors by column chromatography (0.7 g; eluent: 1% methanol in chloroform). A total of 1.04 g (87%) of the acetal *IVa*, m.p. 99 – 101 °C, was obtained.

The acetals *IVb* – *IVd* were obtained likewise. The yields and physico-chemical characteristics are given in Table I.

TABLE VIII
Yields and physico-chemical characteristics of the prostaglandin E_2 analogs *XIII*

Compound	Yield, % m.p.[a], °C	Formula (M.w.)	Calculated/Found			
			% C	% H	% hal.	% S
XIIIek	89	$C_{26}H_{27}ClO_8$	62.09	5.41	7.05	
		(502.9)	61.86	5.32	7.01	
XIIIdl	92	$C_{28}H_{32}O_7S$	65.61	6.29		6.25
		(512.6)	65.42	6.14		6.12
XIIIel	89	$C_{26}H_{27}ClO_7S$	60.17	5.24	6.83	6.18
		(519.0)	59.93	5.08	7.08	6.02
XIIIeo	94	$C_{28}H_{29}ClO_7$	65.56	5.70	6.91	
		(513.0)	65.36	5.53	7.16	

(±)-[(3aα,4α,5β,6aα)]-Hexahydro-5-hydroxy-4-[(*E*)-3,3-ethylenedioxy-4-(4-methylphenoxy)-1-butenyl]-2*H*-cyclopenta[*b*]furan-2-one (*Va*)

To a solution of the acetal *IVa* (1.9 g, 3.52 mmol) in absolute methanol (100 ml) and anhydrous 1,2-dichloroethane (50 ml) was added freshly annealed potassium carbonate (4 g, 29 mmol). The mixture was stirred at room temperature for 6 h, inorganic salts were filtered off, and the filtrate was diluted with water (20 ml) and made acidic with citric acid to pH ≈ 5. After phase separation, the aqueous layer was extracted with 1,2-dichloroethane (6 × 10 ml) and the combined organic extracts were dried with anhydrous magnesium sulfate. The solvent was evaporated at a reduced pressure, and the distillation residue (2.1 g) was chromatographed (70 g of SiO_2; eluent: 2% methanol in chloroform). The obtained oil was crystallized from a benzene–heptane mixture to give 1.25 g (99%) of the hydroxy derivative *Va*, m.p. 117 – 118 °C.

The hydroxy derivatives *Vb* – *Ve* were prepared likewise. The yields and physico-chemical characteristics are given in Table II.

(±)-[(3aα,4α,5β,6aα)]-5-(*tert*-Butyldimethylsilyloxy)hexahydro-4-[(*E*)-3,3-ethylenedioxy-4-(4-methylphenoxy)-1-butenyl]-2*H*-cyclopenta[*b*]furan-2-one (*VIa*)

A mixture of the hydroxy derivative *Va* (1.13 g, 3.13 mmol), imidazole (1.6 g, 23.6 mmol), *tert*-butyldimethylsilyl chloride (1.8 g, 12 mmol), and anhydrous dimethylformamide (30 ml) was stirred at room temperature for 12 h, decomposed with water (100 ml), and diluted with toluene (150 ml). After phase separation, the aqueous layer was extracted with toluene (3 × 25 ml) and the combined organic extracts were washed with saturated sodium hydrogen carbonate solution (2 × 30 ml) and dried with anhydrous magnesium sulfate, and the solvent was evaporated. Crystallization of the solid residue from a diethyl ether–hexane mixture gave 1.38 g (93%) of the lactone *VIa*, m.p. 90 – 91 °C.

The yields and physico-chemical characteristics of the silyl derivatives *VIa* – *VIe* so prepared are given in Table III.

(±)-[(3aα,4α,5β,6aα)]-5-(*tert*-Butyldimethylsilyloxy)hexahydro-4-[(*E*)-3,3-ethylenedioxy-4-(4-methylphenoxy)-1-butenyl]-2*H*-cyclopenta[*b*]furan-2-ol (*VIIa*)

To a solution of the lactone *VIa* (1.12 g, 2.36 mmol) in toluene (90 ml) at −78 °C under argon was added 1 M solution of diisobutylaluminium hydride in hexane (4.5 ml, 4.5 mmol) so rapidly that the reaction mixture temperature did not exceed −60 °C. The reaction was terminated in 30 min by adding 2-propanol (0.9 ml). The mixture was heated slowly to room temperature, diluted with water (6.2 ml), and stirred for approximately 1 h till the separation of a precipitate, which was filtered off and extracted with toluene (3 × 20 ml). The solvent was evaporated from the combined extracts, and the crude product (1.2 g) was crystallized from a diethyl ether–heptane mixture to obtain 1.1 g (98%) of white crystals of the lactol *VIIa*, m.p. 82 – 83 °C.

The yields and physico-chemical characteristics of the lactols *VIIa* – *VIIe* so prepared are given in Table IV.

(±)-11-(*tert*-Butyldimethylsilyloxy)-16-(3-chlorophenoxy)-15-deoxy-15,15-ethylenedioxy-5-(5-methoxycarbonyl-2-furyl)-1,2,3,4,17,18,19,20-octanorprostaglandin $F_{2\alpha}$ (*IXek*)

Method A: A 1.4 M solution of potassium *tert*-butoxide in tetrahydrofuran (4.4 ml, 6.1 mmol) was added dropwise to a water-cooled suspension of the phosphonium salt *VIIIk* (2.7 g, 6.1 mmol) in anhydrous tetrahydrofuran (30 ml) under argon. The mixture was stirred at room temperature for 30 min, and a solution of the lactol *VIIe* (865.9 mg, 1.74 mmol) in anhydrous tetrahydrofuran (25 ml) was added to the solution of the ylide cooled to approximately 0 °C. In 1 h, the temperature was

increased to approximately 20 °C, and stirring was continued for another 8 h. The solvent was then distilled off and the residue was filtered through a silica gel column (20 g; eluent: 20% ethyl acetate in toluene). The crude product was chromatographed on 20 g of silica gel (eluent: 1% methanol in chloroform) to obtain 1.014 g (94%) of the protected prostaglandin $F_{2\alpha}$ *IXek* in the form of a yellowish oil. Other derivatives of the series *IX* were obtained likewise.

Method B: A mixture of the lactol *VIIe* (624 mg, 1.26 mmol), phosphonium salt *VIIIk* (2.0 g, 4.58 mmol), freshly annealed potassium carbonate (2 g), and anhydrous dimethoxyethane (200 ml) under nitrogen was stirred at room temperature for 12 h. Further proceeded as in Method *A*. Other derivatives were obtained likewise.

The yields and physico-chemical characteristics of derivatives *IX* prepared by the two methods are given in Table V.

(±)-11-(*tert*-Butyldimethylsilyloxy)-16-(3-chlorophenoxy)-15-deoxy-15,15-ethylenedioxy-5-(5-methoxycarbonyl-2-furyl)-1,2,3,4,17,18,19,20-octanorprostaglandin E_2 (*XIIek*)

Thioanisole (1.2 g, 9.7 mmol) dissolved in toluene (5 ml) was added to a stirred solution of freshly prepared *N*-chlorosuccinimide (1.1 g, 8.1 mmol) in toluene (100 ml) at approximately 0 °C so rapidly that the temperature did not exceed +1 °C. After cooling the mixture to –25 °C, the PG $F_{2\alpha}$ silyl derivative *IXek* (979.8 mg, 1.58 mmol) dissolved in toluene (60 ml) was added and the mixture was stirred for 2 h at –30 to –25 °C. The reaction was terminated by adding triethylamine (1.75 g, 17.5 mmol) in toluene (10 ml), and after heating the system slowly to 0 °C, ether (30 ml) was added. The mixture was washed with water (30 ml), saturated sodium chloride solution (2 × 30 ml), and water (30 ml). The organic phase was dried with anhydrous magnesium sulfate and the solvent was removed by evaporation. The residue was treated by column chromatography (eluent: 1% methanol in chloroform) to obtain 731 mg (75%) of product *XIIek* in the form of a yellowish oil.

The protected analogues of 15,15-acetal of prostaglandin E_2 *XIIdl*, *XIIel* and *XIIeo* were obtained likewise. Their physico-chemical data are given in Table VI.

(±)-16-(3-Chlorophenoxy)-15-deoxy-15,15-ethylenedioxy-5,5-methoxycarbonyl-2-furyl)-1,2,3,4,17,18,19,20-octanorprostaglandin $F_{2\alpha}$ (*XIek*)

To a solution of the protected derivative *IXek* (301.7 mg, 0.49 mmol) in tetrahydrofuran (15 ml) under a calcium chloride tube at approximately 0 °C was added 1 M solution of tetrabutylammonium fluoride in tetrahydrofuran (1.2 ml, 1.2 mmol), and the solution was stirred at 0 °C for 2.5 h. Chloroform (30 ml) was added, and the reaction mixture was washed with saturated sodium chloride solution (15 ml) and water (2 × 15 ml) and dried with anhydrous magnesium sulfate. Solvent was evaporated off and the residue was purified by column chromatography (eluent: 3% methanol in chloroform) to obtain 218.2 mg (88%) of the derivative *XIek* as a yellowish oil.

The derivatives of 15,15-acetal of prostaglandin $F_{2\alpha}$ and E_2, *XI* and *XIII*, respectively, were prepared likewise. Their physico-chemical data are given in Tables VII and VIII, respectively.

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