SYNTHETIC ANALOGUES OF PROSTAGLANDINS $F_{2\alpha}$ AND E_2

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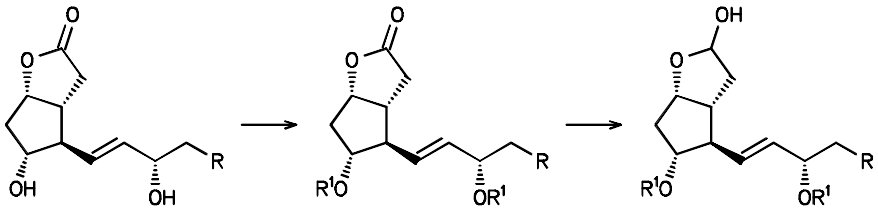
The synthesis of new derivatives of prostaglandins $F_{2\alpha}$ and E_2 *XIIa,b – XVa,b* and *XXa,b – XXIIIa,b* containing the furan or thiophene nucleus in the upper chain has been accomplished starting from [3aα,4α,5β,6aα]-(±)-hexahydro-5-hydroxy-4-((*E*)-(3α)-hydroxy-1-octenyl)-2*H*-cyclopenta[*b*]furan-2-one (*Ia*) and [3aα,4α,5β,6aα]-(±)-hexahydro-5-hydroxy-4-[4-(3-chlorophenoxy)-(3α)-hydroxy-1-butenyl]cyclopenta[*b*]furan-2-one (*Ib*). The diols *Ia* and *Ib* have been converted into the above-mentioned analogues of prostaglandins $F_{2\alpha}$ and E_2 by protecting the hydroxyl groups, subsequent reduction and Wittig reaction with the ylides prepared from the phosphonium salts *IV – VII*, and final deprotection (or oxidation plus deprotection).

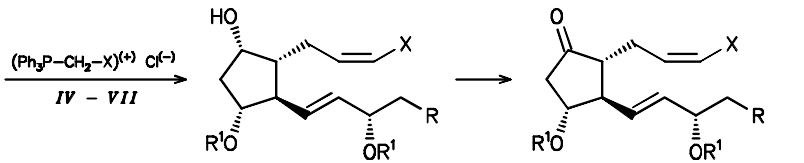
At present, the synthetic analogues of prostaglandins form the active component of a number of preparations used for treatment of illnesses of reproduction organs and for synchronization of rutting season of domestic animals[1 – 4].

In the context of the systematic studies of new prostaglandin analogues[5 – 7] with the aim of finding more efficient and more stable analogues, particularly for the enzymatic β-oxidation of the upper chain in vivo, we have prepared – in a practically standard way – a series of derivatives of prostaglandin $F_{2\alpha}$ (*XIIa,b – XVa,b*) and prostaglandin E_2 (*XXa,b – XXIIIa,b*) containing the furan or thiophene nucleus in the upper chain. For the starting materials we adopted the commercially available [3aα,4α,5β,6aα]-(±)-hexahydro-5-hydroxy-4-((*E*)-(3α)-hydroxy-1-octenyl)-2*H*-cyclopenta[*b*]furan-2-one (diol *Ia*) and [3aα,4α,5β,6aα]-(±)-hexahydro-5-hydroxy-4-[4-(3-chlorophenoxy)-(3α)-hydroxy-1-butenyl]cyclopenta[*b*]furan-2-one (diol *Ib*). These diols were converted into the respective bis-*O*-(tetrahydropyran-2-yloxy) derivatives *IIa,b* by the reaction with 3,4-dihydro-2*H*-pyran in dichloromethane catalyzed with *p*-toluenesulfonic acid, and the subsequent regioselective reduction with diisobutylaluminium hydride[8] in toluene at ca −78 °C gave the respective lactols *IIIa,b* in almost quantitative yields.

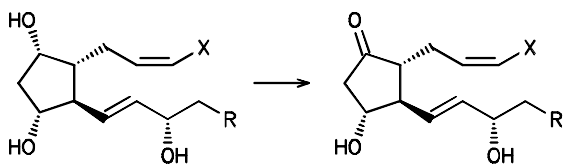
In the following step, these lactols were submitted to the Wittig reaction (with the ylides generated in situ from the corresponding phosphonium salts *IV – VII* on treatment with a strong base) to give the required bis-*O*-(tetrahydropyran-2-yloxy) derivatives of the prostaglandins $F_{2\alpha}$ *VIIIa,b – XIa,b* (Scheme 1). The conversion of phosphonium salts into the ylides was achieved either by potassium *tert*-butoxide in



Ia, Ib *IIa, IIb* *IIIa, IIIb*



VIII(a, b) – XI(a, b) *XVI(a, b) – XIX(a, b)*

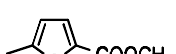


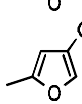
XII(a, b) – XV(a, b) *XX(a, b) – XXIII(a, b)*

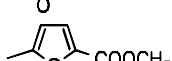
In formulae *I – III, VIII – XXIII* : *a*, R = $-(CH_2)_3CH_3$

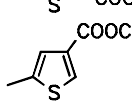
b, R = $-O-C_6H_4-Cl$

R^1 = THP

In formulae *IV, VIII, XII, XVI, XX* : X = 

In formulae *V, IX, XIII, XVII, XXI* : X = 

In formulae *VI, X, XIV, XVIII, XXII* : X = 

In formulae *VII, XI, XV, XIX, XXIII* : X = 

SCHEME 1

anhydrous tetrahydrofuran[9] or by anhydrous potassium carbonate[10]. In our case the latter way was found more advantageous with regard to both the procedure and yield (Table I).

The oxidation of the bistetrahydropyranyl derivatives of $PGF_{2\alpha}$ (*VIIIa,b – XIa,b*) with chromium trioxide in pyridine (the Collins reagent[11]) gave high yields of the corresponding protected derivatives of PGE_2 *XVIa,b – XIXa,b* (Scheme 1, Table II).

The protecting tetrahydropyranyl groups were removed with the help of an ion exchanger in H^+ cycle[12]. The physico-chemical characteristics and yields of the final analogues of prostaglandins $F_{2\alpha}$ and E_2 *XIIa,b – XVa,b* and *XXa,b – XXIIIa,b*, respectively, are given in Tables III and IV.

The phosphonium salts *IV – VII* were obtained in usual way, i.e. by the reaction of the respective chloromethyl derivative with triphenylphosphine in boiling benzene or toluene in the presence of catalytic amount of dimethylformamide[13]. The yields and physico-chemical characteristics of the salts *IV – VII* prepared are given in Table V.

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 Tesla BS 567 apparatus in deuteriochloroform except for those of the phosphonium salts *IV – VII* which were measured in perdeuteriodimethyl sulfoxide; tetramethylsilane was used as the internal standard. The spectra of phosphonium salts *IV* and *VI* were measured with a Bruker 400 apparatus. The values of chemical shifts are given in the δ units (ppm). The mass spectra were measured with a JEOL DX 200 and a JEOL DX 300 apparatuses at the ionization energy of 70 eV. The ionic species are presented in *m/z* units (% of relative intensity). The IR spectra were measured with a Perkin–Elmer 325 apparatus in chloroform except for those of the phosphonium salts *IV – VII* which were measured in KBr pellets.

Chemicals

Starting materials. [3aα,4α,5β,6aα]-(±)-hexahydro-5-hydroxy-4-((*E*)-(3α)-hydroxy-1-octenyl)-2*H*-cyclopenta[*b*]furan-2-one (*Ia*) and [3aα,4α,5β,6aα]-(±)-hexahydro-5-hydroxy-4-[(*E*)-4-(3-chlorophenoxy)-(3α)-hydroxy-1-butenyl]-2*H*-cyclopenta[*b*]furan-2-one (*Ib*) were products of Spolana Neratovice. Methyl 2-chloromethyl-5-furancarboxylate (*XXIV*), methyl 2-chloromethyl-4-furancarboxylate (*XXV*), methyl 2-chloromethyl-5-thiophenecarboxylate (*XXVI*), ethyl 2-chloromethyl-4-thiophenecarboxylate (*XXVII*) were prepared by known procedures[6,14].

[3aα,4α,5β,6aα]-(±)-Hexahydro-5-(tetrahydropyran-2-yloxy)-4-((*E*)-(3α)-(tetrahydropyran-2-yloxy)-1-octenyl)-2*H*-cyclopenta[*b*]furan-2-one (Lactone *IIa*)

A catalytic amount of freshly remelted *p*-toluenesulfonic acid was added to a solution of diol *Ia* (4.05 g; 15.1 mmol) in 1,2-dichloroethane (150 ml) and then 3,4-dihydro-2*H*-pyran (3.17 g; 37.7 mmol) was added drop by drop. The reaction mixture was stirred at room temperature 3 h and then washed with saturated sodium hydrogencarbonate solution (20 ml) and saturated sodium chloride solution (20 ml). The organic portions were dried with anhydrous magnesium sulfate, and the solvents were evaporated to leave 6 g crude oily product which was purified by column chromatography. Yield 5.87 g (89%) bistetrahydropyranyl derivative *IIa*, slightly yellowish oil. For

TABLE I
THP derivatives of prostaglandin $F_{2\alpha}$ *VIIIa,b – XIa,b*

Product	Starting material/ phosphonium salt	Yield, % in procedure A/B	Infrared spectra, cm^{-1}	^1H NMR spectra				
				CH_3/OCH_3	H-13, H-14	H-5, H-6	aromatic H	hetero-aromatic H
VIIIa	*IIIa* *IV*	75 88	3 610 w, 3 520 m, 3 020 s, 2 950 s, 2 860 s, 1 740	0.87 t 3.87 s	5.37 m, 5.54 m	6.28 d, 6.44 m		6.25 d, 7.12 d
VIIIb	*IIIb* *IV*	91 93	3 600 w, 3 500 w, 3 010 s, 2 950 s, 2 870 s, 1 720 s	 3.84 s	5.53 m, 5.71 m	6.22 d, 6.46 m	6.78 m, 7.17 m, 6.91 m, 2 H	6.20 d , 7.12 d
IXa	*IIIa* *V*	47 72	3 600w, 3 420 m, 3 020 s, 2 940 s, 2 880 s, 1 725 s	0.88 t 3.82 s	5.36 m, 5.38 m	6.20 – – 6.51 m		6.32 d, 7.20 d
IXb	*IIIb* *V*	51 75	3 600 w, 3 480 w, 3 020 s, 2 960 s, 2 880 s, 1 720 s	 3.80 s	5.42 – – 5.75 m	6.18 – – 6.42 m	6.75 m, 7.16 m, 6.89 m, 2 H	6.35 d, 7.22 d
Xa	*IIIa* *VI*	75 79	3 600 w, 3 400 m, 3 010 s, 2 940 s, 2 870 s, 1 710 s	0.88 t 3.88 s	5.33 m, 5.52 m	6.21 – – 6.51 m		6.83 d, 7.62 d
Xb	*IIIb* *VI*	82 89	3 600 w, 3 400 m, 3 010 s, 2 940 s, 2 870 s, 1 710 s	 3.85 s	5.53 m, 5.75 m	6.28 m, 6.50 d	6.79 m, 7.18 m, 6.90 m, 2 H	6.76 d, 7.64 d
XIa	*IIIa* *VII*	56 84	3 600 w, 3 380 w, 3 010 s, 2 940 s, 2 870 s, 1 710 s	0.88 t	5.38 – – 5.68 m	5.98 m, 6.41 d		7.22 d, 7.59 d
XIb	*IIIb* *VII*	79 89	3 600 w, 3 500 w, 3 010 s 2 950 s, 2 870 s, 1 710 s		5.30 – – 5.63 m	5.98 m, 6.33 m	6.73 m, 7.20 m, 6.90 m, 2 H	7.08 d, 7.38 d

TABLE II
THP derivatives of prostaglandin E_2 *XVIa,b – XIXa,b*

Product	Starting material	Yield, %	Infrared spectra, cm^{-1}	^1H NMR spectra				
				CH_3/OCH_3	H-13, H-14	H-5, H-6	aromatic H	hetero-aromatic H
XVIa	*VIIIa*	76	3 020 m, 2 950 s, 2 860 m, 1 745 s, 1 720 s	0.88 t 3.88 s	5.25 – – 5.76 m	6.26 m, 6.46 m		6.22 d, 7.12 d
XVIb	*VIIIb*	83	3 010 s, 2 950 s, 2 880 m, 1 745 s, 1 720 s	 3.84 s	5.45 – – 5.93 m	6.24 m, 6.53 m	6.78 m, 7.19 m, 6.88 m, 2 H	6.19 d, 7.11 d
XVIIa	*IXa*	75	3 020 m, 2 940 s, 2 880 m, 1 745 s, 1 725 s	0.86 s 3.86 s	5.36 m, 5.58 m	6.18 – – 6.49 m		6.32 d, 7.20 d
XVIIb	*IXb*	80	3 025 s, 2 965 s, 2 885 m, 1 740 s, 1 720 s	 3.88 s	5.40 – – 5.70 m	6.20 – – 6.52 m	6.74 m, 7.18 m, 6.89 m, 2 H	6.35 d, 7.20 d
XVIIIa	*Xa*	77	3 010 s, 2 940 s, 2 870 m, 1 740 s, 1 710 s	0.88 s 3.86 s	5.12 – – 5.73 m	6.35 – – 6.66 m		6.92 d, 7.62 d
XVIIIb	*Xb*	78	3 015 m, 2 945 s, 2 870 m, 1 740 s, 1 715 s	 3.86 s	5.54 m, 5.68 m	6.30 m, 6.50 m	6.80 m, 7.18 m, 6.89 m, 2 H	6.85 d, 7.62 d
XIXa	*XIa*	81	3 010 s, 2 940 s, 2 870 s, 1 745 s, 1 710 s	0.82 s	5.01 – – 5.56 m	6.03 m, 6.35 m		7.20 d, 7.59 d
XIXb	*XIb*	77	3 010 m, 2 950 s, 2 870 m, 1 745 s, 1 715 s		5.30 – – 5.63 m	5.98 m, 6.33 m	6.73 m, 7.20 m, 6.90 m, 2 H	7.08 d, 7.38 d

TABLE III
Derivatives of prostaglandin $F_{2\alpha}$ *XIIa,b – XVa,b*

Product	Starting material	Yield, %	Formula (M.w.)	Calculated/Found				Infrared spectra, cm^{-1}
				% C	% H	% Cl	% S	
XIIa	*VIIIa*	79	$C_{22}H_{32}O_6$	67.32	8.22			3 610 m, 3 420 s, 3 005 s,
			(392.5)	67.03	8.14			2 940 s, 2 860 s, 1 725 s
XIIb	*VIIIb*	87	$C_{24}H_{27}ClO_7$	62.27	5.88	7.66		3 600 m, 3 420 s, 3 010 s,
			(462.9)	61.99	5.74	7.81		2 940 s, 1 720 s
XIIIa	*IXa*	68	$C_{22}H_{32}O_6$	67.32	8.22			3 620 m, 3 420 m, 3 020 s,
			(392.5)	67.11	8.10			2 940 s, 2 860 s, 1 730 m
XIIIb	*IXb*	70	$C_{24}H_{27}ClO_7$	62.27	5.88	7.66		3 600 m, 3 410 s, 3 010 s,
			(462.9)	62.03	5.78	7.92		2 940 s, 1 720 s
XIVa	*Xa*	85	$C_{22}H_{32}O_5S$	64.68	7.89		7.85	3 620 m, 3 420 s, 3 020 s,
			(408.6)	64.55	7.82		7.86	2 940 s, 2 860 s, 1 710 s
XIVb	*Xb*	68	$C_{24}H_{27}ClO_6S$	60.18	5.68	7.40	6.69	3 600 m, 3 420 s, 3 010 s,
			(479.0)	60.01	5.61	7.55	6.72	2 930 s, 1 720 s
XVa	*XIa*	73	$C_{23}H_{34}O_5S$	65.37	8.11		7.59	3 610 m, 3 400 s, 3 020 s,
			(422.6)	65.08	7.89		7.50	2 940 s, 2 860 s, 1 710 s
XVb	*XIb*	84	$C_{25}H_{29}ClO_6S$	60.91	5.93	7.19	6.50	3 610 w, 3 440 m, 3 020 m,
			(493.0)	60.78	5.86	7.32	6.32	2 960 m, 2 940 m, 1 710 s

TABLE IV
Derivatives of prostaglandin E_2 *XXa,b – XXIIIa,b*

Product	Starting material	Yield, %	Formula (M.w.)	Calculated/Found % C	% H	% Cl	% S	Infrared spectra, cm^{-1}
XXa	*XVIa*	85	$C_{22}H_{30}O_6$ (390.5)	67.67 67.41	7.74 7.55			3 620 w, 3 430 m, 3 015 m, 2 940 s, 2 870 m, 1 745 s, 1 720 s
XXb	*XVIb*	89	$C_{24}H_{25}ClO_7$ (460.9)	62.54 62.28	5.47 5.26	7.69 7.83		3 600 w, 3 410 w, 3 010 s, 2 945 s, 1 745 s, 1 720 s
XXIa	*XVIIa*	83	$C_{22}H_{30}O_6$ (390.5)	67.67 67.55	7.74 7.66			3 610 w, 3 410 w, 3 020 m, 2 950 s, 2 870 m, 1 745 s, 1 730 s
XXIb	*XVIIb*	84	$C_{24}H_{25}ClO_7$ (460.9)	62.54 62.38	5.47 5.19	7.69 7.93		3 620 w, 3 420 w, 3 020 m, 2 950 s, 1 740 s, 1 720 s
XXIIa	*XVIIIa*	91	$C_{22}H_{30}O_5S$ (406.5)	65.00 64.87	7.44 7.23		7.89 7.65	3 620 w, 3 410 m, 3 010 m, 2 960 s, 2 860 m, 1 745 s, 1 710 s
XXIIb	*XVIIIb*	88	$C_{24}H_{25}ClO_6S$ (477.0)	60.44 60.22	5.28 5.15	7.43 7.66	6.72 6.66	3 620 w, 3 400 m, 3 010 m, 2 940 s, 1 740 s, 1 715 s
XXIIIa	*XIXa*	79	$C_{23}H_{32}O_5S$ (420.6)	65.69 65.48	7.67 7.43		7.62 7.44	3 600 w, 3 420 w, 3 015 m, 2 960 s, 2 860 m, 1 750 s, 1 720 s
XXIIIb	*XIXb*	83	$C_{25}H_{27}ClO_6S$ (491.0)	61.16 60.99	5.54 5.32	7.22 7.51	6.53 6.38	3 610 w, 3 420 w, 3 020 m, 2 960 s, 2 870 m, 1 740 s, 1 710 s

TABLE V
Phosphonium salts *IV* – *VI*

Salt	Starting material	Yield, % M.p., °C	Formula (M.w.)	Calculated/Found				Infrared spectra, cm^{-1}	Mass spectra *m/z* (rel.%)
				% C	% H	% Cl	% P		
IV	*XXIV*	92 219 – 221	$C_{25}H_{22}ClO_3P$ (436.8)	68.73 69.18	5.04 5.37	8.13 8.49	7.10 6.81	3 050 m, 1 700 s, 1 590 m	399(53) (M – HCl – 1) 262(50) (Ph_3P)
V	*XXV*	97 166 – 172	$C_{25}H_{22}ClO_3P$ (436.8)	68.73 68.56	5.04 5.27	8.13 8.21	7.10 6.99	3 060 m, 1 710 s, 1 590 m	399(33) (M – HCl – 1) 262(100) (Ph_3P)
VI	*XXVI*	92 192 – 194	$C_{25}H_{22}ClO_2PS$ (452.9)	66.30 66.50	4.90 5.33	7.83 8.15	6.84 6.96	3 060 m, 1 705 s, 1 590 s	416(72) (M – HCl) 262(100) (Ph_3P)
VII	*XXVII*	80 212 – 218	$C_{26}H_{24}ClO_2PS$ (466.9)	66.88 66.77	5.14 5.32	7.61 7.91	6.65 6.55	3 060 m, 1 725 s, 1 595 m	429(20) (M – HCl – 1) 262(100) (Ph_3P)

$C_{25}H_{40}O_6$ (436.6) calculated: 68.78% C, 9.23% H; found: 68.52% C, 9.24% H. IR spectrum: 3 020 s, 2 950 s, 2 860 s, 1 770 s, 1 030 s. ^{1}H NMR spectrum: 0.90 t (CH_3); 5.31 – 5.70 m, 2 H (H-13, H-14); 1.14 – 2.07 m, 20 H; 2.07 – 3.15 m, 6 H; 3.30 – 4.35 m, 6 H; 4.50 – 5.31 m, 3 H. Mass spectrum: 250 (34) (M – THP – OTHP)$^+$, 179 (18) (M – THP – OTHP – C_5H_{11})$^+$, 85 (100) (THP).

In analogous way, diol *Ib* was converted into the bistetrahydropyranyl derivative *IIb*, slightly yellowish oil, yield 90%. For $C_{27}H_{35}ClO_7$ (507.0) calculated: 63.96% C, 6.96% H, 6.99% Cl; found: 63.92% C, 6.97% H, 6.98% Cl. ^{1}H NMR spectrum: 1.46 – 1.86 m, 12 H (CH, CH_2, cyclopentane ring and THP); 2.08 – 2.22 and 2.37 – 2.83 m, 6 H (CH_2CO, CH, CH_2); 3.45 – 3.54 and 3.78 – 4.18 m, 7 H (CH_2O, CH, CH_2); 4.43 – 4.50 and 4.65 – 4.72 and 4.85 – 5.04 m, 4 H (CHO); 5.47 – 5.55 m, 2 H (H-13, H-14); 6.85 – 7.30 m, 4 H (arom. H).

[3aα,4α,5β,6aα]-(±)-Hexahydro-5-tetrahydropyran-2-yloxy)-4-((*E*)-(3α)-(tetrahydropyran-2-yloxy)-1-octenyl)-2*H*-cyclopenta[*b*]furan-2-ol (Lactol *IIIa*)

A 20% solution of DIBAH in hexane (19 ml, 19 mmol) was added to a cold (−78 °C) solution of lactone *IIa* (3.34 g, 7.76 mmol) in toluene (200 ml) under nitrogen at such a rate as to keep the temperature below −60 °C. After 30 min, the reaction was finished by adding 2-propanol (0.85 ml). Then the mixture was heated to room temperature and diluted with water (17 ml), stirred ca 1 h (until a precipitate was formed), and the solid was collected by suction and washed with chloroform (4 × 20 ml). The solvents were evaporated to give 3.29 g (98%) derivative *IIIa* as a yellowish oil, uniform according to TLC. For $C_{25}H_{42}O_6$ (438.6) calculated: 68.46% C, 9.65% H; found: 68.64% C, 9.49% H. IR spectrum: 3 600 m, 3 400 m, 3 030 s, 2 960 s, 2 860 s, 1 020 s. ^{1}H NMR spectrum: 0.86 t (CH_3); 5.12 – 5.72 m, 2 H (H-13, H-14); 1.20 – 2.45 m, 27 H; 3.30 – 4.12 m, 7 H; 4.50 – 4.70 m, 2 H; 4.80 – 4.95 m, 1 H. Mass spectrum: 264 (68) (M – THP – C_5H_{11} – H_2O)$^+$, 235 (43) (264 – CHO)$^+$, 85 (100) (THP)$^+$.

In analogous way, lactone *IIb* was converted to lactol *IIIb*, yield 96% of oily product. For $C_{27}H_{37}ClO_7$ (509.0) calculated: 63.71% C, 7.33% H, 6.96% Cl; found: 63.92% C, 7.44% H, 7.05% Cl. ^{1}H NMR spectrum: 1.42 – 1.88 and 1.95 – 2.08 and 2.36 – 2.52 m, 18 H (CH, CH_2, cyclopentane ring and THP group); 2.93 – 3.10 bs, 1 H (OH); 3.41 – 3.55 and 3.76 – 4.10 m, 7 H (CH_2O, CH, CH_2); 4.45 – 4.52 and 4.58 – 4.80 m, 4 H (2 × OCHO, CHO); 5.46 – 5.56 and 5.61 – 5.9 m, 3 H (H-13, H-14, OCHO); 6.76 – 7.27 m, 4 H (arom. H). Mass spectrum: 322 (6) (M – THP – OTHP)$^+$, 304 (5) (322 – H_2O)$^+$, 85 (100) (THP)$^+$.

(±)-5-(5-Methoxycarbonyl-2-furyl)-11,15-bis-*O*-(tetrahydropyran-2-yloxy)-1,2,3,4-tetranorprostaglandin $F_{2\alpha}$ (*VIIIa*)

Procedure A: A solution of 1.477 M potassium *tert*-butoxide in tetrahydrofuran (1.95 ml, 2.89 mmol) was added dropwise to a suspension of phosphonium salt *IV* (1.26 g, 2.89 mmol) in tetrahydrofuran (10 ml) under nitrogen with cooling in water bath. The mixture was stirred at room temperature 30 min, cooled to ca 0 °C, and a THF solution (5 ml) of lactol *IIIa* (333.1 mg, 0.76 mmol) was added thereinto. The mixture was stirred at 0 °C 1 h and at room temperature 6 h, whereafter the reaction was finished by adding 4 M solution of sodium hydrogensulfate (0.4 ml), water (0.8 ml), and saturated sodium chloride solution (2.4 ml). The layers were separated, and the aqueous phase was washed successively with ethyl acetate (4 × 5 ml) and chloroform (3 × 5 ml). Combined organic portions were dried with anhydrous magnesium sulfate and the solvents were evaporated to leave 1.04 g oil which on purification by column chromatography (silica gel, 45 g; toluene–ethyl acetate 4 : 1) gave 53 mg starting lactol and 318.1 mg (75%) product *VIIIa* (yellowish oil). Its spectral characteristics are given in Table I. The other analogues of $PGF_{2\alpha}$ (*VIIIb* – *XIa,b*) given in Table I were prepared in the same way.

Procedure B: A mixture of lactol *IIIa* (0.51 g; 1.17 mmol), phosphonium salt *IV* (1.28 g, 2.93 mmol), freshly annealed potassium carbonate (0.89 g), and dry methanol (10 ml) was stirred under nitrogen at room temperature 2 h. The reaction mixture was evaporated until almost dry, diluted with chloroform (10 ml), and acidified with 1% hydrochloric acid to pH 6. The aqueous layer was washed with chloroform (3 × 10 ml) and combined organic phases were dried with anhydrous magnesium sulfate, evaporated, and the residue was submitted to column chromatography (silica gel; toluene–ethyl acetate 4 : 1) to give 575.3 mg (88%) compound *VIIIa* as a light yellow oil. The results and spectral characteristics of the derivatives prepared in this way are given in Table I.

(±)-16-(3-Chlorophenoxy)-11,15-bis-*O*-(tetrahydropyran-2-yloxy)-5-(5-methoxycarbonyl-2-furyl)-1,2,3,4,17,18,19,20-octanorprostaglandin E_2 (*XVIb*)

Pyridine (2.8 ml) and dry chromium trioxide (910 mg, 9.1 mmol) were added to a solution of compound *VIIIb* (0.89 g, 1.4 mmol) in 1,2-dichloroethane (5 ml). The reaction mixture was stirred at room temperature 7 h, the inorganic salts were removed by suction and washed with 1,2-dichloroethane (2 × 5 ml), the solvents were evaporated, and the raw oily residue was purified by column chromatography (silica gel; 2% methanol in chloroform) to give 729.4 mg (83%) protected analogue of prostaglandin E_2 *XVIb* as a yellowish oil (Table II). Table II gives the results and spectral characteristics of the PGE_2 derivatives *XVIa,b – XIXa,b* prepared by this procedure.

(±)-5-(5-Methoxycarbonyl-2-furyl)-1,2,3,4-tetranorprostaglandin $F_{2\alpha}$ (*XIIa*)

A mixture of bis-THP derivative *VIIIa* (176 mg, 0.31 mmol), methanol (2 ml), acetone–water (7 : 3, 7 ml), and ion exchanger in H^+ cycle (450 mg Dowex 50X8-200) was stirred at room temperature 24 h. The ion exchanger was collected by suction and washed with the acetone–water mixture (7 : 3, 2 × 1 ml). The solvents were distilled off in vacuum and the residue was extracted with ethyl acetate (5 × 5 ml). Combined organic phases were dried with anhydrous magnesium sulfate, evaporated, and the residue was purified by column chromatography (silica gel, 10 g; benzene–acetic acid–methanol 16 : 1 : 1) to give 96.7 mg (79%) product *XIIa* as a yellowish oil (Table III) The other derivatives of $F_{2\alpha}$ series (*XIIb – XVa,b*) and E_2 series (*XXa,b – XXIIIa,b*) prepared in this way, their yields and spectral characteristics are given in Tables III and IV, respectively.

Triphenyl[(5-methoxycarbonyl-2-furyl)methyl]phosphonium Chloride (*IV*)

A mixture of methyl 2-chloromethyl-5-furancarboxylate (*XXIV*) (7.0 g, 40 mmol), triphenylphosphine (15.8 g, 60 mmol), anhydrous toluene (60 ml), and dimethylformamide (0.6 ml) was refluxed 10 h. The separated crystals were collected by suction, washed with benzene (3 × 20 ml), and dried in air. Yield 16.0 g (92%) white crystalline phosphonium salt *IV*, m.p. 219 – 221 °C (ref.[15] gives m.p. 224 °C). The spectral characteristics are given in Table V.

The other phosphonium salts were prepared similarly (Table V). ^{1}H NMR spectra: compound *IV*: 3.75 s, 3 H (OCH_3); 5.69 d, 2 H (CH_2); 7.72 – 7.95 m, 15 H (arom. H); 6.40 t, 1 H; 7.23 dd, 1 H (furan H); compound *V*: 3.62 s, 3 H (OCH_3); 5.68 d, 2 H (CH_2); 7.36 – 8.08 m, 15 H (arom. H); 6.54 s, 1 H, 7.64 s, 1 H (furan H); compound *VI*: 3.78 s, 3 H (OCH_3); 5.89 d, 2 H (CH_2); 7.76 – 7.97 m, 15 H (arom. H); 6.91 t, 1 H, 7.64 dd, 1 H (thiophene H); compound *VII*: 4.24 q, 2 H (OCH_2); 5.96 d, 2 H (CH_2); 7.44 – 8.14 m, 15 H (arom. H); 7.19 s, 1 H, 8.26 s, 1 H (thiophene H); 1.22 t, 3 H (CH_3).

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