Addition of Thallium Triacetate to $PGF_{2\alpha}$ Methyl Ester and Related Compounds in Acetic Acid. Nuclear Magnetic Resonance Spectral Study of Novel Dioxatricyclic and Oxabicyclic Products

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Addition of $Tl(OAc)_3$ in acetic acid to prostaglandin $F_{2\alpha}$ methyl ester (1) and its congeners (4) and (5) gave, with participation of 9-OH, the bicyclic enol ethers (26) which reacted *in situ* with a further equivalent of $Tl(OAc)_3$ to yield as the main products the dioxatricyclononane derivatives (2), (6), and (9) and (3), (7), and (10), respectively. Elucidation of the structure of the products by ^1H and ^{13}C n.m.r. is presented and a mechanism of the transformations based on model studies is proposed.

With the objective of finding a convenient route for the transformation of F-type prostaglandins to prostacyclines we investigated the reaction of $PGF_{2\alpha}$ methyl ester (1) with thallium triacetate (TTA) in acetic acid. In a preliminary paper [1] we reported that (1) was transformed by TTA to the new tricyclic prostaglandin derivatives (2) and (3a and b) both functionalized at C-7. Thus TTA [2] behaved quite differently from other electrophiles used so far for prostaglandin transformations [3] and this may be due to the fact that the initially formed C–Tl bond underwent ready heterolysis and the resulting carbonium ion was trapped by 11-OH as an internal nucleophile. In this paper we report the extension of the reaction to other systems (4) and (5) with the characteristic functionalities of (1), *i.e.* 9- and 11-OH and the 5*Z*-double bond and some further compounds without 11-OH [(18) and (19)]. These studies were carried out to ascertain the role of the 11-hydroxy-function and to determine the stereochemistry of the products.

The best conversion of $PGF_{2\alpha}$ (1) to the main products (2) and (3a and b) (70—75%) can be achieved with 2.5—3.0 mol. equiv. TTA. 1.0—1.1 mol. equiv. TTA afforded only small amounts of (2) and (3a and b) along with unchanged (1).[1] Similarly, reaction of the benzyl ether (4) [4] with 2.5—3.0 mol. equiv. TTA in acetic acid at room temperature for 24 h yielded two products, both less polar than (4). The i.r. spectrum of the minor product (6), (15%) contained no hydroxy band. The more polar main product (7a and b) (45%), an inseparable mixture of epimers exhibited in the i.r. spectrum a carbonyl band at 1 730 cm^{-1} and a less intense hydroxy band, the latter disappearing when the product was subjected to acid-catalysed methanolysis to give (15).

Reaction of the diol (5) with 2.5—3.0 mol. equiv. TTA gave similar results, *i.e.* a less polar acid sensitive minor product (9) (17%) showing a sharp carbonyl band but no hydroxy absorption in the i.r. as well as a more polar mixture of epimers (10a and b) (38%) as the major product, also containing an acetal type hydroxy, which could be converted into (16) by acid-catalysed methanolysis.

The constitution and stereochemistry of the novel compounds were determined by a detailed analysis of their ^1H and ^{13}C n.m.r. spectra. The relevant data are compiled in Tables 1 and 2. The spectral data disclosed that the less polar, acid sensitive products (2), (6), and (9), on the one hand, and the inseparable mixtures of epimers (3a and b), (7a and b), and (10a and b) on the other, feature common dioxatricyclononane skeletons and are 8,9-dioxatricyclo[$3.3.1.0^{3,7}$]nonane and 3,9-dioxatricyclo[$4.2.1.0^{4,8}$]nonane derivatives, respectively. (In this paper, the numbering of atoms in these and related systems follows the convention adopted for prostanoids.) For brevity the presentation of spectral evidence for these tricyclic structures is restricted to the examples of (2) and (3a and b).

According to i.r. and ^1H and ^{13}C n.m.r. data both (2) and (3a and b) contain a tetrasubstituted cyclopentane ring carrying the unaltered alkyl side chain at C-12 and two OR substituents attached to C(9) and C(11). The spectral data also disclosed the presence of a methyl ester group [methyl group in (9) and (10a and b)] and the lack of a *Z*-5,6 double bond. The most significant novel structural element, common to both (2) and (3a and b) is an –O–C–O– grouping as shown by the quaternary ^{13}C signal at δ 107.66 for (2) and 107.00 and 106.00 p.p.m. for the major and minor epimers of (3a and b), respectively.

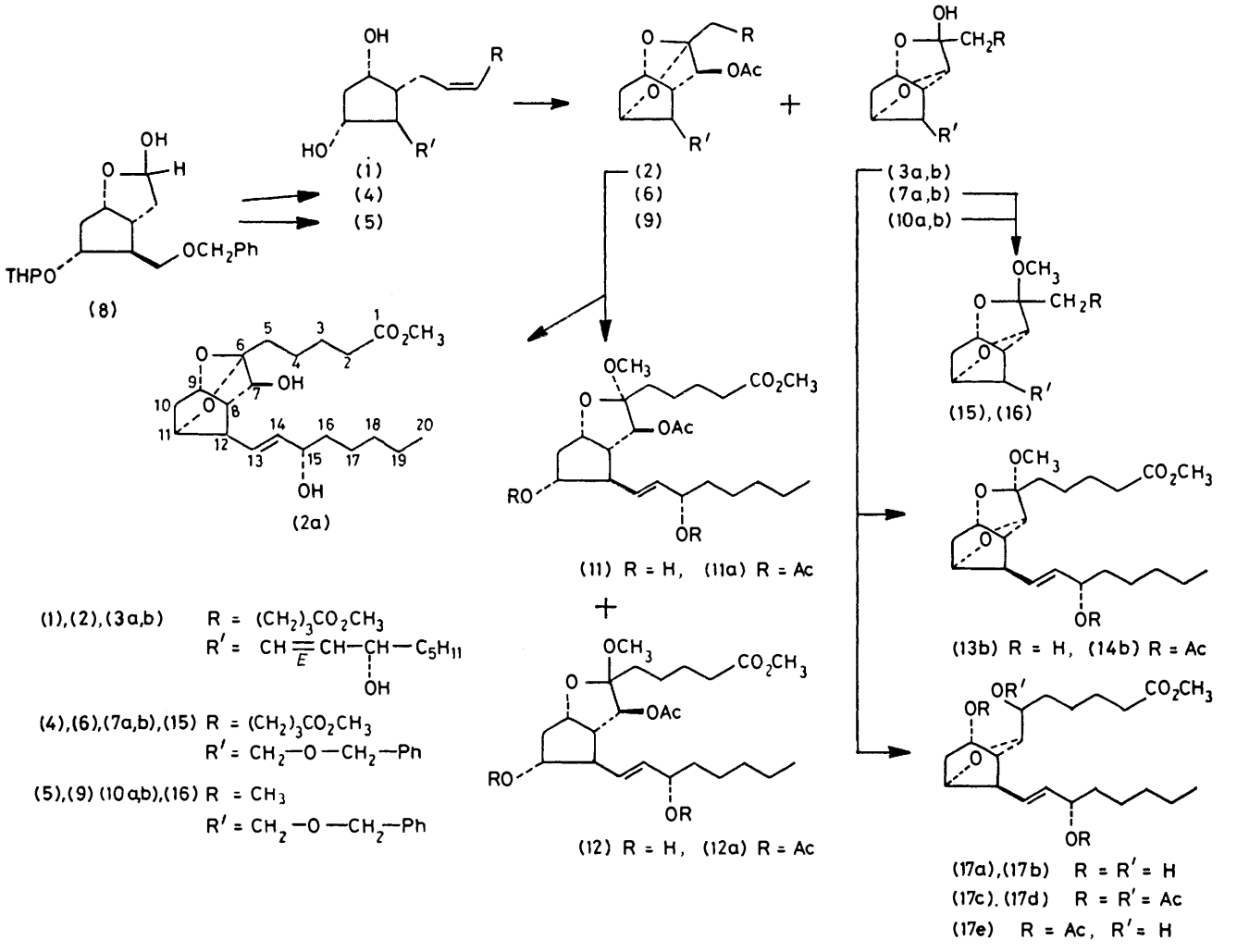
An accurate mass measurement of $M^{+\cdot}$ for (2) gave $C_{23}H_{36}O_7$ as the molecular formula. The spectral data also disclosed the presence of an acetoxy group, which on treatment with methanol in the presence of potassium carbonate was readily converted into a hydroxy function (2a). The characteristic ^{13}C shifts accompanying deacetylation located the OAc group at C-7 ($\delta_{2a} - \delta_2 = -1.03$). Typical β-deacetylation shifts were also noted for the ^{13}C resonances of C-8 ($\delta_{2a} - \delta_2 = +2.21$) and the quaternary –O–C–O– carbon ($\delta_{2a} - \delta_2 = +1.35$), which assigned the latter to C(6). The count of available oxygen atoms left only two oxygens to be

attached to three carbons, namely C(9), C(11), and C(6) which settled the constitution as (2).

The *exo*-configuration of 7-OAc followed clearly from the small ^1H–^1H coupling constant ($^3J_{7,8}$ 0.5 Hz) indicating a nearly 90° dihedral angle between 7- and 8-H.

Supporting evidence for the internal acetal function was provided by transacetalization. Treatment of (2) with methanol in the presence of boron trifluoride–ether at 25 °C for 1 h gave two polar products. The (12) are hemicyclic methyl acetals of the 7-acetoxy-6-oxo-$PGF_{1\alpha}$ methyl ester and epimers at C(6).

The ^1H–^1H coupling constants in (11) and (12) are markedly larger than the corresponding values in the dioxatricyclononane (2) (*cf.* Table 1). The most significant deviations are exhibited by the cyclopentane protons, a result which may be explained in terms of conformational changes associated with the opening of the acetal bond. The smaller couplings in (2) indicate



spectral data clearly showed the presence of newly formed OH and OMe groups and thereby proved the conversion of the dioxatricyclononane system into the epimeric bicyclic acetals (11) and (12). In principle, transacetalization of (2) might result in the cleavage of either of the C(9)–O–C(6) and C(11)–O–C(6) bonds and preliminary spectral analysis, in fact, suggested that (11) and (12) were constitutional isomers.[1] Closer scrutiny of the ^1H and ^{13}C spectra and, in particular, the acetylation induced spectral changes (see Table 1) disclosed, however, that both (11) and (12) have the same bicyclic skeleton formed from (2) through the rupture of the C(11)–O–C(6) bond. In fact (11) and that the pertinent dihedral angles in the highly strained dioxatricyclononane system are all between 45 and 100° while they are substantially larger in (11) and (12) as much of the strain is relieved by the cleavage of the C(11)–O–C(6) bonds. Presumably the same conformational changes are reflected by the absence of a four-bond $^4J_{9,11}$ coupling in the ^1H spectra of (11) and (12). The relatively large value (2 Hz) of this coupling in (2) indicates near coplanarity of 9- and 11-H attributable to the highly strained geometry of the dioxatricyclononane skeleton. Some characteristic changes in the ^{13}C chemical shifts associated with ring opening become apparent from the data in Table 2. The larger δ values

of the C(8), C(10), and C(13) resonances in (11) and (12) may be ascribed to the lack of γ-interactions which cause substantial upfield shifts for the same signals in the sterically crowded (2).

Comparison of ^1H and ^{13}C spectral data for (11) and (12) disclosed that an inversion of the configuration at C(6) gives rise to a significant conformational change in the bicyclic skeleton. A most remarkable consequence of this is reflected by the value of $^3J_{7,8}$ which agrees in (11) with the 0.5 Hz observed for (2) whereas it is 5.5 Hz in (12). Owing to simultaneous changes both in configuration and conformation, the n.m.r. data alone proved to be insufficient for determining the stereochemistry at C(6). The steric disposition of the 6-OMe group [*endo* and pseudoaxial in (11), and *exo* and pseudoaxial in (12)] could be, however, deduced from information gleaned by comparative ^1H and ^{13}C n.m.r. analyses of related bicyclic systems [5] for which the configuration at C(6) was independently established by ring-closure experiments.

The structural elucidation of the other group of tricyclic derivatives, (3a, b), (7a, b), and (10a, b), followed a similar procedure. A molecular formula of $C_{21}H_{34}O_6$ was found for (3a, b) by mass spectrometry. By exchange with D_2O, the ^1H n.m.r. spectrum disclosed that besides the 15-OH, the molecule possesses an additional OH function. Treatment of (3a, b) with methanol in the presence of boron trifluoride–ether at 25 °C for 15 min gave (13b), one of the isomeric methyl acetals (13a, b), which, upon acetylation with acetic anhydride in pyridine, yielded the corresponding monoacetate (14b). The relationship between (3b) and (14b) is based on the coincidence of chemical shift values of carbon atoms not affected by methylation. Evaluation of the methylation shifts, on the other hand, disclosed that acetalization occurred at the quaternary –O–C–O– carbon atom [(14b) — (3b) = +2.6 p.p.m.] and that this carbon atom is to be assigned to position 6. {Methylation shifts were also noted for C-5 [(14b) — (3b) = —5.6 p.p.m.] and C-7 [(14b) — (3b) = —0.7 p.p.m.] resonances.} The marked difference in the methylation shifts for C(5) and C(7) may be used for a tentative assignment of the stereochemistry at C(6). Irrespective of its actual (*exo* or *endo*) orientation, the 6-OMe group should enter a γ-gauche steric interaction with 5-H, an effect which has to be invoked to account for the large shielding of the C(5) resonance on methylation. A similar steric effect for 7-H, however, would be expected to occur only with an *exo*-oriented 6-OMe group. The lack of a substantial upfield shift of the C(7) resonance upon methylation, therefore, may be interpreted by assuming an *endo*-orientation for 6-OMe in (14b) and, accordingly, an *endo*-orientation for the 6-OH group in (3b).

The treatment of (3a, b) with sodium borohydride resulted in the reduction of the masked oxo function and yielded a separable pair of triols (17a, b) epimeric at C(6). Comparison of the ^1H and ^{13}C n.m.r. spectra of triols and their di- and tri-acetates (17c—e) showed the OH groups to be attached to C(6), C(9), and C(15), *i.e.*, the hemiacetal ring in (3a, b) indeed involved the C(6)–O–C(9) linkage. Contrary to expectation,[3e] no oxo-form

TABLE 1

^1H Chemical shifts [a] and coupling constants [b]

	Compound					
	(2)	(11)	(12)	(3a,b)	(17a)	(17c)
6-H					3.97 ($^3J_{6,7}$ 10.5) [d]	5.2 ($^3J_{6,7}$ 10.2)
7-H	4.96 ($^3J_{7,8}$ 0.5)	4.90 ($^3J_{7,8}$ 0.5)	5.19 ($^3J_{7,8}$ 5.5)	3.92 + 3.95 ($^3J_{7,8}$ 3.0, $^4J_{7,9}$ 1.0)	3.97 ($^3J_{7,8}$ 2.0, $^4J_{7,9}$ 1.5)	4.08 ($^3J_{7,8}$ 2.0, $^4J_{7,9}$ 1.5)
8-H	2.86 ($^3J_{8,9}$ 4.5, $^3J_{8,12}$ 1.5)	>2.0 ($^3J_{8,9}$ 8.0, $^3J_{8,12}$ 10.0)	2.51 ($^3J_{8,9}$ 7.0, $^3J_{8,12}$ 5.5)	2.89 + 3.10 ($^3J_{8,9}$ 4.5, $^3J_{8,12}$ 1.0)	2.51 ($^3J_{8,9}$ 4.0, $^3J_{8,12}$ 1.0)	2.70 ($^3J_{8,9}$ 4.0, $^3J_{8,12}$ 1.0)
9-H	4.77 ($^3J_{9,10}$ 4.0 + 0.5, $^4J_{9,11}$ 2.0)	4.58 ($^3J_{9,10}$ 8.0 + 5.5)	4.57 ($^3J_{9,10}$ 7.0 + 3.5)	4.48 + 4.52 ($^3J_{9,10}$ 6.5 + 1.5, $^4J_{9,11}$ 1.0)	4.40 ($^3J_{9,10}$ 9.5 + 5.5)	5.20 ($^3J_{9,10}$ 9.5 + 5.0) [d]
11-H	4.32 ($^3J_{10,11}$ 1.5 + 1.5, $^3J_{11,12}$ 1.5)	3.60 ($^3J_{10,11}$ 10.5 + 6.5, $^3J_{11,12}$ 10.0)	3.97 ($^3J_{10,11}$ 6.5 + 5.5 [c] $^3J_{11,12}$ 6.0 [c])	4.15 + 4.08 ($^3J_{10,11}$ 1.5 + 1.5, $^3J_{11,12}$ 1.5)	4.17 ($^3J_{10,11}$ 2.0 + 0.5, $^3J_{11,12}$ 2.0)	4.18 ($^3J_{10,11}$ 2.0 + 0.5, $^3J_{11,12}$ 2.0)
12-H	3.00 ($^3J_{12,13}$ 3.5)	2.70 ($^3J_{12,13}$ 7.5)	2.78 ($^3J_{12,13}$ 6.0)	2.95 ($^3J_{12,13}$ 3.5)	2.97 ($^3J_{12,13}$ 2.0)	3.03 ($^3J_{12,13}$ 2.0)
13-H, 14-H	5.38 + 5.52 ($^3J_{13,14}$ 15.5, $^3J_{14,15}$ 5.0)	5.4 + 5.5 ($^3J_{13,14}$ 15.0, $^3J_{14,15}$ 6.0)	5.4 + 5.5 ($^3J_{13,14}$ 15.0, $^3J_{14,15}$ 6.0)	5.42 + 5.55 ($^3J_{13,14}$ 15.5, $^3J_{14,15}$ 7.0 [c])	5.57 + 5.65 ($^3J_{13,14}$ 15.5, $^3J_{14,15}$ 4.5)	5.65 ($^3J_{13,14}$ 15.5 $^3J_{14,15}$ 4.5)
15-H	4.05 ($^3J_{15,16}$ 6.0 + 6.0)	3.96 ($^3J_{15,16}$ 6.0 + 6.0 [c])	4.03 ($^3J_{15,16}$ 6.0 + 6.0 [c])	3.9 ($^3J_{15,16}$ 6.0 + 6.0 [c])	4.05 ($^3J_{15,16}$ 5.0 + 6.0)	5.18 ($^3J_{15,16}$ 5.0 + 6.0)
OH	1.6	2.7—2.85	1.8—1.9	4.3 + 4.6 + 1.6	1.6 + 4.3	
CO_2CH_3	3.66	3.57	3.64	3.56	3.66	3.64
OCH_3		3.14	3.24			1.98
OAc	2.06	1.95	2.04			2.02 2.02

[a] In p.p.m. from internal Me_4Si in $CDCl_3$ solution. [b] In Hz. [c] Measured for acetylated derivative. [d] Measured for diacetylated derivative (17e).

TABLE 2

^{13}C Chemical shifts [a]

	(2) [b]	(11) [b]	(12) [b]	(3a)	(3b) [b]	(14b) [b]	(17a) [c]	(17b) [c]	(17c) [c]	(17d) [c]	(17e) [c]	(6) [b]	(9) [b]	(10a) [b]	(10b) [b]
C(1)	174.0	173.9	174.0	174.2		173.9	173.8	174.0	173.7	173.6	173.7	173.9			
C(2)	34.0	33.8	33.9	34.0		34.0	34.1	34.2	34.0	33.9	34.1	34.0			
C(3)	25.1	25.1	25.1	25.2		25.1	25.3	25.1	25.2	25.2	25.2	25.2			
C(4)	22.9	23.3	22.8	23.3	23.8	24.1	26.1	25.7	24.3	25.2	25.3	22.9	7.6	8.1	8.4
C(5)	30.9	29.5	31.8	37.8	36.5	30.9	33.2	35.1	33.0	31.1	35.6	31.0	24.4	30.9	29.4
C(6)	107.7	112.8	107.8	106.0	107.0	109.6	71.5	70.6	74.4 [d]	75.0 [d]	72.8	107.9	108.4	106.5	107.5
C(7)	81.4	79.8	81.2	82.6	83.9	83.2	85.3	85.3	82.3	83.5	85.5	81.6	81.1	82.4	83.6
C(8)	47.6	53.9	51.8	51.0	49.6	49.5	49.3	50.8	46.9	47.0	46.8	45.9	45.9	49.3	47.8
C(9)	80.8	80.4	79.1	77.8	78.5	78.3	70.0	70.4	73.1 [d]	73.0 [d]	73.5	79.1	79.1	77.9	78.6
C(10)	36.4	40.9	39.5	39.2	39.8	39.9	39.1	39.0	36.9	36.6	36.7	36.5	36.5	39.1	39.6
C(11)	78.4	75.9	77.7	78.9	79.1	78.9	79.9	79.8	79.1	78.7	79.0	78.7	78.7	77.1	77.3
C(12)	53.0	52.9	55.0	52.7	51.9	51.7	53.7	53.9	53.0	53.4	53.0	51.2	51.2	50.7	49.8
C(13)	128.7	131.9	131.8	125.1	126.1	129.1	125.6	125.6	128.5	128.4	128.8				
(C14)	135.3	136.1	135.1	135.0	136.7	131.8	137.4	137.4	132.9	132.9	132.8				
C(15)	72.4	73.0	73.0	72.3		74.4	72.4	72.4	74.4	74.4	74.5				
C(16)	37.4	37.3	37.2	37.1		34.3	37.9	37.9	34.7	34.7	34.7				
C(17)	25.1	25.1	25.1	25.1		24.8	25.6	25.7	25.4	25.4	25.4				
C(18)	31.7	31.9	31.8	31.8		31.5	32.3	32.3	31.9	31.9	31.9				
C(19)	22.6	22.6	22.6	22.6		22.5	23.1	23.1	22.9	22.9	22.9				
C(20)	14.0	14.1	14.1	14.0		13.9	14.3	14.3	14.2	14.2	14.2				
OAc	21.2 + 170.3	21.1 + 169.4	21.0 + 170.4			21.2 + 170.1		20.8 +	169.2 169.5 170.7	20.7 20.9 + 21.0	169.6 170.0 170.0	20.7 20.9 +	169.6 169.8	21.1 + 170.2	21.2 + 170.3
CO_2Me	51.4	51.5	51.5	51.5		51.30	51.1	51.1	50.9		51.0	50.9		51.4	
OMe		47.8	47.9			48.2									
CH_2O														69.8	69.8	67.5	68.1
OCH_2Ph														73.1	73.1	73.3	
Ph														127.6	127.5	127.6	
														127.8	127.8	127.9	
														128.5	128.5	128.5	
														138.1	138.0	138.0	

[a] In p.p.m. from internal Me_4Si. [b] In $CDCl_3$ solution. [c] In C_6D_6 solution. Solvent shifts ($\delta_{C_6D_6} - \delta_{CDCl_3}$) were found generally to be <0.5 p.p.m. [d] Assignments may be interchanged.

containing the hemiacetals (3a, b) could be detected in the reaction mixture.

The high strain inherent in the novel dioxatricyclononanes (3a, b) is again reflected in the generally low values of skeletal vicinal interproton coupling constants (*cf.* Table 1) as well as by the occurrence of significant four-bond couplings ($^4J_{7,9}$, $^4J_{9,11}$) in the ^{1}H n.m.r. spectra. A remarkable difference between (2) and (3a, b) is the higher $^3J_{7,8}$ value in the latter (3 Hz), which reflects the different geometries of the two ring systems.

Cleavage of the C(9)–O–C(6) bonds should not result in a major alteration of the overall molecular geometry and this assumption is clearly borne out by the similarities between the ^{1}H and ^{13}C n.m.r. parameters of the esters (17a, b) and (3a, b), respectively. The shielding differences for C(5), C(6), and C(9) (*cf.* Table 2) are clearly due to changes in substitution.

The configurational difference at C(6) gave rise to small but distinct chemical shift variations in the ^{1}H and ^{13}C n.m.r. spectra of (17a, b) and their triacetates (17c, d) (see Tables 1 and 2 and Experimental section). These are most apparent for 8-H and the carbon atoms adjacent to C(6). Another noteworthy difference is provided by the non-equality of the ^{13}C β-acetylation shifts in the two isomers (17c) [−0.2 for C(5), −3.0 p.p.m. for C(7)] and (17d) [−4.0 for C(5), and −1.8 p.p.m. for C(7)]. Although these spectral differences were indicative of the nature and site of isomerism, they proved insufficient for assigning the actual configurations at C(6).

The common tricyclic skeleton of the product molecules (2), (6), (9), (3a, b), (7a, b), and (10a, b) show that the conversions of $PGF_{2\alpha}$ and its analogues outlined above follow a unique pathway. In fact, compounds containing the all-*cis*-2-(alk-2*Z*-enyl)cyclopentane-1,4-diol moiety all provided dioxatricyclononanes and the main direction of the reaction was independent of both the temperature and molar ratio of the substrate and TTA.

The role of 11-OH as a determinant of these reactions is of mechanistic interest. Information in this regard was gleaned by conversion of the model compounds (18) and (19) which lack this particular functional group.

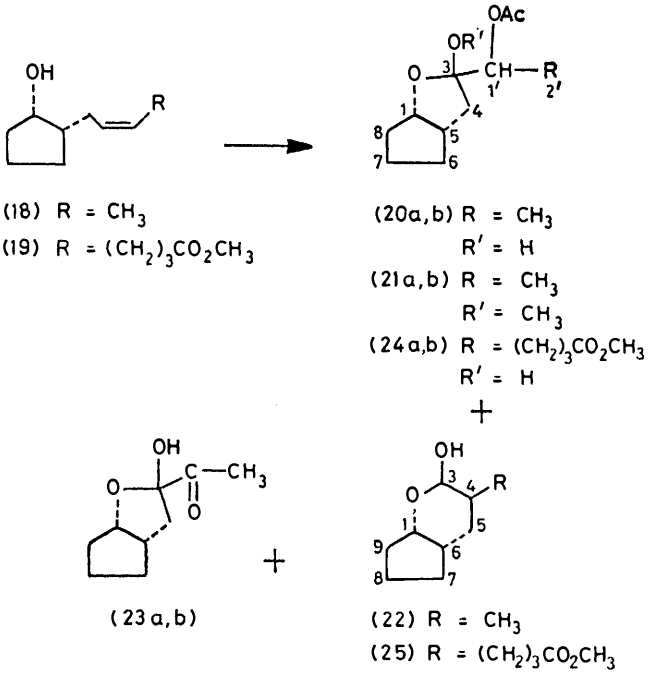
The reaction of (18) with 3 mol. equiv. TTA in acetic acid at room temperature for 3—4 h yielded three main products in addition to some unchanged (18) and minor by-products. The most polar product (20a, b) (*ca.* 60%) could be transformed with methanol containing boron trifluoride–ether, to a mixture of epimeric hemicyclic acetals (21a, b). According to the ^{1}H n.m.r. spectrum of (21a, b), the acetyl group (δ 2.04 and 2.05) is in the side chain, which is indicated by the presence of the one-proton quartets at δ 5.27 and 5.28 (1-H) and the doublet methyl signals (δ 1.21 and 1.23).

The second main product (22) formed in 8% yield was a mixture of the four possible diastereoisomeric *cis*-fused 3-hydroxy-4-methyl-2-oxabicyclo[4.3.0]nonanes. According to t.l.c. the original mixture contained (22) in the acetyl form which then rapidly hydrolysed to (22) during work-up and column chromatography. By ^{1}H and ^{13}C n.m.r., the constitution and relative configuration of the three major components of the mixture could be assigned (see Experimental section). Insufficient information was, however, obtained for the fourth component, which was formed only in traces.

The third identified product obtained in *ca.* 2% yield by the oxidation of (18) was 3-acetyl-3-hydroxy-2-oxa-1α,5α-bicyclo[3.3.0]octane (23a, b), *i.e.* the hemiacetal tautomers of an αβ-diketone. According to the ^{1}H and ^{13}C n.m.r. spectra the major epimer (75%) was that with the acetyl group in the *exo*-orientation.

The reaction of (19) under similar conditions with 3 mol. equiv. TTA gave (24a, b) and (25), the analogues of (20a, b) and (22), respectively.

Knowing the structure of the products formed from $PGF_{2\alpha}$ methyl ester and its congeners on oxidation with TTA in acetic acid, one can envisage the reaction mechanisms shown in Schemes 1 and 2.

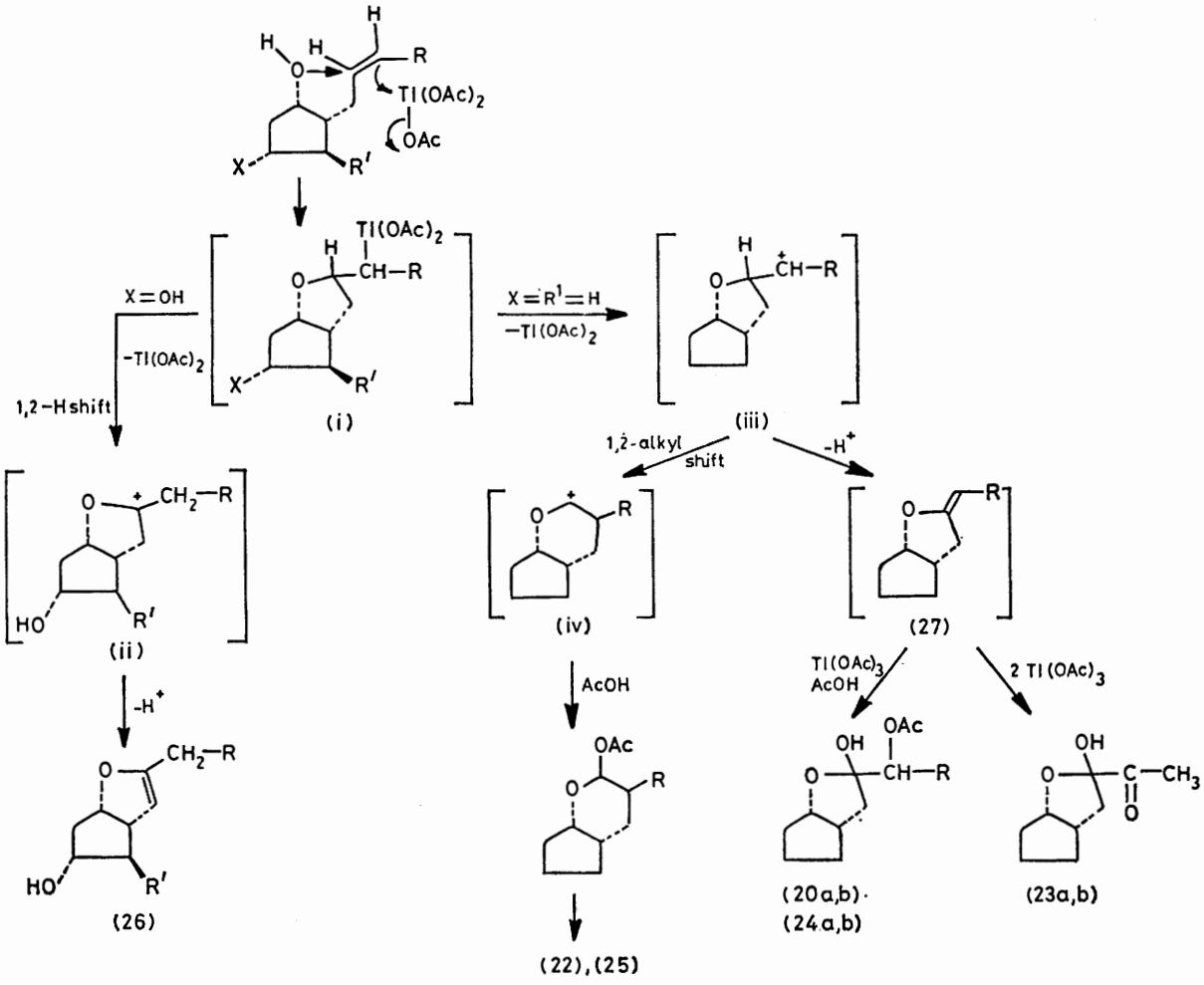


Regiospecific concerted attack of TTA as an electrophile on the sterically favourably disposed 9-OH gives rise to a thalliated bicyclic intermediate (i). Fast heterolysis of the C–Tl bond [6] produces a secondary carbonium ion or similar species at C(5). The latter is then stabilized, yielding intermediates which provide, on further oxidation, the end-products.

The most favourable way to stabilize the carbonium ion derived from (i) is a 1,2-hydride shift. This leads to a tertiary carbonium ion at C(6) (ii) stabilized by the non-bonding electron pair at the adjacent oxygen. Coulomb interaction between this carbonium ion as a hard electrophile and 11-OH as a hard nucleophile ensures additional decrease in the free energy of the corresponding transition state and thus becomes the driving force of the process. The ion (ii) is stabilized by the loss of a proton attached to C(7), giving a Δ^6-

PGI_1-type intermediate (26). Compound (26) could not be isolated from the reaction mixture presumably because, as an enol ether, it is a soft nucleophile with a higher HOMO than the isolated double bond in the starting material and therefore reacts faster with TTA which is a soft electrophile. This is the reason why 1 mol. equiv. TTA is insufficient for the complete conversion of the starting material.

Formation of the products (2) and (3a, b) from the enol ether (26) may be rationalized as shown in Scheme 2.



SCHEME 1

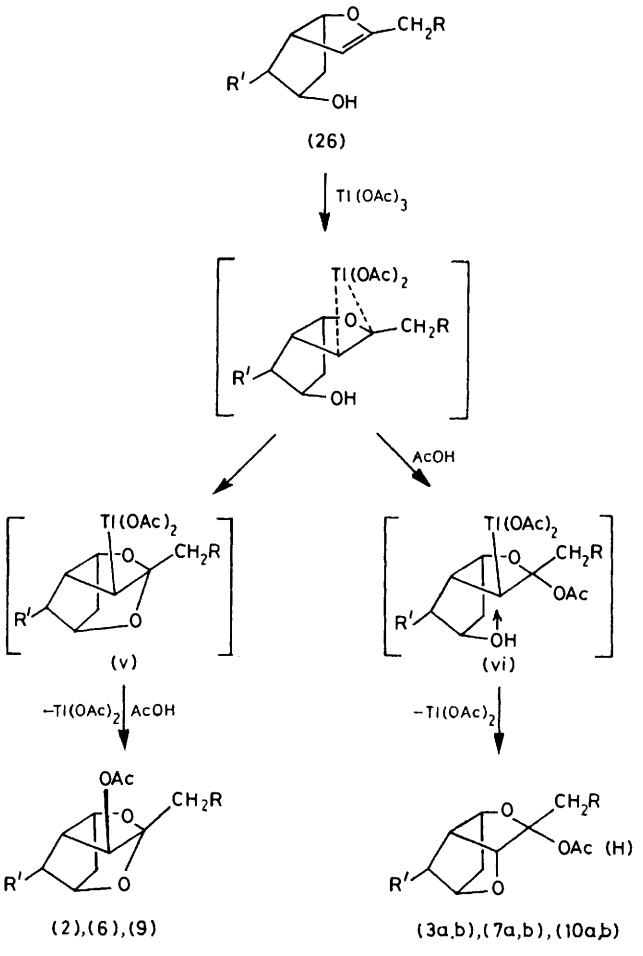
The attack of the electrophile is both regio- and stereospecific and directed towards C(7). For the developing carbonium ion at C(6) there is a competition between 11-OH as an internal and the solvent as an external electrophile leading to (v) and (vi), respectively. The concluding step of the sequence is heterolysis of the C–Tl bond, followed by capture of the carbonium ion at C(6) by the solvent to give (2) or by the 11-OH to yield, after hydrolysis, (3a, b). Our hypothesis about the intermediacy of (26) was supported by the fact that the reaction of Δ^6-PGI_1 methyl ester [7,8] [26; R = $(CH_2)_3CO_2CH_3$, R′ = $CH\overset{E}{=}CHCH(OH)C_5H_{11}$] with 1 mol. equiv. TTA in acetic acid gave (2) and (3a, b) in the same ratio as (1).

In models lacking an 11-OH group, stabilization of the carbonium ion generated by the heterolysis of the primary bicyclic thalliated intermediate (i) follows a different route. It is reasonable to assume that, due to the lack of Coulomb interaction with the 11-OH (a hard electrophile), no 1,2-hydride shift takes place in this case. The secondary carbonium ion is therefore best stabilized by deprotonation at C(6) to yield the exocyclic enol ether (27). This cannot be isolated owing to its faster transformation by TTA compared with the starting material. Compounds (20a, b) can be derived from (27) by further attack by 1 mol. equiv. TTA followed by double nucleophilic attack by the solvent. The minor product (23a, b) can also be deduced from (27) by oxidation with a further 2 mol. equiv. of TTA.

Products (22) and (25), which contain a six-membered ring, can be derived from the secondary carbonium ion (iii) by a 1,2-alkyl shift and capture of the rearranged carbonium ion (iv) by the solvent.

An unexpected feature of the reaction of the models

studied was that, contrary to what would be anticipated from the reaction mechanism, except for the hemiacetals (22) and (25), only hemiacetals and not their acylated forms could be isolated or detected. This may be due to traces of water in the solvent or, rather, to the



SCHEME 2

extreme instability of the sterically crowded hemiacetal acetates.

Compound (5) was prepared from the bicyclic hemiacetal (8) [9] by condensation with ethylidenetriphenylphosphorane followed by deprotection and column chromatography.

The model compounds (18) and (19) were prepared by reducing *cis*-(2-hydroxycyclopentyl)acetic acid lactone [10] with di-isobutylaluminium hydride and condensing the resulting lactol with either ethylidenetriphenylphosphorane to provide (18) or with (4-carboxybutyl)triphenylphosphorane to give (19) [11] upon esterification with diazomethane.

EXPERIMENTAL

^1H and ^{13}C n.m.r. spectra were recorded on a Varian XL-100 Fourier transform spectrometer operating at 100.1 and 25.16 MHz, respectively. Mass spectra were taken on Varian MAT SM-1 instrument. I.r. spectra were recorded with a Spektromom 2000 instrument. T.l.c. was carried out on DC-Fertigplatten Kieselgel 60 F_{254} (Merck) and spots were developed with phosphomolybdic acid in ethanolic solution. Column chromatography was performed on silica gel 60 (Merck; 70—230 mesh).

Reaction of $PGF_{2\alpha}$ Methyl Ester (1) *with Thallium Triacetate.*—Thallium triacetate (11.4 g) in acetic acid (290 ml) was added to a solution of compound (1) (3.68 g) in acetic acid (40 ml) and the solution was stirred for 24 h at room temperature. The solution was evaporated (at 1 mmHg), diluted with water (200 ml), and extracted with ethyl acetate (3 × 150 ml). The combined extracts were washed with water, with aqueous sodium hydrogen carbonate, and finally with brine, dried ($MgSO_4$), and evaporated to give a dark yellow oil (5.7 g). The crude product was chromatographed on silica (600 g) and elution with ethyl acetate–hexane (2 : 1) gave 7β-*acetoxy*-15*S*-*hydroxy*-6,9α;-6,11α-*dioxidoprost*-13*E*-*enoic acid methyl ester* (2) as an oil (1.05 g, 24%) (Found: M^+, 424.241 9. $C_{23}H_{36}O_7$ requires M, 424.246 1). Further elution with the same solvent gave 6*R*,*S*;15*S*-*dihydroxy*-6,9α;7,11α-*dioxidoprost*-13*E*-*enoic acid methyl ester* (3a, b) as a colourless oil (1.97 g, 51%) (Found: M^+, 382.234 4. $C_{21}H_{34}O_6$ requires M, 382.235 5).

7β,15S-*Dihydroxy*-6,9α;6,11α-*dioxidoprost*-13E-*enoic Acid Methyl Ester* (2a).—To a solution of (2) (15 mg) in methanol (2 ml) a catalytic amount of potassium carbonate was added and the mixture was stirred for 15 min at room temperature. The solution was neutralised with dilute hydrochloric acid, diluted with ethyl acetate, washed with aqueous sodium hydrogencarbonate and brine, and dried ($MgSO_4$). The hydroxy-compound (2a) (13 mg, 95%), isolated as an oil by evaporation, was homogeneous by t.l.c. [ethyl acetate–hexane (2 : 1)], δ_H ($CDCl_3$) 2.82 (1 H, m, $J_{8,9}$ 4.5, $J_{8,12}$ 1.5 Hz, 8-H), 2.84 (1 H, m, $J_{12,13}$ 4.0 Hz, 12-H), 4.29 (1 H, m, $J_{10,11} = J_{11,12}$ = 1.5 Hz, 11-H), 4.75 (1 H, m, $J_{9,10}$ 3.5 + 1, $J_{9,11}$ 2 Hz, 9-H), 3.66 (1 H, d, $J_{7,8}$ 0.5 Hz, 7-H), 5.4 (1 H, dd, $J_{13,14}$ 15.5 Hz, 13-H), 5.5 (1 H, dd, $J_{14,15}$ 5 Hz, 14-H), 3.83 (1 H, m, $J_{15,16}$ 6 + 6 Hz, 15-H), and 3.65 (3 H, s, CO_2CH_3); δ_C ($CDCl_3$) 174.00 (C-1), 34.02 (C-2), 25.19 (C-3), 23.09 (C-4), 30.67 (C-5), 109.01 (C-6), 80.37 (C-7), 49.77 (C-8), 80.37 (C-9), 36.37 (C-10), 78.10 (C-11), 52.75 (C-12), 129.12 (C-13), 135.0 (C-14), 72.53 (C-15), 37.42 (C-16), 25.09 (C-17), 31.74 (C-18), 22.58 (C-19), and 13.96 p.p.m. (C-20).

Reaction of Diol (4) *with Thallium Triacetate.*—Thallium triacetate (3.26 g) in acetic acid (60 ml) was added to a solution of diol (4) (1.0 g) in acetic acid (30 ml) and the solution was stirred for 24 h at room temperature. The solution was then worked up as in the first example. The crude product (1.2 g) was chromatographed on silica (150 g) and elution with ethyl acetate–hexane (2 : 1) gave 2-acetoxy-4-benzyloxymethyl-1-(4-methoxycarbonylbutyl)-8,9-dioxatricyclo[3.3.1.$0^{3,7}$]nonane (6) (175 mg, 15%) as an oil, homogeneous by t.l.c. [ethyl acetate–hexane (2 : 1)]; $\nu_{max.}$ 1 735 cm^{-1} (C=O); *m/e* 418 (M^+, 10%), 216 (15), 143 (39), 125 (9), 111 (21), 107 (14), and 91 (100); δ_H ($CDCl_3$) 2.69 (1 H, m, $J_{8,9}$ 5, $J_{8,12}$ 1.5 Hz, 8-H), 2.70 (1 H, m, J_{12,CH_2} 7 + 8 Hz, 12-H), 4.46 (1 H, m, $J_{10,11}$ 1.5 + 2, $J_{11,12}$ 2 Hz, 11-H), 4.72 (1 H, m, $J_{9,10}$ 3.5 + 0.5, $J_{9,11}$ 2 Hz, 9-H), 4.95 (1 H, d, $J_{7,8}$ 0.5, 7-H), 2.04 (3 H, s, $OCOCH_3$), 3.23 (2 H, m, J_{gem} 10 Hz, CH_2O), 3.64 (3 H, s, CO_2CH_3), 4.46 (2 H, s, OCH_2Ph), and 7.28 (5 H, aromatic); δ_C ($CDCl_3$) 173.94 (C-1), 33.98 (C-2), 25.19 (C-3), 22.88 (C-4), 30.99 (C-5), 107.86 (C-6), 81.55 (C-7), 45.90 (C-8), 79.14 (C-9), 36.48 (C-10), 78.65 (C-11), 51.22 (C-12), 69.81 (CH_2O), 73.09 (OCH_2Ph), 51.37 (CO_2CH_3), 170.21 + 21.13 ($OCOCH_3$),

127.58, 127.78, 128.48, and 138.08 (aromatic). Further elution with the same solvent gave 7-benzyloxylmethyl-2-hydroxy-2-(4-methoxycarbonylbutyl)-3,9-dioxatricyclo-[4.2.1.$0^{4,8}$]nonane (7a, b) (467 mg, 45%), as an oil; $\nu_{max.}$ 3 350 (OH) and 1 730 cm^{-1} (C=O); δ_H ($CDCl_3$) 2.85 + 3.04 (1 H, m, $J_{8.9}$ 4.5 Hz, $J_{8.12}$ 1.5 Hz, H-8), 2.65 + 2.71 (1 H, m, $J_{12.CH_2}$ 7.5 + 7.5 Hz, H-12), 3.90 + 3.93 (1 H, dd, $J_{7.8}$ 3, $J_{7.9}$ 1 Hz, H-7), 4.18 + 4.4 (1 H, m, $J_{9.10}$ 6 + 2 Hz, 9-H), 4.27 (1 H, m, $J_{10.11}$ 1.5 + 1.5, $J_{11.12}$ 1.5 Hz, 11-H), 3.27 (2 H, m, J_{gem} 10.5 Hz, CH_2O), 3.59 (3 H, s, CO_2CH_3), 4.41 (2 H, s, OCH_2Ph), and 7.32 (5 H, aromatic).

Reaction of Diol (5) *with Thallium Triacetate*.—Thallium triacetate (3.7 g) in acetic acid (60 ml) was added to a solution of diol (5) (1 g) in acetic acid (30 ml) and the solution was stirred for 24 h at room temperature. Following the usual work-up the crude product (1.26 g) was chromatographed on silica (150 g). Elution with ethyl acetate–hexane (1 : 2) gave 2-acetoxy-4-benzyloxymethyl-1-ethyl-8,9-dioxatricyclo[3.3.1.$0^{3,7}$]nonane (9) (221 mg, 17%) as an oil, homogeneous by t.l.c. [ethyl acetate–hexane (1 : 2)]; $\nu_{max.}$ 1 725 cm^{-1} (C=O); δ_H ($CDCl_3$); 0.93 (3 H, t, $J_{4.5}$ 7.5 Hz, 4-H), 2.69 (1 H, m, $J_{8.9}$ 4.5, $J_{8.12}$ 1.5 Hz, H-8), 2.71 (1 H, m, $J_{12.CH_2}$ 7 + 8 Hz, 12-H), 4.46 (1 H, m, $J_{10.11}$ = $J_{11.12}$ = 1.5 + 2 Hz, 11-H), 4.72 (1 H, m, $J_{9.10}$ 4.5 + 1.5 Hz, 9-H), 4.97 (1 H, d, $J_{7.8}$ 0.5 Hz, 7-H), 2.04 (3 H, s, $OCOCH_3$), 3.23 (2 H, m, J_{gem} 10 Hz, CH_2O), 4.46 (2 H, s, OCH_2Ph), and 7.30 (5 H, aromatic). Further elution with the same solvent gave 7-benzyloxymethyl-2-ethyl-2-hydroxy-3,9-dioxatricyclo[4.2.1.$0^{4,8}$]nonane (10a, b) (401 mg, 38%) as an oil, homogeneous by t.l.c. [ethyl acetate–hexane (1 : 2)]; $\nu_{max.}$ 3 350 cm^{-1} (OH); δ_H ($CDCl_3$) 0.96 + 1.0 (3 H, t, $J_{4.5}$ 7.5 Hz, 4-H), 2.92 + 3.12 (1 H, m, $J_{8.9}$ 4, $J_{8.12}$ 1.5 Hz, 8-H), 2.73 + 2.78 (1 H, m, $J_{12.CH_2}$ 7.5 + 8, 12-H), 3.98 + 4.02 (1 H, dd, $J_{7.8}$ 3, $J_{7.9}$ 1 Hz, 7-H), 4.35 (1 H, m, $J_{10.11}$ = $J_{11.12}$ = 1.5 Hz, 11-H), 4.51 (1 H, m, $J_{9,10}$ 6 + 2 Hz, H-9), 3.35 (2 H, m, J_{gem} 10 Hz, CH_2O), 4.47 (2 H, s, OCH_2Ph), and 7.30 (5 H, aromatic).

endo- *and* exo-*Methyl Acetals of* 7β-*Acetoxy*-6-*oxo*-$PGF_{1\alpha}$ *Methyl Ester* (11 and (12).—To a solution of compound (2) (1.0 g) in methanol (10 ml) a catalytic amount of boron trifluoride–ether was added. After 1 h at room temperature the solution was neutralised with sodium hydrogencarbonate, the solvent was removed, the product was diluted with ethyl acetate, washed with water, aqueous sodium hydrogencarbonate, and finally with brine, dried ($MgSO_4$), and evaporated to give a light yellow oil (980 mg). The crude product was chromatographed on silica (120 g) and elution with ethyl acetate gave *exo*-methyl acetal (12) (240 mg, 22%) as an oil, homogeneous by t.l.c. (ethyl acetate). Further elution with the same solvent gave *endo*-methyl acetal (11) (680 mg, 63%) as an oil, homogeneous by t.l.c. (ethyl acetate). Treatment of *endo*-methyl acetal (11) with acetic anhydride in pyridine yielded the triacetate (11a) as an oil; δ_H ($CDCl_3$) 3.01 (1 H, m, $J_{8.12}$ 10, $J_{11.12}$ 10, $J_{12.13}$ 4 Hz, 12-H), 4.60 (1 H, m, $J_{8.9}$ 7.5, $J_{9.10}$ 5.5 + 8 Hz, 9-H), 4.73 (1 H, m, $J_{10.11}$ 7 + 10, $J_{11.12}$ 10 Hz, 11-H), 4.99 (1 H, d, $J_{7.8}$ 0.5 Hz, 7-H), 5.14 (1 H, m, $J_{14.15}$ 5.5, $J_{15,16}$ 6 + 6 Hz, 15-H), 5.54 (2 H, m, H-13 + -14), 3.59 (3 H, s, CO_2CH_3), and 3.17 (3 H, s, OCH_3). Similar treatment of *exo*-methyl acetal (12) gave the triacetate (12a) as an oil; δ_H ($CDCl_3$) 2.66 (1 H, m, $J_{8.9}$ 7, $J_{8.12}$ 3.5 Hz, 8-H), 3.00 (1 H, m, $J_{11.12}$ 5, $J_{12.13}$ 4 Hz, 12-H), 4.62 (1 H, m, $J_{9.10}$ 3 + 7 Hz, 9-H), 4.99 (1 H, m, $J_{10.11}$ 4.5 + 4 Hz, 11-H), 5.18 (1 H, m, $J_{14.15}$ 5.5, $J_{15.16}$ 6 + 6 Hz, 15-H), 5.23 (1 H, d, $J_{7.8}$ 6 Hz, 7-H), 5.55 (2 H, m, H-13 + -14), 3.66 (3 H, s, CO_2CH_3), and 3.27 (3 H, s, OCH_3).

6,9α;7,11α-*Dioxido*-15S-*hydroxy*-6-endo-*methoxyprost*-13E-*enoic Acid Methyl Ester* (13b) *and* 15S-*Acetoxy*-6,9α;7,11α-*dioxido*-6-endo-*methoxyprost*-13E-*enoic Acid Methyl Ester* (14b).—To a solution of compound (3a, b) (1 g) in methanol (10 ml) a catalytic amount of boron trifluoride–ether was added. After 1 h at 25 °C the solution was worked up as in the previous example. The crude product (1.1 g) was chromatographed on silica (100 g) with ethyl acetate–hexane (1 : 1). Elution gave the *endo*-methyl acetal (13b) (600 mg, 58%) as an oil; *m/e* 396 (M^+), 365 (60%), and 281 (100); $\nu_{max.}$ 3 350 (OH) and 1 730 cm^{-1} (C=O); δ_H ($CDCl_3$) 3.60 (3 H, s, $COOCH_3$) and 3.12 (3 H, s, OCH_3). Treatment of the methyl acetal (13b) (70 mg) with an excess of acetic anhydride in pyridine at 25 °C for 30 min furnished the acetate (14b). The mixture was diluted with water (5 ml), extracted with ether (3 × 5 ml), and the ethereal solution was washed with dilute hydrochloric acid and brine, dried ($MgSO_4$), and evaporated to give crude (14b) as a yellow oil. The product was chromatographed on silica (8 g) with ethyl acetate–hexane (1 : 1) to give pure (14b) (65 mg, 84%) as an oil, *m/e* 438 (M^+, 0.7%), 407 (30), 323 (43), 222 (100), 204 (34), 175 (33), and 133 (19); δ_H ($CDCl_3$) 2.88 (1 H, m, $J_{8.9}$ 4.5, $J_{8,12}$ 1 Hz, 8-H), 3.02 (1 H, m, $J_{12.13}$ 3.5 Hz, 12-H), 4.07 (1 H, m, $J_{10.11}$ = $J_{11.12}$ = 1.5 Hz, 11-H), 4.48 (1 H, m, $J_{9.10}$ 6.5 + 1, $J_{9.11}$ 1 Hz, 9-H), 3.70 (1 H, dd, $J_{7.8}$ 3, $J_{7.9}$ 0.5 Hz, 7-H), 5.4 (1 H, dd, $J_{13.14}$ 15 Hz, 13-H), 5.5 (1 H, dd, $J_{14.15}$ 7 Hz, 14-H), 5.06 (1 H, m, $J_{15.16}$ 6 + 6 Hz, 15-H), 3.57 (3 H, s, CO_2CH_3), 3.11 (3 H, s, OCH_3), and 1.94 (3 H, s, $OCOCH_3$).

6-*Hydroxy*-7,11α-*oxido*-11-*deoxy*-$PGF_{1\alpha}$ *Methyl Ester* (17a,b). Sodium borohydride (5—6 equiv.) was added to a solution of (3a, b) (100 mg) in ethanol (4 ml) at 0 °C. After 24 h the excess of reagent was destroyed with acetic acid. The solvent was removed, the residue was diluted with water, extracted with ethyl acetate, washed with brine, dried ($MgSO_4$), and evaporated. The crude material (105 mg) was chromatographed on silica (20 g). Elution with ethyl acetate-hexane (3 : 1) gave first ester (17a) (20 mg, 20%), and then (17b) (14 mg, 14%), epimers of unknown relative configuration at C(6), as oils, homogeneous by t.l.c.; $\nu_{max.}$ 3 370 (OH) and 1 735 cm^{-1} (C=O); *m/e* 384 (M^+); (17b) δ_H ($CDCl_3$) 2.40 (1 H, m, $J_{8.9}$ 4 Hz, $J_{8.12}$ 1 Hz, 8-H), 2.97 (1 H, m, $J_{12.13}$ 2 Hz, 12-H), 4.17 (1 H, m, $J_{10.11}$ 2 + 0.5, $J_{11.12}$ 2 Hz, 11-H), 4.40 (1 H, m, $J_{9.10}$ 9.5 + 5 Hz, 9-H), 3.97 (1 H, m, $J_{7.8}$ 2, $J_{7.9}$ 1.5 Hz, 7-H), 3.97 (1 H, m, $J_{6.7}$ 10.5 Hz, 6-H), 5.57 (1 H, m, $J_{13.14}$ 15.5 Hz, 13-H), 5.65 (1 H, m, $J_{14.15}$ 4.5, 14-H), 4.05 (1 H, m, $J_{15.16}$ 5 + 6 Hz, 15-H), and 3.66 (3 H, s, CO_2CH_3). Treatment of triol (17a) with acetic anhydride in pyridine yielded the triacetate (17c) as an oil (80%). Similar treatment of triol (17b) with acetic anhydride yielded the triacetate (17d) (75%) together with some 9,15-diacetate (17e) as oils: (17d) δ_H ($CDCl_3$) 2.61 (1 H, m, $J_{8.9}$ 4, $J_{8.12}$ 1 Hz, 8-H), 3.03 (1 H, m, $J_{12.13}$ 2 Hz, 12-H), 4.18 (1 H, m, $J_{10.11}$ 2 + 0.5, $J_{11.12}$ 2 Hz, 11-H), 5.2 (1 H, m, $J_{9.10}$ 9.5 + 5 Hz, 9-H), 4.05 (1 H, m, $J_{7.8}$ 2, $J_{7.9}$ 2 Hz, 7-H), 5.2 (1 H, m, $J_{6.7}$ 11 Hz, 6-H), 5.62 (2 H, m, H-13 + -14), 5.2 (1 H, m, $J_{15.16}$ 5 + 6 Hz, 15-H), 2.02 (3 H, s, $OCOCH_3$), 2.06 (3 H, s, $OCOCH_3$), 2.08 (3 H, s, $OCOCH_3$), and 3.65 (3 H, s, $COOCH_3$); (17e) δ_H (C_6D_6) 2.74 (1 H, m, $J_{8.9}$ 4, $J_{8,12}$ 1 Hz, 8-H), 2.87 (1 H, m, $J_{12.13}$ 2 Hz, 12-H), 3.97 (1 H, m, $J_{10.11}$ 2 + 0.5, $J_{11.12}$ 2 Hz, 11-H), 5.4 (1 H, m, $J_{9.10}$ 9.5 + 5 Hz, 9-H), 3.69 (1 H, m, $J_{7.8}$ 2, $J_{7.9}$ 1.5 Hz,

7-H), 4.08 (1 H, m, $J_{6,7}$ 10.5 Hz, 6-H), 5.50 (2 H, m, H-13 + -14), 5.6 (1 H, m, 15-H), 1.73 (3 H, s, $OCOCH_3$), 1.79 (3 H, s, $OCOCH_3$), and 3.47 (3 H, s, $OCOCH_3$).

Reaction of 2-cis-(*But*-2*Z*-*enyl*)*cyclopentanol* (18) *with Thallium Triacetate.*—Thallium triacetate (17.05 g) in acetic acid (175 ml) was added to a solution of compound (18) (2.5 g) in acetic acid (25 ml) and the solution was stirred for 4 h at room temperature. The solvent was evaporated (at 1 mmHg), diluted with water (100 ml), stirred for 30 min, and extracted with ethyl acetate (6 × 40 ml). The combined solutions were washed with saturated aqueous sodium hydrogencarbonate and brine, dried (Na_2SO_4), and evaporated. The crude product (3 g) was chromatographed on silica (300 g). Elution with hexane–ethyl acetate (3 : 1) gave a mixture of two compounds (22) and (23a, b) (340 mg). Further elution with the same solvent gave 3-(1-acetoxyethyl)-3α,β-hydroxy-2-oxabicyclo[3.3.0]-octane (20a, b) (1.96 g, 60%) as an oil; $\nu_{max.}$ 3 350 (OH) and 1 738 cm^{-1} (C=O); On treatment of (20a, b) (200 mg) with methanol (10 ml) in the presence of boron trifluoride–ether for 1 h at room temperature followed by the usual work-up the 3-(1-acetoxyethyl)-3α,β-methoxy-2-oxabicyclo[3.3.0]-octane (21a, b) was obtained as an oil, homogeneous by t.l.c. [hexane–ethyl acetate (4 : 1)]; $\nu_{max.}$ 1 735 cm^{-1} (C=O); δ_H ($CDCl_3$) 1.23 + 1.21 * (3 H, d, $J_{2,1}$ 6.5 Hz, 2′-H), 5.28 + 5.27 * (1 H, q, 1′-H), 1.73 + 2.18 (2 H, m, $J_{4,4}$ 13, $J_{4,5}$ 7.5 + 3.5 Hz, 4-H), 2.81 (1 H, m, $J_{1,5}$ 5 Hz, 5-H), 4.47 + 4.60 * (1 H, m, 1-H), 3.21 + 3.24 * (3 H, s, OCH_3), and 2.04 + 2.05 * (3 H, s, $OCOCH_3$).

A mixture of compounds (22) and (23a, b) was rechromatographed on silica (50 g) and elution with dichloromethane–acetone (15 : 1) gave 3-acetyl-3α,β-hydroxy-2-oxabicyclo[3.3.0]octane (23a, b) (55 mg, 2%) as an oil, homogeneous by t.l.c. [dichloromethane–acetone (15 : 1)]; $\nu_{max.}$ 3 340 (OH) and 1 720 cm^{-1} (C=O); δ_H(C_6D_6) 1.92 + 1.85 * (3 H, s, $COCH_3$), 2.58 + 2.25 * (1 H, m, $J_{1,5}$ 7 Hz, 5-H), 4.58 + 4.40 * (1 H, m, $J_{1,8}$ 5 + 1 Hz, H-1); δ_C (C_6D_6) 23.01 + 22.51 * (C-2′), 205.40 (C-1′), 105.90 (C-3), 43.23 + 42.41 * (C-4), 42.08 + 35.05 * (C-5), 86.44 + 88.85 * (C-1), 33.15 + 30.15 * (C-8), 23.83 + 24.38 * (C-7), and 33.69 + 32.69 * p.p.m. (C-6).

Further elution with the same solvent gave 3-hydroxy-4-methyl-2-oxabicyclo[4.3.0]nonane (22) (150 mg, 8%) as an oil, homogeneous by t.l.c. [dichloromethane–acetone (15 : 1)]; δ_H ($CDCl_3$) 0.88 + 0.91 + 0.94 (3 H, d, CH_3), 4.11 + 4.67 + 4.87 (1 H, dd, $J_{3,4}$ 7.5 + 6 + 2, $J_{3,OH}$ 2.5 + 2 + 5 Hz, 3-H), 3.74 + 4.30 + 4.31 (1 H, m, 1-H), and 2.57 + 2.80 + 3.04 (1 H, d, OH); δ_C (C_6D_6) 94.85 + 99.32 + 101.08 (C-3), 39.67 + 39.99 + 40.44 (C-4), 33.14 + 33.42 + 33.42 (C-5), 29.04 + 32.09 + 35.64 (C-6), 71.82 + 72.10 + 79.98 (C-1), 26.95 + 27.51 + 27.51 + 32.81 + 32.81 + 32.81 (C-7 + -9), 23.00 + 23.39 + 24.27 (C-8), and 17.01 + 17.25 + 18.90 p.p.m. (CH_3).

Reaction of Compound (19) *with Thallium Triacetate.*—Thallium triacetate (2.6 g) in acetic acid (30 ml) was added to a solution of compound (19) (1.0 g) in acetic acid (30 ml). After 24 h the usual work-up gave the crude product (1.33 g) which was chromatographed on silica (100 g). Elution with hexane-ethyl acetate 2 : 1 gave the isomers of 3-hydroxy-4-(3′-methoxycarbonylpropyl)-2-oxabicyclo[4.3.0]nonane (25) (118 mg, 11%) as an oil; $\nu_{max.}$ 3 340 (OH) and 1 735 cm^{-1} (C=O). Treatment of (25) (50 mg) with methanol (2 ml) in the presence of boron trifluoride–ether gave the methyl acetal of (25) as an oil; $\nu_{max.}$ 1 737 cm^{-1} (C=O); δ_H ($CDCl_3$) 3.88 + 4.26 + 4.45 (1 H, d, $J_{3,4}$ 7.5 + 5.5 + 2 Hz, 3-H), 3.90 + 4.05 + 4.12 (1 H, m, 1-H), 3.65 (3 H, s, CO_2CH_3), and 3.34 + 3.35 + 3.42 (3 H, s, OCH_3). Further elution with the same solvent gave 3-(1′acetoxy-4′-methoxycarbonylbutyl)-3α,β-hydroxy-2-oxabicyclo[3.3.0]octane (24a, b) (178 mg, 13%) as an oil, homogeneous by t.l.c. [hexane–ethyl acetate (2 : 1)]; $\nu_{max.}$ 3 350 (OH) and 1 730br cm^{-1} (C=O); δ_H ($CDCl_3$) 2.7—2.9 (1 H, m, 5-H), 4.94 + 5.00 (1 H, m, 1-H) 4.68 + 4.71 (1 H, m, 1-H), 2.04 + 2.06 (3 H, s, $OCOCH_3$), and 3.64 (3 H, s, CO_2CH_3). On treatment of (24a, b) (50 mg) with methanol (2 ml) in the presence of boron trifluoride–ether the methyl acetal of (24a, b) was obtained, $\nu_{max.}$ 1 735 cm^{-1} (C=O); δ_H ($CDCl_3$) 2.65—2.85 (1 H, m, $J_{1,5}$ 5 Hz, 5-H), 5.19 + 5.21 (1 H, m, $J_{1,2}$ 4 + 7.5 Hz, 1-H), 4.51 + 4.54 (1 H, m, 1-H), 2.02 + 2.03 (3 H, s, OAc), 3.66 (3 H, s, CO_2CH_3), and 3.17 + 3.21 (3 H, s, OCH_3).

* Denotes minor component.

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