Tautomerism of the Enedione System of 15-Oxoprostaglandin D_2

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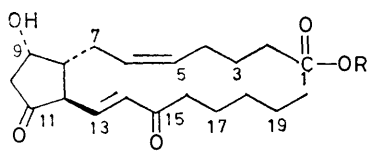
Oxidation of prostaglandin $F_{2\alpha}$ methyl ester by chromic acid yielded 15-oxoprostaglandin D_2 methyl ester and the *Z*- and *E*-tautomers of the isomeric 12-ene, which were separated by partition chromatography and characterized. After equilibration in acidified water the relative proportions of (*Z*)-12-ene, (*E*)-13-ene, and (*E*)-12-ene were 1.0 : 0.88 : 0.89. In contrast, the proportions of the corresponding isomers of the simpler 1-(2-oxocyclopentyl)oct-1-en-3-one were 1.0 : <0.02 : 5.7, indicating that the side chain at C-8 in the prostaglandin markedly affects the equilibrium position. In both systems the contribution from enolic forms was small.

We have been interested recently in the biological properties of certain 15-oxoprostaglandins (15-oxo-PGs).[1] In particular we wished to study 15-oxo-PGD_2 (1a).† This substance contains an enedione system susceptible to keto–enol tautomerism and movement of the 13,14-double bond into the 12,13-position. In addition the β-ketol ring system of (1a) may readily undergo dehydration to the αβ-unsaturated ketone (*cf.* dehydration of PGE to PGA compounds [2]).



(1) a; R = H
b; R = Me

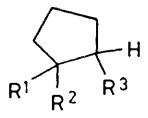
For comparison we attempted to prepare a model compound (1*E*)-1-(2-oxocyclopentyl)oct-1-en-3-one (15) by deacetalization of either of the acetals (6) and (14). These acetals were prepared *via* intermediates (2)—(5) and (7)—(13), respectively. The acetal (6) required refluxing with either toluene-*p*-sulphonic acid in acetone or oxalic acid in acetone–water for cleavage to occur. Analysis by high performance liquid chromatography (h.p.l.c.) with detection by u.v. illumination revealed no trace of the enedione (15) during the reaction, and the product was a mixture of the enediones (17a and b). This material was also obtained by deacetalization of the very acid-labile (16), easily obtained by deconjugation of (6).[3]

The acetal group in (14) was more readily cleaved.[4] In water, at room temperature, an immediate u.v. scan following addition of 0.01N-HCl revealed a chromophore with $\lambda_{max.}$ 234 nm. Subsequent scans at 2 min intervals showed an increase in intensity of the chromophore coupled with a regular shift of the wavelength maximum. After 15 min the process was complete and $\lambda_{max.}$ was 247 nm. Similar results were obtained with 0.01N-HCl and 5% H_2O in MeOH ($\lambda_{max.}$ 230 nm after 1 min shifting to 243 nm after 15 min). Addition of base after either 1 or 15 min gave a strong 415 nm (lime-green) absorption due to the enolate ion (20). Attempts were made to isolate the 1 min incubation product, presumably (15),

† (5*Z*,13*E*)-9α-Hydroxy-11,15-dioxoprosta-5,13-dienoic acid.

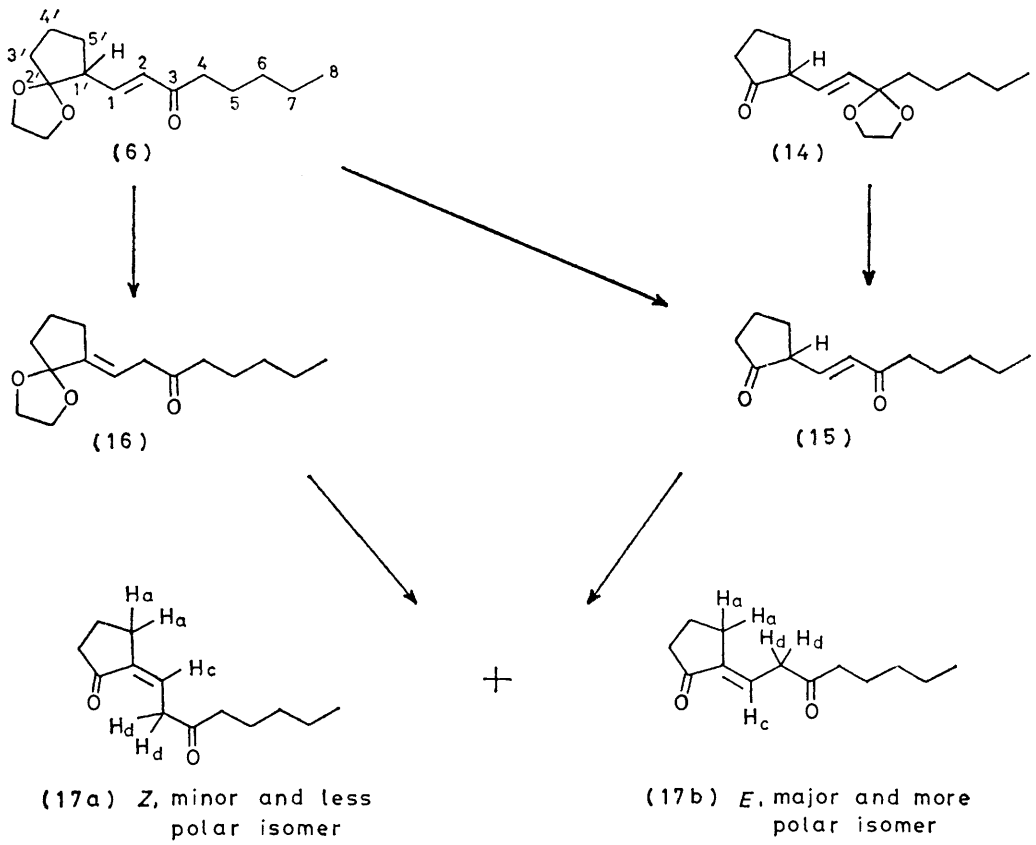
[1] R. L. Jones, *Acta Biol. Med. Germ.*, 1976, **35**, 1091.
[2] N. H. Andersen, *J. Lipid Res.*, 1969, **10**, 320.
[3] H. J. Ringold and S. K. Malhotra, *J. Amer. Chem. Soc.*, 1965, **87**, 3228, and references therein.
[4] J. J. Brown, R. H. Lenard, and S. Bernstein *J. Amer. Chem. Soc.*, 1964, **86**, 2183.

by extraction into ether. Subsequent analysis however revealed only the presence of (17a and b) and unchanged (14). A similar result was obtained when transacetalization with oxalic acid in acetone was carried out. It H.p.l.c. was used to assess purity. Compounds (17a and b) have identical u.v. spectra and very similar i.r. spectra. However ^{1}H n.m.r. spectroscopy enabled the isomers to be distinguished. The less polar enedione



	R^1 R^2	R^3
(2)	O	CO_2Et
(3)	$O[CH_2]_2O$	CO_2Et
(4)	$O[CH_2]_2O$	CH_2OH
(5)	$O[CH_2]_2O$	CHO

	R^1	R^2	R^3
(7)	OH	H	CO_2Et
(8)	OThp	H	CO_2Et
(9)	OThp	H	CH_2OH
(10)	OThp	H	CHO
(11)	OThp	H	CH:CH·CO·C_5H_{11}
(12)	OH	H	CH:CH·CO·C_5H_{11}
(13)	OH	H	CH:CH·C·C_5H_{11}



The protons on C-5′, -1′, -1, and -2 are referred to as H_a, H_b, H_c, and H_d in all compounds shown above

appears therefore that (15) is highly labile and readily rearranges to (17a and b).

The ratio of (17a) to (17b) after acid-catalysed deacetalization was consistently 1 : 7 or 1 : 8. The isomers were separated by straight-phase partition chromatography with lipophilic stationary and moving phases. showed one olefinic proton signal at δ 6.2 (tt) whereas that of the more polar enedione was at δ 6.7 (tt); the C-2 methylene signals are at δ 3.85 and 3.25, respectively. Hence the less polar ene-dione has the *Z*-configuration (17a) and the more polar enedione the *E*-configuration (17b), since the ring carbonyl group deshields the olefinic

proton in (17b) but not in (17a), and deshields the methylene protons in (17a) but not in (17b).[5] In addition the allylic coupling constants (J_{ac}) for the less and the more polar diones are 2.25 and 2.75 Hz, respectively. Since $J(transoid) > J(cisoid)$ by *ca.* 0.4 Hz in cyclic systems,[5] this confirms the previous assignment. Interconversion of the resolved enediones occurs rapidly in acidic aqueous solution and at equilibrium the ratio of (17a) to (17b) was estimated to be 1 : 6.1 by h.p.l.c. (Table). No peak corresponding to the (1*E*)-isomer (15) was detected.

Relative proportions of enedione isomers

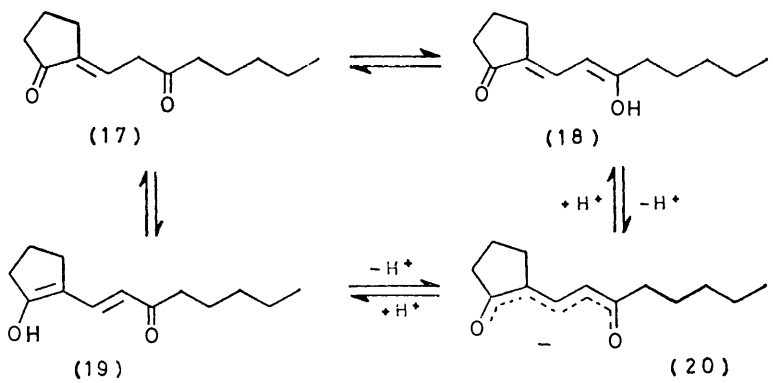
Compound	Treatment		Proportions of isomers † 1(1′)*Z*	1(2)*E*	1(1′)*E*
(*E*)-1-(2-Oxocyclopentyl)oct-1-en-3-one (15)	(A) Deacetalization of (6) with aq. 0.1N-HCl or (14) with aq. 0.01N-HCl		1.0	<0.02	7.9
			1.0	<0.02	7.1
	(B) Aq. 0.1% AcOH for 1 h at 25 °C		1.0	<0.02	5.7
	(C) 0.01N-KOH in H_2O for 5 min at 25 °C, neutralization, and extraction with ether		1.0	<0.02	6.1
			12*Z*	13*E*	12*E*
15-Oxo-PGD_2 methyl ester	(D) Oxidn. by CrO_3, extraction with ether, and liquid-gel chromatography	Expt. 1	1.0	4.0	0.50
		Expt. 2	1.0	4.3	0.90
		Expt. 3	1.0	0.66	0.25
	(B) for 1 h at 25 °C		1.0	0.88	0.89
	(C)		1.0	0.70	0.62
15-Oxo-PGD_2	(D)		1.0	3.2	0.51
	(B)		1.0	0.57	0.53
	(C)		1.0	0.48	0.41

† Relative proportions determined by h.p.l.c. with detection by u.v. illumination.

The absence of a maximum between 300 and 350 nm in the u.v. spectra of (17a) and (17b) in water, dichloromethane, dioxan, or n-hexane indicates that there is negligible conjugated enol contribution in these solvents. In both methanol and ethanol however there is a significant absorption at 334 nm, consistent [6] with structure (18) or (19). If we assume an $\varepsilon_{max.}$ value of 15 000 for these species, the enol contribution to (17) in these solvents is *ca.* 10%. It is of interest to compare these results with those for the enedione system in cholest-4-ene-3,7-dione, which exists almost entirely as 3-hydroxycholesta-3,5-dien-7-one [$\lambda_{max.}$ 322 nm (ε 13 500)].[7]

The addition of base to either (17a) or (17b) gives an immediate and stable 415 nm chromophore. This is presumably due to the enolate ion (20). Neutralization with discharge of the green chromophore gives an intense, but transient, 337 nm chromophore (ε *ca.* 11 000). This is due to rapid protonation on oxygen to give a conjugated enol, (18) and/or (19). With loss of the 337 nm chromophore, the 243 nm chromophore due to the αβ-enone in (17a and b) is re-established. The sequence can be repeated with little loss of material.

Treatment of (17b) in methanol–diethyl ether with an excess of diazomethane gave two products. The minor product is an enol methyl ether [$\lambda_{max.}$ (MeOH) 330 nm (ε 13 300)] from addition of diazomethane to an enolic OH [*cf.* 3-methoxycholesta-3,5-dien-7-one, $\lambda_{max.}$ (EtOH) 310 nm (ε 13 800) [7]]. The i.r. spectrum shows $\nu_{C=O}$ 1 708 cm^{-1} and a very strong $\nu_{C=C}$ band at 1 610 cm^{-1}, consistent with structure (21) since $\nu_{C=O}$ in (22) would be expected to be *ca.* 1 670 cm^{-1}. The mass spectrum of the isolated enol ether (M^+ 222) shows intense peaks at *m/e*



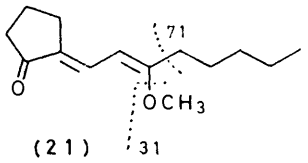
191 (M − 31) and 151 (M − 71) (base peak) and no loss of 99 m.u. from the molecular ion. The *O*-n-butyloxime derivative (M^+ 293) shows intense peaks at *m/e* 262 (M − 31) and 222 (M − 71). Cleavage α to the oxime group to lose the terminal C_5 unit (M − 71) is not favoured [study of alkyloxime derivatives of (6), (14), and 15-oxo-PGs] and therefore these data also support structure (21). Compounds with properties identical

[5] S. D. Brookes, S. Sternhell, B. K. Tidd, and W. B. Turner, *Austral. J. Chem.*, 1965, **18**, 373.

[6] L. F. Fieser and M. Fieser, 'Steroids,' Rheinhold, New York, 1959.

[7] C. W. Greenhalgh, H. B. Henbest, and E. R. H. Jones, *J. Chem. Soc.*, 1952, 2378; J. Barnett, B. E. Ryman, and F. Smith *ibid*, 1946, 526.

with those of (21) can also be derived from either (6) or (14) by treatment with 0.05N- and 0.01N-HCl respectively in pure methanol. Transacetalization and elimination of a molecule of methanol would account for these substances.



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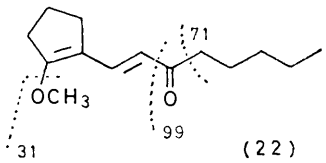

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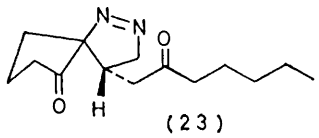


(23)

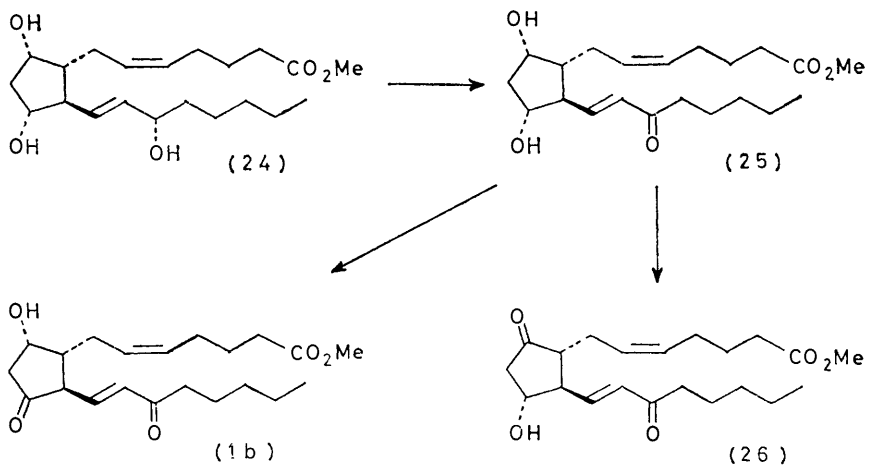
The major product from treatment of (17b) with diazomethane (and the only one formed if the reaction is carried out in pure diethyl ether) is a pyrazoline (23) formed by 1,3-dipolar addition [$\lambda_{max.}$ (MeOH) 324 nm (ε 300); $\nu_{max.}$ (film) 1 750 and 1 715 (C=O), and 1 550 cm^{-1} (N=N)].[8] This compound was not fully characterized.

Careful oxidation of $PGF_{2\alpha}$ methyl ester (24) with chromic acid results in rapid oxidation of the allylic 15-hydroxy-group followed by oxidation of the ring hydroxy-substituents. The products, 15-oxo-PGD_2 (1b), 15-oxo-PGE_2 (26), and 15-oxo-$PGF_{2\alpha}$ (25) methyl esters, were separated by liquid-gel partition chromatography.

u.v. and i.r. data were obtained for the pure compound, its n.m.r. spectrum was difficult to interpret. This was due to the small quantity of material available (re-chromatography was necessary to remove traces of 15-oxo-PGE_2) and to some isomerization to the other two isomers.

In two of three chromic acid oxidations performed on $PGF_{2\alpha}$ methyl ester the major substance isolated was the (*E*)-13-ene, whereas in the other the (*Z*)-12-ene predominated. As with the model compound, equilibration of the separate isomers was complete after treatment with aqueous 0.1% acetic acid for 1 h at 25 °C; a slight excess of the (*Z*)-12-ene isomer was found (Table). It appears therefore that in two instances the kinetic product of the chromic acid oxidation was isolated with little equilibration having taken place during the reaction and subsequent extraction. Equilibration of the system with base, followed by rapid neutralization at 0 °C and extraction into ether, also produced the (*Z*)-12-ene as the major component.

The 15-oxo-PGD_2 free acid isomers could be separated by chromatography with liphophilic solvent mixtures containing a trace of acetic acid. However, evaporation of the eluate resulted in concentration of the acetic acid and consequent equilibration of the isomers. The tautomer identification is based solely on u.v. and h.p.l.c. measurements in comparison with the methyl ester. The Table shows that 15-oxo-PGD_2 (13*E*) was the major isomer produced and that after equilibration the isomer ratios are similar to those for the methyl ester.



The first three zones, a—c, contained isomers of 15-oxo-PGD_2 methyl ester, each giving an immediate and stable 415 nm chromophore in methanolic base, and bis-(*O*-n-butyloxime) and trimethylsilyl derivatives identical by g.l.c.–mass spectrometry. Zone d contained 15-oxo-PGE_2 (500 nm chromophore in base [9]) and zone e 15-oxo-$PGF_{2\alpha}$ (no change with base).

Zones a and b contained the (*Z*)-12-ene-11,15-dione and the (*E*)-13-ene-11,15-dione, respectively (from analysis of u.v., i.r., and n.m.r. spectra). Zone c probably contained the (*E*)-12-ene-11,15-dione: although

The differences in the tautomer ratios at equilibrium between the model cyclopentanone–octenone system and the prostaglandin system must be attributable to the presence of the side chain at C-8. Thus in the (12*E*)-, but not the (12*Z*)- or (13*E*)-prostaglandin isomer, there is considerable interaction between the two side chains. This accounts for the finding that the (12*E*)-prostaglandin isomer is less favoured than the corresponding

[8] T. V. Van Auken and K. L. Rinehart, jun., *J. Amer. Chem. Soc.*, 1962, **84**, 3736.

[9] E. Ånggård and B. Samuelsson, *Arkiv Kemi*, 1966, **25**, 293.

isomer in the model enedione and that an appreciable amount of (13*E*)-prostaglandin isomer is present.

EXPERIMENTAL

U.v. and i.r. spectra were measured with Cary 118C and Perkin-Elmer 237 spectrophotometers, respectively. N.m.r. spectra were measured with a Varian HA 100 spectrometer, with tetramethylsilane as internal standard. G.l.c.–mass spectrometry was performed on all products and intermediates using an LKB 9000 spectrometer (3 m, 3% OV1 column). *O*-n-Butyloxime derivatives were prepared by heating with an excess of n-butylhydroxylamine hydrochloride in dry pyridine at 60 °C for 1 h and trimethylsilyl derivatives by heating with bis(trimethylsilyl)trifluoroacetamide at 60 °C for 15 min. ' Carbon values ' relate to the retention times of the C_{16} to C_{26} straight-chain fatty acid methyl esters.

Liquid-gel partition chromatography was carried out with N1114-51%-LH-20 gel, 50 ± 5 μm particle size (equivalent in polarity to the commercially available Lipidex 5000) in n-hexane–dichloroethane.[10] High performance liquid chromatography (h.p.l.c.) was performed with a Dupont 848 instrument using a Zorbax ODS column and n-hexane–propan-2-ol (10 : 1) as eluant. All compounds were subjected to t.l.c. on Keiselgel G plates, followed by treatment with phosphomolybdic acid (110 °C for 15 min) to assess purity.

2,2-*Ethylenedioxycyclopentanecarbaldehyde* (5).—Ethyl 2-oxocyclopentanecarboxylate (2) (50 g) was acetalized by boiling in benzene (300 ml) with ethylene glycol (20 g) and a trace of toluene-*p*-sulphonic acid, under a Dean–Stark head. The mixture was poured into aqueous 5% sodium hydroxide and the organic phase was separated, washed, and dried ($MgSO_4$). The acetal (3) was added slowly to an excess of lithium aluminium hydride (8.0 g) in ether (300 ml). After the initial reaction the mixture was boiled a further 30 min, and then wet ether was added to remove the excess of hydride. The inorganic salts were precipitated with aqueous 5% sodium hydroxide. Anhydrous magnesium sulphate was added after 30 min and the clear ethereal solution was filtered. Evaporation left the pure (g.l.c.) alcohol (4) (yield 85%), which was employed directly in the next stage. Pyridinium chlorochromate (41 g), and anhydrous sodium acetate (3.1 g) were stirred in dry methylene chloride (200 ml). The alcohol (4) (20 g) in methylene chloride (100 ml) was added to the mixture in one portion. The mixture was stirred at room temperature for 2 h. After dilution with dry ether the solution was decanted and the black residue stirred with more ether; the ethereal solutions were combined, washed with aqueous 5% sodium hydroxide, then saturated sodium chloride solution, and evaporated to give the crude aldehyde (5). Chromatography on magnesium silicate in light petroleum gave an *oil* (12.7 g, 64%), n_D^{25} 1.475 5 (Found: C, 61.5; H, 7.9. $C_8H_{12}O_3$ requires C, 61.5; H, 7.7%), $\nu_{max.}$ (film) 1 721 cm^{-1} (C=O).

2-*Tetrahydropyranyloxycyclopentanecarbaldehyde* (10).—The oxo-ester (2) (50 g) was stirred at room temperature in ethanol (500 ml). Sodium borohydride (6.5 g) was added slowly over 2 h. After a further 1 h the mixture was poured into water, acidified, and extracted with ether. The crude alcohol (7) was treated with a 10% excess of dihydropyran in methylene chloride containing a trace of toluene-*p*-sulphonic acid to give the ether (8). Reduction with lithium aluminium hydride with alkaline work-up as before, followed by oxidation by pyridinium chlorochromate, gave the aldehyde (10). Chromatography on magnesium silicate in light petroleum gave an *oil* (18.1 g, 28.5%), n_D^{25} 1.472 0 (Found: C, 71.1; H, 9.2. $C_{11}H_{18}O_3$ requires C, 71.45; H, 9.5%), $\nu_{max.}$ (film) 1 718 cm^{-1} (C=O).

(E)-1-(2,2-*Ethylenedioxycyclopentyl*)*oct*-1-*en*-3-*one* (6).—Sodium hydride (0.48 g of 50% dispersion in oil) was washed with anhydrous light petroleum and then dissolved in 1,2-dimethoxyethane (DME) (30 ml). Dimethyl 2-oxoheptylphosphonate (2.5 g) was added in DME (10 ml) over 30 min at room temperature with stirring under dry nitrogen. After 1 h a thick precipitate had formed and the acetal aldehyde (5) (1.88 g) in DME (5 ml) was added over 30 min. The mixture was stirred for 1 h, the reaction quenched, and the product taken into ether. The material was purified by partition chromatography to give an *oil* (2.3 g, 76%), n_D^{25} 1.484 0 (Found: C, 71.4; H, 9.7. $C_{15}H_{24}O_2$ requires C, 71.45; H, 9.5%), $\lambda_{max.}$ (MeOH) 232.5 nm (ε 10 700), $\nu_{max.}$ (CCl_4) 1 680 (C=O) and 1 633 cm^{-1} (C=C), δ($CDCl_3$) 0.9 (3 H, t, Me), 1.2—2.0 (12 H, m, CH_2), 2.5 (2 H, t, $COCH_2$), 2.7 (1 H, m, CH), 3.8 (4 H, s, $O[CH_2]_2O$), 6.1 (1 H, dd, olefinic, J_{cd} 16.0, J_{bd} 1.2 Hz), and 6.8 (1 H, dd, olefinic, J_{cd} 16.0 J_{bc} 8.5 Hz).

(E)-3,3-*Ethylenedioxy*-1-(2-*oxocyclopentyl*)*oct*-1-*ene* (14).—The aldehyde (10) (12 g) underwent the Wittig reaction as above to give a 68% yield of product (11). The crude material was stirred in 50% aqueous acetic acid (40 ml) at 45 °C for 4 h. The reaction was quenched with water and the product (12) was taken into ether. The crude hydroxyenone was acetalized in the usual way and then the alcohol was oxidized with pyridinium chlorochromate and purified by partition chromatography to yield an *oil* (1.08 g, 16.5%), n_D^{25} 1.480 6 (Found: C, 71.1; H, 9.2. $C_{11}H_{28}O_3$ requires C, 71.45; H, 9.5%), ε_{210} (MeOH) 1 850, $\nu_{max.}$ (CCl_4) 1 749 cm^{-1}, δ($CDCl_3$) 0.9 (3 H, t, Me), 1.9—2.4 (12 H, m, CH_2), 2.6—2.9 (3 H, m, $CH{\cdot}CO{\cdot}CH_2$), 3.9 (4 H, s, $O[CH_2]_2O$), 5.5 (1 H, dd, olefinic, J_{cd} 16.0, J_{bd} 1.5 Hz), and 5.8 (1 H, dd, olefinic J_{cd} 16.0, J_{bc} 5.2 Hz).

(E)-(2,2-*Ethylenedioxycyclopentylidene*)*octan*-3-*one* (16).—The acetal (6) (1.0 g) was stirred at 0 °C in t-butyl alcohol (2 ml). Potassium t-butoxide [from potassium (0.165 g)] in t-butyl alcohol (5 ml) was slowly added. After 30 min the mixture was poured into ice-cold pH 6.0 acetate buffer and the product extracted into ether. Purification of the material was difficult due to ready cleavage of the acetal group (complete loss in 5 s with 0.001N-HCl). Partition chromatography with a trace of triethylamine in the eluant gave a pale yellow oil (0.51 g, 51%), ε_{210} (MeOH) 3 300, $\nu_{max.}$ (CCl_4) 1 720 cm^{-1} (C=O), δ($CDCl_3$) 0.9 (3 H, t, CH_3), 1.0—1.9 (12 H, m, CH_2), 2.4 (2 H, t, $COCH_2$), 3.1 (2 H, dt, CH_2: J_{cd} 7.3, J_{ad} 1.3 Hz), 4.0 (4 H, m, $O[CH_2]_2O$), 5.8 (1 H, tt, olefinic, J_{cd} 7.3, J_{ac} 2.7 Hz); *O*-n-butyloxime *M*, 323.

1-(2-*Oxocyclopentylidene*)*octan*-3-*one* (17a *and* b).—Deacetalization of any of the acetal ketones (6), (14), and (16) gave a mixture of (17a and b) (in >90% yield), which were separated by liquid gel partition chromatography (0.9 and 1.1 bed volumes; hexane–dichloroethane, 70 : 30); h.p.l.c. elution at 1.1 and 1.6 bed volumes [Found (for the mixture): C, 75.0; H, 9.7. Calc. for $C_{13}H_{20}O_3$: C, 75.0; H, 9.6%], n_D^{25} 1.490 9.

The *Z*-isomer (17a) showed $\lambda_{max.}$ (n-hexane) 240, $\lambda_{max.}$ (MeOH) 243 and 334 (ε 6 200 and 1 080), $\lambda_{max.}$ (MeOH +

[10] A. R. Brash and R. L. Jones, *Prostaglandins*, 1974, **5**, 441.

KOH) 415 nm (ε 26 500), $\nu_{max.}$ (CCl_4) 1 723 (C=O) and 1 650 cm^{-1} (C=C), δ($CDCl_3$) 0.9 (3 H, t, CH_3), 1.0—2.7 (14 H, m, CH_2), 3.85 (2 H, dt, CH_2, J_{cd} 7.1, J_{ad} 2.0 Hz), 6.2 (1 H, tt, olefinic, J_{cd} 7.1, J_{ac} 2.25 Hz).

The *E*-isomer (17b) showed $\lambda_{max.}$ (n-hexane) 240, $\lambda_{max.}$ (MeOH) 243 and 334 (ε 6 400 and 1 130), $\lambda_{max.}$ (MeOH + KOH) 415 nm (ε 34 100), $\nu_{max.}$ (CCl_4) 1 730 (C=O) and 1 655 cm^{-1} (C=C), δ($CDCl_3$) 0.9 (3 H, t, CH_3), 1.1—2.6 (14 H, m, CH_2), 3.25 (2 H, dt, CH_2, J_{cd} 7.5, J_{ad} 1.6 Hz), 6.7 (1 H, tt, olefinic, J_{cd} 7.5, J_{ac} 2.75 Hz).

Both (17a and b) gave a single peak ('carbon value' 17.0) on g.l.c. and identical mass spectra, *m/e* 208 (M^+). In addition each substance formed a bis-(*O*-n-butyloxime), running as one major peak on g.l.c. ('carbon value' 20.2), and having identical mass spectra, *m/e* 350 (M^+).

15-*Oxo-PGD*$_2$ *Methyl Ester* (1b).—Jones reagent (0.50 ml) was added to $PGF_{2\alpha}$ methyl ester (250 mg) in acetone (10 ml) at −30 °C and the mixture stirred for 10 min. After addition of methanol (*ca.* 1 ml), the mixture was partitioned between diethyl ether and water. The ether phase was washed with water, dried (Na_2SO_4), and evaporated. The residue was purified by liquid-gel partition chromatography (hexane–dichloroethane, 70 : 30). The following data refer to substances greater than 95% pure as judged by h.p.l.c. (elution at 1.6, 1.9 and 2.6 bed volumes).

Zone a (1.0 bed volume), $\lambda_{max.}$ (hexane) 241, $\lambda_{max.}$ (MeOH) 243, $\lambda_{max.}$ (MeOH + KOH) 415 nm (ε 35 100), $\nu_{max.}$ (CCl_4) 1 744 (CO_2Me), 1 725 (C=O), and 1 650 cm^{-1} (C=C), δ($CDCl_3$) 0.9 (3 H, t, CH_3), 1.0—3.0 (20 H, m, aliphatic), 3.6 (3 H, s, CH_3), 3.9 (2 H, m, CH_2), 4.5br (1 H, OH), 5.5 (2 H, t, olefinic, H-5 and -6, *J* 4.5 Hz), 6.2 (1 H, td, olefinic, $J_{13.14}$ 7.0, $J_{8.13}$ 2.5 Hz).

Zone b (1.3 bed volume), $\lambda_{max.}$ (hexane) 233.5 (ε 10 000), $\lambda_{max.}$ (MeOH) 236, $\lambda_{max.}$ (MeOH + KOH) 415 nm (ε 36 600), $\nu_{max.}$ (CCl_4) 1 744 (C=O and CO_2Me), 1 682 (C=O), 1 630 (C=C), and 980 cm^{-1} (C=C), δ($CDCl_3$) 0.9 (3 H, t, CH_3), 1.0—3.0 (20 H, m, aliphatic), 3.6 (3 H, s, CH_3), 4.5br (1 H, OH), 5.5 (2 H, t, olefinic, H-5 and -6, *J* 4.5 Hz), 6.2 (1 H, dd, olefinic H-14, $J_{13.14}$ 16.0, $J_{12.14}$ 0.8 Hz), 6.7 (1 H, dd, olefinic H-13, $J_{13,14}$ 16.0, $J_{12.13}$ 7.8 Hz).

Zone c (1.5 bed volume), $\lambda_{max.}$ (hexane) 239 $\lambda_{max.}$ (MeOH) 243, $\lambda_{max.}$ (MeOH + KOH) 415 nm (ε 33 000), $\nu_{max.}$ (CCl_4) 1 745sh (CO_2Me), 1 731 (C=O), and 1 655 cm^{-1} (C=C).

Material from each of these zones was converted into *O*-n-butyloximes and trimethylsilyl derivatives. Each gave 4 peaks ('carbon values' 27.4, 27.8, 28.0, and 28.6) on g.l.c. with correspondingly identical mass spectra (M^+ 578).

15-*Oxo-PGD*$_2$ (1a).—$PGF_{2\alpha}$ was treated with Jones reagent as above. The liquid-gel chromatography solvent contained 0.1% acetic acid to suppress ionization of the carboxy-group. In h.p.l.c. the enedione isomers (415 nm chromophore with base) were eluted at 1.5, 1.7, and 2.3, 15-oxo-PGE_2 at 2.0, and 15-oxo-$PGF_{2\alpha}$ at 2.8 bed volume.

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