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THE PUNAGLANDINS: 10-CHLOROPROSTANOIDS FROM THE OCTOCORAL *TELESTO RIISEI*[1]

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ABSTRACT.—*Telesto riisei*, an octocoral from Hawaii, produces nineteen highly functionalized prostanoids, the punaglandins, which are characterized by various oxygenation at C-5, -6, -7, and -12, and a 10-chloro-9-cyclopentenone moiety. The absolute stereochemistry of the 10-chloroprostanoids is epimeric to that of the Pacific marine prostanoids without halogen. The punaglandins have shown anti-inflammatory and antitumor activity. A synthetic 10-thiomethyl derivative enhances in vivo mineralization in human osteoblasts.

Perhaps no other scientific communication in the field of marine natural products generated as much interest in the ocean and its resources among biomedical researchers as Weinheimer and Spraggins's 1969 paper on the isolation of prostaglandins from a Caribbean gorgonian coral (1). Prostaglandins were available either by tedious isolation from mammalian sources, where they occur in minute concentration, or by inefficient laboratory syntheses. They were not yet available commercially, but here was a report stating that an obscure invertebrate animal, which few people had heard of and even fewer had ever seen, contained prostaglandins in excess of 1% of the dry weight of the animal. The intensive worldwide search that followed in order to discover additional marine sources of prostaglandins proved disappointing. Ten years elapsed before a new marine prostaglandin was isolated from a red alga (2). By then, numerous laboratory syntheses (3) had been fully developed and interest in natural sources of prostaglandins had waned. Then in 1982, two Japanese laboratories independently isolated from an Okinawan stoloniferous octocoral, *Clavularia viridis*, a series of prostaglandins oxygenated at C-4 and C-11, named clavulones (4) and claviridenones (5). Simultaneously, we had isolated the punaglandins,[3] highly functionalized prostaglandins, chloro-substituted at C-10, from a telestacean octocoral *Telesto riisei* Duchassaing and Michelotti (family Telestidae) (6–9).

We had first collected this animal in 1976 at Enewetak atoll, Marshall Islands, and isolated two pregnanes (10). *T. riisei* is part of the fouling community and was introduced to Hawaii, probably on ships' bottoms, as it was first observed in Pearl Harbor (11). Our initial Hawaii collection site was Pupukea, O'ahu; subsequently, we regularly collected it in the entrance channel to the Ala Wai boat harbor in shallow and silty water. Our initial Hawaii collection yielded no pregnanes, but, surprisingly, two new prostaglandins, punaglandins 1 [**1**] and 3 [**5**] (9). Subsequent research resulted in a total of 19 punaglandins, though not all were present in each collection. In this paper we will emphasize those compounds not previously (9) described, their stereochemistry and biological activity.

RESULTS AND DISCUSSION

Freeze-dried animals were extracted with petroleum ether; the residue was dissolved in MeOH-H_2O (7:3) and partitioned against hexane. The punaglandins (0.1% of dry coral) were found in the aqueous MeOH. They were purified by cc on Si gel, followed by

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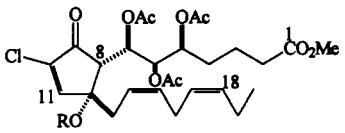
[3]"Puna" means coral in Hawaiian.



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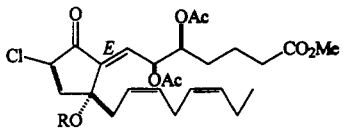
3 R=H, 17,18-dihydro
4 R=Ac, 17,18-dihydro



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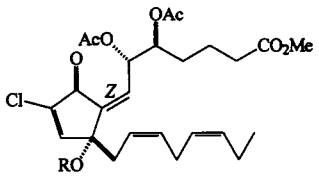

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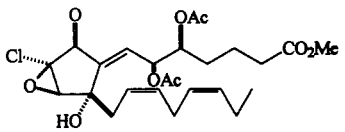
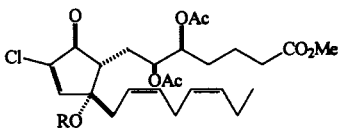
12 R=Ac, 17,18-dihydro



13
14 17,18-dihydro



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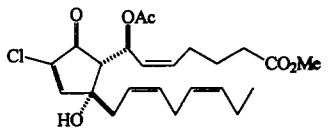
16 R=Ac
17 R=H, 17,18-dihydro



18
19 17,18-dihydro

repeated reversed-phase hplc steps. The structural features exhibited by the punaglandins include a 12-OH (rather than a 12-OAc), which is found in twelve, and a $\Delta^{7,8}$ which is found in ten compounds, four of these with *Z*-geometry. Nine punaglandins are saturated at C-7,8; six of these bear acetoxy functions at C-7. Two each are 5,6-olefins (**18**,**19**) or 10,11-epoxy (**13**,**14**) compounds. Common to all 19 compounds is the α-chloro-α,β-cyclopentenone moiety-altogether an unusual display of functionality, as compared with their terrestrial counterparts.

Because of the rich and varied functionality of the punaglandins, relative stereochemistry could be deduced from nmr spectral data (Tables 1–3). There was evidence to suggest that all members of the series had the same stereocenters. For example, optical rotations were positive and of the same order of magnitude, and nmr coupling constants between protons at vicinal chiral carbons were comparable in all cases where determination was possible. Substitution that is trans- between C-8 and C-12 was demonstrated by an nOe between H-8 and H_2-13. The magnitude of the H-5, 6, 7 coupling constants of 1–4 Hz was compatible with a threo configuration. For the erythro relationship, *J* values of 6–10 Hz are typical (12,13).

The structures of the two 10,11-epoxides [**13**, **14**] could be deduced from the results of nmr experiments, the molecular formula, and the fact that these compounds still had uv spectra of α,β-unsaturated ketones, i.e., 7,8 rather than 10,11-enones. H-11 in **13** now resonated at 3.96 ppm vs. 7.26 in the olefins; two new carbon signals were seen at 91 and 67 ppm; and H-11 or H_2-13 when irradiated showed nOe enhancement. We made numerous attempts to confirm the stereochemical assignments by chemical

TABLE 1. ^{1}H-Nmr Data of Punaglandins **1**–**7** (δ, multiplicity, *J* in Hz).[a]

Position	Compound						
	1[b]	**2**	**3**[b]	**4**	**5**	**6**	**7**
H_2-2	2.2, m	2.3, s	2.3, m	2.3, t	2.3, m	2.3, t	2.3, m
H_2-3	1.6, m	1.6, m	1.6, m	1.6, m	1.6, m	1.6, m	1.6, m
H_2-4	1.6, m	1.6, m	1.6, m	1.6, m	1.6, m	1.6, m	1.6, m
H-5	5.18, ddd (5.3, 5.3, 7.5)	5.3, m	5.18, ddd (5.3, 5.3, 7.5)	5.27, br dt (1.1)	5.25, m	5.2, m	5.25, m
H-6	5.61, dd (5.3, 5.3)	5.3, m	5.61, dd (5.3, 5.3)[c]	5.33, dd (1.1, 7.8)	6.02, dd (4.3, 9.1)	5.86, dd (4.1, 9.4)	6.01, dd (4.3, 9.1)
H-7	5.34, dd (4.2, 5.3)	5.3, m	5.31, dd (4.2, 5.3)	5.50, dt (1.7, 7.8)	6.35, d (9.1)	6.47, d (9.4)	6.33, d (9.1)
H-8	2.75, d (4.2)	3.1, d	2.74, d (4.2)	3.01, d (1.7)			
H-11	7.26, s	7.8, s	7.26, s	7.82, s	7.27, s	7.59, s	7.25, s
H-13$_a$	2.53, dd (7.0, 14.7)	3.5, dd	2.48, dd (7.3, 14.4)	2.87, dd (8.3, 10.2)	3.01, dd (8.1, 14.3)	3.33, dd (8.7, 14.0)	2.95, dd (8.5, 13.5)
H-13$_b$	2.45, dd (8.1, 14.7)	2.9, dd	2.40, dd (7.9, 14.4)	2.77, dd (8.3, 10.2)	2.68, dd (7.0, 14.3)	2.8, dd (6.6, 14.0)	2.62, dd (7.2, 13.5)
H-14	5.30, ddd (7, 8.1, 10.8)	5.3, m	5.25, ddd (7.3, 7.9, 10.9)	5.10, dt (2.4, 7.8)	5.25, m	5.2, m	5.25, m
H-15	5.61, dt (7,10.8)	5.7, dt	5.63, dt (7, 10.9)	5.58, dt (2.4, 7.8)	5.53, m	5.46, dt (7.0, 10.6)	5.52, dt (6.7, 10.9)
H_2-16	2.78, m	2.8, t	1.95, m	2.09, m	2.74, br dd (7.1, 7.1)	2.70, t (7.0)	2.0, m
H-17	5.24, dt (1, 7, 10.6)	5.3, m	1.26, m	1.26, m	5.2, m	5.2, m	1.3, m
H-18	5.41, dt (7, 10.6)	5.6, dt	1.26, m	1.26, m	5.41, m	5.38, ddd (2, 7, 10.2)	1.3, m
H_2-19	2.05, m	2.1, m	1.26, m	1.26, m	2.05, m	1.9, m	1.3, m
H_3-20	1.00, t (7.5)	0.9, t	0.85, t (6.7)	0.86, t (6.0)	0.94, t (7.5)	0.94, t (7.5)	0.86, t (7.1)
H_3-OMe	3.65, s	3.6, s	3.65, s	3.65, s	3.65, s	3.63, s	3.63, s
H_3-OAc	2.11, s	2.2, s	2.09, s	2.14, s	2.09, s	2.10, s	2.10, s
H_3-OAc	2.08, s	2.1, s	2.06, s	2.05, s	2.05, s	2.08, s	2.05, s
H_3-OAc	2.00, s	2.0, s	1.98, s	1.99, s		2.05, s	
H_3-OAc		1.9, s		1.90, s			
H-OH[c]	3.57, s		3.48, s		3.50, s		3.63, s

[a]Recorded at 300 MHz in $CDCl_3$ unless otherwise noted.
[b]Recorded at 500 MHz.
[c]Exchangeable, variable.

manipulation which would produce a crystalline derivative suitable for X-ray diffraction studies or a compound that would lend itself to chiroptical measurements. All of these failed (14).

Experiments designed to lead to a crystalline bromobenzoate first focused on the C-12 alcohol. A C-12 benzoate might also have been used in the application of the exciton-chirality method. However, C-12 was too hindered to react. Reduction of the C-9 carbonyl was successful, but subsequent esterification resulted in transesterification with the C-7 acetate and concomitant formation of the C-7,8 olefin. Enzymatic hydrolysis (pig liver esterase) (15) of the acetates, then to be replaced by more suitable esters, led only to hydrolysis of the C-1 ester; the free acid failed to undergo esterification with 9-anthryldiazomethane (16).

Once the Japanese workers had established the absolute configuration of the clavulones (17) and claviridenones (18), we assumed that the absolute stereochemistry of the punaglandins had been solved. This proved to be a hasty and incorrect assumption. Independent syntheses in two laboratories proved (19–21) that the absolute stereochemistry of the punaglandins was enantiomeric at C-12 to the clavulones and claviridenones. Even more startling is the fact that a single animal, *Clavularia viridis*, which subsequently also yielded 10-haloprostanoids (22,23) has the capability of biosynthesizing enantiomeric halogenated and non-halogenated prostanoids.

TABLE 2. ^{1}H-Nmr Data of Punaglandins **8–13** (δ, multiplicity, *J* in Hz).[a]

Position	Compound					
	8	**9**	**10**	**11**	**12**	**13**
H_2-2	2.3, m	2.3, m	2.3, m	2.3, m	2.3, m	2.3, m
H_2-3	1.6, m	1.6, m	1.6, m	1.6, m	1.6, m	1.6, m
H_2-4	1.6, m	1.6, m	1.6, m	1.6, m	1.6, m	1.6, m
H-5	5.07, m	5.1, m	5.18, dt (3.4)	5.2, m (3.4)	5.2, m	5.2, m
H-6	5.86, dd (4.1, 9.2)	6.32, dd (3.5, 7.7)	6.46, dd (3.4, 7.7)	6.32, dd (3.6, 7.8)	6.46, dd (3.9, 7.8)	5.98, dd (4.2, 9.0)
H-7	6.47, d (9.2)	6.08, d	6.1, d	6.07, d	6.09, d	6.54, d (9.0)
H-11	7.6, s	7.20, s	7.53, s	7.20, s	7.53, s	3.96, s
H-13$_a$	3.31, dd (6.6, 14.3)	2.59, dd (7.7, 14.5)	2.88, dd (6.7, 14.5)	2.56, dd (8, 14)	2.86, dd	2.8, m
H-13$_b$	2.77, dd (6.6, 14.3)	2.47, dd (7.3, 14.5)	2.63, dd (6.7, 14.5)	2.44, dd (8, 14)	2.58, dd	2.8, m
H-14	5.1, dt (6.6, 10.7)	5.1, m	5.15, ddd (6.7, 7.5, 10.6)	5.2, m	5.2, m	5.2, m
H-15	5.49, dt (6.7, 10.7)	5.36, dt (7.2, 10.9)	5.53, dt (7.3, 10.6)	5.57, dt (7.6, 10.9)	5.54, dt (8.8, 10.7)	5.58, m
H_2-16	1.94, t (6.7)	2.74, dd (6.4, 7.2)	2.73, t (4.8)	1.97, m	1.9, m	2.7, m
H-17	1.3, m	5.1, m	5.20, dt (4.8, 10.5)	1.3, m	1.3, m	5.2, m
H-18	1.3, m	5.2, m	5.40, dt (7.0, 10.5)	1.3, m	1.3, m	5.4, m
H_2-19	1.3, m	2.0, m	2.07, m	1.3, m	1.3, m	2.0, m
H_3-20	0.86, t (6.3)	0.95, t (7.5)	0.95, t (7.5)	0.87, t (6)	0.87, t (6.1)	0.94, t (7.5)
H_3-OMe	3.64, s	3.64, s	3.64, s	3.64, s	3.64, s	3.65, s
H_3-OAc	2.11, s	2.10, s	2.10, s	2.10, s	2.10, s	2.08, s
H_3-OAc	2.09, s	2.03, s	2.02, s	2.03, s	2.02, s	2.03, s
H_3-OAc	2.06, s		2.00, s			2.00, s
H-OH[b]		3.5, s		2.79, s		3.67, s

[a]Recorded at 300 MHz in $CDCl_3$.
[b]Exchangeable, variable.

The biological activities of the punaglandins proved to be as varied as those of the mammalian prostanoids (24). Anti-inflammatory activity of punaglandins is documented in a U.S. Patent (25), although this activity was eclipsed by the promising antitumor activity, which was studied extensively. When the activity of the 7,8-olefins [**5** and **7**] against cultured L1210 mouse leukemia cells was compared with corresponding clavulones (12-OAc rather than 12-OH and lacking 10-Cl), the punaglandins were more potent by one order of magnitude (26). The activities of the punaglandins in vitro and in vivo against Ehrlich ascites cells were the strongest of any prostaglandins: furthermore, cytotoxicities almost equaled those of vincristine. Although the 10-chloropunaglandins proved to be too toxic for clinical use, replacement of chlorine with methylthio and side-chain modification yielded a substance which enhanced in vitro mineralization of human osteoblasts and may lead to an agent in the treatment of osteoporosis (27). Recognition that the $\Delta^{7,8}$ structural feature is necessary for antitumor activity has prompted the synthesis of Δ^7 prostaglandin A_1 methyl ester, which is under preclinical study for the treatment of chemotherapeutically resistant ovarian cancer (28).

Discovery of the role of prostaglandins in mammalian systems was a challenging undertaking. Equally intriguing is the question of what function the marine eicosanoids might play in the physiology and/or ecology of certain octocorals. A possible defensive

TABLE 3. ^{1}H-Nmr Data of Punaglandins **14–19** (δ, multiplicity, *J* in Hz).[a]

Position	Compound					
	14	**15**	**16**	**17**	**18**	**19**
H_2-2	2.3, m	2.3, t	2.3, m	2.3, m	2.3, m	2.3, t
H_2-3	1.5, m	1.6, m	1.6, m	1.6, m	1.6, m	1.7, m
H_2-4	1.5, m	1.6, m	1.6, m	1.6, m	1.6, m	2.19, dt (6.7, 7)
H-5	5.2, m	5.11, br d (3.4)	5.0, m	5.11, br d (3.4)	5.3, m	5.57, dt (6.7, 10.7)
H-6	5.97, dd (4.4, 8.9)	5.1, m	5.3, m	5.28, ddd (1.2, 3.4, 8)	5.8, t	5.83, dd (9.6, 10.7)
H-7	6.55, d (8.9)	a: 2.16, dd (7.7, 15.2) b: 1.73, dd (7.8, 15.2)	1.9, m	a: 2.12, ddd (4.5, 15.4) b: 1.73, ddd (1.2, 8.4, 15.4)	5.9, dd	5.94, dd (3.3, 9.6)
H-8		2.67, dd (7.7, 7.8)	3.2, t	2.66, dd (4.5, 8.4)	2.6, d	2.66, d (3.3)
H-11	3.95, s	7.30, s	7.5, s	7.29, s	7.3, s	7.26, s
H-13$_a$	2.85, dd (8, 4)	2.80, dd (8.0, 8.5)	3.0, dd	2.77, dd (1.4, 13.5)	2.5, dd	2.53, dd (8.1, 14.7)
H-13$_b$	2.76, dd (8, 4)	2.65, dd (4.6, 8.5)	2.3, m	2.10, dd (1.4, 13.5)	2.4, dd	2.38, dd (7.1, 14.7)
H-14	5.2, m	5.1, m	5.2, dd (8, 10)	5.28, ddd (1.4, 6.5, 11.1)	5.3, m	5.32, ddd (7.1, 8.1, 11.2)
H-15	5.59, m	5.62, dt (7.5, 10)	5.5, ddd (1, 7, 10.8)	5.65, dt (6.4, 11.1)	5.6, dt	5.64, dt (6.7, 7.0)
H_2-16	1.5, m	2.77, t	2.6, t	2.03, dt (6.2, 6.4)	2.7, t	2.00, dt (6.7, 7.0)
H-17	1.2, m	5.1, m	5.2, dt (10.5)	1.3, m	5.3, m	1.3, m
H-18	1.2, m	5.38, m	5.4, m	1.3, m	5.3, m	1.3, m
H_2-19	1.2, m	2.0, t	2.0, m	1.3, m	2.2, m	1.3, m
H_3-20	0.86, t (6.0)	0.94, t (7.3)	0.95, t (7)	0.85, t (6.2)	0.9, t	0.86, t (6.7)
H_3-OMe	3.66, s	3.64, s	3.6, s	3.65, s	3.6, s	3.65, s
H_3-OAc	2.09, s	2.09, s	2.2, s	2.11, s	2.0, s	1.98, s
H_3-OAc	2.03, s	2.08, s	2.2, s	2.10, s		
H_3-OAc			2.1, s			
H-OH[b]	3.55, s	2.58, s		2.54, s	3.2, s	3.18, s

[a]Recorded at 300 MHz in $CDCl_3$.
[b]Exchangeable, variable.

role of the prostaglandins in the Caribbean gorgonian *Plexaura homomalla* was studied by Gerhart (29) in the laboratory and in the field. He concluded that the compounds provide protection against predatory reef fish by inducing vomiting and subsequent avoidance of the coral, which indeed is not heavily predated. Pawlik and Fenical (30) raised objections to some of Gerhart's conclusions on some relatively minor points, as discussed by Coll (31).

In our observations over the years, *Telesto riisei* appears to be free of predation. According to the literature (32) the coral does have a predator, a nudibranch, *Tritonia wellsi* Marcus (33) (family Tritoniidae). We collected one specimen of a *Tritonia* sp. on colonies of *Telesto* in Papua New Guinea. Positive identification of punaglandins in the *Tritonia* extract was not possible, but a MeOH extract showed distinct punaglandin signals in its ^{1}H-nmr spectrum (14).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Optical rotations were recorded on a Rudolf Research Autopol II polarimeter. Ir spectra were recorded on either a Nicolet MX-5 FTIR or a Perkin-Elmer 467

instrument. Uv spectra were recorded on either a Cary 14 or a Beckman DU-7 spectrophotometer. Electron impact mass spectra were recorded on a Varian MAT 311. A Nicolet NT 300 with an Oxford magnet was used to record 300 MHz ^{1}H- and 75 MHz ^{13}C-nmr spectra. ^{1}H-Nmr chemical shifts are reported in ppm with the chemical shift of residual solvent protons used as internal standards. ^{13}C-nmr chemical shifts are reported in ppm using natural abundance ^{13}C of the solvent as an internal standard. All chromatographic solvents were distilled from glass before use.

ISOLATION OF THE PUNAGLANDINS.—Collections of *Telesto riisei* were made by scuba at −10 m. Before freeze-drying a blue encrusting sponge was removed. The freeze-dried coral was then subjected to Soxhlet extraction with petroleum ether. After removal of petroleum ether at reduced pressure, the crude residue was dissolved in MeOH-H_2O (7:3) and partitioned against hexane. The aqueous MeOH fraction (0.1–0.2% dry wt, 5–10% crude extract) was concentrated and the residue passed over Bio-sil A, 200–400 mesh, with petroleum ether-EtOAc (7:3). Repeated reversed-phase hplc was required to purify any given punaglandin.

Punaglandin 1 [**1**].—Obtained in (0.05% dry wt[4]: [α]D +10.6° (*c*=2.4, MeOH); ir ν max ($CHCl_3$) 3500, 3430, 2930, 2860, 1740, 1610, 1375, 1235, 1025 cm^{-1}; uv λ max (MeOH) 228 (7900) nm; eims (30 eV) *m/z* 496 (3), 478 (5), 447 (17), 418 (25), 387 (100), 358 (22), 327 (37), 267 (58); dcims *m/z* 574 (100); ^{1}H nmr, see Table 1; ^{13}C nmr (125 MHz, $CDCl_3$) δ 196.0 (s), 173.8 (s), 171.3 (s), 170.5 (s), 170.4 (s), 158.1 (d), 136.1 (s), 134.6 (d), 132.9 (d), 126.0 (d), 121.5 (d), 77.2 (s), 72.9 (d), 71.6 (d), 70.0 (d), 53.4 (d), 51.8 (q), 39.4 (t), 33.5 (t), 30.1 (t), 25.8 (t), 21.1 (q), 21.0 (q), 20.9 (q), 20.7 (t), 20.2 (t), 14.3 (q).

Punaglandin 1 acetate [**2**].—Obtained in <0.001% dry wt: ^{1}H nmr, see Table 1.

Punaglandin 2 [**3**].—Obtained in 0.05% dry wt: [α]D +8.8° (*c*=1.9, MeOH); ir ν max (CH_2Cl_2) 3420 (br), 2920, 1730 (br), 1375, 1230, 1045 cm^{-1}; uv λ max (MeOH) 227 (7500) nm; eims (70 eV) *m/z* 498 (1), 480 (1), 467 (4), 447 (5), 387 (100), 327 (100), 285 (28); cims *m/z* 541 (7), 499 (58), 481 (30), 439 (13), 421 (100), 361 (59); high-resolution peak matched *m/z* 499 (499.21350) for $C_{25}H_{36}{}^{35}ClO_8$, calcd, 499.20988; dcims *m/z* 576 ($M^+ + NH_4$); ^{1}H nmr, see Table 1; ^{13}C nmr (125 MHz, $CDCl_3$) δ 196.0 (s), 173.8 (s), 171.9 (s), 170.6 (s), 170.4 (s), 158.2 (d), 136.8 (s), 136.0 (d), 121.1 (d), 77.2 (s), 72.9 (d), 71.7 (d), 70.0 (d), 53.5 (d), 51.9 (q), 39.5 (t), 33.5 (t), 31.7 (t), 30.2 (t), 29.3 (t), 27.6 (t), 22.7 (t), 21.1 (q), 21.0 (q), 20.9 (q), 20.2 (t), 14.2 (q).

Punaglandin 2 acetate [**4**].—Obtained in 0.001% dry wt: [α]D +10° (*c*=0.6, MeOH); ir ν max ($CHCl_3$) 2960, 2920, 2870, 1740 (br), 1440, 1370, 1225, 1030 cm^{-1}; uv λ max ($CHCl_3$) 242 (5600) nm; eims (70 eV) *m/z* 387 (2.6), 378 (1.0), 327 (3.8), 308 (1.2), 279 (42.5), 167 (66.6), 149 (99.5), 43 (100); ^{1}H nmr, see Table 1; ^{13}C nmr (75 MHz, $CDCl_3$) δ 195.0, 173.3, 170.7, 169.9, 169.9, 169.3, 155.1, 137.7, 136.4, 120.0, 83.8, 72.7, 71.1, 69.5, 52.9, 51.6, 33.4, 31.4, 30.3, 29.0, 27.5, 22.5, 21.6, 21.0, 20.8, 20.6, 20.4, 14.0.

Punaglandin 3 [**5**].—Obtained in 0.01% dry wt: [α]D +66.8° (*c*=0.54, MeOH); ir ν max ($CHCl_3$) 3100–3600 (br), 2960, 2940, 1725, 1680 (sh), 1378, 1235, 1110–990 (br) cm^{-1}; uv λ max (MeOH) 238 (8600) nm; eims (25 eV) *m/z* 478 (1), 418 (14), 387 (50), 376 (14), 358 (26), 327 (100), 275 (30), 267 (38), 253 (30), 235 (35); ^{1}H nmr, see Table 1; ^{13}C nmr (75 MHz, $CDCl_3$) δ 186.6 (s), 173.8 (s), 171.1 (s), 169.9 (s), 155.7 (d), 140.5 (s), 137.2 (s), 133.1 (d), 132.5 (d), 130.5 (d), 126.1 (d), 122.0 (d), 77.2 (s), 73.7 (d), 69.8 (d), 51.7 (q), 35.6 (t), 33.2 (t), 29.6 (t), 25.6 (t), 20.8 (q), 20.8 (q), 20.5 (t), 20.2 (t), 14.2 (q).

Punaglandin 3 acetate [**6**].—Obtained in 0.005% dry wt: [α]D +31° (*c*=2.7, $CHCl_3$); ir ν max ($CHCl_3$) 3020, 2960, 2940, 2929, 2870, 1744 (br), 1370, 1220 (br), 1020 (br) cm^{-1}; uv λ max ($CHCl_3$) 251 (8000) nm; eims (70 eV) *m/z* 538 (0.1), 496 (0.1), 478 (0.3), 436 (0.3), 387 (7.0), 376 (8.4), 358 (10.9), 345 (5.3), 327 (25.9), 285 (12.5), 253 (26.2), 235 (25.4), 207 (21.5), 43 (100); ^{1}H nmr, see Table 1; ^{13}C nmr (75 MHz, $CDCl_3$) δ 185.4, 173.6, 170.1, 169.9, 169.3, 151.5, 135.4, 133.8, 132.7, 130.4, 125.9, 121.5, 120.9, 83.3, 73.3, 69.6, 51.6, 33.9, 33.3, 30.0, 25.7, 21.6, 20.8, 20.7, 20.6, 20.2, 14.2.

Punaglandin 4 [**7**].—Obtained in 0.005% dry wt: [α]D +46.3° (*c*=1.6, MeOH); ir ν max ($CHCl_3$) 3150–3600 (br), 2930, 2860 (sh), 1725, 1675 (sh), 1375, 1150–1300 (br), 1000–1100 (br) cm^{-1}; uv λ max (MeOH) 240 (6900) nm; eims (70 eV) *m/z* 420 (2), 387 (23), 378 (8), 360 (6), 347 (19), 327 (100), 285 (44), 267 (84), 253 (74), 235 (82); ^{1}H nmr, see Table 1; ^{13}C nmr (75 MHz, $CDCl_3$) δ 186.8 (s), 173.8 (s), 171.1 (s), 169.8 (s), 155.7 (d), 140.4 (s), 137.2 (s), 135.2 (d), 130.6 (d), 121.5 (d), 77.3 (s), 73.7 (d), 69.8 (d), 51.7 (q), 35.6 (t), 33.2 (t), 31.5 (t), 29.6 (t), 29.0 (t), 27.4 (t), 22.5 (t), 20.8 (q), 20.8 (q), 20.2 (t), 14.0 (q).

Punaglandin 4 acetate [**8**].—Obtained in 0.001% dry wt: [α]D +9.4° (*c*=3.6, $CHCl_3$); ir ν max (film) 3020, 2960, 2920, 2860, 1740 (br), 1680, 1440, 1370, 1220 (br), 1020 cm^{-1}; uv λ max ($CHCl_3$) 249 (6700)

[4]Average yields are reported; actual yields and proportions varied among collections.

nm; eims (70 eV) *m/z* 540 (3.2), 498 (0.8), 480 (0.5), 462 (1.6), 438 (2.2), 420 (3.8), 387 (25.1), 378 (23.5), 327 (50.6), 308 (29.3), 266 (41.4), 253 (44.2), 237 (37.5), 222 (43.4), 207 (37.3), 43 (100); ^{1}H nmr, see Table 2; ^{13}C nmr (75 MHz, $CDCl_3$) δ 185.9, 173.6, 170.6, 170.3, 169.8, 152.1, 139.0, 137.6, 136.3, 130.8, 120.9, 83.8, 73.7, 70.0, 52.1, 34.4, 33.8, 32.0, 30.5, 29.4, 27.9, 23.0, 22.1, 21.2, 21.2, 21.1, 14.5.

Z-Punaglandin 3 [**9**].—Obtained in 0.001% dry wt: eims (70 eV) *m/z* 436 (1.2), 418 (0.9), 387 (5.2), 376 (4.1), 345 (7.5), 327 (41.7), 285 (28.2), 43 (100); ^{1}H nmr, see Table 2.

Z-Punaglandin 3 acetate [**10**].—Obtained in <0.001% dry wt: [α]D +19° (*c*=1.8, $CHCl_3$); uv λ max ($CHCl_3$) 255 (9000), 242 (7900) nm; eims (70 eV), *m/z* 538 (3.5), 478 (2.4), 436 (2.8), 418 (12.5), 387 (16.3), 376 (20.8), 366 (11.2), 358 (23.0), 345 (13.4), 327 (28.6), 43 (100); ^{1}H nmr, see Table 2; ^{13}C nmr (75 MHz, $CDCl_3$) δ 193.8, 173.7, 170.0, 169.6, 169.5, 150.1, 139.6, 136.5, 136.0, 133.7, 132.7, 125.8, 120.9, 82.1, 74.0, 69.9, 51.6, 35.3, 33.4, 30.0, 25.7, 21.6, 20.8, 20.8, 20.6, 20.6, 14.2.

Z-Punaglandin 4 [**11**].—Obtained in 0.001% dry wt: ^{1}H nmr, see Table 2.

Z-Punaglandin 4 acetate [**12**].—Obtained in 0.001% dry wt: [α]D +11° (*c*=1.8, $CHCl_3$); uv λ max (MeOH) 254 (5300), 241 (5100) nm; eims (70 eV) *m/z* 540 (3.2), 480 (0.9), 438 (2.7), 429 (2.6), 420 (3.5), 387 (18.6), 378 (17.2), 360 (14.1), 327 (27.9), 308 (20.4), 285 (14.9), 43 (100); ^{1}H nmr, see Table 2; ^{13}C nmr (75 MHz, $CDCl_3$) δ 190.8, 176.3, 173.7, 173.4, 173.1, 149.0, 142.5, 136.5, 135.8, 135.7, 120.6, 82.3, 74.0, 69.8, 51.6, 35.4, 33.5, 31.5, 30.0, 29.0, 27.5, 23.1, 22.6, 21.6, 20.8, 20.6, 14.0.

Punaglandin 3 epoxide [**13**].—Obtained in 0.001% dry wt: [α]D +16° (*c*=3.0, MeOH); ir ν max (neat) 3483 (br), 3010, 2960, 2875, 1736 (br), 1375, 1223 (br), 1024 cm^{-1}; uv λ max ($CHCl_3$) 245 (7400) nm; eims (70 eV) *m/z* 512 (0.1), 494 (0.8), 403 (3.4), 343 (24.3), 283 (18.9), 43 (100); ^{1}H nmr, see Table 2; ^{13}C nmr (75 MHz, $CDCl_3$) δ 187.3 (s), 173.6 (s), 170.7 (s), 169.9 (s), 139.9 (d), 138.6 (s), 133.9 (d), 132.8 (d), 125.9 (d), 120.9 (d), 93.1 (s), 73.6 (d), 69.5 (d), 66.7 (d), 51.8 (q), 34.2 (t), 33.2 (t), 29.7 (t), 29.6 (t), 25.7 (t), 20.8 (q), 20.7 (q), 20.6 (t), 20.2 (t), 14 (q).

Punaglandin 4 epoxide [**14**].—Obtained in 0.001% dry wt: [α]D +22.5° (*c*=0.8, MeOH); eims (70 eV) *m/z* 514 (0.2), 496 (4), 436 (1), 423 (5), 403 (7), 343 (39), 283 (22), 269 (22), 43 (100); ^{1}H nmr, see Table 3.

Punaglandin 5 [**15**].—Obtained in 0.002% dry wt: [α]D +10.2° (*c*=4.7, $CHCl_3$); ir ν max ($CHCl_3$) 3450 (br), 3010, 2960, 2930, 2870, 1748, 1600, 1440, 1380, 1230, 1170, 1040 cm^{-1}; uv λ max ($CHCl_3$) 244 (5000) nm; eims (70 eV) *m/z* 480 (0.4), 419 (5.9), 389 (9.4), 387 (8.1), 329 (31.4), 285 (10.8), 43 (100); ^{1}H nmr, see Table 3; ^{13}C nmr (75 MHz, $CDCl_3$) 196.6, 171.1, 170.7, 170.6, 157.5, 134.6, 134.3, 132.9, 125.9, 121.6, 77, 73.7, 72.2, 55.1, 51.6, 38.7, 35.9, 33.4, 30.0, 29.9, 25.7, 20.9, 20.6, 20.2, 14.2.

Punaglandin 5 acetate [**16**].—Obtained in 0.01% dry wt: [α]D +8° (*c*=1.2, MeOH); uv λ max ($CHCl_3$) 240 (4500) nm; eims (70 eV) *m/z* 480 (4.9), 420 (27.4), 407 (13.6), 378 (12.4), 360 (25.6), 329 (33.4), 269 (29.2), 43 (100); ^{1}H nmr, see Table 3; ^{13}C nmr (75 MHz, $CDCl_3$) δ 197, 173.0, 170.5, 170.3, 169.9, 155.6, 133.4, 132.8, 125.7, 123.0, 121.0, 85.5, 72.8, 72.3, 52.2, 52, 36, 35, 33.4, 30.0, 26.4, 25.7, 21.5, 21.0, 20.9, 20.6, 14.2.

Punaglandin 6 [**17**].—Obtained in 0.002% dry wt: [α]D +14° (*c*=0.9, $CHCl_3$); ir ν max (CCl_4) 3450 (br), 3010, 2950, 2920, 2750, 1720 (br), 1600, 1440, 1370, 1230 (br), 1030 cm^{-1}, uv λ max ($CHCl_3$) 231 (5300) nm; eims (70 eV) *m/z* 409 (4.1), 329 (31.8), 315 (5.4), 269 (28.1), 255 (28.6), 43 (100); eims (25 eV) *m/z* 482 (0.9), 329 (100), 269 (37.9), 255 (16.3), 173 (20.1), 107 (32.1), 60 (18.6), 43 (42.5), 36 (19.6); ^{1}H nmr, see Table 3; ^{13}C nmr (75 MHz, $CDCl_3$) δ 196.7, 173.5, 170.6, 170.6, 157.6, 136.2, 134.4, 121.3, 78.9, 72.2, 72.1, 55.1, 51.6, 35.8, 33.4, 31.5, 30.0, 29.0, 27.5, 25.5, 22.5, 21.1, 20.8, 20.6, 14.0.

Punaglandin 7 [**18**].—Obtained in <0.001% dry wt: ^{1}H nmr, see Table 3.

Punaglandin 8 [**19**].—Obtained in <0.001% dry wt: Ir ν max ($CHCl_3$) 3300–3600 (br), 2929, 2860, 1730, 1375, 1200–1250 (br) cm^{-1}; uv λ max (MeOH) 227 (6900) nm; eims (70 eV) *m/z* 380, 362, 349, 269 (100), 237; ^{1}H nmr, see Table 3.

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