fashion *via* a superexchange mechanism. Direct metal–metal interaction is believed to be magnetically unimportant because of the relatively large Mn(2)–Mn(1) distance of 2.716 Å.

The acetonitrile and diffuse reflectance spectra of the dimer, which are similar, bear a striking resemblance to the spectra of tris(2,2′-bipyridine)manganese(III) and tris(*o*-phenanthroline)manganese(III).[1] The spectral features of the Mn(IV) ion are expected to be superimposed upon those of the Mn(III) ion; however, the Mn(IV) transitions are of sufficiently high energy and low probability to be obscured by the strong charge-transfer absorptions lying at energies greater than 20 kK, and, thus, the spectrum of the dimer is essentially that of the Mn(III) ion.

On the basis of the structural, spectroscopic, and magnetic data, we conclude that it is appropriate to describe this dinuclear complex as being composed of superexchange coupled Mn(III) and Mn(IV) atoms and that the superexchange cannot involve extensive delocalization of the one e_g electron. The $\chi(T)$ data were fit by a nonlinear least-squares technique to a simple isotropic Heisenberg spin Hamiltonian

$$\mathcal{H} = -2J\mathbf{S}_1 \cdot \mathbf{S}_2$$

for a $2\text{-}{}^3/_2$ spin system. The energy levels $\epsilon_{1/2} = 0$, $\epsilon_{3/2} = -3J$, $\epsilon_{5/2} = -8J$, and $\epsilon_{7/2} = -15J$ were used together with $g = 2.003$ and assuming TIP $= 60 \times 10^{-5}$ cgs unit. The best fit was for $J/k = -147°$.

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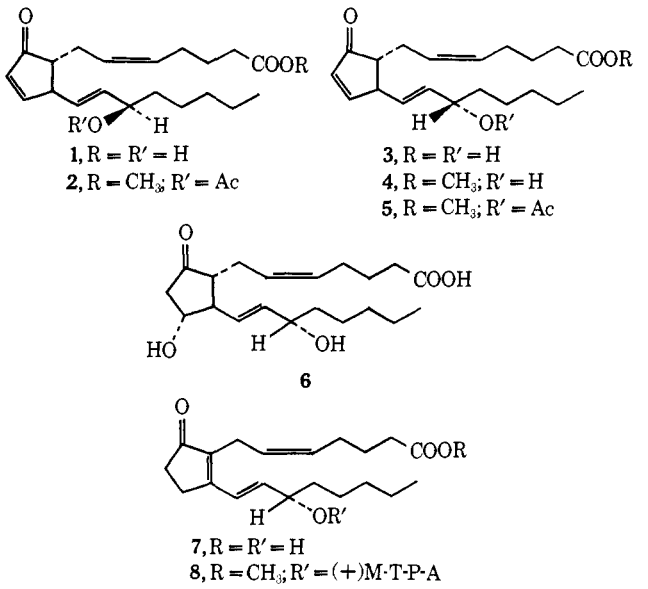
Occurrence of Esters of (15*S*)-Prostaglandin A_2 and E_2 in Coral

Sir:

All known natural mammalian prostaglandins have the *S* configuration at the C_{15} asymmetric center.[1] A recent report by Weinheimer and Spraggins[2] described the isolation from a soft coral, the gorgonian *Plexaura homomalla* occurring in coastal waters off Florida, of a prostaglandin, (15*R*)-PGA_2 (**1**) and its acetate, methyl ester (**2**), having the "nonmammalian" configuration at C_{15}. We have now found that some forms of *P. homomalla* contain, instead of the (*R*)-prostaglandins, esterified derivatives of (15*S*)-PGA_2 (**3**) and (15*S*)-PGE_2 (**6**) identical with the prostaglandins derived from mammalian sources. Also, in some single specimens of this gorgonian, both (15*R*)- and (15*S*)-prostaglandins may occur.

Specimens of *P. homomalla* that are immediately frozen in liquid nitrogen or Dry Ice upon collection and then extracted with organic solvents give essentially only the prostaglandin 15-acetate, methyl esters. However, coral samples that are allowed to stand in water or methanol at ambient temperatures for some time after collection undergo hydrolysis or methanolysis, giving mixtures containing PGA_2 and its methyl ester upon extraction. The (15*R*) and (15*S*) forms of these two prostaglandins differ slightly in silica gel tlc polarity, using the AIX system,[3] the (15*R*) isomers being less polar, so that preliminary identification in coral extracts can be made. During the processing of a recent collection of *P. homomalla*, a single specimen was analyzed and surprisingly found to contain prostaglandins of the (15*S*) configuration. Since then, numerous specimens from various locations in the Caribbean area have been found to contain (15*S*)-PGA_2 and its methyl ester. From many of these, no (15*R*)-prostaglandins could be detected but spots having the tlc mobility and color reactions of (15*S*)-PGE_2 and its methyl ester were observed. Furthermore, from some individual specimens, spots corresponding to both (15*R*)- and (15*S*)-PGA_2 and their methyl esters were seen.[4,5]



Additional confirmation of configuration at C_{15} in coral-derived (15*S*)-PGA_2 was obtained by conversion to (15*S*)-PGE_2 and (15*S*)-$PGF_{2\alpha}$[6] and by base-catalyzed rearrangement to (15*S*)-PGB_2 (**7**). The latter exhibited a positive Cotton effect in the optical rotatory dispersion curve identical with that obtained from mammalian-derived (15*S*)-PGB_2 and the mirror image of that obtained from coral (15*R*)-PGB_2.[7]

The method of Dale, Dull, and Mosher[8] was also

(1) D. A. Nugteren, D. A. VanDorp, S. Bergström, M. Hamberg, and B. Samuelsson, *Nature (London)*, 212, 38 (1966).
(2) A. J. Weinheimer and R. L. Spraggins, *Tetrahedron Lett.*, 5183 (1969).
(3) M. Hamberg and B. Samuelsson, *J. Biol. Chem.*, 241, 257 (1966).
(4) After the completion of this work we learned from Professor Bengt Samuelsson (Royal Veterinary College, Stockholm) that a careful analysis of *P. homomalla* from Florida waters disclosed the presence of a small amount of the (15*S*) isomer of the PGA compounds together with the predominant (15*R*) isomer; R. Light and B. Samuelsson, *Eur. J. Biochem.*, in press.
(5) A single dried specimen was also obtained and found to contain (15*R*)- and (15*S*)-PGB_2 as determined by the nmr spectrum of its (+)-α-methoxy-α-trifluoromethylphenyl acetates (see below).
(6) G. L. Bundy, W. P. Schneider, F. H. Lincoln, and J. E. Pike, *J. Amer. Chem. Soc.*, 94, 2123 (1972).
(7) Private communication from Dr. W. C. Kreuger of The Upjohn Co.
(8) J. A. Dale, D. L. Dull, and H. S. Mosher, *J. Org. Chem.*, 34, 2543 (1969).

useful in confirming the configuration of the PGB compounds at C_{15} and for estimating the composition of mixtures of enantiomers,[9,10] since the (+)-α-methoxy-α-trifluoromethylphenyl acetates (MTPA) of (15*R*)- and (15*S*)-PGB_2 methyl esters showed several differences in the proton and fluorine nuclear magnetic resonance spectra.[11]

The prostaglandins extracted from a specimen of the *S* form of *P. homomalla* after enzymatic hydrolysis were purified by column chromatography. Based on frozen wet weight of coral, the amounts of (15*S*)-PGA_2 (1.4%) and (15*S*)-PGA_2 methyl ester (0.4%) obtained are comparable to the amounts of (15*R*)-prostaglandins obtained from the (*R*) form of *P. homomalla*. In addition,[6] 0.06% of crystalline (15*S*)-PGE_2, mp 63–66.5°, was isolated and shown to be identical in physical and biological properties with mammalian PGE_2.[12]

These findings, in addition to providing a novel and possibly useful natural source of primary prostaglandins,[6] also raise many intriguing biochemical questions about the origin and role of prostaglandins in marine organisms, some of which are under investigation.

(9) J. Muenzer, Senior Thesis, Kalamazoo College, Kalamazoo, Mich., June 1970.

(10) U. Axen, J. E. Pike, and W. P. Schneider on "The Total Synthesis of Natural Products," Vol. III, J. ApSimon, Ed., Wiley, New York, N. Y., in press.

(11) In the proton magnetic spectrum, the doublet from the proton at C_{13} occurred centered at δ 6.79 (J = 16 Hz) for the (15*S*) isomer and at 6.89 (J = 16 Hz) for the (15*R*) isomer. The chemical-shift differences for the methoxyl protons were too small to be useful since they were closely coupled quartets due to splitting by the three fluorine atoms five bonds distant (Varian A-60-A, $CDCl_3$, tetramethylsilane internal reference). The fluorine magnetic resonance spectrum (obtained from Midwest Research Institute at 94.1 MHz in $CDCl_3$ relative to external trifluoroacetic acid) of the 15-epimers showed absorption frequencies of 675 ((*R*) isomer) and 687 ((*S*) isomer) for the trifluoromethyl groups, broadened enough by splitting from the methoxyl protons to make accurate integration difficult without comparison with computer-calculated spectra.

(12) Infrared and nuclear magnetic resonance spectroscopy, mixture melting point, and chromatographic behavior (several systems) all were identical. We are grateful to Dr. J. R. Weeks and coworkers, The Upjohn Company, for the biological assays.

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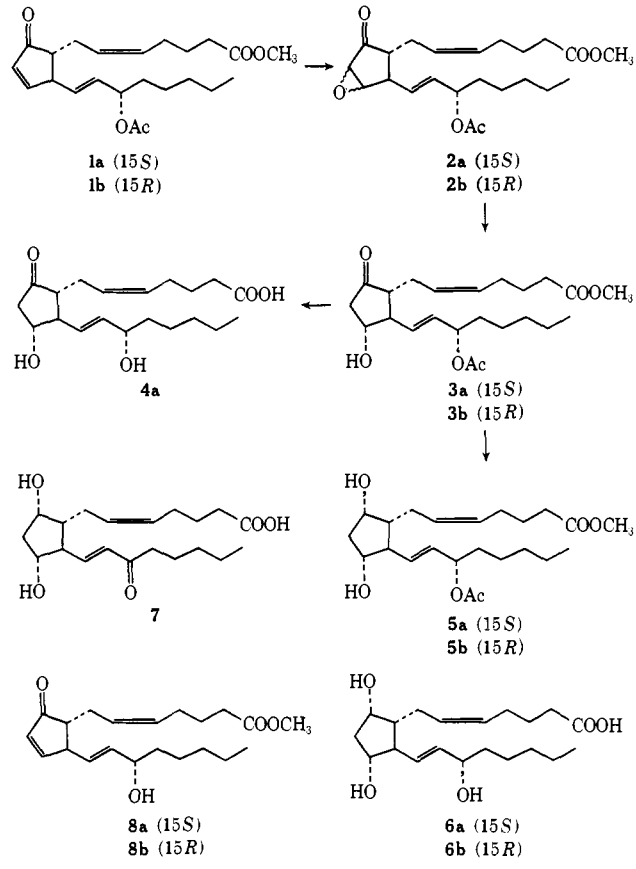
The Synthesis of Prostaglandins E_2 and $F_{2\alpha}$ from (15*R*)- and (15*S*)-PGA_2

Sir:

Ester derivatives of both (15*S*)- and (15*R*)-PGA_2 are readily obtainable from the gorgonian *Plexaura homomalla* found in the Caribbean area.[1,2] This communication describes the conversion of these materials to the biologically important[3] primary prostaglandins PGE_2 and $PGF_{2\alpha}$. (15*S*)-Prostaglandin A_2, acetate, methyl ester (**1a**) from coral extracts[2] was epoxidized with alkaline hydrogen peroxide[4] to a mixture of isomeric 10,11-epoxides (**2a**). Without separation, the mixture was reduced with chromous acetate[5] in acetic acid or aluminum amalgam[6] to give, after separation by silica gel chromatography, **3a**, the 15-acetate, methyl ester of PGE_2, in 56% yield along with 25% of the corresponding 11-epimer. The diester **3a** was hydrolyzed[7] to give PGE_2 (**4a**), obtained crystalline, mp 66–68°, in 90% yield, and identical in all respects[8] with PGE_2 obtained from mammalian sources. The 11β isomer of PGE_2 obtained similarly was noncrystalline, slightly less polar than **4a** on silica gel, showing characteristic downfield shifts of the $C_{13,14}$ olefinic protons in the nmr spectrum and characteristic fine structure differences in the circular dichroism curve.[9]



Reduction of PGE_2 with sodium borohydride leads directly to $PGF_{2\alpha}$.[10] Compound **3a** was also converted to its 11-trimethylsilyl ether and reduced with sodium borohydride to a mixture of 9α and 9β alcohols separated by silica gel chromatography; use of this protecting group increases the 9α:9β ratio obtained on reduction of the 9-ketone.[11] After hydrolysis $PGF_{2\alpha}$

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(3) S. Bergström, L. A. Carlson, and J. R. Weeks, *Pharm. Rev.*, 20, 1 (1968).

(4) F. Weitz and A. Scheffer, *Chem. Ber.*, 54, 2327 (1921).

(5) W. Cole and P. L. Julian, *J. Org. Chem.*, 19, 131 (1954).

(6) L. F. Fieser and M. Fieser in "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967.

(7) The hydrolysis was effected by an acetone-insoluble esterase: E. G. Daniels, The Upjohn Company, unpublished observations.

(8) P. W. Ramwell, J. E. Shaw, G. B. Clarke, M. F. Grostic, D. G. Kaiser, and J. E. Pike, *Progr. Chem. Fats Other Lipids*, 9, 231 (1968).

(9) Private communication, W. C. Krueger, The Upjohn Co.

(10) J. E. Pike, F. H. Lincoln, and W. P. Schneider, *J. Org. Chem.*, 34, 2139 (1969).

(11) The conversion of (15*R*)-PGA_2, acetate, methyl ester from coral to mammalian prostaglandins was first described at the N. Y. Academy of Sciences Meeting, Sept 17–19, 1970; G. L. Bundy, F. H. Lincoln, N. A. Nelson, J. E. Pike, and W. P. Schneider, *Ann. N. Y. Acad. Sci.*, 180, 76 (1971).