Figure 2. The temperature dependence of the quadrupolar splitting patterns of the neat dimer or "twin" (**1**) mesophase (left) and the analogue polymer (**2**) in the eutectic mixture (right).

(rigid body reorientation, libration and internal isomerization) for averaging the electric field gradient at the deuterons, i.e., averaging the orientation of the C–D bond vectors relative to the nematic director.[7] For flexible alkyl chains the number of $\Delta\nu_i$ resolved in the quadrupolar splitting pattern reflects the degree of differential averaging of the electric field gradient at the various methylene segments and is determined by the facility of isomerization at the respective positions along the chain.[8,9]

Figure 1 shows the evolution of the quadrupolar splitting pattern for 1,10-disubstituted decane-d_{20} *solutes* in nematic solvents as a function of the substituent size. A comparison of the spectra of the disubstituted decanes with the corresponding *n*-alkane and molecular modeling suggest that the CD_2 segments closest to the chain ends are the most effectively averaged and exhibit the smallest $\Delta\nu_i$.[9,10] Replacing the bromines with mesogenic cores (Figure 1b) increases the splittings as the larger and more orientationally restricted substituents impose additional constraints on the isomerization of the labeled spacer chain. Embedding an alkyl spacer into the backbone of a linear polymer (Figure 1c) further constrains the spacer chain.

Figure 2 shows the *T* dependence of the ^{2}H NMR spectra of the neat dimer and the polymer eutectic liquid crystals. The behavior of the former is reminiscent of that exhibited by *n*-alkanes (dissolved in nematic solvents) and alkyl chains appended to conventional, low molar mass thermotropic mesogens: On lowering the temperature the nematic order increases yielding larger $\Delta\nu_i$. And, as reported here for the dimer, this increase in the $\Delta\nu_i$ always occurs with the relative $\Delta\nu_i$ *diverging* at low temperature.[3,7] By contrast in the polymer eutectic, the width of the quadrupolar splitting pattern increases on lowering the temperature, but at comparable reduced temperatures, the $\Delta\nu_i$ *converge* to and coalesce at some limiting value $\Delta\nu_0 = 80$ kHz.

In one idealized limit of an all-trans chain perfectly aligned parallel to the director, the calculated quadrupolar splitting is $\Delta\nu_t = |3/2qS_{CD}| = 126$ kHz where the quadrupole coupling constant $q = 168$ kHz and the methylene C–D bond-order parameter $S_{C}D = -1/2$; i.e., the C–D bond vector is normal to the nematic director. Even at the lowest temperatures $\Delta\nu_0 \ll \Delta\nu_t$ implying that there is still considerable mobility of the C–D bond vector. The observed coalescence ($\Delta\nu_i \rightarrow \Delta\nu_0$) suggests that, concomitant with the increased nematic order, averaging of the C–D bond vector orientation becomes independent of the methylene segment's proximity to the mesogenic cores.

These marked differences in the ^{2}H NMR data for the DLC

and the PLC reflect the distinctly different abilities of the spacer chain to accommodate the increasing orientational constraints imposed on the mesogenic cores terminating the respective chains and raise additional questions about the relationship of the dimer mesophase to that of the polymer. The thermodynamic characteristics of oligomeric polymer precursors (amplified *even–odd* phenomena relative to that of low molar mass mesogens) asymptotically approach those of the corresponding PLC at rather low degrees of polymerization (≤ 10).[2b] As the ^{2}H NMR observations reported here clearly show averaged conformational differences between the dimer and the polymer, it would be interesting to ascertain the *critical degree of polymerization* above which the spacer dynamics of the oligomer cross over to behavior characteristic of the polymer.

Punaglandins: Halogenated Antitumor Eicosanoids from the Octocoral *Telesto riisei*[1]

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Marine prostaglandins, first discovered in a gorgonian,[2] have since been isolated from other invertebrates and from red algae.[3] An algal metabolite, hybridalactone,[4] and the octocoral-derived clavulones,[5] claviridenones,[6] feature C-12 oxygenation, which has led Corey[7] to suggest a distinctive biosynthetic pathway for these marine eicosanoids. The punaglandins,[8] which are described here, are also characterized by C-12 oxygen and unprecedented C-10 chlorine functions. One of the Δ^7 compounds, punaglandin 3 (**3**), inhibits L 1210 leukemia cell proliferation with an IC_{50} value of 0.02 $\mu g/mL$, which represents 15-fold greater activity than is shown by the corresponding clavulone.[9]

Telesto riisei, a source of the punaglandins, is an octocoral that lacks symbiotic algae.[10] A 1976 collection from Enewetak furnished two pregnanes;[11] the punaglandins were isolated from collections of *T. riisei* at several Oahu sites.

Refluxing hexane extraction of the freeze-dried animal (760 g) yields a residue (9.5 g), of which 1.9 g partitions into 80% $MeOH/H_2O$, containing the punaglandins. Column chromatography on Biosil A (hexane/EtOAc, 7:3) monitored at 254 nm yields four fractions which are in order of elution, punaglandin 4 (**4**, 0.08% of freeze-dried animal), 3 (**3**, 0.1%), 2 (**2**, 0.2%), and 1 (**1**, 0.8%) as almost colorless oils, each further purified by HPLC (Lichrosorb Magnum RP-18, 80% $MeOH/H_2O$).[12]

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1

2　**17,18-dihydro-1**

3

4　**17,18-dihydro-3**

5

6　**17,18-dihydro-5**

a
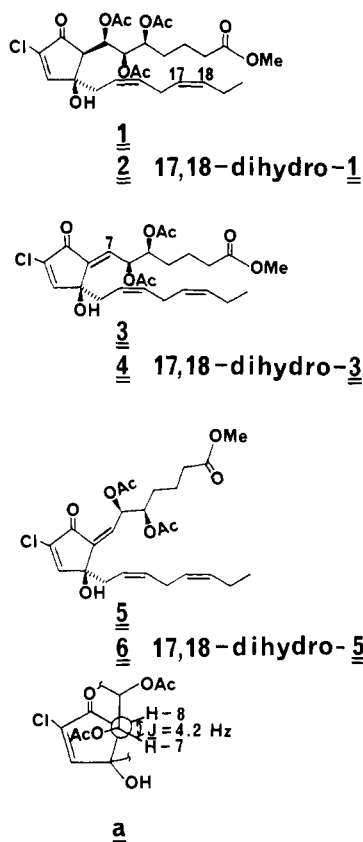
Desorption–chemical ionization MS[13] revealed molecular ions and the presence of chlorine, which was confirmed by combustion analysis. The 17,18-dihydro relationship of **1** and **2** and of **3** and **4** is evident from ^{1}H and ^{13}C NMR data and from their formulas, each pair differing by two mass units. The structure of **1**, $C_{27}H_{37}ClO_{10}$, was deduced as follows: Three acetates (δ 171.3, 170.5, 170.4, 2.11, 2.08, 2.00, all singlets; 1740 cm^{-1}) and one methyl ester (δ 173.8, 3.65) account for eight oxygens and four of nine unsaturations. An α,β-enone (228 nm, ϵ 7900; δ 196.0 s, 136.1 s, 158.1 d, 7.26 s) and a 3° hydroxyl (3500 cm^{-1}; δ 77.2 s) complete the oxygen functions and leave three unsaturations. Two of these are Z olefins (δ 134.6, 132.9, 126.0, 121.5, all doublets; δ 5.30, 5.61, $J = 10.8$ Hz, 5.24, 5.41 $J = 10.6$ Hz) and the last must be a ring for lack of additional low-field NMR signals.

Extensive decoupling experiments at 500 MHz fully documented all protons from C-2 to C-8 and C-13 to C-20 and hence both side chains. A 3° hydroxyl at C-12 was supported by the nonequivalence of the C-13 ^{1}H NMR signals (δ 2.53, 2.45) and their only coupling to H-14 (δ 5.30, $J = 7.0$ Hz), thereby unequivocally placing chlorine at C-10.

Punaglandin 1 (**1**) loses HOAc when treated with pyridine[14] affording a 3:1 mixture of (Z)-7,8-punaglandin 3 (**5**)[12] and **3**. The predominant Z isomer has an $H_{6,7}$ coupling constant of 7.7 Hz vs. 9.1 Hz for the E isomer. This assignment is further confirmed by comparing the chemical shifts of H-6 (6.02 ppm) and H-7 (6.35 ppm) in the E isomer **3** with those of H-6 (6.32 ppm) and H-7 (6.08 ppm) in the Z isomer **5**. The downfield shift of H-6 and the upfield shift of H-7 when going from E to Z is caused by the anisotropy of the C-9 carbonyl and is analogous to observations in the claviridenone series.[15] Under the same reaction conditions, **2** is transformed into (Z)-7,8-punaglandin 4 (**6**)[12] and its E isomer, also in a ratio of 3:1. These reactions show that all four punaglandins belong to the same stereochemical series. The relative

stereochemistry of the five centers was deduced as follows. The trans relationship of the two side chains was proven by irradiating H_2-13 at ~2.5 ppm and observing a strong NOE of the H-8 signal at 2.75 ppm. The three acetates at C-5, C-6, and C-7 must have all-threo configuration since $J_{5,6} = J_{6,7} = 5.3$ Hz.[16] Finally, H-7 must be gauche to H-8 ($J = 4.2$ Hz), as the less favorable Z isomer can only predominate, as it does in the HOAc elimination, if H-8 and AcO-7 are anti to each other, as in *a*. If one assumes that the punaglandins have the same stereochemistry as other marine eicosanoids,[17,18] our structures also represent the correct absolute stereochemistry.

Supplementary Material Available: Full physical data and ^{1}H NMR spectra of compounds **1** and **6** (10 pages). Ordering information is given on any current masthead page.

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Nucleophilic Addition of Azide Ion to Benzene Oxide: A Reinvestigation

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The reaction of benzene oxide (**1**) with sodium azide in H_2O at room temperature affords *trans*-6-azidocyclohexa-2,4-dien-1-ol (**2**) as the major product.[1] The 220-MHz ^{1}H NMR spectrum of **2** indicated the presence of a minor amount of 4-azidocyclohexa-2,5-dien-1-ol (**3**) for which stereochemistry was not assigned.[2] The reaction of **1**-$3,6$-$^2H_2$ with N_3^- gave the 1,2-azido alcohol as a mixture of deuterium-labeled isomers **2**-$2,5$-$^2H_2$ and **2**-$3,6$-$^2H_2$ in addition to **3**-$2,5$-$^2H_2$, and it was concluded that both trans-1,2 and trans-1,6 addition of N_3^- to **1** occurs to form **2**.[1]

Recent observations of facile (room temperature) [3,3]-sigmatropic rearrangements (Claisen rearrangements) involving

(13) We thank Professor K. Nakanishi (Columbia) for these determinations.

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(2) Dienol **3** shows absorptions at δ 6.32 and 6.26 (H_2, H_6 or H_3, H_5), 4.52 (H_1), and 4.04 (H_4). The absorption reported previously at 4.78 ppm apparently was due to the hydroxyl proton; the absorption for H_4 at 4.04 ppm was obscured by the absorption for H_6 of **2** at 4.09 ppm and the absorption of H_2, H_6 or H_3, H_5 was obscured by the absorption for H_3 of **2** at 6.04 ppm in the 220-MHz spectrum.