clude that at 77 K any disorder in this system takes place on a time scale slower than $\sim 10^{-11}$ s. Further studies to elucidate this question are planned.

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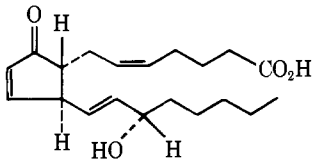
Chiral Synthesis of Prostaglandins from Carbohydrates. Synthesis of (+)-15-(*S*)-Prostaglandin A_2

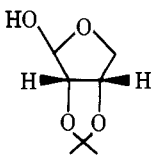
Sir:

Traditional syntheses of natural prostaglandins[1] involve at least one resolution. We have been devoting some effort to total syntheses of these substances which would not require separation of enantiomers, and now record the first total synthesis of a natural prostaglandin, PGA_2 (**1**)[2] from a simple sugar. The specific route we chose features the use of two Claisen rearrangements: one to produce the necessary trans geometry of a double bond (**3** → **4**) and the other as the means of transferring the chirality of a carbon-oxygen bond to that of a nonadjacent carbon-carbon bond (**5** → **7**).

Reaction of 2,3-isopropylidene-L-erythrose[3] (**2**) with 3 equiv of vinyl magnesium chloride in 1:3 tetrahydrofuran: methylene chloride (4 h, 0°) gave, in 96% yield, the vinyl carbinol **3** bp 97–101° (0.2 mm)[4] which, after protection of the primary alcohol as its methyl carbonate (1.05 equiv of methyl chloroformate in pyridine; 3 h at −30°, 1 h at 0°), bp 106–108° (90% yield), was submitted to Claisen rearrangement by heating with 10 equiv of trimethyl orthoacetate[5] (140°, 3 h with 0.1 equiv of propionic acid; additional 0.05 equiv after 1 and 2 h) to give the unsaturated ester **4** bp 136–138° (0.1 mm) in 83% yield: $[\alpha]^{25}D$ −37.8° (*c* 1.0, $CHCl_3$); δ 5.43 (H_B, q, J_{AB} = 15 Hz, J_{BC} = 7 Hz), 5.8 (H_A, m).[6]



1



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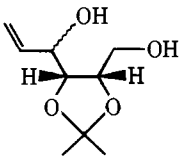

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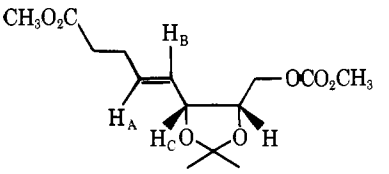
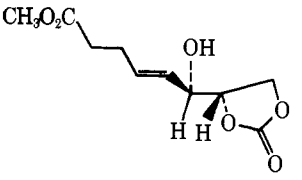


4

The choice of a chloroformate ester for the protection of the primary alcohol group was essential to the success of the next Claisen rearrangement which requires that the allylic alcohol function, which is masked as its acetonide in **4**, be made selectively available. Indeed, hydrolysis of the acetonide (25% aqueous acetic acid, 120°, 1 h), followed by treatment with triethylamine (1 equiv in methylene chloride, 1 h, 25°) gave the allylic alcohol-cyclic carbonate **5** as a colorless liquid: ν (neat) 3450, ~1790, 1730. Claisen rearrangement of **5** to **7** was now carried out with the orthoester **6**[7] (2 equiv, xylene, 160°, 1 h). After removal of excess side chain (florisil, hexane), the cyclic carbonate function of **7** was hydrolyzed from the resulting trimethyl ester **7** (0.1 equiv of potassium carbonate in dry methanol, 30 min, 25°) and the diol **8** was obtained[8] in an overall yield of 59% from the acetonide **4**.



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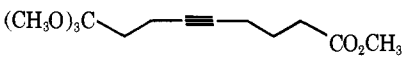

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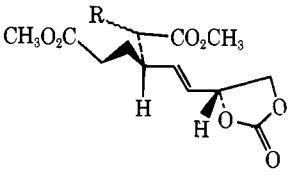

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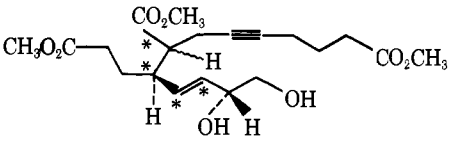
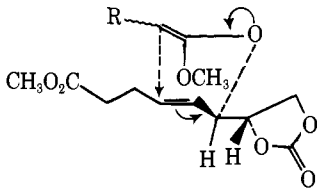


8

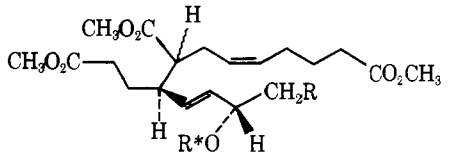
We were confident that the crucial transfer of chirality implied in **5** → **7** would take place with the carbonate ring equatorial in the chair transition state, as shown in **5***. On the other hand, there is no special steric preference for the

chain R in **5***, and it would therefore be expected that the Claisen product **7** would be a mixture, as shown. In fact, the ^{13}C NMR spectrum of **8** shows doubling of the peaks at ~44, 50, 131, and 133 ppm (attributed to the four starred carbon atoms) with an apparent ratio not far from 50:50. The correctness of the assumption that the epimeric mixture only involves C_8 (which in this particular synthesis is irrelevant because the center is epimerizable to the correct arrangement at the end) follows from the sequel.

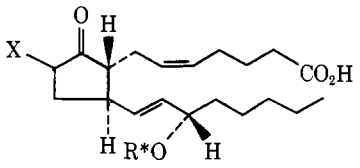


5*

The carbinol function in **8**, having served its purpose, was now transformed into an *n*-pentyl group. Semihydrogenation (5% palladium–barium sulfate in methanol (quinoline) of the triple bond, tosylation (1.1 equiv of tosyl chloride in pyridine, 7 days at −20°), and protection of the secondary hydroxyl (ethyl vinyl ether) gave, after purification on florisil (50% ether–hexane), the tosylate **9**, R = OTs, in 79% overall yield (crude) from **8**. Coupling with lithium dibutylcuprate[9] (5 equiv of ether, −40°, 2 h) led to the required **9**, R = butyl in 67% yield as a colorless oil.



9



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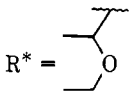

Cyclization (10 equiv of potassium *tert*-butoxide in tetrahydrofuran, 45 min, 25°) and hydrolysis (0.5 *N* sodium hydroxide, reflux, 10 min), followed by acidification (phosphate buffer), gave the keto acid **10**, X = H,[8] in which the acid chain has now been equilibrated to the correct epimer, in 77% yield from **9**, R = butyl (δ 0.8–2.6 (31 H), 3.3–4.2 (m, 3 H), 4.7 (m, 1 H, O-C*H*-O), 5.2–5.8 (m, 4 H), 8.4 (b s, 1 H, CO_2H); ν (neat) 1740, 1710; mass spectrum P^+ 391 (408 − 17)).

Final transformation to natural PGA_2 became possible when it was found that the selective introduction of the α-phenylseleno group[10] could be carried out on the dianion of the ketoacid **10**, X = H, (2.2 equiv of lithium diisopropylamide, tetrahydrofuran, 1 h, −78°, followed by 3 equiv of phenyl selenyl chloride). Oxidation of the product **10**, X = SePh, with sodium periodate (4 equiv of aqueous methanol, 10 min, 25°) and removal of the ethoxyethyl protecting group gave, after purification (silica gel), the desired PGA_2 (**1**) in 46% overall yield from **10**, X = H. The TLC behavior, uv[11] ($\lambda_{max}^{C_2H_5OH}$ 217 nm, log ε 4.03), ^1H NMR and, more particularly, the ^{13}C NMR,[12] and rotation[13] ($[\alpha]^{20}D$ + 130 (*c* 1.26, $CHCl_3$)) confirmed the structure of the synthetic natural PGA_2, thus obtained in 7.7% overall yield from **2**.

Acknowledgment. We thank the National Institutes of Health and the National Science Foundation for their support of this work.

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(7) The necessary orthoester **6** was synthesized starting with the 1-ethoxyethyl ether of 3-butyn-1-ol via the ethoxyethyl ether of 7-chloro-3-heptyn-1-ol and of 7-hydroxy-5-pentynenitrile. Conversion to methyl 8-cyano-5-octynoate (hydrogen chloride in methanol, 0.5 h reflux; toluenesulfonyl chloride–pyridine, 6 h, 25°; sodium cyanide–dimethyl sulfoxide, 3 h, 70°) and, finally, formation of the orthoester (dry hydrogen chloride–methanol–ether, 14 days, −20°, followed by methanol in pentane, 4 days, 25°).
(8) Eluted from silica gel after removal of low polarity impurities with 10–20% ether in hexane.
(9) Cf. C. R. Johnson and G. A. Dutra, *J. Am. Chem. Soc.*, **95**, 7777, 7783 (1973). These couplings were performed using cuprates made with purified cuprous iodide (G. B. Kauffman and L. A. Teter, *Inorg. Synth.*, **7**, 9 (1963)).
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Environmental Control of Reactions: Enhancement of μ-Oxo Dimer Formation from Iron(III) Porphyrins in Organized Monolayer Assemblies as a Model for Membrane Catalysis

Sir:

The involvement of metalloporphyrins and related compounds bound in membranes or similar ordered environment has led us to investigate the behavior of simple surfactant metalloporphyrins in the structurally similar environment provided by fatty acid type monolayer films and organized monolayer assemblies.[1-4] In recent studies of other surfactant molecules containing reactive chromophores, we have found that reactivity in the semirigid monolayer assembly is often quite different from behavior of the same compounds in solution. Of particular interest has been the finding that extremely high effective local concentrations of reactive molecules can be obtained, permitting the occurrence of bimolecular phenomena not observable with the same molecules in solution. Among the prominent reactions observed with different systems are dimerization,[5] photodimer formation,[6] and formation of fluorescent excimers.[7] In studies with the dioctadecyl ester of mesoporphyrin IX, we found efficient dimer production when mixed films of the porphyrin and arachidic acid were spread on water surfaces.[5] In the present paper we report an extension of our investigation to a study of surfactant iron(III) porphyrins.