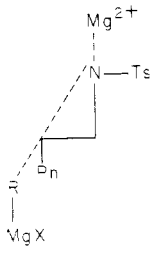
generally used in the previous cases (cf. entries 10 and 11). The presence of the excess reagent caused ring opening to become completely regiospecific without affecting the isolated yield. The ubiquitous push–pull mechanism again nicely accommodates this result wherein the excess Grignard reagent, functioning as a Lewis acid, now provides a tug on nitrogen and increases the extent of bond rupture in the transition state. The increased ionizing power of the solvent does, of course, also play an important role here.[13]



These studies, while indicating several new areas for exploration, should provide some needed guidelines for the reactions of organometallics with N-activated aziridines. The use of these compounds in natural product synthesis is currently being explored.

Experimental Section

General Procedures. The ^1H NMR spectra were taken on a Varian T-60 instrument, using tetramethylsilane as an internal standard. IR spectra were recorded on a Perkin-Elmer 700 spectrometer. The cuprous iodide was prepared from cupric sulfate, potassium iodide, and sodium thiosulfate. The ether was dried by distillation from sodium–benzophenone ketyl. The organolithium and -magnesium reagents were obtained from commercial sources.

Reaction of Aziridine I with Lithium Dimethylcuprate (Entry 5). To 114 mg (0.6 mmol) of freshly dried cuprous iodide in 7 mL of ether cooled to 0 °C was added 0.84 mL of methyllithium (1.4 M, 1.2 mmol). After the solution was stirred for 10 min at 0 °C and 30 min at room temperature, the cuprate was cooled to −70 °C and 96 mg (0.5 mmol) of *N*-carbethoxy-2-phenylaziridine was added. The reaction mixture was gradually warmed to 0 °C and maintained at this temperature for 6 h. The mixture was then quenched by addition of 8 mL of a saturated ammonium chloride solution and the product extracted with ether. The crude isolated material was purified by silica gel chromatography with methylene chloride as eluent to yield 101 mg (98%) of the ring-opened product: IR ($CHCl_3$) 3600–3500, 1720 cm^{-1}; NMR (CCl_4) δ 7.23 (s, 5 H), 4.83 (broad s, 1 H), 4.33 (q, 2 H, J = 7 Hz), 3.25 (m, 2 H), 2.83 (m, 1 H), 1.34 (d, 3 H, J = 7 Hz), 1.17 (t, 3 H, J = 7 Hz); mass spectrum (70 eV) m/e 207 (M^+).

Reaction of Aziridine I with Methyl Copper–Boron Trifluoride (Entry 8). To 190 mg (1 mmol) of freshly dried cuprous iodide in 3 mL of ether cooled to 0 °C was added dropwise 0.75 mL of methyllithium (1.4 M, 1 mmol). After 30 min at 0 °C, the methylcopper was cooled to −70 °C and 0.13 mL (1 mmol) of boron trifluoride etherate was added. The resulting mixture was stirred for 10 min, and then 94 mg (0.5 mmol) of *N*-carbethoxy-2-phenylaziridine was added. The reaction mixture was gradually warmed to room temperature and kept at this temperature for an additional 1 h. Workup as in the above experiment gave 96 mg (95%) of the ring-opened carbamate.

Reaction of Aziridine II with Allylmagnesium Bromide (Entry 12). To a solution of 68 mg (0.25 mmol) of *N*-tosyl-2-phenylaziridine in 2 mL of ether initially cooled to 0 °C was added 0.8 mL of a 1.3 M solution of allylmagnesium bromide in ether. The reaction mixture was stirred at room temperature for 24 h, quenched by addition of 8 mL of a saturated ammonium chloride solution, and extracted with ether. The crude isolated product was purified by silica gel chromatography with 10% ethyl acetate–hexane as eluent to afford 74 mg (94%) of the ring-opened product: IR ($CHCl_3$) 3700, 3600, 1340, 1170 cm^{-1}; NMR (CCl_4) δ 7.63 (d, 2 H, J = 7 Hz), 6.90–7.40 (m, 7 H), 5.84–4.70 (m, 3 H), 4.40 (broad t, 1 H), 2.14–3.65 (m, 5 H), 2.36 (s, 3 H); mass spectrum (70 eV) m/e 306, 250, 177 (base).

Reaction of Aziridine II with an Allyloxy Carbanion (Entry 13). To a solution of the allylic organometallic derived from *sec*-butyllithium treatment of the tetrahydropyranyl ether of methallyl alcohol (2 mmol in 3 mL of THF)[9] cooled to −70 °C was added a freshly prepared solution of magnesium bromide (312 mg, 1.70 mmol) in 2 mL of ether. After 10 min of stirring, 68 mg (0.25 mmol) of *N*-tosyl-2-phenylaziridine in 0.5 mL of THF was added, and the reaction mixture was maintained at −70 °C for 3 h. The mixture was quenched with 8 mL of a saturated ammonium chloride solution and extracted with ether. The crude isolated product was purified by silica gel chromatography with 25% ethyl acetate–hexane as eluent to yield 60 mg (56%) of the ring-opened product: IR ($CHCl_3$) 3700, 3600, 1340, 1170 cm^{-1}; NMR (CCl_4) δ 7.60–7.96 (overlapping d, 2 H), 7.00–7.49 (m, 7 H), 5.00 (broad s, 1 H), 4.75–4.96 (m, 2 H), 4.27–4.60 (m, 1 H), 3.85–4.25 (m, 1 H), 2.65–3.70 (m, 5 H), 2.27 (s, 3 H), 1.17–1.90 (m, 9 H); mass spectrum (70 eV) m/e 155, 84 (base).

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Registry No. I, 70197-04-5; II, 24395-14-0; III, 4164-25-4; CH_3Li, 917-54-4; $H_2C{=}C{=}C(OMe)Li$, 61186-66-1; CH_3MgBr, 75-16-1; $CH_2{=}CHCH_2MgBr$, 1730-25-2; $(CH_3)_2CuLi$, 15681-48-8; $(n\text{-}Bu)_2CuLi$, 24406-16-4; $(CH_2{=}CH)_2CuLi$, 22903-99-7; $CH_3Cu{\cdot}BF_3$, 70197-05-6; $CH_2{=}C(CH_3)CH(O\text{-}THP)Li$, 70197-06-7; 2-phenylaziridine, 1499-00-9; ethyl 2-phenylpropylcarbamate, 70197-07-8; ethyl 2-bromo-2-phenylethylcarbamate, 63409-27-8; ethyl 2-phenylhexylcarbamate, 55150-58-8; ethyl 1-phenylhexylcarbamate, 70197-08-9; *N*-tosyl-1-phenylpropylamine, 70197-09-0; *N*-tosyl-2-phenylpropylamine, 70197-10-3; *N*-tosyl(2-phenyl-4-pentenyl)amine, 70197-11-4; *N*-tosyl(4-methyl-2-phenyl-3-tetrahydropyronyloxy-4-pentenyl)amine, 70197-12-5.

(13) L. A. Paquette, "Principles of Modern Heterocyclic Chemistry", W. A. Benjamin, New York, 1968.

Synthesis of a Key Chiral Intermediate for 12-Hydroxyprostaglandins

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Grieco and co-workers recently described the synthesis of (±)-12-hydroxyprostaglandin $F_{2\alpha}$ methyl ester and reported that, when compared to $PGF_{2\alpha}$, the substance has a comparable activity in terminating pregnancy in the hamster but has minimal smooth muscle stimulating activity on gerbil colon and hamster uterine strips.[1] The 12-OH-$PGF_{2\alpha}$ would appear, therefore, to possess luteolytic activity with a diminished potential for side effects such as diarrhea. We wish to report here a remarkably simple synthesis of one of their key intermediates (**5b**) in optically active form having the absolute configuration corresponding to that of natural prostaglandins.

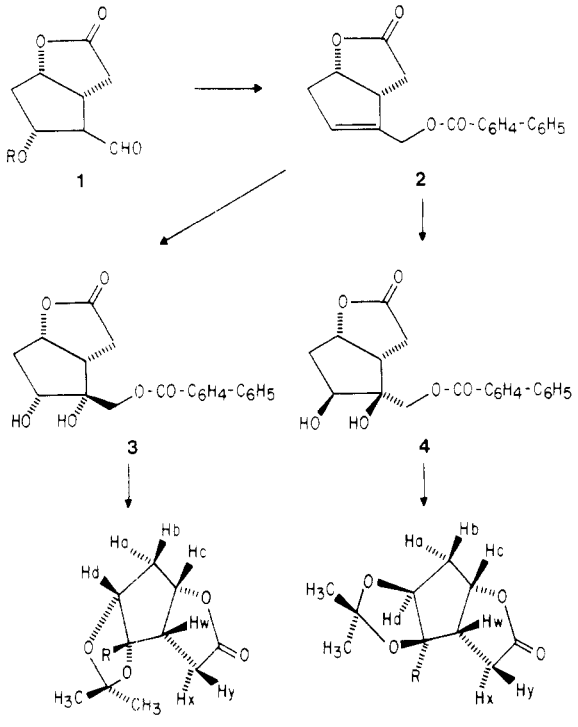
Optically active intermediates of type 1 are available by many synthetic routes,[2-5] and such compounds are readily

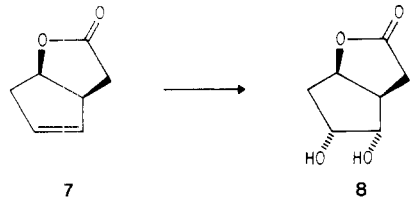
(1) P. A. Grieco, Y. Yokoyama, G. P. Withers, F. J. Okuniewicz, and C.-L. J. Wang, *J. Org. Chem.*, **43**, 4178 (1978).
(2) E. J. Corey, T. K. Schaaf, W. Huber, U. Koelliker, and N. M. Weinshenker, *J. Am. Chem. Soc.*, **92**, 397 (1970).

0022-3263/79/1944-2790$01.00/0

converted to our starting material **2**.[6] In the synthesis of thromboxane B_2, we reported the hydroxylation of **2** in near quantitative yield with a catalytic amount of osmium tetroxide and a molecular equivalent of *N*-methylmorpholine *N*-oxide to yield a mixture of cis glycols **3** and **4**.[6] The more abundant higher melting isomer (mp 155–156 or 166–167 °C) crystallizes readily from the mixture while the less abundant lower melting isomer (mp 144–146 °C) is difficult to obtain pure, but in one instance this isomer was obtained by fractional crystallization (separation of **3** and **4** by chromatography is difficult).

At the time, we recognized the potential of isomer **3** for the preparation of 12-hydroxyprostaglandins of normal configuration and began work to determine the configuration of the glycols. Prior to our work, it had been reported that treatment of **7** with osmium tetroxide–sodium





perchlorate yields 80–92% of the cis glycol **8**, hydroxylation occurring from the less hindered exo face.[7] By analogy, one might expect to obtain the undesirable "exo" glycol **4** as the major product from hydroxylation of **2**; however, as will be seen below, this is not the case.

In preparation for the synthesis of 12-hydroxyprostaglandins, the isomeric glycols were converted to their respective acetonides **5a** and **6a**, and removal of the *p*-phenylbenzoate protective group from each by transesterification afforded the respective alcohols **5b** and **6b**. Further chemical elaboration of material corresponding to **5b** by standard procedures[2] would lead to 12-hydroxyprostaglandins of natural configuration.[1] It was at this point that we attempted to identify the isomers corresponding to **5b** and **6b**.

Inspection of structure **5b** reveals the presence of a unique acetonide methyl group relatively close to the lactone carbonyl—the other methyl group being considerably further away as are the acetonide methyl groups in structure **6b**. The use of lanthanide shift reagents and NMR spectroscopy should be capable of detecting the unique methyl group and thereby reveal which sample corresponds to **5b**. However, use of europium shift reagent tris(2,2,6,6-tetramethyl-3,5-heptanedionato)europium [Eu(thd)$_3$; Resolve-Al^{TM}] with samples corresponding to **5b** and **6b** did not allow a distinction between the isomers presumably due to europium complexation at more than one center. To limit complexation to the lactone carbonyl, isomers **5b** and **6b** were converted to their respective trimethylsilyl ethers **5c** and **6c**. Examination of the ^{1}H NMR spectra of these isomeric silyl ethers obtained with increasing concentrations of tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium [Eu(fod)$_3$; Resolve-Al EuFOD^{TM}] showed that the acetonide derived from the higher melting glycol has the unique methyl group. With material corresponding to **5c**, the acetonide methyl groups underwent shifts of 1.32 and 0.41 ppm while the methyl groups of material corresponding to **6c** experienced shifts of only 0.22 and 0.20 ppm under comparable conditions. These results allowed definitive assignments of structure to the various compounds prepared, and our substance **5b** appears to be essentially the same[8] as the corresponding compound prepared by a different route by Grieco and co-workers.[1]

More recently we have had occasion to hydroxylate **2** and to convert the glycol mixture directly to **5a** and **6a** (easily separated by chromatography) in yields of 70 and 26%, respectively. Removal of the ester protective group from **5a** proceeds in essentially quantitative yield. Thus key intermediate **5b** is readily available from the common intermediates used in the synthesis of prostaglandins.

Experimental Section

Melting points were determined with a Thomas-Hoover melting point apparatus and are uncorrected. Nuclear magnetic resonance (NMR) spectra were obtained on a Varian A-60D or Varian XL-100 spectrometer, and chemical shifts are reported as δ (parts per million) relative to tetramethylsilane as an internal standard. Infrared spectra were recorded as 10% (w/v) solutions in chloroform using a Perkin-Elmer 137 or Perkin-Elmer 197 spectrophotometer. Mass spectra were determined on a CEC 21-110 high resolution mass spectrometer or a Varian MAT CH5 or CH7 mass spectrometer. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. R_f values were determined using Analtech precoated 250 μm silica gel GF thin-layer chromatography plates. Column chromatograms utilized E. Merck silica gel (70–230 mesh ASTM). Extracts were dried over magnesium sulfate.

[3a*S*-(3aα,4β,5β,6aα)]-3,3a,4,5,6,6a-Hexahydro-4,5-dihydroxy-4-[[([1,1′-biphenyl]-4-ylcarbonyl)oxy]methyl]-2*H*-cyclopenta[*b*]furan-2-one (3) and [3a*S*-(3aα,4α,5α,6aα)]-3,3a,4,5,6,6a-hexahydro-4,5-dihydroxy-4-[[([1,1′-biphenyl]-4-ylcarbonyl)oxy]methyl]-2*H*-cyclopenta[*b*]furan-2-one (4). To a solution of 32.7 g (98 mmol) of [3a*R*-(3aα,6aα)]-3,3a,6,6a-tetrahydro-4-[[([1,1′-biphenyl]-4-ylcarbo-

(3) J. S. Bindra and R. Bindra, "*Prostaglandin* Synthesis", Academic Press, New York, 1977, pp 62, 178, 197, 229, 230, 232, and 270.
(4) A. Mitra, "The Synthesis of Prostaglandins", Wiley-Interscience, New York, 1977.
(5) K. G. Paul and F. Johnson, *J. Am. Chem. Soc.*, **98**, 1285 (1976).
(6) N. A. Nelson and R. W. Jackson, *Tetrahedron Lett.*, 3275 (1976).
(7) L. Gruber, I. Tömösközi, E. Major, and G. Kovács, *Tetrahedron Lett.*, 3729 (1974).

(8) Except that our compound is optically active and was obtained as a crystalline material.

nyl)oxy]methyl]-2*H*-cyclopenta[*b*]furan-2-one (**2**),[6] 300 mL of acetone, and 40 mL of water was added a solution of 500 mg of osmium tetroxide in 25 mL of *tert*-butyl alcohol followed by a solution of 17.5 g (114 mmol) of *N*-methylmorpholine *N*-oxide dihydrate in 25 mL of water. The mixture was stirred at room temperature for 1.5 h when 0.57 mL (10 mmol) of acetic acid was added to the mixture, and most of the acetone was removed in vacuo. The residue was diluted with 300 mL of tetrahydrofuran and 1 L of ethyl acetate, and the resulting mixture was washed with a mixture of 250 mL of saturated brine and 15 mL of 12 M hydrochloric acid and a mixture of saturated brine and saturated aqueous sodium bicarbonate and was then dried and concentrated in vacuo. The residue was diluted with 250 mL of ethyl acetate for crystallization and afforded 19.1 g of the desired isomer **3**, mp 166–167 °C (in an earlier preparation, a different polymorph of this isomer was obtained from ethyl acetate, mp 155–156 °C): $R_f \simeq 0.67$ in ethyl acetate; mass spectrum for bis(trimethylsilyl ether) derivative, significant ions at *m/e* 512 (M^+, weak), 497.1821 ($M^+ - CH_3$; Calcd for $C_{26}H_{33}O_6Si_2$: 497.1816), 331, 301, 299, 255, 198, 181, 89, 68, and 59. Anal. Calcd for $C_{21}H_{20}O_6$: C, 68.47; H, 5.47. Found: C, 68.57; H, 5.46.

The filtrate from the crystallization above was concentrated to yield 13.6 g of a semisolid mixture of isomers **3** and **4**. The isomer mixture is difficult to separate chromatographically; however, in one experiment, the lower-melting isomer **4** was obtained pure in 13% yield by a fractional crystallization from ethyl acetate and had mp 144–146 °C: $R_f \simeq 0.57$ in ethyl acetate; mass spectrum for bis(trimethylsilyl ether) derivative, significant ions at *m/e* 512 (M^+, weak), 497.1821 ($M^+ - CH_3$; Calcd for $C_{26}H_{33}O_6Si_2$: 497.1816), 422, 331, 301, 181, 153, and 145. Anal. Calcd for $C_{21}H_{20}O_6$: C, 68.47; H, 5.47. Found: C, 68.41; H, 5.41.

[3a*R*-(3aα,4aα,7aα,7bα)]-3a,4,4a,7,7a,7b-Hexahydro-7b-[[([1,1′-biphenyl]-4-ylcarbonyl)oxy]methyl]-2,2-dimethyl-6*H*-furo[3′,2′:3,4]cyclopenta[1,2-*d*]-1,3-dioxol-6-one (5a). A solution of 1.6 g of glycol isomer **3** (mp 165–166 °C), 20 mL of acetone, and 4 drops of 70% perchloric acid was allowed to stand at room temperature for 40 min. The mixture was diluted with 125 mL of ethyl acetate, and the solution was washed with saturated brine, dried, and concentrated in vacuo. Trituration of the residue with benzene afforded 2.1 g of product **5a**, mp 82–90 °C (gas evolution, benzene solvate by NMR): $R_f \simeq 0.44$ in 1:1 ethyl acetate–hexane; NMR ($CHCl_3$) δ 1.40 (s, CH_3), 1.48 (s, CH_3), 1.88 (apparent t, J = 5 Hz), 2.14 (apparent t, J = 5.5 Hz), 4.42 (s, CH_2O), 4.72 (apparent d, J = 5.5 Hz, H_d hydrogen), 4.97 (apparent t, J = 5 Hz, H_c hydrogen), 7.23–8.16 (m's, 9 aromatic H's), 7.33 (s, 6 H's, C_6H_6); mass spectrum *m/e* 408 (M^+) and other ions of decreasing intensity at 181, 393, 153, 152, 394, 182, 43, 55, 198, 197; $[\alpha]^{25}_D$ −15° (*c* 1.00, $CHCl_3$). Anal. Calcd for $C_{24}H_{24}O_6 \cdot C_6H_6$: C, 74.05; H, 6.22. Found: C, 74.12; H, 6.31.

[3a*R*-(3aα,4aα,7aα,7bα)]-3a,4,4a,7,7a,7b-Hexahydro-7b-(hydroxymethyl)-2,2-dimethyl-6*H*-furo[3′,2′:3,4]cyclopenta[1,2-*d*]-1,3-dioxol-6-one (5b). To a mixture of 2.0 g of ester **5a** (benzene solvate), 25 mL of anhydrous methanol, and 4 mL of dry methylene chloride under nitrogen and at room temperature was added with stirring 1.0 mL of 4.4 N (25%) methanolic sodium methoxide. After the reaction had continued for 20 min, 0.3 mL of acetic acid and 5 mL of ethyl acetate were added, and the mixture was concentrated in vacuo to remove methanol. The residue was mixed with 60 mL of ethyl acetate and 1 g of Celite, and the mixture was filtered. The filtrate was concentrated in vacuo, and the residue was chromatographed in a dry-packed column of 200 g of silica gel deactivated with 40 mL of ethyl acetate. Elution of the column with ethyl acetate afforded methyl *p*-phenylbenzoate ($R_f \simeq 0.90$ in ethyl acetate) followed by 0.93 g of product **5b** which crystallized on standing, mp 94.5–95.5 °C: $R_f \simeq 0.29$ in ethyl acetate; NMR[9] ($CDCl_3$) δ 1.40 (CH_3), 1.45 (CH_3), 2.54 (H_a), 2.04 (H_b), 2.90 (H_x), 2.70 (H_y), 2.85 (H_w), 3.66 (CH_2O), 4.65 (H_d), 5.02 (H_c); J values in Hz, J_{ab} = 17.0, J_{bd} = 4.7, J_{bc} = 5.5, J_{ac} = 0.0, J_{ad} = 0.0, J_{xy} = 18, J_{wy} = 9.9, J_{wx} = 0.0, J_{cw} = 6.5; IR ($CHCl_3$) medium to strong bands at 3590, 3470, 3010, 2990, 2940, 1765, 1420, 1410, 1385, 1375, 1365, 1350, 1295, 1245, 1240, 1220, 1200, 1165, 1140, 1120, 1090, 1040, 1020, 990, 950, 895 cm^{-1}; $[\alpha]^{25}_D$ −55° (*c* 2.00, $CHCl_3$); mass spectrum *m/e* 213.0765 ($M^+ - CH_3$; Calcd for $C_{10}H_{13}O_5$, 213.0763) and other ions of decreasing intensity at 43, 214, 107, 153, 135, 55, 171, 179, and 79. Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.07. Found: C, 58.19; H, 7.18.

[3a*R*-(3aα,4aα,7aα,7bα)]-3a,4,4a,7,7a,7b-Hexahydro-7b-((trimethylsilyloxy)methyl)-2,2-dimethyl-6*H*-furo[3′,2′:3,4]cyclopenta[1,2-*d*]-1,3-dioxol-6-one (5c). A mixture of 0.70 g of alcohol **5b**, 5 mL of anhydrous tetrahydrofuran, 5 mL of hexamethyldisilazane, and 1 mL of chlorotrimethylsilane was stirred at room temperature for 20 h then concentrated in vacuo. The residue was slurried with benzene and filtered through a pad of Celite, and the filtrate was concentrate in vacuo. The residue was chromatographed *rapidly* (10 min) in a column of 30 g of silica gel wet packed with 2:3 ethyl acetate–hexane. Cold (0 °C) eluant of the same composition was passed through the column under nitrogen pressure and afforded 0.85 g of product **5c**: mp 54–55 °C; $R_f \simeq 0.30$ in 1:3 ethyl acetate–hexane; NMR ($CDCl_3$) δ 1.36 (CH_3), 1.45 (CH_3), 2.56 (H_a), 1.96 (H_b), 2.90 (H_x), 2.80 (H_y), 2.80 (H_w), 3.62 (CH_2O), 4.60 (H_d), 4.98 (H_c); J values in Hz, J_{ab} = 16.0, J_{bd} = 5.2, J_{bc} = 6.0, J_{ac} = 0.0, J_{ad} = 0.0, J_{xy} = 18.3, J_{wy} = 10.0, J_{wx} = 0.0, J_{cw} = 6.0; mass spectrum *m/e* 285.1163 ($M^+ - CH_3$; Calcd for $C_{12}H_{21}O_5Si$, 285.1158) and other ions of decreasing intensity at 73, 75, 43, 197, 135, 286, 225, 59, 107. Anal. Calcd for $C_{14}H_{24}O_5Si$: C, 55.97; H, 8.05. Found: C, 56.35; H, 8.22.

[3a*S*-(3aα,4aβ,7aβ,7bα)]-3a,4,4a,7,7a,7b-Hexahydro-7b-[[([1,1′-biphenyl]-4-ylcarbonyl)oxy]methyl]-2,2-dimethyl-6*H*-furo[3′,2′:3,4]cyclopenta[1,2-*d*]-1,3-dioxol-6-one (6a). A solution of 0.90 g of glycol isomer **4** (mp 144–146 °C), 15 mL of acetone, and 3 drops of 70% perchloric acid was allowed to stand at room temperature for 40 min. The mixture was diluted with 100 mL of ethyl acetate, and the solution was washed with saturated brine, dried, and concentrated in vacuo. The residue was chromatographed in a dry-packed column of 200 g of silica gel deactivated with 40 mL of ethyl acetate. The column was eluted with 1:1 ethyl acetate–hexane and gave 0.91 g of product **6a**: mp 129.5–130.5 °C (from benzene); $R_f \simeq 0.67$ in 1:1 ethyl acetate–hexane; NMR ($CHCl_3$) δ 1.38 (s, CH_3), 1.48 (s, CH_3), 4.54 (s, CH_2O), 4.63 (apparent d, J = 5 Hz, H_d hydrogen), 5.24 (apparent q, J = 7.5 Hz, H_c hydrogen), 7.25–8.14 (m's, 9 aromatic H's); $[\alpha]^{25}_D$ +45° (*c* 1.47, $CHCl_3$); mass spectrum *m/e* 408 (M^+) and other ions of decreasing intensity at 181, 78, 393, 198, 152, 153, 182, 77, 394, 52. Anal. Calcd for $C_{24}H_{24}O_6$: C, 70.57; H, 5.92. Found: C, 70.81; H, 5.95.

[3a*S*-(3aα,4aβ,7aβ,7bα)]-3a,4,4a,7,7a,7b-Hexahydro-7b-(hydroxymethyl)-2,2-dimethyl-6*H*-furo[3′,2′:3,4]cyclopenta[1,2-*d*]-1,3-dioxol-6-one (6b). Following the procedure described above for the preparation of isomer **5b**, 0.91 g of ester **6a** was converted by ester interchange with methanol and sodium methoxide to a mixture of **6b** and methyl *p*-phenylbenzoate. The mixture was chromatographed in a dry-packed column of 150 g of silica gel deactivated with 20 mL of acetone and 10 mL of methylene chloride. Elution of the column with 1:4 acetone–methylene chloride afforded methyl *p*-phenylbenzoate ($R_f \simeq 0.91$ in ethyl acetate) followed by 0.50 g of product **6b** as an oil: $R_f \simeq 0.59$ in ethyl acetate; NMR[9] ($CDCl_3$) δ 1.38 (CH_3), 1.50 (CH_3), 2.60 (H_a), 1.95 (H_b), 2.71 (H_x), 2.60 (H_y), 3.10 (H_w), 3.78 (CH_2O), 4.57 (H_d), 5.25 (H_c); J values in Hz, J_{ab} = 15.0, J_{bd} = 5.0, J_{bc} = 7.2, J_{ac} = 7.1, J_{ad} = 1.0, J_{xy} = 19.0, J_{wy} = 10.8, J_{wx} = 0.0, J_{cw} = 7.0; IR ($CHCl_3$) medium to strong bands at 3580, 3480, 3005, 2985, 2935, 1765, 1380, 1370, 1360, 1240, 1225, 1170, 1125, 1085, 1060, 1030, 990, 895, 855 cm^{-1}; $[\alpha]^{25}_D$ +52° (*c* 1.42, $CHCl_3$); mass spectrum *m/e* 213.0761 ($M^+ - CH_3$; Calcd for $C_{10}H_{13}O_5$ 213.0763) and other ions of decreasing intensity at 43, 78, 55, 135, 107, 153, 79, 197.

[3a*S*-(3aα,4aβ,7aβ,7bα)]-3a,4,4a,7,7a,7b-Hexahydro-7b-((trimethylsilyl)oxymethyl)-2,2-dimethyl-6*H*-furo[3′,2′:3,4]cyclopenta[1,2-*d*]-1,3-dioxol-6-one (6c). Following the procedure described above for the preparation of isomer **5c**, 0.30 g of alcohol **6b** was converted to crude product **6c** which was chromatographed *rapidly* (10 min) as described above but using 35:65 ethyl acetate–hexane as eluant. Concentration of appro-

(9) Less detailed but more conventional spectral descriptions are as follows. (a) For **5b**: NMR ($CDCl_3$) δ 1.40 (s, CH_3), 1.45 (s, CH_3), 1.84 (apparent t, J = 5 Hz), 2.11 (apparent t, $J \simeq 5$ Hz), 3.05 (t, $J \simeq 5$ Hz, OH), 3.63 (d, $J \simeq 5$ Hz, CH_2O), 4.65 (apparent d, $J \simeq 5$ Hz H_d hydrogen), 5.02 (apparent t, J = 5 Hz, H_c hydrogen. (b) For **6b**: NMR ($CDCl_3$) δ 1.33 (s, CH_3), 1.46 (s, CH_3), 3.18 (t, J = 5 Hz, OH), 3.75 (d, J = 5 Hz, CH_2O), 4.52 (apparent d, $J \simeq 5$ Hz, H_d hydrogen), 5.20 (apparent q, $J \simeq 7.5$ Hz, H_c hydrogen).

priate fractions afforded 200 mg of product **6c** containing a trace of a slightly more polar impurity and 150 mg of pure **6c**: $R_f \simeq$ 0.36 in 1:3 ethyl acetate–hexane; NMR ($CDCl_3$) δ 1.33 (CH_3), 1.46 (CH_3), 2.54 (H_a), 1.94 (H_b), 2.70 (H_x), 2.60 (H_y), 3.05 (H_w), 3.74 (CH_2O), 4.50 (H_d), 5.20 (H_c); J values in Hz, J_{ab} = 15.0, J_{bd} = 5.0, J_{bc} = 6.5, J_{ac} = 7.5, J_{ad} = 0.0, J_{xy} = 18.0, J_{wy} = 10.0, J_{wx} = 0.0, J_{cw} = 6.5; mass spectrum m/e 285.1163 ($M^+ - CH_3$; Calcd for $C_{13}H_{21}O_5Si$ 285.1158) and other ions of decreasing intensity at 73, 75, 197, 43, 225, 59, 135, 55, 183.

Conversion of 2 to 5a and 6a. Following the procedure described above for the preparation of **3** and **4**, 1.5 g of **2**, 15 mL of acetone, 1.8 mL of water, and 20 mg of osmium tetroxide in 1 mL of *tert*-butyl alcohol was stirred with 0.81 g of *N*-methylmorpholine *N*-oxide and 1.2 mL of water for 1.5 h and then worked up as described above to yield 2.1 g of a crude mixture of **3** and **4**. This mixture, in 25 mL of acetone, was treated with 2 drops of 70% perchloric acid for 40 min and was then worked up as described above to give 2.1 g of a mixture of acetonides **5a** and **6a** which was chromatographed in a column of 250 g of silica gel. The column was eluted with 1:1 ethyl acetate–hexane and fractions of about 17 mL each were collected. Fractions 15–21 afforded 0.48 g (26%) of isomer **6a**, mp 129–130.5 °C, while fractions 38–55 afforded 1.46 g of **5a** which, on trituration with benzene, gave 1.53 g (70%) of **5a** benzene solvate, mp 82.5–90 °C. The infrared and NMR spectra of these samples of **5a** and **6a** are essentially identical with those reported above.

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Registry No. 2, 62158-45-6; **3**, 62158-46-7; **3**-2(Me_3Si) derivative, 70456-71-2; **4**, 62210-95-1; **4**-2(Me_3Si) derivative, 70493-35-5; **5a**, 70456-72-3; **5b**, 70493-36-6; **5c**, 70456-73-4; **6a**, 70493-37-7; **6b**, 70493-38-8; **6c**, 70493-39-9.

Reinvestigation of Dihalotriphenoxyphosphoranes

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In 1883, Noack[1] was the first to prepare dibromotriphenoxyphosphorane, $(PhO)_3PBr_2$, by the addition of bromine to triphenyl phosphite. Since then, many dihalophosphoranes of this type have been prepared and studied.[2-6] The characterization of the above adducts has been based primarily on hydrolytic and elemental analysis data. Recently, Ramirez and co-workers[6] applied ^{31}P NMR to study the product derived from the reaction of chlorine with triphenyl phosphite. Attempts to prepare highly purified samples of these dihalo adducts by Rydon and Tonge[5] were unsuccessful. In the case of the dibromo adduct, elemental analysis was consistent with a structure corresponding to bromotetraphenoxyphosphorane rather than the expected dibromotriphenoxyphosphorane. A conductometric study of the reaction of triphenyl phosphite with bromine in acetonitrile was carried out by Harris and Payne.[4] They postulated that the reaction between triphenyl phosphite and bromine proceeded in two well-defined stages (eq 1 and 2). In the first step, a steep rise in the conductance was observed, whereas no such change occurred in the second step.

$$2(PhO)_3P + Br_2 \rightleftharpoons (PhO)_4PBr + (PhO)_2PBr$$
$$\downarrow\uparrow$$
$$(PhO)_4P^+ + Br^- \quad (1)$$

$$2(PhO)_3P + 2Br_2 \rightleftharpoons 2(PhO)_3PBr_2 \rightleftharpoons$$
$$(PhO)_3PBr^+ + (PhO)_3PBr_3^- \quad (2)$$

We have reinvestigated the reaction of triphenyl phosphite with halogens utilizing ^{31}P NMR spectroscopy. The results of this study are reported herein.

Experimental Section

All ^{31}P NMR spectra were obtained on a Varian CFT-20 NMR spectrometer operating at 32.19 MHz. Chemical shifts are reported in terms of the δ scale relative to 85% phosphoric acid as the external reference. All spectra were recorded by using deuterated chloroform as the solvent with and without the use of the external reference. Triphenyl phosphite was purchased from Eastman Organic Chemicals.

Reaction and Discussion

I. Reaction of Triphenyl Phosphite and Bromine. Following the procedure of Rydon and Tonge,[5] a white solid and a pale yellow solid were obtained from the reaction of triphenyl phosphite with a 0.5 molar and a 1 molar equiv of bromine, respectively, in chlorobenzene. The ^{31}P NMR chemical shifts[7] of the white solid and the pale yellow solid are +22.5 and −4.5 ppm, respectively, relative to 85% phosphoric acid. The former chemical shift corresponds to bromotetraphenoxyphosphorane and the latter to dibromotriphenoxyphosphorane. The ^{31}P NMR shift of bromotetraphenoxyphosphorane was previously reported at +26 ppm by Nesterov et al.[8] The assignment of the resonance at −4.5 ppm to dibromotriphenoxyphosphorane was based on the fact that when a limiting amount of triphenyl phosphite was added into the solution containing the pale yellow solid, the peak at −4.5 ppm decreased, and two new peaks at −228.2 and +22.4 ppm corresponding to phosphorus tribromide[9] and bromotetraphenoxyphosphorane appeared in approximately a 1:3 ratio. A slight excess of triphenyl phosphite caused the peak at −4.5 ppm to disappear and resulted in a spectrum exhibiting peaks at −199.4, −175.3, −128.2, and +22.5 ppm corresponding to phenyl phosphorodibromidite,[9,10] diphenyl phosphorobromidite,[9,10] triphenyl phosphite, and bromotetraphenoxyphosphorane, respectively.

Table I presents the results of ^{31}P NMR studies of triphenyl phosphite with 0.25, 0.5, 0.75, and 1 molar equiv amounts of bromine. When 0.25 molar equiv of bromine was added to triphenyl phosphite, bromotetraphenoxyphosphorane, diphenyl phosphorobromidite, and unreacted triphenyl phosphite were observed. When 0.5 molar equiv of bromine was added to triphenyl phosphite, phenyl phosphorodibromidite was observed in addition to the aforementioned compounds. When 0.75 molar equiv of bromine was added to triphenyl phosphite, the phosphorus compounds observed were bromotetraphenoxyphosphorane, diphenyl phosphorobromidite, phenyl phosphoro-

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