29, 119245-39-5; 30, 119245-40-8; cyclohexanone, 108-94-1; bi-1-cyclohexen-1-yl, 1128-65-0.

Supplementary Material Available: Tables of positional parameters, bond angles, bond lengths, and general temperature factor expressions (4 pages); observed and calculated reflections for 3(*R**)-(2-oxocyclohex-1(*S**)-yl)-[1(*S**),1′(*R**)-bicyclohexyl]-2,2′-dione (**25**) (3 pages). Ordering information is given on any current masthead page.

Notes

Iodine Oxidation of α-Tocopherol and Its Model Compound in Alkaline Methanol: Unexpected Isomerization of the Product Quinone Monoketals

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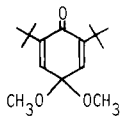
Iodine in alkaline methanol has been shown to bring about the oxidative coupling or oxidation of the alkyl substituent of alkylphenols.[1] The reagent has also been employed in the synthesis of bichalcones.[2] To extend the scope of this oxidation, the author initiated a study of 4-alkoxyphenols, including α-tocopherol (**3b**) and its model compound, 2,2,5,7,8-pentamethylchroman-6-ol (**3a**), whose chemical oxidation has been extensively investigated in connection with the biological antioxidant activity shown by the former.[3]

Dropwise addition of a methanolic solution of I_2 (1 mol equiv) to a solution of 2,6-di-*tert*-butyl-4-methoxyphenol in methanol containing excess KOH under N_2 at room temperature (ca. 10 °C), immediately afforded *p*-benzoquinone dimethyl ketal **1** in over 90% yield. Likewise, dimethyl ketal **2** was obtained from 2,3,5,6-tetramethyl-4-methoxyphenol in 54% yield. Model compound **3a**, a



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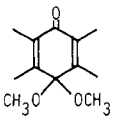

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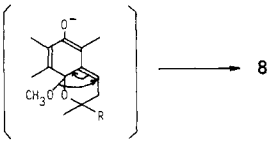
cyclic ether fused to a benzene ring, was subjected to similar iodine oxidation at room temperature. An oily product, isolated in 67% yield after extractive workup of the reaction mixture, is assigned 8a-methoxychroman-6-one **4a** based on its spectral data (see the Experimental Section). $NaBH_4$ reduction of the product to the parent phenol **3a** and acid hydrolysis to give *p*-benzoquinone **10a** are consistent with structure **4a**.[4] Chromanone **4a** was also obtained by treating **3a** with benzoyl peroxide in refluxing methanol[4] but in somewhat lower yield. Surprisingly, however, **4a** was no longer formed when the same iodine oxidation of **3a**, which is quite rapid even at 10 °C, was carried out at 50 °C. The crystalline major product (ca. 30%) obtained is isomeric with **4a**. Its structure, 4-methoxychroman-6-ol **8a**, is based on the following spectral observations. The IR spectrum suggests the presence of a hydroxyl group(s), and the UV spectrum exhibits a marked resemblance to that of the parent phenol **3a**. The ^1H NMR spectrum indicates that C-4 bears a methoxy group (δ 3.36) and a hydrogen (δ ca. 4.2). Treatment of **8a** with acid afforded 3,4-dehydrochroman-6-ol **9a**. It is notable that oxidation at C-4 has been quite rare in the chroman-6-ol series. The distinct products from reactions at the different temperatures are reconciled by the experiments which follow. Oxidation of **3a** with I_2 at room temperature followed by warming before the workup, gave rise to **8a** (48%), but no **4a** was detected. It is, therefore, assumed that **4a** isomerizes to **8a** (70%) in hot methanol in the presence of the alkali. The principal byproduct in this isomerization reaction is **9a** (15%), which is assumed not to derive from **8a** since prolonged heating neither increased the yield of **9a** appreciably nor decreased that of **8a**. Chromane **8a** remained virtually intact after being heated in alkaline methanol.

Iodine oxidation of (2*RS*,4′*R*,8′*R*)-**3b** at room temperature in the same manner afforded 8a-methoxy-α-tocopherone (**4b**) (68%) as an inseparable mixture of diastereomers. After exposure to alkaline methanol at 60 °C **4b** was converted into isomeric 4-methoxy-α-tocopherol (**8b**), isolated as a pair of diastereomers (72% in total) whose stereochemistry has not been determined. The rearrangement of **4b** was accompanied by formation of 3,4-dehydro-α-tocopherol (**9b**) (19%).

The benzoquinone monoketals from the 4-alkoxyphenols are probably formed by the solvolysis of the primary products, 4-alkoxy-4-iodocyclohexa-2,5-dien-1-ones. The apparently unprecedented dienone–phenol rearrangement of **4a** and **4b** is tentatively thought to proceed as shown in Scheme I. Protonation of enolate anion **6** and subsequent attack of methanol at the 4-position with simultaneous loss of the C-8a methoxy group would furnish 8.[5] If the proton attached to C-3 in enol **7** is removed, **9** is expected to form. Further investigation of the structural requirements for this isomerization is needed since ketal **2**, bearing no cyclic ether function, did not tend to isom-



6

(1) Omura, K. *J. Org. Chem.* **1984**, *49*, 3046.
(2) Ali, S. M.; Ilyas, M. *J. Org. Chem.* **1986**, *51*, 5415.
(3) For recent examples, see: (a) Suarna, C.; Craig, D. C.; Cross, K. J.; Southwell-keely, P. T. *J. Org. Chem.* **1988**, *53*, 1281. (b) Matsuo, M.; Matsumoto, S. *J. Org. Chem.* **1987**, *52*, 3514. (c) Winterle, J.; Dulin, D.; Mill, T. *J. Org. Chem.* **1984**, *49*, 491. (d) Clough, R. L.; Yee, B. G.; Foote, C. S. *J. Am. Chem. Soc.* **1979**, *101*, 683.
(4) Goodhue, C. T.; Risley, H. A. *Biochemistry* **1965**, *4*, 854.
(5) Unless **6** is protonated, the attack by the nucleophilic solvent would be unlikely since C-4 is nucleophilic. This protonation, however, may not necessarily be required if **8** is formed by migration of the C_4–C_{4a} double bond with concomitant intramolecular 1,3-shift of the 8a-methoxy group.

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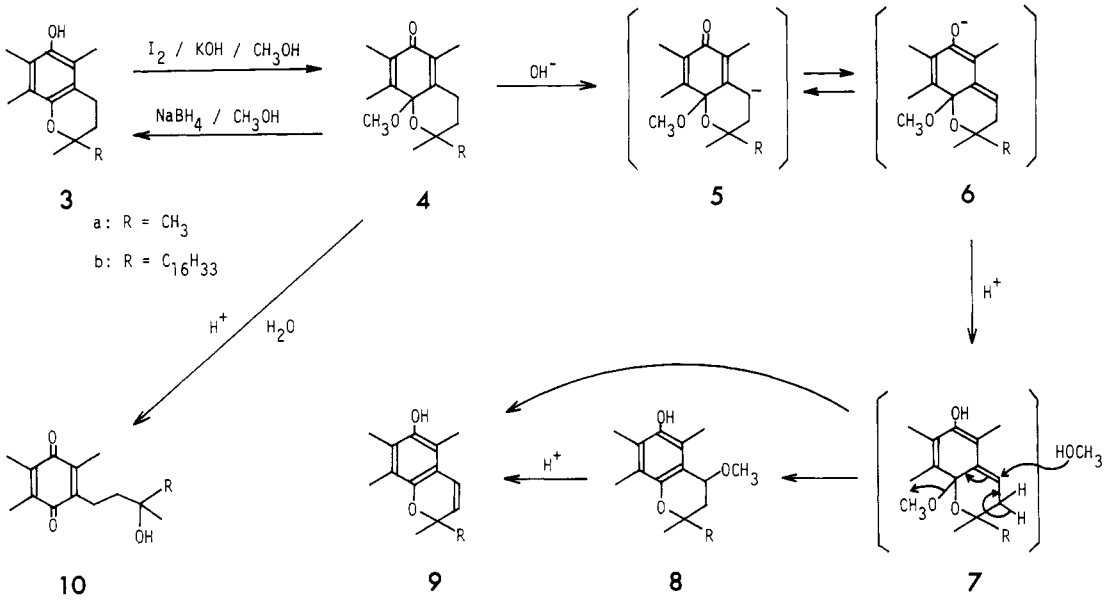
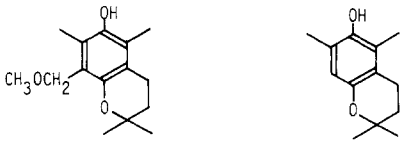
Scheme I



erize when kept in hot alkaline methanol. In the isomerization of **4a**, which principally affords **8a**, formation of 8-(methoxymethyl)chroman-6-ol **11** might also be expected. Indeed, **11** was isolated after a careful analysis of the reaction mixture, but in extremely low yield (0.5%). Although the location of the methoxymethyl group at the 8-position did not seem unambiguous from the spectral data alone, the product was identical in all respects with the compound obtained by treatment of 2,2,5,7-tetramethylchroman-6-ol (**12**) with formaldehyde/hydrochloric acid[6] and subsequent methanolysis. A preliminary ex-



11

12

amination suggested that 2,2,4,6,7-pentamethylcoumaran-5-ol, with a five-membered heterocyclic ring, is also methoxylated by the iodine oxidation to the corresponding 7a-methoxycoumaran-5-one, which appears to undergo a similar, facile isomerization to **4** in alkaline methanol.

The results obtained here offer a simple method of introducing a methoxy function at C-4 in **3** and possibly other related chroman-6-ols. In addition, a convenient one-pot synthesis of chromenol **9** from chromanol **3** was devised. Thus the iodine oxidation of **3a** and **3b** at room temperature, followed by heating and acidification with hydrochloric acid, gave **9a** (61%) and **9b** (69%), respectively. The same chromenols have been prepared by the DDQ oxidation of acetylated **3** and subsequent deacetylation.[7] This study is being continued to explore a new aspect of the chemistry of vitamin E.

Experimental Section

Melting points are uncorrected. Unless otherwise stated, ^{1}H NMR spectra were recorded at 60 MHz. ^{13}C NMR spectra were obtained at 22.49 MHz. UV spectra were measured in cyclohexane. Column chromatography was performed on silica gel (Merck, 70–230 mesh) or basic alumina (Merck, 70–230 mesh, activity grade III). Unless specifically noted, TLC was carried out on silica gel.

Preparation of *p*-Benzoquinone Monoketals. 8a-Methoxy-2,2,5,7,8-pentamethylchroman-6-one (4a). To a stirred solution of **3a**[8] (3.520 g, 16 mmol) in methanol (100 mL) containing KOH (9.0 g, 0.16 mol) was dropwise added at room temperature (ca. 10 °C) a solution of I_2 (4.064 g, 16 mmol) in methanol (30 mL) under N_2 over a period of 20 min. The color of the iodine solution was immediately discharged as it was added. After the mixture was kept at room temperature for 10 min under N_2, it hardly contained **3a** or **8a** (described below) as indicated by TLC. The reaction mixture was poured into cold water (500 mL) and extracted with ether (2 × 200 mL). The combined extracts were washed with ether, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to leave an oily residue. The residue was chromatographed on basic alumina (100 g) with petroleum ether to afford **4a** (2.68 g, 67%) as a pale yellow oil: ^{1}H NMR (CCl_4) δ 2.78 (s, 3 H), ca. 2.3 (m, 2 H), 1.82 (s, 9 H), ca. 1.7 (m, 2 H), 1.38 (s, 3 H), 1.10 (s, 3 H); IR (CCl_4) 1677, 1636 cm^{-1}; UV 237 nm (log ϵ 4.14); HRMS calcd for $C_{15}H_{22}O_3$ *m/e* 250.1568, found 250.1571.

By use of the procedure described for the preparation of **4b**,[4] **3a** was allowed to react with benzoyl peroxide in refluxing methanol to yield **4a** (46%), identical with the sample obtained above (TLC on neutral alumina, ^{1}H NMR, and IR). $NaBH_4$ (0.3 g) was added at once to a solution of **4a** (103 mg) in methanol (10 mL), and the mixture was stirred for 30 min at room temperature under N_2. Addition of dilute HCl to the reaction mixture followed by filtration afforded **3a** (84 mg, 93%), mp 93–95 °C. A solution of **4a** (62 mg) in methanol (5 mL) containing 0.1 N HCl (5 drops) was allowed to stand at room temperature for 30 min to give after workup an orange oil of **10a** (47 mg, 81%), identical with an authentic sample prepared by the $FeCl_3$ oxidation of **3a** in ethanol[9] (TLC, ^{1}H NMR, and IR).

8a-Methoxy-α-tocopherone (4b). A similar procedure described for **4a** was followed, with use of (2*RS*,4′*R*,8′*R*)-**3b** (861 mg, 2 mmol), I_2 (508 mg, 2 mmol), KOH (1.5 g, 27 mmol), and methanol (32 mL total), to give **4b** (a mixture of a pair of diastereomers) (629 mg, 68%) as a pale yellow oil, identical with an authentic sample (TLC on neutral alumina, ^{1}H NMR, and IR) prepared by the oxidation of the same **3b** with benzoyl peroxide in refluxing methanol:[4] ^{1}H NMR (CCl_4) δ 2.78 (s, 3 H), ca. 2.4 (m, 2 H), 1.82 (s, 9 H), 1.35 (s), 1.04 (s); IR (CCl_4) 1678, 1640 cm^{-1}; UV 237 nm (log ϵ 4.09). The ^{1}H NMR spectrum (90 MHz) in C_6H_6

(6) John, W.; Rathmann, F. H. *Ber. Dtsch. Chem. Ges. A* **1941**, *74*, 890.
(7) (a) Burton, G. W.; Doba, T.; Gabe, E. J.; Hughes, L.; Lee, F. L.; Prasad, L.; Ingold, K. U. *J. Am. Chem. Soc.* **1985**, *107*, 7053. (b) Mayer, H.; Isler, O. In *Methods in Enzymology*; McCormick, D. B., Wright, L. D., Eds.; Academic Press: New York, 1971; Part C, Vol. 18, pp 241–348.
(8) Smith, L. I.; Ungnade, H. E.; Hoehn, H. H.; Wawzonek, S. *J. Org. Chem.* **1939**, *4*, 311.
(9) John, W.; Dietzel, E.; Emte, W. *Z. Physiol. Chem.* **1939**, *257*, 173.

exhibited two singlets (OCH_3) at δ 2.59 and 2.60. The ^{13}C NMR spectrum in $CDCl_3$ showed two signals (C-8a) at 94.37 and 94.48.

4,4-Dimethoxy-2,6-di-*tert*-butylcyclohexa-2,5-dien-1-one (1). A similar procedure described for **4a** was followed, with use of 2,6-di-*tert*-butyl-4-methoxyphenol (200 mg, 0.85 mmol), I_2 (216 mg, 0.85 mmol), KOH (0.55 g, 10 mmol), and methanol (25 mL total), to give a pale yellow oil (209 mg, 93%) whose ^1H NMR and IR spectra were in accord with those reported for **1**.[10] As the product thus obtained was practically pure as suggested by TLC, further purification by column chromatography was not undertaken. If the reaction mixture after addition of I_2 was acidified with 6 N HCl, 2,6-di-*tert*-butyl-*p*-benzoquinone was obtained in nearly quantitative yield, mp 65–68 °C (lit.[10] mp 67–68 °C).

4,4-Dimethoxy-2,3,5,6-tetramethylcyclohexa-2,5-dien-1-one (2). A similar procedure described for **4a** was followed, by use of 2,3,5,6-tetramethyl-4-methoxyphenol[11] (540 mg, 3 mmol), I_2 (762 mg, 3 mmol), KOH (1.7 g, 30 mmol), and methanol (38 mL total), to give **2** (343 mg, 54%) as colorless crystals, identical with an authentic sample[11] (melting point, ^1H NMR, and IR), mp 52–53 °C (petroleum ether) (lit.[11] mp 56 °C).

A solution of **2** (700 mg, 3.3 mmol) in methanol (30 mL) containing KOH (1.9 g, 34 mmol) was kept at 50 °C for 1.5 h under N_2. The cooled mixture was poured into water, and extracted with ether. The extract was washed with water, dried, and evaporated to leave **2** (628 mg, 90% recovery).

Preparation of 4-Methoxychroman-6-ols. 4-Methoxy-2,2,5,7,8-pentamethylchroman-6-ol (8a). To a stirred solution of **3a** (880 mg, 4 mmol) in methanol (25 mL) containing KOH (2.26 g, 40 mmol), was dropwise added at 50 °C a solution of I_2 (1.016 g, 4 mmol) in methanol (10 mL) under N_2 over a period of 10 min. The mixture was kept at 50 °C for 20 min under N_2. TLC (neutral alumina) indicated that it hardly contained **4a**. The reaction mixture was cooled, poured into cold water (400 mL), and extracted with ether (2 × 200 mL). The combined extracts were washed with water, dried, and evaporated to leave an oily residue, which was chromatographed on silica gel (25 g) with benzene to afford **8a** (288 mg, 29%) as colorless crystals: mp 124–125 °C (methanol); ^1H NMR ($CDCl_3$) δ 4.29 (s, 1 H, exchangeable with D_2O), ca. 4.2 (m, 1 H), 3.36 (s, 3 H), 2.14 (s, 6 H), 2.09 (s, 3 H), ca. 1.7 (m, 2 H), 1.35 (s, 6 H); IR ($CHCl_3$) 3595, 3375 (br) cm^{-1}; UV 302 nm (log ϵ 3.63); MS *m/e* 250 (M^+). Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.78; H, 8.93.

To a stirred solution of **3a** (3.520 g, 16 mmol) in methanol (100 mL) containing KOH (9.0 g, 0.16 mol) was dropwise added at room temperature a solution of I_2 (4.067 g, 16 mmol) in methanol (30 mL) under N_2 over a period of 20 min. The mixture was heated to and kept at 50 °C for 40 min under N_2. The cooled mixture was worked up as described above to leave a crystalline residue, recrystallization of which from petroleum ether afforded **8a** (1.46 g, 37%). The filtrate was condensed, and the residue was chromatographed on silica gel (50 g). Elution with benzene gave an oily mixture (659 mg) containing **9a** (described below) as the major component. Further elution yielded additional **8a** (464 mg, 12%).

A solution of **4a** (4.860 g, 19.4 mmol) in methanol (200 mL) containing KOH (11.3 g, 0.20 mol) was kept at 50 °C for 40 min under N_2. The mixture, which no longer contained **4a** as indicated by TLC (neutral alumina), was cooled and worked up as described above. Recrystallization of the residue from isopropyl ether gave **8a** (3.08 g, 63%). The filtrate was evaporated, and the residue was chromatographed on silica gel (40 g). Elution with benzene gave **9a** (649 mg, 15%) as a yellow oil, which was crystallized from hexane to furnish the pure product: colorless crystals; mp 69–70 °C (lit.[7a] mp 70.3–71.8 °C); IR ($CHCl_3$) 3595, 3410 (br) cm^{-1}; UV 334 nm (log ϵ 3.51), 280 (3.89), 271 (3.93), 233 (4.25), 222 (4.22); MS *m/e* 218 (M^+). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.75; H, 8.45. The ^1H NMR spectrum was in agreement with that reported for **9a**.[7a] Further elution gave additional **8a** (345 mg, 7%). Continued elution yielded an oil (72 mg), which was subjected to preparative TLC on silica gel ($CHCl_3$/methanol, 20:1) to give **11** (25 mg, 0.5%) as an oil. The oil was crystallized from hexane to provide an analytical sample as colorless crystals: mp 84.5–85.5 °C; ^1H NMR ($CDCl_3$) δ 4.49 (s, 2 H), 4.37 (s, 1 H, exchangeable with D_2O), 3.28 (s, 3 H), ca. 2.6 (m, 2 H), 2.19 (s, 3 H), 2.08 (s, 3 H), ca. 1.7 (m, 2 H), 1.26 (s, 6 H); IR ($CHCl_3$) 3585, 3380 (br) cm^{-1}; UV 302 nm (log ϵ 3.68); MS *m/e* 250 (M^+). Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.83; H, 8.91. The reaction was repeated, but the mixture was kept at 50 °C for 2.5 h instead of 40 min to afford **8a** (71%) and **9a** (17%).

A solution of **8a** (2.00 g, 8 mmol) in acetone (25 mL) containing 6 N HCl (20 drops) was allowed to stand at room temperature for 2.5 h. Addition of the mixture into water and extractive workup with ether gave a residue, which was chromatographed (silica gel) to give **9a** (1.71 g, 98%). A solution of **8a** (1.00 g, 4 mmol) in methanol (40 mL) containing KOH (2.27 g, 41 mmol) was kept at 50 °C for 4 h under N_2. Addition of the mixture into water and extractive workup with ether gave **8a** (997 mg, 100% recovery).

4a-Methoxy-α-tocopherol (8b). A heterogeneous mixture[12] of **4b** (3.22 g, 7 mmol), KOH (12 g, 0.21 mol), and methanol (200 mL) was stirred at 60 °C for 1 h under N_2. The cooled mixture was worked up as described for **8a**, and the residual oil was chromatographed on silica gel (60 g). Elution with petroleum ether/benzene (10:1) gave **9b** (569 mg, 19%) as a yellow oil, identical with an authentic sample (TLC, ^1H NMR, and IR) obtained by alkaline hydrolysis of 3,4-dehydro-α-tocopheryl acetate, which was prepared by the DDQ oxidation of α-tocopheryl acetate:[7b] ^1H NMR (CCl_4) δ 6.38 (d, J = 10 Hz, 1 H), 5.42 (d, J = 10 Hz, 1 H), 3.95 (s, 1 H, exchangeable with D_2O), ca. 2.1 (m, 9 H), 1.28 (s, 3 H); IR (CCl_4) 3600, 3450 (br) cm^{-1}; UV 335 nm (log ϵ 3.51), 281 (3.89), 272 (3.93), 234 (4.26), 222 (4.21). Further elution provided **8b** (less polar isomer) (989 mg, 31%) as a light yellow oil, which became a pasty solid when kept in a refrigerator: R_f 0.34 ($CHCl_3$); ^1H NMR (CCl_4) δ ca. 4.1 (m, 1 H), 4.00 (s, 1 H, exchangeable with D_2O), 3.28 (s, 3 H), 2.06 (s, 3 H), 2.02 (s, 6 H), 1.26 (s, 3 H); IR (CCl_4) 3610, 3375 (br) cm^{-1}; UV 302 nm (log ϵ 3.65); HRMS calcd for $C_{30}H_{52}O_3$ *m/e* 460.3913, found 460.3910. Continued elution provided **8b** (polar isomer) (1.31 g, 41%) as a light yellow oil: R_f 0.19 ($CHCl_3$); ^1H NMR (CCl_4) δ ca. 4.2 (m, 1 H), 3.99 (s, 1 H, exchangeable with D_2O), 3.29 (s, 3 H), 2.06 (s, 3 H), 2.01 (s, 6 H), 1.25 (s, 3 H); IR (CCl_4) 3610, 3375 (br) cm^{-1}; UV 302 nm (log ϵ 3.61); HRMS calcd for $C_{30}H_{52}O_3$ *m/e* 460.3913, found 460.3950.

Hydrolysis of each isomer of **8b** with hydrochloric acid in acetone at room temperature gave **9a** in ca. 90% yield.

One-Pot Synthesis of 9a and 9b. To a stirred solution of **3a** (440 mg, 2 mmol) in methanol (100 mL) containing KOH (3.9 g, 70 mmol) was dropwise added at room temperature a solution of I_2 (508 mg, 2 mmol) in methanol (10 mL) under N_2 over a period of 8 min. The mixture was heated to and kept at 60 °C for 1 h under N_2. To the hot mixture was dropwise added 6 N HCl (20 mL) under N_2 over a period of 7 min. The resulting mixture was stirred at 60 °C for 1 h. The cooled mixture was poured into water and extracted with ether. The extract was washed successively with water, aqueous $Na_2S_2O_3$, and water, dried, and evaporated. The resulting oily residue was chromatographed on silica gel (20 g) with petroleum ether/benzene (10:1) to give a yellow oil, which crystallized slowly upon standing. Recrystallization from hexane afforded **9a** (265 mg, 61%) as colorless crystals, mp 68–70 °C. The filtrate was evaporated to leave a crystalline residue (75 mg), which proved to be a mixture of **3a** and **9a**.

The reaction of **3b** (861 mg, 2 mmol) was performed and the reaction mixture was worked up in the same manner as described above for **9a**. Column chromatography of the residual mixture of products on silica gel (45 g) with petroleum ether/benzene (10:1) furnished **9b** (594 mg, 69%). Further elution gave an oil (153 mg), which proved to be a mixture of **3b** and **9b**.

Preparation of 8-(Methoxymethyl)-2,2,5,7-tetramethylchroman-6-ol (11). By adaptation of the procedure described for the preparation of 2,2-dimethylchromans from phenols,[13] a solution of isoprene (21 mL) in petroleum ether (60 mL) was

(10) Nilsson, A.; Palmquist, U.; Pettersson, T.; Ronlân, A. *J. Chem. Soc., Perkin Trans. 1* **1978**, 696.

(11) Martius, C.; Eilingsfeld, H. *Justus Liebigs Ann. Chem.* **1957**, *607*, 159.

(12) Owing to its relatively low solubility in methanol, **4b** dissolved in that solvent only partially even at 60 °C under the given condition.

(13) Ahluwalia, V.; Arora, K. K.; Jolly, R. S. *J. Chem. Soc., Perkin Trans. 1* **1982**, 335.

dropwise added to a stirred mixture of 2,6-dimethylhydroquinone (28.0 g), 85% H_3PO_4 (23 mL), and petroleum ether (60 mL) over a period of 2.5 h, and the mixture was vigorously stirred for 3 h. The oily residue, obtained after workup, was chromatographed on silica gel (135 g) with petroleum ether to give a crystalline product, which was recrystallized from petroleum ether to yield **12** (13.1 g, 31%) as colorless crystals: mp 92–93.5 °C (lit.[14] mp 91–92 °C). The ^1H NMR, IR, and UV spectra were in accord with those reported for **12**.[14]

By adaptation of the procedure described for the preparation of 5-(chloromethyl)-4-methoxy-2,3,6-trimethylphenol from 4-methoxy-2,3,6-trimethylphenol,[6] a mixture of **12** (5.00 g), 37% HCHO (4.30 g) and concentrated HCl (50 mL) was stirred vigorously for 24 h. Filtration of the mixture afforded a colorless solid (5.63 g): ^1H NMR ($CDCl_3$) δ 4.69 (s, unexchangeable with D_2O); IR (CCl_4) 3605, 3420 (br) cm^{-1}. Attempted purification by recrystallization proved unsuccessful. This crude product (5.63 g) was dissolved in methanol (30 mL), and the solution was kept at room temperature for 20 min. The mixture was poured into water and extracted with ether. The extract was washed successively with water, aqueous $NaHCO_3$, and water, dried, and evaporated. Column chromatography of the oily residue on silica gel (140 g) with benzene yielded **11** (3.47 g) as colorless crystals, identical with that described above (melting point, TLC, ^1H NMR, and IR).

Acknowledgment. I am grateful to Professor K. Naya (Kwansei Gakuin University) for NMR spectra with a JEOL FX-90Q spectrometer and to Dr. P. T. M. Kenny and Mr. M. Sakaidani (Suntory Institute for Bioorganic Research) for high-resolution mass spectra.

(14) Lars, J.; Nilsson, G.; Sievertsson, H.; Selander, H. *Acta Chem. Scand.* **1968**, *22*, 3160.

Synthesis of Perfluorotetraalkyl Orthocarbonates Using Elemental Fluorine

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An extraordinarily significant application of direct fluorination is in the synthesis of oxygen-containing fluorocarbons that are inaccessible by other techniques. Thus, recent research on the synthesis of "spherical" fluorocarbons in our laboratory has led to the preparation of perfluorotetraalkyl orthocarbonates [$C(OCR_f)_4$] by controlled direct elemental fluorine reactions.

Hydrocarbon orthocarbonates are generally synthesized by the action of sodium alkoxides on trichloronitromethane or trichloromethanesulfenyl chloride.[1] Perfluorotetraalkyl orthocarbonates are inaccessible via conventional fluoroorganic techniques. While fluorinated alkoxides are known, they are very weak nucleophiles and, at the temperatures required for reaction, are highly dissociated or undergo competing side reactions.[2] The main difficulty in the fluorination of ester compounds lies in the susceptibility of the ester linkage toward attack by hydrogen fluoride. The direct fluorination method employed by our laboratory has been very successful in fluorination of other acid-sensitive compounds such as crown ethers,[3] branched dialkyl ethers,[4] and polyesters.[5]

Scheme I. Reaction Scheme of Tetraalkyl Orthocarbonates

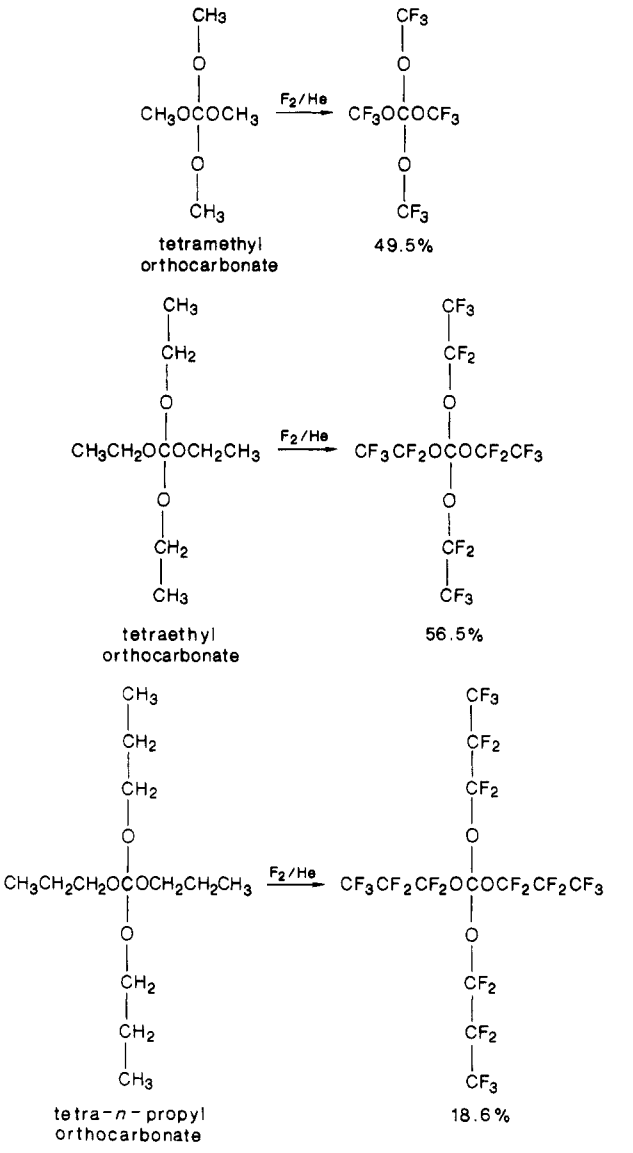

Table I. Comparison of Boiling Points

compound	bp, °C	compound	bp, °C
$C(OCH_3)_4$	114	$C(OC_2F_5)_4$	80
$C(OC_2H_5)_4$	160	$C(OC_3F_7)_4$	132
$C(OC_3H_7)_4$	224	$C(CF_2OCF_3)_4$	130
$C(OCF_3)_4$	20.8	$C(CF_2OC_2F_5)_4$	170

$C(OCF_3)_4$ and $C(OC_2F_5)_4$ were obtained directly from the hydrocarbons in 49.5% and 56.5% yield, respectively. The direct fluorination of $C(OCH_2CH_2CH_3)_4$ yields the compound $C(OCF_2CF_2CF_3)_4$ in an 18.6% yield. It has previously been reported that perfluoro orthocarbonates such as perfluorotetramethyl and perfluorotetraethyl orthocarbonate rearrange during reactions with elemental fluorine and that only very low yields are possible.[6] The reaction scheme appears in Scheme I and a comparison of boiling points appears in Table I. It should be noted

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(3) Lin, W. H.; Bailey, W. I., Jr.; Lagow, R. J. *J. Chem. Soc., Chem. Commun.* **1985**, 1350.
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(5) Persico, D. F.; Gerhardt, G. E.; Lagow, R. J. *J. Am. Chem. Soc.* **1985**, *107*, 1197.
(6) Adcock, J. L.; et al. *J. Fluorine Chem.*, in press.

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