(1:1 hexane–EtOAc) afforded 14 mg (54%) of ketone 7 as a colorless oil, which was homogeneous by TLC analysis: IR ($CHCl_3$) 1720 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.23 (d, J = 7.8 Hz, ArH), 6.95 (t, J = 7.7 Hz, ArH), 6.86 (dd, J = 17.6 and 10.9 Hz, C*H*=CH_2), 6.83 (t, J = 7.1 Hz, ArH), 6.75 (t, J = 7.7 Hz, ArH), 5.23 (dd, J = 10.9 and 1.3 Hz, C=CH), 5.02 (dd, J = 17.6 and 1.2 Hz, C=CH), 4.88 (AB q, J_{AB} = 10.9 Hz, ν_{AB} = 17.6 Hz, NCH_2O), 3.66 (s, H-5), 3.53 (m, OCH_2CH_2), 3.18 (1 H, m), 3.00 (1 H, d, J = 9.4 Hz), 2.39–2.41 (3 H, m), 2.03 (1 H, d, J = 18.5 Hz), 1.96 (s, NCH_3), 1.86 (1 H, d, J = 9.4 Hz), 1.80 (1 H, dd, J = 18.5 and 6.9 Hz), 0.82–0.95 (m, CH_2CH_2Si), 0.12 (9 H, s, $SiCH_3$); ^{13}C NMR (125 MHz, C_6D_6) δ 218.8, 178.9, 142.5, 138.9, 126.6, 122.1, 111.8, 109.4, 72.6, 69.1, 65.6, 60.0, 59.7, 58.2, 55.8, 53.7, 47.7, 44.6, 42.5, 36.2, 17.3, −1.8; high-resolution MS (CI, methane) m/z 451.2389 (451.2417 calcd for $C_{26}H_{35}N_2O_3Si$).

Base-Promoted Epimerization of 7 To Afford 10 and Deprotection To Afford Oxindole Ketone 11. A solution of 7 (19 mg, 0.042 mmol), acetone (3 mL), and 1 N NaOH (0.3 mL) was maintained at 23 °C for 45 min. The reaction solution was then diluted with CH_2Cl_2 (10 mL), and the organic phase was washed with 1 N NaOH (10 mL), dried (K_2CO_3), and concentrated to give 19 mg of impure 10. Purification of a comparable sample by flash chromatography on silica gel (1:1 hexanes–EtOAc) provided a pure sample of the more polar oxindole ketone epimer 10: IR ($CHCl_3$) 1712, 1727 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 7.6 Hz, ArH), 7.23 (td, J = 6.6 and 1.2 Hz, ArH), 7.03 (td, J = 7.7 and 1.0 Hz, ArH), 6.29 (dd, J = 10.8 and 17.8 Hz, CH_2=C*H*), 5.44 (d, 1 H, J = 10.0 Hz, CH_2=C), 5.42 (d, 1 H, J = 17.7 Hz, CH_2=C), 5.10 (AB q, J_{AB} = 10.9 Hz, ν_{AB} = 67.4 Hz, NCH_2O), 3.52 (m, OCH_2CH_2), 3.25 (m, 1 H), 3.10 (m, 1 H), 2.98 (d, 1 H, J = 9.8 Hz, NCH_2), 2.57 (m, 1 H), 2.45 (s, 1 H), 2.32 (s, NCH_3), 2.25 (d, 1 H, J = 17.9 Hz, CH_2), 2.17 (d, 1 H, J = 9.8 Hz, NCH_2), 2.17 (m, 1 H, CH_2), 0.88 (m, 2 H, CH_2Si), −0.47 (s, 9 H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 216.5, 177.7, 141.5, 139.2, 132.8, 128.0, 127.2, 122.5, 116.4, 109.3, 71.5, 69.3, 66.0, 61.3, 60.8, 60.4, 55.8, 51.8, 46.9, 46.3, 42.1, 37.1, 17.7, −1.4; MS (CI, isobutane) m/z 451 (MH), 333, 108.

The crude sample of epimer 10 (19 mg) was dissolved in 6 N HCl (2 mL) and maintained at 23 °C for 1 h. This solution was then diluted with CH_2Cl_2 (20 mL) and basified by the careful addition of saturated aqueous $NaHCO_3$. The resulting mixture was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic layers were dried (K_2CO_3) and concentrated. Purification of the residue by flash chromatography (9:1 $CHCl_3$–MeOH) afforded 14 mg (ca. 100%) of ketone 11, which was homogeneous by TLC analysis. This sample was crystallized by the vapor diffusion method (EtOAc–hexane) to give crystals suitable for single-crystal X-ray analysis: ^1H NMR (500 MHz, $CDCl_3$) δ 8.44 (bs, NH), 7.82 (d, J = 7.8 Hz, ArH), 7.18 (td, J = 7.7 and 1.0 Hz, ArH), 6.96 (td, J = 7.7 and 1.0 Hz, ArH), 6.86 (d, J = 7.6 Hz, ArH), 6.29 (dd, J = 17.7 and 10.8 Hz, CH_2=C*H*), 5.44 (d, J = 10.8 Hz, CH=C), 5.42 (d, J = 17.7 Hz, CH=C), 4.00 (bs, NCH), 3.24 (m, 1 H), 3.09 (m, 1 H), 3.00 (d, 1 H, J = 9.8 Hz, NCH_2), 2.56 (m, 1 H), 2.51 (s, 1 H), 2.35 (s, NCH_3), 2.33 (d, 1 H, J = 18.0 Hz, CH_2), 2.16 (dd, 1 H, J = 18.0 and 6.5 Hz, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 216.2, 179.5, 140.5, 139.1, 133.9, 128.0, 127.4, 121.9, 116.5, 109.6, 71.4, 60.9, 60.7, 60.3, 55.9, 51.8, 46.9, 46.4, 42.1, 37.2; high-resolution MS (CI, methane) m/z 321.1583 (321.1603 calcd for $C_{20}H_{21}N_2O_2$, MH).

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Supplementary Material Available: X-ray crystallographic data for 11 (5 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Oxidation of 2′-Hydroxyacetophenones with Thallium(III) Nitrate in Methanol

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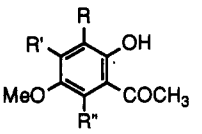
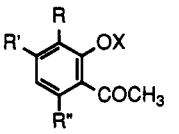
Introduction

Thallium(III) compounds have been used as unique oxidizing agents in synthetic methodology.[1] McKillop et al.[2] have examined the oxidation of phenols with thallium(III) nitrate (TTN) and found that phenols with an electron-releasing substituent at the 4-position are easily converted into 4,4-disubstituted cyclohexa-2,5-dienone derivatives. The oxidation of phenols bearing electron-attracting substituents such as hydroxyacetophenones, however, have not been studied in detail.[2-4] In this paper, we wish to report on the mechanism of oxidation of 2′-hydroxyacetophenones and unique features of the products as part of our work to establish a method for the synthesis of isoflavonoids.[5,6]

Results

The reactivities of hydroxy-substituted acetophenones in the oxidation with TTN were examined qualitatively. The 5′-methoxyacetophenones **1a–e** were oxidized and the reactivities greatly enhanced with increasing number of methoxy groups. 2′-Hydroxy-4′,6′-dimethoxyacetophenone (**1f**) disappeared within a few minutes and reappeared when the mixture was treated with hydrochloric acid, suggesting that **1f** formed a complex with TTN.





1a R=R'=R"=H
1b R=R"=H, R'=OMe
1c R=H, R'=R"=OMe
1d R=R"=OMe, R'=H
1e R=R'=R"=OMe
1f X=R=H, R'=R"=OMe
1g X=Me, R=H, R'=OH, R"=OMe
1h X=Me, R=H, R'=R"=OMe
1i X=R=R'=H, R"=OMe
1j X=Me, R=R'=H, R"=OMe
1k X=H, R=R'=R"=OMe

The oxidation products and conditions for 2′-hydroxyacetophenones with a methoxy group at the 5′- and/or 3′-positions are summarized in Table I. The acetophenone **1a** was oxidized with 2 equiv of TTN to give a mixture of 2-acetyl-3-hydroxy-4,4-dimethoxy-2,5-cyclohexadienone (**5a**) and 2-acetyl-3-hydroxy-6,6-dimethoxy-2,4-cyclohexadienone (**6a**), a tautomer of **5a** (the ratio, ca. 3:1) (Scheme I). The oxidation of **1b** with an equivalent of TTN afforded a mixture of a small amount of 2-acetyl-4,4,5-trimethoxy-2,5-cyclohexadienone (**2b**) and its methanol adduct (**3b**). The treatment of these products with aqueous acetonitrile formed a hydrate (**4b**) which was converted into a mixture of **2b** and **4b** (ca. 1:1) by the evaporation of the solvent. The trimethoxy- and tetramethoxyacetophenones **1c**, **1d**,[7] and **1e** were rapidly oxidized within a few minutes to give **2c**,[2] **2d**, and **2e**, which were gradually demethylated with increasing reaction time

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Table I. Oxidation Conditions of 2'-Hydroxyacetophenones and Their Products[a]

starting material	method	molar ratio of TTN to 1	reactn temp (°C)	reactn time (min)	product	mp (°C)	recrystn solvent	yield (%)
1a	A	2.2	40	120	5a+6a	oil		85
1b	A	1.1	10	120	3b+2b	oil		ca. 80
1c	B	1.1	−5 to −10	5–10	2c	91–92	Et_2O	80
1d	B	1.1	−5 to −10	5–10	2d	99–100	$CHCl_3$–Et_2O	70
1e	B	1.1	−5 to −10	5–10	2e	oil		90
1k	A	1.1	0	45	6k	89–90	Et_2O–hexane	22
					5c	84–85	aqueous MeOH	4
10	B	1.1	0	5–10	11	118–119	$CHCl_3$–Et_2O	82

[a] MS spectra for the products except for 5a and 6a showed the molecular ion peak, respectively.

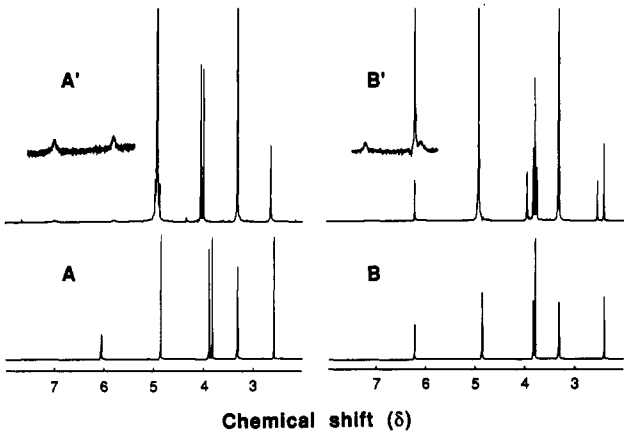


Figure 1. ^1H NMR spectra of the reaction mixture of the acetophenones 1f and 1h (each 5 mg) with TTN (12–13 mg) in methanol-d_4 (0.5 mL). A and B: original spectra of 1f and 1h, respectively. A' and B': spectra of the reaction mixture of 1f and 1h after 5 and 60 min, respectively.

or by the treatment with dilute hydrochloric acid in methanol to give triketone derivatives (Scheme II). The oxidation of 1k and subsequent demethylation afforded 2-acetyl-3-hydroxy-5,6,6-trimethoxy-2,4-cyclohexadienone (6k), a tautomer of 5c, but the yield was low because the product 6k was slowly isomerized to 5c in an acidic medium and partly decomposed during workup.

Discussion

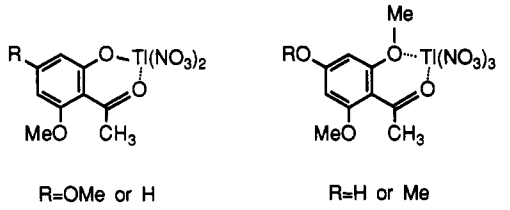
Mechanistic Observation of the Reaction. The results show that all oxidations gave the corresponding quinone monoacetal (2) as a first product and the products are easily converted into unique triketone derivatives (5 or 6). Regarding the TTN oxidation of phenols, McKillop et al.[2] have reported that the oxidation proceeded not via O-thallation but via ipso-thallium. On the other hand, the fact that 1f forms a thallium complex suggests that complexation with the hydroxy group in acetophenones is the initial step of the oxidation such as in the case of the oxidation of flavonols with TTN.[8] Therefore, the interaction of TTN with acetophenones 1f–1j which were not oxidized under the mild conditions was examined by ^1H NMR and the representative spectra are shown in Figure 1.

In the spectra for 1f, the signals of the two methoxy and acetyl groups shifted paramagnetically within 5 min upon addition of TTN and those of the two aromatic protons collapse simultaneously to appear as two broad signals

Table II. ^1H NMR Spectral Data for Acetophenones 1f–1j in Methanol-d_4 upon Addition of TTN[a]

compd	$COCH_3$	OMe	arom. H
1f	2.57 s	3.82 s, 3.88 s	6.04 d', 6.06 d'
complex	2.64 s	4.00 s, 4.05 s	5.81 b, 7.00 b
1g	2.39 s	3.75 s (6 H)	6.09 s (2 H)
complex	2.52 s	3.75 s, 3.86 s	5.92 b, 7.00 b
1h	2.40 s	3.78 s (6 H), 3.82 s	6.22 s (2 H)
complex	2.54 s	3.75 s, 3.95 s, 3.96 s	6.10 b, 7.20 b
1i	2.63 s	3.90 s	6.49 dd,[b] 7.37 t, 6.53 dd
complex	2.71 s	4.00 s	6.16 b, 8.96 b, 7.19 b
1j[c]	2.41 s	3.79 s (6 H)	6.67 d (2 H), 7.32 t

[a] s, singlet; d, doublet (J = 8.0–8.5 Hz); d', doublet (J = 2.0–2.5 Hz); dd, doublet of doublets (J = 8.0–8.5, 2.0–2.5 Hz); t, triplet (J = 8.0–8.5 Hz); b, broad. [b] C_3-proton. [c] The signals for the complex of 1j were not observed within 2 h.



R=OMe or H R=H or Me

Figure 2. Assumed structures of the cyclic thallium complexes.

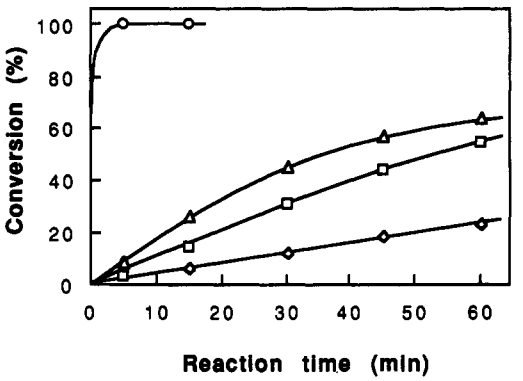


Figure 3. Complexation time courses of the acetophenones (5 mg) with TTN (12–13 mg) in methanol-d_4 at 25 °C. The conversions were calculated from the integration of the signals for the acetyl methyl proton in the ^1H NMR spectra: 1f, ○; 1g, △; 1h, □; 1i, ◇.

(1) McKillop, A.; Taylor, E. C. In *Comprehensive Organometallic Chemistry*; Wilkinson, J., Ed.; Pergamon: Oxford, 1982; Vol. 7, pp 465–513.
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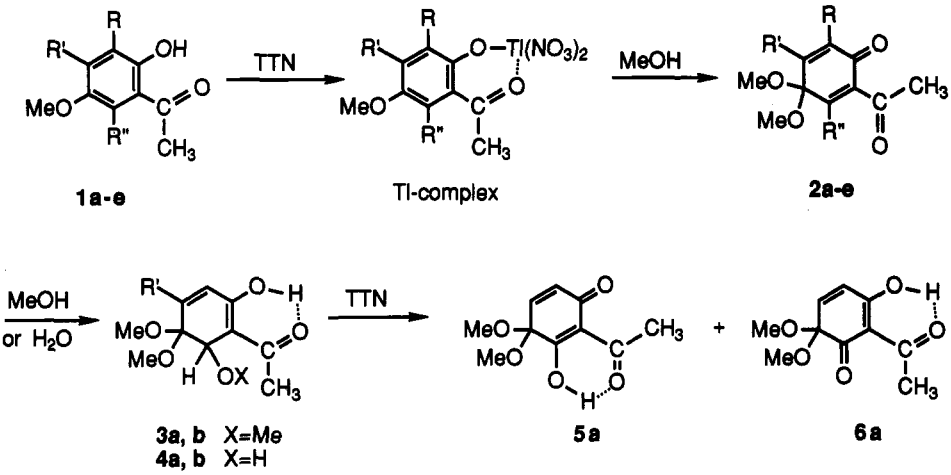
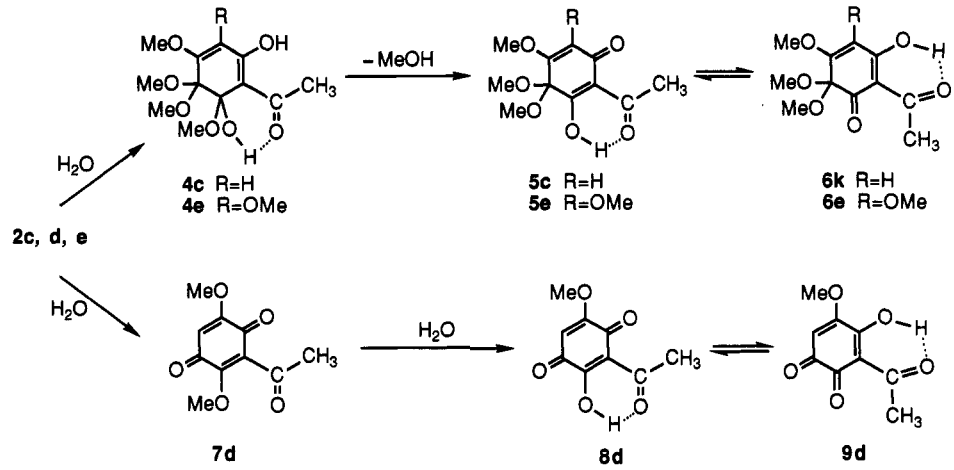
(8) Singh, Om V.; Khanna, M. S.; Tanwar, M. P.; Garg, C. P.; Kapoor, R. P. *Synth. Commun.* **1990**, *20*, 2401–2408.

Scheme I[a]



[a] a, R = R′ = R″ = H; b, R = R″ = H, R′ = OMe; c, R = H, R′ = R″ = OMe; d, R = R″ = OMe, R′ = H; e, R = R′ = R″ = OMe.

Scheme II



(Figure 1), suggesting that **1f** rapidly forms a complex with TTN. The spectra for the other acetophenones are not changed immediately by the addition of TTN, but the signals for a newly formed complex appear clearly with increasing reaction times (Table II). In the spectra for **1g** and **1h**, a singlet for the two equivalent methoxy groups splits into two singlets in the complexes and that for the aromatic protons is also changed to two broad signals. The splitting pattern of these spectra is very similar to that of the spectrum for **1f** (Figure 1 and Table II). These results show that the symmetrical acetophenones such as **1g** and **1h** are converted into unsymmetrical molecules by the formation of the thallium complex. It is considered that the acetophenones form a cyclic thallium complex as shown in Figure 2. The complexation is greatly accelerated by the existence of the 2′-hydroxy group and by increasing the electron density of the carbonyl group, and the rates decrease in the order **1f**, **1g**, **1h**, **1i**, and **1j** as shown in Figure 3. The results suggest that TTN coordinates easily to an electron-rich oxygen atom such as a carbonyl or hydroxyl oxygen atom and that the oxidation of the 2′-hydroxyacetophenones with TTN proceeds via O-thallation as shown in Scheme I.

That is, the thallium complex of **1** is converted into the quinone monoacetal (**2**) by the addition of methanol and elimination of thallium moiety. Since the 3-position in **2** is highly activated by the resonance of the 2,3-carbon–carbon double bond with two carbonyl groups, **2** have a tendency to form the addition product of methanol or water (**3** or **4**) and the final product is controlled by the stability of **2**, **3**, or **4** under the reaction conditions. For example, **2b** with no substituent at the 3-position exists as its methanol adduct (**3b**) in the reaction mixture. The monoacetal **2a** exists also as its methanol adduct (**3a**) or hydrate (**4a**), but further oxidation of **3a** or **4a** proceeds to give the triketone derivatives **5a** and **6a** because the reactivities of these adducts are higher than that of the starting material **1a** (Scheme I). This result is supported by the ^1H NMR study of the reaction of **1a** with TTN in methanol-d_4. The reaction of acetophenones **1c**, **1d**, and **1e** with the 6′-methoxy group proceeds rapidly under very mild conditions and resultant monoacetals (**2**) are obtained in high yield, since the attack of the solvent to the 3-position in **2** is suppressed by the steric hindrance of the 3-methoxy group. These results show also that the oxidation of **1k** with no substituent at the 5′-position forms a triketone derivative **6k** via the hydrolysis of the corresponding *o*-quinone monoacetal by a similar mechanism described for the hydrolysis of **2c** (vide infra).

Hydrolysis of Quinone Monoacetals. The above mechanistic observation shows also that the demethylation of **2** to **5** proceeds by hydrolysis of the 3-methoxy group as shown in Scheme II. The mechanism is supported by the following fact: the interaction of **5c** with $H_2{}^{18}O$ afforded **5c**-^{18}O only, but the hydrolysis of **2c** using $H_2{}^{18}O$ gave **5c**-$^{18}O_2$, which had exchanged two oxygen atoms. The hydrolysis of **2c** gave **5c** only, but that of **2e** afforded a mixture of **5e** and its tautomer **6e** (5:1), suggesting that

Table III. ^{1}H NMR Spectral Data for 2-Acetyl-4,4-dimethoxycyclohexa-2,5-dienones 2, 2-Acetyl-3-hydroxy-4,4-dimethoxycyclohexa-2,5-dienones 5, and Their Derivatives in $CDCl_3$[a]

compd	$COCH_3$	C_3-OMe	C_4-OMe	C_5-OMe	C_6-OMe	C_3-H	C_5-H	C_6-H	OH
5a	2.63 s		3.42 s (6 H)				6.84 d	6.38 d	18.03
6a	2.69 s		3.46 s (6 H)				6.67 d	6.29 d	
2b	2.53 s		3.36 s (6 H)	3.83 s		7.13 s		5.60 s	
3b	2.18 s	3.25 s	3.20 s, 3.43 s	3.80 s		4.32 s		5.32 s	16.00 bs
4b	2.19 s		3.24 s, 3.49 s	3.80 s		4.60 d		5.36 s	16.08 s
2c[b]	2.44 s	4.03 s	3.34 s (6 H)	3.81 s				5.63 s	
5c[b]	2.60 s		3.37 s (6 H)	3.90 s				5.56 s	18.42 s
6k	2.51 s		3.46 s (6 H)	3.87 s				5.39 s	17.27 s
2d	2.40 s	4.10 s	3.34 s (6 H)		3.72 s		5.33 s		
7d[c]	2.45 s	4.01 s			3.89 s		5.80 s		
8d	2.761 s				3.91 s		6.11 s		17.54 s
9d	2.755 s				3.95 s		6.22 s		17.66 s
2e	2.43 s	4.03 s	3.35 s (6 H)	3.79 s	4.16 s				
5e	2.61 s		3.35 s (6 H)	3.80 s	4.22 s				18.31 s
6e	2.71 s		3.41 s (6 H)	3.79 s	4.15 s				17.80 s
11[d]		3.96 s	3.39 s (6 H)	3.81 s (6 H)				5.67 s	
12[d]			3.39 s (6 H)	3.84 s or 3.89 s				5.62 s	18.35 s

[a] s, singlet; d, doublet (J = 10.5 Hz): the numbering of the compounds **3b** and **4b**, **6a**, **6k**, **6e**, and **9d** was shown on the basis of the compounds **2b**, **5a**, **5c**, **5e**, and **8d**, respectively. [b] ^{13}C NMR data for **2c**: δ 32.6 (Me), 52.2 (2 C, C_4-OMe), 56.3, 60.0 (C_5- and C_3-OMe), 96.7 (C_4), 104. 3 (C_6), 124.2 (C_2), 160.8, 165.5 (C_3 and C_5), 184.1 (C_1), 200.2 (-CO-). Those for **5c**: 26.6 (Me), 52.3 (2 C, C_4-OMe), 56.8 (C_5-OMe), 93.9 (C_4), 100.0 (C_6), 107.6 (C_2), 170.5 (C_5), 187.9, 189.3 (C_1 and C_3), 199.4 (-CO-). [c] The data were obtained from the spectra for the incomplete hydrolytic product of **2d** at 0 °C for 30 min. [d] The data are those for the cyclohexadienone moiety in **11** or **12**.

the isomerization of **5** was affected by their substituents. On the other hand, **2d** was hydrolyzed to a mixture of 2-acetyl-3-hydroxy-6-methoxybenzoquinone (**8d**) and 3-acetyl-4-hydroxy-5-methoxy-*o*-benzoquinone (**9d**), a tautomer of **8d**, (3:1) without formation of **5d**. One of the reasons is that the β-methoxyvinyl functionality at the 5,6-positions accelerates the hydrolysis of the *gem*-methoxy groups. Actually, the ^{1}H NMR spectrum for the incomplete hydrolytic product of **2d** showed the presence of **8d** and 2-acetyl-3,6-dimethoxybenzoquinone (**7d**), and no signal attributed to the *gem*-methoxy groups was observed at all. The reason why the *gem*-methoxy groups in **2e** are hardly hydrolyzed albeit the existence of the 6-methoxy group can be explained as follows: the effective interaction of the β-methoxyvinyl functionality toward the *gem*-methoxy groups is hindered sterically by the 5-methoxy group.

Characterization of the Oxidation Products and a Revised Structure of the Oxidation Products with TTN from 2′-Hydroxy-4′,5′,6′-trioxygenated Chalcones. The ^{1}H NMR data for the products obtained here are summarized in Table III. In the ^{1}H NMR spectra for the demethylated products (**5c**) of **2c**, the signal for the methoxy group at δ 4.03 in **2c** disappears and a new signal for a chelated hydroxy group appears at δ 18.42. Furthermore, its ^{13}C NMR spectra exhibits the existence of three carbonyl carbon atoms at a range of δ 188 to 200. The results show clearly that the product is a unique triketone derivative. The product **6k** is gradually isomerized to **5c** and its ^{1}H NMR spectral pattern is similar to that of **5c**, showing that the two products (**5c** and **6k**) have a single configuration, respectively, and **6k** is a tautomer of **5c**. In the NOE experiment of the two tautomeric compounds, a small NOE (3%) was observed in the chelated hydroxyl proton in **6k** by the irradiation of the olefinic proton, but the irradiation of the olefinic or chelated hydroxyl protons in **5c** did not cause any NOE. Furthermore, the signal of the olefinic proton in **5c** agreed very closely with that in **2c**, but that in **6k** appeared at a higher field. Thus, the structures of **5c** and **6k** are revealed to be 2-acetyl-3-hydroxy-4,4,5-trimethoxy-2,5-cyclohexadienone and 2-acetyl-3-hydroxy-5,6,6-trimethoxy-2,4-cyclohexadienone.

The product from **1b** was separated into **2b** and **3b** contaminated with **2b**, by silica gel column chromatography. The compound **3b** was produced from **2b** by treatment of methanol and its ^{1}H NMR spectrum showed the existence of four methoxy groups and a chelated hydroxy group, suggesting that **3b** is a methanol adduct. The methoxyl functionality introduced is confirmed to be the C_3-position in **3b** from the following facts: the signals of the *gem*-methoxy groups appear as two singlets and the signal at δ 7.13 for the C_3-proton in **2b** is largely shifted diamagnetically to the signal at δ 4.32. Thus, the structure of **3b** was shown to be 1-acetyl-2-hydroxy-4,5,5,6-tetramethoxy-1,3-cyclohexadiene

On the other hand, in the oxidatin of 6′-hydroxy-2′,3′,4′-trioxygenated chalcones with TTN in methanol, McKillop et al.[2] have reported that their oxidation products are hydrolyzed gradually under the oxidation conditions or in acidic media to give the quinone monohemiacetals. Our results, however, suggest that the structure of the products hydrolyzed is not the hemiacetal but the triketone derivative such as **5c**. Thus, we reexamined the oxidation of 6′-hydroxy-2′,3′,4,4′-tetramethoxychalcone (**10**) with TTN in methanol. The oxidation proceeded smoothly to give the corresponding quinone monoacetal (**11**), which was easily hydrolyzed to 3-hydroxy-4,4,5-trimethoxy-2-[3-(4-methoxyphenyl)acryloyl]cyclohexa-2,5-dienone (**12**), a derivative of **5c** (Table III). Thus, the hemiacetal structure proposed by McKillop et al. must be revised to **12**.

Experimental Section

All melting points were determined in glass capillaries and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker 400 spectrometer (400 MHz) using tetramethylsilane as internal standard and chemical shifts are given in δ values. MS spectra were taken on a Shimazu QP 1000 spectrometer. Column chromatography was carried out on Kieselgel 60 (70–230 mesh; Merck). Elemental analyses were performed with a Yanaco CHN corder, Model MT-2, and the values of all crystalline compounds are within 0.3% of theoretical values. TTN·3H_2O was obtained from Aldrich (usual safety precaution is encouraged).

General Method for the Oxidation of 2′-Hydroxyacetophenones. Method A. A cooled solution of TTN·3H_2O (1.07 g; 2.4 mmol) in methanol (15 mL) was added to a stirred solution of the acetophenone (2 mmol) in methanol (30–40 mL) and the mixture was allowed to stand with stirring. The mixture was concentrated to 20–25 mL under reduced pressure and diluted with chloroform (50–60 mL). After the precipitate was filtered

off, the filtrate was shaken with ice (ca. 50 g) and extracted with chloroform. The extract was washed with cooled water, dried over anhydrous sodium sulfate, and then passed through a short column of silica gel using chloroform as eluent. The eluate was evaporated under reduced pressure to give the oxidation products (Table I).

Only **6k** was sensitive against silica gel and a large amount of **6k** was decomposed by column chromatography. Therefore, the reaction mixture which was obtained from the mixture of **1k** (500 mg) and TTN·3H_2O (1.2 g) was treated as follows. To the reaction mixture diluted with chloroform was added 3% hydrochloric acid (5 mL), and the mixture was additionally stirred at 0 °C for 5–10 min. The mixture was shaken with ice (ca. 50 g) and extracted with chloroform. The extract was washed with ice-cooled 0.1–0.2% hydrochloric acid and water, dried, and then concentrated. The residue was crystallized from ether–hexane and the crystal (A) and mother liquor (B) were obtained. After A was washed with a small amount of water (yellow material was removed), the crystals were treated with ether and the insoluble material was removed (**1k** was recovered, 40 mg) and recrystallized to give **6k** (120 mg). The mother liquor B was chromatographed over a silica gel column using chloroform as eluent to give **5c** (20 mg) from the second fraction.

Method B. A cooled solution (−5 to −10 °C) of TTN (1.07 g, 2.4 mmol) in methanol (25 mL) was added with stirring to a cooled solution (−5 to −10 °C) of the acetophenone or chalcone (**10**) (2 mmol) in methanol (50 mL) and the mixture was allowed to stand with stirring in an ice–salt bath. To the mixture was added a suspension of sodium hydrogen carbonate (0.8 g) in water (3–5 mL), and the mixture was additionally stirred for 5–10 min in an ice–salt bath. The separated precipitate was filtered off using a small amount of active carbon. The filtrate was concentrated to 20–25 mL under reduced pressure, diluted with chloroform, shaken with ice (ca. 50 g), and then extracted with chloroform. The extract was washed with water, dried over anhydrous sodium sulfate, and then concentrated under reduced pressure to give the quinone monoacetal (Table I).

Hydrolysis of the Quinone Monoacetals 2c, 2e, 2d, and 11. To the solution of the quinone monoacetal (ca. 50 mg) in methanol (5–10 mL) was added 5% hydrochloric acid (0.2–0.5 mL), and the mixture was allowed to stand at room temperature until the starting material disappeared (1–2 h) (in the case of the hydrolysis of **11**, the crystal of **12** was separated). The mixture was diluted with water and the product separated was collected by filtration or extraction with ether to give the desired compound in good yield. **5c**: mp 83–85 °C (from methanol); EIMS, 242 (M^+). Mixture of **5e** and **6e** (ratio, 5:1): oily material; EIMS, 272 (M^+). Mixture of **8d** and **9d** (ratio, 3:1): mp 135–136 °C dec (from EtOAc–hexane) (reaction time, 4 h). **12**: mp 138–140 °C (from methanol) (lit.[2] mp 139–140 °C); EIMS, 360 (M^+).

Hydrolysis of 2c in $H_2{}^{18}O$. To a solution of **2c** in methanol (200 μL) containing $H_2{}^{18}O$ (50 μL) was added 10% hydrochloric acid (6 μL), and the mixture was allowed to stand at room temperature for 1.5 h. The mixture was diluted with water and the crystals separated were collected to give the hydrolyzed product. EIMS (20 eV); m/z (rel intensity) M^+ 246 (33.8) [$C_{11}H_{14}O_4{}^{18}O_2$]; 244 (14.6) [$C_{11}H_{14}O_5{}^{18}O$]; 242 (2.5) [$C_{11}H_{14}O_6$].

Exchange Reaction between 5c and $H_2{}^{18}O$. **5c** was dissolved into a mixture of methanol (100 μL) and $H_2{}^{18}O$ (10 μL) and was allowed to stand at room temperature for 20 h: EIMS (20 eV); m/z (rel intensity) M^+ 244 (19.5) [$C_{11}H_{14}O_5{}^{18}O$]; 242 (1.0). The exchange reaction between **2c** and $H_2{}^{18}O$ was not observed under the same conditions.

Registry No. **1a**, 705-15-7; **1b**, 20628-06-2; **1c**, 22248-14-2; **1d**, 72424-28-3; **1e**, 3162-28-5; **1b**, 90-24-4; **1g**, 13246-14-5; **1h**, 832-58-6; **1i**, 703-23-1; **1j**, 2040-04-2; **1k**, 7507-98-4; **2b**, 138008-71-6; **2c**, 57197-14-5; **2d**, 138008-72-7; **2e**, 138008-73-8; **3b**, 138059-63-9; **5a**, 138008-69-2; **5c**, 138008-75-0; **5e**, 138008-79-4; **6a**, 138008-70-5; **6e**, 138008-77-2; **6k**, 138008-74-9; **7d**, 6172-59-4; **8d**, 138008-80-7; **9d**, 138008-81-8; **10**, 3877-67-6; **11**, 138008-76-1; **12**, 138008-78-3; thallium trinitrate, 13746-98-0.

Supplementary Material Available: Tables of ^1H NMR data for the adducts **3a** and **4a** and the time course of the oxidation of **1a** and details of the synthetic method for 4′-hydroxy-2′,6′-dimethoxyacetophenone preparation (2 pages). Ordering information is given on any current masthead page.

The Reaction of Carboxylate Nucleophiles with *tert*-Butyldimethylphenoxysilanes in Dimethylformamide

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We have examined the reaction of a series of carboxylate anions with a series of *tert*-butyldimethylphenoxysilanes (**1a–d**) in the polar aprotic solvent dimethylformamide (DMF). The reaction is an example of nucleophilic substitution at silicon (Scheme I) and is characterized by values for β_{Nuc} of 1.0 and β_{Lg} of −1.9. Scheme I depicts the reaction as involving nucleophilic attack of a carboxylate anion on a tetravalent silicon center; however, it is probable that the species actually undergoing substitution is a silicon center coordinated with a molecule of DMF.[1–7] Presumably the silicon center expands its valence shell by coordinating with a molecule of DMF; the pentavalent silicon species then undergoes reaction with the nucleophile.[1–7] It is well-known that pentavalent silicon centers are more reactive than tetravalent silicon centers.[8,9] In Scheme I any complexation with solvent is omitted for clarity.

The reaction of nucleophiles with silicon substrates cannot be studied in protic solvents. When nucleophiles and silicon substrates are allowed to react in protic solvents, the usual reaction is a general base catalyzed addition of solvent; direct substitution by the nucleophilic reagent is not observed.[10–17] The general base catalyzed addition of solvent can be avoided by examining the reaction in an aprotic solvent. DMF is a useful aprotic solvent for studying nucleophilic substitution reactions[18] since the high dielectric constant[19] (ϵ = 36.7) makes it possible to dissolve anionic nucleophiles. In addition pK_a values for many carboxylic acids and phenols have been determined in DMF,[20,21] allowing one to construct linear

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