the blue solution was stirred for 20 min, during which time the blue color disappeared. The ammonia was evaporated, and brine was added to destroy the excess lithium. The product was taken up in ether (100 mL). Evaporation of the solvent gave a colorless oil (37 mg), which was separated by column chromatography [hexane–EtOAc (1:4)], yielding the triol 4 (8 mg): ^{1}H NMR ($CDCl_3$) δ 5.80 (dd, 1 H, J = 11, 17 Hz), 4.90 (d, 1 H, J = 17 Hz), 4.89 (d, 1 H, J = 11 Hz), 4.81 (d, 1 H, J = 1 Hz), 4.57 (br s, 1 H), 3.66 (dd, 2 H, J = 6, 11 Hz), 3.37 (d, 1 H, J = 10 Hz), 1.95 (m, 1 H), 1.69 (s, 3 H), 1.55 (m), 1.20 (s, 3 H), 1.16 (s, 3 H), 0.99 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 150.3 (d), 148.0 (s), 112.0 (t), 109.9 (t), 79.1 (d), 73.2 (s), 63.5 (t), 52.9 (d), 46.0 (d), 40.0 (s), 40.0 (t), 39.5 (d), 31.7 (t), 29.7 (t), 25.6–24.9 (4 peaks), 23.4 (q), 16.7 (q); MS m/z 322 (M^+). The same product was not obtained when the reaction was carried out in the nitrogen atmosphere.

Reduction of 1 with Lithium in Ethylamine. Ethylamine (ca. 10 mL) was dried with Na, and the dry ethylamine was introduced into a two-necked flask connected with a dry ice trap. Lithium (18 mg, 2.6 mmol) was dissolved, and a solution of 1 (49 mg, 161 μmol) in dry THF (0.5 mL) was added to the blue solution. The reaction mixture was stirred for 1.5 h, and ethylamine was evaporated on a water bath (25 °C). The residue was treated with brine, and the product was extracted with ether (100 mL). Evaporation of the ether gave a crude material (49 mg), which was purified by a short silica gel column [hexane–EtOAc (5:1)] to produce the pure diol 5 (45 mg, 91.3%) as a colorless oil: IR (film) 3400, 1465, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.24 (t, 1 H, J = 7 Hz, H-15), 3.41 (m, 1 H, H-17), 2.20 (m, 2 H, H-16), 1.90 (sept, 1 H, J = 7 Hz, H-10), 1.83 (tt, 1 H, J = 4, 12 Hz, H-4), 1.65 (s, 3 H, H-14), 1.47 (m, H-5), 1.39 (m, H-3), 1.28 (m, H-6), 1.24 (s, 3 H, H-20), 1.18 (s, 3 H, H-19), 1.14 (dd, 1 H, J = 3, 12 Hz, H-2), 0.89 (d, 3 H, J = 7 Hz, H-11), 0.82 (s, 3 H, H-7), 0.79 (t, 3 H, J = 7 Hz, H-9), 0.75 (d, 3 H, J = 7 Hz, H-12); ^{13}C NMR ($CDCl_3$) δ 145.0 (s), 118.4 (d), 77.8 (d), 72.7 (s), 48.2 (d), 38.3 (t), 36.4 (s), 34.6 (t), 30.4 (t), 27.6 (t), 27.2 (t), 26.7 (d), 25.3 (q), 24.6 (q), 23.8 (q), 20.2 (q), 18.6 (q), 15.0 (q), 7.7 (q); $[\alpha]^{26}_D$ +25.7° (c 0.04, $CHCl_3$); CIMS m/z 309 (M^+ – 1); HREIMS calcd for $C_{20}H_{34}O$ ($M - H_2O$) 290.2610, found 290.2610.

Ozonization of the Diol 5. Ozone was introduced into a solution of 5 (41.3 mg, 134 μmol) in methanol (10 mL) at –78 °C for 15 min. The excess ozone was removed by applying nitrogen stream, and dimethyl sulfite (0.4 mL) was added. The mixture was allowed to stand at room temperature, and methanol was evaporated on a rotary evaporator. After brine was added onto the residue, the product was taken up into hexane–ether (1:1). The crude material (45.0 mg) was purified by short column chromatography (hexane–EtOAc) to yield pure ketone 6 (24.1 mg, 85.8%): $[\alpha]^{25}_D$ + 27° (c 0.06, $CHCl_3$); IR (film) 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.25 (tt, 1 H, J = 4, 12 Hz, H-4), 2.14 (s, 3 H, H-14), 1.94 (sept, 1 H, J = 7 Hz, H-10), 1.70 (m, 1 H, H-3), 1.61 (qd, 1 H, J = 4, 13 Hz, H-5), 1.14 (dd, 1 H, J = 3, 12 Hz, H-2), 0.90 (d, 3 H, J = 7 Hz, H-12), 0.83 (s, 3 H, H-7), 0.79 (t, 3 H, J = 8 Hz, H-9), 0.78 (d, 3 H, J = 7 Hz, H-12); ^{13}C NMR ($CDCl_3$) δ 212.4 (s), 52.5 (d), 47.8 (d), 37.6 (t), 36.3 (s), 34.5 (t), 28.1 (d), 25.3 (q), 24.6 (t), 24.6 (q), 24.0 (t), 19.9 (q), 18.4 (q), 7.6 (q); MS m/z 210 (M^+), 181 (M – 29), 167 (M – 43); HREIMS calcd for $C_{14}H_{26}O$ 210.1984, found 210.2000.

Baeyer–Villiger Reaction of the Ketone 6. m-Chloroperbenzoic acid (25 mg, 0.15 mmol) was added to a solution of the ketone 6 (18.1 mg, 86 μmol) in dry chloroform (1 mL), and the mixture was stirred at 50 °C for 16 h. The residue obtained on evaporation of the solvent was purified by short column chromatography [hexane–EtOAc (95:5)] to give the acetate 7 (18.3 mg, 94.3%): IR (film) 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.64 (tt, 1 H, J = 5, 11 Hz, H-4), 2.04 (s, 3 H, H-14), 1.89 (sept, 1 H, J = 7 Hz, H-10), 1.79 (m, 1 H, H-3), 1.70 (tdd, 1 H, J = 2, 5, 11 Hz, H-5), 1.45 (dq, 1 H, J = 5, 11 Hz, H-5), 1.20 (dd, 1 H, J = 3, 12 Hz, H-2), 0.90 (d, 3 H, J = 7 Hz, H-11), 0.83 (s, 3 H, H-7), 0.79 (t, 3 H, J = 8 Hz, H-9), 0.78 (d, 3 H, J = 7 Hz, H-12); ^{13}C NMR ($CDCl_3$) δ 170.7 (s), 74.7 (d), 46.4 (d), 36.0 (t), 34.1 (t), 27.9 (t), 27.6 (t), 25.3 (d), 24.4 (q), 21.5 (q), 21.5 (q), 19.8 (q), 18.4 (q), 7.7 (q); CIMS m/z 227 (M^+ + 1); MS m/z 166 (M – 60), 151 (166 – Me), 137 (166 – Et), 123 (166 – Ac); HREIMS calcd for $C_{12}H_{22}$ (M – AcOH) 166.1721, found 166.1723.

Hydrolysis of the Acetate 7. A solution of 7 (9.0 mg, 40 μmol) in MeOH (1 mL) was treated with 5 drops of a 1 M aqueous NaOH solution, and the mixture was allowed to stand for 2 h. The mixture was neutralized, the methanol was evaporated, and the residue was extracted with ether (100 mL). The crude product was purified by short column chromatography (hexane–EtOAc) to afford pure 8 (7.3 mg, 99.2%): IR (film) 3330 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.52 (tt, 1 H, J = 5, 11 Hz, H-4), 1.89 (sept, 1 H, J = 7 Hz, H-10), 1.77 (m, 1 H, H-3), 1.70 (tdd, J = 3, 5, 12 Hz, H-5), 1.56 (m, 1 H, OH), 1.13 (dd, 1 H, J = 3, 13 Hz, H-2), 0.89 (d, 3 H, J = 7 Hz, H-11), 0.84 (s, 3 H, H-7), 0.78 (t, 3 H, J = 8 Hz, H-9), 0.78 (d, 3 H, J = 7 Hz, H-12); ^{13}C NMR ($CDCl_3$) δ 72.2 (d), 46.6 (d), 36.3 (t), 35.9 (s), 34.2 (t), 31.7 (t), 31.6 (t), 25.2 (d), 24.5 (q), 19.9 (q), 18.5 (q), 7.7 (q); MS m/z 184 (M^+), 155 (M – 29), 137 (M – 47); HREIMS calcd for $C_{12}H_{22}$ ($M - H_2O$) 166.1721, found 166.1720.

Synthesis of the (*R*)-MTPA Ester of the Alcohol 8. A solution of 8 (1.0 mg, 5.4 μmol) in dry pyridine (20 μL) was treated with (+)-MTPA chloride (2.5 μL, 13 μmol), and the solution was allowed to stand for 16 h. *N,N*-Dimethyl-1,3-propanediamine (2.5 μL) was added to quench the excess chloride, and after 30 min, the pyridine was evaporated by applying nitrogen stream. The residue was subjected to preparative TLC [hexane–EtOAc (9:1)] to give the MTPA ester 9 (0.8 mg, 50%). The (*S*)-MTPA ester was obtained in the same manner. The ^{1}H NMR data of the (*R*)- and (*S*)-MTPA esters are summarized in Table II.[12]

Synthesis of the (*R*)-MTPA Ester of the Diol 5. The diol 5 (1 mg, 3.2 μmol) was dissolved in dry pyridine (20 μL), and (+)-MTPA chloride (1.2 μL, 6.3 μmol) was added. After 15 h, *N,N*-dimethyl-1,3-propanediamine (2.5 μL) was added, and the mixture was allowed to stand for 30 min. The solvent was evaporated and the residue was subjected to preparative TLC [hexane–EtOAc (8:2)] to give the MTPA ester 5a (0.5 mg, 30%). The (*S*)-MTPA ester was obtained in the same manner. The ^{1}H NMR data of the (*R*)- and (*S*)-MTPA esters are summarized in Table I.[12]

Supplementary Material Available: ^{1}H NMR data for the (*R*)- and (*S*)-MTPA esters of diol 5 and 9 and NMR spectra of 1, 3, 4, 5, 6, 7, 8, (*R*)- and (*S*)-MTPA ester of 5, and (*R*)- and (*S*)-9 (18 pages). Ordering information is given on any current masthead pages.

(12) Available as supplementary material.

Reaction of $Na_2Fe(CO)_4$ with an Unsaturated Aziridinium Ion. Unprecedented Rearrangement of an Alkyltetracarbonylferrate Intermediate

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Received September 20, 1991

As a potential approach for forging the sixth ring of the complex oxindole alkaloid gelsemine (6),[1] we recently considered the sequence outlined in Scheme I. A key step in this plan would be carbonylation of the unsaturated aziridinium ion 2 with an anionic metal complex to form the cyclopentanone ring of the hexacyclic ketone 4. Baeyer–Villiger oxidation of this latter intermediate could plausibly allow development of the final hydropyran ring of the target alkaloid (4 → 5 → 6). Earlier studies in our laboratories had led to an expeditious sequence for preparing the hexacyclic aziridine 1.[2–5] Moreover, these in-

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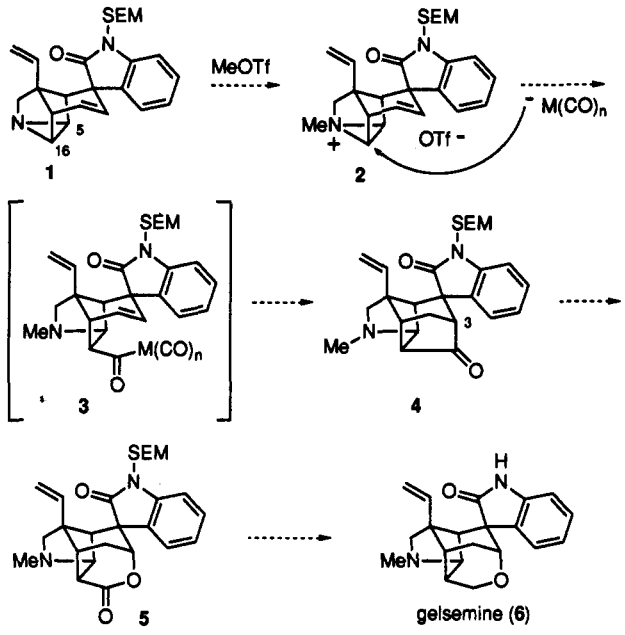
0022-3263/92/1957-1035$03.00/0

Scheme I



vestigations had demonstrated that the oxindole ring of this intermediate effectively blocked access of nucleophiles to the proximal aziridine carbon such that ring opening of **2** with cyanide anion occurred regioselectively at C(16).[5] Disodium tetracarbonylferrate[6] was an obvious choice for initially exploring the sequence proposed in Scheme I, since it is a powerful nucleophile and is known to react with 3-alkenyl tosylates or halides to afford cyclopentanones upon protonolysis.[6-8] Although the reaction of $Na_2Fe(CO)_4$ with aziridines or aziridinium ions has not, to our knowledge, been previously examined, this anion is known to cleave the ring of doubly activated cyclopropanes.[9]

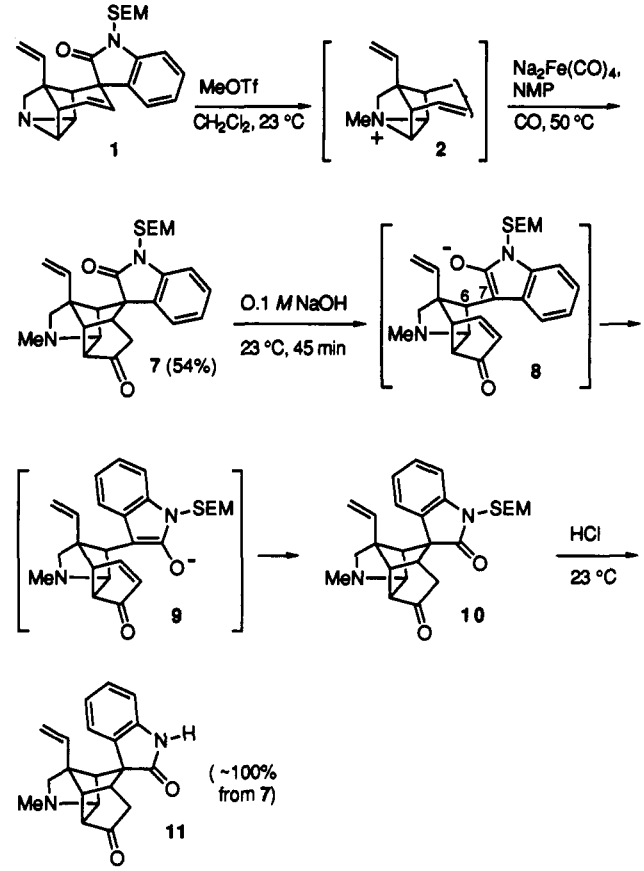
(1)[6c]

We disclose herein the first example of the reaction of $Na_2Fe(CO)_4$ with an aziridinium cation. We moreover report that the reaction of aziridinium ion **2** with this anionic metal complex does not lead to the expected hexacyclic cyclopentanone **4**, but rather occasions an unprecedented carbon skeletal rearrangement to afford an isomeric hexacyclic ketone.

Results and Discussion

When a $CDCl_3$ solution of aziridine **1**[5] was treated at room temperature with an equivalent of methyl triflate,

Scheme II[a]



[a] NMP = *N*-methyl-2-pyrrolidone.

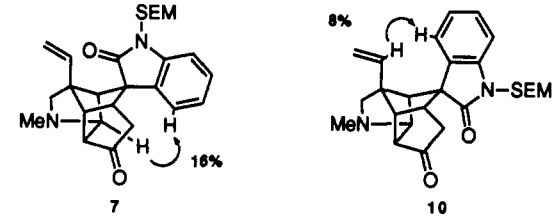


Figure 1. NOE data for spirooxindoles **7** and **10**.

the diagnostic signals[10] of the C(5) and C(16) methine hydrogens (broad singlets at δ 2.39 and 2.79) were replaced with broad singlets at 3.94 and 4.57 ppm. A new methyl singlet at δ 3.28 was also present. These new signals are diagnostic of the formation of the *N*-methylaziridinium ion **2**.[11] The reactivity of $Na_2Fe(CO)_4$ is known to be markedly enhanced in dipolar aprotic solvents.[12] Thus, aziridine **1** was treated at room temperature in CH_2Cl_2 with 1 equiv of $MeOSO_2CF_3$, and after 1 h the solvent was removed to afford the crystalline *N*-methylaziridium ion **2**, which was dissolved in *N*-methyl-2-pyrrolidone and treated with 5 equiv of the dioxane complex of $Na_2Fe(CO)_4$ (Scheme II). After purging with CO, the reaction mixture was heated at 50 °C under a CO atmosphere for 14 h and finally hydrolyzed at room temperature with acetic acid. After purification on silica gel, a single carbonylation product **7** was isolated in 54% yield. High-resolution mass

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(4) Earley, W. G.; Oh, T.; Overman, L. E. *Tetrahedron Lett.* **1988**, *29*, 3785.
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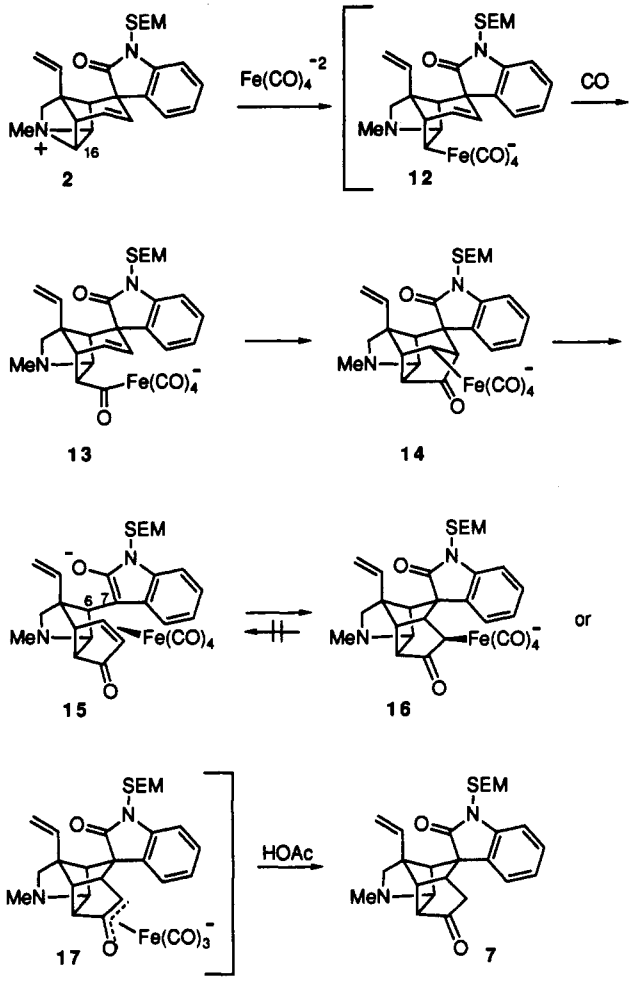
(10) ^1H NMR assignments were established by extensive homonuclear decoupling and NOE experiments.
(11) Crist, D. R.; Leonard, N. J. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 962.
(12) Collman, J. P.; Finke, R. G.; Cawse, J. N.; Brauman, J. I. *J. Am. Chem. Soc.* **1977**, *99*, 2515.

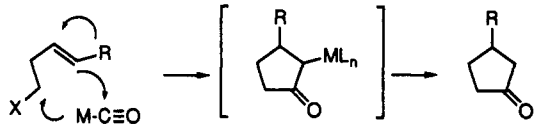
Scheme III



spectroscopy established that the molecular composition of this material was that expected for product **4**. However, a detailed analysis of the ^{1}H NMR spectrum made this structural assignment untenable. Moreover, when **7** was treated with dilute base it was quantitatively converted to an isomer **10**, which appeared to differ from **7** only in the orientation of the spirooxindole functionality. ^{1}H NMR NOE studies were fully consistent with this interpretation (Figure 1). Facile epimerization at the spirocyclic center also rules out structure **4** for the carbonylation product. However, this isomerization would be consistent with structural formulation **7**. This material, being a 1,5-dicarbonyl, could epimerize at C(7) by a process involving retro-Michael fragmentation to **8**, rotation of the C(6)–C(7) single bond (**8** → **9**) and intramolecular Michael cyclization of **9** to afford **10**. The driving force for this isomerization would be placement of the smaller oxindole carbonyl group, rather than the larger aryl ring, on the more hindered concave α face of the tetracyclic azacycloundecane ring system.[2,4] Conclusive evidence for the structure of **10** was secured by removal of the SEM group to provide the crystalline hexacyclic ketone **11**, an intermediate which was amenable to single-crystal X-ray analysis.

The formation of **7** from the reaction of aziridinium ion **2** with $Na_2Fe(CO)_4$ is striking, since the hexacyclic skeleton of **7** is more highly strained than that of the expected product **4**.[13] A plausible mechanism for this conversion is proposed in Scheme III. Ring opening of **2** at C(16) would initially generate the alkylferrate **12**, which in analogy to studies with simpler substrates[6-8] would be expected to undergo sequential CO and alkene insertion to afford **14**. We propose that due to the low basicity of an oxindole enolate anion, **14** is not stable but rather undergoes β-elimination to give the tetracarbonyliron alkene complex **15**, a stable 18-electron species. Collapse of this intermediate at the β-carbon of the enone, more rapidly than rotation of the C(6)–C(7) bond, would afford the hexacyclic iron enolate **16**. The stability of this intermediate, or a related oxy-η^3-allyl intermediate **17**, could provide the driving force for the molecular rearrangement.[14] Tetracarbonyliron alkene complexes are well-characterized[15,16] and are particularly stable when the alkene is substituted with electron-withdrawing groups.[15] The proposed conversion of **15** → **16** derives direct precedent from the studies of Roberts on the addition of malonate anions to tetracarbonyliron alkene complexes.[17,18]

To the best of our knowledge, the carbon skeletal rearrangement uncovered in this study is unprecedented in organometallic chemistry. In its simplest terms it can be formulated as depicted in eq 2 where R is a carbon appendage. Although the facility of this rearrangement in



(2)

the system studied here undermined our initial synthesis objective, the recognition of this transformation could lead to productive future applications in other synthesis areas. We also note that the occurrence of a similar rearrangement for the specific case of R = H[14] is not, to our knowledge, ruled out in the previously reported[6,7] reactions of $Na_2Fe(CO)_4$ with unsaturated tosylates or halides.

Experimental Section[19]

Sequential Reaction of Aziridine 1 with Methyl Trifluoromethanesulfonate and Disodium Tetracarbonylferrate. Preparation of Hexacyclic Oxindole Ketone 7. Methyl triflate (6.5 μL, 0.058 mmol) was added to a solution of aziridine **1** (23.6 mg, 0.058 mmol) in CH_2Cl_2 (1.0 mL) at 23 °C. After 1 h the solvent was removed under a flow of argon and the flask containing the white solid residue was evacuated and taken into a drybox.

Inside the drybox, *N*-methyl-2-pyrrolidone (1.0 mL) was added, followed by the disodium tetracarbonylferrate–dioxane complex (100 mg, 0.29 mmol). The flask containing the resulting yellow solution was sealed, removed from the drybox, and purged with CO. The resulting mixture was then heated in a 50 °C oil bath under an atmosphere of CO. After 14 h the yellow-red solution was allowed to cool to 23 °C and acetic acid (200 μL) was added. The resulting solution was stirred for 1 h at 23 °C, diluted with CH_2Cl_2 (40 mL), washed with 0.1 N HCl (40 mL) followed by saturated aqueous $NaHCO_3$ (20 mL), dried (K_2CO_3), and concentrated. Purification of the residue by flash chromatography

(13) The heat of formation of **7** is 3.5 kcal/mol higher than that of **4** by molecular mechanics calculations (MMX force field).

(14) The irreversible rearrangement of a (γ-oxoalkyl)ferrate intermediate to an iron enolate by a process involving transfer of hydrogen has been suggested in another context, see: Cooke, M. P.; Parlman, R. M. *J. Am. Chem. Soc.* **1975**, *97*, 6863.

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(18) Roberts, B. W.; Ross, M.; Wong, J. *J. Chem. Soc., Chem. Commun.* **1980**, 428.

(19) General experimental details have been published.[20] The disodium tetracarbonylferrate–dioxane complex (1:1.5) was prepared as described in ref 21.

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(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).

Acknowledgment. Support of this investigation by the Heart, Lung and Blood Institute of the National Institutes of Health (HL-25854) is gratefully acknowledged. NMR, mass spectra, and X-ray analyses employed instrumentation acquired with the assistance of NSF Shared Instrumentation Grants. We particularly wish to thank Dr. J. Ziller, Director of the UCI X-Ray Crystallography Laboratory, for the structural determination of 11. We also thank Dr. William Nugent, DuPont Central Research and Development, for helpful discussion.

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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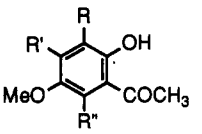
Received May 24, 1991

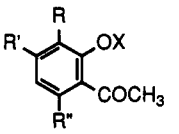
Introduction

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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0022-3263/92/1957-1038$03.00/0