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Selective Oxidation of the α-Methylene of the Bridge in Ferrocenophanes with Silver Oxide or Silver Perchlorate/Sodium Methoxide

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Synopsis. The treatment of ferrocenophanes with AgO, Ag_2O or $AgClO_4/CH_3ONa$ in methanol gave oxidized products at the α-methylene of the bridge. In the reaction of $[m][n]$ferrocenophanes (m, n=3, 4, 5; $m>n$), the α-methylene of the longest bridge $[m]$ was oxidized in preference to that of the shorter bridge $[n]$. A reaction mechanism via a radical and/or cation species on the α-methylene of the bridge is proposed.

A selective oxidation of the α-methylene of the bridge in ferrocenophanenes with a silver oxide or perchlorate/CH_3ONa system has been found during progress in a study concerning multibridged ferrocenophanes. We synthesized a number of multibridged ferrocenophanes[1] containing perbridged superferrocenophane;[2] demetalation of those phanes was subsequently planned to prepare virious kinds of cage compounds comprising the carbon frameworks of the phanes. Since multibridged phanes are not susceptibile to demetalation under reduction conditions,[3] we designed the following methods. The ferrocene nuclei are oxidized with silver salt followed by treatment with alkoxide to be labilized; the resulting methoxylation complexes on the cyclopentadienyl (η^5-C_5H_5, Cp) ring are then decomposed by catalytic hydrogenetion to yield a demetalation framework. A model reaction of demetalation using [4](1,1′)ferrocenophane (**1a**) was examined prior to the reaction of multibridged ferrocenophanes. The compound (**1a**) in methanol was oxidized with AgO to generate the corresponding ferricenium ion; the ion was treated with CH_3ONa in methanol. However, no expected complex was given; only oxidation products (**1b** and **1c**) at the α-carbon of the bridge were afforded in fairly good yields (ca. 70%) (Chart 1).

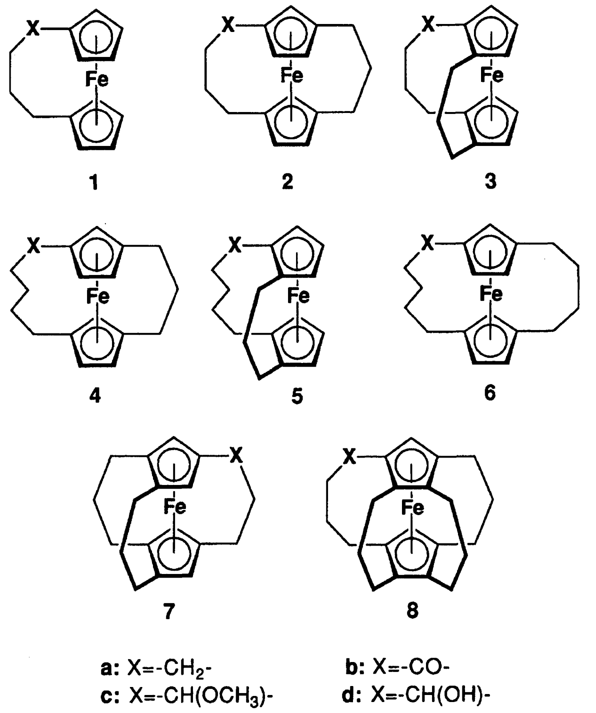


Chart 1.

Accordingly, the interesting oxidation with silver oxide in the presence of alkoxide was applied to several ferrocenophanes having different bridging modes from each other. The use of $AgClO_4$ instead of AgO also afforded oxygenetion products at the α-methylene carbon, although the substitution served to slow down the rate of oxidation. The results in the reactions using Ag_2O were almost comparable with those of $AgClO_4$. The selected result of each ferrocenophane in the reaction with silver compounds are summarized in Table 1. The reactions were monitered by TLC; each reaction was allowed to continue until the starting material either disappeared or until the spots of the products remained unchanged. The structures of the products were confirmed by their spectroscopies, by comparing them with authentic samples, or by interconversion reactions between the related compounds (as described in the experimental section). The configurations of methoxyl and hydroxyl derivatives about the arrangement of the substituent were not confirmed. The materials other than the compounds described in Table 1 were decomposition products.

In order to examine the reaction mechanism of the oxidation, the reaction of **1a** with the following reagents was run: (1) AgO without methoxide in methanol, (2) AgO/*t*-BuOK in *t*-butyl alcohol, (3) AgO without alkoxide in *t*-butyl alcohol, (4) AgO in benzene, and (5) $NaClO_4/CH_3ONa$ in methanol. All of the reactions under those conditions gave no or only a slight amount of oxidation product. Therefore, silver salt and methoxide ion are essential for oxidation of the phane, and butyl alcohol is not appropriate as a solvent in the oxidation due to its viscosity. The ferricenium salt ($[\mathbf{1a}]^+ \cdot ClO_4^-$) of **1a** was prepared by a reaction with $AgClO_4$, and was isolated; the salt was treated with sodium methoxide in methanol to give ketone **1b**, but was treated with ascorbic acid to recover only **1a**. Moreover, a treatment of methoxyl derivative (**1c**) with AgO/CH_3ONa in methanol afforded an oxo compound (**1b**). It is there-

Table 1. Oxidation of Ferrocenophanes with Silver Salts and Sodium Methoxide in Methanol

Substrate	Reagent	Reaction time	Products (%)			Recovered **a** (%)
			b	**c**	**d**	
1a	AgO	45 min	47	24	—	—
2a	AgO	6 h	19	34	—	—
3a	$AgClO_4$	45 h	—	10	18	45
4a	$AgClO_4$	45 min	6	16	21	7
5a	$AgClO_4$	24 h	17	—	12	33
6a	$AgClO_4$	9 h	4	6	16	16
7a	$AgClO_4$	12 h	54	15	—	—
7a	AgO	45 min	59	—	—	10
8a	$AgClO_4$	24 h	15	—	—	9

fore evidenced that the oxidation proceeds via action of CH_3ONa to the ferricenium ion, and that **1c** is an intermediate product of **1b**. Those oxidations of **1a** and **1c** did not result from a reaction with dioxygen in air, since almost similar results were obtained under either an argon atmosphere or in air.

From those results we propose the oxidation mechanism summarized in Scheme 1, in which monobridged phane **1a** is represented as the substrate. The generation of α-carbocation and/or α-carboradical was supported by the fact that the longer methylene chain in **2a**—**6a** and **8a** is oxidized in preference to the shorter one. The stabilities of α-carbocations and α-carboradicals on [3]-, [4]-, and [5]methylene bridges increase in this order, because π-conjugation between the cation or the radical sp^2 carbon and the Cp ring is more effective in the longer bridge than in the shorter one, due to the good planality of the sp^2 plane with the Cp ring plane in the longer bridge. The unusual stability of α-ferrocenyl carbocations is well known;[4] we have demonstrated that the carbocations of the α-methylene of the bridge in ferrocenophanes are stable in solution.[5] The selective oxidation of the isolated bridge at the 4,4′-positions in **7a** should be caused by the low steric hindrance compared with that of the other bridges. A decrease in the yield of oxidation product in **8a** is due to an instability of the substrate. The production of hydroxyl compounds might be caused by an attack by water to the reaction intermediates when the reaction mixture was worked up, since the yields of the hydroxyl compounds were not reproducible.

The oxidation of hydroxymethylarenes with Ag_2CO_3 to afford formylarenes[6] and the reaction of alkylarenes with AgO under acidic conditions to give the corresponding acylarenes[7] were reported as examples of oxidations with silver compounds. However, the oxidation of methylene with silver oxide or a silver salt/alkoxide system has not been found, to the best of our knowledge. The oxidation of 1,2,3,4-tetrahydronaphthalene under the same conditions as those given in Table 1 yielded no expected oxidation product. Therefore, the extraordinary stabilization of the cation or radical center with a neighboring effect of the ferrocene moiety should contribute to the progress of oxygenetion in the reaction with our oxidation system.

Experimental

Ferrocenophanes (**1a**,[8] **2a**,[9] **3a**,[10] **4a**,[11] **5a**,[11] **6a**,[11] **7a**,[12] and **8a**[13]) provided as the substrate were prepared according to the already reported method.

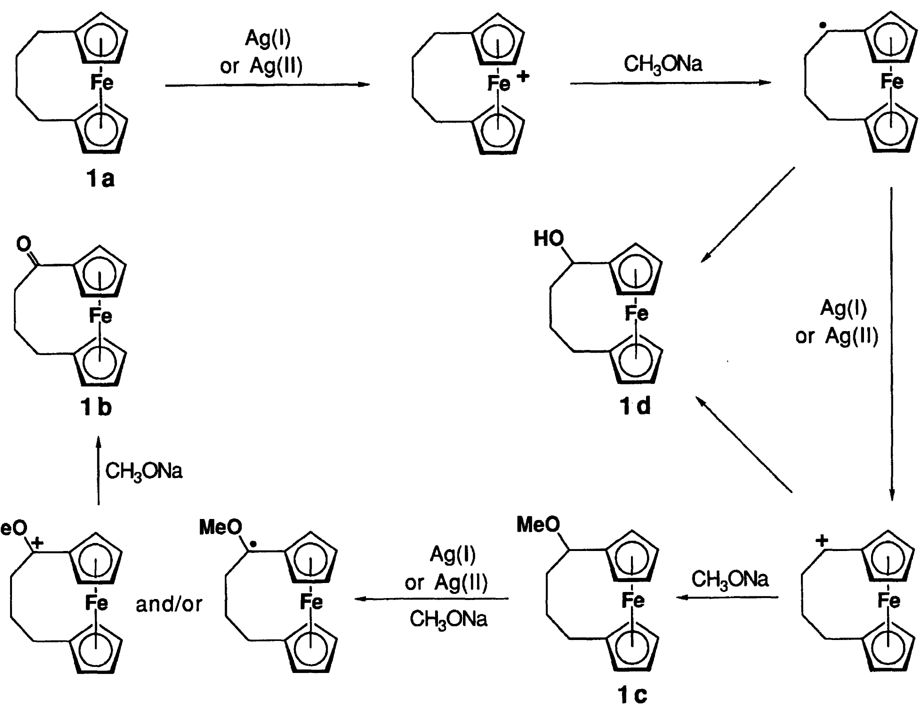
The procedure for oxidation in **7a** is described as a typical example: An excess amount of $AgClO_4$ (3.0 g) was added to a solution of 1.47 g (4.79 mmol) of $[3_3]$ (1,2,4)-ferrocenophane (**7a**) in 100 ml of methanol; the mixture was stirred at room temperature for ca. 30 min. To the resulting greenish-blue suspension was added dropwise a large excess of CH_3ONa, which was prepared from Na (2 g) and methanol (50 ml); the reaction mixture was stirred at room temperature for 12 h. The progress of the reaction was checked by thin-layer chromatography. The reaction mixture was filtered through a short column of silica gel with methanol/ether eluent. The solvent was evaporated in vacuo, and benzene and water were added to the resulting concentrated mixture. The organic layer was washed with saturated aq NaCl, dried over Na_2SO_4, and evaporated. The residue was column-chromatographed on silica gel with benzene/ethyl acetate (10/1) used as an eluent. The first and second bands yielded 235 mg of **7c** (15%) and 821 mg (54%) of **7b**, respectively. Ketone **7b** disagreed with 1-oxo$[3_3]$-(1,2,4)ferrocenophene,[12] but agreed with 7-oxo$[3_3]$(1,2,4)-ferrocenophane.[12] 7-Methoxy$[3_3]$(1,2,4)ferrocenophane (**7c**) gave a yellow oil; ^{1}H NMR ($CDCl_3$) δ=1.10—2.50 (16H, m, CH_2), 3.22 (3H, s, OCH_3), 3.60 (1H, m, 7-H of bridge), 3.76, 3.85, and 4.05 (1H, 2H and 1H, each m, Cp-H).

Found: M^+, *m/z* 336.1177. Calcd for $C_{20}H_{24}OFe$: M, 336.1180.

The oxidation of **7c** under the same conditions as that of **7a** gave only ketone **7b** in quantitative yield. Therefore, it was confirmed that **7c** was substituted with the methoxy group at the 7-position of the 4,4′-bridge.

A reaction using AgO was carried out according to the same procedure as that described above, except for using silver(I) salt.

The oxidation reactions of the other ferrocenophanes were also carried out according to the same procedure. Several ketones of the products were identified by comparison with authentic samples (**1b**,[8] **2b**,[14] and **4b**[14]) prepared via an



Scheme 1.

alternate route. The spectral data of **2b**, **4b**—**6b**, and **8b** were as described below. The positions of the carbonyl groups in **2b** and **4b**—**6b** were supported by the facts that they were in disagreement with the corresponding isomeric ketones, 5-oxo[4][3](1,3)-,[9] 6-oxo[5][3](1,3)-,[11] 6-oxo[5][3]-(1,2)-,[15] and 6-oxo[5][4](1,3)ferrocenophanes,[11] respectively. The structure of **8b** was also confirmed by the spectroscopies of [3$_4$](1,2,3,4)ferrocenophane derived from **8b**.[16]

1-Oxo[4][3](1,3)ferrocenophane (2b). A reddish-brown oil; IR (neat liquid) 1645 (C=O); ^{1}H NMR (CDCl$_3$) δ=1.60—2.70 (12H, m, CH$_2$), 3.90 and 3.97 (each 2H, m, Cp), 4.39 and 4.46 (each 1H, AB part of an ABX system, 2-, and 5-H of Cp).

Found: M$^+$, m/z 294.0709. Calcd for $C_{17}H_{18}OFe$: M, 294.0706.

1-Oxo[5][3](1,3)ferrocenophane (4b). A reddish-brown oil; IR (neat liquid) 1650 (C=O); ^{1}H NMR (CDCl$_3$) δ=1.50—3.00 (14H, m, CH$_2$), 3.90, 4.34, and 4.70 (1H, 3H and 1H, each, m, Cp-H), 4.62 (1H, t, J=1.4 Hz, 2-H of Cp).

Found: M$^+$, m/z 308.0860. Calcd for $C_{18}H_{20}OFe$: M, 308.0862.

6-Oxo[5][3](1,2)ferrocenophane (5b). A reddish-brown oil; IR (neat liquid) 1650 (C=O); ^{1}H NMR (CDCl$_3$) δ=0.80—3.00 (14H, m, CH$_2$), 3.80, 4.09, 4.12, and 4.46 (each 1H, m, Cp-H), 4.06 (1H, t, J=3.0 Hz, 2′-H of Cp), 4.41 (1H, t, J=2.8 Hz, 2-H of Cp).

Found: M$^+$, m/z 308.0856. Calcd for $C_{18}H_{20}OFe$: M, 308.0862.

6-Oxo[5][4](1,3)ferrocenophane (6b). A reddish-yellow oil; IR (neat liquid) 1655 (C=O); ^{1}H NMR (CDCl$_3$) δ=1.60—2.70 (16H, m, CH$_2$), 3.99, 4.42, and 4.60 (2H, 1H, and 1H each m, Cp-H), 4.04 (1H, t, J=1.5 Hz, 2′-H of Cp), 4.67 (1H, t, J=1.5 Hz, 2-H of Cp).

Found: M$^+$, m/z 322.1006. Calcd for $C_{19}H_{22}OFe$: M, 322.1018.

6-Oxo[4][3$_3$](1,2,3,4)ferrocenophane (8b). Yellow prisms: mp 180 °C (decomp); IR (KBr) 1645 (C=O); ^{1}H NMR (CDCl$_3$) δ=1.50—2.70 (24H, m, CH$_2$), 3.86 (1H, s, 5′-H of Cp), 4.24 (1H, s, 5-H of Cp).

Found: C, 73.85; H, 6.97%, M$^+$, m/z 374.1323. Calcd for $C_{23}H_{26}OFe$: 73.80; H, 7.00%, M, 374.1331.

Methoxyl and hydroxyl derivatives were assigned by the mass, ^{1}H NMR and IR spectroscopies and by the results that the oxidation products of those agreed with the corresponding ketones. $AgClO_4$ or AgO_2/CH_3ONa and MnO_2 were used for the oxidation of methoxyl and hydroxyl derivatives, respectively. The ^{1}H NMR spectra of methoxyl and hydroxyl derivatives were shown to be mixtures of stereoisomers about the arrangement of the methoxy or hydroxy group. The signals of the methoxy protons were detected at δ=3.1—3.4 in the spectra of the methoxyl derivatives. The OH stretching bands in the IR spectra of hydroxyl derivatives were found at 3300—3350 cm^{-1}. The position of the substituent in **3c** and **3d** was supported by the results that their oxidation products disagreed with 5-oxo[4][3](1,2)ferrocenophane,[10] but agreed with 1-oxo[4][3]-(1,2)ferrocenophane.[14]

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