Excellent Chiral Induction by Diene Iron-Tricarbonyl Moiety. I: Diastereoselective [4+2] Type Cycloaddition of 1-Azatriene Iron-Tricarbonyl Complex

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Received September 29, 1994; accepted December 13, 1994

The $LiClO_4$-catalyzed cycloaddition reaction of 1-azatriene iron-tricarbonyl complex with Danishefsky's diene proceeds in a highly stereoselective manner to give a diastereomerically pure 2-substituted dehydropiperidinone derivative. The stereochemistry of the major cycloadduct was determined to be 6*RS*,1′*SR* by X-ray crystallographic analysis.

Key words [4+2] type cycloaddition; aldimine; 1-azatriene iron-tricarbonyl complex; 1-methoxy-3-(trimethylsilyloxy)-1,3-butadiene; lithium perchlorate; dehydropiperidinone

Heterocyclic compounds involving the piperidine ring system, such as nojirimycin, porantheridine, and swainsonine, have attracted much interest by virtue of their varied and clinically useful biological actions (Fig. 1). Therefore, construction of the piperidine skeleton constitutes a continuing major challenge in synthetic organic chemistry. In particular, [4+2] type cycloadditions between imine-dienophiles and dienes have received much attention as a versatile synthetic tool for piperidine derivatives.[1,2] The majority of the reported investigations on this topic have dealt with the diastereoselectivity of C-1 or C-2 substituted chiral dienes[3] and chirally modified dienophiles derived from chiral aldehydes[4] or chiral amines,[5] although Lewis acids have also received increasing attention as chiral catalysts for asymmetric cycloadditions.[6] With the aim of developing a superior diastereoselective [4+2] type cycloaddition, our own investigations in this area have been focused on the stereodirecting potential of **2**, which was demonstrated to be a good acceptor in nucleophilic addition with organometallic reagents.[7] Our synthetic route is depicted in Chart 1. Several 2-monosubstituted or 2,6-disubstituted piperidine-type natural products could be derived from the dehydropiperidinone (**3**) by the stereoselective introduction of the appropriate substituents at the C-2 position. Cycloaddition of 1-methoxy-3-(trimethylsilyloxy)-1,3-butadiene (Danishefsky's diene) with the imine complex (**2**) would afford **3** if the addition reaction proceeds with the desired high stereoselectivity. Preparation of **2** can be readily achieved from commercially available hexadienal according to reported procedures.[8] After examination of many experimental conditions, we found that the [4+2] type cycloaddition of Danishefsky's diene with **2b** took place in a highly stereoselective manner in the presence of a catalytic amount of a perchlorate salt such as lithium perchlorate ($LiClO_4$) or magnesium perchlorate ($MgClO_4$) suspended in dichloromethane (CH_2Cl_2), yielding **3b** as a sole product.

This report details the highly diastereoselective [4+2] type cycloaddition of Danishefsky's diene with the imine complex (**2**) and determination of the stereochemistry of the major cycloadduct (**3b**) by X-ray crystallographic analysis.[9]

Results and Discussion

The racemic dienal complex (**1**) was prepared from the corresponding dienal according to the reported procedures.[8] Condensation of **1**[7] with benzylamine ($BnNH_2$)

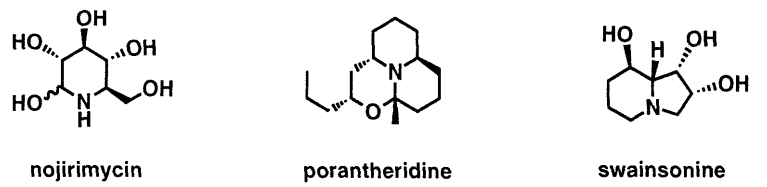

Fig. 1

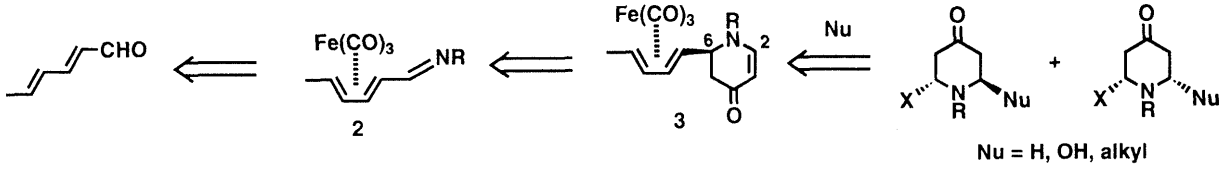

Chart 1

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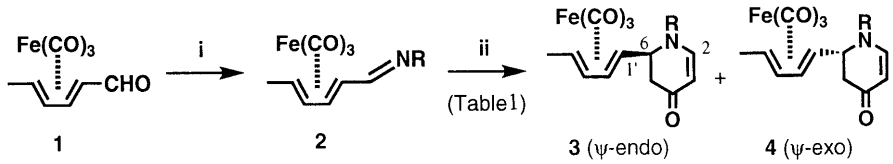

1 2 3 (ψ-endo) 4 (ψ-exo)

i) RNH_2, MS 3A, benzene; ii) Danishefsky's diene, Lewis Acid (see Table 1)

a: R = Bn, b: R = *p*-$MeOC_6H_4$, c: R = Ph, d: R = *p*-ClC_6H_4

Chart 2

Table 1. [4+2] Type Cycloaddition Reaction of Danishefsky's Diene with 1-Azatriene Iron-Tricarbonyl Complexes (**2a—d**) Mediated by Several Lewis Acids

Run	Substrate	Reaction conditions	Yield[a] (%)	de (**3**/**4**)
1	**2a**	$AlCl_3$ (1.1 eq), CH_2Cl_2, −78°C→−30°C, 5 h	7	—
2		$LiClO_4$ (1.1 eq), CH_2Cl_2, r.t., 8 h	30	—
3	**2b**	$AlCl_3$ (1.1 eq), CH_2Cl_2, −78°C→−30°C, 6 h	72	58[b]
4		$AlCl_3$ (0.2 eq), CH_2Cl_2, −78°C→−30°C, 6 h	28	45[c]
5		TMSOTf (1.1 eq), CH_2Cl_2, −78°C→−30°C, 8 h	77	74[b]
6		$LiClO_4$ (5 M solution), ether, r.t., 1 h	89	86[c]
7		$LiClO_4$ (2.0 eq), CH_2Cl_2, r.t., 3 h	87	81[c]
8		$LiClO_4$ (1.1 eq), CH_2Cl_2, r.t., 3 h	80	>95[c]
9		$LiClO_4$ (0.2 eq), CH_2Cl_2, r.r., 8 h	93	>95[c]
10		$LiClO_4$ (0.2 eq), THF, r.t., 8 h	73	77[c]
11		$Mg(ClO_4)_2$ (1.0 eq), CH_2Cl_2, r.t., 6 h	80	>95[c]
12	**2c**	$AlCl_3$ (1.1 eq), CH_2Cl_2, −78°C→−30°C, 6 h	70	30[b]
13		$LiClO_4$ (0.2 eq), CH_2Cl_2, r.t., 2 h	92	81[b]
14	**2d**	$LiClO_4$ (0.2 eq), CH_2Cl_2, r.t., 0.5 h	82	79[b]

a) Isolated yields of cycloadducts **3** and **4**. *b*) Determined from the isolated yields. *c*) Deduced from the 500 MHz ^{1}H-NMR spectra of the diastereomeric mixture.

readily afforded the imine (**2a**) in a quantitative yield. Initially, the imine complex (**2a**) was allowed to react with Danishefsky's diene in various solvents (CH_2Cl_2, tetrahydrofuran (THF), ether) in the presence of various Lewis acids ($AlCl_3$, $LiClO_4$, $ZnCl_2$, $BF_3 \cdot Et_2O$). However, contrary to our expectation, the addition product was obtained in low yield and recovery of most of **1** was always observed (Table 1, runs 1 and 2). After these unsuccessful experiments, it was found, as shown in Table 1 (runs 3—10), that when the *p*-methoxyphenylimine (PMP-imine) complex (**2b**), prepared similarly to **2a**, was used under typical reaction conditions, the [4+2] type cycloaddition could proceed smoothly, giving rise to a separable mixture of cycloadducts (**3b** and **4b**) in reasonable yields with different ratios of **3b** and **4b** depending on the Lewis acid employed. Although reaction of **2b** with conventional Lewis acids, such as aluminum chloride ($AlCl_3$)[10] and trimethylsilyl triflate (TMSOTf),[11] resulted in a moderate stereoselectivity even at low temperature, irrespective of their amount, treatment of **2b** with a catalytic or stoichiometric amount of $LiClO_4$ at room temperature provided **3b** diastereoselectively in good yields.[12] The $LiClO_4$-promoted cycloaddition requires a less-than-equivalent addition of $LiClO_4$ and use of CH_2Cl_2 as a solvent for high stereoselectivity. In order to clarify the role of $LiClO_4$, the cycloaddition with another perchlorate salt, $Mg(ClO_4)$, was investigated and the same high stereoselectivity (de >95%) was observed (run 11). Therefore, these experiments strongly indicate the importance of the metal perchlorates for excellent stereoselectivity.

Next, we examined the electronic effect of the aromatic ring of **2b** by comparison with the electron-deficient aldimines complexes (**2c** and **2d**). Reaction of **2c** and **2d** with Danishefsky's diene in the presence of a catalytic amount of $LiClO_4$ in CH_2Cl_2 at room temperature gave a diastereomixture of **3c**/**4c** and **3d**/**4d** with lower stereoselectivity (81% and 79% de) (runs 13 and 14). Since a more electron-rich aldimine complex (**2b**, *p*-$MeOC_6H_4$ > **2c**, Ph > **2d**, *p*-ClC_6H_4) tends to exhibit higher stereoselectivity, the PMP substituent of **2b** holds the key to success in the diastereoselective [4+2] type cycloaddition. This trend of stereoselectivity might be attributed to the chelation ability of the aldimine nitrogen (*vide infra*).

The stereochemistries of diastereomeric **3b—d** and **4b—d** were deduced from comparisons of their *Rf* values[13] and 500 MHz proton nuclear magnetic resonance (^{1}H-NMR) spectra.[7b] All of the major adducts (**3b—d**) have smaller *Rf* values than the minor ones (**4b—d**) and furthermore, the signals of the H_6 protons in **3b—d** were observed as a doublet of doublets (dd) between 4.0—4.3 ppm, whereas those in **4b—d** were observed as a doublet of doublets of doublets (ddd) between 3.6—3.8 ppm. These results indicate that **3b—d** and **4b—d** should be the *ψ-endo* and *ψ-exo* diastereomers,[13] respectively. In order to identify definitively the stereochemistry, we carried out an X-ray analysis of **3b**, and the crystal structure is depicted in Fig. 2. It is clear that **3b** is the *ψ-endo* diastereomer, that is, **3b** has (6*RS*,1′*SR*)-configuration. The stereochemistries of the remaining cycloadducts (**3c, d** and **4b—d**) would be (6*RS*,1′*SR*) and (6*RS*,1′*RS*), respectively, based on their *Rf* values and ^{1}H-NMR spectra mentioned above.

From the stereochemical form of the major products,

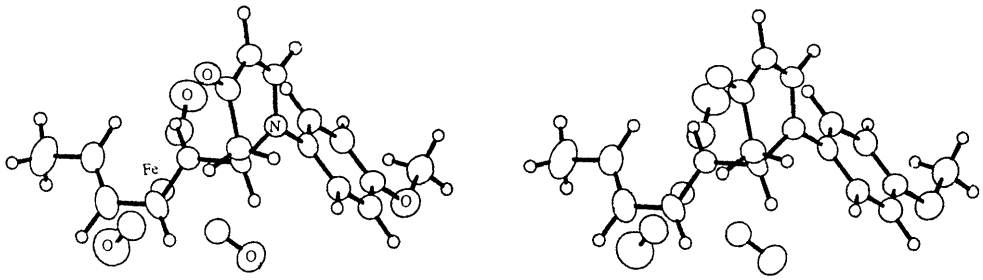

Fig. 2

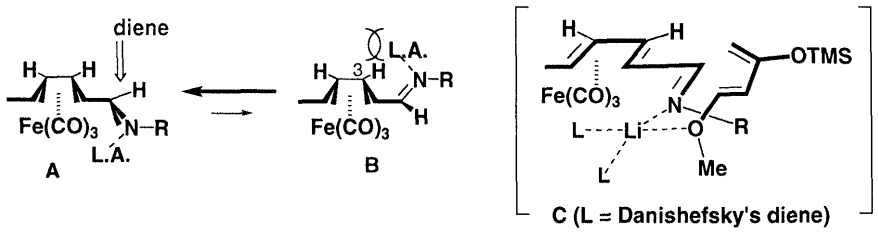

Fig. 3

the reaction process should be described as follows, by analogy with the nucleophilic addition of organometals (Fig. 3).[7] In the presence of Lewis acids, the transoid conformation A is considered to be more stable than the cisoid one B owing to the severe steric repulsion between the substituents of nitrogen and the vinyl proton at C-3. Consequently, the diene should approach preferentially from the *re*-face of the C=N bond in conformation A and the (6*RS*,1′*SR*)-diastereomers (**3b—d**) are predominantly obtained. The requirement of less-than-equivalent $LiClO_4$ for high stereoselectivity suggests that the imine reacts with the diene intramolecularly *via* coordination with Li^+, as in transition state C in Fig. 3.[14] The coordination of excess diene to the Li^+ as a Lewis acid ligand (L) should induce severer steric hindrance than would occur with other conventional Lewis acids.[15] In addition, strong chelating ability of the imine would enhance the steric hindrance of the transition state by shortening the Li–N bond length. In view of these factors, it is reasonable that, in the series of aromatic aldimine complexes (**2b—d**), **2b** shows the best diastereoselectivity under the conditions with a catalytic amount of $LiClO_4$.

As mentioned above, we have succeeded in developing a highly stereoselective [4+2] type cycloaddition of Danishefsky's diene with the PMP-imine (**2b**) in the presence of a catalytic amount of a perchlorate salt, $LiClO_4$ or $MgClO_4$, suspended in CH_2Cl_2. Since the optically active dienal complex (**1**) can be prepared on a large scale, this methodology provides a versatile route to chiral dehydropiperidinones and various optically active piperidine alkaloids.

Experimental

All melting points were determined with a Yanagimoto MP-21 melting point apparatus and are uncorrected. Measurements of optical rotations were carried out using a Nihon Bunko DIP-360 digital polarimeter. IR spectra measurements were performed with a Horiba FT-210 IR spectrometer. ^{1}H-NMR spectra were measured with a JEOL JNM-GX 500 spectrometer (500 MHz). ^{13}C-NMR spectra were measured with a Varian VXR-200 spectrometer (50 MHz). All signals are expressed as ppm downfield from tetramethylsilane used as an internal standard (ε value). The following abbreviations are used: singlet (s), doublet (d), triplet (t), multiplet (m), broad (br). Mass spectra were taken with a Shimadzu QP1000 GCMS spectrometer and a JEOL JMS-D300 mass spectrometer. Unless otherwise noted, all reactions were performed using anhydrous solvents. Merck Kieselgel 60 was used as an adsorbent for column chromatography.

***N*-{(2*RS*,5*SR*)-(2*E*,4*E*)-Tricarbonyliron[(η^4-2,5)-2,4-hexadienylidene]}*p*-methoxyphenylamine (2b)** A mixture of (2*RS*,5*SR*)-(2*E*,4*E*)-tricarbonyliron[(η^4-2,5)-2,4-hexadienal] (250 mg, 1.06 mmol), prepared according to the reported procedure,[8] *p*-anisidine (130 mg, 1.06 mmol), molecular sieves 3A (300 mg), and dry benzene (5 ml) was stirred at room temperature for 2 h. Concentration of the reaction mixture *in vacuo* gave the desired product (361 mg, 100%). **2b**: IR (KBr): 2029 (CO), 1952 (CO), 1618, 1508, 1273, 1244, 1038 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 7.62 (1H, d, J=7.6 Hz, ArN=CH), 7.03 (2H, d, J=9.0 Hz, Ar-H), 6.86 (2H, d, J=9.0 Hz, Ar-H), 5.69 (1H, dd, J=8.4, 4.9 Hz, C3-H), 5.23 (1H, dd, J=9.0, 4.9 Hz, C4-H), 3.80 (3H, s, OMe), 1.79 (1H, dd, J=8.4, 7.6 Hz, C2-H), 1.59 (1H, m, C5-H), 1.49 (3H, d, J=6.0 Hz, C5-Me). MS *m/z*: 341 (M^+, 1.0), 313 (52), 200 (100).

***N*-{(2*RS*,5*SR*)-(2*E*,4*E*)-Tricarbonyliron[(η^4-2,5)-2,4-hexadienylidene]}benzylamine (2a)** This compound was prepared in quantitative yield (960 mg) from **1** (697 mg, 2.95 mmol) and benzylamine (121 mg, 2.95 mmol) by the same procedure as described for the preparation of **2b**. **2a**: IR (KBr): 3030—2830, 2044 (CO), 1971 (CO), 1639, 1495, 1030 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 7.49 (1H, d, J=7.7 Hz, BnN=CH), 7.21—7.36 (5H, m, Ph), 5.55 (1H, dd, J=8.4 and 4.8 Hz, C3-H), 5.17 (1H, dd, J=7.4 and 4.8 Hz, C4-H), 4.52 (2H, s, PhC$\underline{H}_2$), 1.67 (1H, dd, J=8.4, 7.7 Hz, C2-H), 1.50—1.40 (4H, m, C5-H and C5-Me). MS *m/z*: 325 (M^+, 0.2), 298 (12), 269 (99), 241 (100).

***N*-{(2*RS*,5*SR*)-(2*E*,4*E*)-Tricarbonyliron[(η^4-2,5)-2,4-hexadienylidene]}phenylamine (2c)** This compound was prepared in quantitative yield (405 mg) from **1** (307 mg, 1.30 mmol) and aniline (121 mg, 1.30 mmol) by the same procedure as described for the preparation of **2b**. **2c**: IR (KBr): 2044 (CO), 1978 (CO), 1618, 1589 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 7.62 (1H, d, J=7.4 Hz, ArN=CH), 7.26—7.32 (3H, m, Ph), 7.03 (2H, d, J=8.4 Hz, Ph), 5.72 (1H, dd, J=8.4 and 5.0 Hz, C3-H), 5.25 (1H, dd, J=8.4, 5.0 Hz, C4-H), 1.77 (1H, dd, J=8.4, 7.4 Hz, C2-H), 1.62 (1H, m, C5-H), 1.50 (3H, d, J=5.8 Hz, C5-Me). MS *m/z*: 311 (M^+, 1.5), 255 (73), 170 (100).

***N*-{(2*RS*,5*SR*)-(2*E*,4*E*)-Tricarbonyliron[(η^4-2,5)-2,4-hexadienylidene]}*p*-chlorophenylamine (2d)** A mixture of **1** (291 mg, 1.23 mmol), *p*-chloroaniline (157 mg, 1.23 mmol), molecular sieves 3A (350 mg), and dry benzene (5 ml) was refluxed for 12 h. The reaction mixture was filtered through a pad of Celite, and concentration of the filtrate *in vacuo* gave the desired product **2d** (425 mg, 100%). **2d**: IR (KBr): 2048 (CO), 1979 (CO), 1618, 1489, 1463, 1151, 1091 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz)

δ: 7.60 (1H, d, J=7.1 Hz, ArN=CH), 7.27 (2H, d, J=8.3 Hz, Ar), 6.95 (2H, d, J=8.3 Hz, Ar), 5.73 (1H, dd, J=8.6, 4.9 Hz, C3-H), 5.26 (1H, dd, J=8.6, 5.1 Hz, C4-H), 1.72 (1H, m, C2-H), 1.61 (1H, m, C5-H), 1.50 (3H, d, J=6.0 Hz, C5-Me). MS m/z: 345 (M^+, 0.7), 317 (10), 261 (100).

(6*RS*,1′*SR*,4′*RS*)-(1′*E*,3′*E*)-Tricarbonyliron[2,3-didehydro-1-*p*-methoxyphenyl-6-(η⁴-1′,4′)-1′,3′-pentadienylpiperidin-4-one] (3b) and (6*RS*,1′*RS*,4′*SR*)-(1′*E*,3′*E*)-Tricarbonyliron[2,3-didehydro-1-*p*-methoxyphenyl-6-(η⁴-1′,4′)-1′,3′-pentadienylpiperidin-4-one] (4b) Experimental procedures for Table 1, runs 3, 5, and 9 will be described as representative examples: a) Run 3, [$AlCl_3$–CH_2Cl_2]: Danishefsky's diene (39.4 mg, 0.229 mmol) was added to a solution of the imine **2b** (26.0 mg, 0.0762 mmol) and $AlCl_3$ (11.1 mg, 0.0838 mmol) in CH_2Cl_2 (2 ml) at −78 °C and the resulting solution was stirred at −78 °C for 3 h and then allowed to warm slowly to −30 °C over an additional 3 h. The reaction was quenched with aqueous $NaHCO_3$ solution, and the mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried over anhydrous $MgSO_4$, then concentrated *in vacuo*. The residue was chromatographed (hexane : AcOEt = 1 : 1) to give **4b** (4.7 mg, 15%) and **3b** (17.9 mg, 57%).

b) Run 5, [TMSOTf–CH_2Cl_2]: Danishefsky's diene (33.3 mg, 0.193 mmol) was added to a solution of the imine **2b** (33.0 mg, 0.0967 mmol) and TMSOTf (23.6 mg, 0.106 mmol) in CH_2Cl_2 (2 ml) at −78 °C and the resulting solution was stirred at −78 °C for 3 h and then allowed to warm slowly to −30 °C over an additional 5 h. The reaction was quenched with aqueous $NaHCO_3$ solution, and the mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried over anhydrous $MgSO_4$, then concentrated *in vacuo*. The residue was chromatographed (hexane : AcOEt = 1 : 1) to give **4b** (3.8 mg, 10%) and **3b** (26.7 mg, 67%).

c) Run 9, [$LiClO_4$–CH_2Cl_2]: Lithium perchlorate (1.6 mg, 0.0150 mmol) was added to a solution of the imine **2b** (25.6 mg, 0.0752 mmol) and Danishefsky's diene (40.2 mg, 0.233 mmol) in CH_2Cl_2 (1 ml) at room temperature and the resulting suspension was stirred at room temperature for 8 h. The reaction was quenched with aqueous $NaHCO_3$ solution, and the mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried over anhydrous $MgSO_4$, then concentrated *in vacuo*. The residue was chromatographed (hexane : AcOEt = 1 : 1) to give **3b** as a sole product (28.6 mg, 93%). **3b**: yellow crystals, mp 170.0 °C (AcOEt). *Anal.* Calcd for $C_{20}H_{19}FeNO_5$: C, 58.70; H, 4.68; N, 3.42. Found: C, 58.78; H, 4.77; N, 3.34. IR (KBr): 2040 (CO), 1965 (CO), 1643 (C=O), 1579, 1510, 1247, 1036 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 7.30 (1H, dd, J=7.7, 1.7 Hz, C2-H), 7.17 (2H, m, Ar-2″H), 6.95 (2H, m, Ar-3″H), 5.12 (1H, d, J=7.7 Hz, C3-H), 5.07 (2H, m, C2′-H and C3′-H), 4.08 (1H, br dd, J=6.8, 6.0 Hz, C6-H), 3.84 (3H, s, OMe), 3.08 (1H, dd, J=16.2, 6.0 Hz, C5-H), 2.58 (1H, br d, J=16.2 Hz, C5-H), 1.36 (3H, d, J=6.8 Hz, C4′-Me), 1.24 (1H, dd, J=7.7, 6.8 Hz, C1′-H), 1.09 (1H, dq, J=8.6, 6.8 Hz, C4′-H). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ: 211.5 (CO), 190.2 (C4), 157.4 (Ar-4″C), 148.8 (Ar-1″C), 137.2 (Ar-2″C), 123.0 (Ar-3″C), 114.8 (C2), 100.1 (C3), 85.8 (C3′), 80.5 (C2′), 61.4 (C6), 58.8 (C1′), 56.9 (C4′), 55.5 (OMe), 42.5 (C5), 18.8 (C4′-Me). MS m/z: 409 (M^+, 0.1), 382 (1.8), 354 (19.1), 326 (100). **4b**: yellow crystals, mp 123.5 °C (AcOEt). *Anal.* Calcd for $C_{20}H_{19}FeNO_5$: C, 58.70; H, 4.68; N, 3.42. Found: C, 58.49; H, 4.77; N, 3.46. IR (KBr): 2042 (CO), 1974 (CO), 1645 (C=O), 1579, 1510, 1325, 1282, 1248, 1200, 1180 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 7.10 (1H, d, J=7.7 Hz, C2-H), 7.08 and 6.95 (each 2H, m, Ar-2″ and 3″H), 5.11 (1H, d, J=7.7 Hz, C3-H), 4.81 (1H, dd, J=8.6, 4.3 Hz, C2′-H), 4.42 (1H, dd, J=8.6, 4.3 Hz, C3′-H), 3.86 (3H, s, OMe), 3.61 (1H, ddd, J=10.3, 6.8, 3.4 Hz, C6-H), 3.09 (1H, dd, J=16.2, 6.8 Hz, C5-H), 2.66 (1H, dd, J=16.2, 3.4 Hz, C5-H), 1.36 (3H, d, J=6.0 Hz, C4′-Me), 1.29 (1H, dd, J=10.3, 8.6 Hz, C1′-H), 1.22 (1H, dq, J=8.6, 6.0 Hz, C4′-H). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ: 210.8 (CO), 190.5 (C4), 158.2 (Ar-4″C), 149.9 (Ar-1″C), 137.6 (Ar-2″C), 126.2 (Ar-3″C), 114.9 (C2), 100.0 (C3), 86.0 (C3′), 82.0 (C2′), 64.6 (C6), 59.0 (C1′), 56.5 (C4′), 55.5 (OMe), 43.6 (C5), 18.9 (C4′-Me). MS m/z: 409 (M^+, 1.4), 381 (11.1), 353 (57.2), 325 (100), 257 (22).

(6*RS*,1′*SR*,4′*RS*)-(1′*E*,3′*E*)-Tricarbonyliron[2,3-didehydro-1-benzyl-6-(η⁴-1′,4′)-1′,3′-pentadienylpiperidin-4-one] (3a) By the same procedure as described for the preparation of **2b** in run 9, **3a** were prepared in 35% (17.2 mg) yield, starting from the imine **2a** (41.0 mg, 0.126 mmol), Danishefsky's diene (65.1 mg, 0.378 mmol), and $LiClO_4$ (2.7 mg, 0.021 mmol). **3a**: a yellow oil. IR (KBr): 2038 (CO), 1971 (CO), 1641 (C=O), 1583, 1209, 1160 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 7.28—8.39 (5H, m, Ph), 7.09 (1H, d, J=7.1 Hz, C2-H), 4.93—5.14 (3H, m, C3-H, C2′-H and C3′-H), 4.62 (1H, d, J=15.4 Hz, PhCH_2), 4.52 (1H, d, J=15.4 Hz, PhCH_2), 3.24 (1H, dd, J=8.1, 6.6 Hz, C6-H), 2.83 (1H, dd, J=16.5, 6.6 Hz, C5-H), 2.33 (1H, d, J=16.5 Hz, C5-H), 1.42 (3H, d, J=6.0 Hz, C4′-Me), 1.25—1.39 (2H, m, C1′-H and C4′-H). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ: 212.0 (CO), 189.5 (C4), 152.1 (Ph-1″C), 136.8 (Ph), 129.0 (Ph), 128.3 (Ph), 127.2 (C2), 98.0 (C3), 86.1 (C3′), 80.8 (C2′), 59.5 (C6), 59.0 (C1′), 57.7 (Ph-C), 56.9 (C4′), 43.8 (C5), 19.0 (C4′-Me). MS m/z: 393 (M^+, 1.0), 365 (7.7), 337 (30), 309 (100).

(6*RS*,1′*SR*,4′*RS*)-(1′*E*,3′*E*)-Tricarbonyliron[2,3-didehydro-1-phenyl-6-(η⁴-1′,4′)-1′,3′-pentadienylpiperidin-4-one] (3c) and (6*RS*,1′*RS*,4′*SR*)-(1′*E*,3′*E*)-Tricarbonyliron[2,3-didehydro-1-phenyl-6-(η⁴-1′,4′)-1′,3′-pentadienylpiperidin-4-one] (4c) By the same procedure as described for the preparation of **2b** in run 9, **4c** and **3c** were prepared in 8.8% (6.3 mg) and 83% (59.3 mg) yield, respectively, starting from the imine **2c** (58.7 mg, 0.189 mmol), Danishefsky's diene (97.4 mg, 0.566 mmol), and $LiClO_4$ (4.0 mg, 0.0376 mmol). **3c**: yellow crystals, mp 117.5 °C (EtOH). *Anal.* Calcd for $C_{19}H_{17}FeNO_4$: C, 60.18; H, 4.52; N, 3.69. Found: C, 60.16; H, 4.52; N, 3.72. IR (KBr): 2042 (CO), 1967 (CO), 1649 (C=O), 1579, 1495, 1340, 1215 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 7.43 (2H, dd, J=7.7, 7.7 Hz, Ph-2″H), 7.40 (1H, d, J=7.7 Hz, C2-H), 7.23 (2H, d, J=7.7 Hz, Ph-3″H), 7.22 (1H, dd, J=7.7, 7.7 Hz, Ph-4″H), 5.20 (1H, d, J=7.7 Hz, C3-H), 5.15 (1H, dd, J=8.5, 5.1 Hz, C2′-H), 5.06 (1H, dd, J=8.5, 5.1 Hz, C3′-H), 4.24 (1H, dd, J=6.0, 6.0 Hz, C6-H), 3.06 (1H, dd, J=16.3, 6.0 Hz, C5-H), 2.61 (1H, d, J=16.3 Hz, C5-H), 1.36 (3H, d, J=6.0 Hz, C4′-Me), 1.18 (1H, dd, J=8.5, 6.0 Hz, C1′-H), 1.10 (1H, dq, J=8.5, 6.0 Hz, C4′-H). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ: 211.4 (CO), 190.5 (C4), 147.4 (Ph), 143.5 (Ph), 129.6 (Ph), 125.0 (Ph), 120.3 (C2), 101.2 (C3), 85.5 (C3′), 80.5 (C2′), 60.3 (C6), 58.7 (C1′), 57.1 (C4′), 41.6 (C5), 18.7 (C4′-Me). MS m/z: 379 (M^+, 2.0), 351 (20), 323 (100), 295 (100), 239 (14), 227 (29). **4c**: yellow crystals, mp 117.0 °C (EtOH). *Anal.* Calcd for $C_{19}H_{17}FeNO_4$: C, 60.18; H, 4.52; N, 3.69. Found: C, 60.00; H, 4.69; N, 3.73. IR (KBr): 2042 (CO), 1980 (CO), 1957 (CO), 1645 (C=O), 1578, 1495, 1259, 1201 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 7.45 (2H, dd, J=7.7, 7.7 Hz, Ph-2″H), 7.30 (1H, dd, J=7.7, 7.7 Hz, Ph-4″H), 7.20 (1H, d, J=7.7 Hz, C2-H), 7.16 (2H, d, J=7.7 Hz, Ph-3″H), 5.17 (1H, d, J=7.7 Hz, C3-H), 4.80 and 4.48 (each 1H, dd, J=8.5, 5.1 Hz, C2′-H and C3′-H), 3.79 (1H, ddd, J=9.4, 6.8, 2.6 Hz, C6-H), 3.12 (1H, dd, J=16.2, 6.8 Hz, C5-H), 2.67 (1H, dd, J=16.2, 2.6 Hz, C5-H), 1.35 (3H, d, J=6.0 Hz, C4′-Me), 1.35 (1H, dd, J=9.4, 8.5 Hz, C1′-H), 1.22 (1H, dq, J=8.5, 6.0 Hz, C4′-H). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ: 210.7 (CO), 190.5 (C4), 148.5 (Ph), 144.5 (Ph), 129.9 (Ph), 126.3 (Ph), 123.9 (C2), 100.9 (C3), 86.1 (C3′), 81.7 (C2′), 63.8 (C6), 59.1 (C1′), 56.4 (C4′), 43.5 (C5), 18.9 (C4′-Me). MS m/z: 379 (M^+, 1.7), 351 (16), 323 (76), 295 (100), 239 (12).

(6*RS*,1′*SR*,4′*RS*)-(1′*E*,3′*E*)-Tricarbonyliron[2,3-didehydro-1-*p*-chlorophenyl-6-(η⁴-1′,4′)-1′,3′-pentadienylpiperidin-4-one] (3d) and (6*RS*,1′*RS*,4′*SR*)-(1′*E*,3′*E*)-Tricarbonyliron[2,3-didehydro-1-*p*-chlorophenyl-6-(η⁴-1′,4′)-1′,3′-pentadienylpiperidin-4-one] (4d) By the same procedure as described for the preparation of **2b** in run 9, **4d** and **3d** were prepared in 8.8% (5.1 mg) and 73% (42.5 mg) yield, respectively, starting from the imine **2d** (48.4 mg, 0.40 mmol), Danishefsky's diene (72.4 mg, 0.420 mmol), and $LiClO_4$ (3.0 mg, 0.0280 mmol). **3d**: yellow crystals, mp 162.0 °C (EtOH). *Anal.* Calcd for $C_{19}H_{16}ClFeNO_4$: C, 55.17; H, 3.90; Cl, 8.57; N, 3.39. Found: C, 55.16; H, 4.02; Cl, 8.30; N, 3.32. IR (KBr): 2042 (CO), 1969 (CO), 1651 (C=O), 1599, 1581, 1576, 1495, 1321, 1296, 1213, 1198, 1086 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 7.40 (2H, d, J=8.6 Hz, Ar-2″H), 7.33 (1H, d, J=7.7 Hz, C2-H), 7.16 (2H, d, J=8.6 Hz, Ar-3″H), 5.20 (1H, d, J=7.7 Hz, C3-H), 5.13 and 5.07 (each 1H, dd, J=8.6, 5.1 Hz, C2′-H and C3′-H), 4.17 (1H, dd, J=6.0, 5.1 Hz, C6-H), 3.05 (1H, dd, J=16.2, 6.0 Hz, C5-H), 2.61 (1H, d, J=16.2 Hz, C5-H), 1.37 (3H, d, J=6.0 Hz, C4′-Me), 1.06—1.16 (2H, m, C1′-H and C4′-H). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ: 211.4 (CO), 190.5 (C4), 147.1 (Ar-1″C), 142.2 (Ar-4″C), 129.9 (Ar-2″C), 129.7 (Ar-3″C), 121.8 (C2), 101.8 (C3), 85.7 (C3′), 80.5 (C2′), 60.7 (C6), 59.0 (C1′), 56.7 (C4′), 42.0 (C5), 18.8 (C4′-Me). MS m/z: 413 (M^+, 1.5), 387 (5.1), 385 (15.1), 359 (22), 357 (66), 331 (80), 329 (100), 261 (19.1). **4d**: yellow crystals, mp 190.5 °C (EtOH). *Anal.* Calcd for $C_{19}H_{16}ClFeNO_4$: C, 55.17; H, 3.90; Cl, 8.57; N, 3.39. Found: C, 55.18; H, 4.01; Cl, 8.56; N, 3.34. IR (KBr): 2044 (CO), 1977 (CO), 1971 (CO), 1653 (C=O), 1597, 1583, 1493, 1261, 1200 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 7.42 (2H, d, J=8.6 Hz, Ar-2″H), 7.13 (1H, d, J=8.6 Hz, C2-H), 7.12 (2H, d, J=8.6 Hz, Ar-3″H), 5.19 (1H, d, J=8.6 Hz, C3-H), 4.83 (1H, dd, J=8.6, 5.1 Hz, C2′-H), 4.49 (1H, dd, J=8.6, 5.1 Hz, C3′-H), 3.73 (1H, ddd, J=9.4, 6.0, 3.4 Hz, C6-H), 3.10 (1H, dd, J=16.2 and 6.0 Hz, C5-H), 2.67 (1H, dd, J=16.2 and

3.4 Hz, C5-H), 1.36 (3H, d, J=6.0 Hz, C4′-Me), 1.29 (1H, dd, J=9.4, 8.6 Hz, C1′-H), 1.23 (1H, dq, J=8.6, 6.0 Hz, C4′-H). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ: 214.7 (CO), 190.6 (C4), 148.6 (Ar-1″C), 144.5 (Ar-4″C), 129.9 (Ar-2″C), 126.3 (Ar-3″C), 123.9 (C2), 101.0 (C3), 86.1 (C3′), 81.7 (C2′), 63.9 (C6), 59.1 (C1′), 56.4 (C4′), 43.5 (C5), 18.9 (C4′-Me). MS m/z: 413 (M^+, 0.6), 387 (1.8), 385 (5.7), 359 (8.8), 357 (25.4), 331 (34), 329 (100), 261 (8.0).

X-Ray Analysis of 3b A crystal was mounted on a Rigaku AFC-5R diffractometer, and the cell parameters and the intensity data were measured with graphite-monochromated Mo K_α (λ=0.71069 Å) radiation at 18 °C. The iron atomic coordinates were obtained by the heavy atom isomorphous replacement method and the other atomic coordinates were obtained by successive Fourier transforms with the phases of the iron atom.[16] The parameters of non-hydrogen atoms were refined by the block-diagonal least-squares method with anisotropic temperature factors.[17] The hydrogen atoms were located from a difference Fourier synthesis, and refined with isotropic temperature factors. Chemical formula $C_{20}H_{18}FeNO_5$; M.W. 408.214; monoclinic; space group $P2_{1/C}$; Z=4; unit cell dimensions a=13.371(5) Å, b=11.475(3) Å, c=12.365(3) Å, β=92.2(3)°, V=1895.8(9) Å^3, $D_{cal.}$=1.4303 gcm^{-3}; μ(Mo K_α)=66.58 mm^{-1}; crystal size 0.5×0.4×0.6 mm. Of the total of 7069 reflections up to the 2θ range of 2°—60°, 6851 independent reflections were measured and the absorption correction was applied for all reflections whose χ-angle was 90°.[18] The structure was refined with 3579 reflections which were above the 3σ (I) level. The final R value was 0.0787.

Acknowledgments This work was supported by a Grant-in-Aid for Scientific Research on Priority Area of Reactive Organometallics No.05236101 from the Ministry of Education, Science and Culture, Japan and also by a grant from Takeda Chemical Industries, Ltd. Foundation. We are grateful to Professor Yukiteru Katsube for advice on X-ray crystallographic analysis.

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