Stereospecific 1,3-Migration of an $Fe(CO)_3$ Group on Acyclic Conjugated Polyenes: Application to Remote and Iterative Asymmetric Induction

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The stereochemical outcome of the 1,3- and 1,5-migration of an $Fe(CO)_3$ group on (acyclic polyene)-$Fe(CO)_3$ complexes and their application to stereoselective construction of remote and contiguous stereogenic centers are described. Treatment of the [(η^4-4−7)triene]$Fe(CO)_3$ complexes **1a**−**d** bearing an electron-withdrawing group on the terminal position of an uncomplexed olefin with a base such as $KN(SiMe_3)_2$ (KHMDS) and $LiCH_2CN$ induced the 1,3-migration reaction of the $Fe(CO)_3$ group, giving the [(η^4-2−5)triene]$Fe(CO)_3$ complexes **2a**−**d** in moderate to good yields, depending on the electron-withdrawing groups. From an experiment using the chiral (trienenitril)$Fe(CO)_3$ complex **5**, it is revealed that the 1,3-migration proceeds with inversion of configuration. Similarly, the 1,5-migration reaction of the[(η^4-6−9)tetraenone]$Fe(CO)_3$ complexes **9** occurred with a catalytic amount of KHMDS, giving the [(η^4-2−5)tetraenone]$Fe(CO)_3$ complexes **10** with retention of configuration. Furthermore, we have succeeded in the first regio- and stereoselective nucleophilic substitution of the (3,5-diene-1,2-diol) $Fe(CO)_3$ complexes (**15** → **24a**−**h**) with various nucleophiles via the ortho esters **21**. By using iterative manipulation of the above two reactions, remote stereocontrol of the terminal substituents on acyclic polyene (**9** → **12**) and construction of contiguous stereogenic centers (**19**, **28**) have been achieved.

Introduction

Coordination of 1,3-dienes to an $Fe(CO)_3$ group moderates the reactivity of the unsaturated system to some nucleophilic and electrophilic reactions and also influences the reactivity of functional groups attached to the diene system in terms of chemo- and stereoselectivity.[1] Thus far, extensive research has been undertaken to construct stereogenic centers adjacent to the (diene)Fe-$(CO)_3$ group[2,3] as well as to theoretically understand the factors governing the diastereoselectivity of the reactions.[4] Although the $Fe(CO)_3$ group is a very efficient chiral auxiliary for 1,2- and 1,3-asymmetric induction (AI), there are few examples that have achieved remote asymmetric induction[5] of higher than 1,4-AI. To overcome this drawback, several ingenious methods such as the Mukaiyama−aldol reaction of a silyl enol ether of a π-allytricarbonyliron lactone complex[6a] and stereodefined hydroxyl group-mediated alkylation with an organotitanium reagent,[6b] have been developed. As an extension of the 1,2-migration of the $Fe(CO)_3$ group, which has been

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(1) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987. *Transition Metals in Total Synthesis*; Harrington, P. J., Ed.; John Wiley & Sons: New York, 1990. Pearson, A. J. *Iron Compounds in Organic Synthesis*; Academic Press: London, 1994.

(2) Grée, R. *Synthesis* **1989**, 341−355. Grée, R.; Lellouche, J. P. In *Advances in Metal-Organic Chemistry*; Liebeskind. L. S., Ed.; JAI Press: Greenwich, CT, 1995; Vol. 4, pp 129−273. Iwata, C.; Takemoto, Y. *Chem. Commun*. **1996**, 2497−2504. Knölker, H.-J. *Chem. Soc. Rev*. **1999**, *28*, 151−157.

(3) 1,2-AI: Harvey, D. F.; Selchau, V. B. *J. Org. Chem*. **2000**, *65*, 2282−2286. Roush, W. R.; Works, A. B. *Tetrahedron Lett*. **1997**, *38*, 351−354. Wasicak, J. T.; Craig, R. A.; Henry, R.; Dasgupta, B.; Li, H.; Donaldson, W. A. *Tetrahedron* **1997**, *53*, 4185−4198. Takemoto, Y.; Takeuchi, J.; Matsu, E.; Iwata, C. *Chem. Pharm. Bull*. **1996**, *44*, 948−955. Takemoto, Y.; Takeuchi, J.; Morio, K.; Nakamoto, T.; Iwata, C. *Chem. Pharm. Bull*. **1996**, *44*, 940−947. Ripoche, I.; Gelas, J.; Grée, D.; Grée, R.; Troin, Y. *Tetrahedron Lett*. **1995**, *36*, 6675−6678. Wada, C. K.; Roush, W. R. *Tetrahedron Lett*. **1994**, *35*, 7351−7354. Tao, C.; Donaldson, W. A. *J. Org. Chem*. **1993**, *58*, 2134−2143. 1,3-AI: Frank-Neumann, M.; Geoffroy, P.; Gumery, F.; Bissinger, P. *Tetrahedron Lett*. **2000**, *41*, 4213−4217. Nakanishi, S.; Kumeta, K.; Sawai, Y.; Takata, T. *J. Organomet. Chem*. **1996**, *515*, 99−101. Marchand, N. J.; Grée, D. M.; Martelli, J. T.; Grée, R. L.; Toupet, L. J. *J. Org. Chem*. **1996**, *61*, 5063−5072. 1,4-AI: Franck-Neumann, M.; Colson, P.-J.; Geoffroy, P.; Taba, K. M. *Tetrahedron Lett*. **1992**, *33*, 1903−1906.

(4) González-Blanco, Ó.; Branchadell, V.; Grée, R. *Chem. Eur. J*. **1999**, *5*, 1722−1727 and references therein.

(5) Dorling, E. K.; Thomas, E. J. *Tetrahedron Lett*. **1999**, *40*, 471−474. Tamai, Y.; Hattori, T.; Date, M.; Koike, S.; Kamikubo, Y.; Akiyama, M.; Seino, K.; Takayama, H.; Oyama, T.; Miyano, S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1685−1694. Mitchell, H. J.; Nelson, A.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1899−1914. Sugiura, M.; Yagi, Y.; Wei, S.-Y.; Nakai, T. *Tetrahedron Lett*. **1998**, *39*, 4351−4354. Evans, D. A.; Coleman, P. J.; Côté, B. *J. Org. Chem*. **1997**, *62*, 788−789. Magnus, N.; Magnus, P. *Tetrahedron Lett*. **1997**, *38*, 3491−3494 and references therein.

(6) (a) Ley, S. V.; Cox, L. R. *Chem. Commun*. **1998**, 227−228. Ley, S. V.; Cox, L. R.; Middleton, B.; Worrall, J. M. *Chem. Commun*. **1998**, 1339−1340. Ley, S. V.; Cox, L. R.; Worrall, J. M. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3349−3354. (b) Bärmann, H.; Prahlad, V.; Tao, C.; Yun, Y. K.; Wang, Z.; Donaldson, W. A. *Tetrahedron* **2000**, *56*, 2283−2295. Bell, P. T.; Dasgupta, B.; Donaldson, W. A. *J. Organomet. Chem*. **1997**, *538*, 75−82.

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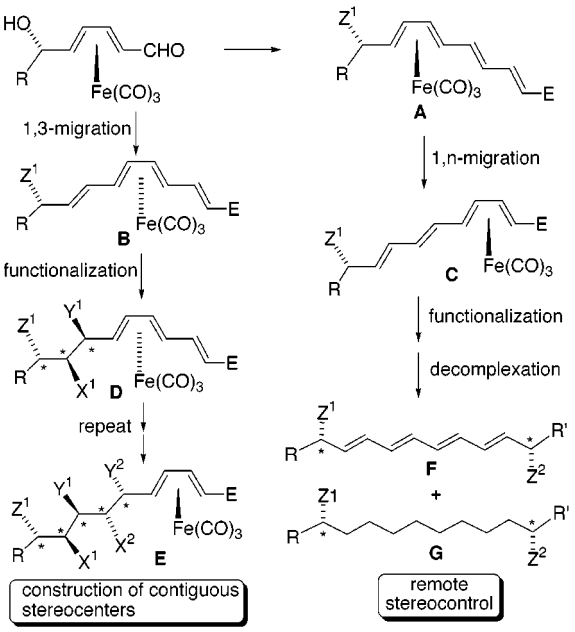
Scheme 1. Remote Stereocontrol Based on the 1,3-Migration Concept



already reported by us,[7] we are currently interested in applying a 1,3-migration[8−13] of the $Fe(CO)_3$ group on triene complexes. Our general strategy is shown in Scheme 1, which includes three main topics: (1) whether the 1,3-migration of the $Fe(CO)_3$ group on chiral polyene complexes proceeds in a stereospecific manner or not (**A** → **B** or **C**), (2) the stereoselective introduction of two functional groups on the uncomplexed olefin of the migrated products (**B** → **D** → **E**), and (3) remote stereocontrol of the terminal substituents on acyclic polyene (**C** → **F** or **G**). In this paper, we present a full account of our investigation into the stereospecific 1,3-migration of the $Fe(CO)_3$ group and the stereoselective construction of remote and contiguous stereogenic centers.[8]

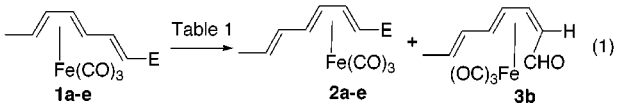
Results and Discussion

The 1,3-Migration of an $Fe(CO)_3$ Group on (Triene)$Fe(CO)_3$ Complexes and Determination of Their Stereochemistry. First, 1,3-migration of the racemic triene complexes **1a**,[9c] bearing an ester group, was investigated under several basic conditions (eq 1, Table 1). Although the ester complex **1a** was not transformed into the desired 1,3-migrated product **2a** under thermal[9] and Lewis-acidic[10] conditions, treatment of **1a** with 0.3 equiv of potassium bis(trimethylsilyl)amide (KHMDS) at 0 °C gave **2a** in 71% yield along with the recovered starting material (Table 1, entry 1). In the series of the amide bases, the potassium cation is crucial for the 1,3-migration reaction, because the corresponding lithium and sodium amide (LHMDS and NHMDS) were less effective under similar conditions (Table 1, entries 2 and 3). In addition, weaker bases such as sodium hydride[11] and *n*-Bu_4NF (TBAF) could be used in place of KHMDS, if the reaction was performed with an excess amount of the base or for a longer reaction time (Table 1, entries 4 and 5). We next examined the 1,3-migration reaction of **1b**−**e** bearing other electron-withdrawing substituents. Treatment of the aldehyde **1b**[12a] with 0.3 equiv of KHMDS afforded the migrated product **2b** in moderate yield (35%) due to the recovery of **1b** (31%) and generation of the (2*Z*)-aldehyde complex **3b** (4%) (Table 1, entry 6). On the other hand, the same reaction of the ketone **1c**[12a] proceeded smoothly, giving the desired product **2c** in a reasonable yield (Table 1, entry 7). In the case of the nitrile complex **1d**,[9c] the 1,3-migration with a catalytic amount of KHMDS was not effective, resulting in recovery of the starting material as an *E*- and *Z*-isomeric mixture in a ratio of 3:2 (Table 1, entry 8). To our surprise, subjection of **1d** to 2 equiv of $LiCH_2CN$ at 0 °C for 30 min led to exclusive formation of **2d** in 91% yield (Table 1, entry 9).[12,13] This result is in conflict with the previous report, which described that no 1,3-migration from **1d** to **2d** had been observed by the similar treatment.[12a] In contrast to **1a**−**d**, subjection of the benzylidene complex **1e** to $LiCH_2CN$ in THF (2 equiv, 0 °C) provided no migration product (Table 1, entry 10). Thus, we found that the 1,3-migration of the $Fe(CO)_3$ group on the triene complexes **1a**−**d** required the presence of strong electron-withdrawing groups on the conjugated polyene system and was induced by the bases such as KHMDS and $LiCH_2CN$. To clarify the driving

Table 1. 1,3-Migration of Conjugated Triene $Fe(CO)_3$ Complexes 1a−e[a]

			yield[b] (%)	
entry	substrate	reaction conditions	product	substrate
1	**1a**	$KN(SiMe_3)_2$ (0.3 equiv)	**2a** (71)	**1a** (25)
2		$NaN(SiMe_3)_2$ (0.2 equiv)	**2a** (9)	**1a** (75)
3		$LiN(SiMe_3)_2$ (0.9 equiv)	**2a** (2)	**1a** (89)
4		NaH (1.5 eq.), 1 h	**2a** (78)	**1a** (15)
5		*n*-Bu_4NF (0.3 equiv), 1 h	**2a** (43)	**1a** (46)
6	**1b**	$KN(SiMe_3)_2$ (0.3 equiv)	**2b**, **3b** (39)[c]	**1b** (31)
7	**1c**	$KN(SiMe_3)_2$ (0.3 equiv)	**2c** (56)	**1c** (9)
8	**1d**	$KN(SiMe_3)_2$ (0.3 equiv)	**2d** (13)[d]	**1d** (79)[d]
9		$LiCH_2CN$ (2 equiv)	**2d** (91)[d]	**1d** (trace)[d]
10	**1e**	$LiCH_2CN$ (2 equiv)	**2e** (trace)	**1e** (76)

[a] Reactions were performed in dry THF under a nitrogen atmosphere for 30 min. [b] Isolated yield, unless otherwise described. [c] Isolated as a mixture of (2*E*)- and (2*Z*)-adducts in a ratio of 35/4. [d] Calculated from the ^1H NMR spectra.



a: E = CO_2Et, **b**: E = CHO, **c**: E = $COCH_3$, **d**: E = CN, **e**: E = Ph

(7) Takemoto, Y.; Ishii, K.; Miwa, Y.; Taga, T.; Ibuka, T.; Nakao, S.; Tanaka, T. *Tetrahedron Lett.* **2000**, *41*, 85−88. Takemoto, Y.; Ishii, K.; Honda, A.; Okamoto, K.; Yanada, R.; Ibuka, T. *Chem. Commun.* **2000**, 1445−1446.

(8) Takemoto, Y.; Yoshikawa, N.; Baba, Y.; Iwata, C.; Tanaka, T.; Ibuka, T.; Ohishi, H. *J. Am. Chem. Soc.* **1999**, *121*, 9143−9154. Takemoto, Y.; Baba, Y.; Yoshikawa, N.; Iwata, C.; Tanaka, T. Ibuka, T. *Chem. Commun.* **1998**, 1911−1912. Takemoto, Y.; Yoshikawa, N.; Iwata, C. *J. Chem. Soc., Chem. Commun.* **1995**, 631−632. The similar 1,2-migration reaction of the $Fe(CO)_3$ group has been reported by the French group: Braun, A.; Toupet, L.; Lellouche, J.-P. *J. Org. Chem.* **1996**, *61*, 1914−1915.

(9) (a) Whitlock, H. W., Jr.; Markezich, R. L. *J. Am. Chem. Soc.* **1971**, *93*, 5290−5291. (b) Whitlock, H. W., Jr.; Reich, C.; Woessner, W. D. *J. Am. Chem. Soc.* **1971**, *93*, 2483−2492. (c) Goldschmidt, Z.; Bakal, Y. *J. Organomet. Chem.* **1984**, *269*, 191−200.

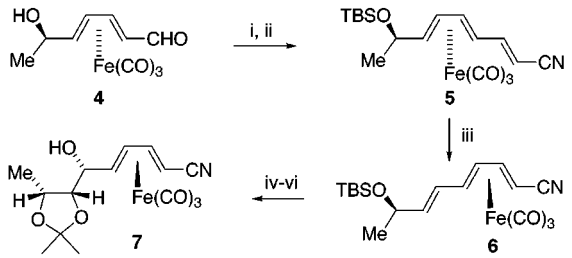
(10) Martina, D.; Brion, F. *Tetrahedron Lett.* **1982**, *23*, 865−868.

(11) Pinsard, P.; Lellouche, J.-P.; Beaucourt, J.-P.; Toupet, L.; Schio, L.; Grée, R. *J. Organomet. Chem.* **1989**, *371*, 219−231.

(12) (a) Hafner, A.; von Philipsborn, W.; Salzer, A. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 126−127. (b) Adams, C. M.; Cerioni, G.; Hafner, A.; Kalchhauser, H.; von Philipsborn, W.; Prewo, R.; Schwenk, A. *Helv. Chim. Acta* **1988**, *71*, 1116−1142.

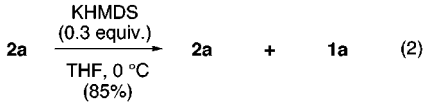
(13) Wada, A.; Fujioka, N.; Imai, H.; Shichida, Y.; Ito, M. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 423−426. Wada, A.; Hiraishi, S.; Takamura, N.; Date, T.; Aoe, K.; Ito, M. *J. Org. Chem.* **1997**, *62*, 4343−4348.

Scheme 2[a]



[a] Key: (i) TBSOTf, pyridine, 0 °C, 97%; (ii) $(EtO)_2P(O)CH_2CN$, NaH, THF, 0 °C, 84% [(*E*)-**5**/(*Z*)-**5**/**6** = 62/11/11); (iii) $LiCH_2CN$ (3 equiv), THF, 0 °C, 48% (100% based on the consumed starting material); (iv) OsO_4, pyridine, −20 °C; $NaHSO_3$, rt, 80% (β/α = 95/5); (v) HF·pyridine, 0 °C, 100%; (vi) $Me_2C(OMe)_2$, *p*-TsOH, MS 4A, benzene, acetone, rt, 24%.

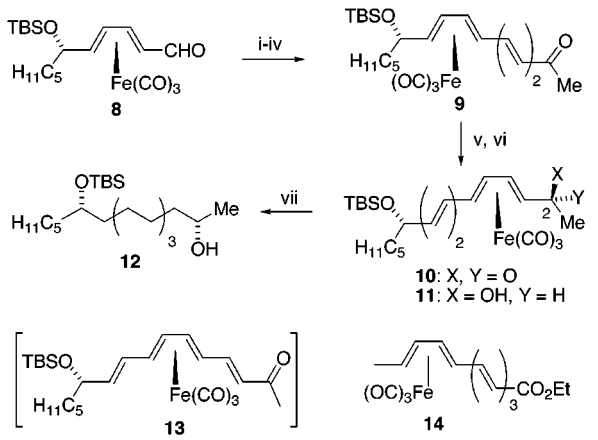
force of this 1,3-migration of the $Fe(CO)_3$ group, the migration product **2a** was subjected to the base-catalyzed conditions. The reaction of **2a** with a catalytic amount of KHMDS at 0 °C provided a mixture of **2a** and **1a** in a ratio of 6/1 (eq 2). The result indicates that the 1,3-migration of the (triene)$Fe(CO)_3$ complexes is an equilibrium reaction, and the thermodynamically more stable complex **2a** tends to be produced predominantly. The thermodynamic stability of **2a** would be attributed to the stronger d−π* orbital interaction (back-donation) between the iron atom and the complexed diene moiety.



Although the 1,3-migration of the $Fe(CO)_3$ group has been reported under several conditions,[9−13] stereochemical studies on the metal shift using chiral substrates were, to our knowledge, previously without example. We therefore examined the stereochemical behavior of the $Fe(CO)_3$ group in the 1,3-migration of the chiral nitrile complex **5**, which had been synthesized from the known compound **4**[14] in two steps (Scheme 2). The same treatment of **5** with $LiCH_2CN$ (3 equiv) as **1d** gave the migrated product **6** in 48% yield as a single diastereomer with **5** (52%). The 1,3-migration reaction of **5** always furnished the same product **6**, irrespective of the base employed [0.3 equiv of KHMDS (21%), 6.8 equiv of NaH (45%)], and a diastereomer of **6** could not be observed in all cases. The relative configuration of **6** was unambiguously determined by an X-ray crystallographic analysis (see Figure S1 in the Supporting Information) of **7**, which had been transformed from **6** in three steps. By comparing the stereochemistry of (4*S*,8*R*)-**5** with that of (2*R*,8*R*)-**6**, it is revealed that the $Fe(CO)_3$ group would migrate with inversion of configuration on the triene moiety. To clarify the role of $LiCH_2CN$, the reaction mixture of **5** and $LiCH_2CN$ in THF was quenched with CD_3OD and CH_3CO_2D, but no deuterated products of **6** were obtained. The mechanistic details have not been clarified at this stage, but from the results described above, reagents such as KHMDS and $LiCH_2CN$ possibly function as a nucleophile, but not a base.

(14) Takemoto, Y.; Baba, Y.; Noguchi, I.; Iwata, C. *Tetrahedron Lett.* **1996**, *37*, 3345−3348. Takemoto, Y.; Baba, Y.; Honda, A.; Nakao, S.; Noguchi, I.; Iwata, C.; Tanaka, T.; Ibuka, T. *Tetrahedron* **1998**, *54*, 15567−15580.

Scheme 3[a]



[a] Key: (i) $(EtO)_2P(O)CH_2CN$, NaH, THF, 0 °C (82%); (ii) DIBAL-H, −50 °C (75%); (iii) *n*-Bu_3P, CH_2Cl_2 (71%); (iv) $CH_3COCH_2P(O)(OMe)_2$, $LiOH·H_2O$, MeO H (72%); (v) $KN(SiMe_3)_2$, THF, 0 °C (70%); (vi) $NaBH_4$, MeOH (72%); (vii) H_2O_2, 1M NaOH; H_2, PtO_2 (89%).

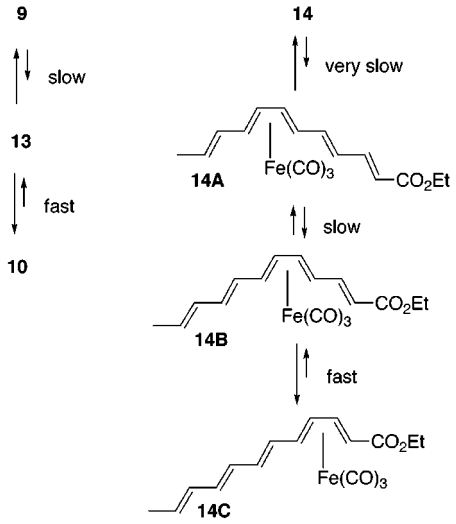
The 1,*n*-Migration of an $Fe(CO)_3$ Group on (Polyene)$Fe(CO)_3$ Complexes and Application to Remote Stereocontrol of Terminal Substituents on Acyclic Polyene. To extend the applicability of the 1,3-migration reaction to asymmetric synthesis, we next undertook the 1,*n*-migration (n = 5, 7) of the chiral (polyene)$Fe(CO)_3$ complexes **9**, prepared from **8**[14] as shown in Scheme 3. The key reaction in this case would be an iterative 1,3-migration reaction of the $Fe(CO)_3$ group (i.e., 1,5- and 1,7-migration). Then we investigated the migration reaction of **9** with several bases. Although we could not obtain the migration product by treatment of **9** with NaH and TBAF, the reaction of **9** with 0.3 equiv of KHMDS in THF at 0 °C provided the 1,5-migration product **10** in 70% yield. In the latter case, 1,3-migration product **13**, an intermediate of the 1,5-migration reaction, could not be observed in the crude reaction mixture. In contrast to **9**, the same treatment of the pentenoate complex **14** with KHMDS gave no migrated products, resulting in recovery of most of the starting material. We could not succeed in the migration of the $Fe(CO)_3$ group of **14** despite many experiments under various reaction conditions. The different behavior between **9** and **14** may be explained by the reaction rate of the second step in Scheme 4. Namely, in the former case, the isomerization of **9** into **13** may be slow but the following isomerization of **13** into **10** would be fast. Therefore, the 1,5-migration product **10** was produced in good yield. In contrast, in the latter case, both isomerization reactions of **14** → **14A** and **14A** → **14B** might be slow and consequently none of **14C** could be obtained.

Generally, the reduction of the (trienone)$Fe(CO)_3$ complexes such as **9** with sodium borohydride gave a nearly equimolar ratio of the two diastereomeric trienol complexes.[15] However, the reduction of the migrated product **10** provided the β-alcohol **11** as the single isomer in 72% yield.[16] Namely, the results demonstrate that the iterative 1,3-migration of the $Fe(CO)_3$ group can be applied

(15) Nunn, K.; Mosset, P.; Gree, R.; Saalfrank, R. W. *J. Org. Chem.* **1992**, *57*, 3359−3364. Franck-Neumann, M.; Colson, P.-J.; Geoffroy, P.; Taba, K. M. *Tetrahedron Lett.* **1992**, *33*, 1903−1906.

(16) Franck-Neumann, M.; Bissinger, P.; Geoffroy, P. *Tetrahedron Lett.* **1997**, *38*, 4473−4476. Clinton, N. A.; Lillya, C. P. *J. Am. Chem. Soc.* **1970**, *92*, 3058−3064.

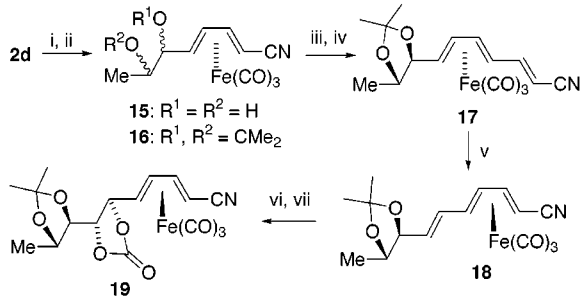
Scheme 4



to controlling remote stereogenic centers across conjugate polyenes. The stereochemistry of the C-2 of **11** was determined by the following chemical transformation (**11** → **12**) and the MTPA-ester method.[17] The desired *syn*-2,11-diol **12** was easily synthesized in 89% yield by reaction of **11** with 30% hydrogen peroxide in the presence of 1N NaOH solution and subsequent hydrogenation on platinum oxide in AcOEt. The absolute stereochemistry of the C-2 of **12** was revealed to be (*S*)-configuration by comparing the ^{1}H NMR spectra of their corresponding (*R*)- and (*S*)-MTPA esters. The above result and the stereochemical outcome[16] of the $NaBH_4$ reduction of the (dienone)$Fe(CO)_3$ complexes revealed that the 1,5-migration of the $Fe(CO)_3$ group should occur with retention of configuration as a result of a double inversion mechanism.

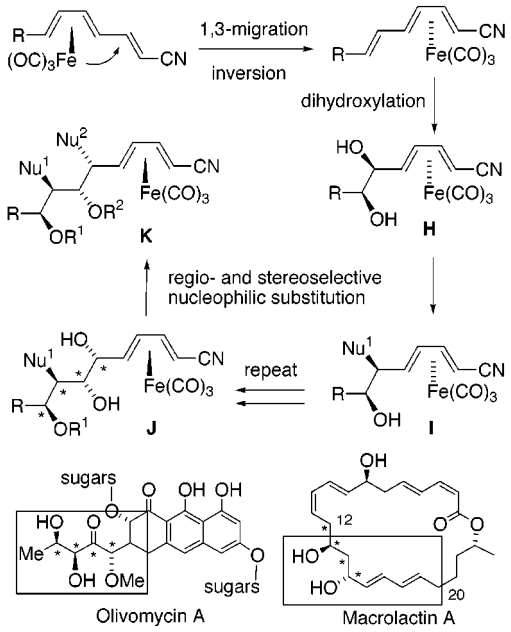
Regio- and Stereoselective Functionalization of Uncomplexed Olefin of the Migrated Products and Construction of Contiguous Chiral Centers Using Iterative 1,3-Migration of an $Fe(CO)_3$ Group. We finally investigated the stereoselective construction of contiguous stereogenic centers by the iterative 1,3-migration of the $Fe(CO)_3$ group. The nitrile **2d** was employed as the starting material for the purpose. As shown in Scheme 5, the diols **15** were synthesized stereoselectively as an inseparable mixture (anti/syn = 9/1) from **2d** by the OsO_4-mediated dihydroxylation.[18] After conversion of **15** into the acetonide **16** and separation of the two diastereomers, the α,*β*-unsaturated nitrile **17** was synthesized by the DIBAL-reduction and olefination of **16** in good yield. The second 1,3-migration of **17** proceeded smoothly with 2 equiv of $LiCH_2CN$ to give **18** in 65% yield. The OsO_4-mediated dihydroxylation of **18** occurred with high anti selectivity (anti/syn = 98/2), and the subsequent protection of the resulting diol gave rise to the 1,2-*syn*-2,3-*anti*-3,4-*syn*-tetraol derivative **19**, which could be converted into a side chain of olivomycin A (Scheme 6). The relative stereochemistry of **19** was unambiguously determined by an X-ray crystallographic analysis (see Figure S2 in the Supporting Information). It is important to note that 1,2-syn-2,3-anti-3,4-syn-

Scheme 5[a]



[a] Key: (i) OsO_4, pyridine, 0 °C; $NaHSO_3$, rt, 92% (*β*/α = 9/1); (ii) $Me_2C(OMe)_2$, *p*-TsOH, $CHCl_3$, 0 °C, 78%; (iii) DIBAL-H, toluene, −78 °C, 92%; (iv) $(EtO)_2P(O)CH_2CN$, NaH, THF, 0 °C, 79% (*E*/*Z* = 4.3/1); (v) $LiCH_2CN$, THF, −78 to 0 °C, 65%; (vi) OsO_4, pyridine, 0 °C; $NaHSO_3$, rt, 70% (*β*/α = 2/98); (vii) (imidazole)$_2$CO, benzene, rt, 82%.

Scheme 6. Asymmetric Synthesis of 1,3-Polyols Using 1,3-Migration of an $Fe(CO)_3$ Group



tetrasubstituted products such as **19** could be obtained by the iterative 1,3-migration procedure, while the same manipulation using 1,2-migration of the $Fe(CO)_3$ group previously reported by us, produced another diastereomer, 1,2-anti-2,3-anti-3,4-anti-tetrasubstituted one.[7]

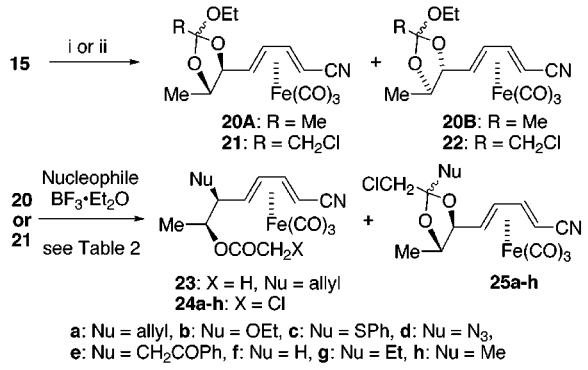
As an extension of the iterative 1,3-migration procedure, we next investigated the nucleophilic substitution of (dienediol)$Fe(CO)_3$ complexes (**H** → **I**) with various nucleophiles (Scheme 6). If the regio- and stereoselective transformation of **H** into **I** could be established, the 1,3-polyol derivatives **K** such as macrolactin A would be synthesized via **J** by an iterative manipulation of the three-step sequence (1,3-migration, dihydroxylation, and nucleophilic substitution). There are few reports concerning the nucleophilic substitution of the 1,2-diol derivatives,[6c] while numerous nucleophilic substitutions of mono-alcohol derivatives have been developed.[19] Initial substitution experiments were performed with di-

(17) Ohtani, I.; Kusumi, J.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092−4096. Yoshida, W. Y.; Bryan, P. J.; Baker, B. J.; McClintock, J. B. *J. Org. Chem.* **1995**, *60*, 780−782.

(18) Gigou, A.; Lellouche, J.-P.; Beaucourt, J.-P.; Toupet, L.; Grée, R. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 755−757.

(19) (a) Clinton, N. A.; Lillya, C. P. *J. Am. Chem. Soc.* **1970**, *92*, 3058−3064. (b) Uemura, M.; Minami, T.; Yamashita, Y.; Hiyoshi, K.; Hayashi, Y. *Tetrahedron Lett.* **1987**, *28*, 641−644. (c) Roush, W. R.; Wada, C. K. *Tetrahedron Lett.* **1994**, *35*, 7347−7350.

Scheme 7[a]



[a] Key: (i) $MeC(OEt)_3$, PPTS, CH_2Cl_2; (ii) $ClCH_2C(OEt)_3$, PPTS, CH_2Cl_2, **21** (80%), **22** (8.7%).

acetate[19a,b] and dichloroacetate,[19c] prepared from **15** under standard conditions (Scheme 7). Treatment of these diester complexes with allyltrimethylsilane and BF_3·Et_2O (2 equiv) in CH_2Cl_2 provided none of the allylation product and the starting material was recovered, respectively. The reaction with stronger Lewis acids such as $TiCl_4$ and TMSOTf at higher temperature resulted in the formation of decomplexed products. Suspecting that the electron-withdrawing nitrile substituent and the adjacent acyloxy group were interfering with the carbocation formation of diester $Fe(CO)_3$ complexes, we next examined the cyclic ortho ester derivatives **20A** and **21**, which were prepared from **15** and $CH_3C(OEt)_3$ or $ClCH_2C(OEt)_3$ in the presence of PPTS in CH_2Cl_2.[20] Although the former ortho esters **20A** and **20B** were used for the next reaction without any purification, the latter **21** could be purified by column chromatography and separated from the minor diastereomer **22**. The reaction of **20** with allyltrimethylsilane and BF_3·Et_2O (2 equiv) in CH_2Cl_2 at −78 °C was sluggish, but it proceeded more smoothly with warming to 0 °C and gave the desired product **23** in 42% yield along with unidentified products. In contrast to **20**, the same reaction of **21** as that of **20** proceeded smoothly even at −78 °C to provide the allylation product **24a** in good yield (77%) as the only diastereomer observed by 500 MHz ^1H NMR analysis of the crude reaction mixture. However, when allyltributylstannane was employed as a nucleophile, **24a** was obtained only in 34% yield together with the acetal **25a** as a major product (40%). The stereochemistry of **24a** was unambiguously established by an X-ray crystallographic analysis (see Figure S3 in the Supporting Information). It is evident that the substitution reaction of **21** proceeded with retention of configuration in the same manner as that of the (dienol)$Fe(CO)_3$ complexes, from the structure of **24a**.[19] The different reactivity between **20A** (X = H) and **21** (X = Cl) would be attributed to stability of their corresponding intermediates, the cyclic oxonium ion **L** and the η^5-(pentadienyl)iron(1+) cation **M** (Scheme 8). Namely, the chloride destabilizes the oxonium ion **L** (X = Cl) by a positive inductive effect and makes the η^5-(pentadienyl)iron(1+) cation **M** more predominant. Consequently, the desired product **24a** is obtained with high stereoselectivity. In addition, the ratio of **24**/**25** is also affected by the nucleophilicity of the nucleophiles such as allyltrimethylsilane and allyltributylstannane. When stronger nucleophiles are employed, the ratio of **24**/**2**5 tends to become lower, because the nucleophilic addition may complete before the conversion of **L** into **M** reaches an equilibrium state.

Scheme 8

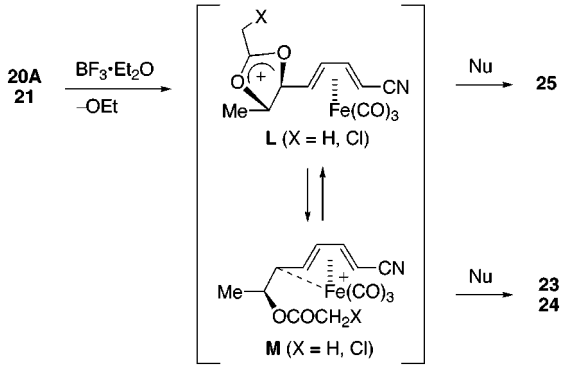


Table 2. Nucleophilic Substitution of 2-chloro-1-ethoxyethylidene Ortho Ester $Fe(CO)_3$ Complex 21[a]

			yield[b] (%)	
entry	Nu	reaction conditions	**24a**−**h**	**25a**−**h**
1	allyl	CH_2=$CHCH_2TMS$, CH_2Cl_2, −78 °C	**24a** (77)	**25a** (0)
2	EtO	EtOH, THF, rt	**24b** (93)	**25b** (0)
3	PhS	PhSH, THF, 0 °C	**24c** (89)	**25c** (0)
4	N_3	$TMSN_3$, THF, 0 °C	**24d** (83)	**25d** (0)
5	$PhCOCH_2$	CH_2=C(OTMS)Ph, CH_2Cl_2, −50 °C	**24e** (70)[c]	**25e** (8)[c]
6	H	Et_3SiH, CH_2Cl_2, −78 °C	**24f** (56)	**25f** (0)
7	Et	Et_3Al, CH_2Cl_2, −78 °C	**24g** (62)	**25g** (17)
8	Me	Me_2Zn, dioxane, 0°C	**24h** (38)[c]	**25h** (9)[c]

[a] Reactions were performed with 2 equiv of BF_3·Et_2O under a nitrogen atmosphere. [b] Isolated yield. [c] Calculated from the ^1H NMR spectra.

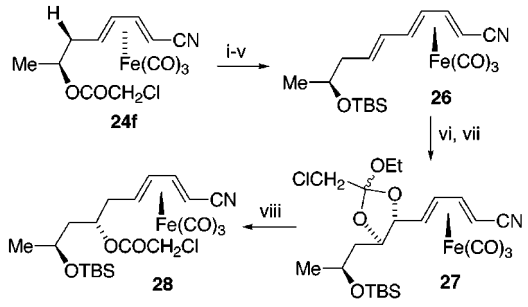
Furthermore, we undertook the nucleophilic substitution of **21** with other nucleophiles (Table 2). Treatment of **21** with ethanol (10 equiv) and BF_3·Et_2O (2 equiv) in THF at room temperature gave the ethyl ether **24b** in 93% yield (Table 2, entry 2). Similarly, the reactions of **21** with either thiophenol or trimethylsilyl azide at 0 °C provided **24c** and **24d**, as the only observed products in 83−89% yield (Table 2, entries 3 and 4). The silyl enol ether of methyl pheny ketone could be employed as a carbonic nucleophile for the substitution reaction, giving the alkylation product **24e** in 70% yield (Table 2, entry 5). The regioselective reduction with triethylsilane and alkylation with trialkylaluminum[19b] and dialkylzinc[21] were also promoted by BF_3·Et_2O, providing the corresponding products **24f**−**h** in moderate yields (Table 2, entries 6−8). The relative stereochemistry of **24b**−**h** was elucidated from the result of the X-ray analysis of **24a**.

To clarify the synthetic utility of this method, we finally examined the stereoselective synthesis of the 1,3-*anti*-diol **28** from **24f** by iterative manipulation (Scheme 9). The dihydroxylation and ortho esterification of the 1,3-migration product **26**, easily synthesized from **24f** in five steps, afforded the desired ortho ester **27** in 54% yield in

(20) Oku, A.; Numata, M. *J. Org. Chem*. **2000**, *65*, 1899−1906. Ohtake, H.; Ikegami, S. *Org. Lett.* **2000**, *2*, 457−460. Wifp, P.; Tsuchimoto, T.; Takahashi, H. *Pure Appl. Chem*. **1999**, *71*, 415−421. Wang, W.; Kong, F. *J. Org. Chem*. **1998**, *63*, 5744−5745. Kita, Y.; Yoshida, Y.; Mihara, S.; Furukawa, A.; Higuchi K.; Fang, D.-F.; Fujioka, H. *Tetrahedron* **1998**, *54*, 14689−14704.

(21) Almena Perea, J. J.; Ireland, T.; Knochel, P. *Tetrahedron Lett*. **1997**, *38*, 5961−5964.

Scheme 9[a]



[a] Key: (i) K_2CO_3, MeOH, 86%; (ii) TBSOTf, pyridine, 97%; (iii) DIBAL-H, toluene, 90%; (iv) $(EtO)_2P(O)CH_2CN$, NaH, THF, 86% (E/Z = 8/1); (v) $LiCH_2CN$, THF, 80%; (vi) OsO_4, pyridine; $NaHSO_3$, 81%; (vii) $ClCH_2C(OEt)_3$, PPTS, CH_2Cl_2, 67%; Et_3SiH, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 52%.

a 95/5 ratio. The reaction of **27** with triethylsilane in the presence of $BF_3{\cdot}$etherate proceeded smoothly to give the aimed 1,3-*anti*-diol **28** as the single isomer. Thus we have succeeded in the construction of the C12−C20 segment of macrolactin A (Scheme 6).

Conclusion

In conclusion, we have demonstrated the stereochemical outcome of the base-catalyzed 1,3- and 1,5-migration of the (polyene)$Fe(CO)_3$ complexes and succeeded in the first regio- and stereoselective substitution of the (3,5-diene-1,2-diol)$Fe(CO)_3$ complexes via the ortho esters. By using iterative manipulation of the above two reactions, we have also developed a novel remote and contiguous asymmetric induction method with the sole chiral auxiliary.

Experimental Section

Ethyl (2*SR*,5*RS*,2*E*,4*E*,6*E*)-Tricarbonyliron [(η^4-2−5)-Octa-2,4,6-trienoate] 2a (Table 1, Entry 1). A 0.5 M solution of $KN(TMS)_2$ in toluene (0.16 mL, 0.078 mmol) was added dropwise to a solution of **1a** (80.0 mg, 0.261 mmol) in dry THF (2 mL) at 0 °C under an argon atmosphere, and the mixture was stirred for 1 h. After being quenched with an aqueous NH_4Cl solution, the mixture was extracted with hexane/AcOEt (5:1). The extract was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, hexane/AcOEt = 10/1) to give **2a** (56.6 mg, 71%) and **1a** (20.0 mg, 25%). **(Table 1, Entry 2).** The same treatment of **1a** (20 mg, 0.065 mmol) with a 0.6 M solution of $NaN(TMS)_2$ in toluene (22 μL, 0.013 mmol) as described for the synthesis of **2a** (Table 1, entry 1) gave the crude mixture, which was purified by column chromatography (SiO_2, hexane/AcOEt = 10/1) to give **2a** (1.7 mg, 9%) and **1a** (15.0 mg, 75%). **(Table 1, Entry 3).** The same treatment of **1a** (20 mg, 0.065 mmol) with a 0.5 M solution of $LiN(TMS)_2$ in THF (0.118 mL, 0.0588 mmol) as described for the synthesis of **2a** (Table 1, entry 1) gave the crude mixture, which was purified by column chromatography (SiO_2, hexane/AcOEt = 10/1) to give **2a** (0.5 mg, <2%) and **1a** (17.8 mg, 89%). **(Table 1, Entry 4).** To a stirred solution of **1a** (100 mg, 0.327 mmol) in dry THF (1 mL) was added NaH (19.6 mg, 0.491 mmol) at 0 °C under an argon atmosphere, and the mixture was stirred at room temperature for 2 h. The reaction mixture was treated by the same procedure described above to give **2a** (77.8 mg, 78%) and **1a** (14.9 mg, 15%). **(Table 1, Entry 5).** To a stirred solution of **1a** (33.4 mg, 0.098 mmol) in dry THF (1 mL) was added TBAF (an 1.0 M solution in THF, 0.033 mL) at 0 °C under an argon atmosphere, and the mixture was stirred for 1 h. The reaction mixture was treated by the same procedure described above to give **2a** (14.3 mg, 43%) and **1a** (15.3 mg, 46%). **2a**: a yellow oil; IR (KBr) 2054, 1988, 1709 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14 (d, 1H, J = 7.9 Hz), 1.22 (t, 3H, J = 7.3 Hz), 1.64 (dd, 3H, J = 1.8, 6.7 Hz), 2.13 (dd, 1H, J = 9.2, 9.8 Hz), 4.09 (q, 2H, J = 7.3 Hz), 5.28 (dd, 1H, J = 5.5, 9.2 Hz), 5.46 (ddd, 1H, J = 1.2, 9.8, 15.0 Hz), 5.74 (ddd, 1H, J = 1.2, 5.5, 7.9 Hz), 5.75−5.82 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.5, 18.3, 45.7, 60.4, 64.6, 82.5, 84.1, 129.2, 131.6, 172.2, 210.2; MS (FAB) m/z 307 (MH^+, 48), 278 (34), 250 (78), 223 (44), 121 (100). Anal. Calcd for $C_{13}H_{14}FeO_5$: C, 51.01; H, 4.61. Found: C, 51.12; H, 4.66.

(4*S*,7*R*,8*R*,2*E*,4*E*,6*E*)-Tricarbonyliron [(η^4-4−7)-8-*tert*-Butyldimethylsilyloxy-2,4,6-nonatrienenitrile] (*E*)-5. To a stirred solution of **4** (1.1 g, 4.13 mmol) in pyridine (15 mL) was added TBSOTf (2.9 mL, 12.4 mmol) at 0 °C under a nitrogen atmosphere. After 1.5 h, brine was added to the reaction mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo, and pyridine was removed azeotropically with toluene. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 15/1) to gave TBS-ether (1.50 g, 97%) as yellow crystals: $[\alpha]^{27}_D$ +111 (c = 1.00, $CHCl_3$); IR (KBr) 1682, 1992, 2060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.87 (s, 9H), 1.33−1.35 (m, 1H), 1.34 (d, 3H, J = 6.1 Hz), 1.56−1.59 (m, 1H), 3.65 (dq, J = 6.1, 8.5 Hz, 1H), 5.39 (dd, 1H, J = 4.9, 8.5 Hz), 5.78 (dd, 1H, J = 4.9, 7.9 Hz), 9.30 (d, 1H, J = 4.3 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.2, −4.1, 18.0, 25.6, 25.8, 55.0, 70.0, 70.8, 82.2, 87.2, 196.0; MS (EI) m/z 352 (2.2), 296 (52), 240 (15), 147 (100). Anal. Calcd for $C_{16}H_{24}FeO_5Si$: C, 50.53; H, 6.36. Found: C, 50.76; H, 6.26.

To a suspension of NaH (10.0 mg, 0.251 mmol) in dry THF (1 mL) was added dropwise $(EtO)_2P(O)CH_2CN$ (0.041 mL, 0.251 mmol) at 0 °C under an argon atmosphere, and the mixture was stirred for 10 min at room temperature. To the resulting mixture was added slowly a solution of the TBS-ether (86.7 mg, 0.228 mmol) in dry THF (1 mL) at 0 °C, and the whole was stirred for 1 h. After being quenched with an aqueous NH_4Cl solution, the mixture was extracted with AcOEt. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, hexane/AcOEt = 20/1) to give (*E*)-**5** (57.0 mg, 62%), (*Z*)-**5** (10.4 mg, 11%), and **6** (10.2 mg, 11%). (*E*)-**5**: yellow crystals; $[\alpha]^{26}_D$ +122 (c = 1.01, $CHCl_3$); IR (KBr) 2214, 2052, 1990, 1612 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.06 (s, 3H), 0.07 (s, 3H), 0.86 (s, 9H), 1.32 (d, J = 6.1 Hz, 3H), 1.47 (dd, 1H, J = 8.5, 8.5 Hz), 1.61 (dd, J = 8.5, 10.5 Hz, 1H), 3.57 (dq, J = 6.1, 8.5 Hz, 1H), 5.22 (dd, 1H, J = 4.9, 8.5 Hz), 5.31 (d, 1H, J = 15.9 Hz), 5.34 (dd, J = 4.9, 8.5 Hz, 1H), 6.47 (dd, 1H, J = 10.4, 15.9 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.3, −4.2, 18.0, 25.6, 25.7, 55.8, 69.1, 71.0, 83.1, 85.2, 95.8, 118.0, 154.6, 209.9; MS (EI) m/z 375 (2.0), 348 (17), 320 (52), 187 (100). Anal. Calcd for $C_{18}H_{25}FeNO_4Si$: C, 53.60; H, 6.25; N, 3.47. Found: C, 53.70; H, 6.09; N, 3.40. (*Z*)-**5**: yellow crystals; $[\alpha]^{30}_D$ −715 (c = 0.95, $CHCl_3$); IR (KBr) 2214, 2052, 1971, 1597 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.07 (s, 6H), 0.87 (s, 9H), 1.35 (d, J = 6.1 Hz, 3H), 1.67 (dd, 1H, J = 5.5, 8.5 Hz), 2.04 (dd, J = 8.5, 10.4 Hz, 1H), 3.61 (dq, J = 6.1, 6.1 Hz, 1H), 5.09 (d, 1H, J = 11.0 Hz), 5.24 (dd, 1H, J = 5.5, 8.5 Hz), 5.35 (dd, J = 5.5, 8.5 Hz, 1H), 6.28 (dd, 1H, J = 10.4, 11.0 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.24, −4.15, 18.0, 25.6, 25.8, 54.2, 69.4, 71.1, 83.4, 85.5, 94.8, 116.5, 153.9, 209.9; MS (EI) m/z 375 (1.8), 319 (21), 187 (100). Anal. Calcd for $C_{18}H_{25}FeNO_4Si$: C, 53.60; H, 6.25; N, 3.47. Found: C, 53.73; H, 6.18; N, 3.45.

(2*R*,5*S*,6*S*,7*R*,8*R*,2*E*,4*E*)-Tricarbonyliron [(η^4-2−5)-Octa-6-hydroxy-7,8-*O*-isopropylidene-2,4-nonadienenitrile] 7. To a solution of **6** (171 mg, 0.430 mmol) in pyridine (1 mL) was added dropwise a solution of OsO_4 (200 mg, 0.787 mmol) in pyridine (2 mL) at −20 °C under argon atmosphere, and the whole was stirred for 30 min. The resulting mixture was quenched with a saturated $NaHSO_3$ solution at room temperature for 12 h. After being quenched with brine, the mixture was extracted twice with AcOEt. The extracts were washed with an aqueous NH_4Cl solution, water, and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude residue was

purified by column chromatography (SiO_2, hexane/AcOEt = 3/1) to give α-diol (142 mg, 80%) and *β*-diol (4.8 mg, 3%). α-Diol: yellow crystals; mp 145−147 °C (hexane/AcOEt); $[\alpha]^{24}_D$ −69.5 (*c* = 1.00, $CHCl_3$); IR (KBr) 3460, 2220, 2067, 2002 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.09 (s, 3H), 0.10 (s, 3H), 0.47 (d, 1H, *J* = 7.3 Hz), 0.87 (s, 9H), 1.19 (d, 3H, *J* = 6.7 Hz), 1.42 (dd, 1H, *J* = 7.3, 7.3 Hz), 2.51 (d, 1H, *J* = 9.8 Hz), 3.27 (d, 1H, *J* = 7.9 Hz), 3.63 (s, 1H), 3.89 (d, 1H, *J* = 6.1 Hz), 4.06−4.12 (m, 1H), 5.55−5.62 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) *δ* −5.1, −4.6, 17.8, 19.8, 24.3, 25.7, 63.9, 71.4, 72.9, 75.9, 82.1, 87.2, 121.3; MS (EI) *m*/*z* 381 (0.2), 353 (0.4), 131 (11), 75 (100). Anal. Calcd for $C_{18}H_{27}FeNO_6Si$: C, 49.43; H, 6.22; N, 3.20. Found: C, 49.43; H, 6.03; N, 3.14. *β*-Diol: a yellow oil; $[\alpha]^{30}_D$ −70.0 (*c* = 0.23, $CHCl_3$); IR (KBr) 3473, 2220, 2065, 1996 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.07 (s, 3H), 0.10 (s, 3H), 0.33 (d, 1H, *J* = 8.5 Hz), 0.87 (s, 9H), 1.21 (dd, 1H, *J* = 6.1, 9.2 Hz), 1.25 (d, 3H, *J* = 6.1 Hz), 2.63 (d, 1H, *J* = 7.9 Hz), 2.93 (d, 1H, *J* = 3.7 Hz), 3.17 (ddd, 1H, *J* = 3.1, 4.9, 7.9 Hz), 3.57 (m, 1H), 3.96 (dq, 1H, *J* = 3.1, 6.1 Hz), 5.46 (dd, 1H, *J* = 4.9, 9.2 Hz), 5.57 (dd, 1H, *J* = 4.9, 8.5 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) *δ* −4.8, −3.8, 17.9, 20.6, 23.7, 25.7, 65.3, 68.7, 72.4, 79.3, 81.4, 85.7, 121.4; MS (FAB) *m*/*z* 438 (MH^+, 28), 159 (55), 136 (57), 73 (100); HRMS (FAB) calcd $C_{18}H_{28}FeNO_6Si$ (MH^+) 438.1034, found 438.1040.

To a stirred solution of the α-diol (54.6 mg, 0.125 mmol) in THF (1 mL) was added HF·pyridine complex (20.7 M, 2.0 mL) at 0 °C under a nitrogen atmosphere. After 3 h, a saturated $NaHCO_3$ solution was added to the reaction mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 1/3) to give the triol (40.4 mg, 100%) as a yellow oil: $[\alpha]^{24}_D$ −91.0 (*c* = 0.76, $CHCl_3$); IR (KBr) 3311, 2222, 2064, 2000, 1977 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.48 (d, 1H, *J* = 7.5 Hz), 1.27 (d, 3H, *J* = 6.3 Hz), 1.42 (dd, 1H, *J* = 6.3, 8.7 Hz), 2.33 (s, 1H), 2.68 (s, 1H), 3.19 (s, 1H), 3.34 (s, 1H), 3.90 (d, 1H, *J* = 5.7 Hz), 4.00 (m, 1H), 5.58 (dd, 1H, *J* = 5.4, 8.7 Hz), 5.61 (dd, 1H, *J* = 5.4, 7.7 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) *δ* 19.5, 24.2, 63.7, 70.6, 71.5, 76.3, 82.1, 87.0, 121.3; MS (FAB) *m*/*z* 324 (MH^+, 4), 307 (51), 137 (86), 136 (100); HRMS (FAB) calcd $C_{12}H_{14}FeNO_6$ (MH^+) 324.0170, found 324.0168.

To a solution of the triol (15.0 mg, 0.046 mmol) and 2,2-dimethoxypropane (8.5 *μ*L, 0.069 mmol) in a mixture of benzene (0.8 mL) and acetone (0.1 mL) were added *p*-TsOH (2.0 mg, 0.009 mmol) and molecular sieves 4A (15.0 mg), and the whole was stirred at room temperature for 1 h. The mixture was filtered through a pad of Celite, and the filtrate was concentrated in vacuo. After being quenched with water, the mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude residue was purified by preparative TLC (SiO_2, CH_2Cl_2/AcOEt = 5/1) to give **7** (4.1 mg, 24%) as yellow crystals: mp 172−173 °C (benzene); $[\alpha]^{30}_D$ −88.7 (*c* = 0.43, $CHCl_3$); IR (KBr) 3439, 2220, 2064, 1996 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.41 (d, 1H, *J* = 6.9 Hz), 1.25 (dd, 1H, *J* = 5.1, 8.1 Hz), 1.35 (d, 3H, *J* = 6.3 Hz), 1.37 (s, 3H), 1.49 (s, 3H), 2.43 (d, 1H, *J* = 6.0 Hz), 3.61 (m, 1H), 3.95 (dd, 1H, *J* = 3.0, 6.6 Hz), 4.37 (dq, 1H, *J* = 6.3, 6.6 Hz), 5.57 (dd, 1H, *J* = 5.1, 8.1 Hz), 5.60 (dd, 1H, *J* = 5.1, 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) *δ* 14.9, 24.1, 24.6, 27.1, 64.3, 70.4, 73.0, 80.2, 81.9, 86.3, 108.2, 121.4; MS (EI) *m*/*z* 336 (3.3), 307 (25), 280 (24). Anal. Calcd for $C_{15}H_{17}FeNO_6$: C, 49.61; H, 4.72; N, 3.86. Found: C, 49.90; H, 4.71; N, 3.83.

(2*R*,3*S*,6*R*,11*R*,3*E*,5*E*,7*E*,9*E*)-Tricarbonyliron [(*η*⁴-3−6)-Hexadeca-2-hydroxy-11-*tert*-butyldimethylsilyloxy-3,5,7,9-tetraene] 11. Under an argon atmosphere, to a solution of **10** (12.1 mg, 0.0241 mmol) in MeOH (0.5 mL) was added slowly $NaBH_4$ (0.90 mg, 0.024 mmol) at −78 °C, and the whole was stirred at −50 °C for 4 h. After being quenched with a saturated $NaHCO_3$ solution, the mixture was extracted with AcOEt. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, hexane/AcOEt = 5/1) to give **11** (8.7 mg, 72%) as a yellow oil: $[\alpha]^{25}_D$ +89.3 (*c* = 0.283, $CHCl_3$); IR ($CHCl_3$) 3570, 2040, 1980 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) *δ* 0.01 (s, 3H), 0.04 (s, 3H), 0.89 (s, 9H), 0.90 (m, 3H), 1.20−1.40 (m, 9H), 1.36 (d, 3H, *J* = 6.2 Hz), 1.90 (dd, 1H, *J* = 8.4, 10.5 Hz), 2.18 (d, 1H, *J* = 2.4 Hz), 3.79 (m, 1H), 4.10 (ddd, 1H, *J* = 5.9, 7.3, 11.9 Hz), 5.18 (dd, 1H, *J* = 4.9, 8.1 Hz), 5.25 (dd, 1H, *J* = 4.9, 8.4 Hz), 5.61 (dd, 1H, *J* = 10.5, 14.9 Hz), 5.66 (dd, 1H, *J* = 7.3, 14.9 Hz), 6.03 (dd, 1H, *J* = 10.5, 14.9 Hz), 6.22 (dd, 1H, *J* = 10.5, 14.9 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) *δ* −4.8, −4.3, 14.0, 18.2, 22.6, 24.9, 25.9, 26.0, 31.8, 38.2, 63.2, 69.6, 69.8, 73.2, 79.8, 81.6, 129.0, 131.0, 133.6, 137.5.

(2*R*,11*R*)-2-Hydroxy-11-*tert*-butyldimethylsilyloxyhexadecane 12. To a solution of **11** (8.7 mg, 0.017 mmol) in MeOH (0.5 mL) was added a 30% H_2O_2 solution (20 mg, 0.17 mmol) and a 1 M NaOH solution (170 *μ*L, 0.17 mmol) at 0 °C under an argon atmosphere, and the whole was stirred for 1 h. After being quenched with an aqueous NH_4Cl solution, the mixture was extracted with AcOEt. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The mixture of the residue, $PtO_2 \cdot 2H_2O$ (5.5 mg, 0.021 mmol), and AcOEt (1 mL) was stirred at room temperature for 15 h under a hydrogen atmosphere (1 atm). After being filtrated with the Celite, the mixture was concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, hexane/AcOEt = 5/1) to give **12** (5.7 mg, 89%) as a colorless oil: $[\alpha]^{25}_D$ +3.7 (*c* = 0.32, $CHCl_3$); ^1H NMR ($CDCl_3$, 270 MHz) *δ* 0.01 (s, 3H), 0.04 (s, 3H), 0.89 (s, 9H), 0.90 (m, 3H), 1.19 (d, 3H, *J* = 6.2 Hz), 1.20−1.29 (m, 24H), 3.62 (m, 1H), 3.78 (m, 1H); MS (CI) *m*/*z* 373 (MH^+, 30), 239 (100); HR-MS (CI) calcd for $C_{22}H_{49}O_2Si$ (MH^+) 373.3502, found 373.3512.

(2*SR*,5*RS*,6*RS*,7*SR*,2*E*,4*E*)-Tricarbonyliron [(*η*⁴-2−5)-Octa-6,7-isopropylidenedioxy-2,4-dienonitrile] 16. A mixture of **10** (220 mg, 0.751 mmol), 2,2-dimethoxypropane (276 *μ*L, 2.25 mmol), *p*-TsOH (7.1 mg, 0.038 mmol), and $CHCl_3$ (7.5 mL) was stirred at 0 °C for 2 h under an argon. After being quenched with an aqueous $NaHCO_3$ solution, the mixture was extracted with AcOEt. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, hexane/AcOEt = 5/1) to give **16** (194 mg, 78%) and the diastereomer of **16** (21.3 mg, 8.5%): IR ($CHCl_3$) 2220, 2070, 2000 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) *δ* 0.49 (dd, 1H, *J* = 1.1, 7.8 Hz), 1.02 (ddd, 1H, *J* = 0.8, 6.2, 7.6 Hz), 1.36 (d, 3H, *J* = 5.9 Hz), 1.38 (s, 6H), 3.48 (dd, 1H, *J* = 6.2, 8.4 Hz), 3.83 (qd, 1H, *J* = 5.9, 8.4 Hz), 5.52 (ddd, 1H, *J* = 1.1, 4.9, 7.6 Hz), 5.65(ddd, 1H, *J* = 0.8, 4.9, 7.8 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) *δ* 17.3, 24.5, 26.8, 27.1, 59.6, 77.9, 82.8, 82.8, 86.0, 108.4, 121.0, 171.0; MS (FAB) *m*/*z* 334 (MH^+, 92), 306 (37), 264 (100), 250 (54). Anal. Calcd for $C_{14}H_{15}FeNO_5$: C, 50.48; H, 4.54; N, 4.20. Found: C, 50.53; H, 4.61; N, 4.21.

(4*SR*,7*RS*,8*RS*,9*SR*,2*E*,4*E*,6*E*)-Tricarbonyliron (*η*⁴-4−7)-Deca-8,9-isopropylidenedioxy-2,4,6-trienonitrile] 17. A 1.0M solution of DIBAL-H in toluene (114 *μ*L, 0.114 mmol) was added to a solution of **16** (25.4 mg, 0.0763 mmol) in toluene (0.8 mL) at −78 °C under an argon atmosphere, and the whole was stirred for 1.5 h. After being quenched with a saturated $NaHCO_3$ solution, the mixture was extracted three times with AcOEt. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, hexane/AcOEt = 5/1) to give the aldehyde (23.5 mg, 92%): IR ($CHCl_3$) 2060, 1990, 1680 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) *δ* 1.21 (m, 2H), 1.31 (d, 3H, *J* = 5.9 Hz), 1.33 (s, 6H), 3.44 (dd, 1H, *J* = 7.3, 8.1 Hz), 3.81 (qd, 1H, *J* = 5.9, 8.1 Hz), 5.58 (dd, 1H, *J* = 4.9, 8.1 Hz), 5.84 (ddd, 1H, *J* = 0.5, 4.9, 8.6 Hz), 9.35 (d, 1H, *J* = 4.1 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) *δ* 17.5, 26.9, 27.2, 55.0, 59.9, 77.9, 83.0, 83.3, 86.2, 108.3, 195.8; MS (FAB) *m*/*z* 337 (MH^+, 95), 280 (28), 252 (49), 194 (100). Anal. Calcd for $C_{14}H_{16}FeO_6$: C, 50.03; H, 4.80. Found: C, 50.03; H, 4.80. The same treatment of the aldehyde (70 mg, 0.21 mmol) as described for the synthesis of **5** gave the crude mixture, which was purified by column chromatography (SiO_2, hexane/AcOEt = 10/1) to give **17** (47.9 mg, 64%) and 2*Z*-isomer of **17** (11.2 mg, 15%). **17**: a yellow oil; IR ($CHCl_3$) 2220, 2060, 1995 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) *δ* 1.15 (dd, 1H, *J* = 7.3, 7.8 Hz), 1.39 (s, 6H), 1.40 (d, 3H, *J* = 5.9 Hz), 1.66 (dd, 1H, *J* = 7.3, 10.5

Hz), 3.43 (dd, 1H, J = 7.8, 7.8 Hz), 3.86 (qd, 1H, J = 5.9, 7.8 Hz), 5.36 (d, 1H, J = 15.9 Hz), 5.39−5.50 (m, 2H), 6.51 (dd, 1H, J = 10.5, 15.9 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 17.6, 27.0, 27.3, 56.0, 58.9, 77.5, 77.8, 83.6, 84.1, 84.5, 96.4, 108.3, 154.3; MS (FAB) m/z 360 (MH^+, 57), 331 (42), 303 (82), 275 (42), 218 (100). Anal. Calcd for $C_{16}H_{17}FeNO_5$: C, 53.51; H, 4.77; N, 3.90. Found: C, 53.45; H, 4.98; N, 3.61.

(2*SR*,5*RS*,6*RS*,7*SR*,2*E*,4*E*)-Tricarbonyliron [(η^4-2−5)-Octa-6,7-(1-ethoxy-2-chloro)ethylidenedioxy-2,4-dienonitrile] 21 and (2*SR*,5*RS*,6*SR*,7*RS*,2*E*,4*E*)-Tricarbonyliron [(η^4-2−5)-Octa-6,7-(1-ethoxy-2-chloro)ethylidenedioxy-2,4-dienonitrile] 22. Orthochloroacetic acid triethyl ester (100 μL, 0.522 mmol) and PPTS (8.7 mg, 0.035 mmol) were successively added to a solution of **10** (102 mg, 0.348 mmol) in dry CH_2Cl_2 (3.4 mL) at 0 °C under an argon atmosphere. The resulting mixture was stirred at room temperature for 1.5 h. After being quenched with an aqueous $NaHCO_3$ solution, the mixture was extracted with AcOEt. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, hexane/AcOEt = 5/1) to give **21** (111 mg, 80%) and **22** (12.1 mg, 8.7%) as diastereomixtures. **21**: a yellow oil; IR ($CHCl_3$) 2220, 2070, 1995 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.56 (m, 1H), 1.00 (m, 1H), 1.21 (t, 3H, J = 7.3 Hz), 1.43 (d, 3H, J = 5.9 Hz), 3.54−3.76 (m, 5H), 4.06−4.22 (qd, 1H, J = 5.9, 8.1 Hz), 5.54−5.73 (m, 2H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ (major) 15.1, 17.6, 25.2, 45.8, 57.8, 58.1, 79.2, 83.7, 85.8, 87.0, 119.5, 121.5; (minor) 15.0, 17.3, 25.1, 46.7, 57.5, 57.9, 80.9, 83.3, 84.2, 86.0, 119.5, 121.5; MS (FAB) m/z 432 (M^+ + Cl, 10), 397 (M^+, 23), 369 (100). Anal. Calcd for $C_{15}H_{16}ClFeNO_6$: C, 45.31; H, 4.06; N, 3.52. Found: C, 45.11; H, 4.00; N, 3.57. **22**: a yellow oil; IR ($CHCl_3$) 2220, 2075, 2015 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.49 (m, 1H), 1.06 (dd, 1H, J = 8.1, 8.9 Hz), 1.23 (t, 3H, J = 7.0 Hz), 1.38 (d, 3H, J = 5.9 Hz), 3.44−3.76 (m, 5H), 3.95−4.22 (qd, 1H, J = 5.9, 14.3 Hz), 5.37 (dd, 1H, J = 4.6, 8.1 Hz), 5.64 (dd, 1H, J = 4.6, 7.3 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ (major) 15.0, 16.5, 24.4, 46.7, 57.9, 58.4, 79.1, 82.9, 87.0, 87.8, 94.8, 119.2; (minor) 14.9, 16.5, 24.6, 46.7, 57.5, 59.2, 80.4, 82.8, 86.5, 86.6, 94.8, 121.0; MS (FAB) m/z 432 (M^+ + Cl, 13), 397 (M^+, 58), 369 (100).

(2*SR*,5*RS*,6*RS*,7*SR*,2*E*,4*E*)-Tricarbonyliron [(η^4-2−5)-Octa-6-allyl-7-acetoxy-2,4-dienonitrile] 23. Orthoacetic acid trimethyl ester (34.7 μL, 0.260 mmol) and PPTS (3.4 mg, 0.013 mmol) were added to a solution of **15** (38.0 mg, 0.130 mmol) in dry CH_2Cl_2 (1.2 mL) at 0 °C under an argon atmosphere, and the resulting mixture was stirred for 30 min. After being quenched with an aqueous $NaHCO_3$ solution, the mixture was extracted with AcOEt. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. To a solution of the crude mixture of **20A** and **20B** in dry CH_2Cl_2 (1.2 mL) were added allyltrimethylsilane (207 μL, 1.30 mmol) and BF_3·ether complex (69 μL, 0.33 mmol) at −78 °C, and the whole was stirred at 0 °C for 1 h. After being quenched with an aqueous $NaHCO_3$ solution, the mixture was extracted with AcOEt. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, hexane/AcOEt = 10/1) to give **23** (19.0 mg, 42%) as yellow crystals: mp 74 °C (hexane); IR ($CHCl_3$) 2220, 2070, 1985, 1730 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.40 (dd, 1H, J = 1.1, 7.8 Hz), 1.11 (dd, 1H, J = 9.2, 9.7 Hz), 1.27 (d, 3H, J = 6.2 Hz), 1.57 (m, 1H), 2.05 (s, 3H), 2.02−2.38 (m, 2H), 4.94 (dq, 1H, J = 2.7, 6.2 Hz), 5.07 (dd, 1H, J = 1.4, 17.3 Hz), 5.14 (dd, 1H, J = 1.4, 10.0 Hz), 5.22 (ddd, 1H, J = 1.1, 5.1, 9.2 Hz), 5.59 (ddd, 1H, J = 1.1, 5.1, 7.8 Hz), 5.78 (dddd, 1H, J = 7.3, 7.3, 10.0, 17.3 Hz); MS (FAB) 359 (M^+, 45), 331 (100), 303 (6), 275 (9). Anal. Calcd for $C_{16}H_{17}FeNO_5$: C, 53.51; H, 4.77; N, 3.90. Found: C, 53.50; H, 4.96; N, 3.74.

(2*SR*,5*RS*,6*RS*,7*SR*,2*E*,4*E*)-Tricarbonyliron [(η^4-2−5)-Octa-6-allyl-7-chloroacetoxy-2,4-dienonitrile] 24a. To a solution of **21** (38.8 mg, 0.0976 mmol) in dry CH_2Cl_2 (0.8 mL) was successively added allyltrimethylsilane (155 μL, 0.976 mmol) and BF_3·ether complex (41 μL, 0.195 mmol) at −78 °C. The whole was stirred for 1.5 h at −78 °C. After the same workup as described for **23**, the crude residue was purified by column chromatography (SiO_2, hexane/AcOEt = 5/1) to give **24a** (29.5 mg, 77%) as yellow crystals: mp 95 °C (hexane); IR ($CHCl_3$) 2220, 2070, 1990, 1750, 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.41 (d, 1H, J = 7.6 Hz), 1.12 (dd, 1H, J = 8.9, 9.4 Hz), 1.34 (d, 3H, J = 6.8 Hz), 1.56 (m, 1H), 2.11−2.42 (m, 2H), 4.11 (s, 2H), 5.00 (dq, 1H, J = 2.4, 6.8 Hz), 5.08 (dd, 1H, J = 1.4, 17.0 Hz), 5.16 (dd, 1H, J = 1.4, 9.2 Hz), 5.22 (dd, 1H, J = 4.9, 8.9 Hz), 5.61 (dd, 1H, J = 4.9, 7.6 Hz), 5.70−5.86 (dddd, 1H, J = 7.3, 7.3, 9.2, 17.0 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 15.7, 24.4, 37.7, 41.0, 47.1, 63.7, 75.6, 81.6, 88.1, 118.5, 121.5, 134.8, 166.6; MS (FAB) m/z 428 (M^+ + Cl, 26), 393 (M^+, 81), 365 (82), 267 (100). Anal. Calcd for $C_{16}H_{16}ClFeNO_5$: C, 48.82; H, 4.10; N, 3.56. Found: C, 48.67; H, 4.08; N, 3.27.

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Supporting Information Available: Experimental procedure for the preparation of **2b**−**d**, **6**, **9**, **10**, **15**, **18**, **19**, **24b**−**h**, and **26**−**28**. X-ray structural information of **7**, **19**, and **24a**. ^{1}H NMR spectra of **2b**,**c**, **9**−**12**, **18**, **19**, **24c**−**f**,**h**, and **26**−**28**. This material is available free of charge via the Internet at http://pubs.acs.org.

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