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Dynamic Diastereoselectivity during Iron Carbonyl Mediated Spirocyclization Reactions

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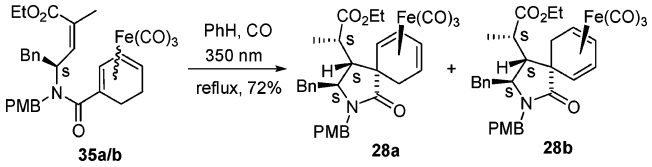


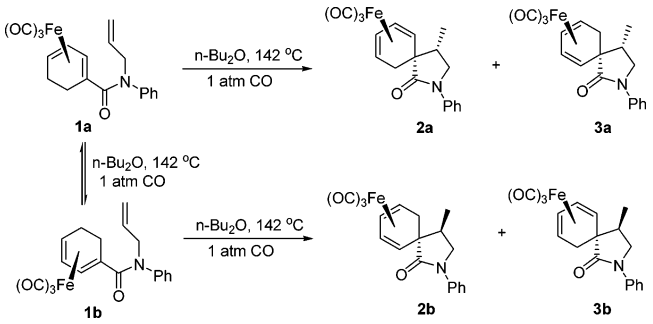
Dynamic diastereoselectivity during $Fe(CO)_3$ promoted [6 + 2] ene spirocyclization of **35a** and **35b**, having a chiral center on the pendent side chain, was investigated and gave rise to products **28a** and **28b** instead of four possible isomers. From this reaction, two chiral centers are generated, with absolute stereochemistry determined by the double bond geometry and the chiral center already present. **28a**/**b** and the diene product from demetallation of **28a** are proposed as potential intermediates for total synthesis of 18-deoxycytochalasin H. Furthermore, a stepwise second cyclization and a tandem double cyclization mediated by the $Fe(CO)_3$ moiety was investigated.

Introduction

The iron(0) tricarbonyl moiety has been widely applied to promote isomerization of olefinic compounds,[1] formation of carbon−carbon bonds, and for diene protection[2] because of its compatibility with a wide range of functional groups, environmentally friendly nature, and efficient catalytic ability. The $Fe(CO)_3$ moiety can also be used as a stereochemical directing group during reactions of neighboring functionality.[3]

A few years ago, an $Fe(CO)_3$ promoted [6 + 2] ene type of cyclization was developed in our laboratory to provide spirocyclic lactams as final products.[4] A simple example is outlined in Scheme 1, although the pendent double bond in the substrate can be further substituted with a variety of functional groups. Initially, subjection of substrates **1a** and **1b**, a pair of interconvertible enantiomers derived from racemic complexed acids, to thermal reaction conditions affords lactams **2a** and **2b**, respectively. While the actual cyclization is stereospecific, subsequent rearrangement of the diene in lactam **2a**, via an iron-mediated hydride shift, produces compound **3a** and, similarly, **3b** is obtained from **2b**. Finally, four isomers, two pairs of enantiomers (**2a**/**3a** and **2b**/**3b**), are provided through this spirocyclization reaction. While several approaches[4,5] have been developed to control the loss of regio- or stereochemistry caused by postcyclization diene rearrangement, none of them adequately address the racemization caused by precyclization interconversion of two substrate enantiomers. To a great extent, the application of this methodology to organic synthesis is limited by all the above disadvantages. Our previous work also showed precyclization racemization could be avoided by introduction

SCHEME 1. An Example of $Fe(CO)_3$ Promoted [6+2] ene Type of Spirocyclization



(1) Uma, R.; Crevisy, C.; Grée, R. *Chem. Rev.* **2003**, *103*, 27−51.

(2) (a) Pearson, A. J. *Iron Compounds in Organic Synthesis*; Academic Press: San Diego, CA, 1994. (b) Evans, G.; Johnson, B. F. G.; Lewis, J. *J. Organomet. Chem.* **1975**, *102*, 507.

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(4) Pearson, A. J.; Zettler, M. W. *J. Am. Chem. Soc.* **1989**, *111*, 3908−3918.

(5) (a) Pearson, A. J.; Wang, X. *J. Am. Chem. Soc.* **2003**, *125*, 638−639. (b) Pearson, A. J.; Dorange, I. B. *J. Org. Chem.* **2001**, *66*, 3140−3145.

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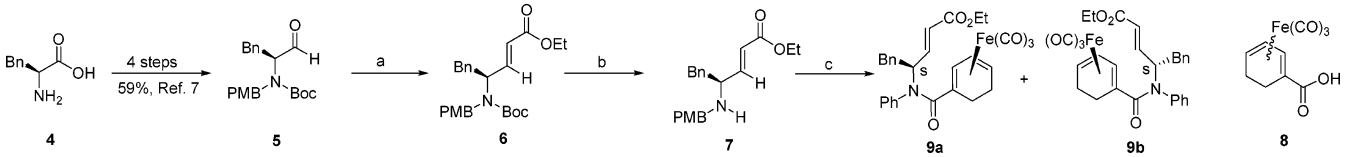
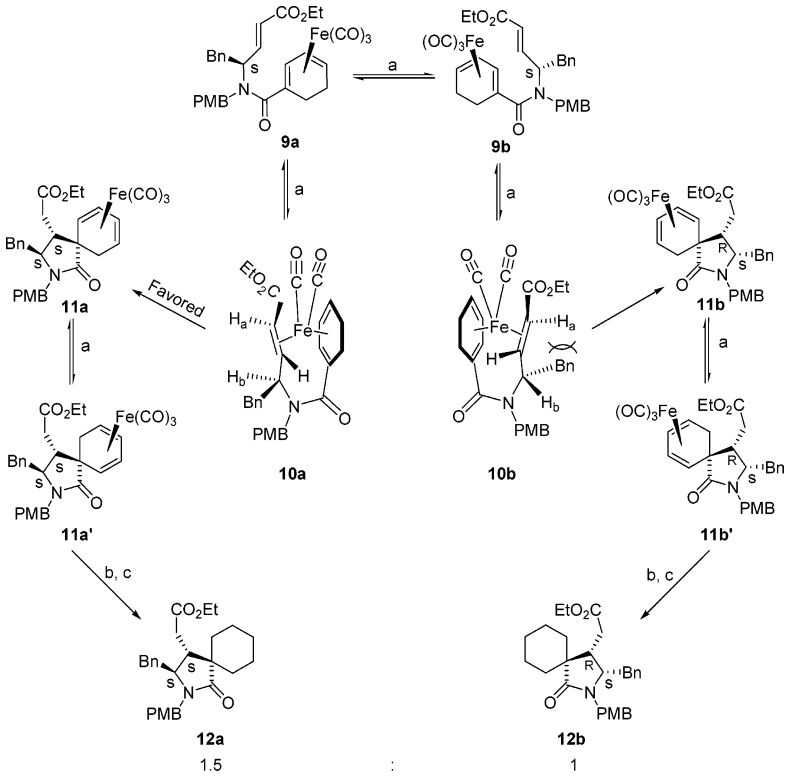
SCHEME 2. Synthesis of Substrates 9a and 9b[a]



[a] Reagents and conditions: (a) Triethyl phosphonoacetate, BuLi, THF, −78 °C, then **5** in THF −78−0 °C, 53%. (b) TFA, CH_2Cl_2, 0 °C, 96%. (c) **8**, DIEA, MsCl, CH_2Cl_2, 0 °C, then **7**, rt, 82%.

SCHEME 3. Spirocyclization of Substrates 9a and 9b[a]



[a] /lp;&-5q;1Reagents and conditions: (a) *n*-Bu_2O, CO, 142 °C. (b) Sat. $CuCl_2$ in EtOH. (c) 10% Pd/C, H_2, MeOH, 50% yield over three steps.

of substituents on the cyclohexadienyl ring, but this requires an often difficult optical resolution of the starting material.[6] This inspired us to further explore the stereochemistry of this cyclization reaction to obtain optically pure products. Our investigation focused on what is essentially a dynamic kinetic resolution using substrates with a chiral center on the pendent side chain. We also consider its potential application to the total synthesis of 18-deoxycytochalasin H, a natural product that is a potent HIV-1 protease inhibitor. A preliminary communication of part of this work has previously been published.[7]

Results and Discussion

Considering the ready accessibility of starting material and the possibility that introduction of a chiral center on the pendent olefinic side chain can produce, to some extent, a new chirality inducing factor, substrates **9a** and **9b** were designed and prepared starting with the known aldehyde **5** (Scheme 2), which was derived in 59% yield over four steps from L-phenylalanine (**4**).[8] Unsaturated ester *E*-**6** was obtained from aldehyde **5** through a Horner−Wadsworth−Emmons reaction,[9] accompanied by formation of the *Z* isomer (*E*:*Z*/1.4:1), which was separated chromatographically. Amine deprotection occurred by treatment with TFA to afford **7** quantitatively, which was coupled with racemic complexed acid **8** to afford the expected substrates, two diastereomers **9a** and **9b**, in 82% combined yield.

Heating substrates **9a** and **9b** in *n*-Bu_2O under CO atmosphere at 142 °C generated several inseparable products which could not be fully characterized by ^1H NMR spectroscopy. Without further purification, the mixture of these products was demetallated with $CuCl_2$, followed by hydrogenation over 10% Pd/C to lead to two major products, **12a** and **12b** in ratio of 1.5 to 1, in 50% isolated yield over three steps. Compounds **12a** and **12b** were easily characterized and the stereochemistry of **12a** was determined from the NOE difference NMR spectrum.

On the basis of our understanding of the likely mechanism, the spirocyclization of substrates **9a** and **9b** is outlined in Scheme 3 and involves reaction intermediates **10a** and **10b**. The

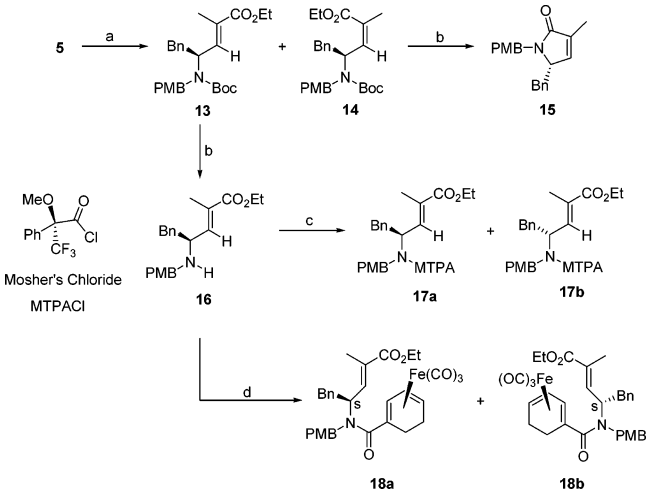
(6) (a) Pearson, A. J.; Zettler, M. W. *J. Chem. Soc., Chem. Commun.* **1987**, 1243−1245. (b) Birch, A. J.; Bandara, B. M. R. *Tetrahedron Lett.* **1980**, *21*, 2981−2982.

(7) Pearson, A. J.; Wang, X. *Tetrahedron Lett.* **2005**, *46*, 3123−3126.

(8) Dondoni, A.; Perrone, D.; Merino, P. *J. Org. Chem.* **1995**, *60*, 8074−8080.

(9) Udwary, D. W.; Casillas, L. K.; Townsend, C. A. *J. Am. Chem. Soc.* **2002**, *124*, 5294−5303.

SCHEME 4. Preparation of Substrates 18a and 18b[a]

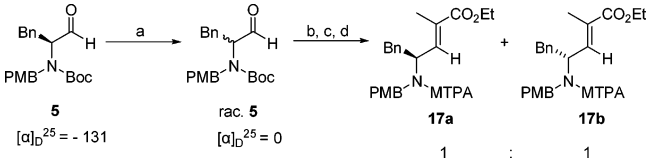


[a] Reagents and conditions: (a) Method A: ethyl 2-(diethoxyphosphoryl)propionate, BuLi, THF, −78 °C, 67% for **13**, 14% for **14**; method B: ethyl 2-(diethoxyphosphoryl)propionate, DBU, LiCl, MeCN, 0 °C, 65% for **13**, 13% for **14**; method C: (carbethoxyethylidene)triphenylphosphorane, CH_2Cl_2, 73% for **13**, 13% for **14**. (b) TFA, CH_2Cl_2, quantitatively. (c) Mosher's chloride, DIEA, CH_2Cl_2, amine **16**, method A: 82%, ee = 94%; method B: 78%, ee = 74%; method C: 85%, ee = 71%. (d) **8**, DIEA, MsCl, CH_2Cl_2, 0 °C, then **16**, rt, 81%.

facial orientation of the prochiral alkene side chain shown for **10a**/**b** corresponds to that which leads to the stereochemistry shown for the conversion of **1a** to **2a**/**b** in Scheme 1. Since both demetallation and hydrogenation were complete, the ratio of direct cyclization products **11a**/**a′** over **11b**/**b′** can also be deduced as 1.5 to 1 from the ratio of **12a** over **12b**. Considering the difference in configurations of intermediates **10a** and **10b**, we speculate that the stereoselectivity of this reaction is due to different steric hindrance effects in these structures. In intermediate **10b**, eclipsed H_a and Bn experience a repulsive interaction, which is relieved in **10a** because H_a and H_b are now eclipsed. Therefore, the spirocyclization reaction favors the pathway through intermediate **10a**, and equilibration between **9a** and **9b** (via metal-mediated H-shifts) gives rise to **11a** as the major product. Even though the stereoselectivity was not as good as we hoped, these results encouraged us to investigate this reaction further.

Replacement of H_a with a sterically more demanding substituent should introduce greater steric hindrance in intermediate **10b**, which may lead to much better stereocontrol if our rationale on the selectivity is correct. On the basis of this proposition, substrates **18a** and **18b** were prepared (Scheme 4) starting with aldehyde **5** via a Horner−Wadsworth−Emmons reaction. Several reaction conditions were applied for conversion of aldehyde **5** to compounds **13** and **14**. Method A (ethyl 2-(diethoxyphosphoryl) propionate, *n*-BuLi, THF, −78 °C) furnished 67% of **13** and 14% of **14**, and further Boc deprotection of compound **13** gave rise to free secondary amine **16** with 94% ee, which was determined by converting amine **16** to Mosher amides **17a** and **17b**. Method B (ethyl 2-(diethoxyphosphoryl) propionate, LiCl, DBU, MeCN, 0 °C)[10] afforded 65% and 13% of **13** and **14**, respectively, however, the deprotection product **16** showed only 74% ee. The milder method C ((carbethoxyethylidene) triphenylphosphorane, CH_2Cl_2)[11] gave even poorer ee, 71%, for compound **16**. So, finally, secondary amine **16** prepared using method A was taken on to the coupling reaction with racemic complexed acid **8** to provide the desired substrates **18a** and **18b**. Deprotection of compound **14** spontaneously afforded lactam **15** instead of the corresponding free secondary amine, which is also the reason why only substrates **18a** and **18b** with pendent *E* olefin were prepared via this route. The analogous *Z* olefins were obtained by a different route, described later.

SCHEME 5. Preparation of 17a and 17b from Racemic Amine 16[a]



[a] Reagents and conditions: (a) DBU, LiCl, MeCN, 0 °C, 85%. (b) Ethyl 2-(diethoxyphosphoryl)propionate, DBU, LiCl, MeCN, 0 °C, 69%. (c) TFA, CH_2Cl_2, quantitatively. (d) Mosher's chloride, DIEA, CH_2Cl_2, racemic amine **16**, 41% for **17a** and 42% for **17b**.

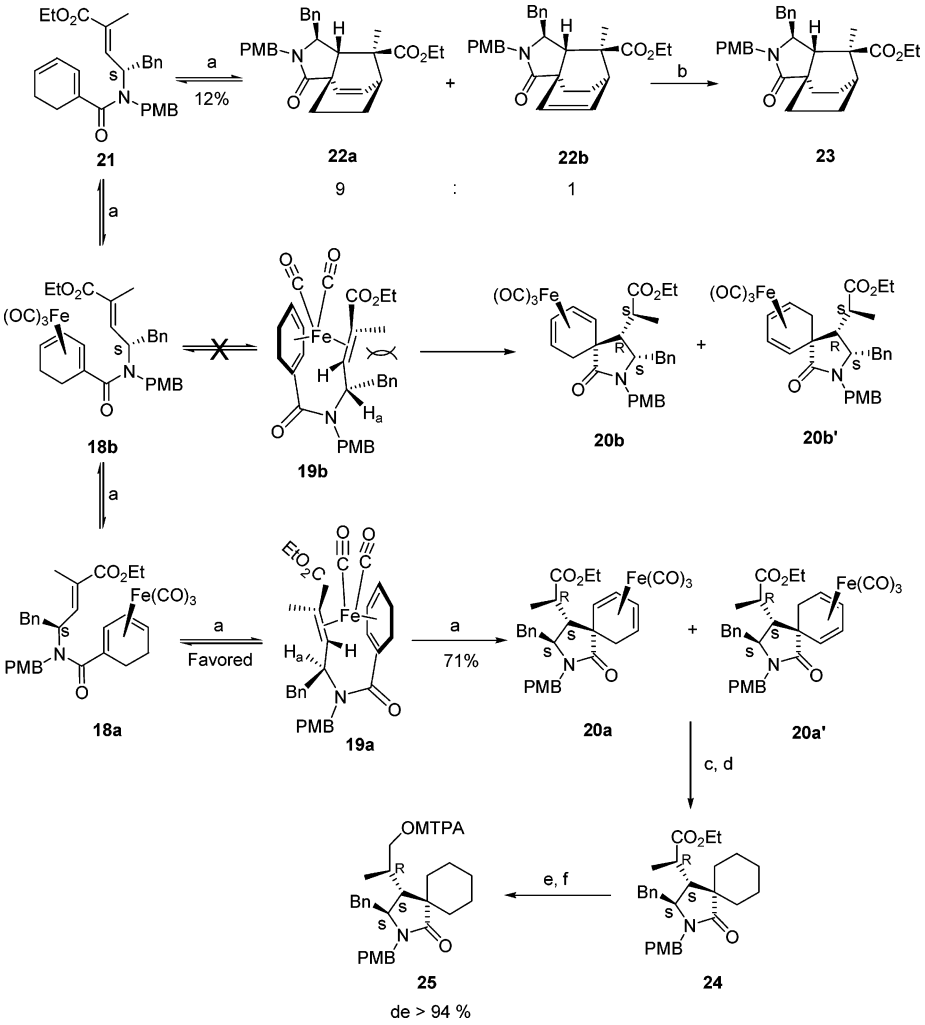
As mentioned above, the optical purity of free amine **16** was determined by conversion to Mosher amides **17a** and **17b**. The ^{1}H NMR spectrum of **17a**/**b** showed four isomers in different ratios, which made optical purity measurement difficult because of the uncertainty concerning the presence of amide resonance rotamers of **17a** and **17b**. To confirm this, racemic amine **16** was prepared (Scheme 5). First, aldehyde **5** was racemized by treatment with DBU in the presence of LiCl in acetonitrile, confirmed by the change of specific rotation from −131 to 0. Subsequent subjection of racemic **5** to method B conditions described in Scheme 4, followed by Boc-removal with TFA and amidation with Mosher's chloride, provided two chromatographically separable products **17a** and **17b** in 1:1 ratio. Variable temperature ^{1}H NMR spectra confirmed the presence of rotamers for both of them. Comparison with these ^{1}H NMR spectra allowed determination of the optical purity of amines **16** prepared earlier.

With substrates **18a** and **18b** in hand, spirocyclization was investigated under thermal conditions (in *n*-Bu_2O, reflux, and under CO atmosphere). Gratifyingly, only spirocyclic lactams **20a** and **20a′** were isolated and no compounds **20b** or **20b′** could be observed in the crude mixture of products (Scheme 6). These results indicate that the increased steric hindrance between methyl and benzyl groups in **19b** suppresses formation of this intermediate, and spirocyclization proceeds only via intermediate **19a**. Equilibration between **18a** and **18b** under these reaction conditions channels the conversion through **19a** to afford only **20a** which subsequently rearranges to afford the mixture of **20a** and **20a′**. These results further support our rationale on the diastereoselectivity of this type of spirocyclization. However, only 35% of expected products **20a** and **20a′** were obtained reproducibly under thermal conditions. Major side products were characterized to be **22a** and **22b** in 9:1 ratio and in 36% yield, which might be derived from demetallated intermediate **21** followed by an immediate intramolecular Diels−Alder reaction. Compounds **22a** and **22b** were confirmed to be products of

(10) Dixon, D. J.; Foster, A. C.; Ley, S. V. *Org. Lett.* **2000**, *2*, 123−125.

(11) (a) Horigome, M.; Motoyoshi, H.; Watanabe, H.; Kitahara, T. *Tetrahedron Lett.* **2001**, *42*, 8207−8210. (b) Nieman, J. A.; Coleman, J. E.; Wallace, D. J.; Piers, E.; Lim, L. Y.; Roberge, M.; Andersen, R. J. *J. Nat. Prod.* **2003**, *66*, 183−199.

SCHEME 6. Spirocyclization of Substrates 18a and 18b[a]

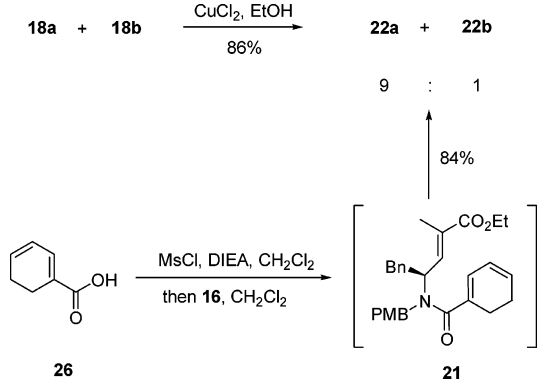


[a] Reagents and conditions: (a) Benzene, CO, 85 °C, 350 nm, 67% for compound **20a** and **20a′**, 4% for decomplexed **20a** and **20a′**, 12% for **22a** and **22b**. (b) 10% Pd/C, H_2, MeOH, 98%. (c) Method A: Me_3NO, benzene, 81%; Method B: sat. $CuCl_2$ in EtOH, 83%. (d) 10% Pd/C, H_2, MeOH, 88%. (e) $LiBH_4$, Et_2O, 90%. (f) Mosher's chloride, DIEA, toluene, 100 °C, 72%.

endo/exo cycloaddition by converting them to a single hydrogenation product, **23**. After a series of optimization experiments, photothermal reaction conditions (benzene, CO, 85 °C, 350 nm) afforded the best yield, 67%, for compounds **20a** and **20a′** with formation of their demetallation products in 4% yield, and Diels−Alder products **22a** and **22b** in 12% yield. Then, demetallation with copper(II) chloride in ethanol followed by hydrogenation converted products **20a** and **20a′** to the same compound **24**, whose optical purity was determined (ee > 94%) through reduction with $LiBH_4$, followed by esterification with Mosher's chloride to furnish compound **25**. Thus, no stereochemical leakage occurs throughout the reaction sequence, and the cyclization event itself is stereospecific.

As previously mentioned, major side products during the reaction in Scheme 6 were two [4 + 2] cycloaddition products in 9:1 ratio. Treatment of **18a** and **18b** with copper(II) chloride at room temperature also gave compounds **22a** and **22b** in 9:1 ratio and in 86% yield (Scheme 7). However, we did not have any proof whether this cyclization might be promoted by the $Fe(CO)_3$ moiety or derived directly from demetallated compound **21**, via a simple intramolecular Diels−Alder reaction. Attempted

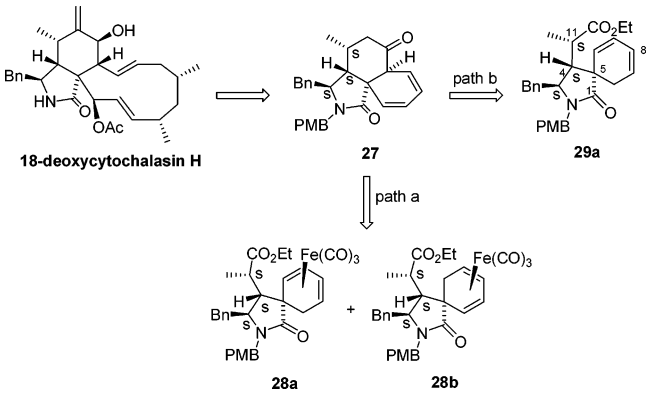
SCHEME 7. Investigation of Diels−Alder Reaction on the Basis of Substrate 18a and 18b



synthesis of compound **21** via the acyl mesylate from acid **26**[12] and amine **16** afforded only **22a** and **22b** in 9:1 ratio and in 84% yield. This result confirms that uncomplexed compound **21** undergoes spontaneous intramolecular Diels−Alder reaction

(12) Gradén, H.; Hallberg, J.; Kann, N.; Olsson, T. *J. Comb. Chem.* **2004**, *6*, 783−788.

SCHEME 8. A Possible Approach to 18-Deoxycytochalasin H

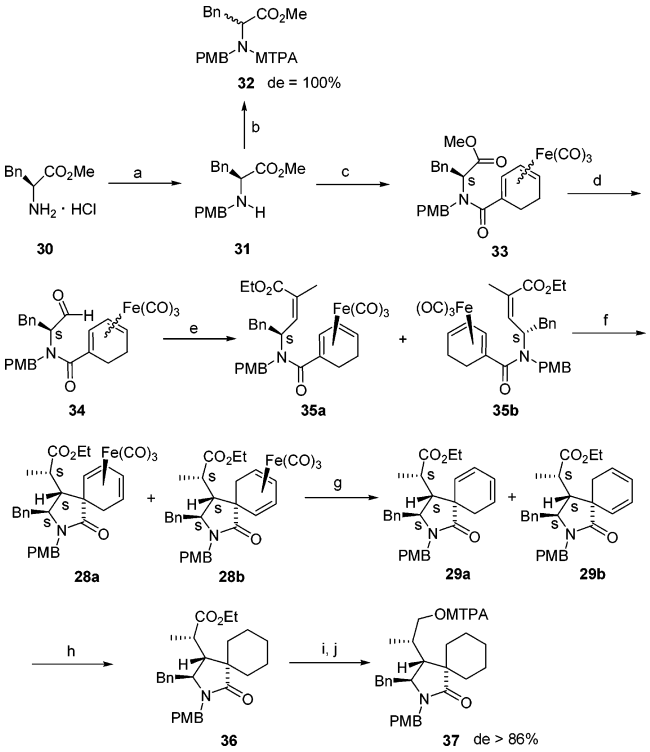


as soon as it is formed. More importantly, it further confirms the need to use diene−$Fe(CO)_3$ complexes stoichiometrically, because coordination of the diene with $Fe(CO)_3$ prevents Diels−Alder cycloaddition and allows the substrate to follow a [6 + 2] ene pathway, thereby increasing molecular diversity that is accessible from such materials.

18-Deoxycytochalasin H (Scheme 8) is a potent HIV-1 protease inhibitor, and its derivatives can regulate plant growth.[13] The presence of a densely substituted spirolactam skeleton in its structure attracted our interest because this type of subunit is produced from our ene type cyclization. One can envision 18-deoxycytochalasin H to be accessible from an intermediate such as **27** by further manipulation of the cyclohexadiene, and **27** might in turn be available from **28a**/**b**. Alternatively, **27** might also be available from **29a**, which can be obtained from demetallation of **28a**, via a series of transformations. As intermediates for total synthesis, compounds **29a** and **28a**/**b** require S, S, and S chirality at C3, C4, and C11, respectively, however, compounds **20a** and **20a′**, prepared from the spirocyclization reaction in Scheme 6, show one different chiral center, R, at C11. On the basis of our understanding of the mechanism of this [6 + 2] ene spirocyclization reaction, intermediate **29a** with the same chirality as 18-deoxycytochalasin H, or its complexed precursors, **28a** and **28b**, should be accessible from precursors **35** (Scheme 9) having a pendent trisubstituted *Z* olefin.

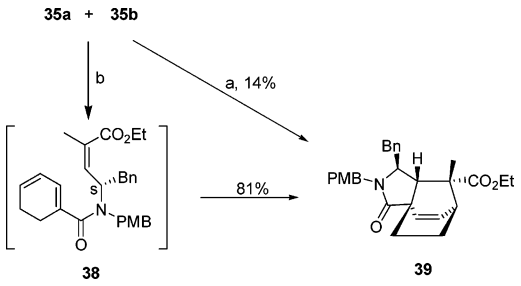
Since deprotection of compound **14** resulted in spontaneous cyclization to give lactam **15** instead of a free secondary amine (Scheme 4), substrates **35a** and **35b** were prepared as outlined in Scheme 9 starting with ethyl L-phenylalanine hydrochloride (**30**). Known secondary amine **31**[14] was prepared according to a published procedure[15] by treating **30** with sodium hydroxide followed by anisaldehyde and a catalytic amount of acetic acid and then reduction with lithium borohydride. The optical purity of secondary amine **31** (ee = 100%) was also determined by conversion to the Mosher amide **32**. As far as we are aware, the optical purity of **31** obtained by this route has not previously been determined. Subsequent coupling of amine **31** with complexed acid **8** led to amide **33**, as two diastereomers, which could be converted in 56% yield over two steps to substrates

SCHEME 9. Preparation and Spirocyclization Reaction of Substrates 35a and 35b[a]



[a] Reagents and conditions: (a) NaOH, MeOH, then *p*-methoxybenzaldehyde, AcOH, MeOH, 0 °C; $NaBH_4$, 82%. (b) Mosher's chloride, DIEA, reflux, 91%. (c) **8**, DIEA, MsCl, CH_2Cl_2, 0 °C, then **31**, 40 °C, 75%. (d) DIBAl-H, Et_2O, −78 °C, 80%. (e) Ethyl 2-[bis(2,2,2-trifluoroethyl)phosphono]propionate, KH, THF, −78 °C, 70%. (f) Benzene, CO, 350 nm, 85 °C, 72%. (g) Sat. $CuCl_2$ in EtOH, 80%. (h) 10% Pd/C, H_2, MeOH, 84% (ee > 86%). (i) $LiBH_4$, Et_2O. (j) Mosher's chloride, DIEA, benzene, 80 °C, 70% over two steps.

SCHEME 10. Diels−Alder Reaction from Substrates 35a and 35b[a]



[a] Reagents and conditions: (a) Benzene, CO, 350 nm, 85 °C, 14%, side product from spirocyclization. (b) Sat. $CuCl_2$ in EtOH, 81%.

35a and **35b** through DIBAl-H reduction and a Still−Gennari phosphonate olefination reaction.[16]

As expected, subjection of substrates **35a** and **35b** to photothermal conditions furnished spirocyclic lactams **28a** and **28b**, two diastereomers, as the only [6 + 2] ene spirocyclization products in 72% yield. As before, excellent dynamic diastereoselectivity resulted from different steric hindrance in the two diastereomeric reaction intermediates. We also isolated 4%

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(14) Bonache, M. A.; Cativiela, C.; Garcia-Lopez, M. T.; Gonzalez-Muniz, R. *Tetrahedron Lett.* **2006**, *47*, 5883−5887.

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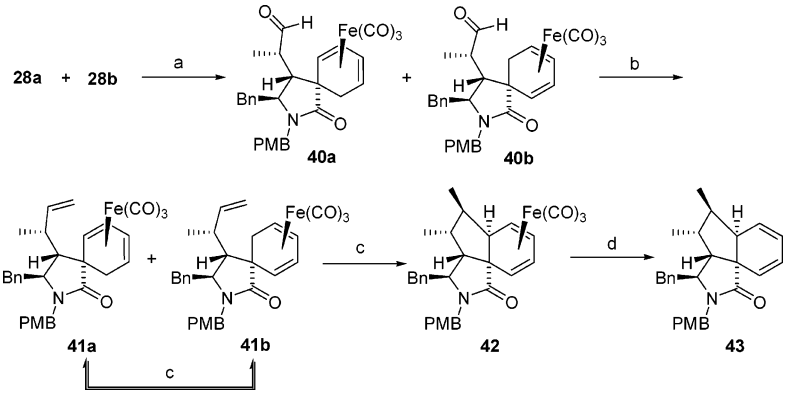
(16) (a) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405−4408. (b) Dakin, L. A.; Langille, N. F.; Panek, J. S. *J. Org. Chem.* **2002**, *67*, 6812−6815.

SCHEME 11. Exploration of a Second $Fe(CO)_3$ Promoted Cyclization[a]



[a] Reagents and conditions: (a) DIBAl-H, Et_2O, −78 °C, 77%. (b) Methyltriphenylphosphonium bromide, *n*-BuLi, THF, 0 °C to rt, 92%. (c) Mesitylene, CO, 350 nm, 160 °C, 52%. (d) Sat. $CuCl_2$ in EtOH, 72%.

combined yield of compounds **20a** and **20a′**, which we attribute to formation of substrates **18a** and **18b** through *Z* double bond isomerization of **35a** and **35b** under the reaction conditions. Diels−Alder reaction products were also formed through decomplexed intermediate **38** to give rise to compound **39**, in this case in 14% yield (Scheme 10). When substrates **35a** and **35b** were subjected to demetallation (sat. $CuCl_2$ in EtOH), the product **38** underwent spontaneous Diels−Alder reaction to provide **39** as a single stereoisomer in 81% yield. This also confirmed that the [6 + 2] ene spirocyclization reaction, described in Scheme 9, needs to be promoted by stoichiometric $Fe(CO)_3$ and is not directly accessible from **38** by any catalytic method.

Compounds **28a** and **28b** were demetallated with copper chloride in ethanol to afford decomplexed dienes **29a** and **29b** in 80% yield, which were hydrogenated to a single compound **36** in 84% yield. We attempted to determine the optical purity of compound **36** by conversion to the Mosher ester **37**, ^1H NMR of which indicated its diastereomeric purity to be greater than 86%, but this could not be determined accurately. On the basis of analysis of the reactions in Scheme 9, the most likely point for partial racemization to occur is during conversion of aldehyde **34** to substrates **35a** and **35b** in the presence of a strong base, KH, and not during the spirocyclization reaction.

The stereochemistry at C3 and C4 in compounds **29a** and **29b** was confirmed by NOESY, however, the chirality of C11 on the side chain of this spirocyclic structure was assigned to be S on the basis of the reaction mechanism but could not be confirmed by NMR spectroscopy. Meanwhile, we also wanted to explore the possibility of a second cyclization reaction through introduction of a second double bond on the side chain. Substrates for this model study, **41a** and **41b**, were prepared from spirocyclization products **28a** and **28b** through a reduction of ester to aldehydes **40a** and **40b** and subsequent Wittig reaction (Scheme 11). Investigation of the [6 + 2] ene-type cyclization of **41a**/**b** showed that the best isolated yield, 52% with 25% of recovered starting materials, was obtained using more forcing photothermal conditions in mesitylene at 160 °C for 9 h, affording **42** as the only characterizable product. Prolonged reaction time gave poorer yield, possibly because of decomposition of product **42** at high temperature. On the basis of the reaction mechanism, only substrate **41a** can directly undergo cyclization to afford compound **42**; however, substrate **41b** is isomerized to **41a** under thermal equilibration and then undergoes cyclization to afford **42**. Treatment of **42** with copper chloride in ethanol furnished demetallated compound **43** in 72% yield.

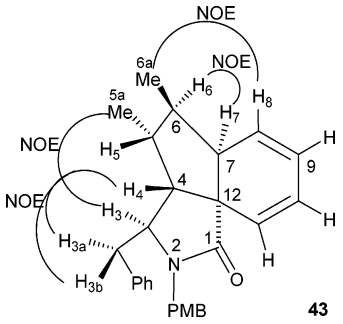
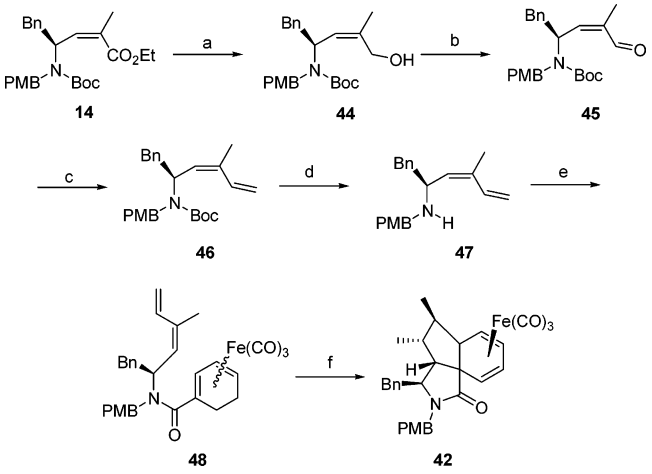


FIGURE 1. Determination of the stereochemistry for compound **43**.

The stereochemistry of compound **43** was confirmed by 2D COSY and NOESY spectra (Figure 1). A strong NOE was observed between Me_{5a} protons and H_3 and H_4 and both of H_{3a} and H_{3b}, but no NOE was observed between H_3 and H_5, which indicated that the stereochemical relationship is trans for H_3 with H_4 and cis for H_4 with H_5. Since the chirality of C7 is fixed by the reaction mechanism via alkene coordination to Fe, the stereochemistry at C6 was confirmed by the cis relationship between H_6 and H_7, which results in a strong NOE between them, and no NOE between H_7 and Me_{6a}, while the latter showed strong NOE with H_8. This assignment also confirms the S stereochemistry assigned for the side chain propionate moiety of **29a**/**b** discussed earlier. While **43** is clearly not convertible to **27**, and therefore is not a viable intermediate on route to 18-deoxycytochalasin H, the success of this tandem sequence provides the impetus for development of a more appropriate homologous reaction.

The success of the above stepwise second $Fe(CO)_3$ promoted cyclization encouraged us to explore a tandem double cyclization on the basis of a substrate with a conjugated diene in the pendent side chain. The involvement of the iron complex in multiple steps described in Schemes 9 and 11 might be avoided through this tandem approach. Substrate **48** was prepared starting with intermediate **14**, which was the side product during preparation of **13**. Reduction of **14** with DIBAl-H at rt led to alcohol **44** in 92% yield. Subsequent attempts to oxidize allylic alcohol **44** to *Z*-α, *β* unsaturated aldehyde **45** with MnO_2, PCC, Dess Martin reagent, or Swern oxidation were compromised because double bond isomerization occurred to give rise to *E*-α, *β* unsaturated

SCHEME 12. Investigation of a Tandem Double Cyclization Mediated by the $Fe(CO)_3$ Moiety[a]



[a] Reagents and conditions: (a) DIBAl-H, CH_2Cl_2, rt, 92%. (b) $Fe(CO)_4PPh_3$, Me_3NO, benzene, 71%. (c) Methyltriphenylphosphonium bromide, *n*-BuLi, THF, −78 °C − rt, 85%. (d) Me_3SiI, $CHCl_3$, 50 °C, then acetic acid, 53%. (e) **8**, DIEA, MsCl, CH_2Cl_2, 0 °C, then **47**, 40 °C, 83%. (f) Benzene, CO, 350 nm, reflux, 10%.

aldehyde which was inseparable from **45**. Recently, a new method for oxidation of allylic alcohols to aldehydes was developed in our laboratory by using $Fe(CO)_4PPh_3$ as catalyst and Me_3NO as oxidant in benzene solution.[17] Subjection of **44** to this reaction afforded aldehyde **45** in 71% yield without any formation of *E* isomer. Diene **46** was obtained through a Wittig reaction in the presence of methyltriphenylphosphonium bromide and *n*-BuLi, and subsequent Boc removal with Me_3SiI gave rise to free secondary amine **47** in 53% yield,[18] which was used in the next step without further purification. Finally, coupling of amine **47** with racemic complexed acid **8** furnished the desired substrate **48** as two diastereomers. Unfortunately, subjection of **48** to photothermal conditions in benzene provided only 10% of expected product **42**, accompanied by many uncharacterized side products. Other attempts under different reaction conditions led to even poorer yield. Consequently, the better approach to these multicyclic structures is via the interrupted tandem sequence of Schemes 9 and 11.

Conclusions

We have shown that spirocyclization using our iron-promoted [6 + 2] ene-type reaction can be used to produce densely substituted spirolactams in high optical purity, using a single stereogenic center as a control element. This procedure is akin to a dynamic kinetic resolution and allows a racemic mixture of planar chiral diene iron complexes such as **8** to be converted to a single enantiomer of the product. A second ene-type cyclization allows the construction of a tricyclic structure, again with complete stereocontrol. Provided this second cyclization can be engineered to produce a six-membered ring as in structure **27** (rather than the five-membered ring from the present work), we envision that this technology can be used to produce the main structural features present in the 18-deoxycytochalasin H molecule. Those studies are currently underway in our laboratory.

(17) Pearson, A. J.; Kwak, Y. *Tetrahedron Lett.* **2005**, *46*, 5417−5419.
(18) Takeuchi, H.; Fujimoto, T.; Hoshino, K.; Motoyoshiya, J.; Kakehi, A.; Yamamoto, I. *J. Org. Chem.* **1998**, *63*, 7172−7179.

Experimental Section

General Procedure for the Thermally Induced Cyclization. The appropriate amide was dissolved in freshly distilled *n*-Bu_2O ether (0.02 mmol/mL) under argon in a dried glass round bottomed flask. The air in the solution was removed by freeze−pump−thaw method three times, followed by bubbling with Ar for 10 min and then with CO for 10 min. The solution was refluxed under a balloon of CO for 8−20 h. The cooled reaction mixture was filtered through Celite and was concentrated in vacuo. Flash chromatography or preparative TLC separation yielded the desired products. Deviations from this procedure are noted in the experimental description for specific compounds.

General Procedure for the Photothermally Induced Cyclization. The appropriate amide was dissolved in freshly distilled toluene, xylene, or mesitylene (0.01−0.02 mmol/mL) under argon in a dried quartz tube or a glass round bottomed flask. The air in the solution was removed by freeze−pump−thaw method three times followed by bubbling with Ar for 10 min and then with CO for 10 min. The reaction flask was put into an oil bath heated to the boiling point of the solvent being used and was irradiated in a Rayonet reactor with a 350-nm light source with magnetic stirring for 3−24 h under a balloon of CO. The cooled reaction mixture was filtered through Celite and was concentrated in vacuo. Flash chromatography or preparative TLC separation yielded the desired products. Deviations from this procedure are noted in the experimental description for specific compounds.

General Procedure for Demetallation. Method A: To the solution of complexed intermediate in benzene was added trimethylamine oxide (30 equiv). The reaction mixture was stirred for 24 h at rt and then was filtered through Celite and was concentrated in vacuo. Purification by flash chromatography or preparative TLC afforded the pure products. Method B: To a small vial was added the iron carbonyl complex (0.1 mmol) and sat. $CuCl_2$ solution in EtOH (2.5 mL). The solution was stirred at rt for 18−24 h and then was concentrated in vacuo. After water (4 mL) was added to the residue, the mixture was extracted with ether (3 mL × 3). The organic layer was washed with brine, was dried (Na_2SO_4), was filtered, and was concentrated in vacuo. The crude products were purified by preparative TLC or flash chromatography.

[(4*S*,2*E*)-Ethyl 4-(*N*-(4-methoxybenzyl)cyclohexa-1,3-dienecarboxamido)-5-phenylpent-2-enoate]tricarbonyliron (9a and 9b). To a solution of complexed carboxylic acid **8** (123 mg, 0.47 mmol) and diisopropylethylamine (92 μL, 0.56 mmol) in freshly distilled CH_2Cl_2 (6.0 mL) under argon at 0 °C was quickly added methanesulfonyl chloride (47 μL, 0.60 mmol). Stirring was continued at this temperature for 1 h. Diisopropylethylamine (169 μL, 1.02 mmol) was added followed by a solution of amine **7** (236 mg, 0.70 mmol) in freshly distilled CH_2Cl_2 (2.0 mL). The temperature was allowed to reach rt and then the reaction mixture was stirred for 24 h. After CH_2Cl_2 (15 mL) was added, the organic layer was washed with 1 N HCl (5 mL × 2) and brine (5 mL × 2), was dried (Na_2SO_4), was filtered, and was concentrated in vacuo. Flash chromatography (Hex:EA/4:1) allowed partial separation of **9a** and **9b** (223 mg, 82% combined yield). One diastereomer: R_f = 0.50 (Hex:EA/4:1). $[\alpha]_D^{25} = -29$ (c = 0.84, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ7.25−7.05 (7H), 6.92 (br, 1H), 6.81 (dt, J = 8.8, 2.0 Hz, 2H), 6.16 (br, 1H), 5.56 (br, 1H), 5.28 (br, 1H), 4.42 (br, 1H), 4.13 (q, J = 7.2 Hz, 2H), 3.80 (s, 3H), 3.83−3.70 (m, 1H), 3.52−3.40 (2H), 3.05 (br, 1H), 1.92−1.62 (3H), 1.42−1.36 (m, 1H), 1.23 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 166.2, 159.3, 146.0, 129.7, 128.9, 128.7, 126.9, 122.7, 114.4, 85.7, 70.8, 64.6, 62.1, 60.6, 55.5, 53.6, 38.0, 27.0, 23.9, 14.4. HRMS (FAB) calcd for MH^+ ($C_{31}H_{32}FeNO_7$) 586.1528, found, 586.1529. The other diastereomer: R_f = 0.51 (Hex:EA/4:1). $[\alpha]_D^{25} = -53$ (c = 0.90, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ7.27−7.05 (8H), 6.88 (d, J = 8.4 Hz, 2H), 5.97 (d, J = 4.0 Hz, 1H), 5.56 (d, J = 16.4 Hz, 1H), 5.23 (dd, J = 6.0, 4.8 Hz, 1H), 4.84 (d, J = 15.6 Hz, 1H), 4.13 (q, J = 68 Hz, 2H), 4.22−4.05

(2H), 3.80 (s, 3H), 3.38−3.36 (m, 1H), 3.20−3.10 (br, 2H), 1.96−1.80 (2H), 1.78−1.64 (m, 1H), 1.44−1.33 (m, 1H), 1.24 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 166.3, 159.4, 146.3, 138.2, 129.5, 128.9, 128.8, 128.7, 126.9, 122.4, 114.5, 85.1, 84.7, 77.4, 64.1, 61.2, 60.6, 55.5, 38.0, 27.0, 26.5, 24.7, 14.4. HRMS (FAB) calcd for MH^+ ($C_{31}H_{32}FeNO_7$) 586.1528, found, 586.1556.

Ethyl 2-[(3*S*,4*S*)-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-zaspiro-[4.5]decan-4-yl]acetate (12a) and Ethyl 2-[(3*S*,4*R*)-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]decan-4-yl]acetate (12b). The mixture of **9a** and **9b** (71 mg, 0.121 mmol) in *n*-Bu_2O (8 mL) was subjected to thermal cyclization conditions under reflux for 12 h. Rapid purification by flash chromatography (Hex:EA/2:1) afforded **11a** and **11b** together with three other isomers, which were inseparable and were used without further purification. According to general procedure method A for demetallation, to the above mixture was added sat. $CuCl_2$ in ethanol (2.0 mL). Stirring was continued for 18 h. Evaporation in vacuo gave the crude products as a pale yellow oil. To a solution of this oil in MeOH (4.0 mL) was added 10% Pd/C (39 mg), and the mixture was stirred under H_2 for 15 h. After filtration to remove the catalyst, the solvent was evaporated in vacuo. Purification by flash chromatography (hexanes: EA/2:1) afforded compounds **12a** and **12b** in 1.5:1 ratio and in 50% combined yield over three steps. **12a**: R_f = 0.50 (Hex:EA/2:1). $[\alpha]_D^{25}$ = −5 (c = 1.12, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ7.30−7.20 (3H), 7.05 (d, J = 6.4 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 6.79 (d, J = 8.8 Hz, 2H), 4.98 (ABq, J = 14.8 Hz, 1H), 3.99−3.76 (2H), 3.78 (s, 3H), 3.72 (ABq, J = 14.8 Hz, 1H), 3.22−3.18 (m, 1H), 2.98 (dd, J = 14.0, 6.4 Hz, 1H), 2.83 (dd, J = 14.0, 7.2 Hz, 1H), 2.41−2.37 (m, 1H), 2.32 (dd, J = 14.8, 4.4 Hz, 1H), 1.94−1.87 (m, 1H), 1.83 (dd, J = 14.8, 10.4 Hz, 1H), 1.85−1.76 (1H), 1.74−1.64 (2H), 1.59−1.24 (6H), 1.09 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.6, 172.5, 159.2, 138.2, 129.6, 129.5, 128.9, 128.8, 126.9, 114.1, 61.8, 60.7, 55.4, 46.3, 44.3, 41.9, 40.9, 35.6, 35.4, 29.1, 25.6, 22.5, 22.4, 14.3. HRMS (FAB) calcd for MH^+ ($C_{28}H_{36}NO_4$) 450.2644, found, 450.2649. **12b**: R_f = 0.60 (Hex:EA/2:1). $[\alpha]_D^{25}$ = −72 (c = 0.85, $CHCl_3$). ^{1}H NMR (400 MHz, C_6D_6): δ7.03−6.94 (5H), 6.83 (d, J = 8.8 Hz, 2H), 6.61 (d, J = 8.8 Hz, 2H), 5.20 (ABq, J = 14.8 Hz, 1H), 4.0−3.95 (m, 1H), 3.80−3.65 (2H), 3.22 (ABq, J = 14.8 Hz, 1H), 3.18 (s, 3H), 2.80−2.70 (2H), 2.47 (dd, J = 14.0, 8.8 Hz, 1H), 2.43−2.37 (m, 1H), 2.22−2.08 (3H), 1.76−1.68 (2H), 1.66−1.58 (m, 1H), 1.50−1.42 (2H), 1.17−1.05 (3H), 0.84 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.8, 172.5, 159.0, 139.1, 129.3, 129.2, 129.1, 128.9, 126.8, 114.1, 60.9, 57.9, 55.4, 44.7, 44.4, 44.3, 37.7, 34.4, 31.3, 30.9, 25.9, 22.3, 22.2, 14.3. HRMS (FAB) calcd for MH^+ ($C_{28}H_{36}NO_4$) 450.2644, found, 450.2646.

[(4*S*,2*E*)-Ethyl 4-(*N*-(4-methoxybenzyl)cyclohexa-1,3-diene-carboxamido)-2-methyl-5-phenylpent-2-enoate]tricarbonylir-on (18a) and (18b). To a solution of methanesulfonyl chloride (76.6 μL, 0.99 mmol) in freshly distilled CH_2Cl_2 (2.5 mL) under argon in a dried round-bottom flask at 0 °C was slowly added a solution of carboxylic acid 8 (175 mg, 0.66 mmol) and diisopropylethylamine (0.14 mL, 0.86 mmol) in freshly distilled CH_2Cl_2 (2.0 mL). Stirring was continued at this temperature for 1 h. Then, diisopropylethylamine (0.24 mL, 1.45 mmol) was added followed by a solution of amine 16 (465 mg, 1.32 mmol) in freshly distilled CH_2Cl_2 (2.0 mL). The temperature was allowed to rise to rt and the reaction mixture was stirred for 20 h and was quenched with 1 N HCl (3 mL), and CH_2Cl_2 (20 mL) was added. The organic layer was washed with 1 N HCl (3 mL) and brine (5 mL), was dried (Na_2SO_4), was filtered, and was concentrated in vacuo. The crude products were partially purified by flash chromatography (Hex:EA/8:1) to provide **18a** and **18b** in 81% combined yield. One diastereomer (163 mg, 41%): R_f = 0.35 (Hex:EA/3:2). $[\alpha]_D^{25}$ = +11.9 (c = 1.20, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ7.22−7.04 (5H), 6.93 (d, J = 9.6 Hz, 2H), 6.82−6.79 (2H), 6.20 (s, br, 1H), 5.30 (t, J = 4.8 Hz, 1H), 4.69 (ABq, J = 16 Hz, 1H), 4.36 (d, J = 16.4 Hz, 1H), 4.20−4.04 (3H), 3.80 (s, 3H), 3.45−340 (2H), 2.93 (dd, J = 13.6, 8.0 Hz, 1H), 1.87−1.68 (3H), 1.41−1.34 (m, 1H), 1.37 (d, J = 1.60 Hz, 3H), 1.22 (t, J = 7.2 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 174.2, 167.8, 159.1, 138.5, 138.1, 129.9, 129.5, 128.5, 128.4, 128.3, 126.5, 114.2, 85.6, 85.5, 85.5, 85.4, 64.5, 60.6, 59.5, 55.3, 38.5, 26.8, 23.6, 14.2, 12.2, 12.1. HRMS (FAB) calcd for MH^+ ($C_{32}H_{34}FeNO_7$) 600.1685, found, 600.1685. Further purification by flash chromatography (1.5% CH_3OH in CH_2Cl_2) afforded the other diastereomer (160 mg, 40%). R_f = 0.30 (1.5% MeOH in CH_2Cl_2). $[\alpha]_D^{25}$ = −16.1 (c = 4.12, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ7.21−7.06 (7H), 6.87 (d, J = 8.8 Hz, 2H), 5.94 (d, J = 1.2 Hz, 1H), 5.20 (dd, J = 5.2, 1.2 Hz, 1H), 5.00−4.80 (s, br, 1H), 4.45−4.20 (s, br, 1H), 4.14 (q, J = 7.2 Hz, 2H), 3.80 (s, 3H), 3.35 (d, J = 6.0 Hz, 1H), 3.17 (dd, J = 13.2, 8.0 Hz, 1H), 2.98 (dd, J = 12.8, 8.8 Hz, 1H), 1.95−1.35 (4H), 1.28 (s, 9H), 1.26 (t, J = 7.2 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 173.7, 167.9, 159.1, 137.7, 129.9, 129.6, 129.5, 128.4, 128.3, 126.5, 114.3, 114.2, 84.6, 84.2, 73.5, 63.7, 60.7, 59.5, 55.4, 26.3, 24.7, 14.2, 12.4. HRMS (FAB) calcd for MH^+ ($C_{32}H_{34}FeNO_7$) 600.1685, found, 600.1684.

[(2*R*)-Ethyl 2-[(3*S*,4*S*,5*S*)-6,9,η-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]deca-6,8-dien-4-yl]propanoate]tricarbonyliron (20a) and [(2*R*)-Ethyl 2-[(3*S*,4*S*,5*R*)- 6,9,η-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]deca-6,8-dien-4-yl]propanoate]tricarbonyliron (20a′). According to the general procedure for photothermally induced cyclizaton, a mixture of **18a** and **18b** (22.5 mg, 37.6 μmol) was refluxed in benzene (5.5 mL) in a dried quartz tube for 5.5 h to afford inseparable **20a** and **20a′** (15.1 mg, 67%) and the diene from demetallation of **20a** and **20a′** (0.7 mg, 4%) and the Diels−Alder reaction products **22a** and **22b** (2.0 mg 12%). **20a** and **20a′**: R_f = 0.36 (Hex:EA/2:1). ^{1}H NMR (400 MHz, $CDCl_3$), mixture of two isomers: δ7.34−6.76 (18H, two isomers), 5.77−5.74 (m, 1H, one isomer), 5.54−5.49 (2H, two isomers), 5.24−5.21 (m, 1H, another isomer), 4.87 (ABq, J = 14.8 Hz, 1H, another isomer), 4.67 (ABq, J = 14.4 Hz, 1H, one isomer), 3.78 (s, 3H, one isomer), 3.77 (s, 3H, another isomer), 4.00−2.3 (20H, two isomers), 2.20−1.80 (4H, two isomers), 1.13 (t, J = 6.8 Hz, 3H, another isomer), 0.99 (t, J = 7.2 Hz, 3H, one isomer), 0.59 (d, J = 7.2 Hz, 3H, one isomer), 0.42 (d, J = 6.8 Hz, 3H, another isomer). ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.6, 177.6, 176.7, 174.8, 174.7, 159.5, 159.4, 137.8, 137.6, 130.6, 130.5, 130.0, 129.7, 129.0, 128.9, 128.6, 128.3, 127.2, 126.9, 114.2, 114.1, 8.5, 86.9, 86.0, 82.5, 68.2, 63.0, 60.8, 60.7, 59.8, 59.2, 58.4, 57.8, 55.4, 51.1, 50.6, 50.0, 47.6, 45.7, 45.5, 45.1, 41.0, 40.3, 39.4, 38.8, 34.0, 14.2, 13.9, 10.7, 10.5. HRMS (FAB) calcd for MH^+ ($C_{32}H_{34}FeNO_7$) 600.1685, found, 600.1670. **22a** and **22b**: R_f = 0.40 (Hex:EA/2:1). ^{1}H NMR (400 MHz, $CDCl_3$) major isomer **22a**: δ7.21−6.68 (9H), 6.32 (dd, J = 6.8, 8.0 Hz, 1H), 6.13 (d, J = 8.0 Hz, 1H), 5.00 and 3.86 (ABq, J = 15.2 Hz, 2H), 4.15 (dq, J = 7.2, 1.2 Hz, 2H), 3.78 (s, 3H), 3.63−3.31 (m, 1H), 3.04−3.00 (m, 1H), 2.89−2.80 (3H), 1.69−1.50 (3H), 1.24 (t, J = 6.8 Hz, 3H), 0.85 (s, 3H). Minor isomer **22b**: δ7.21−6.68 (9H), 6.60 (d, J = 8.0, 1H), 6.22 (dd, J = 6.0, 8.0 Hz, 1H), 5.07 and 3.86 (ABq, J = 14.4 Hz, 2H), 4.06 (dq, J = 7.2, 1.2 Hz, 2H), 3.79 (s, 3H), 2.98−2.92 (m, 1H), 2.72−2.76 (m, 1H), 2.45−2.43 (m, 1H), 1.19 (t, J = 7.2 Hz, 3H), 0.93 (s, 3H), other peaks overlap with peaks of major isomer. ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.1, 177.0, 158.8, 138.5, 134.3, 132.4, 129.2, 129.1, 129.0, 128.6, 126.7, 113.9, 61.3, 59.1, 55.4, 50.6, 49.2, 48.4, 43.6, 41.7, 40.3, 27.6, 20.9, 20.3, 14.4. HRMS (FAB) calcd for MH^+ ($C_{29}H_{34}NO_4$) 460.2488, found, 460.2496.

(2*R*)-Ethyl 2-[(3*S*,4*S*,5*S*)-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]deca-6,8-dien-4-yl]propanoate and (2*R*)-Ethyl 2-[(3*S*,4*S*,5*R*)-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro-[4.5]deca-6,8-dien-4-yl]propanoate. Method A: According to the general procedure method A for demetallation, *E* products **20a** and **20a′** (13.8 mg, 23.0 μmol) were demetallated at rt for 24 h. Purification by flash chromatography (Hex:EA/3:1) provided two isomers (8.5 mg, 81%) as colorless oils. Method B: According to the general procedure method B for demetallation, *E* products **20a** and **20a′** (13.0 mg, 21.7 μmol) were demetallated for 24 h at rt. Purification by preparative TLC (Hex:EA/3:1) afforded two isomers

(8.3 mg, 83%) as colorless oils. One isomer: $R_f = 0.56$ (Hex:EA/2:1). $[\alpha]_D^{25} = +35.0$ ($c = 0.26$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ7.33−6.79 (9H), 6.11 (dd, $J = 4.2$, 9.6 Hz, 1H), 5.97−5.92 (m, 1H), 5.77−5.73 (m, 1H), 5.57 (d, $J = 9.6$ Hz, 1H), 5.07 (ABq, $J = 14.8$ Hz, 1H), 3.90−3.67 (2H), 3.83 (ABq, $J = 14.4$ Hz, 1H), 3.80 (s, 3H), 3.57−3.55 (m, 1H), 2.93 (d, $J = 5.6$ Hz, 2H, 2.79−2.75 (m, 1H), 2.64 (dd, $J = 3.2$, 4.0 Hz, 1H), 2.47−2.41 (m, 1H), 1.88 (dd, $J = 6.8$, 17.2 Hz, 1H), 1.11 (t, $J = 7.2$ Hz, 3H), 0.66 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.6, 175.4, 159.3, 137.7, 130.3, 130.0, 128.9, 128.4, 127.4, 127.1, 125.1, 125.0, 124.3, 114.1, 60.6, 57.9, 55.5, 47.8, 44.6, 44.4, 40.6, 40.1, 34.6, 14.2, 12.8. HRMS (FAB) calcd for MH^+ ($C_{29}H_{34}NO_4$) 460.2488, found, 460.2449. The other isomer: $R_f = 0.64$ (Hex:EA/2:1). $[\alpha]_D^{25} = -86.0$ ($c = 0.45$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ7.31−6.80 (9H), 6.04−5.98 (2H), 5.89−5.85 (m, 1H), 5.69 (d, $J = 8.0$ Hz, 1H), 4.89 (ABq, $J = 14.4$ Hz, 1H), 3.98 (ABq, $J = 14.4$ Hz, 1H), 3.79 (s, 3H), 3.75−3.67 (m, 1H), 3.49−3.38 (2H), 3.04−2.96 (2H), 2.74 (dd, $J = 13.6$, 8.0 Hz, 1H), 2.49−2.48 (m, 1H), 2.45−2.40 (m, 1H), 2.21 (dd, $J = 19.6$, 6.4 Hz, 1H), 1.02 (t, $J = 7.6$ Hz, 3H), 0.61 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.5, 174.7, 159.4, 137.9, 130.7, 130.5, 129.8, 128.8, 128.7, 126.8, 126.0, 124.4, 124.3, 114.2, 60.7, 58.0, 55.5, 48.3, 47.2, 45.1, 43.1, 41.0, 26.2, 14.1, 11.9. HRMS (FAB) calcd for MH^+ ($C_{29}H_{34}NO_4$) 460.2488, found, 460.2496.

(2*R*)-Ethyl 2-[(3*S*,4*S*)-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]decadien-4-yl]propanoate (24). Following the procedure used to prepare **12a** and **12b**, the (2*R*)-ethyl 2-[(3*S*, 4*S*)-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]deca-6,8-dien-4-yl]propanoate mixture (8.5 mg, 18.5 μmol) was hydrogenated to afford **24** (9.3 mg, 88%) as a colorless oil, which was purified by preparative TLC (2% MeOH in CH_2Cl_2). $R_f = 0.30$ (2% MeOH in CH_2Cl_2). $[\alpha]_D^{25} = -14.9$ ($c = 0.68$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ7.3−6.79 (9H), 4.81 (ABq, $J = 14.8$ Hz, 1H), 3.95 (ABq, $J = 14.4$ Hz, 1H), 3.79 (s, 3H), 3.75−3.67 (m, 1H), 3.54−3.50 (m, 1H), 3.42−3.34 (m, 1H), 3.05 (dd, $J = 5.6$, 13.2 Hz, 1H), 2.71 (dd, $J = 8.4$, 13.6 Hz, 1H), 2.58−2.52 (m, 1H), 2.46−2.45 (m, 1H), 1.90−1.60 (6H), 1.55−1.23 (4H), 1.03 (t, $J = 6.8$ Hz, 3H), 0.62 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.0, 175.1, 159.3, 138.2, 130.5, 129.7, 128.9, 128.8, 126.8, 114.0, 60.6, 58.0, 55.4, 46.5, 44.6, 43.7, 41.1, 38.7, 37.2, 28.7, 25.7, 23.1, 22.6, 14.2, 11.3. HRMS (FAB) calcd for MH^+ ($C_{29}H_{38}NO_4$) 464.2800, found, 464.2820.

(2*R*)-2-[(3*S*,4*S*)-3-Benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro-[4.5]decadien-4-yl]propyl (2*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (25). To a solution of **24** (5.3 mg, 11.4 μmol) in freshly distilled ether (0.2 mL), was carefully added $LiBH_4$ (1.51 mg, 68.6 μmol) at rt. After stirring was continued for 2 h, the reaction mixture was quenched with water (1 mL) and was extracted with ether (3 mL × 3). The ether layer was washed with brine (1 mL), was dried (Na_2SO_4), was filtered, and was concentrated in vacuo. The crude product was purified by preparative TLC (2% MeOH in CH_2Cl_2) to afford (2*R*)-2-[(3*S*, 4*S*)-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]decadien-4-yl]propanol (4.3 mg, 90%) as a colorless oil. $R_f = 0.25$ (2% MeOH in CH_2Cl_2). $[\alpha]_D^{25} = -3.4$ ($c = 0.36$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ7.38−6.86 (9H), 4.95 and 4.07 (ABq, $J = 14.4$ Hz, 2H), 3.81 (s, 3H), 3.26 (dd, $J = 4.0$, 12.8 Hz, 1H), 3.12 (dd, $J = 4.4$, 7.6 Hz, 1H), 2.79 (dd, $J = 4.2$, 11.2 Hz, 1H), 2.54 (dd, $J = 11.6$, 12.8 Hz, 1H), 2.33−2.28 (2H), 1.85−1.26 (12H), 0.24 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.7, 159.4, 138.4, 130.7, 129.8, 129.1, 128.8, 127.4, 114.2, 65.6, 57.1, 55.5, 46.6, 44.4, 39.8, 39.1, 37.8, 34.0, 28.5, 25.7, 23.2, 22.6, 11.2. HRMS (FAB) calcd for MH^+ ($C_{27}H_{36}NO_3$) 422.2695, found, 422.2698.

To a solution of this alcohol (2.9 mg, 6.9 μmol) in freshly distilled toluene (0.15 mL) was added diisopropylethylamine (11.5 μL, 69 μmol) and Mosher's chloride (10.4 μL, 55.0 μmol). Then, the reaction mixture was heated to 100 °C and was stirred for 16 h at this temperature. The cooled reaction mixture was quenched with 1 N HCl (0.5 mL) and was extracted with ether (1 mL × 3). The combined organic layer was washed with brine (1 mL), was dried (Na_2SO_4), was filtered, and was concentrated in vacuo. Residual solvent was removed under vacuum oil pump for 12 h to afford **25** (3.1 mg, 72%, de > 94%) as a colorless oil. $R_f = 0.30$ (Hex:EA/2:1). ^1H NMR (400 MHz, $CDCl_3$): δ7.40−6.82 (14H), 4.96 and 3.93 (ABq, $J = 14.8$ Hz, 2H), 3.81 (s, 3H), 3.44 (q, $J = 0.8$ Hz, 3H), 3.39 (dd, $J = 6.8$, 10.8 Hz, 1H), 3.18−3.14 (2H), 3.08 (dd, $J = 8.0$, 10.8 Hz, 1H), 2.57 (dd, $J = 10.4$, 14.0 Hz, 1H), 2.14 (s, 1H), 2.00−1.69 (6H), 1.60−1.14 (5H), 0.31 (d, $J = 6.8$ Hz, 3H). ^{19}F NMR (400 MHz, $CDCl_3$): δ67.49 (s, 3F, major isomer), 67.53 (s, 3F, minor isomer). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.1, 166.3, 159.4, 138.0, 132.3, 130.7, 129.8, 129.5, 129.2, 128.6, 127.5, 127.2, 114.1, 108.2, 77.4, 76.7, 69.4, 57.8, 55.5, 46.7, 44.4, 41.9, 40.4, 37.5, 31.5, 28.5, 25.6, 23.0, 22.3, 11.6. HRMS (FAB) calcd for MH^+ ($C_{37}H_{43}F_3NO_5$) 638.3093, found, 638.3060.

[(2*S*)-Methyl 2-(*N*-(4-methoxybenzyl)cyclohexa-1,3-dienecarboxamido)-3-phenylpropanoate]tricarbonyliron (33). To a solution of methanesulfonyl chloride (0.17 mL, 2.16 mmol) in freshly distilled CH_2Cl_2 (8 mL) at 0 °C under argon in a dried round-bottom flask was slowly added a solution of carboxylic acid **8** (382 mg, 1.44 mmol) and diisopropylethylamine (0.31 mL, 1.87 mmol) in freshly distilled CH_2Cl_2 (5 mL). Stirring was continued at this temperature for 1 h, and then diisopropylethylamine (0.52 mL, 3.17 mmol) was added followed by a solution of amine **31** (777 mg, 2.60 mmol) in freshly distilled CH_2Cl_2 (4 mL). The temperature was raised to 40 °C and the reaction mixture was stirred for 24 h. After the reaction mixture was cooled to rt, CH_2Cl_2 (30 mL) was added and the solution was washed with 1 N HCl (20 mL × 3) and brine (20 mL × 2), was dried (Na_2SO_4), was filtered, and was concentrated in vacuo. The crude products were purified by flash chromatography (Hex:EA/4:1) to provide **33** as a yellow viscous liquid. One isomer was obtained in 38% yield after a further purification by gravity chromatography (1% MeOH in CH_2Cl_2). $R_f = 0.55$ (Hex:EA/2:1). $[\alpha]_D^{25} = -84$ ($c = 1.21$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ7.27−6.76 (9H), 6.21 (s, br, 1H), 5.30 (s, br, 1H), 4.76 (ABq, $J = 14.8$ Hz, 1H), 3.84−3.78 (br, 1H), 3.80 (s, 3H), 3.64−3.58 (br, 1H), 3.58 (s, 3H), 3.44−3.22 (3H), 1.95−1.41 (4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ173.6, 171.2, 159.5, 130.2, 129.9, 128.6, 126.8, 114.1, 113.9, 110.0, 86.3, 85.7, 69.1, 64.7, 60.4, 55.5, 54.5, 52.1, 35.0, 27.2, 23.6. HRMS (FAB) calcd for MH^+ ($C_{28}H_{28}FeNO_7$) 546.1216, found, 546.1208. The other isomer was obtained in 37% yield. $R_f = 0.45$ (Hex:EA/2:1). $[\alpha]_D^{25} = -135$ ($c = 0.68$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ7.28−7.09 (7H), 6.88 (d, $J = 8.8$ Hz, 2H), 6.03 (d, $J = 4.4$ Hz, 1H), 5.23 (dd, $J = 6.0$, 4.4 Hz, 1H), 4.92 (ABq, $J = 16.0$ Hz, 1H), 3.88−3.73 (2H), 3.81 (s, 3H), 3.67 (s, 3H), 3.55 (dd, $J = 14.4$, 6.0 Hz, 1H), 3.77 (d, 5.6 Hz, 1H), 3.09 (dd, $J = 14.0$, 7.6 Hz, 1H), 1.96−1.44 (4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ195.8, 173.5, 170.8, 159.5, 139.1, 129.6, 129.0, 128.7, 127.7, 126.7, 114.4, 85.2, 84.6, 64.0, 61.3, 55.5, 53.1, 52.4, 35.6, 26.3, 24.7. HRMS (FAB) calcd for MH^+ ($C_{28}H_{28}FeNO_7$) 546.1216, found, 546.1202.

[*N*-(4-Methoxybenzyl)-*N*-((2*S*)-1-formyl-2-phenylethyl)cyclohexa-1,3-diene carboxamide]tricarbonyliron (34). To a solution of ester **33** (503 mg, 0.92 mmol) in Et_2O (4.4 mL) at −78 °C was added dropwise DIBAl-H (1.5 M in toluene, 2.45 mL, 3.68 mmol). After stirring at this temperature for 15 min, MeOH (4.4 mL) was added slowly, followed by saturated NaK tartrate (8 mL) at −78 °C. Then, the reaction mixture was allowed to warm to rt and was extracted with diethyl ether (15 mL × 3). The combined extract was dried (Na_2SO_4) and concentrated. Flash chromatography (Hex:EA/3:1) provided pure products **34**. One diastereomer (208 mg, 44%): $R_f = 0.60$ (Hex:EA/2:1). $[\alpha]_D^{25} = -79$ ($c = 1.71$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ9.35 (s, 1H), 7.36−6.85 (9H), 6.25 (d, $J = 4.0$ Hz, 1H), 5.35 (dd, $J = 6.0$, 4.8 Hz, 1H), 4.96 (ABq, $J = 14.0$ Hz, 1H), 3.80 (s, 3H), 3.53−3.51 (m, 1H), 3.37−3.30 (2H), 3.16−3.05 (2H), 2.02−1.41 (4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ197.2, 173.7, 159.8, 138.8, 129.9, 129.7, 128.8, 127.4, 127.0, 114.9, 86.3, 85.9, 67.3, 65.8, 65.6, 55.5, 53.8, 32.7, 27.7, 23.1.

HRMS (FAB) calcd for MH^+ ($C_{27}H_{26}FeNO_6$) 516.1112, found, 516.1100. The other diastereomer (171 mg, 36%): $R_f = 0.50$ (Hex:EA/2:1). $[\alpha]_D^{25} = -115$ ($c = 1.36$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ9.50 (s, 1H), 7.31−6.88 (9H), 6.06 (d, $J = 4.0$ Hz, 1H), 5.27 (dd, $J = 5.6$, 5.2 Hz, 1H), 5.00 and 3.77 (ABq, $J = 16.8$ Hz, 2H), 3.80 (s, 3H), 3.56 (dd, $J = 14.0$, 5.2 Hz, 1H), 3.47−3.40 (2H), 3.02 (dd, $J = 14.0$, 8.0 Hz, 1H), 1.98−1.47 (4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ196.4, 173.8, 159.7, 138.8, 129.4, 129.0, 128.4, 127.4, 126.9, 114.9, 85.3, 85.2, 69.5, 66.6, 64.6, 55.6, 52.4, 33.5, 26.7, 24.5. HRMS (FAB) calcd for MH^+ ($C_{27}H_{26}FeNO_6$) 516.1112, found, 516.1098.

[(4*S*,2*Z*)-Ethyl 4-(*N*-(4-methoxybenzyl)cyclohexa-1,3-dienecarboxamido)-2-methyl-5-phenylpent-2-enoate]tricarbonyliron (35a) and (35b). To a solution of ethyl 2-[bis(2,2,2-trifluoroethyl)phosphono]propanoate (347 mg, 1.00 mmol) in THF (6 mL) at 0 °C was carefully added potassium hydride (35% in oil, 68.7 mg, 0.60 mmol). The reaction was maintained at 0 °C for 30 min and then was cooled to −78 °C, and aldehyde **34** (344 mg, 0.67 mmol) in THF (5 mL) was added. The reaction mixture was stirred at −78 °C for 3 h and then was allowed to warm to 0 °C, was quenched with 1 N HCl (25 mL), and was extracted with diethyl ether (20 mL × 3). The combined organic layer was washed with brine (10 mL × 2) and was dried (Na_2SO_4). The solvent was evaporated in vacuo and the residue was further purified by flash chromatography (Hex:EA/6:1) to provide inseparable products **35a** and **35b** (251 mg, 70%). $R_f = 0.70$ (Hex:EA/2:1). ^1H NMR (400 MHz, $CDCl_3$) two diastereomers: δ7.20−6.56 (10H), 6.22, 5.70 (br, 1H), 5.31, 5.05 (br, 1H), 6.27−4.30 (3H), 3.93 (q, $J = 7.2$ Hz, 2H), 3.79, 3.78 (s, 3H), 3.60−3.22 (2H), 2.98 (dd, $J = 12.8$, 5.6 Hz, 1H), 1.84, 1.80 (d, $J = 1.2$ Hz, 3H), 2.0−1.0 (7H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 173.8, 167.3, 167.2, 159.0, 139.5, 139.2, 129.9, 129.8, 128.9, 128.7, 128.5, 128.4, 126.4, 114.5, 114.3, 114.0, 85.9, 83.8, 71.2, 64.9, 60.8, 60.6, 60.4, 55.5, 55.4, 54.3, 37.8, 27.0, 26.2, 25.5, 23.4, 20.7, 20.5, 14.2. HRMS (FAB) calcd for MH^+ ($C_{32}H_{34}FeNO_7$) 600.1685, found, 600.1682.

[(2*S*)-Ethyl 2-[(3*S*,4*S*,5*S*)-6,9,η-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]deca-6,8-dien-4-yl]propanoate]tricarbonyliron (28a) and [(2*S*)-Ethyl 2-[(3*S*,4*S*,5*R*)- 6,9,η-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]deca-6,8-dien-4-yl]propanoate]tricarbonyliron (28b). According to the general procedure for photothermally induced cyclization, a mixture of **35a** and **35b** (24.3 mg, 0.04 mmol) was refluxed in 5.5 mL of benzene under CO atmosphere for 5.5 h. Preparative TLC (1% THF in CH_2Cl_2) provided two isomers **28a** and **28b** in 72% combined yield. One isomer (12.6 mg, 52%, yellow sticky oil): $R_f = 0.55$ (Hex:EA/2:1 two developments). $[\alpha]_D^{25} = +64$ ($c = 0.84$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ7.35−6.84 (9H), 5.53 (dd, $J = 4.2$, 4.2 Hz, 1H), 5.28−5.25 (m, 1H), 4.48 and 4.43 (ABq, $J = 14.8$ Hz, 2H), 3.87−3.54 (2H), 3.79 (s, 3H), 3.54−3.50 (m, 1H), 3.36−3.32 (m, 1H), 2.95 (dd, $J = 13.2$, 4.4 Hz, 1H), 2.74−2.65 (2H), 2.50 (dd, $J = 6.8$, 1.2 Hz, 1H), 2.07 (dd, $J = 2.0$, 2.4 Hz, 1H), 2.02−1.92 (2H), 1.05 (t, $J = 7.2$ Hz, 3H), 0.56 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ211.9, 177.9, 173.8, 159.3, 137.1, 130.5, 130.2, 129.3, 128.9, 127.3, 114.1, 88.5, 82.7, 69.1, 64.0, 60.6, 60.5, 55.5, 51.0, 49.6, 46.3, 41.4, 38.3, 34.3, 15.4, 14.2. HRMS (FAB) calcd for MH^+ ($C_{32}H_{34}FeNO_7$) 600.1685, found, 600.1673. The other isomer (4.9 mg, 20%, yellow sticky oil): $R_f = 0.65$ (Hex:EA/2:1 two developments). $[\alpha]_D^{25} = -10$ ($c = 0.38$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ7.30−6.82 (9H), 5.76−7.72 (m, 1H), 5.53−5.50 (m, 1H), 4.66 and 4.11 (ABq, $J = 14.8$ Hz, 2H), 3.93−3.84 (2H), 3.78 (s, 3H), 3.62 (dd, $J = 10.8$, 4.0 Hz, 1H), 3.14−3.10 (2H), 2.91 (dq, $J = 6.8$, 2.0 Hz, 1H), 2.80 (dd, $J = 13.2$, 4.4 Hz, 1H), 2.2−2.11 (2H), 2.00 (dd, $J = 15.2$, 3.6 Hz, 1H), 1.93 (d, $J = 1.6$ Hz, 1H), 1.15 (t, $J = 6.8$ Hz, 3H), 0.46 (d, $J = 8.8$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ174.3, 173.8, 167.3, 167.2, 159.0, 139.5, 139.2, 129.9, 129.8, 128.9, 128.7, 128.5, 128.4, 126.4, 114.3, 114.0, 85.9, 83.8, 71.2, 64.9, 60.8, 60.6, 60.4, 55.5, 55.4, 64.3, 37.8, 27.0, 25.5, 23.4, 20.7, 20.5, 14.2. HRMS (FAB) calcd for MH^+ ($C_{32}H_{34}FeNO_7$) 600.1685, found, 600.1673. Products **20a** and **20a′** from *E*-substrates were also obtained in 3% yield and Diels−Alder products **39** in 14% yield. Characterizations for **39** are included in the Supporting Information.

(2*S*)-Ethyl 2-[(3*S*,4*S*,5*S*)-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]deca-6, 8-dien-4-yl]propanoate (29a) and (2*S*)-Ethyl 2-[(3*S*,4*S*,5*R*)-3-benzyl-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]deca-6,8-dien-4-yl]propanoate (29b). According to the general procedure for demetallation method B, *Z*-products **28a** and **28b** (15.6 mg, 26.0 μmol) and sat. $CuCl_2$ solution in EtOH (0.7 mL) were mixed. Stirring was continued at rt for 24 h. The crude products were purified by preparative TLC (Hex:EA/3:1) to afford **29a** and **29b** in 80% combined yield. **29a** (3.7 mg, 31%, colorless oil): $R_f = 0.40$ (Hex:EA/2:1). $[\alpha]_D^{25} = +37$ ($c = 0.31$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.31−6.82 (9H), 6.06 (dd, $J = 10.0$, 5.2 Hz, 1H), 5.94−5.90 (m, 1H), 5.75−5.71 (m, 1H), 5.55 (d, $J = 9.6$ Hz, 1H), 4.87 and 4.24 (ABq, $J = 15.2$ Hz, 2H), 3.99−3.89 (2H), 3.80 (s, 3H), 3.67−3.63 (m, 1H), 2.87−2.74 (3H), 2.45−2.38 (m, 1H), 2.22 (dd, $J = 4.4$, 4.8 Hz, 1H), 1.85 (dd, $J = 17.6$, 5.6 Hz, 1H), 1.16 (t, $J = 7.2$ Hz, 3H), 0.74 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ178.7, 175.0, 159.3, 137.3, 130.2, 130.0, 128.8, 127.1, 126.7, 125.7, 124.8, 124.1, 114.1, 60.5, 59.8, 55.5, 47.9, 46.9, 45.3, 40.5, 40.3, 35.2, 16.2, 14.3. HRMS (FAB) calcd for MH^+ ($C_{29}H_{34}NO_4$) 460.2488, found, 460.2475. 29b (5.8 mg, 49%, colorless oil): $R_f = 0.60$ (Hex:EA/ 2:1). $[\alpha]_D^{25} = -20$ ($c = 0.48$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ7.28−6.83 (9H), 6.03−5.95 (2H), 5.89−5.84 (m, 1H), 5.68 (dd, $J = 8.4$, 1.2 Hz, 1H), 4.56 and 4.43 (ABq, $J = 14.8$ Hz, 2H), 4.01−3.86 (2H), 3.79 (s, 3H), 3.55−3.51 (m, 1H), 2.93−2.83 (2H), 2.58−2.40 (3H), 2.13 (dd, $J = 3.6$, 2.4 Hz, 1H), 1.16 (t, $J = 7.2$ Hz, 3H), 0.56 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ177.6, 174.6, 159.2, 137.8, 131.2, 130.1, 129.8, 129.6, 128.8, 126.9, 126.3, 124.2, 124.0, 114.2, 60.8, 60.7, 55.5, 51.3, 47.5, 46.1, 42.0, 41.0, 26.5, 16.1, 14.2. HRMS (FAB) calcd for MH^+ ($C_{29}H_{34}NO_4$) 460.2488, found, 460.2489.

[(3*S*,4*S*,5*S*)-6,9,η-3-Benzyl-4-((1*S*)-formyl-1-ethyl)-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5] deca-6,8-diene]tricarbonyliron (40a) and [(3*S*,4*S*,5*R*)-6,9,η-3-Benzyl-4-((1*S*)-formyl-1-ethyl)-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5] deca-6,8-diene]tricarbonyliron (40b). To a solution of **28a** and **28b** (21.7 mg, 36.2 μL) in Et_2O (0.3 mL) at −78 °C was added dropwise DIBAl-H solution (1.5 M in toluene, 0.12 mL 181.1 μL). Stirring was continued for 1 h, and the reaction was quenched slowly with MeOH (0.6 mL) immediately followed by addition of sat. KNa tartrate solution (1 mL). The product was extracted with Et_2O (1.5 mL × 3), and the organic layer was dried (Na_2SO_4) and was concentrated, and the residue was purified by flash chromatography (Hex:EA/3:1) to afford two diastereomers **40a** and **40b** (15.6 mg, 77% combined yield). One isomer (11.1 mg, 55%, pale yellow oil): $R_f = 0.50$ (Hex:EA/1:1). $[\alpha]_D^{25} = +54$ ($c = 0.98$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ9.12 (s, 1H), 7.35−6.84 (9H), 5.55 (dd, $J = 5.2$, 5.2 Hz, 1H), 5.30−5.27 (m, 1H), 4.89 and 4.06 (ABq, $J = 14.8$ Hz, 2H), 3.80 (s, 3H), 3.36−3.33 (m, 1H), 3.16−3.12 (m, 1H), 3.06 (dd, $J = 13.2$, 4.4 Hz, 1H), 2.72 (dd, $J = 13.6$, 9.2 Hz, 1H), 2.67−2.60 (m, 1H), 2.49 (dd, $J = 6.4$, 1.2 Hz, 1H), 2.16 (dd, $J = 2.0$, 2.8 Hz, 1H), 2.01−1.88 (2H), 0.49 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ211.8, 202.6, 177.4, 159.5, 136.8, 130.5, 130.1, 129.1, 127.9, 127.5, 114.2, 88.6, 82.7, 68.7, 63.6, 59.4, 55.5, 50.7, 48.4, 46.4, 45.4, 40.7, 34.3, 11.8. HRMS (FAB) calcd for MH^+ ($C_{30}H_{30}FeNO_6$) 556.1423, found, 556.1413. Further purification by a preparative TLC (1.5% THF in CH_2Cl_2) provided the other isomer (4.5 mg, 22%, pale yellow oil). $R_f = 0.60$ (Hex:EA/1:1) or 0.70 (1.5% THF in CH_2Cl_2, three developments). $[\alpha]_D^{25} = -48$ ($c = 0.39$, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ9.20 (d, $J = 1.6$ Hz, 1H), 7.33−6.86 (9H), 5.78−5.75 (m, 1H), 5.53 (dd, $J = 6.4$, 4.4 Hz, 1H), 4.67 and 4.15 (ABq, $J = 14.4$ Hz, 2H), 3.81 (s, 3H), 3.20 (dd, $J = 9.6$, 4.0 Hz, 1H), 3.16−3.13 (m, 1H), 3.04 (dd, $J = 13.2$, 4.0 Hz, 1H), 2.84−2.80 (m, 1H), 2.76 (d, $J = 6.0$ Hz, 1H), 2.27 (dd, $J = 13.2$, 10.8 Hz, 1H), 2.15 (dd, $J = 15.2$, 2.0 Hz, 1H), 2.06−1.99 (2H), 0.39 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR

(100 MHz, $CDCl_3$): δ203.4, 176.3, 159.6, 137.1, 130.5, 129.6, 129.1, 128.1, 127.3, 114.3, 87.1, 85.9, 60.8, 59.9, 59.8, 55.5, 53.3, 52.0, 45.7, 45.5, 40.1, 12.4. HRMS (FAB) calcd for MH^+ ($C_{30}H_{30}FeNO_6$) 556.1423, found, 556.1392.

[(3*S*,4*S*,5*S*)-6,9,η-3-Benzyl-4-((3*R*)-but-1-en-3-yl)-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]deca-6,8-diene]tricarbonyliron (41a) and [(3*S*,4*S*,5*R*)-6,9,η-3-Benzyl-4-((3*R*)-but-1-en-3-yl)-2-(4-methoxybenzyl)-1-oxo-2-azaspiro[4.5]deca-6,8-diene]tricarbonyliron (41b). To a suspension of methyltriphenylphosphonium bromide (98 mg, 0.275 mmol) in THF (2.5 mL) at 0 °C was slowly added *n*-BuLi (2.5 M solution in hexanes, 0.11 mL, 0.275 mmol). After 1 h at this temperature, a solution of aldehydes **40a** and **40b** (61 mg, 0.11 mmol) in THF (2.5 mL) was added quickly. Stirring was continued at 0 °C for 10 min and then the reaction was allowed to reach rt and was maintained at this temperature for 1.5 h. Finally, the reaction was quenched with 1 N HCl (2 mL) and was extracted with Et_2O (4 mL × 3). The organic layer was dried (Na_2SO_4) and was concentrated in vacuo, and the residue was purified by flash chromatography (Hex:EA/4:1) to afford **41a** and **41b** (55 mg, 92% combined yield). One isomer (43 mg, 72%, pale yellow oil): R_f = 0.65 (Hex:EA/2:1). $[\alpha]_D^{25}$ = +42 (*c* = 0.23, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−6.80 (9H), 5.54 (dd, *J* = 6.4, 4.4 Hz, 1H), 5.29−5.26 (m, 1H), 4.97−4.88 (m, 1H), 4.85 and 3.94 (ABq, *J* = 14.4 Hz, 2H), 4.69−4.56 (2H), 3.80 (s, 3H), 3.36−3.25 (m, 1H), 3.19−3.16 (m, 1H), 3.09 (dd, *J* = 13.2, 4.8 Hz, 1H), 2.75 (dd, *J* = 13.6, 9.2 Hz, 1H), 2.63 (dd, *J* = 6.4, 1.2 Hz, 1H), 2.50−2.43 (m, 1H), 2.09 (dd, *J* = 16.0, 3.6 Hz, 1H), 2.05−1.93 (2H), 0.35 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ211.9, 177.9, 159.4, 137.7, 137.6, 130.7, 130.0, 129.0, 128.5, 127.2, 116.3, 114.0, 88.6, 82.6, 69.0, 63.9, 58.1, 55.5, 50.7, 50.6, 45.1, 41.0, 35.9, 33.4, 16.9. HRMS (FAB) calcd for MH^+ ($C_{31}H_{32}FeNO_5$) 554.1630, found, 554.1627. The other isomer (12 mg, 20%, pale yellow oil): R_f = 0.63 (Hex:EA/2:1). $[\alpha]_D^{25}$ = −63 (*c* = 0.19, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ7.31−6.84 (9H), 5.74−5.70 (m, 1H), 5.50 (dd, *J* = 6.4, 4.4 Hz, 1H), 5.15−5.07 (m, 1H), 4.78−4.65 (m, 2H), 4.70 and 4.03 (ABq, *J* = 14.4 Hz, 2H), 3.81 (s, 3H), 3.18−3.10 (2H), 3.03 (dd, *J* = 13.2, 4.4 Hz, 1H), 2.89 (d, *J* = 6.0 Hz, 1H), 2.69−2.65 (m, 1H), 2.32 (d, *J* = 13.2, 10.4 Hz, 1H), 2.12−1.99 (2H), 1.86 (d, *J* = 1.2 Hz, 1H), 0.28 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 159.5, 138.5, 137.7, 130.7, 129.7, 128.9, 128.6, 127.1, 116.3, 114.1, 87.0, 85.8, 60.9, 60.0, 58.8, 55.5, 54.0, 52.1, 45.5, 45.3, 40.2, 36.0, 18.0. HRMS (FAB) calcd for MH^+ ($C_{31}H_{32}FeNO_5$) 554.1630, found, 554.1620.

[(3*S*,3a*R*,4*R*,5*R*,5a*S*)-6,9, η-3-Benzyl-2-(4-methoxybenzyl)-2,3,-3a,4,5,5a-hexahydro-4,5-dimethylindeno[1-c]pyrrol-1-one]tricarbonyliron (42). According to the general photothermally induced cyclization procedure, a mixture of **41a** and **41b** (8.3 mg, 15 μmol) was heated at 160 °C in mesitylene (2.3 mL) under CO atmosphere for 9 h. Preparative TLC (Hex:EA/3:1) provided compound **42** (4.3 mg, 52%). Starting material (25%) was also recovered. R_f = 0.60 (Hex:EA/ 2:1). $[\alpha]_D^{25}$ = +23 (*c* = 0.80, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ7.33−6.83 (9H), 5.37 (dd, *J* = 6.4, 4.4 Hz, 1H), 5.31−5.28 (m, 1H), 5.12 and 3.89 (ABq, *J* = 14.8 Hz, 2H), 3.81 (s, 3H), 3.42−3.87 (m, 1H), 2.94 (d, *J* = 6.4 Hz, 1H), 2.83−2.74 (2H), 2.39 (dd, *J* = 9.2, 3.6 Hz, 1H), 2.35−2.28 (m, 1H), 2.17 (dd, *J* = 6.4, 1.2 Hz, 1H), 2.11 (d, *J* = 8.4 Hz, 1H), 1.24−1.19 (m, 1H), 0.88 (d, *J* = 7.2 Hz, 3H), 0.47 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ212.3, 176.5, 159.3, 136.6, 130.4, 129.6, 128.8, 128.6, 127.1, 114.3, 86.6, 83.6, 67.8, 65.8, 61.4, 55.5, 54.9, 52.1, 51.4, 44.8, 43.3, 41.3, 40.1, 13.8. HRMS (FAB) calcd for MH^+ ($C_{31}H_{32}FeNO_5$) 554.1630, found, 554.1654.

(3*S*,3a*R*,4*R*,5*R*,5a*S*)-2-(4-Methoxybenzyl)-3-benzyl-2,3,3a,4,5,-5a-hexahydro-4,5-dimethylindeno[1-c]pyrrol-1-one (43). According to the general procedure method B for demetallation, compound **42** (10.0 mg, 18.0 μmol) was treated with sat. $CuCl_2$ solution in EtOH (0.5 mL) at rt for 24 h. The purification by preparative TLC (Hex:EA/3:1) afforded **43** (5.3 mg, 72%) as a colorless oil. R_f = 0.40 (Hex:EA/2:1). $[\alpha]_D^{25}$ = −20 (*c* = 0.45, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3/C_6D_6$=1/3): δ7.11−6.73 (9H), 5.84−5.70 (2H), 5.55−5.45 (2H), 5.22 and 3.70 (ABq, *J* = 14.4 Hz, 2H), 3.44−3.40 (m, 1H), 3.34−3.32 (m, 1H), 3.35 (s, 3H), 2.87 (dd, *J* = 13.2, 4.0 Hz, 1H), 2.32 (dd, *J* = 13.6, 9.2 Hz, 1H), 2.26 (dd, *J* = 9.2, 1.6 Hz, 1H), 1.45−1.40 (m, 1H), 1.35−1.28 (m, 1H), 0.77 (d, *J* = 6.4 Hz, 3H), 0.22 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ178.4, 159.4, 137.4, 130.2, 129.8, 128.8, 127.2, 126.9, 125.3, 123.3, 123.30, 114.3, 100.4, 56.7, 56.2, 55.5, 55.3, 47.0, 44.7, 44.4, 44.3, 40.9, 14.2, 13.2. HRMS (FAB) calcd for MH^+ ($C_{28}H_{32}NO_2$) 414.2433, found, 414.2426.

[*N*-(4-Methoxybenzyl)-N-((2*S*,3*Z*)-4-methyl-1-phenylhexa-3,5-dien-2-yl)cyclohexa-1, 3-dienecarboxamide]tricarbonyliron (48). Following the procedure for preparation of **18a** and **18b**, to a solution of methanesulfonyl chloride (7.4 μL, 0.096 mmol) in freshly distilled CH_2Cl_2 (0.3 mL) was slowly added a solution of carboxylic acid **8** (17 mg, 0.065 mmol) and diisopropylethylamine (13.8 μL, 0.083 mmol) in freshly distilled CH_2Cl_2 (0.3 mL). Stirring was continued for 1 h, and then diisopropylethylamine (23.3 μL, 0.141 mmol) was added followed by the solution of amine **47** (32 mg, 0.104 mmol) in freshly distilled CH_2Cl_2 (0.3 mL). The reaction was maintained at rt for 24 h, and then the temperature was allowed to rise to 40 °C, and the reaction mixture was stirred for 10 h. The crude products were purified by flash chromatography (Hex:EA/4:1) to provide two inseparable diastereomers **48** (29 mg, 83%). R_f = 0.75 (Hex:EA/2:1). ^{1}H NMR (400 MHz, $CDCl_3$) two diastereomers: δ7.20−6.77 (9H), 6.26−5.60 (3H), 5.40−4.20 (6H), 3.81 (s, 3H), 3.50−3.14 (2H), 2.88−2.81 (m, 1H), 2.10−1.40 (4H), 1.73, 1.72 (d, *J* = 1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ174.4, 173.7, 168.5, 168.2, 159.0, 139.4, 135.5, 133.3, 133.0, 129.8, 129.7, 128.9, 128.6, 128.5, 128.4, 128.3, 128.1, 126.4, 115.3, 114.3, 114.2, 88.9, 88.8, 86.3, 86.2, 85.7, 84.9, 84.2, 74.2, 71.6, 64.6, 64.0, 63.8, 63.5, 58.1, 55.5, 55.4, 52.5, 40.7, 39.8, 26.8, 26.5, 25.7, 25.6, 24.9, 24.0, 22.8, 19.9, 19.8. HRMS (FAB) calcd for MH^+ ($C_{31}H_{32}FeNO_5$) 554.1630, found, 554.1613.

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Supporting Information Available: Experimental procedures for preparation of compounds **6**−**7**, **13**−**17**, **23**, **31**−**32**, **36**−**39**, and **44**−**47** and copies of NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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