Diastereoselective Synthesis of Nitrogen-Containing Heterobicyclic and -tricyclic Skeletons via Intramolecular Cyclization of (η^4-diene)Fe(CO)$_3$ Complexes Bearing Amino Acid Derivatives

Ming-Chang P. Yeh,* L.-W. Chuang, C.-C. Hwu, J.-M. Sheu, and L.-C. Row

Department of Chemistry, National Taiwan Normal University, 88 Section 4, Ding-Jou Road, Taipei, Taiwan 117, ROC

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Addition of secondary amino acid derivatives to (η^5-pentadienyl)tricarbonyliron cations gives (η^4-diene)tricarbonyliron complexes in high yields with amino ester groups at the terminal position of the diene ligands. Treatments of the adducts containing a sarcosine, phenylalanine, or alanine moiety with lithium diisopropylamide (LDA), under an atmosphere of carbon monoxide, furnish fused 3-azabicyclo[3.3.0]octanecarboxylic acid derivatives. Under the same reaction conditions, intramolecular cyclizations of complexes containing a proline or pipecolinic acid derivative at the terminal position of the diene ligands give 6-azatricyclo-[6.3.0.0^{2,6}]undecane and 7-azatricyclo[7.3.0.0^{2,7}]dodecane ring systems, respectively, whereas treatment of the complex containing a nipecotic acid derivative provides a bridged 8-azatricyclo[6.3.1.0^{2,6}]dodecanecarboxylic acid derivative.

Nitrogen-containing heterocyclic compounds have figured prominently in chemistry due to their useful pharmacological properties, their structural novelty, and their attendant rich chemistry.[1] In spite of the numerous literature on the synthesis of nitrogen-containing heterobicyclic compounds,[2] there have been few reports on the preparation of nitrogen-containing heterobicyclic and -tricyclic compounds promoted by transition metals. Of these reactions, however, formation of fused nitrogen-containing heterobicyclic compounds has so far been restricted to only cobalt-,[3] chromium-,[4] titanium-,[5] nickel-,[6] iron-,[7] or palladium-promoted[8] cyclization of unsaturated molecules. Only limited examples of cobalt-mediated (the Pauson–Khand reaction) coupling reactions of alkyne to alkene followed by radical cyclization to give angularly fused triquinanes containing a nitrogen atom[9a] and a palladium-catalyzed cyclization of a polyenyne to give a linearly fused triquinane containing a nitrogen atom have been explored.[9b] In this paper, we report that nitrogen-containing fused bicyclic, linearly fused tricyclic, and bridged tricyclic skeletons can be constructed by the intramolecular cyclization of the diene–iron complexes bearing amino acid derivatives at the terminal position of the diene ligands.

Preparation of Starting Complexes

The addition of primary amines to the (η^5-pentadienyl)Fe(CO)$_3$ cation (**1a**) is known to proceed by exo attack to produce (η^4-*cis*-dienylamine)Fe(CO)$_3$ complexes and the binuclear species obtained by further reaction with the cation.[10] This has been confirmed in our preliminary investigations; the reaction of the primary amino ester derivative $H_2NCH_2CO_2Et$ with **1a** provided the binuclear species as the major product in 51% yield.

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(1) (a) Jutz, J. C. *Top. Curr. Chem.* **1978**, *73*, 125. (b) Katritzky, A. R. *Tetrahedron* **1980**, *36*, 679. (c) Boger, D. L. *Chem. Rev.* **1986**, *86*, 781. (c) Jones, G. In *Quinolines*; Jones, G., Ed.; Wiley-Interscience: London, 1977; p 1. (d) Dyke, S. F.; Kinsman, R. G. In *Isoquinolines*; Grethe, G., Ed.;Wiley-Interscience: New York, 1981; p 1. (e) Sundberg, R. J. *The Chemistry of Indoles*, Academic Press, New York, **1970**. (f) Cordell, G. A. *Introduction to Alkaloids*; Wiley-Interscience: New York, 1981. (g) Williams, D. R.; Brown, D. L.; Benbow, J. W. *J. Am. Chem. Soc.* **1989**, *111*, 1923. (h) Boger, D. L.; Mullican, M. D. *J. Org. Chem.* **1984**, *49*, 4033. (i) Williams, J. P.; St. Laurent, D. R.; Friedrich, D.; Pinard, E.; Roden, B. A.; Paquette, L. A. *J. Am. Chem. Soc.* **1994**, *116*, 4689. (j) Wang, Z.; Jimenez, L. S. *J. Am. Chem. Soc.* **1994**, *116*, 4977.

(2) (a) Black, D. St. C.; Doyle, J. E. *Adv. Heterocycl. Chem.* **1980**, *27*, 1. (b) Mulzer, J.; Becker, R.; Brunner, E. *J. Am. Chem. Soc.* **1989**, *111*, 7500. (c) Pearson, W. H.; Walavalkar, R.; Schkeryantz, J. M.; Fang, W. K.; Blickensdorf, J. D. *J. Am. Chem. Soc.* **1993**, *115*, 10183. (d) Tückmantel, W.; Andree, G.; Seidel, A.; Schmickler, H.; Lex, J.; Kraka, E.; Haug, M.; Cremer, D.; Vogel, E. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 592. (e) Kato, H.; Arikawa, Y.; Hashimoto, M.; Masuzawa, M. *J. Chem. Soc., Chem. Commun.* **1983**, 938. (f) Tokitoh, N.; Okazaki, R. *J. Am. Chem. Soc.* **1987**, *109*, 1856. (g) Shea, K. J.; Lease, T. G.; Ziller, J. W. *J. Am. Chem. Soc.* **1990**, *112*, 8627. (h) Overman, L. E.; Mendelson, L. T.; Jacobsen, E. J. *J. Am. Chem. Soc.* **1983**, *105*, 6629. (i) Overman, L. E.; Jacobsen, E. J.; Doedens, R. J. *J. Org. Chem.* **1983**, *48*, 3393. (j) Jacobsen, E. J.; Levin, J.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 4329.

(3) (a) Jeong, N.; Hwang, S. H.; Lee, Y. *J. Am. Chem. Soc.* **1994**, *116*, 3159. (b) Chung, Y. K.; Lee, B. Y.; Jeong, N.; Hudecek, M.; Pauson, P. L. *Organometallics* **1993**, *12*, 220. (c) Brown, S. W.; Pauson, P. L. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1205.

(4) (a) Dötz, K. H.; Schäfer, T.; Harms, K. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 176. (b) Audouin, M.; Blandinières, S.; Parlier, A.; Rudler, H. *J. Chem. Soc., Chem. Commun.* **1990**, 23.

(5) Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 4912.

(6) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 1286.

(7) (a) Knölker, H.-J. *Synlett* **1992**, 371. (b) Knölker, H.-J.; Heber, J. *Synlett* **1993**, 924. (c) Knölker, H.-J.; El-Ahl, A.-A.; Weingärter, G. *Synlett* **1994**, 194.

(8) (a) Hegedus, L. S. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1113. (b) van der Schaaf, P. A.; Sutter, J.-P.; Grellier, M.; van Mier, G. P. M.; Spek, A. L.; van Koten, G.; Pfeffer, M. *J. Am. Chem. Soc.* **1994**, *116*, 5134. (c) Bäckvall, J.-E.; Andersson, P. G. *J. Am. Chem. Soc.* **1990**, *112*, 3683. (d) Andersson, P. G.; Bäckvall, J. E. *J. Am. Chem. Soc.* **1992**, *114*, 8696. (e) Grigg, R.; Dorrity, M. J.; Malone, J. F.; Sridharan, V.; Sukirthalingam, S. *Tetrahedron Lett.* **1990**, *31*, 1343. (f) Trost, B. M.; Chen, S.-F. *J. Am. Chem. Soc.* **1986**, *108*, 6053. (g) Trost, B. M.; Scanlan, T. S. *J. Am. Chem. Soc.* **1989**, *111*, 4988. (h) Trost, B. M.; van Vranken, D. L. *J. Am. Chem. Soc.* **1993**, *115*, 444. (i) Trost, B. M.; Marrs, C. M. *J. Am. Chem. Soc.* **1993**, *115*, 6636.

(9) (a) Clive, D. L. J.; Cole, D. C.; Tao, Y. *J. Org. Chem.* **1994**, *59*, 1396. (b) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1993**, *115*, 9421.

(10) (a) Maglio, G.; Palumbo, R. *J. Organomet. Chem.* **1974**, *76*, 367. (b) Maglio, G.; Musco, A.; Palumbo, R. *J. Organomet. Chem.* **1971**, *32*, 127.

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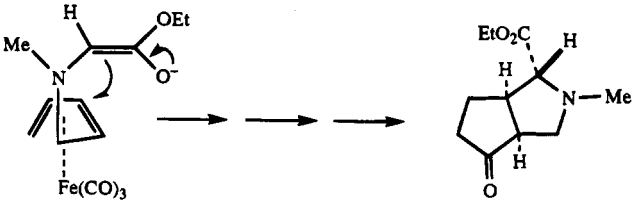
With secondary amino ester derivatives, however, we were able to introduce an amino ester moiety at the C-5 position of the diene ligand under mild reaction conditions.[11] Thus, additions of protected amino acids **2a–h** (1.2 molar equiv) to a stirred suspension of cations **1a–c** at −40 °C for 20 min and 25 °C for 30 min, followed by workup, gave (η^4-*cis*-dienylamine)$Fe(CO)_3$ complexes **3a–j** as the major products after purification by flash column chromatography on silica gel. The yields of the additions were generally high (69–98%; Table 1). It must be mentioned that complexes **3b,d,i,j** were obtained as mixtures of diastereomers and were used for the intramolecular cyclization without further separation. The stereochemistry of **3** was assigned as cis on the basis of comparison of their ^1H NMR spectral data, which were close to those of cis C-5-substituted (η^4-diene)$Fe(CO)_3$ complexes made by addition of functionalized zinc–copper reagents to cation **1**[12] and were consistent with the ^1H NMR spectral data of (η^4-*cis*-dienylamine)$Fe(CO)_3$ complexes reported in the literature.[10b]

Intramolecular Cyclization Reactions

Our cyclization study began with complex **3a**. Treatment of **3a** with 1.2 molar equiv of LDA at −78 °C under an atmosphere of CO provided a major product in 50% yield, identified as the 3-azabicyclo[3.3.0]octanecarboxylic acid derivative **4a** with an incorporated CO at the C-6 position. It is important to note that three new stereogenic centers of compound **4a** are created; however, only the single diastereomer shown was isolated. NMR (nuclear magnetic resonance) spectroscopy studies provided the initial evidence for support of the structural assignments. The ^1H NMR spectrum of compound **4a** exhibited the following: two narrow quartets, centered at δ 4.16, assigned to the two diastereotopic methylene protons of C-10; a doublet of doublets, centered at δ 3.29, assigned to one of the diastereotopic methylene protons at C-4; a singlet at δ 2.97, assigned to the proton at C-2; a multiplet, centered at δ 2.95, assigned to the proton at C-1; a multiplet, centered at δ 2.80, assigned to the proton at C-5; a doublet of doublets, centered at δ 2.55, assigned to one of the diastereotopic methylene protons at C-4; a multiplet, centered at δ 2.36, assigned to the protons at C-7 and C-8; a singlet at δ 2.30, assigned to the methyl protons at the nitrogen atom; a multiplet, centered at δ 2.11, assigned to the protons at C-7; a multiplet, centered at δ 1.94, assigned to the protons at C-8; a triplet, centered at δ 1.24, assigned to the methyl group at C-11. The ^{13}C NMR spectrum of complex **4a** exhibited the following: a signal at δ 219.9, assigned to C-6 (carbonyl of the keto functionality); a signal at δ 172.3, assigned to C-9 (carbonyl of the ester functionality); a signal at δ 73.0, assigned to C-2; a signal at δ 60.7, assigned to C-10; a signal at δ 57.5, assigned to C-4; a signal at δ 50.4, assigned to C-5; a signal at δ 45.7, assigned to C-1; a signal at δ 38.9, assigned to C-7; a signal at δ 37.3, assigned to the methyl carbon at the nitrogen atom; a signal at δ 25.2, assigned to C-8; a signal at δ 14.4, assigned to C-11. Compound **4a** results from anti addition of the α-face of the kinetic enolate **5** at the internal position (C-3) of the diene ligand. None of the product arising from



5 **4a**

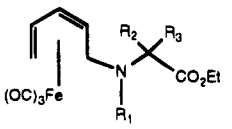
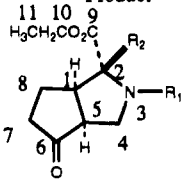
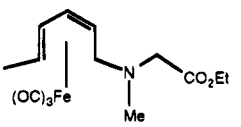
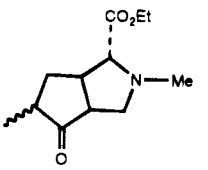
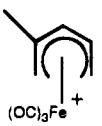
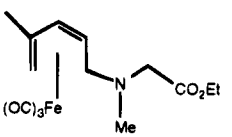
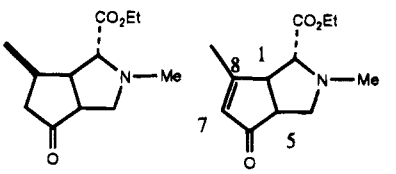
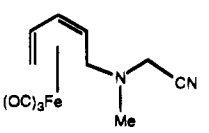
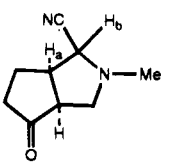
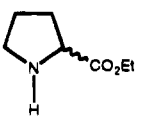
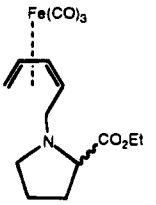
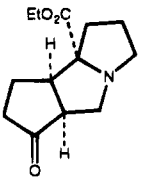
addition at the β-face of **5** has been found. This result agrees closely with the formation of a single diastereomer of fused bicyclo[3.3.0]octanecarboxylic acid derivatives obtained by the intramolecular cyclization of (η^4-diene)$Fe(CO)_3$ complexes bearing functionalized side chains at the terminal position of the diene ligands.[12a] Several examples of cyclization of diene–iron complexes bearing amino acid derivatives are summarized in Table 1.

Several entries in Table 1 deserve special mention. Substrates with tertiary α-carbons **3b–d** (obtained from additions of the phenylalanine and alanine derivatives to cation **1a**, respectively, entries 2–4, Table 1), also underwent intramolecular cyclization to produce 3-azabicyclo[3.3.0]octanecarboxylic acid derivatives **4b–d**, respectively, as the only diastereomeric product in each case. All exo carbethoxy groups of **4b–d** were assigned on the basis of the NOE difference spectrum of **4b** and **4c**. Irradiation of the benzylic protons of **4b** did not result in enhancement of the proton at C-1, while irradiation of the methyl protons at C-2 of **4c** provided enhancement of the exo proton at C-4. No enhancement of protons at C-1 and C-5 was observed. Attempts to assign the relative stereochemistry of **4d** using NOE analysis were unsuccessful. The generation of a single product from intramolecular cyclization of a mixture of diastereomeric dienylamine precursors further substantiates the formation of a common intermediate, *i.e.*, the planar enolate anion as mentioned above. However, intramolecular cyclization of the substrate with an additional methyl group at the terminal position of the diene ligand **3e** gave a mixture of diastereomers in a ratio of 1:1 (entry 5, Table 1), presumably derived from epimerization at the α-carbon (C-7) of the keto group during acid quenching and aqueous workup. The epimerization of the α-carbon (C-7) of the keto group during acid quenching had also been observed in the carbocyclic analog.[12a] It must be mentioned that the ratio of the two diastereomeric products of the carbocyclic analog depended on the isolation processes. Isolation of the reaction mixture immediately after acid quenching afforded a single diastereomer. However, both diastereomers were obtained when the reaction mixture was stirred in trifluoroacetic acid for a long period of time (12 h). Thus, the difference may be due to the epimerization of the α-carbon (C-7) of the keto group during acid quenching. However, isolation of the reaction mixture from the intramolecular cyclization of **3e** with an amino acid derivative at the terminal position of the diene ligand immediately after acid

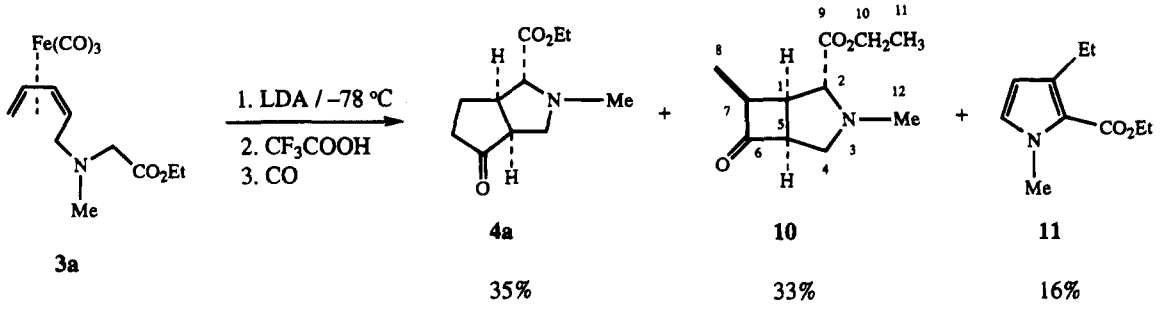
(11) C-Alkylation of protected amino acids to tricarbonyl(η^5-dienyl)-iron cations were reported; see: (a) Dunn, M. J.; Jackson, R. F. W.; Stephenson, G. R. *Synlett* **1992**, 905. (b) Dunn, M. J.; Jackson, R. F. W. *J. Chem. Soc., Chem. Commun.* **1992**, 319. (c) Genet, J.-P.; Hudson, R. D. A.; Meng, W.-D.; Roberts, E.; Stephenson, G. R.; Thorimbert, S. *Synlett* **1994**, 631.

(12) (a) Yeh, M. C. P.; Sheu, B. A.; Fu, H. W.; Tau, S. I.; Chuang, L. W. *J. Am. Chem. Soc.* **1993**, *115*, 5941. (b) Yeh, M. C. P.; Sun, M.-L.; Lin, S.-K. *Tetrahedron Lett.* **1991**, *32*, 113.

Table 1. Synthesis and Intramolecular Cyclization of Complexes 3a–g

Entry	Cation	amino acid derivatives	Complex	Product	Yield (%)
1	 **1a**	$HN(Me)CH_2CO_2Et\cdot HCl$ **2a**	 **3a** $R_1 = Me, R_2 = R_3 = H$	 **4a** $R_1 = Me, R_2 = H$	50%
2	**1a**	$NH(Et)CH(CH_2Ph)CO_2Et$ **2b**	**3b** $R_1 = Et, R_2 = H, R_3 = CH_2Ph$	**4b** $R_1 = Et, R_2 = CH_2Ph$	33%
3	**1a**	$NH(Et)CH(Me)CO_2Et$ **2c**	**3c** $R_1 = Et, R_2 = H, R_3 = Me$	**4c** $R_1 = Et, R_2 = Me$	44%
4	**1a**	$NH(CH_2CH{=}CHCH_3)CH(Me)CO_2Et$ **2d**	**3d** $R_1 = CH_2CH{=}CHCH_3, R_2 = H,$ $R_3 = Me$	**4d** $R_1 = CH_2CH{=}CHCH_3,$ $R_2 = Me$	69%
5	 **1b**	**2a**	 **3e**	 **4e**	36%
6	 **1c**	**2a**	 **3f**	 **4f** : **6** = 1.2 : 1	80%
7	**1a**	$HN(Me)CH_2CN\cdot HCl$ **2e**	 **3g**	 **4g** exo : endo = 1.4 : 1	65%
8	**1a**	 **2f**	 **3h**	 **7**	13%

Scheme 1



quenching gave a mixture of diastereomers of **4e** in a ratio of 1:1. This difference is not understood. It was suggested that the basicity of the nitrogen atom in **4e** may facilitate the epimerization process at the α-carbon (C-7) of the keto group during the isolation process. Surprisingly, intramolecular cycloaddition of the substrate with a methyl group at the internal position (C-2) of the diene ligand, for example complex **3f**, produced the usual type of 3-azabicyclo[3.3.0]octanecarboxylic acid derivative **4f** (46%) along with the 3-azabicyclo-[3.3.0]octenecarboxylic acid derivative **6** (34%) (entry 6, Table 1). The stereochemistry for the carbethoxy group in **4f** assigned as exo was based on the same hypothesis as for the formation of **4a**. Attempts to confirm the relative stereochemistry of **4f** using NOESY measurements were unsuccessful. The tentative assignment of the endo methyl group of **4f** was based on the previous report of the intermolecular nucleophilic addition/carbonylation of diene–iron complexes with either methoxy or methyl substituents at C-2 of the diene ligand.[13] In both cases, cis-3,4-disubstituted cyclopentanones were obtained. Moreover, the stereochemistry for the methyl group at C-8 assigned as endo was consistent with anti addition of the enolate to the diene ligand as shown in Scheme 5. NMR and infrared spectra of **6** exhibited signal patterns corresponding to an α,β-unsaturated ketone. The proton at δ 5.95, a singlet, was assigned to the vinyl proton at C-7; a three-proton singlet at δ 2.19 was assigned to the methyl group at C-9. The carbon at δ 209.2 was assigned to the carbonyl of the keto functionality; two carbons at δ 171.7 and 131.3 were assigned to the vinyl carbons at C-8 and C-7, respectively. The typical absorption at 1703 cm^{-1} for the keto functionality of an α,β-unsaturated ketone in the infrared spectrum of **6** also proved the structural assignments.

3g, a substrate with a (cyanomethyl)methylamino group, also underwent intramolecular cyclization to produce a mixture of exo and endo isomers in a ratio of 1.4:1 (entry 7, Table 1). Unlike an ester group, a cyano group is rather small. Thus, either one of the two α-protons is possibly removed by LDA under the kinetically controlled reaction conditions.[12a] The major isomer assigned as exo is based on ^1H NMR studies. The proton at δ 3.71, a singlet, was assigned to H_b. The coupling constant for H_a-H_b (J_{ab}) of 0 Hz agrees with the 0 Hz coupling constant for similarly disposed trans hydrogens of **4a**. Furthermore, the dihedral angle of 95.26° for $H_a-C_1-C_2-H_b$ analyzed by the molecular modeling (Chem 3D program) of **4g** (exo) is consistent with the angle (95.30°) obtained by X-ray diffraction analysis, which proves the 0 Hz coupling constant for H_a-H_b. The coupling constant for H_a-H_b of the endo isomer of **4g** is 7.8 Hz, which agrees with a dihedral angle ($H_a-C_1-C_2-H_b$) of 37.5° analyzed by molecular modeling (Chem 3D).[14]

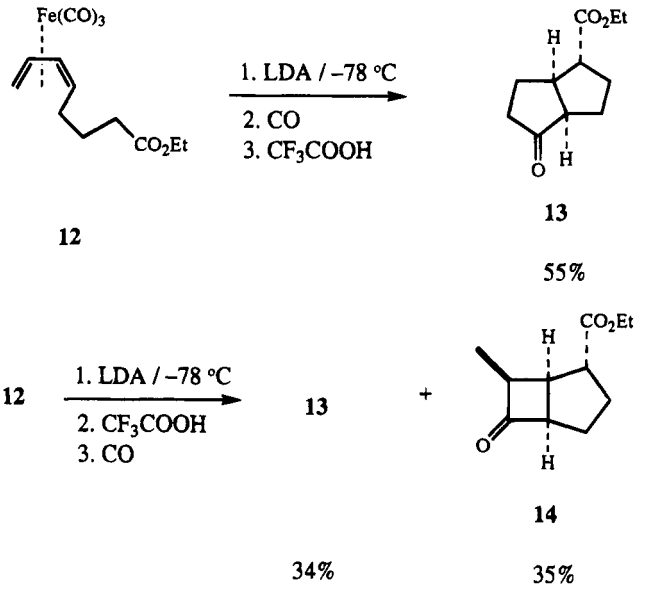
Under the same reaction conditions, we were able to construct the nitrogen-containing linearly fused tricyclo-[6.3.0.$0^{2,6}$]undecanecarboxylic acid derivative **7**, linearly fused tricyclo[7.3.0.$0^{2,7}$]dodecanecarboxylic acid derivative **8**, and the bridged tricyclo[6.3.1.$0^{2,6}$]dodecanecarboxylic acid derivative **9** via intramolecular cyclization of (η^4-1,3-diene)$Fe(CO)_3$ complexes bearing a proline, pipecolinic, and nipecotic acid derivatives, respectively, at the terminal positions of the diene ligands. Attempts to confirm stereochemistries of carbethoxy groups of tricyclic compounds **7–9** using various methods (NOE and NOESY spectra) were unsuccessful. All carbethoxy groups of **7–9** were tentatively assigned as exo on the basis of addition of the α-face of the kinetic enolate at the C-3 position of diene ligands. It is important to note that three new stereogenic centers of the fairly complicated tricyclic compounds **7–9** are created; however, only the single diastereomers shown were isolated.

Interestingly, the reaction undergoes different pathways by direct quenching of the reaction mixture with acid followed by addition of CO. Thus, treatment of complex **3a** with 1.2 molar equiv of LDA at −78 °C under nitrogen for 2 h followed by acid quenching and then addition of CO (14–18 psi) affords **4a** (35%), the 3-azabicyclo[3.2.0]heptanecarboxylic acid derivative **10** (33%), and the pyrrole derivative **11** (16%) after purification by flash column chromatography and distillation under reduced pressure (Scheme 1). NMR (nuclear magnetic resonance) spectroscopy studies provided the initial evidence for support of the structural assignments. The ^1H NMR spectrum of compound **10** exhibited the following: two narrow quartets, centered at δ 4.16, assigned to the two diastereotopic methylene protons of C-10; a multiplet, centered at δ 3.67, assigned to the proton at C-5; a singlet at δ 3.63, assigned to the proton at C-2; a multiplet, centered at δ 3.42, assigned to the proton at C-1; a doublet of doublets, centered at δ 3.12, assigned to one of the diastereotopic methylene protons at C-4; a multiplet, centered at δ 3.07, assigned to the proton at C-7; a doublet of doublets, centered at δ 3.02, assigned to one of the diastereotopic methylene protons at C-4; a singlet at δ 2.43, assigned to the

(13) (a) Semmelhack, M. F.; Bodurow, C. M.; Fewkes, E.; Herndon, J. W.; Knaus, G.; Le, H. T. M.; Sanner, M. *Chem. Scr.* **1985**, *25*, 131. (b) Semmelhack, M. F.; Herndon, J. W.; Liu, J. K. *Organometallics* **1983**, *2*, 1885.

(14) (a) Karplus, M. *J. Am. Chem. Soc.* **1963**, *85*, 2870. (b) Bothner-By, A. A. *Adv. Magn. Reson.* **1965**, *1*, 195.

Scheme 2



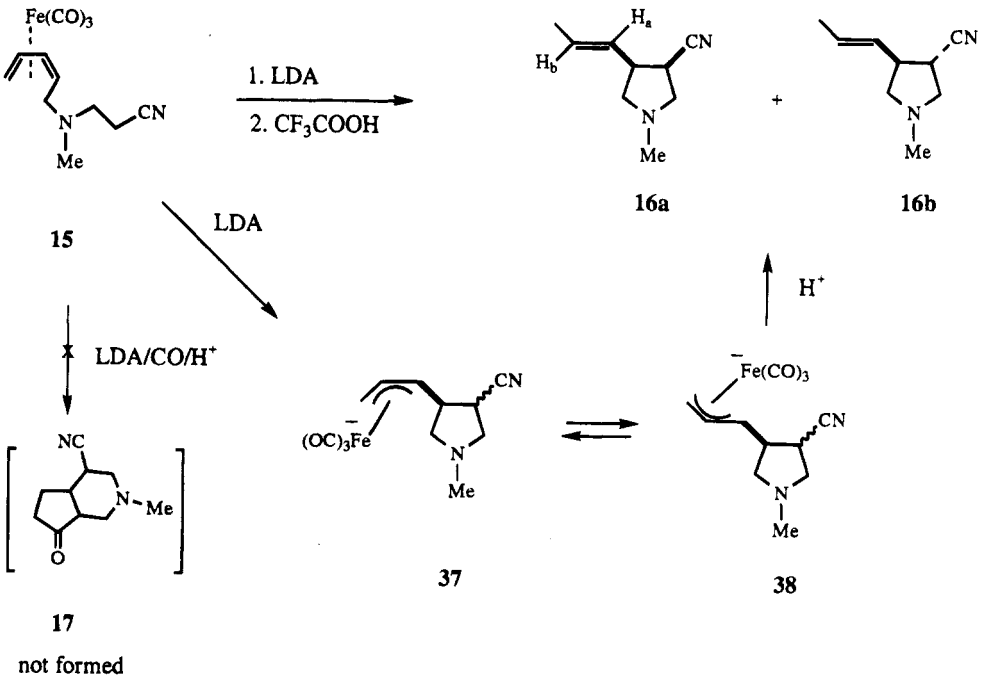
methyl protons at the nitrogen atom; a triplet, centered at δ 1.30, assigned to the methyl protons at C-11; a doublet, centered at δ 1.09, assigned to the methyl protons at C-8. The ^{13}C NMR spectrum of complex **10** exhibited the following: a signal at δ 215.3, assigned to C-6 (carbonyl of the keto functionality); a signal at δ 172.5, assigned to C-9 (carbonyl of the ester functionality); a signal at δ 64.8, assigned to C-2; a signal at δ 62.4, assigned to C-10; a signal at δ 60.2, assigned to C-4; a signal at δ 55.3, assigned to C-5; a signal at δ 55.0, assigned to C-1; a signal at δ 38.7, assigned to C-7; a signal at δ 36.8, assigned to the methyl carbon at the nitrogen atom; a signal at δ 14.4, assigned to C-11; a signal at δ 8.0, assigned to C-8. This result is consistent with the intramolecular cyclization of complex **12** to give the fused bicyclo[3.3.0]octanecarboxylic acid derivative **13** only or both **13** and the fused bicyclo[3.2.0]heptanecarboxylic acid derivative **14**, depending on the quenching process (Scheme 2). Thus, treatment of **12** with LDA under an atmosphere of CO at −78 °C for 2 h and 25 °C for 2 h followed by acid quenching produced **13** as the major product in 55% yield,[12a] whereas reaction of **12** with LDA at −78 °C for 2 h followed by acid quenching and then addition of an atmosphere of CO for 1 h at −78 °C provided **13** (34%) and **14** (35%) (Scheme 2) after purification by flash column chromatography and distillation under reduced pressure. Both methyl groups at C-7 of **10** and **14** were assigned as endo on the basis of their NOESY experiments. It is important to note that the formation of bicyclo[3.2.0]heptane skeletons is limited to the iron−diene complexes bearing no substituents at the C-1 or C-2 position of the diene ligands. For example, treatment of complexes with a methyl group at C-1 (**3e**) or C-2 (**3f**) with LDA at −78 °C followed by acid quenching did not generate bicyclo[3.2.0]heptane or bicyclo[3.3.0]octane skeletons. The major products isolated were cyclopentanecarboxylic acid derivatives; no carbonyl insertion products were obtained.

Increasing the tether length by 1 with complex **15** (Scheme 3) led to a 23% yield of an inseparable mixture of cis and trans isomers of pyrrolidine derivatives **16a,b** in a ratio of 4:3 (obtained by the integration of the ^1H NMR spectrum of the crude mixture). None of the desired internal addition product, for example **17**, was isolated under an atmosphere of N_2 or CO. The stereochemistry of the double bonds of **16a** and **16b** was assigned as trans on the basis of comparison of their ^1H NMR decoupling experiments. A coupling constant of 14.6 Hz for the two vicinal vinyl protons (H_a−H_b) suggested a trans relationship between H_a and H_b.

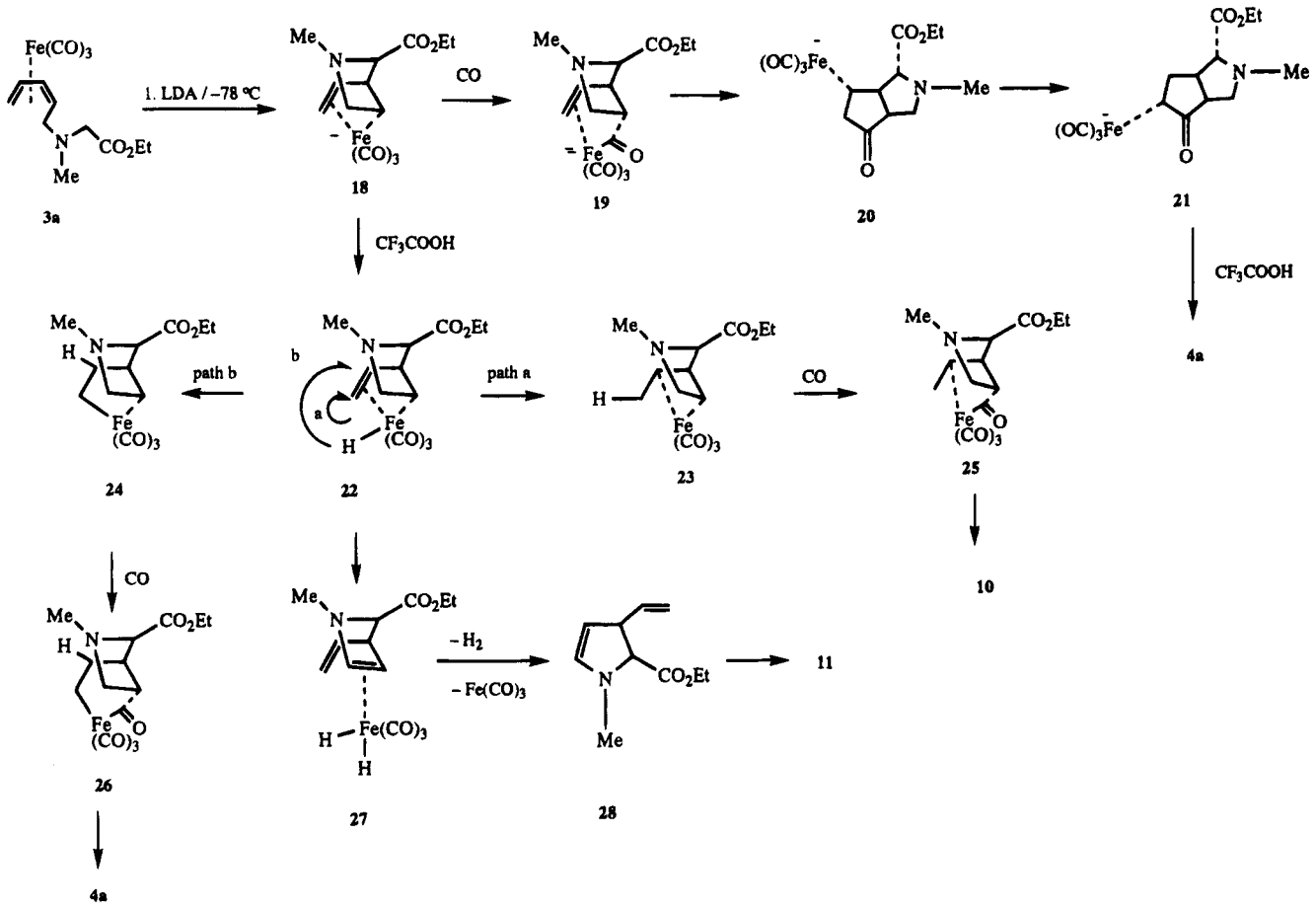
Discussion

The formation of aza-bicyclic and -tricyclic skeletons agrees closely with the mechanism proposed for the intramolecular addition of nucleophiles to acyclic (η^4-diene)$Fe(CO)_3$ complexes bearing functionalized side

Scheme 3



Scheme 4



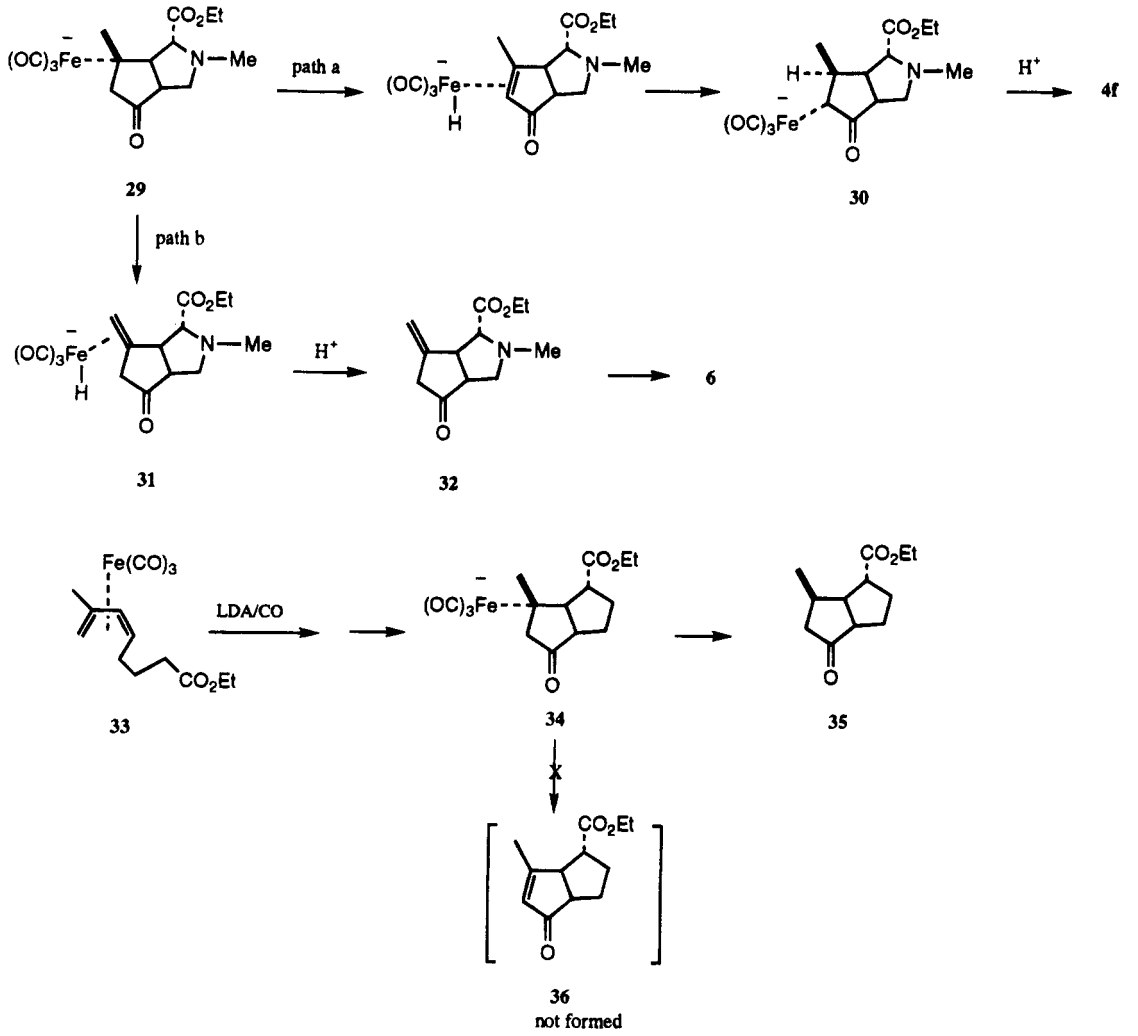
chains at the terminal position of the diene ligands.[12a] Anti addition of the stabilized α-amino enolate anion, obtained from treatment of **3a** with 1.2 molar equiv of LDA, at C-3 of the diene ligand gave the putative homoallyl anion intermediate **18** (Scheme 4). It is important to mention that an α-amino ester enolate anion such as α-lithio-*N*,*N*-dimethylglycine ethyl ester fails to add to (η^4-diene)Fe(CO)$_3$ complexes intermolecularly, under the same reaction conditions. Moreover, the intramolecular addition occurred exclusively at the C-3 position of the diene ligand, and no addition at C-2 was found. Carbonyl insertion was then enhanced by external CO (14−18 psi) to generate the acyliron anion intermediate **19** and intramolecular alkene insertion to give **20**. The postulated initial bicyclic intermediate **20** could rearrange rapidly to the enolate−iron derivative **21**, presumably via a β-hydride elimination/readdition process. Protonation of **21** produced the azabicyclic compound **4a**. Furthermore, intramolecular cyclization of both diastereomers of complexes **3b−d,h−j** under the same reaction conditions (LDA/CO, −78 °C, THF/HMPA) gave only a single diastereomer of cycloadducts **4b−d**, **7**, **8**, and **9**, respectively. The reason for the isolation of a single isomer in each case may derive from the formation of the same kinetic enolates by treatment of both diastereomers with LDA under the kinetically controlled reaction conditions.[15] However, the formation of compound **4a** in Table 1 and Scheme 1 may result from different reaction pathways. Iron−hydride species **22** could be obtained upon direct quenching of **18** with CF_3COOH (Scheme 4). Intramolecular alkene insertion into the iron−hydride bond of **22** would lead to the formation of ferracyclobutane derivative **23** (path a) and ferracyclopentane derivative **24** (path b). Carbonyl insertion was then enhanced by external CO (14−18 psi) to produce ferracyclopentane intermediate **25** and ferracyclohexane intermediate **26**, which after reductive elimination produce the 3-azabicyclo[3.2.0]heptanecarboxylic acid derivative **10**[16,17] and 3-azabicyclo[3.3.0]-octanecarboxylic acid derivative **4a**, respectively. However, detachment of the iron tricarbonyl moiety from the olefin of **22** followed by β-hydride elimination would give **27**. Reductive elimination of **27** followed by decomplexation of the iron tricarbonyl moiety produced **28**. The initially formed product **28** presumably aromatized by migration of the double bond to provide pyrrole derivative **11**. However, insertion of the pendant olefin into the iron−hydride bond of **22** is limited to the complexes bearing no methyl group at the C-1 or C-2 positions of diene−iron complexes. For example, reaction of complexes with a methyl group at C-1 (**3e**) or C-2 (**3f**) with LDA at −78 °C followed by acid quenching did not generate bicyclo[3.2.0]heptane or bicyclo[3.3.0]octane skeletons. The reason for the limitation may be due to the difficulty of insertion of a substituted olefin into the iron−hydride bond of intermediate **22**. Moreover, the

(15) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868.

(16) 3-Azabicyclo[3.2.0]heptanone derivatives can also be obtained by intramolecular [2 + 2] cycloadditions of keteniminium salts derived from β-amino acids: Gobeaux, B.; Ghosez, L. *Heterocycles* **1989**, *28*, 29.

(17) Cyclobutanone derivatives can be isolated by intermolecular nucleophilic addition followed by acid quenching. Semmelhack, M. F.; Le, H. T. M. *J. Am. Chem. Soc.* **1984**, *106*, 2715.

Scheme 5



bicyclic intermediate containing a methyl group at the internal position (C-8) of the diene ligand, for example **29**, might undergo different reaction pathways (Scheme 5). Anion **29** might rearrange to iron enolate **30** (path a) or give **31** (path b) after elimination of the β-hydride at the methyl group. Acid quenching of **31** woud produce **32**, which underwent double isomerization to give the α,β-unsaturated ketone derivative **6**. It must be mentioned that, under the same reaction conditions, intramolecular cyclization of complex **33** provided the bicyclo[3.3.0]octanecarboxylic acid derivative **35** only (Scheme 5), none of the α,β-unsaturated ketone derivative **36** was isolated.[12a] The difference is not clear. It was suggested that the adjacent five-membered ring containing a methyl group at the nitrogen atom may force the methyl group at C-8 to the proximity of the iron center for β-hydride elimination, while β-hydride elimination of the methyl group in the bicyclic anion **34** did not occur. Thus, only **35** was isolated.

Interestingly, intramolecular cycloaddition of the complex bearing a (cyanoethyl)methylamino moiety at the terminal position of the diene ligand (Scheme 3), for example complex **15**, does not give the desired 4-azabicyclo[4.3.0]nonanecarboxylic acid derivative **17** under the same reaction conditions as for the formation of 3-azabicyclo[3.3.0]octanecarboxylic acid derivative **4a**. Treatment of complex **15** with 1.2 molar equiv of LDA at −78 °C for 2 h and 25 °C under an atmosphere of CO for 2 h followed by acid quenching generated pyrrolidine derivatives **16a,b** as the major products. The reason for the difference is not understood. It was assumed that the formation of the (homoallyl)iron anion intermediate containing a nitrogen atom in a six-membered ring was difficult due to the steric congestion, while the stereo requirement for the formation of the (homoallyl)iron anion, for example **18** (Scheme 4), containing a nitrogen atom in a five-membered ring was low. Thus, anion **18** underwent carbonyl insertion, alkene insertion, and protonation to provide the 3-azabicyclo[3.3.0]octanecarboxylic acid derivative **4a**. A plausible mechanism has been proposed for the formation of pyrrolidine derivatives **16a,b**, which is illustrated in Scheme 3. The cyano-stabilized anion obtained from treatment of **15** with LDA may attack at the terminal position of the diene ligand upon raising the reaction temperature to 25 °C to give allyl anion species **37**. The formation of the putative allyl anion complex **37** at 25 °C (thermodynamically controlled reaction conditions) is consistent with a previous report on the intermolecular addition of reactive carbon nucleophiles to acyclic diene–iron complexes.[18] Carbanions such as ester enolates and cyano-stabilized anions are sufficiently reactive to add at the internal position of the diene

(18) (a) Semmelhack, M. F.; Herndon, J. W.; Springer, J. P. *J. Am. Chem. Soc.* **1983**, *105*, 2497. (b) Semmelhack, M. F.; Herndon, J. W. *Organometallics* **1983**, 2, 363.

ligand at −78 °C (kinetically controlled reaction conditions) to generate homoallyl anion species. When the temperature is raised to 25 °C (thermodynamically controlled reaction conditions), anions reverse and add at the terminal position of the diene ligand to produce allyl anion intermediates. The anion intermediate **37** might undergo allyl syn-anti isomerization to give **38**.[19] Protonation of **38** with acid gave pyrrolidine derivatives **16a,b**.

The reactions described herein demonstrate that intramolecular iron-mediated cycloaddition can be a convenient method for the formation of *N*-containing heterobicyclic and -tricyclic compounds. Although the yields of the *N*-containing heterotricyclic compounds **7**−**9** are only moderate, this facile and straightforward approach to the synthesis of fairly complicated systems, with promising relative stereocontrol, may have further applications.

Experimental Section

All reactions were run under a nitrogen atmosphere in oven-dried glassware unless otherwise indicated. Anhydrous solvents or reaction mixtures were transferred via an oven-dried syringe or cannula. Diethyl ether (ether) and tetrahydrofuran (THF) were distilled under nitrogen from a deep blue sodium benzophenone ketyl solution. Methylene chloride was distilled from calcium chloride. Copper cyanide (CuCN), sarcosine ethyl ester hydrochloride, (methylamino)acetonitrile hydrochloride, 3-(methylamino)propionitrile, DL-phenylalanine, DL-alanine, ethyl pipecolinate, ethyl nipecotate, fluoroboric acid (48% in water), and hexafluorophosphoric acid (60% in water) were purchased from Aldrich Chemical Co. and used as received. Cations **1a**−**c** were synthesized according to the literature procedure.[20] Amino acid derivatives **2b,c** were synthesized by protection of DL-alanine and DL-phenylalanine, respectively, following the literature procedure.[21] Compound **2d** was obtained by treatment of DL-alanine with thionyl chloride in ethanol followed by protection of the amino group with *trans*-crotonaldehyde.[21] Compoud **2f** was obtained by protection of the acid group of DL-proline with thionyl chloride in ethanol. Flash column chromatography, following the method of Still,[22] was carried out with E. Merck silica gel (Kieselgel 60, 230−400 mesh) using the indicated solvents. Analytical thin-layer chromatography was performed with silica gel 60 F_{254} plastic plates of 0.2-mm thickness from E. Merck. The term "concentration" refers to the removal of solvent with an aspirator pump (Yamato Instrument Company Model WP-15) with a Buchi Rotovapor-R. The term "under nitrogen" implies that the apparatus was evacuated (oil pump) and then filled with nitrogen three times. The term "flash distillation" refers to a vacuum distillation at 25 °C with a receiver at −78 °C. The term "short-path distillation" refers to the process in which the entire distillation apparatus (a tube closed at one end, held horizontally) with the exception of the collection bulb was slowly heated in an air bath from 25 to 150 °C under vacuum; the distillate was collected at −78 °C, and boiling points for fractions refer to the bath temperature range. Melting points were determined in open capillaries with a Thomas-Hoover apparatus and are uncorrected. ^{1}H nuclear magnetic resonance (NMR) spectra were obtained with a JEOL EX 400 instrument (400 MHz). Chemical shifts are reported in parts per million with either tetramethylsilane (0.00 ppm) or $CHCl_3$ (7.26 ppm) as internal standard. ^{13}C NMR spectra were recorded with JEOL EX 400 (100.4 MHz) spectrometers with $CDCl_3$ (77.0 ppm) as the internal standard. Infrared (IR) spectra were recorded with a JASCO IR-700 spectrometer. Mass spectra were acquired on a JEOL JMS-D 100 spectrometer at an ionization potential of 70 eV and are reported as mass/charge (*m/e*) with percent relative abundance. High-resolution mass spectra were obtained with an AEI MS-9 double-focusing mass spectrometer and a JEOL JMS-HX 110 spectrometer at the Department of Chemistry, Central Instrument Center, Taichung, ROC.

General Procedure for Addition of Amino Acid Derivatives 2a−h to (η^5-pentadienyl)Fe(CO)$_3$ Cation Salts 1a−c. Amino acid derivatives **2** (1.2 molar equiv) and triethylamine (1.2 molar equiv; 2.2 molar equiv was added in the cases of **2a,e,g**) in 5.0 mL of THF at −40 °C was added to a stirred suspension of a cation salt (**1a**−**c**) in 20 mL of THF under nitrogen. A homogeneous solution was obtained after the reaction mixture was stirred at −40 °C for 20 min. The reaction mixture was further stirred at 25 °C for 30 min and was then diluted with 100 mL of 50% ethyl acetate/hexanes. The resultant solution was washed with water (100 mL × 3) and brine (100 mL × 3), dried over anhydrous magnesium sulfate (10 g), and concentrated to give the crude mixture.

General Procedure for Intramolecular Cyclization of (η^4-diene)Fe(CO)$_3$ Complexes 3a−j. In a typical procedure, to a solution of diisopropylamine (0.64 mL, 4.5 mmol) in 4.0 mL of THF under nitrogen at −78 °C was added rapidly, neat, via syringe, a solution of *n*-butyllithium (2.8 mL, 4.5 mmol, 1.6 M) in hexane followed by addition of 0.80 mL of hexamethylphosphoramide. The reaction mixture was stirred at −78 °C for 20 min. With the solution at −78 °C, carbon monoxide was added to the system via a syringe needle and was pressurized to *ca.* 2 psig (always with a positive pressure kept on the system) as measured by a regulator at the CO cylinder. The CO pressure was then released via an additional needle, and the CO was allowed to flow through the system for 20 s. A solution of a diene−iron complex (**3a**−**j**, 4.0 mmol) in 3.0 mL of THF was added dropwise via syringe, the gas exit needle was removed, and the closed system was pressurized to *ca.* 14 psig with CO. The mixture was stirred at −78 °C for 2 h and 25 °C for 2 h. After this time, the mixture was again cooled to −78 °C, the CO needle was removed, and the system was depressurized via insertion of a syringe needle into the septum, which was quickly removed when gas flow could no longer be heard. The reaction mixture was quenched with trifluoroacetic acid (5.0 molar equiv) via a syringe needle and was stirred at 25 °C for 2 h. After this time, the reaction mixture was diluted with a mixture of ethyl acetate/hexanes (1/2, 100 mL). The resultant solution was washed with water (100 mL × 3) and brine (100 mL × 3), dried over anhydrous magnesium sulfate (10 g), and concentrated to give the crude mixture.

[(2−5-η)-1-((Carbethoxymethyl)methylamino)-2,4-pentadiene]tricarbonyliron (3a). The crude mixture obtained from the addition of **2a** (0.74 g, 4.8 mmol) to cation **1a** (1.2 g, 4.0 mmol) was purified via flash column chromatography (silica gel, 5% ethyl acetate/hexanes) to give **3a** (1.2 g, 3.7 mmol, 93%) as a yellow oil: IR (CH_2Cl_2) 3073, 2996, 2976, 2872, 2047, 1977, 1738, 1287, 1192, 1044 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.49−5.44 (m , 2 H), 4.17 (q, J = 7.3 Hz, 2 H), 3.24 (d, J = 16.6 Hz, 1 H), 3.14 (d, J = 16.6 Hz, 1 H), 2.87 (dd, J = 13.2, 9.3 Hz, 1 H), 2.56 (m, 1 H), 2.31 (s, 3 H, NCH_3), 2.07 (dd, J = 13.2, 10.3 Hz, 1 H), 1.81 (d, J = 7.8 Hz, 1 H), 1.49 (d, J = 9.7 Hz, 1 H), 1.27 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 210.7, 170.7, 91.1, 87.6, 60.5, 57.3, 56.0, 54.7, 41.6, 40.2, 14.2; MS (70 eV) *m/e* (relative intensity) 323 (M^+, 5), 295 (15), 267 (27), 250 (32), 239 (83), 207 (100), 171 (52), 151 (62), 129 (98), 100 (32), 99 (73), 67 (92); HRMS (EI) *m/e* calcd for $C_{10}H_{17}NO_2Fe$ (M^+ − 3CO) 239.0608, found 239.0608.

(19) (a) Chang, S.; White, P. S.; Brookhart, M. *Organometallics* **1993**, *12*, 3636. (b) Brookhart, M.; Yoon, J.; Noh, S. K. *J. Am. Chem. Soc.* **1989**, *111*, 4117.

(20) Donaldson, W. A. *J. Organomet. Chem.* **1990**, *395*, 187.

(21) (a). Womack, E. B.; McWhirter, J. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 714. (b) Groneberg, R. D.; Miyazaki, T.; Stylianides, N. A.; Schulze, T. J.; Stahl, W.; Schreiner, E. P.; Suzuki, T.; Iwabuchi, Y.; Smith, A. L.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1993**, *115*, 7593.

(22) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

[(2−5-η)-1-((1-Carbethoxy-2-phenylethyl)ethylamino)-2,4-pentadiene]tricarbonyliron (3b). The crude mixture obtained from the addition of **2b** (1.4 g, 6.1 mmol) to cation **1a** (1.5 g, 5.1 mmol) was purified via flash column chromatography (silica gel, 7% ethyl acetate/hexanes) to give **3b** (2.0 g, 4.7 mmol, 92%) as a 1:1 mixture of diastereomers: IR (CH_2Cl_2) (mixture of diastereomers) 3066, 3030, 2978, 2935, 2872, 2042, 1973, 1724, 1604, 1494, 1454, 1377, 1344, 1286, 1172, 1095, 1068, 1034 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers) δ 7.30−7.17 (m, 10 H, Ph), 5.45 (m, 2 H), 5.31 (dd, J = 7.8, 5.8 Hz, 1 Hz, 1 H), 5.22 (dd, J = 7.8, 5.4 Hz, 1 H), 4.06 (m, 4 H), 3.56 (t, J = 7.8 Hz, 2 H), 3.06−2.60 (m, 8 H), 2.50 (m, 1 H), 2.40−2.20 (m, 4 H), 2.09 (dd, J = 13.7, 9.8 Hz, 1 H), 1,78 (m, 2 H), 1.52 (m, 2 H), 1.16 (t, J = 7.3 Hz, 6 H), 0.99 (t, J = 7.3 Hz, 6 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) (mixture of diastereomers) δ 210.9, 172.6, 172.5, 136.6, 138.5, 129.3, 129.3, 128.2, 128.1, 126.2, 90.8, 90.8, 87.6, 87.6, 65.5, 64.1, 60.2, 60.0, 57.8, 57.2, 50.0, 49.9, 44.6, 43.8, 39.9, 39.8, 36.7, 35.8, 14.3, 14.2, 13.8, 13.7; MS (30 eV) (mixture of diastereomers) m/e (relative intensity) 427 (M^+, 1), 399 (3), 371 (16), 343 (100), 275 (15), 252 (36), 214 (18), 196 (22); HRMS (EI) m/e calcd for $C_{18}H_{25}FeNO_2$ (M^+ − 3CO) 343.1235, found 343.1234.

[(2−5-η)-1-(1-Carbethoxyethylethylamino)-2,4-pentadiene]tricarbonyliron Complex (3c). The crude mixture obtained from the addition of **2c** (0.54 g, 3.7 mmol) to cation **1a** (0.90 g, 3.1 mmol) was purified via flash column chromatography (silica gel, 9% ethyl acetate/hexanes) to give **3c** (0.95 g, 2.7 mmol, 90%) as a yellow oil. Complex **3c** could be further separated into two diastereomers. Diastereomer 1: IR (CH_2Cl_2) 3047, 2991, 2980, 2937, 2046, 1983, 1726, 1452, 1375, 1296, 1280, 1178, 1113, 881, 860 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.46 (m, 1 H), 5.41 (dd, J = 7.3, 5.4 Hz, 1 H), 4.15 (q, J = 6.8 Hz, 2 H), 3.51 (q, J = 7.8 Hz, 1 H), 2.88 (dd, J = 14.2, 2.8 Hz, 1 H), 2.57 (m, 3 H), 2.17 (dd, J = 14.2, 9.8 Hz, 1 H), 1.80 (dd, J = 4.9, 2.0 Hz, 1 H), 1.54 (dd, J = 6.8, 2.0 Hz, 1 H), 1.27 (t, J = 7.3 Hz, 3 H), 1.18 (d, J = 7.8 Hz, 3 H), 1.03 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 210.0, 174.1, 90.9, 87.6, 60.4, 58.7, 57.2, 49.9, 44.6, 39.8, 14.6, 14.3, 13.8; MS (30 eV) m/e (relative intensity) 295 (M^+ − 2CO, 14), 267 (100), 199 (98), 171 (71), 128 (73); HRMS (EI) m/e calcd for $C_{12}H_{21}FeNO_2$ (M^+ − 3CO) 267.0922, found 267.0918. Diastereomer 2: IR (CH_2Cl_2) 3051, 2991, 2980, 2977, 2046, 1959, 1724, 1452, 1377, 1296, 1267, 1178, 1111, 1070, 1022, 829, 815 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.46 (m, 1 H), 5.42 (dd, J = 7.3, 4.9 Hz, 1 H), 4.11 (q, J = 6.8 Hz, 2 H), 3.50 (q, J = 6.8 Hz, 1 H), 2.92 (dd, J = 12.2, 3.9 Hz, 1 H), 2.68 (m, 1 H), 2.52 (m, 1 H), 2.43 (m, 1 H), 2.10 (dd, J = 13.7, 9.8 Hz, 1 H), 1.79 (dd, J = 4.9, 1.9 Hz, 1 H), 1.55 (dd, J = 9.3, 1.9 Hz, 1 H), 1.28 (d, J = 6.8 Hz, 3 H), 1.27 (t, J = 7.3 Hz, 3 H), 0.99 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 210.0, 173.8, 90.8, 87.6, 60.1, 57.5, 57.2, 49.3, 43.9, 39.8, 16.2, 14.3, 13.5; MS (30 eV) m/e (relative intensity) 295 (M^+ − 2CO, 14), 267 (100), 238 (7), 207 (9), 171 (25); HRMS (EI) m/e calcd for $C_{12}H_{21}FeNO_2$ (M^+ − 3CO) 267.0922, found 267.0920.

[(2−5-η)-1-((1-Carbethoxyethyl)((*E*)-2-butenyl)amino)-2,4-pentadiene]tricarbonyliron (3d). The crude mixture obtained from the addition of **2d** (0.20 g, 1.2 mmol) to cation **1a** (0.30 g, 1.0 mmol) was purified via flash column chromatography (silica gel, 9% ethyl acetate/hexanes) to give **3d** (0.26 g, 0.69 mmol, 69%) as a 1:1 mixture of diastereomers. The mixture of diastereomers was further purified by MPLC, and only one of the diastereomers was obtained as a pure compound: IR (CH_2Cl_2) 3055, 2993, 2980, 2939, 2046, 1981, 1724, 1448, 1423, 1377, 1246, 1195, 1151, 1059, 970, 866 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.55−5.39 (m, 4 H), 4.10 (q, J = 7.3 Hz, 2 H), 3.53 (q, J = 7.3 Hz, 1 H), 3.21 (br d, J = 14.1 Hz, 1 H), 2.91 (m, 2 H), 2.53 (m, 1 H), 2.08 (dd, J = 14.2, 4.4 Hz, 1 H), 1.78 (dd, J = 4.4, 2.0 Hz, 1 H), 1.68 (d, J = 6.3 Hz, 3 H), 1.52 (dd, J = 9.3, 2.0 Hz, 1 H), 1.26 (m, 6 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 211.0, 173.8, 128.7, 128.6, 90.9, 87.7, 60.1, 57.2, 52.3, 49.1, 40.0, 39.9, 17.8, 16.0, 14.3; MS (30 eV) m/e (relative intensity) 321 (M^+ − 2CO, 1), 293 (100), 237 (90), 225 (80); HRMS (EI) m/e calcd for $C_{14}H_{23}FeNO_2$ (M^+ − 3CO) 293.1078, found 293.1077.

[(2−5-η)-1-((Carbethoxymethyl)methylamino)-2,4-hexadiene]tricarbonyliron (3e). The crude mixture obtained from the addition of **2a** (1.2 g, 7.2 mmol) to cation **1b** (1.9 g, 6.0 mmol) was purified via flash column chromatography (silica gel, 20% ethyl acetate/hexanes) to give **3e** (1.9 g, 5.7 mmol, 95%) as a yellow oil: IR (CH_2Cl_2) 2963, 2932, 2861, 2020, 1979, 1736, 1454, 1379, 1194 , 1125, 1032, 945, 781 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.19 (m, 2 H), 4.10 (q, J = 7.3 Hz, 2 H), 3.15 (d, J = 16.6 Hz, 1 H), 3.10 (d, J = 16.6 Hz, 1 H), 2.81 (dd, J = 13.2, 3.9 Hz, 1 H), 2.40 (m, 1 H), 2.34 (m, 1 H), 2.29 (s, 3 H, NCH_3), 2.05 (dd, J = 13.2, 10.3 Hz, 1 H), 1.35 (d, J = 5.9 Hz, 3 H), 1.20 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 211.4, 170.7, 94.9, 83.0, 60.5, 57.3, 56.4, 54.4, 41.7, 22.6, 20.3, 14.2; MS (70 eV) m/e (relative intensity) 337 (M^+, 6), 281 (22), 252 (100), 220 (32), 170 (97), 142 (54), 128 (56), 98 (56), 81 (72), 54 (78), 44 (65); HRMS (EI) m/e calcd for $C_{12}H_{19}FeNO_3$ (M^+ − 2CO) 281.0731, found 281.0709.

[(2−5-η)-1-((Carbethoxymethyl)methylamino)-4-methyl-2,4-pentadiene]tricarbonyliron (3f). The crude mixture obtained from the addition of **2a** (0.69 g, 4.5 mmol) to cation **1c** (1.2 g, 4.1 mmol) was purified via flash column chromatography (silica gel, 20% ethyl acetate/hexanes) to give **3f** (1.3 g, 3.9 mmol, 96%) as a yellow oil: IR (CH_2Cl_2) 3065, 3052, 2990, 2984, 2047, 1975, 1744, 1622, 1381, 1283, 1267, 1246, 1188, 1036, 905 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.36 (d, J = 7.3 Hz, 1 H), 4.17 (q, J = 7.3 Hz, 2 H), 3.24 (d, J = 16.6 Hz, 1 H), 3.14 (d, J = 16.6 Hz, 1 H), 2.82 (dd, J = 13.2, 3.9 Hz, 1 H), 2.41 (m, 1 H), 2.31 (s, 3 H, NCH_3), 2.18 (s, 3 H), 2.10 (dd, J = 13.2, 9.8 Hz, 1 H), 1.84 (s, 1 H), 1.51 (s, 1 H), 1.27 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 210.6, 170.7, 108.3, 87.3, 60.5, 57.4, 55.8, 51.1, 42.7, 41.7, 24.3, 14.2; MS (70 eV) m/e (relative intensity) 337 (M^+, 92), 309 (52), 253 (71), 222 (82), 198 (89), 193 (100), 165 (92), 129 (75), 116 (97), 112 (91), 100 (89), 82 (96); HRMS (EI) m/e calcd for $C_{14}H_{19}FeNO_5$ (M^+) 337.0611, found 337.0611.

[(2−5-η)-1-((Cyanomethyl)methylamino)-2,4-pentadiene]tricarbonyliron Complex (3g). The crude mixture obtained from the addition of **2e** (0.84 g, 7.2 mmol) to cation **1a** (1.8 g, 6.0 mmol) was purified via flash column chromatography (silica gel, 15% ethyl acetate/hexanes) to give **3g** (1.6 g, 5.9 mmol, 98%) as a yellow oil: IR (CH_2Cl_2) 3056, 3046, 2992, 2982, 2951, 2234, 2051, 1985, 1616, 1453, 1258, 1125, 1030, 895, 878 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.54 (m, 1 H), 5.44 (dd, J = 6.8, 5.9 Hz, 1 H), 3.57 (d, J = 17.1 Hz, 1 H), 3.44 (d, J = 17.1 Hz, 1 H), 2.68 (dd, J = 13.2, 4.9 Hz, 1 H), 2.47 (m, 1 H), 2.30 (s, 3 H, NCH_3), 2.00 (dd, J = 13.2, 9.8 Hz, 1 H), 1.88 (dd, J = 7.8, 3.4 Hz, 1 H), 1.53 (dd, J = 9.8, 3.4 Hz, 1 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 210.3, 114.5, 91.6, 87.0, 54.6, 53.8, 43.9, 41.3, 40.5; MS (70 eV) m/e (relative intensity) 276 (M^+, 12), 248 (100), 220 (92), 192 (97), 149 (80), 121 (60), 110 (70), 84 (89), 67 (74), 56 (80), 42 (78); HRMS (EI) m/e calcd for $C_{11}H_{12}FeN_2O_3$ (M^+) 276.0196, found 276.0201.

[Ethyl *N*-((2−5-η)-2,4-pentadienyl)prolinate]tricarbonyliron (3h). The crude mixture obtained from the addition of **2f** (0.84 g, 6.0 mmol) to cation **1a** (1.5 g, 5.0 mmol) was purified via flash column chromatography (silica gel, 30% ethyl acetate/hexanes) to give **3h** (1.2 g, 3.3 mmol, 72%) as a yellow oil. Complex **3h** could be further separated into two diastereomers. Diastereomer 1: IR (CH_2Cl_2) 2992, 2984, 2048, 1979, 1736, 1267, 1254, 1097, 889, 869, 848 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.48 (m, 1 H), 5.40 (m, 1 H), 4.17 (q, J = 6.8 Hz, 2 H), 3.18 (m, 1 H), 3.08 (dd, J = 8.8, 6.4 Hz, 1 H), 2.99 (dd, J = 13.2, 4.9 Hz, 1 H), 2.64 (m, 1 H), 2.24 (m, 1 H), 2.08−1.74 (m, 6 H), 1.56 (dd, J = 9.3, 2.5 Hz, 1 H), 1.27 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 210.8, 173.7, 91.2, 87.4, 64.5, 60.6, 55.6, 52.5, 52.3, 40.2, 29.2, 22.8, 14.2; MS (20 eV) m/e (relative intensity) 294 (M^+ − 2CO + 1, 55), 266 (78), 250 (22), 221 (33), 198 (100), 169 (23), 157 (34), 136 (35); HRMS (EI) m/e calcd for $C_{12}H_{19}FeNO_2$ (M^+ − 3CO) 265.0770, found

265.0767. Diastereomer 2: IR (CH_2Cl_2) 2992, 2982, 2048, 1973, 1736, 1283, 1265, 1248, 1183, 910, 882, 833 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.49 (m, 1 H), 5.40 (m, 1 H), 4.18 (q, J = 6.8 Hz, 2 H), 3.09 (m, 2 H), 2.87 (dd, J = 12.7, 5.0 Hz, 1 H), 2.63 (m, 1 H), 2.41 (m, 1 H), 2.18 (t, J = 10.7 Hz, 1 H), 2.07 (m, 1 H), 1.88–1.84 (m, 4 H), 1.48 (dd, J = 8.3, 2.0 Hz, 1 H), 1.28 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 210.7, 174.0, 91.2, 87.6, 64.7, 60.6, 55.4, 53.3, 53.0, 40.4, 29.4, 23.1, 14.2; MS (20 eV) *m/e* (relative intensity) 294 (M^+ − 2CO + 1, 25), 276 (31), 266 (75), 206 (36), 197 (86), 169 (81), 136 (67), 126 (100), 64 (25); HRMS (EI) *m/e* calcd for $C_{13}H_{19}FeNO_3$ (M^+ − 2CO) 293.0719, found 293.0718.

[Ethyl *N*-((2–5-η)-2,4-pentadienyl)pipecolinate]tricarbonyliron (3i). The crude mixture obtained from the addition of **2g** (1.2 g, 6.0 mmol) to cation **1a** (1.5 g, 5.0 mmol) was purified via flash column chromatography (silica gel, 30% ethyl acetate/hexanes) to give **3i** (1.3 g, 3.5 mmol, 70%) as a 1:1 mixture of diastereomers: IR (CH_2Cl_2) (mixture of diastereomers) 3065, 2989, 2049, 1975, 1713, 1275, 1182, 891, 828 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers) δ 5.45 (m, 4 H), 4.19 (m, 4 H), 3.14–3.00 (m, 4 H), 2.83–2.59 (m, 5 H), 2.35 (m, 1 H), 2.17–1.93 (m, 3 H), 1.81–1.70 (m, 12 H), 1.54 (m, 1 H), 1.27 (m, 6 H), 0.88 (m, 1 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) (mixture of diastereomers) δ 210.8, 173.5, 173.3, 91.0, 87.9, 87.8, 64.3, 64.0, 60.5, 60.4, 55.3, 55.1, 54.5, 54.4, 50.8, 49.5, 40.3, 40.0, 30.0, 29.6, 25.3, 25.1, 23.0, 22.4, 14.3; MS (20 eV) (mixture of diastereomers) *m/e* (relative intensity) 308 (M^+ − 2CO + 1, 100), 291 (35), 280 (88), 265 (35), 223 (41), 211 (47), 184 (35), 170 (41), 139 (32); HRMS (EI) *m/e* calcd for $C_{14}H_{21}FeNO_3$ (M^+ − 2CO) 307.0876, found 307.0863.

[Ethyl *N*-((2–5-η)-2,4-pentadienyl)nipecotate]tricarbonyliron (3j). The crude mixture obtained from the addition of **2h** (0.96 g, 6.0 mmol) to cation **1a** (1.5 g, 5.0 mmol) was purified via flash column chromatography (silica gel, 30% ethyl acetate/hexanes), to give **3j** (1.2 g, 3.2 mmol, 64%) as a 1:1 mixture of diastereomers: IR (CH_2Cl_2) (mixture of diastereomers) 3046, 2992, 2982, 2048, 1977, 1725, 1674, 1618, 1283, 1152, 1094, 912, 883 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers) δ 5.46 (m, 4 H), 4.13 (m, 4 H), 3.02 (m, 1 H), 2.75 (m, 3 H), 2.55 (m, 4 H), 2.23 (m, 1 H), 2.02 (m, 2 H), 1.89–1.68 (m, 10 H), 1.55–1.43 (m, 6 H), 1.25 (m, 6 H), 0.86 (m, 1 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) (mixture of diastereomers) δ 210.8, 174.9, 90.9, 87.7, 60.2, 57.6, 57.6, 55.3, 55.0, 54.9, 54.0, 53.5, 52.2, 41.8, 41.7, 40.1, 40.0, 26.8, 26.7, 24.5, 24.3, 14.1; MS (20 eV) (mixture of diastereomers) *m/e* (relative intensity) 335 (M^+ − CO, 1), 307 (15), 279 (100), 211 (31), 207 (16), 183 (12), 139 (36), 67 (15); HRMS (EI) *m/e* calcd for $C_{15}H_{21}FeNO_4$ (M^+ − CO) 335.0827, found 335.0818.

[((2–5-η)-2,4-pentadienyl)methylamino)propionitrile]tricarbonyliron (15). The crude mixture obtained from the addition of 3-(methylamino)propionitrile (0.39 g, 4.2 mmol) to cation **1a** (1.2 g, 3.8 mmol) was purified via flash column chromatography (silica gel, 15% ethyl acetate/hexanes) to give **15** (1.0 g, 3.5 mmol, 91%) as a yellow oil: IR (CH_2Cl_2) 3065, 3029, 2994, 2934, 1998, 1732, 1605, 1464, 1375, 1337, 1238, 1136, 1046, 891, 774, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.50 (m, 2 H), 2.79 (dd, J = 9.6, 4.2 Hz, 1 H), 2.70 (m, 1 H), 2.59–2.52 (m, 2 H), 2.40 (t, J = 6.8 Hz, 2 H), 2.21 (s, 3 H, NCH_3), 1.95 (dd, J = 13.3, 10.0 Hz, 1 H), 1.83 (d, J = 7.5 Hz, 1 H), 1.46 (d, J = 6.7 Hz, 1 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 210.5, 118.6, 91.0, 87.5, 55.8, 54.1, 51.3, 40.6, 40.0, 16.2; MS (70 eV) *m/e* (relative intensity) 290 (M^+, 5), 248 (15), 220 (80), 192 (100), 149 (98), 123 (43), 110 (97), 84 (53), 67 (95), 56 (75), 42 (52), 38 (54); HRMS (EI) *m/e* calcd for $C_{12}H_{14}FeN_2O_3$ (M^+) 290.0353, found 290.0347.

(1*R,2*R**,5*S**)-2-Carbethoxy-3-methyl-6-oxo-3-azabicyclo[3.3.0]octane (4a).** The crude mixture from intramolecular cyclization of complex **3a** (1.2 g, 3.7 mmol) was purified via flash column chromatography (silica gel, 7% ethyl acetate/hexanes) and short-path distillation (0.02 mmHg, 65–75 °C) to give **4a** (0.39 g, 1.9 mmol, 50%) as a colorless liquid: IR (CH_2Cl_2) 2967, 1738, 1449, 1262, 1184, 1100, 1032, 893, 843 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.19–4.13 (m, 2 H), 3.29 (dd, J = 9.8, 9.3 Hz, 1 H), 2.97 (s, 1 H), 2.95 (m, 1 H), 2.80 (m, 1 H), 2.55 (dd, J = 9.3, 4.9 Hz,1 H), 2.36 (m, 2 H), 2.30 (s, 3 H, NCH_3), 2.11 (m, 1 H), 1.94 (m, 1 H), 1.24 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (100.4 MHz , $CDCl_3$) δ 219.9, 172.3, 73.0, 60.7, 57.5, 50.4, 45.7, 38.9, 37.3, 25.2, 14.4; MS (70 eV) *m/e* (relative intensity) 211 (M^+, 10), 166 (30), 138 (100), 111 (30), 97 (40), 82 (50), 71 (60), 57 (100) , 53 (80), 28 (20); HRMS (EI) *m/e* calcd for $C_{11}H_{17}NO_3$ (M^+) 211.1207, found 211.1205.

(1*R,2*R**,5*S**)-2-Carbethoxy-3-ethyl-2-(phenylmethyl)-6-oxo-3-azabicyclo[3.3.0]octane (4b).** The crude mixture from intramolecular cyclization of complex **3b** (0.85 g, 2.0 mmol) was purified via flash column chromatography (silica gel, 16% ethyl acetate/hexanes) to give **4b** (0.21 g, 0.66 mmol, 33%) as a colorless liquid: IR (CH_2Cl_2) 3067, 3045, 2991, 2980, 2937, 2874, 1738, 1714, 1637, 1604, 1496, 1452, 1381, 1296, 1209, 1184, 1159, 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (m, 3 H), 7.14 (d, J = 7.3 Hz, 2 H), 4.16 (q, J = 7.3 Hz, 2 H), 3.57 (d, J = 14.7 Hz, 1 H), 3.30 (dd, J = 7.3, 2.3 Hz, 1 H), 3.05 (q, J = 9.3 Hz, 1 H), 2.96 (m, 1 H), 2.84 (t, J = 9.3 Hz, 1 H), 2.70 (d, J = 14.7 Hz, 1 H), 2.43 (t, J = 9.8 Hz, 1 H), 2.21 (m, 2 H), 2.15 (m, 1 H), 1.88 (m, 2 H), 1.25 (t, J = 6.8 Hz, 3 H), 1.07 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 220.9, 171.6, 137.5, 129.2, 128.3, 126.3, 74.9, 60.4, 53.1, 48.5, 45.5, 43.0, 39.4, 37.2, 23.9, 14.9, 14.5; MS (70 eV) *m/e* (relative intensity) 315 (M^+, 1), 261 (6), 242 (100), 224 (55), 214 (30), 128 (25); HRMS (EI) *m/e* calcd for $C_{19}H_{25}NO_3$ (M^+) 315.1834, found 315.1827.

(1*R,2*R**,5*S**)-2-Carbethoxy-3-ethyl-2-methyl-6-oxo-3-azabicyclo[3.3.0]octane (4c).** The crude mixture from intramolecular cyclization of complex **3c** (0.70 g, 2.0 mmol) was purified via flash column chromatography (silica gel, 9% ethyl acetate/hexanes) and short-path distillation (0.02 mmHg, 83–95 °C) to give **4c** (0.21 g, 0.88 mmol, 44%) as a colorless liquid: IR (CH_2Cl_2) 2993, 2974, 2939, 2845, 1724, 1641, 1467, 1448, 1412, 1379, 1290, 1238, 1159, 1136, 1076, 1022, 912, 881 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.14 (q, J = 7.0 Hz, 2 H), 3.22 (d, J = 6.9 Hz, 1 H), 2.98 (dt, J = 8.3, 7.8 Hz, 1 H), 2.83 (m, 2 H), 2.71 (m, 1 H), 2.29 (t, J = 8.8 Hz, 2 H), 2.22 (m, 1 H), 2.00 (m, 1 H), 1.87 (m, 1 H), 1.30 (s, 3 H), 1.28 (t, J = 7.3 Hz, 3 H), 1.02 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 221.0, 173.9, 70.5, 60.2, 53.3, 48.9, 48.0, 42.6, 39.2, 23.4, 17.2, 14.7, 14.4; MS (70 eV) *m/e* (relative intensity) 239 (M^+, 4), 166 (100), 138 (18), 110 (98), 94 (24), 82 (61); HRMS (EI) *m/e* calcd for $C_{13}H_{21}NO_3$ (M^+) 239.1521, found 239.1519.

(1R*,2R*,5S*)-2-Carbethoxy-3-((*E*)-2-butenyl)-2-methyl-6-oxo-3-azabicyclo[3.3.0]octane (4d). The crude mixture from intramolecular cyclization of complex **3d** (0.26 g, 0.69 mmol) was purified via flash column chromatography (silica gel, 9% ethyl acetate/hexanes) to give **4d** (0.11 g, 0.42 mmol, 61%) as a colorless liquid: IR (CH_2Cl_2) 3043, 2997, 2972, 2939, 2876, 2854, 1726, 1635, 1446, 1413, 1377, 1288, 1230, 1136, 1074, 1020, 970 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.53 (dq, J = 15.2, 6.4 Hz, 1 H), 5.35 (m, 1 H), 4.14 (q, J = 6.8 Hz, 2 H), 3.30 (dd, J = 13.7, 4.9 Hz, 1 H), 3.14 (dd, J = 15.1, 8.8 Hz, 1 H), 3.00 (q, J = 7.8 Hz, 1 H), 2.79 (m, 2 H), 2.72 (dd, J = 13.7, 7.8 Hz, 1 H), 2.28 (dd, J = 9.3, 6.8 Hz, 2 H), 2.02 (m, 1 H), 1.88 (m, 1 H), 1.64 (d, J = 6.4 Hz, 3 H), 1.31 (s, 3 H), 1.28 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 221.0, 174.0, 129.1, 127.1, 70.1, 60.3, 53.8, 50.8, 48.8, 48.1, 39.2, 23.4, 17.7, 17.3, 14.5; MS (70 eV) *m/e* (relative intensity) 265 (M^+, 3), 210 (3), 192 (98), 166 (100), 138 (97), 110 (42), 82 (51), 67 (29), 55 (96); HRMS (EI) *m/e* calcd for $C_{15}H_{23}NO_3$ (M^+) 265.1679, found 265.1674.

2-Carbethoxy-3,7-dimethyl-6-oxo-3-azabicyclo[3.3.0]-octane (4e). The crude mixture from intramolecular cyclization of complex **3e** (1.9 g, 5.7 mmol) was purified via flash column chromatography (silica gel, 20% ethyl acetate/hexanes) to give **4e** (0.46 g, 2.1 mmol, 36%) as a mixture of diastereomers in a 1:1 ratio: IR (CH_2Cl_2) (mixture of diastereomers) 2968, 1740, 1449, 1361, 1260, 1180, 1109, 1044, 894, 802 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers) δ 4.30

(q, J = 7.3 Hz, 2 H), 4.18 (q, J = 7.3 Hz, 2 H), 3.41 (m, 1 H), 3.21 (s, 1 H), 3.00 (m, 1 H), 3.00–2.84 (m, 6 H), 2.54–2.40 (m, 5 H), 2.39 (s, 6 H), 2.39–2.21 (m, 2 H), 1.72 (m, 4 H), 1.35 (m, 2 H), 1.30 (t, J = 7.3 Hz, 3 H), 1.02 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) (mixture of diastereomers) δ 219.8, 219.4, 172.5, 172.1, 73.5, 73.0, 61.8, 60.2, 57.8, 57.2, 51.8, 50.2, 44.4, 43.8, 38.5, 38.2, 37.2, 37.0, 25.4, 25.1, 14.1, 13.3; MS (70 eV) *m/e* (relative intensity) (mixture of diastereomers) 225 (M^+, 5), 195 (10), 162 (12), 150 (100), 122 (13), 108 (68), 94 (45), 85 (52), 82 (95), 67 (48), 55 (52), 51 (18); HRMS (EI) *m/e* calcd for $C_{12}H_{19}NO_3$ (M^+) 225.1364, found 225.1358.

(1*R,2*R**,5*S**,8*R**)-2-Carbethoxy-3,8-dimethyl-6-oxo-3-azabicyclo[3.3.0]octane (4f).** The crude mixture from intramolecular cyclization of complex **3f** (1.3 g, 4.0 mmol) was purified via flash column chromatography (silica gel, 20% ethyl acetate/hexanes) and short-path distillation (0.02 mmHg, 110–130 °C) to give **4f** (0.41 g, 1.8 mmol, 46%) and **6** (0.31 g, 1.4 mmol, 34%) as colorless liquids. **4f**: IR (CH_2Cl_2) 3054, 2994, 2980, 2944, 1740, 1624, 1478, 1445, 1433, 1304, 1182, 1123, 1096, 1059, 907, 893, 856, 845 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.23 (q, J = 7.3 Hz, 2 H), 3.37 (dd, J = 9.3, 8.3 Hz, 1 H), 3.27 (d, J = 6.4 Hz, 1 H), 3.10 (q, J = 7.3 Hz, 1 H), 2.83 (dt, J = 8.3, 3.4 Hz, 1 H), 2.65 (dd, J = 9.3, 3.9 Hz, 1 H), 2.45 (m, 1 H), 2.35 (m, 1 H), 2.34 (s, 3 H, NCH_3), 2.09 (dd, J = 17.5, 13.2 Hz, 1 H), 1.31 (t, J = 7.3 Hz, 3 H), 1.18 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 219.4, 172.7, 66.5, 60.3, 57.7, 52.7, 50.5, 44.2, 38.2, 31.1, 16.3, 14.0; MS (70 eV) *m/e* (relative intensity) 225 (M^+, 100), 196 (15), 163 (18), 153 (100), 150 (100), 122 (10), 108 (58), 94 (32), 83 (50), 82 (100), 67 (95), 55 (50), 51 (12); HRMS (EI) *m/e* calcd for $C_{12}H_{19}NO_3$ (M^+) 225.1364, found 225.1359.

(1*R,2*R**,5*S**)-2-Carbethoxy-3,8-dimethyl-6-oxo-3-azabicyclo[3.3.0]oct-7-ene (6)**: IR (CH_2Cl_2) 3065, 3052, 2980, 2944, 2885, 1740, 1624, 1433, 1381, 1182, 1030, 895, 679 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (s, 1 H), 4.25 (q, J = 6.8 Hz, 2 H), 3.39 (d, J = 4.9 Hz, 1 H), 3.25 (m, 2 H), 3.03 (m, 1 H), 2.75 (dd, J = 9.3, 4.9 Hz, 1 H), 2.38 (s, 3 H, NCH_3), 2.19 (s, 3 H), 1.13 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 209.2, 176.5, 171.7, 131.3, 67.6, 60.7, 55.4, 54.3, 50.4, 38.1, 18.0, 14.2; MS (70 eV) *m/e* (relative intensity) 223 (M^+, 100), 208 (5), 194 (7), 152 (60), 150 (98), 122 (95), 107 (65), 82 (95), 68 (90), 55 (40); HRMS (EI) *m/e* calcd for $C_{12}H_{17}NO_3$ (M^+) 223.1207, found 223.1210.

(1*R,2*R**,5*S**)-2-Cyano-3-methyl-6-oxo-3-azabicyclo-[3.3.0]octane (4g).** The crude mixture from intramolecular cyclization of complex **3g** (1.5 g, 4.3 mmol) was purified via flash column chromatography (silica gel, 20% ethyl acetate/hexanes) and short-path distillation (0.02 mmHg, 65–75 °C) to give **4g** (exo) as a colorless solid (0.26 g, 1.6 mmol, 37%) and **4g** (endo) (0.19 g, 1.2 mmol, 28%) as a colorless liquid.

4g (exo): IR (CH_2Cl_2) 3065, 2966, 2957, 2226, 1744, 1607, 1451, 1304, 1258, 1163 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 (s, 1 H), 3.21 (m, 1 H), 3.15 (d, J = 9.5 Hz, 1 H), 2.76 (dd, J = 8.8, 8.5 Hz, 1 H), 2.65 (dd, J = 9.2, 8.8 Hz, 1 H), 2.42 (s, 3 H, NCH_3), 2.42–2.32 (m, 3 H), 1.81 (m, 1 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 218.4, 116.3, 62.7, 56.8, 49.3, 45.1, 38.6, 37.9, 26.9; MS (70 eV) *m/e* (relative intensity) 164 (M^+, 52), 138 (72), 119 (23), 95 (42), 85 (49), 82 (100), 67 (23), 55 (12); HRMS (EI) *m/e* calcd for $C_9H_{12}N_2O$ (M^+) 164.0949, found 164.0948.

4g (endo): IR (CH_2Cl_2) 3066, 2977, 2967, 2229, 1744, 1605, 1354, 1268, 1156 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.39 (d, J = 7.8 Hz, 1 H), 3.17 (m, 2 H), 2.75 (dd, J = 5.2, 4.5 Hz, 1 H), 2.48 (dd, J = 9.7, 5.2 Hz, 1 H), 2.42 (s, 3 H, NCH_3), 2.39 (m, 1 H), 2.23 (m, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 218.0, 116.7, 61.5, 58.7, 50.2, 42.3, 40.8, 38.7, 24.9; MS (70 eV) *m/e* (relative intensity) 164 (M^+, 52), 138 (72), 119 (15), 95 (32), 85 (49), 82 (100), 67 (23), 55 (12); HRMS (EI) *m/e* calcd for $C_9H_{12}N_2O$ (M^+) 164.0949, found 164.0948.

(1*R,2*R**,8*S**)-2-Carbethoxy-9-oxo-6-azatricyclo[6.3.0.0^{2,6}]-undecane (7).** The crude mixture from intramolecular cyclization of complex **3h** (1.2 g, 3.3 mmol) was purified via flash column chromatography (silica gel, 30% ethyl acetate/hexanes) to give **7** (0.10 g, 0.42 mmol, 13%) as a pale yellow liquid: IR (CH_2Cl_2) 3067, 2991, 2982, 1738, 1423, 1186, 1114 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.21 (q, J = 7.3 Hz, 2 H), 3.30 (dd, J = 15.6, 9.8 Hz, 1 H), 3.18 (m, 1 H), 3.08 (dd, J = 15.1, 7.8 Hz, 1 H), 2.86 (dd, J = 13.7, 9.3 Hz, 2 H), 2.75 (m, 1 H), 2.43 (m, 1 H), 2.36 (m, 1 H), 2.26 (m, 1 H), 2.12 (m, 1 H), 1.91 (m, 1 H), 1.79 (m, 1 H), 1.75 (m, 1 H), 1.66 (m, 1 H), 1.30 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 218.5, 174.2, 82.2, 61.0, 56.5, 54.6, 51.0, 49.9, 38.5, 36.5, 24.3, 23.9, 14.3; MS (70 eV) *m/e* (relative intensity) 238 (M^+ + 1, 87), 164 (99), 135 (45), 125 (55), 100 (100), 79 (99), 67 (31), 55 (23); HRMS (EI) *m/e* calcd for $C_{13}H_{19}NO_3$ (M^+) 237.1365, found 237.1356.

(1*R,2*R**,9*S**)-2-Carbethoxy-10-oxo-7-azatricyclo-[7.3.0.0^{2,7}]dodecane (8).** The crude mixture from intramolecular cyclization of complex **3i** (1.1 g, 2.9 mmol) was purified via flash column chromatography (silica gel, 30% ethyl acetate/hexanes) to give **8** (0.48 g, 0.93 mmol, 32%) as a pale yellow liquid: IR (CH_2Cl_2) 2943, 2860, 1736, 1444, 1334, 1265, 1224, 1141, 1024 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (m, 2 H), 3.34 (dd, J = 9.8, 8.8 Hz, 1 H), 2.98 (dd, J = 9.8, 2.4 Hz, 1 H), 2.93–2.85 (m, 2 H), 2.74 (dd, J = 15.4, 6.3 Hz, 1 H), 2.61 (dd, J = 8.8, 2.4 Hz, 1 H), 2.27 (d, J = 8.8 Hz, 1 H), 2.24 (d, J = 2.9 Hz, 1 H), 2.12 (d, J = 12.7 Hz, 1 H), 1.99 (m, 1 H), 1.91 (m, 1 H), 1.69 (d, J = 13.7 Hz, 1 H), 1.54 (d, J = 12.2 Hz, 1 H), 1.43–1.33 (m, 2 H), 1.25 (t, J = 7.3 Hz, 3 H), 1.17 (m, 1 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 220.9, 175.1, 70.7, 60.1, 54.1, 48.3, 48.1, 45.3, 39.4, 29.1, 24.6, 23.0, 21.5, 14.3; MS (70 eV) *m/e* (relative intensity) 252 (M^+ + 1, 22), 178 (100), 176 (23), 150 (6), 122 (18), 79 (8); HRMS (EI) *m/e* calcd for $C_{14}H_{21}NO_3$ (M^+) 251.1521, found 251.1514.

(1*S,2*R**,6*S**)-1-Carbethoxy-5-oxo-8-azatricyclo[6.3.1.0^{2,6}]-dodecane (9).** The crude mixture from intramolecular cyclization of complex **3j** (1.1 g, 2.9 mmol) was purified via flash column chromatography (silica gel, 30% ethyl acetate/hexanes) to give **9** (0.36 g, 1.4 mmol, 50%) as a pale yellow liquid: IR (CH_2Cl_2) 3399, 3067, 2986, 1721, 1290, 1265, 1246, 1096, 895, 880, 858 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.16 (m, 2 H), 3.26 (dd, J = 18.5, 4.2 Hz, 1 H), 3.10 (m, 1 H), 3.03 (m, 2 H), 2.94 (m, 2 H), 2.81 (d, J = 13.2 Hz, 1 H), 2.73 (m, 1 H), 2.40 (dd, J = 18.5, 8.0 Hz, 1 H), 2.20 (m, 1 H), 2.16 (m, 1 H), 1.95 (m, 2 H), 1.86 (m, 1 H), 1.55 (m, 1 H), 1.41 (t, J = 7.3 Hz, 1 H), 1.28 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 214.3, 172.2, 61.7, 50.1, 48.1, 46.2, 43.3, 40.7, 40.5, 37.0, 32.5, 23.4, 19.5, 14.1; MS (70 eV) *m/e* (relative intensity) 251 (M^+, 62), 194 (8), 178 (43), 169 (98), 140 (48), 97 (30), 96 (100), 56 (12); HRMS (EI) *m/e* calcd for $C_{14}H_{21}NO_3$ (M^+) 251.1521, found 251.1525.

(1*R,2*R**,5*S**,7*S**)-2-Carbethoxy-7-methyl-6-oxo-3-azabicyclo[3.2.0]heptane (10).** To a solution of diisopropylamine (0.85 mL, 6.0 mmol) in 4.0 mL of THF under nitrogen at −78 °C was added rapidly, neat, via syringe, a solution of *n*-butyllithium (3.8 mL, 6.0 mmol, 1.6 M) in hexane followed by addition of HMPA (1.8 mL). The reaction mixture was stirred at −78 °C for 20 min. A solution of complex **3a** (1.4 g, 4.3 mmol) in THF (3.0 mL) was added dropwise via syringe. The mixture was stirred at −78 °C for 2 h. The reaction mixture was quenched with trifluoroacetic acid (1.0 mL) via a syringe needle and was stirred at 25 °C under an atmosphere of CO for 2 h. After this time, the reaction mixture was diluted with an ethyl acetate/hexanes mixture (1/1, 100 mL). The resultant solution was washed with water (100 mL × 3) and brine (100 mL × 3), dried over anhydrous magnesium sulfate (10 g), and concentrated to give the crude mixture. The crude mixture was purified via flash column chromatography (silica gel, 25% ethyl acetate/hexanes) to give **11** (0.25 g, 1.8 mmol, 16%), **10** (0.30 g, 1.4 mmol, 33%), and **4a** (0.32 g, 1.5 mmol, 35%) as colorless oils. **10**: IR (CH_2Cl_2) 2984, 2936, 1775, 1728, 1275, 1254, 1192, 1098, 1030 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.18 (q, J = 7.3 Hz, 2 H), 3.67 (m, 1 H), 3.63 (s, 1 H), 3.42 (m, 1 H), 3.12 (dd, J = 9.3, 8.3 Hz, 1 H), 3.07 (m, 1 H), 3.02 (dd, J = 9.3, 6.8 Hz, 1 H), 2.43 (s, 3 H, NCH_3), 1.30 (t, J = 6.8 Hz, 3 H), 1.09 (d, J = 7.3 Hz, 3 H); ^{13}C NMR (100.4 MHz,

$CDCl_3$) δ 215.3, 172.5, 64.8, 62.4, 60.2, 55.3, 55.0, 38.7, 36.8, 14.4, 8.0; MS (70 eV) *m/e* (relative intensity) 211 (M^+, 10), 154 (30), 138 (95), 128 (10), 82 (10), 67 (15); HRMS (EI) *m/e* calcd for $C_{11}H_{17}NO_3$ (M^+) 211.1207, found 211.1213.

2-Carbethoxy-3-ethyl-1-methylpyrrole (11): IR (CH_2Cl_2) 3063, 3050, 2985, 1727, 1609, 1273, 1105, 895, 828, 818 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.67 (d, J = 2.4 Hz, 1 H), 6.00 (d, J = 2.4 Hz, 1 H), 4.30 (q, J = 7.3 Hz, 2 H), 3.87 (s, 3 H, NCH_3), 2.78 (q, J = 7.3 Hz, 2 H), 1.36 (t, J = 6.8 Hz, 3 H), 1.19 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 164.5, 128.2, 108.2, 76.7, 76.4, 59.9, 37.6, 21.4, 15.0, 14.4; MS (70 eV) *m/e* (relative intensity) 181 (M^+, 37), 166 (12), 149 (100), 136 (34), 125 (32), 112 (26), 67 (28); HRMS (EI) *m/e* calcd for $C_{10}H_{15}NO_2$ (M^+) 181.1102, found 181.1108.

(1*R,2*R**,5*S**,7*S**)-2-Carbethoxy-7-methyl-6-oxobicyclo-[3.2.0]heptane (14)**. To a solution of diisopropylamine (0.85 mL, 6.0 mmol) in 4 mL of THF under nitrogen at −78 °C was added rapidly, neat, via syringe, a solution of *n*-butyllithium (3.8 mL, 6.0 mmol, 1.6 M) in hexane followed by addition of HMPA (1.8 mL). The reaction mixture was stirred at −78 °C for 20 min. A solution of complex **12** (1.5 g, 4.8 mmol) in THF (3.0 mL) was added dropwise via syringe. The mixture was stirred at −78 °C for 2 h. The reaction mixture was quenched with trifluoroacetic acid (1.0 mL) via a syringe needle and was stirred at 25 °C under an atmosphere of CO for 2 h. After this time, the reaction mixture was diluted with an ethyl acetate/hexanes mixture (1/1, 100 mL). The resultant solution was washed with water (100 mL × 3) and brine (100 mL × 3), dried over anhydrous magnesium sulfate (10 g), and concentrated to give the crude mixture. The crude mixture was purified via flash column chromatography (silica gel, 25% ethyl acetate/hexanes) to give **13**[12a] (0.32 g, 1.6 mmol, 34%), and **14** (0.33 g, 1.7 mmol, 35%) as colorless oils. **14**: IR (CH_2Cl_2) 2971, 2876, 1769, 1449, 1375, 1352, 1192, 1157, 1136, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.12 (q, J = 7.2 Hz, 2 H), 3.69 (ddd, J = 6.8, 5.9, 3.4 Hz, 1 H), 3.53 (dq, J = 10.3, 7.8 Hz, 1 H), 3.27 (dd, J = 10.3, 5.9 Hz, 1 H), 2.87 (d, J = 7.8 Hz, 1 H), 2.17 (dd, J = 12.2, 5.8 Hz, 1 H), 1.98 (dd, J = 12.5, 6.1 Hz, 1 H), 1.80−1.62 (m, 2 H), 1.27 (t, J = 7.2 Hz, 3 H), 1.02 (d, J = 7.8 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 216.7, 175.1, 63.5, 60.6, 54.9, 43.9, 37.9, 30.5, 27.4, 14.1, 7.9; MS (70 eV) *m/e* (relative intensity) 196 (M^+, 16), 167 (13), 150 (18), 141 (27), 95 (67), 67 (100), 54 (29); HRMS (EI) *m/e* calcd for $C_{11}H_{16}O_3$ (M^+) 196.1099, found 196.1100.

3-Cyano-4-((*E*)-1-propenyl)-1-methylpyrrolidine (16). The crude mixture from intramolecular cyclization of complex **15** (0.92 g, 2.7 mmol) was purified via flash column chromatography (silica gel, 7% ethyl acetate/hexanes) and short-path distillation (0.02 mmHg, 85−90 °C) to give **16** (0.15 g, 0.67 mmol, 25%) as an inseparable 4:3 mixture of syn and anti isomers: IR (CH_2Cl_2) (mixture of diastereomers) 3019, 2988, 2948, 2849, 2242, 1607, 1424, 1250, 1100, 895, 833, 828 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers) δ 5.62 (m, 2 H), 5.37 (m, 2 H), 3.42 (quin, J = 6.8 Hz, 1 H), 3.04 (quin, J = 7.1 Hz, 1 H), 2.88−2.79 (m, 6 H), 2.71 (m , 2 H), 2.36 (s, 3 H, NCH_3), 2.35 (s, 3 H, NCH_3), 2.34 (m, 2 H), 1.69 (d, J = 6.4 Hz, 3 H), 1.67 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) (mixture of diastereomers) δ 129.4, 127.1, 126.3, 120.7, 120.5, 60.8, 60.5, 58.3, 58.2, 46.6, 40.9, 40.6, 40.5, 33.9, 33.6, 16.8, 12.3; MS (70 eV) (mixture of diastereomers) *m/e* (relative intensity) 150 (M^+, 86), 149 (39), 135 (16), 124 (15), 108 (27), 107 (31), 82 (18), 67 (10), 57 (100); HRMS (EI) *m/e* calcd for $C_9H_{14}N_2$ (M^+) 150.1156, found 150.1153.

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Supporting Information Available: ORTEP diagrams showing the atom-numbering scheme and tables of crystallographic data, positional parameters, and bond lengths and angles for **4g** (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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