Use of a Methoxy Substituent in Controlling the Stereochemistry of Intramolecular Iron-Mediated Diene/Olefin Cyclocoupling

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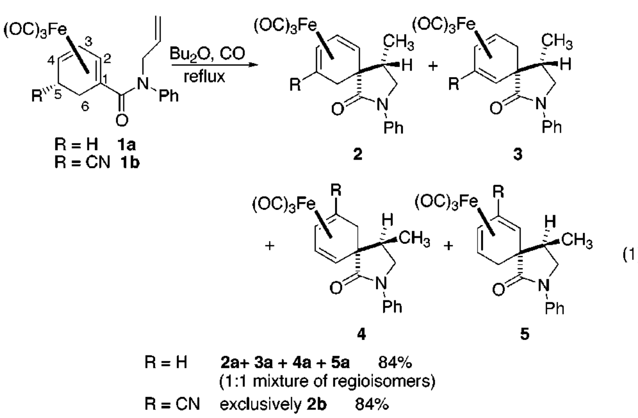
A methodology for stereocontrol during the intramolecular coupling between cyclohexadiene−$Fe(CO)_3$ complexes and pendant alkenes is presented. Introduction of a methoxy group at the C(3) position of the diene moiety controls pre- and postcyclization rearrangements of the diene $Fe(CO)_3$ unit, allowing the preparation of spirolactams with defined relative stereochemistry and with a cyclohexenone framework, thus making this reaction a potentially valuable tool for the construction of quaternary carbon centers.

Introduction

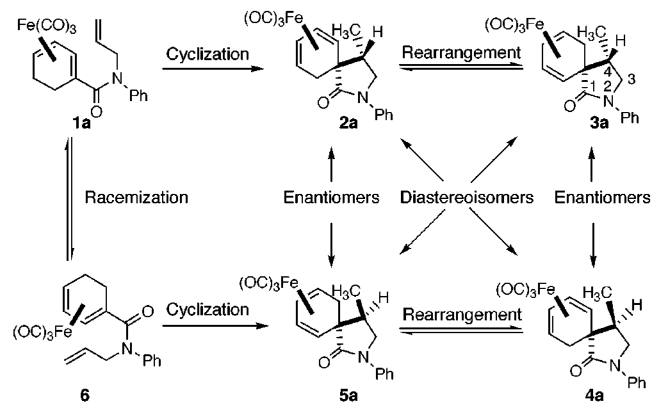
The synthesis of natural products possessing complex molecular structure often requires the construction of quaternary carbon centers.[1] Despite the large number of methods available for the formation of such carbon−carbon bonds, these synthetic reactions often suffer from a lack of general applicability.[2] The construction of spirocenters in an asymmetric fashion is even more restricted.[3]

We previously reported an intramolecular coupling between a diene−$Fe(CO)_3$ complex and a pendant alkene that results in the efficient, stereospecific construction of congested quaternary carbon centers.[4a,b] Allylic amides were found to be the best substrates for these spirocyclizations (eq 1), whereas allylic ester and allylic thioester systems were shown to be limited to substrates having a low degree of substitution on the remote olefinic moiety. This novel spirocyclization had another drawback: when the chiral complex **1a** (eq 1) was reacted



under the thermal cyclization conditions, a complete scrambling of the stereochemistry was observed in the products **2a**, **3a**, **4a**, and **5a**. Thus, although the stereochemistry at the newly formed carbon−carbon bond in these spirocyclizations is defined cis to the metal, a racemic mixture of two diastereoisomers of the spirocomplex is obtained.[4] The explanation for these results is shown in Scheme 1, where stereospecific cyclization of chiral complex **1a** to give **2a** is followed by equilibration to the regioisomeric rearranged diene−$Fe(CO)_3$ complex **3**a.[4,6] The observed loss of absolute stereochemistry is caused by a competing, but slower racemization of the

Scheme 1



(1) For recent examples, see: (a) Srikrishna, A.; Ramachary, D. B. *Tetrahedron Lett.* **2000**, *41*, 2231. (b) Takahashi, M.; Dodo, K.; Hashimoto, Y.; Shirai, R. *Tetrahedron Lett.* **2000**, *41*, 2111. (c) Overman, L. E.; Paone, D. V.; Stearns, B. A. *J. Am. Chem. Soc.* **1999**, *121*, 7702. (d) Honzawa, S.; Mizutani, T.; Shibasaki, M. *Tetrahedron Lett.* **1999**, *40*, 311.

(2) For reviews, see: (a) Corey, E. J.; Guzman-Perez, A. *Angew. Chem., Int. Ed. Engl.* **1998**, *388*. (b) Fuji, K. *Chem. Rev.* **1993**, *93*, 2037. (c) Martin, S. *Tetrahedron* **1980**, *36*, 419. For recent examples of the construction of quaternary carbon, see: (a) Nishimura, N.; Mitsunobu, O. *Tetrahedron Lett.* **2000**, *41*, 2945. (b) Hong, J. H.; Gao, M.; Chu, C. K. *Tetrahedron Lett.* **1999**, *40*, 231. (c) Dwyer, M. P.; Price, D. A.; Lamar, J. E.; Meyers, A. I. *Tetrahedron Lett.* **1999**, *40*, 4765. (d) Yashimata, Y.; Odashima, K.; Koga, K. *Tetrahedron Lett.* **1999**, *40*, 2803. (e) Pigge, F. C.; Fang, S.; Rath, N. P. *Tetrahedron Lett.* **1999**, *40*, 2251.

(3) For a recent review, see: Sannigrahi, M. *Tetrahedron* **1999**, *55*, 9007. For recent examples, see: (a) Xi, C.; Kotora, M.; Nakajima, K.; Takahashi, T. *J. Org. Chem.* **2000**, *65*, 945. (b) Wallace, D. J.; Cowden, C. J.; Kennedy, D. J.; Ashwood, M. S.; Cottrell, I. F.; Dolling, U. *Tetrahedron Lett.* **2000**, *41*, 2027. (c) Takao, K.; Saegusa, H.; Watanabe, G.; Tadano, K. *Tetrahedron: Asymmetry* **2000**, *11*, 453. (d) Tanner, D.; Hagberg, L.; Poulsen, A. *Tetrahedron* **1999**, *55*, 1427. (e) Pigge, F. C.; Fang, S.; Rath; N. P. *Org. Lett.* **1999**, *11*, 1851.

(4) (a) Pearson, A. J.; Zettler, M. *J. Am. Chem. Soc.* **1989**, *111*, 3908. (b) Pearson, A. J.; Alimardanov, A.; Pinkerton, A. A.; Parrish, A. A. *J. Org. Chem.* **1998**, *63*, 6610. (c) Pearson, A. J., Alimardanov, A. *Organometallics* **1998**, 17, 3739.

(5) Pearson, A. J.; Zettler, M. *J. Chem. Soc., Chem. Commun.* **1987**, 1243.

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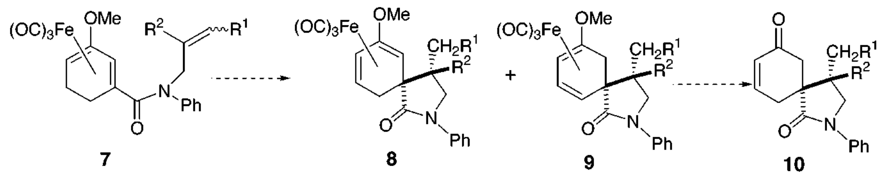
Scheme 2



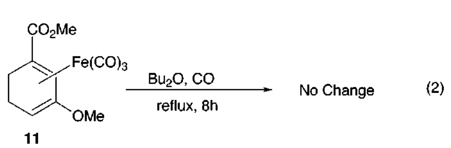
starting material to give the enantiomeric diene−Fe(CO)$_3$ complex **6** which in turn gives spirocomplexes **5a** and **4a** upon cyclization.

However, we have demonstrated that the stereochemical outcome of these spirocyclizations can be controlled by introducing an appropriate group at the C(5) position of the diene−Fe(CO)$_3$ complex (e.g., **1b**, eq 1).[4a,5] Thus, when the chiral optically pure cyano substituted diene−Fe(CO)$_3$ complex **1b** was cyclized, only spirocomplex **2b** was obtained stereospecifically. Unfortunately, the cyclization was restricted to simple remote alkene subunits, and the C(5) substituents were of rather limited value for the synthesis of natural products. The studies to be detailed herein were formulated for the explicit purpose of controlling the stereochemistry during this intramolecular ene-type coupling between diene−Fe(CO)$_3$ complexes and pendant alkene subunits, and to do so in a fashion that will lead to a molecular framework that is potentially useful for the synthesis of natural products.

Results and Discussion

In an effort to overcome the problems outlined above, we directed our attention to the synthesis and reactions of amide complexes **7** (Scheme 2). We anticipated that attaching a methoxy group at the C(3) position of the diene−Fe(CO)$_3$ complex (e.g., **7**, Scheme 2) would prevent the precyclization rearrangement, for obvious thermodynamic reasons (the most stable diene has the structure shown in **7**). Then even if the postcyclization rearrangement could not be avoided (see **8** and **9**), it would not matter as demetalation of the regioisomeric diene−Fe(CO)$_3$ complexes, followed by acidic hydrolysis would lead to a unique cyclohexenone compound **10**.

Our study commenced by testing the propensity of diene−Fe(CO)$_3$ complex **11**[7,8] (eq 2) to rearrange under the thermal conditions utilized for the actual spirocyclization reaction. We were delighted to observe that subjection of **11** to the thermal conditions led to recovery of the starting material with no product of rearrangement (eq 2).[9] This result indicated a means of controlling the



(2)

overall stereochemistry of the spirocyclization reaction.

(6) (a) Alper, H.; LePort, P. C.; Wolfe, S. *J. Am. Chem. Soc.* **1969**, *91*, 7553. (b) Whitesides, T. H.; Neilan, J. P. *J. Am. Chem. Soc.* **1976**, *98*, 63.

(7) The synthesis of complex **11** was achieved starting from *m*-anisic acid in four steps as described in ref 8. The yield of the last step was dramatically improved by purging (using an oxygen free Ar flow) the solution of H_2SO_4/MeOH prior reaction.

(8) Birch, A. J.; Pearson, A. J. *J. Chem Soc., Perkin Trans. 1* **1977**, 638.

(9) Some aromatized product was observed as a minor side product (<5%).

Scheme 3

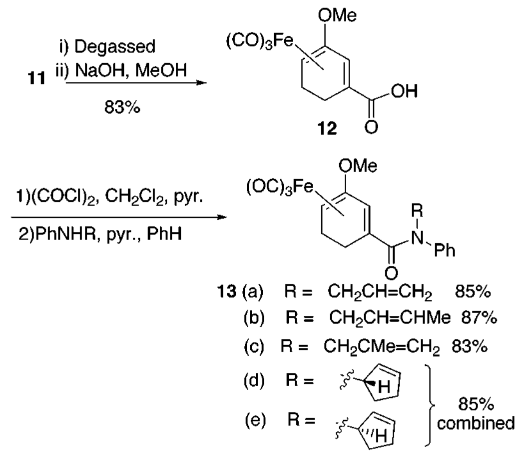
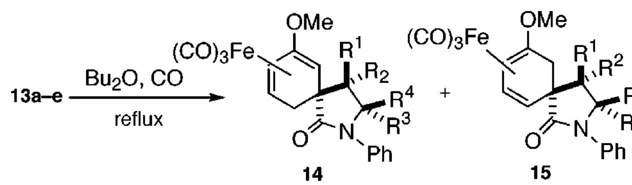


Table 1. Cyclization of 3-Methoxy Allylic Amide Derivatives[a]



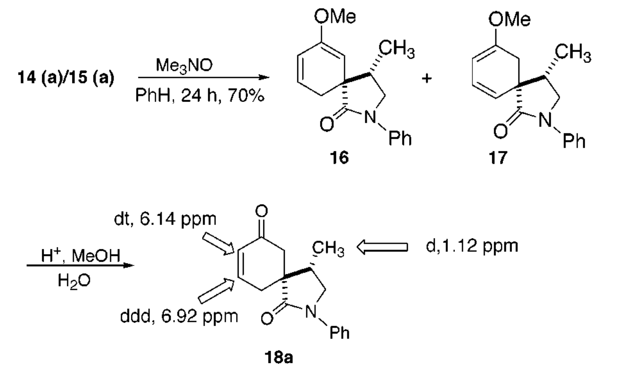
(a) $R_1 = R_3 = R_4 = H$, $R_2 = CH_3$
(b) $R_1 = R_3 = R_4 = H$, $R_2 = Et$
(c) $R_1 = R_2 = CH_3$, $R_3 = R_4 = H$
(d) $R_1 = R_4 = H$, $R_2 = R_3 = CH_2CH_2CH_2$
(e) $R_1 = R_3 = H$, $R_2 = R_4 = CH_2CH_2CH_2$

entry	substrate	reaction conditions	products	yield, %
1	**13a**	A, 8 h	**14a**, **15a**	80
2		B, 2.5 h		80
3	**13b**	A, 6 h	**13b**, **15b**	16
4		B, 2.5 h		85
5	**13c**	A, 6 h	**14c**, **15c**	20
6		B, 2.5 h		88
7	**13d**	A, 8 h	**14d**, **15d**	78[b]
8	**13e**	B, 4 h	No reaction	0
9		A, 8 h	**14e**, **14d**, **15d**	72[b]

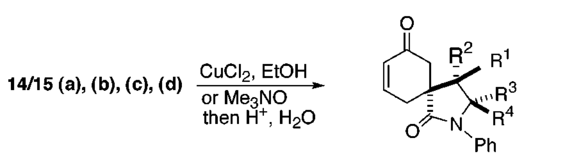
[a] A: Bu_2O, CO, reflux; B: Rayonet, 350 nm, CO, C_6H_6, reflux. [b] Yield based on recovered starting material.

As previously experienced with the related 4-methoxycyclohexadienylcarboxylate complex,[4a] saponification of **11** was somewhat troublesome. These iron complexes proved to be quite sensitive to oxidation, leading to aromatization under the usual basic or acidic hydrolysis conditions when traces of air were present. Therefore, the solution of **11** and aqueous sodium hydroxide (30%) in methanol was thoroughly purged (using an argon flow) prior to the hydrolysis reaction, which allowed carboxylic acid **12** to be isolated as a yellow solid, in good yield (83%) (Scheme 3). Conversion of acid **12** to its acid chloride, followed by treatment with a series of different *N*-allylaniline substrates in the presence of dry pyridine, afforded a series of diene−Fe(CO)$_3$ complexes **13a**−**e** in

Scheme 4



good yield. With the diene−$Fe(CO)_3$ complexes **13** in hand, we were now in position to evaluate their behavior. Thermal spirocyclization of substrate **13a** gave a 1:1 mixture of inseparable isomeric adducts **14a**/**15a**,[10] along with the demetalated materials **16**/**17**, as minor side products (12%) (Table 1, entry 1). This mixture was smoothly converted to the corresponding free ligands **16**/**17** by reaction with trimethylamine *N*-oxide in anhydrous benzene (Scheme 4). Acidic hydrolysis of the isomeric enol ether mixture provided spirocyclohexenone **18a** as a single compound. Evidence that only enone **18a** was obtained was garnered by the existence of a single methyl doublet at 1.1 ppm and by the pattern characteristic of the α,β-unsaturated ketone in the ^{1}H NMR spectrum. The relative stereochemistry between the spirocenter and the lactam side chain follows from our previous work.[4] Conversion of the mixture **14a**/**15a** directly to **18a** was also accomplished in one step using a suspension of copper(II) chloride in ethanol (eq 3).[11]



(3)

18 (a) $R_2 = CH_3$, $R_1 = R_3 = R_4 = H$
(b) $R_2 = Et$, $R_1 = R_3 = R_4 = H$
(c) $R_1 = R_2 = CH_3$, $R_3 = R_4 = H$
(d) $R_2 = R_3 = CH_2CH_2CH_2$, $R_1 = R_4 = H$

With the general concept of this protocol established, we turned our attention to the spirocyclization of more highly substituted unsaturated amides.[12] Unfortunately, when **13b** and **13c** were submitted to thermal cyclization conditions (Bu_2O, CO, reflux), spirocomplexes **14b**/**15b** and **14c**/**15c** were produced in low yield (16% and 20%, respectively) along with numerous uncharacterized side products. Recourse was made instead to the use of photothermal conditions.[4b] Thus, **13b** was heated at 80 °C in anhydrous benzene in a Rayonet photochemical reactor, using a 350 nm light source, to afford the cyclized material **14b/15b** as the anticipated 1:1 mixture of

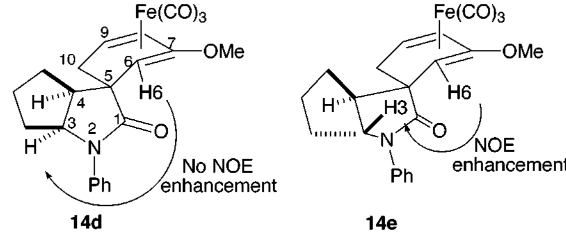


Figure 1. Assignments of stereochemistry of **14d** and **14e** by ^{1}H−^{1}H NOE studies ($CDCl_3$, 200 MHz).

isomers in 85% yield. It may be noted that **13b** was diluted in benzene 33% more than the normal conditions,[4b] in order to avoid formation of side products. The same treatment was applied to **13a** and **13c** which furnished **14a**/**15a** and **14c**/**15c** in 80% and 88% yield, respectively (Table 1, entries 2, 6). In each case, the mixture of regioisomers was smoothly converted to a single cyclohexenone derivative (eq 3).

The final stages of this study consisted in investigating the spirocyclization of the mixture of epimeric complexes **13d/13e**. The product of this cyclization would be of great interest since it would lead to a tricyclic framework having an appreciably congested quaternary carbon center.[4b] Unfortunately, initial attempts to cyclize **13d/13e** under photothermal conditions resulted only in recovery of the starting material. However, when reacted under thermal reaction conditions, this 1:1 mixture of epimers afforded the desired spirocompounds as a complex mixture of regio- and stereoisomers. Refinement of the stereochemistry problem required prior separation of epimers **13d** and **13e,** which was achieved by preparative TLC, using a multiple development technique.[16] As expected, one of the iron amide complexes, the structure of which was later assigned to **13d**, under thermal conditions led to spirolactams **14d**/**15d** as a 1:1.2[10] mixture (78% yield at 64% conversion). Prior work in our laboratory with related molecules hinted that one of the amide complexes (**13e**) might well be unreactive toward cyclization (vide infra).[4b] This presumption proved to be incorrect in that treatment of the other epimer (the structure of which was later assigned to **13e**) under thermal conditions led to the isolation of a mixture of epimerized **13d**/**13e**, and spirocyclized compounds **14d**/**15d**/**14e** as a 1:1.9:1.4 mixture,[10] in 75% yield (based on recovered starting material). The presence of **13d** as well as **14d** and **15d** indicates that a competing epimerization at the allylic amide stereogenic center takes place during the spirocyclization of **13e**. Moreover, a new spirocompound **14e** was observed (Scheme 5), having a ^{1}H NMR spectrum analogous to **14d**, the only difference being a downfield shift of the peaks corresponding to H(3), H(4), and H(9). NOE difference experiments allowed us to unambiguously assign the structure of **14d** and **14e**. Irradiation of H(3) showed a strong NOE enhancement for the signal corresponding to H(6) in compound **14e** (Figure 1). The same experiment with compound **14d** showed no NOE enhancement for H(6) when H(3) was

(10) By integration of ^{1}H NMR.

(11) Thompson, D. J. *J. Organomet. Chem.* **1976**, *108*, 381.

(12) The corresponding amines were prepared according to literature procedures. Reductive *N*-monoalkylation of aniline provided crotylaniline.[13] The direct (and selective) *N*-monoalkenylation of aniline with 2-methyl-2-propenyl-1-mesylate using methylmagnesium bromide as a base afforded methallylaniline.[14] *N*-Cyclopentenylaniline was obtained by treating aniline with 3-chlorocyclopentene at 80 °C in the presence of trimethylamine.[15] The corresponding amide complexes (respectively **13b**, **13c**, **13d/13e**) were obtained from carboxylic acid complex **12** in good yields (Scheme 3).

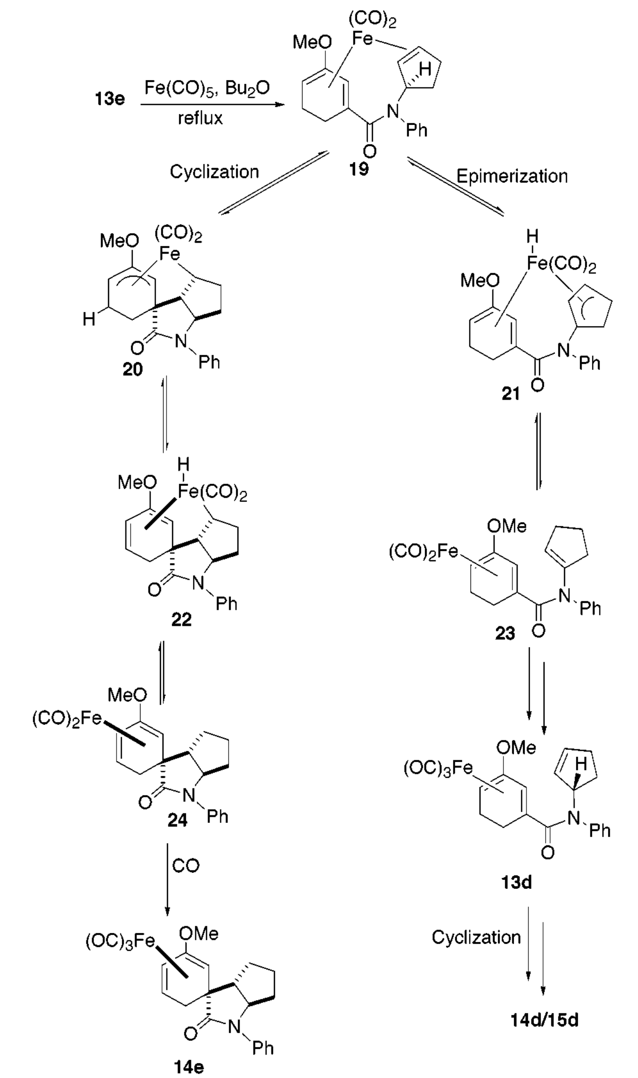
(13) Verardo, G.; Giumanini, A. G.; Strazzolini, P.; Poiana, M. *Synthesis* **1993**, 121.

(14) Yoshida, Y.; Tanabe, Y. *Synthesis* **1997**, 533.

(15) Abdrakhmanov, I. B.; Sharafutdinov, V. M.; Dzhemilev, U. M.; Tal'vinskii, E. V.; Sagitdinov, I. A.; Tolstikov, G. A. *Zh. Prikl. Khim.* **1982**, *55*, 2121.

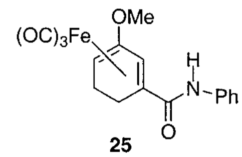
(16) A sequence of elution/drying of the preparative TLC plate was repeated five times.

Scheme 5



irradiated, indicating the remarkable *trans*-octalin structure of **14e**. Based upon the reaction mechanism,[4] this information also established the stereochemistry of the starting material **13e** to be as shown in Scheme 3.

A plausible mechanism that rationalizes the formation of the epimerized mixture of starting complexes **13e/13d** and the formation of spirocyclized compounds **14e**, **14d/15d** is adumbrated in Scheme 5. Under thermal conditions, **13e** first loses a CO ligand to give a 16-electron complex, which is stabilized by coordination of the pendant alkene to the metal (e.g., **19**). Intermediate **19** can be engaged in two competing reactions. Cyclization, followed by H migration leads to **22** which, after reductive elimination and recapture of one CO, gives *trans*-octalin complex **14e**. Due to the strained *trans*-ring junction in metallacyclic intermediate **20**, the energy barrier for the cyclization of **13e** is probably higher than the cyclization of its epimer **13d**. Therefore, insertion into the allylic C−H bond of the pendant alkene competes with direct cyclization and gives rise to π allyl complex **21**. Reductive elimination (**23**), followed by the reverse sequence (of **23** to **21**) yields **13d**, which in turn follows the cyclization path to afford **14d/15d**. It may be noted that we have previously observed a similar isomerization of allyl to vinyl amide side chains during these reactions,[4a] but this is the first time we have noted any epimerization of a cyclopentenylamide substituent. In contrast to our earlier work, intermediate **23** was not isolated, but amide complex **25** (which presumably results from hydrolysis of vinyl amide complex **23**) was obtained as a side product of the spirocyclization of **13e**.



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Conclusions

Described herein is the intramolecular coupling between pendant olefinic moieties and 3-methoxycyclohexadiene−$Fe(CO)_3$ complexes under thermal or photothermal conditions. The C(3) methoxy substituent efficiently controls the stereochemical issues of the spirocyclization by avoiding the precyclization rearrangement, and by facilitating the conversion of two postcyclization rearrangement products to a single compound. Besides its complete stereoselectivity, this methodology leads to a cyclohexenone framework, of potential value for the synthesis of various natural products.

Experimental Section

General experimental and spectroscopic methods are as described elsewhere.[4] The carboxylic acid proton of compound **12** was not detected by ^{1}H NMR. The quaternary carbons of the $Fe(CO)_3$ moiety were not detected by ^{13}C NMR for compounds **12**, **13a**, **13b**, **13c**, **13d**, **13e**, and **14e**.

General Procedure for the Preparation of Allylic Amides. Carboxylic acid **12** was dissolved in freshly distilled CH_2Cl_2 under argon in a flame-dried single-neck round-bottom flask. Two equivalents of freshly distilled oxalyl chloride was added via a syringe at room temperature, followed by 1.1 equiv of anhydrous pyridine. The reaction mixture was stirred at room temperature for 20 min (reaction was monitored by IR) under argon. The solvent was then evaporated in a vacuum. The resulting viscous oil was kept under high vacuum (0.5 mmHg) for 10 min and then dissolved in freshly distilled benzene. Anhydrous pyridine (2 equiv) was added via a syringe, followed by 2 equiv of the appropriate amine. The reaction mixture was stirred under argon for 24 h (reaction can be monitored by TLC). The product mixture was diluted with diethyl ether, washed with 2 N aq HCl and water, dried over $MgSO_4$, and concentrated under vacuum. Flash chromatography on silica gel or preparative TLC separation (EtOAc/hexane, 2:8) afforded the desired racemic allyl amide, usually as a yellow viscous oil. Deviations from this procedure are noted in the experimental data for the specific compound.

General Procedure for the Photothermally Induced Cyclization. The appropriate amide was dissolved in freshly distilled benzene in a flame-dried quartz tube equipped with a reflux condenser under argon. The solution was purged with CO for 1 min. The reaction mixture was heated to 80 °C and irradiated in a Rayonet reactor with 350 nm light source, with magnetic stirring for 2.5 h under a balloon of CO. The cooled product mixture was diluted with ether, filtered through Celite, and concentrated. Flash chromatography or preparative TLC separation (EtOAc/hexanes, 2:8) yielded the desired product. Deviations from this procedure are noted in the experimental data for the specific compound.

General Procedure for the Thermally Induced Cyclization. The appropriate amide was dissolved in freshly distilled *n*-butyl ether under argon. The solution was purged with CO for 1 min and then refluxed under a balloon of CO for 8 h. The cooled product mixture was diluted with ether, filtered through Celite, and concentrated. Flash chromatography or preparative TLC separation (EtOAc/hexanes, 2:8) yielded the desired product. Deviations from this procedure are noted in the experimental data for the specific compound.

General Procedure for the Preparation of α,β Unsaturated Ketone Using Copper Chloride. The mixture of spiroamide complexes was stirred with a saturated solution of $CuCl_2$ in EtOH for 20 h under Ar. The mixture was poured into water and extracted with Et_2O. The ethereal layer gave, after filtration through a plug of silica and removal of the solvent, the crude product, which was purified by flash chromatography or preparative TLC (EtOAc/hexanes, 6:4).

General Procedure for the Preparation of α,β Unsaturated Ketone Using Me_3NO Followed by Acidic Hydrolysis. A dry 1:1 mixture of spirocyclic amide complexes was dissolved in anhydrous C_6H_6. This solution was added via a syringe to a flame-dried round-bottom flask containing 35 equiv of anhydrous Me_3NO under Ar. The reaction mixture was stirred at room temperature under Ar for 16 h (the reaction can be monitored by IR) and then diluted with ether and filtered through Celite. The solution was washed with H_2O, dried over $MgSO_4$, and concentrated. The demetalated product was then dissolved in methanol and added to a solution of oxalic acid (15.5 equiv) in water. The reaction mixture was stirred at room temperature for 24 h and then poured into a sat. aq solution of K_2CO_3 and extracted with ether. Preparative TLC or flash chromatography (EtOAc/hexanes, 6:4) yielded the pure α,β-unsaturated ketone.

Tricarbonyl[1−4-η-(3-Methoxycyclohexa-1,3-diene)carboxylic acid]iron (12). To a solution of the known iron complex ester **11**[8] (5 g, 16.25 mmol) in methanol (degassed 10 min prior to use using an oxygen free Argon flow) was added 12 mL of aq KOH (30%) (degassed 10 min prior to use using an oxygen free Argon flow). The mixture was stirred for 24 h under Ar and then acidified to pH = 3 using a 10% aq HCl solution. The acidic solution was extracted with CH_2Cl_2. The resulting organic layer was washed with water, dried over $MgSO_4$, and concentrated to afford **12** (3.96 g, 83%) as a yellow crystalline solid. Mp 188−190 °C dec IR (cm^{-1}, CH_2Cl_2): 3300−2400, 2068, 1974, 1668. ^1H NMR (200 MHz, $CDCl_3$, δ): 5.69 (d, J = 2.4 Hz, 1H), 3.69 (s, 3H), 3.60 (apparent q, 1H, J = 2.4 Hz), 2.18−1.76 (series of m, 3H), 1.43 (ddd, 1H, J = 13.8, 9.2, 4.2 Hz). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 180.0, 138.9, 69.5, 56.1, 54.6, 54.1, 25.9, 22.4. HRMS (m/z) for $M^+ - CO$ ($C_{10}H_{10}FeO_5$): calculated: 265.9878; found: 265.9882.

Tricarbonyl[*N*-allyl-*N*-phenyl-1−4-η-3-(methoxycyclohexa-1,3-diene)-1-carboxamide]iron (13a). A solution of acid **12** (300 mg, 1.02 mmol) in anhydrous CH_2Cl_2 (3.2 mL) was treated with oxalyl chloride (180 μL) and anhydrous pyridine (90 μL), followed by anhydrous benzene (4.5 mL), anhydrous pyridine (165 μL), and *N*-allylaniline (277 μL) according to the general procedure. Amide complex **13a** (355 mg, 85%) was isolated by flash chromatography as a yellow oil. IR (cm^{-1}, CH_2Cl_2): 2059, 1991, 1634. ^1H NMR (200 MHz, C_6D_6, δ): 7.21−7.08 (series of m, 5H), 6.11 (dddd, 1H, J = 20.7, 11.5, 7.1, 5.6 Hz), 5.73 (d, 1H, J = 1.8 Hz), 5.00 (ddt, 1H, J = 11.5, 2.9, 1.0 Hz), 4.94 (ddt, 1H, J = 20.7, 2.9, 1.0 Hz), 4.62 (ddt, 1H, J = 14.5, 5.5, 1.3 Hz), 4.10 (ddt, 1H, J = 14.5, 5.5, 1.0 Hz), 3.19 (apparent dd, 1H, J = 5.5, 2.7 Hz), 2.94 (s, 3H), 1.71 (ddd, 1H, J = 13.7, 10.8, 2.9 Hz), 1.34 (m, 2H), 1.03 (ddd, 1H, J = 13.7, 7.7, 5.0 Hz), 1.00 (ddd, 1H, J = 13.7, 7.7, 4.8 Hz). (In $CDCl_3$ the OCH_3 singlet occurs at δ 3.4) ^{13}C NMR (50 MHz, $CDCl_3$, δ): 173.5, 143.5, 138.3, 133.3, 129.7, 128.0, 127.6, 117.9, 68.9, 60.2, 55.8, 55.1, 54.1, 26.7, 24.3. HRMS (m/z) for MH^+ ($C_{20}H_{20}FeNO_5$): calculated: 410.0691; found: 410.0698.

Tricarbonyl[*N*-cyclopent-2-en-1-yl-*N*-phenyl-1−4-η-(3-methoxycyclohexa-1,3-diene)-1-carboxamide]iron (13d/13e). A solution of acid **12** (500 mg, 1.7 mmol) in anhydrous CH_2Cl_2 (6.4 mL) was treated with oxalyl chloride (300 μL) and anhydrous pyridine (150 μL), followed by anhydrous benzene (7.5 mL), anhydrous pyridine (275.32 μL), and *N*-cyclopentenylaniline (0.575 g) according to the general procedure. The mixture was then stirred under reflux for 24 h. Amide complexes **13d**/**13e** were isolated as a 1:1 mixture by flash chromatography (317 mg, 85% based on recovered starting material at 51% conversion). Amides **13d**/**13e** were separated by preparative TLC purification (EtOAc/hexanes, 8:2, multiple development). **13d:** IR (cm^{-1}, CH_2Cl_2): 2052, 1979, 1650. ^1H NMR (200 MHz, $CDCl_3$, δ): 7.40−7.12 (series of m, 5H), 5.74 (m, 3H), 5.33 (s, 1H), 3.42 (s, 4H), 2.23−1.16 (series of m, 8H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 173.9, 140.2, 138.1, 135.2, 130.8, 130.2, 129.0, 127.8, 68.6, 64.0, 61.2, 55.9, 54.1, 31.3, 27.9, 27.0, 24.7. HRMS (m/z) for $M^+ - 2CO$ ($C_{20}H_{21}FeNO_3$): calculated: 379.0871; found: 379.0874. **13e:** IR (cm^{-1}, CH_2Cl_2): 2052, 1973, 1631, 1609, 1492. ^1H NMR (200 MHz, $CDCl_3$, δ): 7.38−7.11 (series of m, 5H), 5.79−5.54 (series of m, 4H), 5.52 (s, 3H), 3.46 (m, 1H), 2.34−1.20 (series of m, 8H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 173.5, 140.2, 138.5, 134.9, 130.4, 130.3, 128.9, 127.8, 68.8, 64.8, 61.0, 55.9, 54.2, 32.3, 28.5, 26.8, 24.6. HRMS (m/z) for $M^+ - 2CO$ ($C_{20}H_{21}FeNO_3$): calculated: 379.0871; found: 379.0871.

Tricarbonyl(6−9-η-1-oxo-2-phenyl-4-methyl-7-methoxy-2-azaspiro[4.5]deca-6,8-diene)iron(14a)/Tricarbonyl(7−10-η-1-oxo-2-phenyl-4-methyl-7-methoxy-2-azaspiro[4.5]-deca-7,10-diene)iron (15a). Thermal Cyclization. Amide complex **13a** (205 mg) was heated in *n*-butyl ether (28 mL) according to the general procedure. Flash chromatography (EtOAc/hexane, 2:8) yielded spirocomplexes **14a**/**15b** as a 1:1 mixture of regioisomers (164 mg, 80% yield), demetalated spirocompound **16**/**17** (25 mg, 12%), and starting material **13a** (12.3 mg, 6%). Recrystallization from Et_2O/hexanes (1:5, −78 °C) afforded **14a** as a pale yellow solid. Mp 104−106 °C dec IR (cm^{-1}, CH_2Cl_2): 2042, 1968, 1690. ^1H NMR (200 MHz, $CDCl_3$, δ): 7.61 (m, 2H), 7.33 (t, 2H, J = 7.5 Hz), 7.12 (tt, 1H, J = 7.5, 0.6 Hz), 5.20 (dd, 1H, J = 6.6, 2.1 Hz), 3.86 (dd, 1H, J = 9.8, 6.3 Hz), 3.75 (s, 3H), 3.37 (dd, 1H, J = 9.8, 2.4 Hz), 3.10 (d, 1H, J = 2.1 Hz), 2.74 (dt, 1H, J = 6.6, 2.7 Hz), 2.27 (m, 1H), 1.92 (dd, 1H, J = 14.9, 2.7 Hz), 1.74 (dd, 1H, J = 14.9, 2.7 Hz), 1.26 (d, 3H, J = 7.14 Hz). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 211.2, 176.7, 140.8, 139.7, 128.8, 124.4, 119.4, 67.5, 55.0, 54.7, 54.0, 52.2, 48.9, 39.7, 39.1, 15.7. HRMS (m/z) for $M^+ - CO$ ($C_{19}H_{19}FeNO_4$): calculated: 381.0663; found: 381.0661. **15a:** ^1H NMR (200 MHz, $CDCl_3$, δ): 5.51 (d, 1H, J = 4.6 Hz), 5.01 (dd, 1H, J = 6.3, 4.6 Hz), 4.16 (dd, 1H, J = 10.2, 6.2 Hz), 3.55 (s, 3H), 2.76 (dd, 1H, J = 6.3, 1.3 Hz), 2.46 (d, 1H, J = 15.0 Hz), 2.17 (d, 1H, J = 15.0 Hz), 1.65 (m, 2H), 1.10 (d, 3H, J = 7.2 Hz). **Photothermal cyclization: 13a** (50 mg, 0.12 mmol) was irradiated according to the general procedure to yield spirolactams **14a**/**15a** as a 1:1 mixture of regioisomers (40 mg, 80% yield).

Tricarbonyl[6−9-η-1-oxo-2-phenyl-7-methoxy-2-azaspiro[4.5]-(3,4-*cis*-bicyclo[3.3.0]octane)deca-6,8-diene]-iron (14d). Thermal cyclization: Amide complex **13d** (200 mg, 0.46 mmol) was heated in *n*-butyl ether (29 mL) according to the general procedure. Flash chromatography (EtOAc/hexane, 2:8) yielded spirocomplexes **14d**/**15d** as a 1:1.2 brown mixture of regioisomers (100 mg, 78% yield based on recovered starting material), along with 72 mg of recovered starting material (64% conversion). **14d**/**15d** were separated by preparative TLC (EtOAc/hexane, 2:8, multiple development). Recrystallization from Et_2O/hexanes (1:5, −78 °C) afforded **14d** as an off-white solid. Mp 166−168 °C dec IR (cm^{-1}, CH_2Cl_2): 2049, 1967, 1691. ^1H NMR (200 MHz, $CDCl_3$, δ): 7.47 (dd, 2H, J = 7.5, 1.2 Hz), 7.33 (td, 2H, J = 7.5, 2.0 Hz), 7.13 (tt, 1H, J = 7.5, 1.2 Hz), 5.19 (dd, 1H, J = 6.5, 1.9 Hz), 4.48 (td, 1H, J = 6.6, 2.0 Hz), 3.77 (s, 3H), 3.18 (d, 1H, J = 1.9 Hz), 2.69 (dt, 1H, J = 6.5, 3.2 Hz), 2.50 (q, 1H, J = 6.6 Hz), 2.10−1.56 (series of m, 8H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 211.2, 176.4, 141.5, 138.0, 128.6, 124.8, 122.0, 66.9, 60.5, 55.4, 55.0, 54.0, 51.9, 48.5, 41.8, 31.3, 27.9, 25.1. HRMS (m/z) for $M^+ - CO$ ($C_{21}H_{21}FeNO_4$): calculated: 407.0820; found: 407.0812.

Tricarbonyl[7−10-η-1-oxo-2-phenyl-7-methoxy-2-azaspiro[4.5]-(3,4-*cis*-bicyclo[3.3.0]octane)deca-7,10-diene]-iron (15d). Recrystallization from Et_2O/hexanes (1:5, −78 °C) afforded **15d** as a yellow solid. Mp 172−174 °C dec IR (cm^{-1}, CH_2Cl_2): 2043, 1964, 1697. ^1H NMR (200 MHz, $CDCl_3$, δ): 7.49 (dd, 2H, J = 8.6, 1.4 Hz), 7.36 (td, 2H, J = 8.6, 1.7 Hz), 7.15 (tt, 1H, J = 8.6, 1.4 Hz), 5.49 (dd, 1H, J = 4.5, 1.6 Hz), 4.98 (dd, 1H, J = 6.4, 4.5 Hz), 4.67 (td, 1H, J = 6.5, 1.9 Hz), 3.54 (s, 3H), 2.71 (dd, 1H, J = 6.4, 1.6 Hz), 2.70 (m, 1H), 2.45 (d, 1H, J = 14.8 Hz), 2.28 (d, 1H, J = 14.8 Hz), 1.97 (m, 2H), 1.71−1.52 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 212.5, 175.8, 138.0, 128.8, 124.9, 121.9, 118.8, 79.4, 73.9, 61.9, 60.9, 56.5, 51.3, 49.6, 36.1, 32.0, 27.4, 24.7. HRMS (m/z) for $M^+ - CO$ ($C_{21}H_{21}FeNO_4$): calculated: 407.0820; found: 407.0814. **Photothermal cyclization:** a solution of **13d**/**13e** (43 mg, 0.11 mmol) as a 1:1 mixture of diastereoisomers in 12 mL of benzene was irradiated according to the general procedure to yield only traces of the desired spirocompounds along with 39 mg of recovered starting material after flash chromatography (EtOAc/hexanes, 2/8).

Tricarbonyl(6−9-*η*-1-oxo-2-phenyl-7-methoxy-2-azaspiro[4.5]-(3,4-*trans*-bicyclo[3.3.0]octane)deca-6,8-diene)-iron (14e). Thermal cyclization: Amide complex **13e** (60 mg, 0.2 mmol) was heated in *n*-butyl ether (9 mL) according to the general procedure. Flash chromatography (EtOAc/hexane, 2:8) yielded spirocomplexes **14d**/**15d**/**14e** as a 1:1.9:1.4 brown mixture (72% yield based on recovered starting material, 59% conversion), along with a mixture of **13e**/**13d** (27 mg). **14d**/**15d**/**14e** were separated by preparative TLC (EtOAc/hexane, 2:8, multiple development). Recrystallization from Et_2O/hexanes (1:5, −78 °C) afforded **14e** as a white solid. Mp 160−165 °C dec IR (cm^{-1}, CH_2Cl_2): 2045, 1960, 1690. ^1H NMR (200 MHz, $CDCl_3$, δ): 7.48 (d, 2H, J = 7.7 Hz), 7.35 (td, 2H, J = 7.7, 2.1 Hz), 7.15 (tt, 1H, J = 7.7, 2.1 Hz), 5.25 (dd, 1H, J = 6.8, 1.9 Hz), 4.71 (td, 1H, J = 6.2, 2.2 Hz), 3.58 (s, 3H), 3.20 (d, 1H, J = 1.9 Hz), 2.91 (dt, 1H, J = 6.8, 3.0 Hz), 2.72 (d, 1H, J = 8.6 Hz), 2.13−1.54 (series of m, 8H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 176.2, 138.5, 138.1, 128.8, 124.9, 122.2, 69.1, 61.1, 59.9, 54.7, 53.2, 51.3, 49.0, 34.7, 32.0, 27.7, 24.8. HRMS (m/z) for $M^+ - CO$ ($C_{21}H_{21}FeNO_4$): calculated: 407.0820; found: 407.0820.

4-Methyl-2-phenyl-2-azaspiro[4,5]dec-8-ene-1,7-dione (18a). $CuCl_2$ method: 50 mg (0.12 mmol) of **14a**/**145a** treated with $CuCl_2$ according to the general procedure afforded **18a** (50% yield, 16 mg) after preparative TLC. **Me_3NO method:** A solution of 50 mg of **14a**/**15a** in 8 mL of C_6H_6 was treated with 0.3 g (35 equiv) of Me_3NO according to the general procedure. The product was then dissolved in 5 mL of MeOH and hydrolyzed by a solution of 0.17 g of $(CO_2H)_2$ in 1 mL of H_2O to give after flash chromatography **17a** (70% yield, 22 mg) as yellow solid. Recrystallization from Hexanes/Et_2O (1:5, −78 °C) afforded **18a** as an off-white solid. Mp 83−85 °C. IR (cm^{-1}, CH_2Cl_2): 1696. ^1H NMR (200 MHz, $CDCl_3$, δ): 7.63 (dd, 2H, J = 7.3, 1.2 Hz), 7.38 (td, 2H, J = 7.3, 1.2 Hz), 7.19 (tt, 1H, J = 7.3, 1.2 Hz), 6.92 (ddd, 1H, J = 10.2, 5.2, 2.9 Hz), 6.14 (dt, 1H, J = 10.2, 1.3 Hz), 3.92 (dd, 1H, J = 9.9, 7.4 Hz), 3.42 (dd, 1H, J = 9.9, 5.7 Hz), 2.95 (dt, 1H, J = 19.2, 2.9 Hz), 2.77 (d, 1H, J = 16.5 Hz), 2.58 (br d, 1H, J = 16.5 Hz), 2.48−2.34 (series of m, 2H), 1.12 (d, 3H, J = 7.2 Hz). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 197.2, 174.9, 147.0, 139.2, 129.8, 129.0, 124.9, 119.8, 52.5, 51.0, 40.1, 36.6, 33.7, 15.4. HRMS (m/z) for M^+ ($C_{16}H_{17}NO_2$): calculated: 255.1259; found: 255.1254.

2-Phenyl-2-azaspiro[4.5]-(3,4-*cis*-bicyclo[3.3.0]octane)-dec-8-ene-1,7-dione (18d). Me_3NO method: A solution of 50 mg (0.12 mmol) of **14d**/**15d** in 8.0 mL of C_6H_6 was treated with 0.3 g (35 equiv) of Me_3NO according to the general procedure. The product was then dissolved in 4.5 mL of MeOH and hydrolyzed by a solution of 0.3 g of $(CO_2H)_2$ in 1.1 mL of H_2O to give after flash chromatography **18d** (68% yield, 22 mg) as a colorless oil. IR (cm^{-1}, CH_2Cl_2): 1694. ^1H NMR (200 MHz, $CDCl_3$, δ): 7.50 (apparent d, 2H, J = 7.7 Hz), 7.39 (apparent t, 2H, J = 7.7 Hz), 7.19 (apparent t, 1H, J = 7.7 Hz), 6.90 (ddd, 1H, J = 10.1, 5.7, 2.4 Hz), 6.16 (dd, 1H, J = 10.1, 1.9 Hz), 4.65 (td, 1H, J = 6.9, 2.2 Hz), 3.03 (d, 1H, J = 16.5 Hz), 2.77 (ddd, 1H, J = 18.5, 2.4, 1.9 Hz), 2.61 (d, 1H, J = 16.5 Hz), 2.38 (dd, 1H, J = 18.5, 5.7 Hz), 1.99 (m, 1H), 1.60 (series of m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 197.8, 174.4, 146.3, 137.6, 130.4, 128.9, 125.4, 122.4, 61.5, 54.4, 45.9, 42.1, 35.5, 31.5, 28.4, 25.3. HRMS (m/z) for M^+ ($C_{18}H_{19}NO_2$): calculated: 281.1416; found: 281.1420.

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Supporting Information Available: Figures giving NMR spectra (^1H, ^{13}C) of all new compounds, as well as experimental descriptions and characterization data for compounds **13b**, **13c**, **14/15b**, **14/15c**, **18b**, and **18c**. This material is free of charge via the Internet at http://pubs.acs.org.

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