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Enantiopure η^4-(1-Sulfinyldiene)Iron(0) Tricarbonyl Complexes as Templates for Carbocycle Construction via Ring-Closing Metathesis

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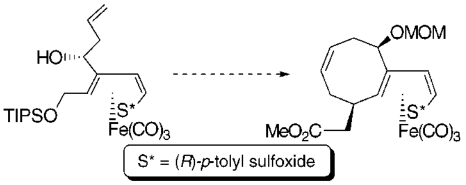
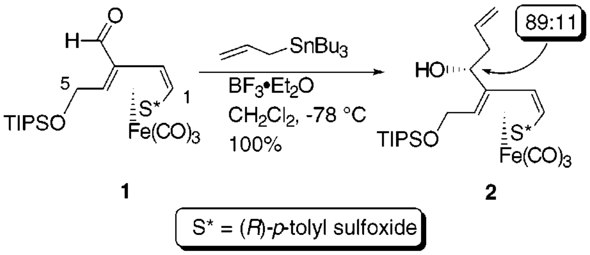
ABSTRACT



Enantiomerically pure 1-(1*Z*,3*E*)-sulfinyl iron(0) dienols have been elaborated to bis-olefins capable of undergoing ring-closing metathesis chemistry. Using Grubbs' ruthenium carbene catalyst, a six-membered carbocycle (with one chiral center) and seven-, eight-, and nine-membered carbocycles (with two chiral centers) have been prepared. Novel transformations include the $LiClO_4$-promoted allylation of an alkylidene malonate and a reductive sulfur–carbon bond cleavage to convert a vinyl sulfoxide into an alkene with SmI_2.

While the use of enantiomerically pure sulfoxides to dictate the absolute stereochemistry of incipient chiral centers is a well-established strategy for asymmetric synthesis,[1] there are few approaches which utilize organotransition metal chemistry in any of the key asymmetric bond-forming events.[2] Our contribution to this area has been the development of an indirect approach which features the use of a sulfoxide to impart planar chirality, in a highly diastereoselective manner, in the preparation of 1-sulfinyl-(1*Z*,3*E*)-dienyl iron(0) tricarbonyl complexes.[3] The planar chirality has then been used to diastereoselectively introduce chiral centers along the periphery of the diene of these complexes.[4] Herein we describe how this methodology may be extended to construct medium-sized carbocycles (six- through nine-membered rings) which contain one or more chiral centers.

We had previously described[4] the synthesis of sulfinyl iron dienal **1** and its diastereoselective conversion to homoallyl alcohol **2**, which could be obtained in diastereomerically pure form following chromatography (eq 1). In seeking to exploit



(1)

this finding, we realized that the terminal alkene would be available to participate in ring-closing metathesis (RCM) chemistry[5] provided that the C_5 silyloxy group could be properly elaborated into a second olefin. Also, we needed to determine whether the Grubbs' catalyst would be compat-

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[1] For recent reviews, see: (a) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Gianneto, P. *Tetrahedron: Asymmetry* **1997**, *8*, 1339. (b) Carreño, C. *Chem. Rev.* **1995**, *95*, 1717. (c) Walker, A. J. *Tetrahedron: Asymmetry* **1992**, *3*, 961.

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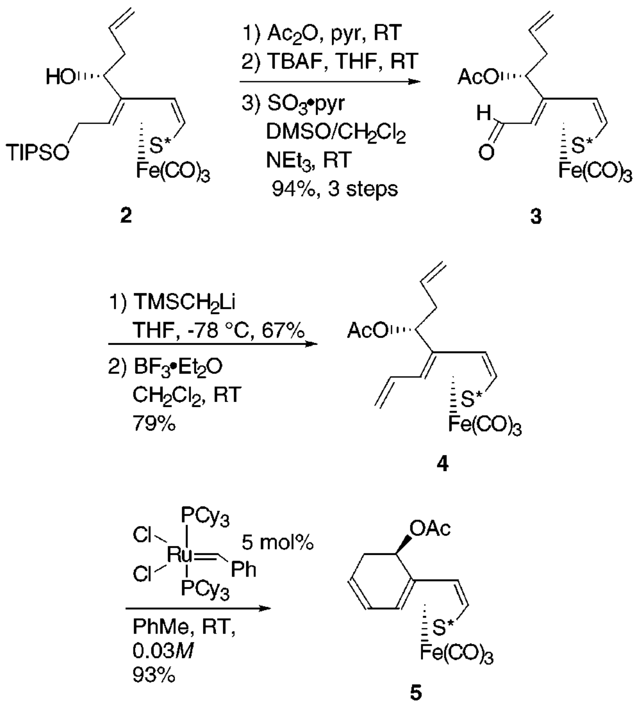
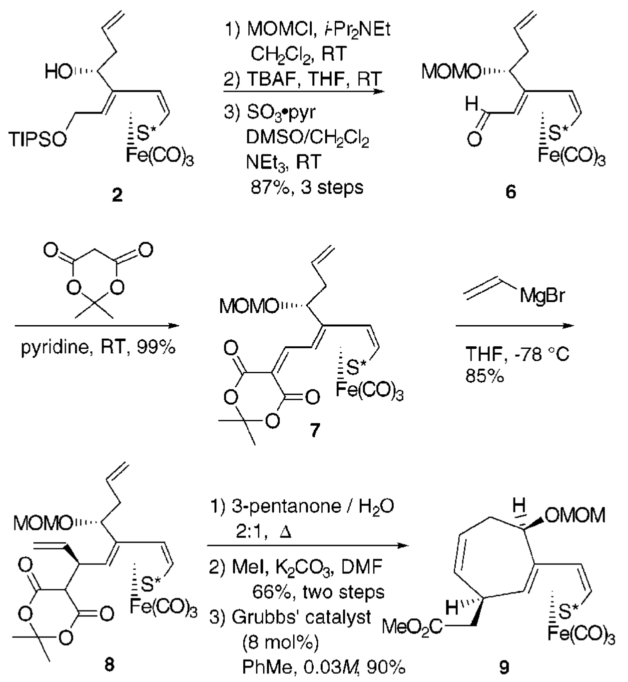
ible with the sulfoxide as well as with the iron tricarbonyl unit, since we were unaware of any precedent for such a transformation. To begin this investigation, **2** was therefore converted into diene **4** by standard Peterson olefination[6] methodology (Scheme 1). We were delighted to subsequently discover that ring-closing metathesis conditions were indeed compatible with our sulfinyl iron dienes, as **4** was readily converted to six-membered carbocycle **5**.

Scheme 1



We next turned our attention toward the synthesis of a seven-membered analogue, realizing that a proper choice of methods for elaboration of the C_5 silyloxy group could provide a carbocycle possessing two chiral centers, not just one as in **5**. Indeed, chemistry first reported by Laabassi and Grée and then later utilized by Roush and co-workers provided an entry into such a metathesis precursor.[7] By employing a protection/desilylation/oxidation sequence similar to that depicted in Scheme 1, homoallyl alcohol **2** was converted into sulfinyl iron dienal **6**, which was then smoothly transformed into the corresponding alkylidene malonate **7** using Meldrum's acid in pyridine (Scheme 2).

Scheme 2



Low-temperature addition of vinylmagnesium bromide to **7** gave adduct **8** *as a single diastereomer*. The stereochemistry at C_5 was assigned by analogy with Roush's findings, based on a presumed nucleophilic addition *anti* to the iron tricarbonyl unit. This assignment was later confirmed by NOE measurements (vide infra). For operational reasons,[8] we chose to hydrolyze and decarboxylate adduct **8** at this point, and the unpurified acid was esterified to provide the metathesis precursor. As before, conversion of this bis-olefin into the seven-membered carbocycle, **9**, using Grubbs' catalyst proceeded in excellent yield. The presumed stereo-

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(2) (a) Adrio, J.; Carretero, J. C. *J. Am. Chem. Soc.* **1999**, *121*, 7411. (b) Buezo, N. D.; Alonso, I.; Carretero, J. C. *J. Am. Chem. Soc.* **1998**, *120*, 7129. (c) Davies, S. G.; Loveridge, T.; Clough, J. M. *Synlett* **1997**, 66. (d) Villar, J. M.; Delgado, A.; Llebaría, A.; Moretó, J. M.; Molins, E.; Miravitlles, C. *Tetrahedron* **1996**, *52*, 10525. (e) Hua, D. H.; Lagneau, N. M.; Chen, Y.; Robben, P. M.; Clapham, G.; Robinson, P. D. *J. Org. Chem.* **1996**, *61*, 4508. (f) Hiroi, K.; Onuma, H.; Arinaga, Y. *Chem. Lett.* **1995**, 1099. (g) Hiroi, K.; Arinaga, Y. *Tetrahedron Lett.* **1994**, *35*, 153. (h) Pérez-Encabo, A.; Perrio, S.; Slawin, A. M. Z.; Thomas, S. E.; Wierzchleyski, A. T.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 629. (i) Ibbotson, A.; Reduto dos Reis, A. C.; Saberi, S. P.; Slawin, A. M. Z.; Thomas, S. E.; Tustin, G. J.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1251.

(3) (a) Paley, R. S.; de Dios, A.; Estroff, L. A.; Lafontaine, J. A.; Montero, C.; McCulley, D. J.; Rubio, M. B.; Ventura, M. P.; Weers, H. L.; Fernández de la Pradilla, R.; Castro, S.; Dorado, R.; Morente, M. *J. Org. Chem.* **1997**, *62*, 6326. (b) Paley, R. S.; Rubio, M. B.; Fernández de la Pradilla, R.; Dorado, R.; Hundal, G.; Martínez-Ripoll, M. *Organometallics* **1996**, *15*, 4672.

(4) Paley, R. S.; Estroff, L. A.; McCulley, D. J.; Martînez-Cruz, L. A.; Sánchez, A. J.; Cano, F. H. *Organometallics* **1998**, *17*, 1841.

(5) For recent reviews on ring-closing metathesis, see: (a) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, 54, 4413. (b) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 371. (c) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036.

(6) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780.

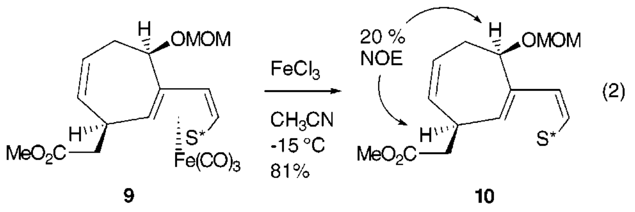
(7) (a) Laabassi, M.; Grée, R. *Tetrahedron Lett.* **1988**, *29*, 611. (b) Wada, C. K.; Roush, W. R. *Tetrahedron Lett.* **1994**, *35*, 7351. (c) Roush, W. R.; Wada, C. K. *J. Am. Chem. Soc.* **1994**, *116*, 2151.

(8) Purification of compounds containing the alkylidene malonate unit, such as **7** and **8**, required incorporation of acetic acid (1 vol %) in the eluant. Since it was often difficult to completely remove the acetic acid in vacuo, we preferred to perform the metathesis reactions on material that did not require this additive for purification.

(9) For a related allylation (of α-alkoxy aldehydes) employing allyltributylstannane in 5.0 M $LiClO_4/Et_2O$, see: Henry, K. J., Jr.; Grieco, P. A.; Jagoe, C. T. *Tetrahedron Lett.* **1992**, *33*, 1817.

(10) For recent examples of successful cyclooctanoid synthesis via RCM, see: (a) Crimmins, M. T.; Choy, A. L. *J. Am. Chem. Soc.* **1999**, *121*, 3033. (b) Delgado, M.; Martín, J. D. *J. Org. Chem.* **1999**, *64*, 4798 and references therein.

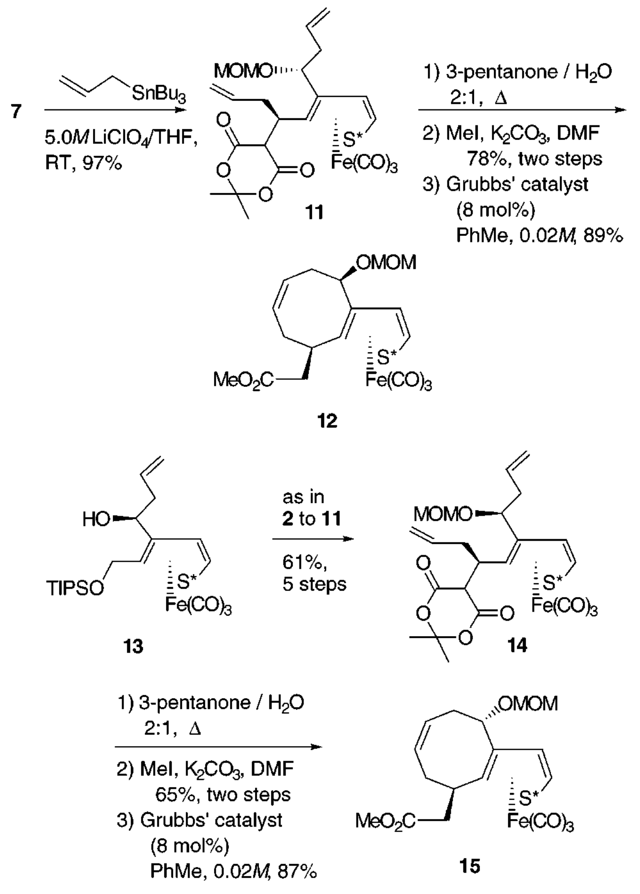
chemical assignment was verified by NOE measurements performed on the decomplexed carbocycle **10**, as shown in eq 2.



(2)

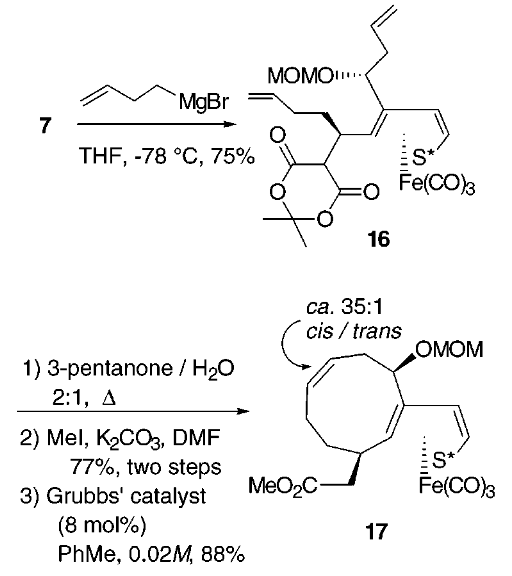
The obvious extension of this chemistry was to utilize allyl Grignard rather than vinyl Grignard in order to explore the feasibility of eight-membered ring synthesis via ring-closing metathesis. When addition of allylmagnesium chloride to alkylidene malonate **7** failed to yield more than trace amounts of the desired adduct, we were forced to seek an alternate set of conditions to effect this transformation. Fortunately, addition of allyl tributylstannane in 5.0 M LiClO$_4$/THF provided the desired adduct **11** as a *single diastereomer*, and in nearly quantitative yield (Scheme 3).[9] Conversion of **11**, as before, by hydrolysis/decarboxylation and esterification afforded the metathesis precursor, and subjecting this material to RCM conditions cleanly provided the eight-membered carbocycle **12** in 89% yield. Since geometric constraints are thought to be required for successful cyclooctanoid synthesis via RCM,[10] it would seem that the *cis* orientation of the olefinic chains about the C$_3$−C$_4$ double bond reduces the number of energetically feasible conformations. The presence of the bulky iron tricarbonyl unit on the α diene face may serve to further narrow the olefins' range of conformations; however its role must remain speculative until the chemistry of the related decomplexed species is explored. Pseudoequatorial or pseudoaxial positioning of the OMOM substituent in the transition state appears to be irrelevant, as the diastereomeric bis-olefin **14**[11] was converted to the corresponding eight-membered carbocycle **15** with equal facility.

Scheme 3



Similar chemistry was used to obtain the nine-membered carbocycle, considered to be even more challenging to prepare by RCM than eight-membered rings.[5c] Alkylidene malonate **8** was treated with 3-butenylmagnesium bromide, and as before, this adduct (**16**) was decarboxylated and esterified to afford a bis-olefin metathesis precursor. Ring-closing metathesis proceeded smoothly to provide nine-membered carbocycle **17**, in good yield (88%) as a 35:1 *cis*/*trans* mixture[12] of double bond isomers (Scheme 4).

Scheme 4



Future utilization of this methodology in natural product synthesis depends on our ability to manipulate the vinyl sulfoxide functionality. While many possibilities exist, here we report an unexpected and, to our knowledge, previously unknown transformation. After removal of the iron tricarbonyl unit from cyclooctanoid **12**, attempted reduction of the sulfoxide (to the corresponding sulfide) with SmI$_2$ gave

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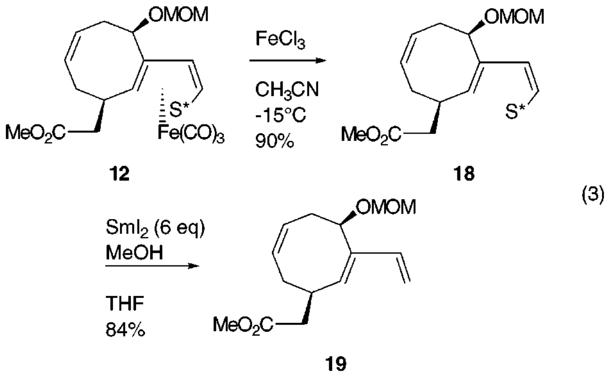
[11] Derived from the minor diastereomer produced from allylation of **1**, which was readily separable from the major diasteromer (**2**) by column chromatography. See ref 4. Details of the conversion of **13** into **14** are provided in the Supporting Information.

[12] This ratio was determined by integration of the ^{1}H NMR spectrum of **17**.

instead the terminal alkene (**19**) in high yield (eq 3). This result suggests additional synthetic strategies, including construction of fused carbocylic ring systems via Diels–Alder chemistry or a second ring-closing metathesis. Progress in these areas will be reported in due course.



(3)

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Supporting Information Available: Experimental procedures and NMR, IR, and mass spectroscopy data for compounds **3**–**12** and **14**–**19** and selected ^{1}H NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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