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A New Paradigm for Cationic Cyclization of Iron Tricarbonyl Diene Complexes with Pendant Alkenes and Arenes

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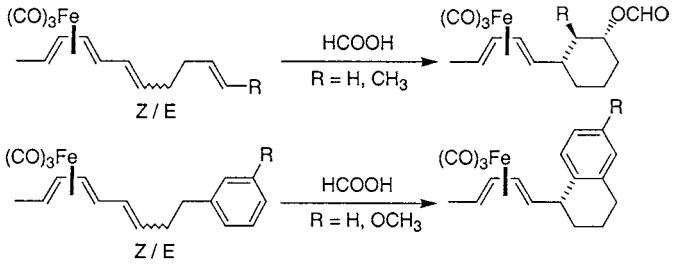
ABSTRACT



A new example of stereospecific cationic cyclization of iron tricarbonyl diene complexes with pendant alkenes and arenes is provided. Protonation of a double bond vicinal to the iron tricarbonyl diene moiety is employed to trigger the cyclization, rather than the previously reported Lewis/protic acid dehydroxylation of diastereomeric alcohols, eliminating one step of separation and avoiding some reactivity problems previously encountered for one of the alcohol diastereoisomers.

Nucleophilic addition to pentadienyliron tricarbonyl complexes is becoming a valuable tool in modern synthetic organic chemistry.[1] Recent efforts in our group have been directed toward cationic cyclization reactions with pendant alkenes and arenes as the nucleophile partner.

The first reported cyclizations of this type[2] employed both secondary alcohols obtained by Grignard addition to the tricarbonyliron sorbaldehyde complex and tertiary alcohols obtained by organolithium reagent additions to tricarbonyliron ketone derivatives. Recent reports of biomimetic cascade cyclization reactions demonstrate the considerable synthetic relevance of this reaction.[3]

The tertiary alcohols can be obtained as pure diastereoisomers, because the starting ketone complex adopts an s-cis configuration.[3] On the other hand, Grignard addition to the tricarbonyliron sorbaldehyde complex leads to a mixture of diastereoisomers, Ψ-endo and Ψ-exo,[4] which although being easily separable, proved to have a marked difference in reactivity for some of the substrates that were prepared.[2c] This may be a serious drawback, because the less reactive isomer, Ψ-endo, is the major product of the Grignard addition. Finding a route that would bypass the diastereomeric alcohols would be of considerable value, mainly because Ψ-endo and Ψ-exo isomers lead to enantiomeric products upon demetallation (Scheme 1; starting with the other enantiomer of tricarbonyliron sorbaldehyde complex would invert the ratio between the resulting enantiomers). The methodology described herein will allow that, given an optically pure starting complex,[5] the final product will be only one enantiomer.

Reported cyclizations of alcoholic substrates using protic acids,[3] rather than the initially used Lewis acids, turned our

(1) (a) Pearson, A. J. *Iron Compounds in Organic Synthesis*; Academic Press: London, 1994. (b) Donaldson, W. A. *Aldrichimica Acta* **1997**, *30* (1), 17−24.

(2) (a) Pearson, A. J.; Alimardanov, A.; Pinkerton, A. A.; Fouchard, D. M.; Kirschbaum, K. *Tetrahedron Lett.* **1998**, *39*, 5919−5922. (b) Franck-Neumann, M.; Geoffroy, P.; Hanss, D. *Tetrahedron Lett.* **1999**, *40*, 8487−8490. (c) Pearson, A. J.; Alimardanov, A. R.; Kerber, W. D. *J. Organomet. Chem.* **2001**, *630*, 23−32.

(3) Franck-Neumann, M.; Geoffroy, P.; Hanss, D. *Tetrahedron Lett.* **2002**, *43*, 2277−2280.

(4) For a definition of Ψ-endo and Ψ-exo nomenclature: Clinton, N. A.; Lillya, C. P. *J. Am. Chem. Soc.* **1970**, *92*, 3058−3064.

(5) (a) Franck-Neumann, M.; Briswalter, C.; Chemla, P.; Martina, D. *Synlett* **1990**, *10*, 637−640. (b) Anson, C. E.; Dave, G.; Stephenson, G. R. *Tetrahedron* **2000**, *56* (15), 2273−2281.

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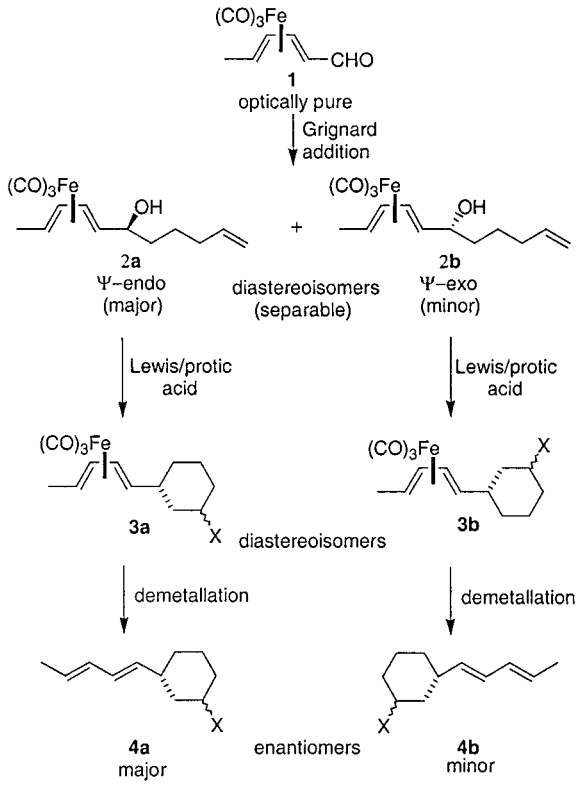
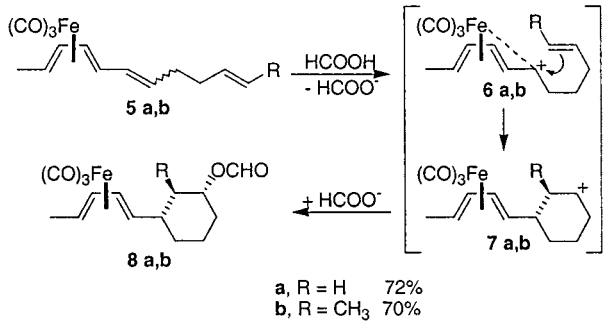
Scheme 1



attention to a new type of substrate that proved to solve the problem encountered earlier. Instead of dehydroxylation of the alcohol, the carbocation that triggers the cyclization process is generated by protonation of a double bond. This process is regioselective, given the fact that only the carbon proximal to the tricarbonyliron diene moiety can receive anchimeric assistance from the iron (Scheme 2). Although

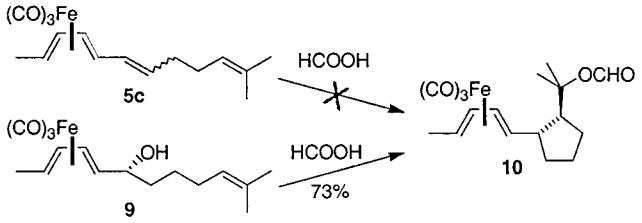
Scheme 2



the Wittig olefination employed to make the starting substrates[6] produces a mixture of *Z*/*E* diastereoisomers, they both generate the same stabilized carbocation, identical to the carbocation that is generated from the Ψ-exo alcohols (which is also the diastereoisomer that gives better results for cyclization). The subsequent intramolecular nucleophile attack then proceeds anti to the tricarbonyliron moiety with respect to the diene plane, leading to the expected stereospecific cyclization. Note that in the case of **5b**, the product **8b** is obtained as a single diastereoisomer with the methyl substituent being equatorial, consistent with the proposed mechanism. The subsequent reaction of the resulting carbocation with the external nucleophile proceeds only equatorially for both **7a** and **7b**.[7]

An attempt to alter the degree of substitution and push the reaction toward formation of a five-membered ring proved to be unsuccessful (Scheme 3). Instead of the

Scheme 3

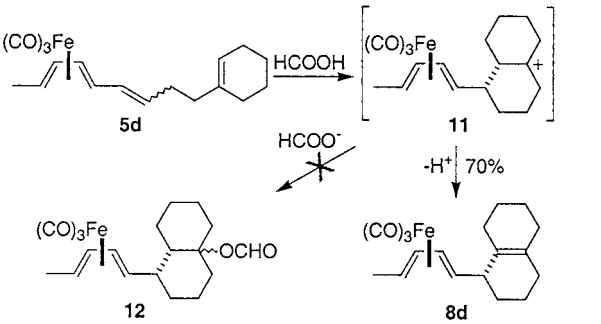


expected product **10**, a complex mixture of formates and elimination products (not isolated) was obtained. In contrast, the corresponding Ψ-exo alcohol **9** was successfully converted to **10**, indicating some degree of complementarity between the two methods.

One possible explanation for the difference in behavior of **5c** and **9** is that competing protonation of the trisubstituted double bond in **5c** occurs, whereas the hydroxyl group of **9** provides a more basic site that is protonated more rapidly.

A pendant cyclohexenyl substrate designed to produce a bicyclic system gave a slightly unexpected result, that is, an elimination product (**8d**) rather than a nucleophile insertion product (**12**, Scheme 4). Most probably, the tertiary carbocation **11** that results from cyclization is too hindered to capture the formate anion.

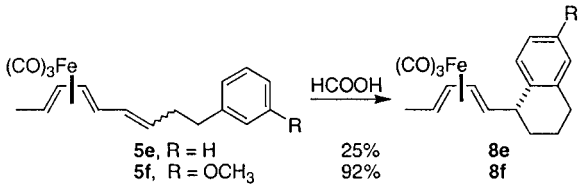
Scheme 4



(6) (a) Taber, D. F.; Rahimizadeh, M.; You, K. K. *J. Org. Chem.* **1995**, *60*, 529−531. (b) Bell, P. T.; Dasgupta, B.; Donaldson, W. A. *J. Organomet. Chem.* **1997**, *538*, 75−82.

For the tertiary alcohol series, there are reports of successful cyclizations of unactivated pendant arenes, but only with protic acids, and of activated pendant arenes with Lewis acid (BF_3).[3] However, for the secondary alcohols, only the pendant activated arene Ψ-exo substrate cyclized successfully upon treatment with a Lewis acid (BF_3).[2c] The new method proved to be successful for the two pendant arene substrates that were tested, both unactivated (**5e**) and methoxy activated (**5f**). Both substrates afforded a single diastereoisomer product. As expected, the cyclization of **5f** occurred in higher yield than that of **5e**.

In summary, we have presented a new type of cationic cyclization of tricarbonyliron diene complexes with pendant alkenes and arenes. The previously employed distereomeric diene alcohols have been replaced by substrates with a triene backbone, which proved to cyclize successfully, simplify the overall procedure, and solve a reactivity problem. At the same time, this methodology provides an enantioselective synthetic route toward any of the above products, provided the starting complex is optically pure.



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Supporting Information Available: Full characterization for compounds **5a**−**f**, **9**, and **10** and a general experimental procedure and full characterization for compounds **8a**,**b**,**d**−**f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) For Lewis acid (BF_3)-mediated cyclizations, both equatorial and axial fluorides were observed. The size of the formate anion may be the cause of exclusive equatorial product formation in the present examples.