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Cationic cyclizations of (diene)iron tricarbonyl complexes with pendant alkenes and arenes

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Dedicated to Professor Myron Rosenblum on the occasion of his 75th birthday

Abstract

Stereospecific annulation reactions, which involve the intramolecular addition of olefinic and aromatic nucleophiles to in situ generated iron tricarbonyl-stabilized dienyl cations, are described. It is found that a simple unactivated olefinic double bond reacts to generate cyclohexane systems in high yield. On the other hand, reaction with aromatic moieties to form substituted tetralins proceeds only for activated aromatic rings; in those cases where less nucleophilic aromatics are used, a competing unproductive rearrangement of the diene–iron tricarbonyl complex occurs.

Keywords: Stereospecific annulation reactions; Substituted tetralins; Diene–iron tricarbonyl complexes

1. Introduction

A recent modification of the well-known nucleophilic addition to pentadienyliron tricarbonyl complexes [1] is an in situ generation and trapping of the transoid cation. It should be noted that Clinton and Lillya [2] have shown that diastereomeric dienol complexes **2** and **4** (Scheme 1), named Ψ-*exo* and Ψ-*endo*, exist in preferred conformations with bulkier hydroxyl and alkyl substituents located at sterically less crowded sites, illustrated in Fig. 1 (the diene is viewed 'edge-on' looking along the C2–C3 bond). It was further shown that solvolyses of the corresponding diastereomeric dinitrobenzoates **1** and **3**, which should exist in preferred conformations similar to those shown in Fig. 1, take place with complete retention of configuration [3]. Moreover, Ψ-*exo* dinitrobenzoate (**1**) was found to undergo solvolysis 60 times faster than the corresponding free ligand, while Ψ-*endo* isomer **3** was solvolyzed slower than the free ligand. These results were explained by the ionization of **1** and **3** with anchimeric assistance from iron with subsequent addition of the nucleophile from the side opposite to iron tricarbonyl unit (i.e. double inversion). The rate difference of solvolyses of Ψ-*exo* and Ψ-*endo* dinitrobenzoates can be rationalized in terms of respective conformations that are required for anchimeric assistance. The Ψ-*exo* diastereomer exists in a preferred conformation with the leaving group oriented favorably for ionization. At the same time, Ψ-*endo* isomer **3** should first undergo rotation around the C2–C3 bond to form a more congested conformer.

In accordance with the proposed mechanism of solvolysis, it was shown that dienediol complexes **5** can cyclize in acidic media with the formation of tetrahydropyrans [4] and tetrahydrofurans [5]. Interestingly, in the case of cycloetherification of **5** ($n = 2$, R = H, R′ = CO_2Me), *E*,*Z*-complex (the result of cyclization after isomerization to the cisoid cation) is formed along with the major *E*,*E*-isomer [4]. The corresponding *E*,*E*-complexes are formed with retention of configuration at the position α to the dieneiron tricarbonyl. On the other hand, Amberlyst-15-catalyzed cycloetherification of **5** ($n = 1$, R = H, R′ = Me) was shown to give a mixture of diastereomers [5]. Formation of tetrahydrofurans in this case is a comparatively slow process, and the products can exist in equilibrium with respective intermediate cations under the reaction conditions. The

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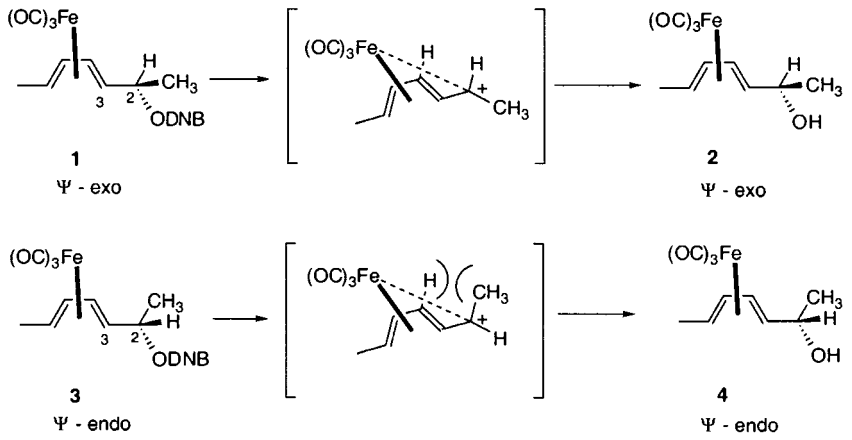


Scheme 1.

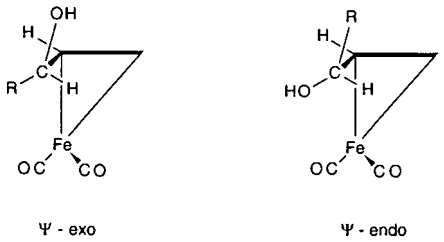
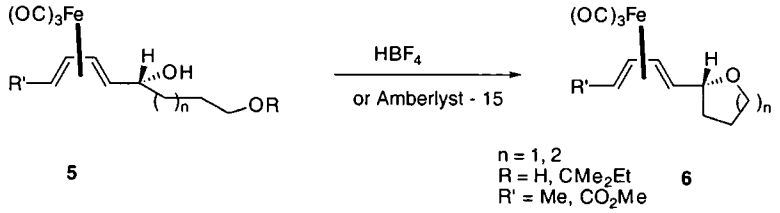
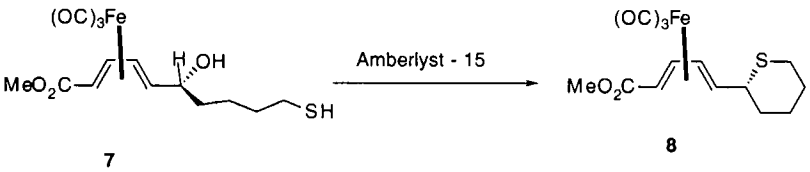


Fig. 1. Preferred conformations of Ψ-*exo* and Ψ-*endo* alcohols.

possible σ-bond rotation in the cationic complexes under these conditions (room temperature, 20 h) can lead to eventual loss of stereochemistry.



Likewise, thiol **7** affords tetrahydrothiopyran (**8**) under the same conditions [6]. It should be pointed out that while Ψ-*exo* **7** reacts with retention of configuration, the Ψ-*endo* isomer in this case gives an essentially 1:1 mixture of diastereomers.



Uemura and coworkers have applied this methodology to carbon–carbon bond formation [7]. Transoid cationic complexes were formed in situ at −78 °C by treatment with Lewis acids. Intermolecular nucleophilic substitutions, for example, using allylsilanes, take place with complete retention of configuration. This methodology was later studied by Roush and Wada [8] and utilized for the synthesis of the *as*-indacene unit of icarugamycin [9].

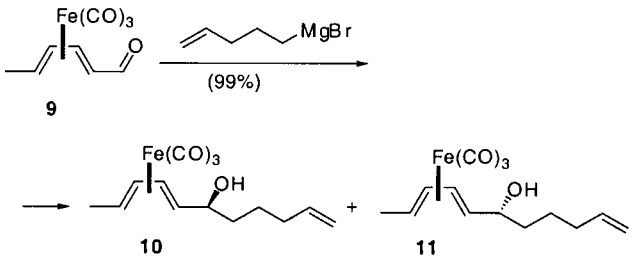
It should be noted that, prior to our own work, there were no reports of intramolecular cyclization of pentadienyliron tricarbonyl cation with the formation of carbocycles. Studies of cyclizations of these cations with pendant alkenes are discussed in this article [10].

2. Results and discussion

2.1. Cyclization of in situ generated (pentadienyl)iron tricarbonyl cation with pendant alkene

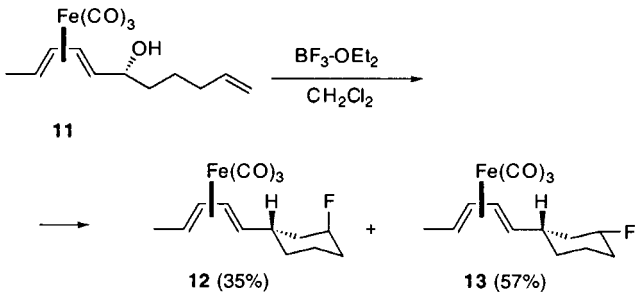
Diastereomeric (1,7,9-undecatrienol)iron tricarbonyl complexes were prepared by Grignard addition to (2,4-hexadienal)iron tricarbonyl (**9**), readily available from 2,4-hexadienal. The diastereomers have strikingly different R_f values on silica gel and, therefore, can be easily separated chromatographically. This behavior has been observed previously for simpler analogs **2** and **4** [2,11]. Flash chromatography separation gave pure **10** and **11** in 61 and 38% yields, respectively. Diastereomeric trienol complexes are expected to exist

in preferred conformations shown in Fig. 1 (R = $(CH_2)_3CH{=}CH_2$). The exposed hydroxy group of the Ψ-*exo* diastereomer would account for its polar behavior, while the unusual non-polar character of Ψ-*endo* diastereomer is in agreement with its stereochemistry with a sterically shielded hydroxy group [2]. Moreover, the assignment of Ψ-*exo* stereochemistry to the more polar diastereomer for the simple dienol complex (Fig. 1, R = Me) was confirmed by X-ray crystallography [12]. On this basis, the relative stereochemistry of the major product **10** of Grignard addition was assigned as *6S,7R* (*6R,7S*) (Ψ-*endo*), and that of the minor product **11** as *6R,7R* (*6S,7S*) (Ψ-*exo*). The formation of the Ψ-*endo* diastereomer as the major product is in agreement with results of Howell et al. for MeMgI addition to aldehyde **9** [13].



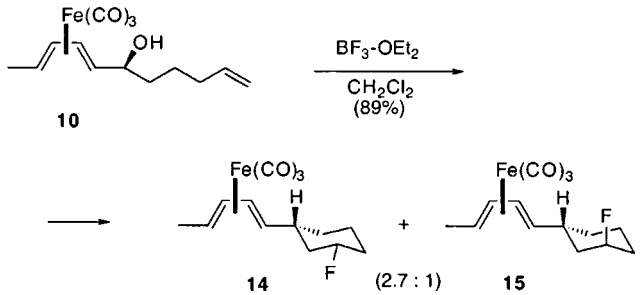
It should be noted that, for the simpler case of (3,5-heptadienol)iron tricarbonyl, it has been shown that the major (Ψ-*endo*) diastereomer can be converted to the minor one (Ψ-*exo*) by treatment with alumina [14].

Treatment of alcohol **11** with three equivalents of BF_3–OEt_2 in CH_2Cl_2 at −78 °C with subsequent warming to room temperature resulted in the formation of two fluorides, **12** and **13**, in 35 and 57% yields, respectively, which were separated chromatographically.



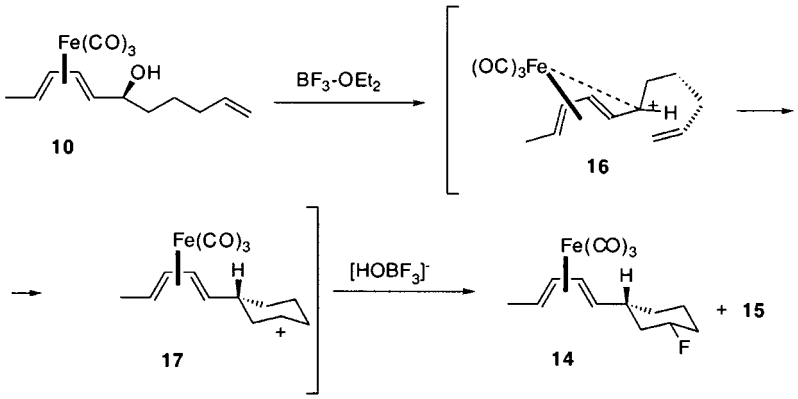
The structures of **12** and **13** as six-membered carbocycles were assigned on the basis of APT ^{13}C-NMR spectra, which clearly exhibit signals of CHF fragments (doublets at 89.07 and 91.52 ppm, respectively), and confirmed by X-ray crystallographic analysis [10]. Due to the steric bulk of the dieneiron tricarbonyl moiety, both epimeric fluorides should exist in a locked chair conformation with the (diene)$Fe(CO)_3$ being in an equatorial orientation. The ^{1}H-NMR spectrum of **13** shows the C*H*F resonance as a dtt with J_{HH} = 10.6 (t), 4.5 Hz (t), characteristic of an axial hydrogen atom. At the same time, its ^{19}F-NMR spectrum exhibits a doublet at −168.61 ppm, characteristic of an equatorial fluoride [15]. On the other hand, the corresponding spectral data for **12** (4.84 ppm, dtt, J_{FH} = 48 Hz, J_{HH} = 4, 2 Hz in ^{1}H-NMR and −182.6 ppm, dt in ^{19}F-NMR spectra) are characteristic of a cyclohexane derivative with an axial fluorine substituent. It should be noted that only one diastereomer of each fluoride was formed during this reaction. The stereochemistry at C3 corresponds to that of C6 of the starting alcohol (i.e. result of the net retention of configuration, as is usual with these systems) [10].

Cyclization of Ψ-*endo* alcohol **10** under the same conditions (BF_3–OEt_2, CH_2Cl_2, −78 °C to room temperature) resulted in the formation of cyclohexyl fluoride complexes **14** and **15** in 89% combined yield, as an inseparable mixture (2.7:1 ratio). Only one epimer of each fluoride was observed in the NMR spectra.

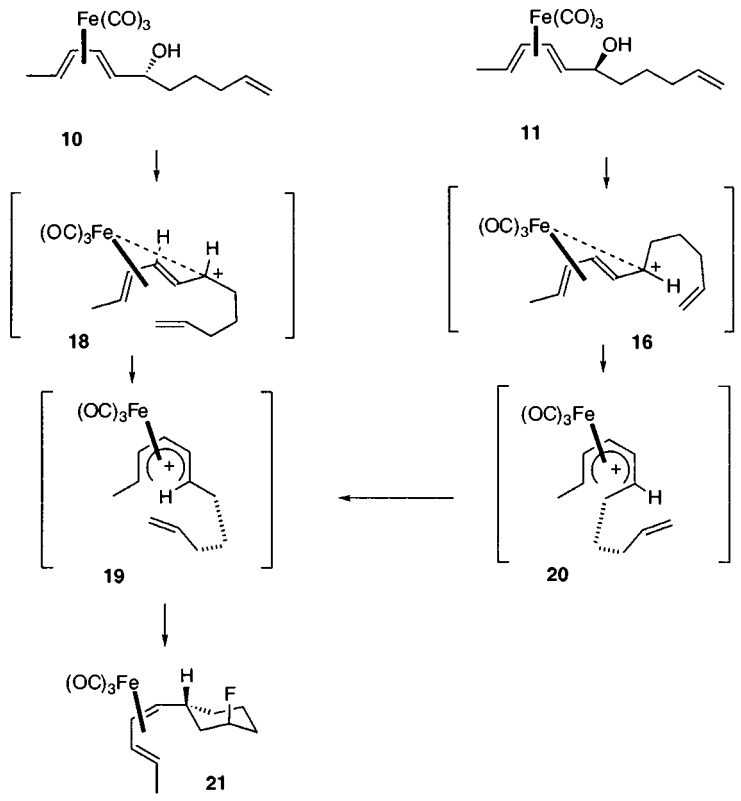


Formation of cyclohexyl fluoride complexes can be explained by Lewis acid (BF_3–OEt_2) induced ionization of the alcohol with anchimeric assistance from the iron atom, leading to the formation of a stabilized transoid (pentadienyl)$Fe(CO)_3$ cation **16** (Scheme 2). Attack of the pendant olefin with accompanying carbon–carbon bond formation would then proceed from the face opposite to iron tricarbonyl, resulting in the product of formal nucleophilic substitution with retention of configuration at the position α to the dieneiron tricarbonyl. Reaction of the resulting cyclohexyl cation **17** with $[BF_3OH]^-$ (or BF_3) as a source of external nucleophile results in the formation of fluorides. To our knowledge, this is the first example of intramolecular cationic carbocyclization of pentadienyliron tricarbonyl complexes with a pendant olefin.

Formation of a six-, rather than five-membered ring can be rationalized in terms of greater stability of secondary versus primary cation. Similar to the case of alcohol complexes (Fig. 1), the conformation of the intermediate cation **17** would be the one with hydrogen atom α to the dieneiron tricarbonyl located in the sterically more crowded site and bulkier methylene groups in less hindered sites. Axial attack of the nucleophile at cation **17** would then be restricted due to the



Scheme 2.



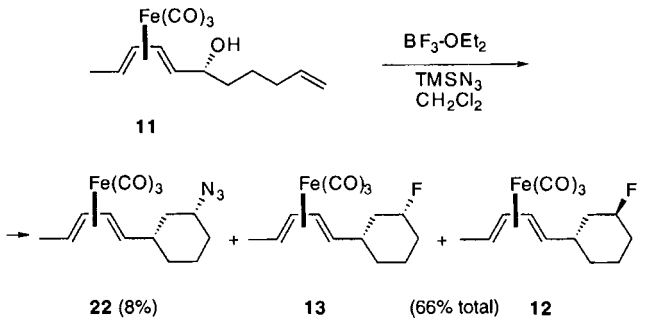
Scheme 3.

steric effect of $Fe(CO)_3$. Accordingly, preferential formation of equatorial fluorides is observed.

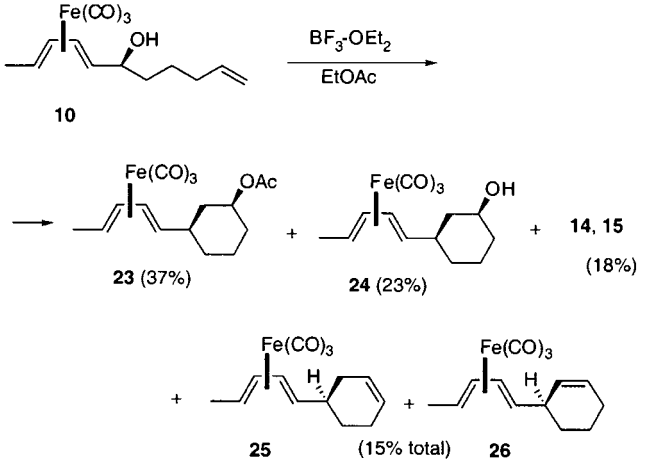
It should be pointed out that the cyclization occurs with an unactivated double bond. The complete retention of configuration at the carbon atom α to the (diene)$Fe(CO)_3$ in the case of Ψ-*endo* alcohol **10** is also noteworthy in view of the report of epimerization during the formation of tetrahydrothiopyrans from the corresponding Ψ-*endo* thiol [6]. Presumably, the irreversible nature of the carbacyclization is responsible for this stereospecificity.

Interestingly, a small amount ($\leq 5\%$) of an inseparable side-product can be seen in ^{1}H- and ^{19}F-NMR spectra of **12** and in the mixture of **14** and **15**. That compound has not been isolated and fully characterized. However, signals observed in the NMR spectra indicate that the compound is an axial cyclohexyl fluoride. A possible side product of cyclization is the (fluorocyclohexyl-*E*,*Z*-pentadiene)iron tricarbonyl (**21**), formed as a result of a reaction with participation of cisoid cations **19** and **20** (Scheme 3). The fact that the same compound is present in product mixtures from both alcohols **10** and **11** can be explained by isomerization of **20** to the more stable isomer **19** before the cyclization takes place. Such an isomerization is characteristic of cisoid cationic complexes [11,16].

In an attempt to introduce nucleophiles other than fluoride, reaction in the presence of azidotrimethylsilane was performed. However, when a 1:1 ratio of BF_3–OEt_2 and $TMSN_3$ was used, only fluorides were produced. Use of a large excess of azidotrimethylsilane (ten equivalents $TMSN_3$, three equivalents BF_3–OEt_2) yielded azide **22** in only 8% yield, with fluorides **12** and **13** still being the major products. This result is rather surprising considering previous reports of azidation with $TMSN_3$ in the presence of BF_3–OEt_2 [17] and in view of the report by Roush and Wada [8] of intermolecular reactions of dienol–$Fe(CO)_3$ complexes to give the corresponding azides.



Treatment of alcohol **10** with BF_3–OEt_2 in EtOAc (-78 °C, then room temperature, 10 min) resulted, after chromatographic separation, in the formation of acetate **23** (37%), alcohol **24** (23%), a mixture of triene complexes **25** and **26** (15%, ca. 4:1 ratio) and fluorides **14** and **15** (18%; yields are based on reacted staring material at 94% conversion). Both acetate **23** and alcohol **24** were obtained as single diastereomers, with equatorial functional groups ($J_{HH} = 11$, 4.3 Hz for H-1 of **23** and 10.5, 4 Hz for H-1 of **24**). Hence, the presence of iron tricarbonyl controls stereochemistry at both C3 and C1 of the resulting cyclohexanol derivatives. Interestingly, control experiments (quenching at -78 °C and reaction at room temperature) show that, unlike the nucleophilic substitution reported by Uemura et al. [7], cationic cyclizations take place at room temperature.

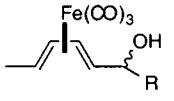


It should be noted that formation of the alcohol is not a result of direct reaction of intermediate cyclohexyl cation with any residual water present in the solvent, since a control experiment showed that no reaction occurs at all in the presence of water. The hydrolysis of initially formed acetate during the work up is also unlikely, as indicated by the fact that acetate **23** remains unchanged under the work up conditions. The mechanism shown in Scheme 4 can explain formation of the observed products. Cation **17** is formed after ionization of alcohol and cationic cyclization.

Reaction of **17** with $[BF_3OH]^-$ or BF_3–OEt_2 present in the solution is responsible for the formation of fluorides. Trapping of **17** with ethyl acetate solvent would result in the formation of intermediate **27** that can be transformed to hemiorthoester **28** upon reaction with $[BF_3OH]^-$. Intermediate **28** can then degrade to alcohol **24** or acetate **23**. Alternatively, acetate **23** can be formed directly from cation **27** as a result of the attack of fluoride ion as base, with subsequent elimination of ethylene. Triene complexes **25** and **26** can form either directly from cation **17** or as a result of elimination from acetate **23**. The observation that the yield of trienes increases with prolonged reaction times indicates that the latter pathway is the major one.

2.2. Cyclization of in situ generated (pentadienyl)iron tricarbonyl cations with pendant aromatic nucleophiles

In an effort to expand the scope of this cyclization reaction, we have explored the use of pendant aryl groups as nucleophiles. This would allow the construction of substituted tetralins, and also eliminate any problems that arise during nucleophilic addition to the carbocation that results from the initial cyclization. Several test compounds (**29**–**36**) were synthesized by Grignard addition of the appropriate arylalkyl magnesium bromide to complex **9**. The diastereomers obtained were separated easily by flash chromatography because of the marked difference in R_f on silica gel between the Ψ-*exo* and Ψ-*endo* stereoisomers. The relative stereochemistries were assigned based on polarity on silica gel as described above, and their identities were confirmed readily by ^{1}H-NMR spectroscopy.

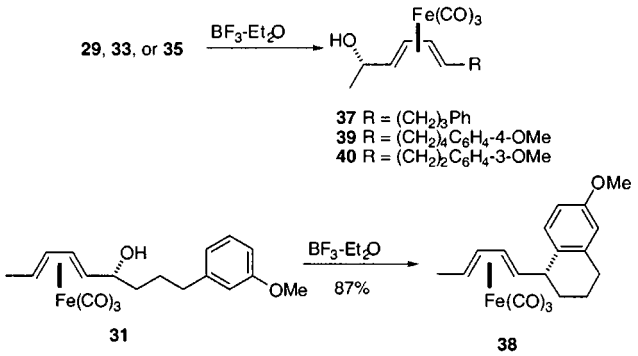


29 (Ψ-exo) R = $(CH_2)_3$Ph
30 (Ψ-endo) R = $(CH_2)_3$Ph
31 (Ψ-exo) R = $(CH_2)_3C_6H_4$-3-OMe
32 (Ψ-endo) R = $(CH_2)_3C_6H_4$-3-OMe
33 (Ψ-exo) R = $(CH_2)_4C_6H_4$-4-OMe
34 (Ψ-endo) R = $(CH_2)_4C_6H_4$-4-OMe
35 (Ψ-exo) R = $(CH_2)_2C_6H_4$-3-OMe
36 (Ψ-endo) R = $(CH_2)_2C_6H_4$-3-OMe

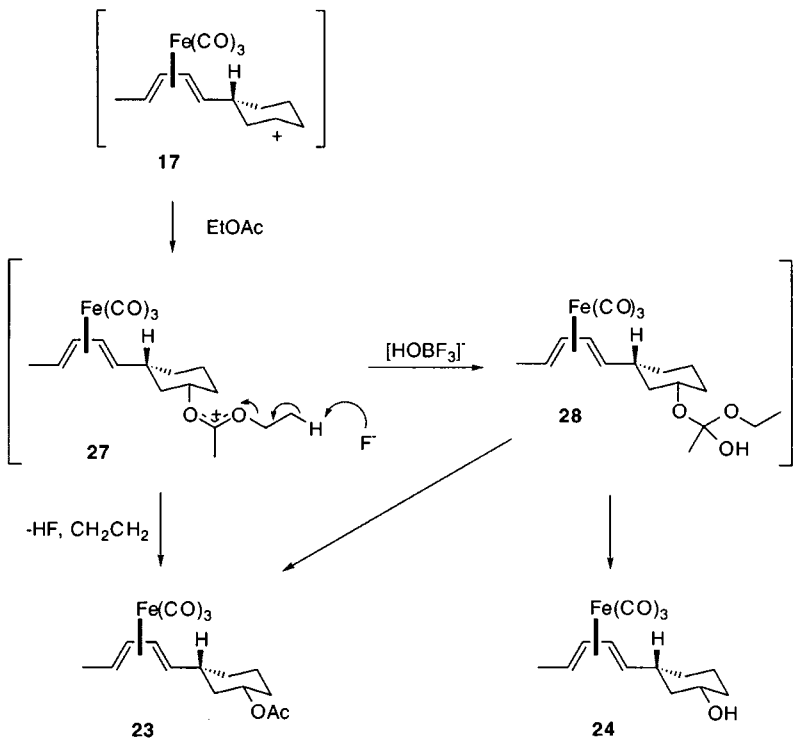
Compound **29** underwent a reaction in the presence of a Lewis acid, however, compound **30** yielded only recovered starting material (in fact **29** did not yield the anticipated cyclization product — instead compound

37 was isolated). The lower reactivity of the Ψ-*endo* diastereomer toward Lewis acids is likely due to the antiperiplanar conformer required for ionization being relatively high energy because the alkyl chain eclipses the external vinylic proton, as noted above. All further studies using these aryl-substituted derivatives therefore concentrated solely on Ψ-*exo* diastereomers.

Under acidic conditions (either BF_3–OEt_2 or H_2SO_4) alcohols **29**, **31**, **33**, and **35** undergo ionization and subsequent nucleophile capture. In the case of **31** cyclization occurred, however, in all other cases the major product resulted from diene rearrangement and recapture of water. All reactions were completely stereoselective.



The cyclization of **31** afforded **38** in 87% yield, but when the pendant nucleophile was insufficiently reactive to capture the dienyl cation a series of products (**37**, **39**, **40**) was generated with dienyl rearrangement dominating the mixture. No product of cyclization was observed for these systems. This type of rearrangement has been observed previously in dienol–iron tricarbonyl systems [18] and was confirmed in this case by COSY ^{1}H-NMR and a proton decoupling experiment on complex **37**. The critical cross-peak observed in the COSY spectrum of **37** was between the doublet of doublets at 1.39 ppm, assigned to the methyl protons, and the multiplet at 3.29 ppm, assigned to the proton on the alcoholic carbon (vide infra). This indicates that the alcoholic carbon is adjacent to a methyl group, a connectivity which could only occur through the rearrangement of the diene as shown. Additionally, the ^{1}H-NMR spectrum of **37** was decoupled selectively at 987 Hz (3.29 ppm) and the methyl doublet of doublets ($J = 6.6$, 3.2 Hz) became a narrow doublet ($J = 3.3$ Hz), further confirming the previous assignment. The mechanism of this rearrangement has been delineated by Takemoto et al. [18]. The possibility of capture of fluoride instead of water was eliminated replacing BF_3–OEt_2 with H_2SO_4 which generated the same mixture of products. Because the targeted cyclization is essentially irreversible, an experiment was designed to test whether the rearranged product could be driven to the desired cyclized product. Thus, compound **37** was stirred in methylene chloride with BF_3–OEt_2 at 0 °C for 24 h. It was hoped that the higher temperature and longer reaction time would promote nucleophilic capture by



Scheme 4.

the arene, however, TLC showed only a partitioning between the same products observed from the reaction of **29**.

3. Conclusions

Stereospecific intramolecular reaction of pendant alkenes and arenes with iron-stabilized dienyl cations can be accomplished in good yield, in those cases where the carbon nucleophile is sufficiently reactive to prevent competing rearrangements of the dienol substrate. The data collected from these experiments suggest that activated aryl nucleophiles, as in complex **31**, are sufficiently reactive to capture iron tricarbonyl–pentadienyl cations intramolecularly, and this is of synthetic utility in the formation of carbon–carbon bonds. The formation of the same fused-ring system from the non-activated nucleophile in **29** was unsuccessful. Complex **33** is activated toward the formation of a spiro-hexadienone system but the loss of aromaticity provides too high an energy barrier for reaction to proceed. Complex **35** was activated toward the formation of an indane system, however, the activation barrier to form the torsionally strained five-membered ring could not be overcome.

4. Experimental

4.1. General procedures

All reactions were carried out under dry, deoxygenated Ar. Tetrahydrofuran and Et_2O were distilled freshly from Na–benzophenone. Methylene chloride was distilled freshly from CaH_2. Pyridine was fractionally distilled from BaO. Column chromatography was performed on flash grade silica gel with eluting solvents reported as V/V ratios. Thin layer chromatography was performed on Sigma–Aldrich K6F Silica Gel 60 Å plates and visualized with UV light, phosphomolybdic acid, or Verghn's reagent. NMR spectra were recorded on a Varian XL200 (200 MHz) or a Varian Gemini 300 (300 MHz) spectrometer in $CDCl_3$ referenced to TMS as an internal standard, unless otherwise noted. NMR samples of organo-iron compounds were prepared by filtering through a plug of basic alumina, Brockman activity III. Since complexes **30**, **33**–**36** did not lead to productive cyclization reactions, they were characterized only by ^{1}H-NMR spectroscopy. Accordingly, only complexes **29** and **37** (the product of its rearrangement) are described here. (2*E*,4*E*)-2,4-hexadienal iron tricarbonyl [11], 1-bromo-3-phenylpropane [19], 1-bromo-3-(3-methoxyphenyl)propane [20], 1-bromo-4-(4-methoxyphenyl)butane [21], and 1-bromo-2-(3-methoxy-phenyl)-ethane [22] were prepared by literature procedures. All compounds were synthesized as racemic mixtures, but for convenience assignment of stereochemistry in naming these compounds refers to one enantiomer.

4.2. (6S*,7R*)-Tricarbonyl[7–10-η^4-(7E,9E)-1,7,9-undecatrien-6-ol]iron (**10**)

To 0.104 g of Mg (4.3 mmol) and 3 ml of dry Et_2O, a solution of 5-bromopent-1-ene (0.53 ml, 4.3 mmol) in 3 ml of dry Et_2O was added slowly under Ar (so that the reaction mixture was refluxing). The mixture was heated on a water bath until all Mg dissolved (ca. 30 min). The resulting Grignard reagent was then slowly added via a cannula to the solution of 0.786 g of (hexadienal)iron tricarbonyl in 4 ml of dry Et_2O at −78 °C under Ar. The reaction mixture was stirred at −78 °C for 30 min, slowly warmed to room temperature (r.t.) and stirred for 3 h, then quenched with saturated NH_4Cl. The Et_2O layer was separated, and the aqueous layer was washed with Et_2O twice. The combined organic fraction was washed with $NaHCO_3$ solution and water, dried over $MgSO_4$, and the solvent was evaporated. Flash chromatography separation (silica gel, EtOAc–hexanes, 1:19–1:5) afforded 0.614 g (61%) of Ψ-*endo* isomer **10** and 0.386 g of Ψ-*exo* isomer **11**. Complex **10** (orange liquid; R_f 0.51 in EtOAc–hexanes, 3:7). IR ($CHCl_3$, cm^{-1}): 3600 (br), 2050, 1980, 1603. ^{1}H-NMR: $\delta = 5.8$ (ddt, 1H, $J = 17$, 10.3, 6.7 Hz, H2), 5.13 (dd, 1H, $J = 8.5$, 5 Hz, H9), 5.08–4.95 (m, 3H, H1, H8), 3.5–3.4 (m, 1H, H6), 2.08 (dt, 2H, $J = 6.7$, 6.7 Hz, H3), 1.63–1.46 (m, 4H, H4, H5), 1.42 (d, 3H, $J = 6$ Hz, H11), 1.31 (d, 1H, $J = 3$ Hz, OH), 1.15 (dq, 1H, $J = 8.5$, 6 Hz, H10), 1.03 (dd, 1H, $J = 8$ Hz, H7). ^{13}C-NMR: $\delta = 212.2$, 138.5, 114.9, 85.3, 80.9, 73.9, 68.7, 58.2, 39.3, 33.7, 25.1, 19.1. HRMS for [M^+] Found: 306.0562. calc.: 306.0554. Complex **11** (orange liquid; R_f 0.29 in EtOAc–hexanes, 3:7). IR ($CHCl_3$, cm^{-1}): 3600 (br), 2949, 2050, 1978. ^{1}H-NMR: $\delta = 5.82$ (ddt, 1H, $J = 17$, 10.2, 6.7 Hz, H2), 5.23 (dd, 1H, $J = 8.7$, 5 Hz, H9), 5.09–4.96 (m, 3H, H1, H8), 3.5–3.4 (m, 1H, H6), 2.16–2.05 (m, 2H, H3), 1.71–1.48 (m, 5H, H4, H5, OH), 1.42 (d, 3H, $J = 6$ Hz, H11), 1.23 (dq, 1H, $J = 8.7$, 6 Hz, H10), 0.97 (dd, 1H, $J = 8.2$ Hz, H7). ^{13}C-NMR: $\delta = 212.1$, 138. 6, 114.8, 86.4, 82.1, 74.1, 64.7, 58.3, 38.1, 33.5, 24.7, 19.2. HRMS for [M^+] Found: 306.0543. Calc.: 306.0554.

4.3. (1R*,3S*,1′R*)-Tricarbonyl{1′–4′-η^4-1-fluoro-[(1′E,3′E)-1′,3′-pentadienyl] cyclohexane}iron (**13**) and (1S,3S,1′R)-tricarbonyl{1′-4′-η^4-1-fluoro-[(1′E,3′E)-1′,3′-pentadienyl] cyclohexane}iron (**12**)

To a solution of alcohol **11** (28 mg) in CH_2Cl_2 (1 ml) was added BF_3–OEt_2 (35 μl, three equivalents) at −78 °C under Ar. The reaction mixture was stirred at −78 °C for 1 h, then at r.t. for 1 min. The reaction was quenched by addition of saturated $KHCO_3$ solu-

tion. The organic layer was separated, washed with saturated $KHCO_3$, water, dried over $MgSO_4$, and concentrated. Preparative TLC separation on silica gel (hexanes, multiple development) afforded 16 mg of complex **13** (57%; more polar product) and 9.5 mg of complex **12** (34%, less polar product). Complex **13** (yellow crystalline compound). M.p. 57–58 °C. IR ($CHCl_3$, cm^{-1}): 2950, 2040, 1971, 998. ^{1}H-NMR: $\delta =$ 5.04 (dd, 1H, $J = 8$, 5 Hz, H8), 5.02 (dd, 1H, $J = 10.7$, 5 Hz, H9), 4.45 (dtt, 1H, $J = 49$, 10.6, 4.5 Hz, H1), 2.21–1.7 (m, 4H), 1.4 (d, 3H, $J = 6$ Hz, H11), 1.36–1.0 (m, 6H), 0.83 (dd, 1H, $J = 8$ Hz, H7). ^{13}C-NMR: $\delta = 212.7$, 212.7, 91.5 (d, $J_{CF} = 173$ Hz), 85.4, 82.2, 68.9, 57.6, 42.7 (d, $J_{CF} = 17$ Hz), 41.3 (d, $J_{CF} = 10$ Hz), 33.7, 32.2 (d, $J_{CF} = 17.8$ Hz), 23.1 (d, $J_{CF} = 11.9$ Hz), 19.1. ^{19}F-NMR ($CDCl_3$, $CFCl_3$ standard): $\delta = -168.6$ (d, $J = 49$ Hz). HRMS for [$M^+ - CO$] Found: 280.0552. Calc. for $C_{13}H_{17}FFeO_2$: 280.0562. Complex **12** (yellow crystalline compound). M.p. 49–51 °C. IR ($CHCl_3$, cm^{-1}): 2942, 2047, 1971, 1564, 957. ^{1}H-NMR: $\delta = 5.03$ (dd, 1H, $J = 10.7$, 5 Hz, H9), 5.02 (dd, 1H, $J = 10$, 5 Hz, H8), 4.84 (dtt, 1H, $J = 48$, 4, 2 Hz, H1), 2.13–1.03 (m, 9H), 1.39 (d, 3H, $J = 6$ Hz, H11), 0.77 (dd, 1H, $J = 10$, 7 Hz, H7). ^{13}C-NMR: $\delta = 89.1$ (d, $J_{CF} = 167$ Hz), 85.2, 82.5, 70.1, 57.3, 40.9 (d, $J_{CF} = 21$ Hz), 37.1, 34.1, 30.3 (d, $J_{CF} = 21$ Hz), 20.2, 19.1. ^{19}F-NMR ($CDCl_3$, $CFCl_3$ standard): $\delta = -182.9$ (dt, $J =$ 48, 45 Hz). HRMS for [M^+] Found: 308.0488. Calc. for $C_{14}H_{17}FFeO_3$: 308.0511. For [$M^+ - 3CO$] Found: 224.0670. Calc. for $C_{11}H_{17}FFe$: 224.0664.

4.4. (1S,3R*,1′R*) and (1R*,3R*,1′R*)-Tricarbonyl-{1′–4′-η⁴-1-fluoro-[(1′E,3′E)-1′,3′-pentadienyl]-cyclohexane}iron (**14**, **15**)*

The alcohol **10** (26 mg) was treated with BF_3–OEt_2 (33 μl, three equivalents) in CH_2Cl_2 as described above. Preparative TLC purification afforded 23 mg (89%) of a mixture of complexes **14** and **15** in a 2.7:1 ratio. IR ($CHCl_3$, cm^{-1}): 2944, 2041, 1971, 998. ^{1}H-NMR: $\delta =$ 5.05–4.87 (m, 2H, H8, H9), 4.9 and 4.42 (dtt, $J = 47$, 4, 2 Hz; dtt, $J = 49$, 10.5, 4.5 Hz, 1H, H1, minor and major epimer, respectively), 2.2–1.47 (m, 4H), 1.4 (d, 3H, $J = 6$ Hz, H11), 1.36–1.0 (m, 6H), 0.84 and 0.76 (dd, $J = 8.5$ Hz; dd, $J = 8.5$ Hz, 1H, H7, major and minor epimer, respectively). ^{19}F-NMR ($CDCl_3$, $CFCl_3$ standard): $\delta = -168.6$ (d, $J = 49$ Hz), -184.0 (dt, $J = 47$, 43 Hz). HRMS for [M^+] Found: 308.0500. Calc. for $C_{14}H_{17}FFeO_3$: 308.0511.

4.5. (1R,3S*,1′R*)-Tricarbonyl{1′–4′-η⁴-1-azido-[(1′E,3′E)-1′,3′-pentadienyl]cyclohexane}iron (**22**)*

To a solution of alcohol **11** (22 mg) in CH_2Cl_2 (1 ml) were added sequentially $TMSN_3$ (95 μl, ten equivalents) and BF_3–OEt_2 (35 μl, three equivalents) at -40 °C under Ar. The reaction mixture was stirred at -40 °C for 1 h, then at r.t. for 5 min. The reaction was quenched by addition of saturated $KHCO_3$ solution. The organic layer was separated, washed with saturated $KHCO_3$, water, dried over $MgSO_4$, and concentrated. Preparative TLC separation on silica gel (hexanes, multiple development) afforded fluorides **12** and **13** (66% combined yield), and azide **22** (2 mg, 8% yield). IR ($CHCl_3$, cm^{-1}): 2938, 2099, 2041, 1973, 1455. ^{1}H-NMR: $\delta = 5.08$–4.97 (m, 2H, H8, H9), 3.32 (ddt, 1H, $J = 15.5$, 11.6, 4 Hz, H1), 2.13–1.67 (m, 6H), 1.4 (d, 3H, $J = 6$ Hz, H11), 1.33–1.05 (m, 6H), 0.79 (dd, $J = 8.9$, 7.7 Hz, H7). HRMS for [$M^+ - CO$] Found: 303.0667. Calc. for $C_{13}H_{17}FeN_3O_2$: 303.0670.

4.6. (1S,3R*,1′R*)-Tricarbonyl{1′–4′-η⁴-3[(1′E,3′E)-1′,3′-pentadienyl]cyclohexyl acetate}iron (**23**)*

To a solution of alcohol **10** (23 mg) in anhydrous EtOAc (1 ml) was added BF_3–OEt_2 (28 μl, three equivalents) at -78 °C under Ar. The reaction mixture was stirred at -78 °C for 20 min, then at r.t. for 10 min. The reaction was quenched by addition of saturated $KHCO_3$ solution. The organic layer was separated, washed with saturated $KHCO_3$, water, dried over $MgSO_4$, and concentrated. Preparative TLC separation on silica gel (CH_2Cl_2–hexanes, multiple development) afforded (in the order of increasing polarity) compounds **25** and **26** (3 mg, mixture, 15%), **14** and **15** (18%, 2.7:1 mixture of epimers), **23** (9 mg, 37%), **10** (1.5 mg), and **24** (5 mg, 23 %). (Yields are based on the amount of consumed starting material.) Complex **23** (yellow crystalline compound). M.p. 102–104 °C. IR ($CHCl_3$, cm^{-1}): 2947, 2045, 1974, 1728, 1258. ^{1}H-NMR: $\delta = 5.05$–4.98 (m, 2H, H8, H9), 4.64 (tt, 1H, $J = 11$, 4.3 Hz, H1), 2.06 (s, 3H, COMe), 2.03–1.72 (m, 4H), 1.39 (d, 3H, $J = 6$ Hz, H11), 1.36–1.02 (m, 6H), 0.81 (dd, 1H, $J = 8$ Hz, H7). ^{13}C-NMR: $\delta = 170.5$, 85.3, 82.3, 72.6, 69.1, 57.4, 41.7, 39.9, 35.8, 31.4, 23.7, 21.5, 19.1. HRMS for [M^+] Found: 348.0647. Calc. for $C_{16}H_{20}FeO_5$: 348.0660. Complex **24** was isolated as a yellow crystalline compound in 23% yield. M.p. 127–128 °C. IR (KBr, cm^{-1}): 3256, 2947, 2854, 2033, 1946, 1072. ^{1}H-NMR: $\delta = 5.05$–4.97 (m, 2H, H8, H9), 3.54 (tt, 1H, $J = 10.5$, 4 Hz, H1), 2.08–1.69 (m, 4H), 1.39 (d, 3H, $J = 6$ Hz, H11), 1.34–0.96 (m, 6H), 0.84 (dd, 1H, $J = 8.5$ Hz, H7). ^{13}C-NMR: $\delta = 85.3$, 82.4, 70.5, 69.6, 57.4, 44.1, 41.9, 35.9, 35.1, 24.0, 19.1. HRMS for [M^+] Found: 306.0547. Calc. for $C_{14}H_{18}FeO_4$: 306.0554. The mixture of complexes **25** and **26** was isolated as a yellow solid in 15% yield (4:1 ratio). IR ($CHCl_3$, cm^{-1}): 2924, 2040, 1966, 1444. ^{1}H-NMR: $\delta = 5.65$–5.61 (m, 2H, H1, H2), 5.09–5.01 (m, 2H, H8, H9), 2.18–1.79 (m, 7H), 1.4 (d, 3H, $J = 6$ Hz, H11), 1.1 (dq, 1H, $J = 7.5$, 6 Hz, H10), 0.92 (dd, 1H, $J = 8.5$ Hz, H7).

^{13}C-NMR: for **25** $\delta = 126.6, 126.2, 85.3, 82.6, 70.5, 57.3, 39.1, 33.7, 32.9, 22.3, 19.2$; for **26** 131.5, 128.0, 85.5, 82.9, 69.5, 57.4, 40.4, 33.3, 25.0, 21.1, 19.2. HRMS for [M^+] Found: 288.0454. Calc. for $C_{14}H_{16}FeO_3$: 288.0449.

4.7. (2R,6R*)-Tricarbonyl[2–5-η⁴-(2E,4E)-9-phenylnonadien-6-ol]iron (**29**)*

To 145 mg of Mg (5.95 mmol; oven-dried, ground) in 2 ml THF containing a crystal of iodine was added dropwise at reflux a solution of 793 mg 1-bromo-3-phenylpropane (3.98 mmol) in 2 ml THF. The resulting mixture was stirred at reflux for 1 h. and then 0.66 ml of the solution was added dropwise to 105 mg (2*E*,4*E*)-hexadienal iron tricarbonyl (0.44 mmol) in 1 ml THF at −78 °C. The reaction was stirred at −78 °C for 30 min and r.t. for 20 min and then quenched with aqueous (aq.) NH_4Cl. The THF layer was removed and the aqueous layer extracted with two portions of Et_2O. The combined organic extracts were washed with $NaHCO_3$ and water, dried over Na_2SO_4, and the solvent was removed under vacuum. Flash chromatography separation (silica gel, 1:5 EtOAc–hexanes) afforded 76 mg of Ψ-*exo* diastereomer **29** (48%) as an orange crystalline solid (R_f 0.26 in 1:3 EtOAc–hexanes). ^{1}H-NMR: $\delta = 7.32–7.18$ (m, 5H), 5.21 (dd, 1H, $J = 8.8, 5.5$ Hz), 5.06 (dd, 1H, $J = 9.5, 5.0$ Hz), 3.44 (m, 1H, H6), 2.63 (t, 2H, $J = 10.8$ Hz), 1.82–1.53 (m, 4H), 1.42 (d, 3H, $J = 9.3$), 1.22 (m, 1H), 0.97 (t, 1H, $J = 11.0$ Hz). ^{13}C-NMR: $\delta = 128.4, 128.3, 125.8, 86.5, 82.0, 81.8, 74.0, 64.4, 58.2, 38.3, 35.9, 27.5, 19.4$. HRMS for [$M^+$] Found: 356.0763. Calc. for $C_{18}H_{20}FeO_4$: 356.0711. The Ψ-*endo* diastereomer **30**, (62 mg, 39%) was isolated as an orange oil (R_f 0.49 in 1:3 EtOAc–hexanes). ^{1}H-NMR: $\delta = 7.41–7.05$ (m, 5H), 5.79 (dd, 1H, $J = 8.9, 5.6$ Hz), 5.23 (dd, 1H, $J = 8.4, 7.1$ Hz), 2.61 (t, 2H, $J = 8.2$ Hz), 2.38 (m, 1H), 1.92 (m, 1H), 1.80–1.45 (m, 4H), 1.41 (d, 3H, $J = 6.4$ Hz), 1.02 (t, 1H, $J = 8.2$ Hz).

4.8. (2R,6R*)-Tricarbonyl[2–5-η⁴-(2E,4E)-9-(3-methoxyphenyl)nonadien-6-ol]iron (**31**)*

To 720 mg of Mg (29.7 mmol; oven-dried, ground) in 20 ml THF with a crystal of iodine was added dropwise at reflux a solution of 6.08 g 1-bromo-3-(3-methoxyphenyl)propane (3.98 mmol) in 20 ml THF. The resulting mixture was stirred at reflux for 1 h. and then 16 ml of the solution was added dropwise to 1.802 g (2*E*,4*E*)-hexadienal iron tricarbonyl (7.63 mmol) in 10 ml THF at −78 °C. The reaction was stirred at −78 °C for 30 min and r.t. for 30 min and then quenched with aq. NH_4Cl. The THF layer was removed and the aqueous layer extracted with two portions of Et_2O. The combined organic extracts were washed with $NaHCO_3$ and water, dried over Na_2SO_4, and the solvent was removed under vacuum. Flash chromatography (silica gel, 1:4 EtOAc–hexanes) afforded 1.512 g of Ψ-*exo* diastereomer **31** (51%) as an orange oil (R_f 0.29 in 1:2 EtOAc–hexanes). IR ($CHCl_3$, cm^{-1}): 3600 (br), 2050, 1980. ^{1}H-NMR: $\delta = 7.21$ (t, 1H, $J = 9.5$ Hz), 6.83–6.70 (m, 3H), 5.22 (dd, 1H, $J = 9.2, 4.8$ Hz), 5.04 (dd, 1H, $J = 7.9, 5.7$ Hz), 3.91 (s, 3H) 3.45 (m, 1H), 2.63 (t, 2H, 12.1 Hz), 1.88–1.35 (m, 5H), 1.41 (d, 3H, $J = 7.3$ Hz), 0.96 (t, 1H, $J = 9.5$ Hz). ^{13}C-NMR: $\delta = 129.5, 120.7, 114.0, 111.3, 86.7, 82.1, 74.8, 64.5, 58.7, 55.4, 38.5, 36.4, 27.7, 19.7$ (4° carbons not detected). HRMS for [M^+] Found: 386.0751. Calc. for $C_{19}H_{22}FeO_5$: 386.0817. From this reaction 1.031 g Ψ-*endo* diastereomer **32** (35%) as an orange oil (R_f 0.29 in 1:2 EtOAc–hexanes) was also isolated. ^{1}H-NMR: $\delta = 7.25$ (t, 1H, $J = 9.5$ Hz), 6.83–6.70 (m, 3H), 5.82 (dd, 1H, $J = 8.9, 4.7$ Hz), 5.21 (dd, 1H, $J = 7.9, 5.5$ Hz), 3.94 (s, 3H) 2.61 (t, 2H, 11.5 Hz), 2.40 (m, 1H), 1.92–1.43 (m, 5H), 1.43 (d, 3H, $J = 5.1$ Hz), 1.19 (t, 1H, $J = 9.2$ Hz). HRMS for [M^+] Found: 386.0866. Calc. for $C_{19}H_{22}FeO_5$: 386.0817.

4.9. (2S,3S*)-Tricarbonyl[3–6-η⁴-(3E,5E)-9-phenylnonadien-2-ol]iron (**37**)*

To a solution of 34 mg of **29** (0.095 mmol) in 1.0 ml CH_2Cl_2 was added 35 μl BF_3–OEt_2 (0.285 mmol) at −78 °C. The reaction mixture was stirred at −78 °C for 1 h and then at r.t. for 1 min and finally quenched with aq. $NaHCO_3$. The organic layer was removed and the aqueous layer extracted twice with CH_2Cl_2. The combined organic extracts were washed with $NaHCO_3$ and water, dried over Na_2SO_4, and the solvent was removed under vacuum. Flash chromatography separation (silica gel, 1:4 EtOAc–hexanes) afforded 26 mg of **37** (42%) as an orange oil (R_f 0.64 in 1:3 EtOAc–hexanes). ^{1}H-NMR: $\delta = 7.30–7.14$ (m, 5H), 5.18–4.98 (m, 2H), 3.27 (m, 1H), 2.61 (t, 2H, $J = 6.6$ Hz), 1.73–1.19 (m, 6H), 0.90 (m, 1H). HRMS for [M^+] Found: 356.0787. Calc. for $C_{18}H_{20}FeO_4$: 356.0711.

4.10. (2R,6R*)-Tricarbonyl[2–5-η⁴-(2E,4E)-5-(6,7,8,9-tetrahydro-12-methoxynapthyl)pentadienyl]iron (**38**)*

To a solution of 52 mg of **31** (0.134 mmol) in 1.6 ml CH_2Cl_2 was added 49μl BF_3–OEt_2 (0.398 mmol) at −78 °C. The reaction mixture was stirred at −78 °C for 1 h and then at r.t. for 1 min and finally quenched with $NaHCO_3$. The organic layer was removed and the aqueous layer extracted with two portions of CH_2Cl_2. The combined organic extracts were washed with $NaHCO_3$ and water and dried over Na_2SO_4. Removal of solvent under vacuum afforded 43 mg of **38** (87%) as an orange oil (R_f 0.60 in 1:3 EtOAc–hexanes). IR ($CHCl_3$, cm^{-1}): 2045, 1973. ^{1}H-NMR: $\delta = 7.28$ (d, 1H, $J = 8.2$ Hz), 6.71 (dd, 1H, $J = 8.4, 2.8$ Hz), 6.58 (d, 1H, $J = 3.0$ Hz), 5.30 (dd, 1H, $J = 9.2, 5.1$ Hz), 5.06 (dd, 1H, $J = 9.2, 4.8$ Hz), 3.76 (s, 3H), 2.74 (t, 2H, $J = 7.6$

Hz), 2.48 (m, 1H), 2.08–1.68 (m, 5H, H2), 2.39 (d, 1H, $J = 6.1$ Hz), 1.12 (t, 1H, $J = 8.4$ Hz). ^{13}C-NMR: $\delta =$ 157.8, 137.7, 132.0, 129.3, 113.5, 111.8, 84.7, 83.4, 71.0, 57.9, 55.3, 42.5, 33.6, 30.1, 21.0, 19.2. HRMS for [M^+] Found: 368.0090. Calc. for $C_{19}H_{20}FeO_4$: 368.0711.

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