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Stereochemical Requirements of Oxidative Cyclizations in Extended Iterative Organoiron-Mediated Routes to Alkaloids

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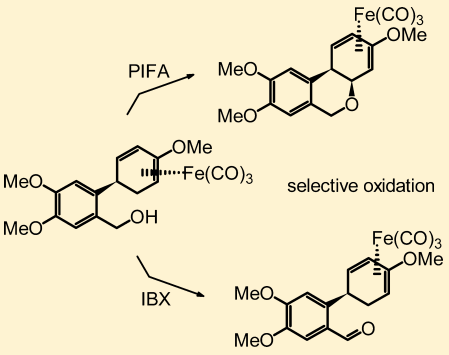
Supporting Information

ABSTRACT: Oxidative cyclization by reaction of benzylic and phenolic OH groups on tricarbonyl(η^4-cyclohexa-1,3-diene)iron(0) complexes has been achieved with the hypervalent iodine oxidant PIFA which was shown to be compatible with the tricarbonyliron complex. The reaction proceeds with substrates with the nucleophilic substituent on the opposite face of the ligand to the iron. IBX gives efficient oxidation of the benzyl alcohol to the aldehyde in the presence of the $Fe(CO)_3$ group. Reduction of 1-arylcyclohexadienyliron(1+) complexes with sodium borohydride to access the *endo* series also gave a novel rearranged 2-aryl reduction product with a 5-*endo* OMe group. The *cis* relative stereochemistry of the oxidative cyclization product, the *exo* delivery of hydride to the 1-arylcyclohexadienyliron(1+) complex, and the 2-aryl-5-*endo*-methoxy relative stereochemistry of the rearranged product were proved by X-ray crystallography.



INTRODUCTION

We have established the strategic utility of our *1,1* iterative strategy[1] to introduce the quaternary center at the heart of the carbon skeleton of the Amaryllidaceae alkaloids.[2] This procedure makes use of a sequence of two nucleophile additions to chiral electrophilic cyclohexadienyliron complexes and has been exemplified by syntheses of *O*-methyljouberti-amine[1a] and mesembrine[3] and formal total syntheses[1b] of lycoramine and maritidine (for examples of these approaches to maritidine **2** and mesembrine **3**, see Figure 1). The complementary *1,2* iterative sequence is illustrated by our work toward hippeastrine.[4] These procedures are referred to as iterative because the same hapticity in the metal complex is employed in each of the electrophilic intermediates.[5] Each nucleophile addition step is linked to the next by a reactivation step which increases the hapticity from η^n to η^{n+1}. The metal provides activation and stereocontrol in each iteration, and its value in the synthesis is increased each time the series of iterations is lengthened.

With tricarbonyliron complexes, intramolecular oxidative cyclization followed by acid catalyzed ring-opening is an attractive reactivation step.[6−8] The cyclization produces an η^4 diene complex with an allylic leaving group, which is converted into the η^5 electrophile by the ring-opening step. We describe here an investigation of the scope and stereochemical requirements of the oxidative cyclization in arylcyclohexadiene complexes, with the aim of developing procedures that would adapt our synthesis[3] of mesembrine to give rapid access to the medically important Amaryllidaceae alkaloid galanthamine **4**[9] and shorten our synthetic route[1b] to maritidine (Figure 2).

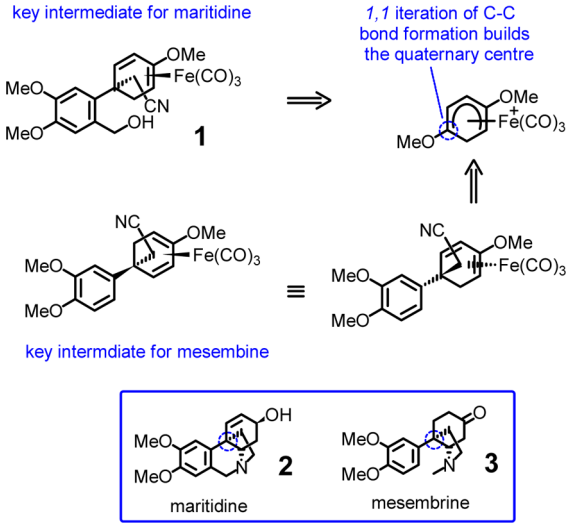


Figure 1. *1,1*-Iterative strategies for the quaternary centers in maritidine and mesembrine.

RESULTS AND DISCUSSION

Two different classes of oxygen-centered nucleophiles [a benzyl alcohol (in **1**) and a phenolic OH (in **5**) (Figure 2)] with substantially different oxidation potentials and nucleophilicities have been compared in this study. Either a widely applicable

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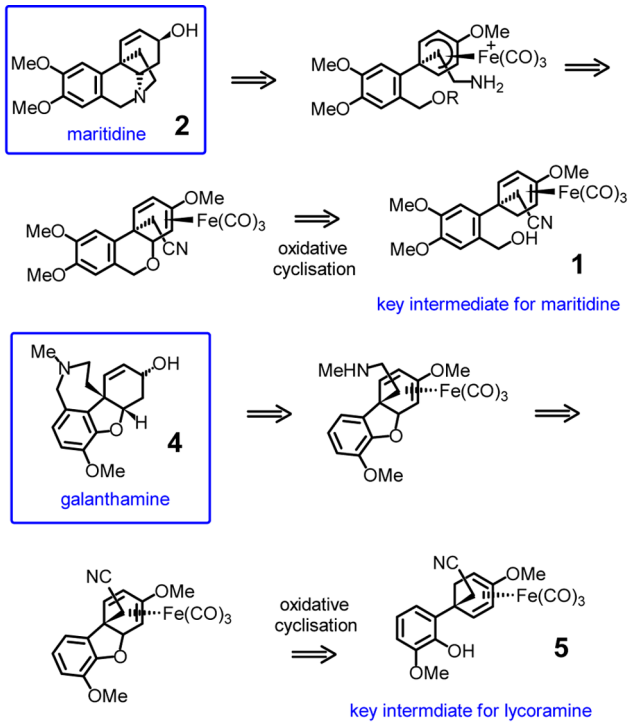
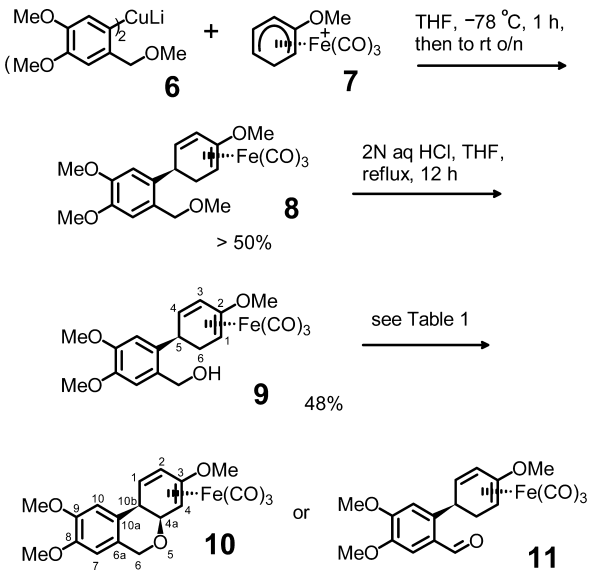


Figure 2. Use of oxidative cyclization to extend the iterative strategy for regiodiverse structural targets such as maritidine and galanthamine.

oxidative cyclization method or two efficient but more specialized procedures are needed. Known oxidants from earlier reports[6−8] of oxidative cyclizations of dieneiron complexes and new reagents have been examined in this work. In particular, the hypervalent iodine reagent phenyliodine bis(trifluoroacetate) (PIFA), which has been used by Ley's group[10] to synthesize oxomaritidine, seemed an attractive option since it is known to be compatible with other organic functionality in the alkaloid target molecules. In order to quickly test a range of oxidizing conditions, a model compound **9** (Scheme 1) was chosen. The substrate **9** contains the (η^4-cyclohexadiene)iron(0) complex and benzyl alcohol structures present in **1** (Figure 2) and was easily made in the racemic series in two steps starting from "Birch's salt"[11] (±)-**7**[12] using a diaryl cuprate reagent **6** generated from the aryllithium reagent used in our earlier studies of the preparation of 1-arylcyclohexadienyliron complexes. The aryllithium and copper iodide produced the diaryl cuprate species **6** which on addition of 2-methoxy salt **7** gave the *exo* adduct **8**, which was taken on to the benzyl alcohol in the presence of a small quantity of methyl 3,4-dimethoxybenzyl ether, which was produced when the excess diaryl cuprate was quenched with water. The alcohol **9** was obtained from **8** by a simple solvolysis procedure[13] in 48% yield after purification by chromatography.

Scheme 1. Study of the Oxidation of the Benzyl Alcohol 9



The majority of oxidative conditions used in this study formed either the aldehyde **11** or the required cyclization product **10**, but the ferrocenium ion procedure, which had proved very effective in the examples examined by Knölker,[12] failed to produce an isolable product or, when used in the presence of sodium carbonate to control the build-up of acid, proved unreactive (Table 1). The hypervalent iodine reagents behaved differently, with IBX showing selectivity for the aldehyde **11** and PIFA producing **10**. The best results with PIFA were obtained using 2,2,2-trifluoroethanol as the solvent, and only traces of the cyclized product were obtained in dichloromethane and none at all in acetonitrile. The ^{1}H NMR spectrum of the cyclized product **10** was easily distinguished from the starting material **9** by the loss of the signals for the methylene group of the cyclohexadiene at 2.39 and 1.68 ppm and the appearance of a doublet of doublets at 4.56 ppm for new H-4a of the 4a,10b-dihydro-3,8,9-trimethoxy-6*H*-dibenzo-[*b*,*d*]pyran ring system. The *cis* coupling constant for $J_{4a,10b}$ is 9.3 Hz, which is comparable to the 9 Hz *cis* coupling observed after a similar oxidative cyclization by Pearson.[7] The benzyl methylene group of **9** changes from a singlet at 4.63 ppm to two doublets at 4.47 and 4.30 ppm for H-6 in **10**. The H-5 signal moves further upfield from ∼3.5 ppm in **9** to 3.12 ppm in **10**, and similarly in the ^{13}C NMR the 5-C signal moves further upfield from 38.2 ppm in **9** to 35.4 ppm in **10**. The product **10** was crystallized, and the *cis* ring fusion was confirmed by X-ray crystallography.[14]

Table 1. Different Conditions Used in the Oxidative Cyclization in Scheme 1

entry	reaction conditions	product and yield
1	IBX, DMSO, rt, 2 h	67% of aldehyde **11**
2	MnO_2, toluene, 120 °C, 3.5 h	formed aldehyde **11**[a]
3	5% $FeCl_3$ on silica, 1 h under vac	trace of product **10**[a]
4	Cp_2FePF_6, CH_2Cl_2, rt, 4 h	no product isolated
5	Cp_2FePF_6, Na_2CO_3, CH_2Cl_2, rt, 12 h	no reaction
6	DDQ, CH_2Cl_2, rt, 1.5 h	formed aldehyde **11**[a]
7	PIFA, CH_2Cl_2, −40 °C, 10 min	trace of product **10**[a]
8	PIFA, MeCN, −40 °C to rt, 12 h	no reaction
9	PIFA, CF_3CH_2OH, −40 °C, 10 min	42% of product **10**

[a]Evidence from thin-layer chromatography.

In the phenolic series (Scheme 2, Table 2), the starting point was the SEM-protected aryllithium reagent used in our lycoramine formal total synthesis.[1b] The corresponding diaryl cuprate reagent **12** was generated at −78 °C and reacted with the salt **7** to give **13** in 30% yield. The SEM group was removed without difficulty with sulfuric acid in methanol/THF to give the desired phenol **14** in 86% yield. In practice it was more efficient (46% overall) to combine the two reactions into a

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Scheme 2. Study of the Oxidation of the Cyclohexadienylphenol 14

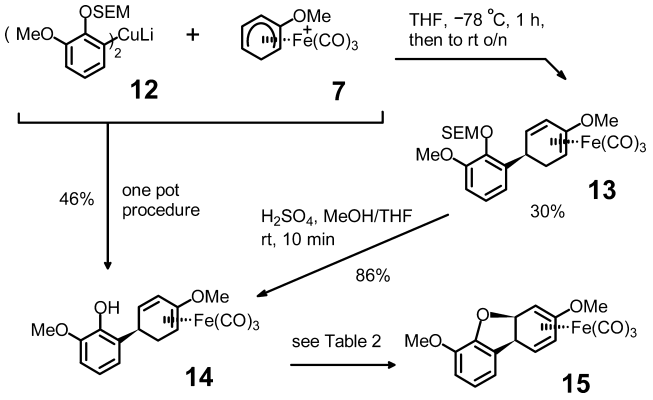


Table 2. Different Conditions Used in the Oxidative Cyclization in Scheme 2

entry	reaction conditions	product and yield
1	MnO_2, toluene, 130 °C, 20 min	no product
2	MnO_2, benzene, 100 °C, 2 h	trace of product **15**[a]
3	10% $FeCl_3$ on silica, 1 h	4% of product **15**
4	CAN, MeOH, rt, 12 h	no product
5	DDQ, CH_2Cl_2, rt, 1 h	no reaction
6	PIFA, CH_2Cl_2, −40 °C, 10 min	no product
7	PIFA, CF_3CH_2OH, −40 °C, 20 min	15% of product **15**[b]

[a]Evidence from thin-layer chromatography. [b]See text.

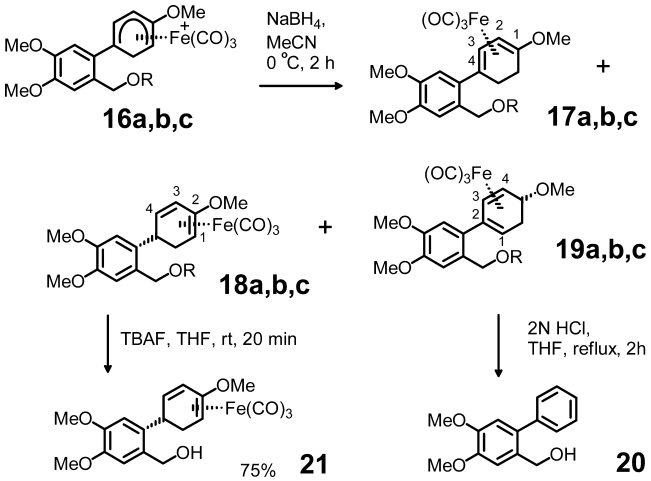
single procedure, treating the crude product from the organocuprate addition with acid for 10 min at room temperature before working up the reaction. The hypervalent iodine reagent PIFA again required the use of 2,2,2-trifluoroethanol as the solvent, and the reaction was rather less efficient than for substrate **9**. In the case of **14**, the product was hard to separate from the byproduct of the reaction and residues from PIFA itself. The ^{1}H NMR of the cyclized product **15** differs from the starting material **14** because of the loss of the C(6) methylene peaks at 2.40 and 1.76 ppm and the appearance of the doublet of doublets at 5.31 ppm. This same product (**15**) was obtained pure but in low yield by oxidation of **14** using $FeCl_3$ on silica. PIFA is capable of promoting the required cyclization under mild conditions and would be suitable for further development as an alternative reagent for the oxidative cyclization of tricarbonyl(η^4-diene)iron(0) complexes with pendant nucleophilic substituents. A supported analogue[15] of the PIFA reagent, if attachment was made at the phenyl group, would be useful to simplify the separation of byproduct from **15**.

The key intermediates **1** and **5** from our synthetic studies[1b] were also examined with PIFA in 2,2,2-trifluoroethanol at −40 °C, conditions that had been suitable to allow oxidative cyclization to occur in the model study. Neither case was successful. The intermediate **5** for lycoramine proved more sensitive than the model compound, and after only 10 min, TLC analysis showed that complete decomposition had occurred. With the benzyl alcohol **1**, no trace of product was observed even after 40 min. The $FeCl_3$ oxidation was also examined, but similarly without success.

There is an important difference between the models and these two "real" systems. Because **1** and **5** are further advanced in the synthetic route and the *1,1* iterative sequence of two nucleophile additions has been completed, the arene substituent, which was introduced first, has been displaced to the *endo* face of the ligand by the introduction of the CH_2CN side chain. The arenes are on the same side of the ring as the metal complex in the two real examples and on the opposite side in the model. The proposed mechanisms both involve intramolecular nucleophile addition to the iron-bound multihapto ligand, and an *exo* stereochemistry for this process would be preferred. Rather than risk wasting precious material from the two synthetic routes, it was decided to examine this stereochemical issue with a second model compound. It was expected that the required *endo* arene complexes could be prepared by borohydride reduction of the 1-aryl-4-methoxycyclohexadienyl electrophiles which were available in much larger amounts because they are at a far earlier stage in the routes to lycoramine and maritidine. In practice, although eventually successful, this reduction step produced unexpected results which raise interesting mechanistic issues.[16]

Reduction of the methyl ether derivative **16a** of **1** with sodium borohydride in acetonitrile at 0 °C was examined first (Scheme 3). Three products were formed, of which two were

Scheme 3. Study of the Reduction of 1-Arylcyclohexadienyliron Complexes (a: R = Me; b: R = Si^{t}BuPh$_2$; c: R = Si^{i}Pr$_3$)



inseparable but appeared from their NMR spectrum to be the expected products of *i* and *ω* hydride addition to the dienyl ligand. These products corresponded to a 47% yield from **16a**. The ^{1}H NMR spectra of structures of this type are characteristic around δ = 5−6 ppm, as the 2-methoxy-5-arylcyclohexadiene complex **18a** has a single "inner" hydrogen at C(3) of the diene and the 1-methoxy-4-arylcyclohexadiene regioisomer **17a** has two. The hydrogen at 5.26 ppm in **18a** showed the typical clear doublet of doublets from coupling to the two hydrogens at C(1) and C(4). In **17a**, the two hydrogens at δ = 5.51 and δ = 5.33 are close together in the spectrum and the coupling between them is difficult to identify. The third product **19a** was obtained pure in 13% yield and was similar to **18a** as it had a single hydrogen (H-3) in the range δ = 5−6 ppm, coupled in the normal fashion to H-4, but the OMe signal did not appear in the expected position for a C(2) methoxy group. The possibility that the *ipso* hydride reduction lacked stereoselectivity was also ruled out because the product **19a** was different to the *exo* adduct **8** prepared earlier as a precursor to **9**. An attempt to isomerize **19a** into one of the other three

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known products caused instead the loss of MeOH to form the trisubstituted biaryl **20**. Both OMe groups were removed in this process, suggesting that the methoxy group on the cyclohexadiene ligand was allylic or rearranged to an allylic position. The solvolysis of the benzylic OMe is comparable to the process that formed **9** and is consistent with our earlier studies.[13] The product **19a** was crystallized and identified by X-ray crystallography[14] as the 2-aryl-5-*endo*-methoxy 1,3-diene complex.

Two silyl-protected benzyl ethers **16b** and **16c** were available from the maritidine project[1b] and were similarly reduced with sodium borohydride in acetonitrile (Scheme 3, Table 3). Again

Table 3. Regioisomer Ratios from the Reduction of the Ethers 16a−c

entry	starting material	product ratio **17**/**18**/**19**	yield (%)
1	**16a** (R = Me)	45:33:22	60
2	**16b** (R = Si^{t}BuPh$_2$)	18:50:32	40
3	**16c** (R = Si^{i}Pr$_3$)	9:25:66	32

the unexpected rearranged 2-aryl products **19b,c** were obtained in 13−21% yield. As might be expected with a more bulky benzyl ether, the ω hydride addition was enhanced when the silyl group was TBDPS (substrate **16b**). Fortunately, however, the minor product was crystalline and was isolated by fractional crystallization. The resulting crystals were of X-ray quality and established the relative stereochemistry, which had been in doubt because hydride addition at substituted positions on cyclohexadienyliron complexes is known sometimes to proceed on the *endo* face. The X-ray structure (see the Supporting Information) shows that the product **18b** was the required *endo* aryl stereoisomer. Removal of the silyl group, however, to form the diastereoisomer of **9**, could not be achieved with TBAF, even in refluxing THF. The problem was finally solved in the TIPS ether series which again gave the 5-*endo* aryl product **18c** which although formed in low yield (the major product was the novel rearranged 2-aryl-5-*endo* methoxy isomer) was obtained pure by crystallization and was successfully converted into **21**, the diastereoisomer of **9**. Fortunately, the desilylation step this time was efficient (75% yield) and proceeded at room temperature. A sufficient amount of the product **21** was obtained to test the stereochemical requirements of the oxidative cyclization. The PIFA oxidation was performed in exactly the same way that afforded 42% yield of **10** from the *exo* isomer **9**. In the *endo* series with **21**, however, no traces of a cyclization product could be identified. It is concluded that the oxidative cyclization of oxygen atoms present as ortho substituents on aryl cyclohexadiene derivatives proceeds only in the *exo* stereoisomer series.

The diastereoisomers described in this work have characteristic ^{1}H NMR signals for the epimeric H-5 protons. The H-5 opposite to the tricarbonyliron group (i.e., *endo* arene; *exo* H) consistently appears downfield from the alternative stereoisomer with the hydrogen on the same side of the ligand as the metal (i.e., *exo* arene; *endo* H). In the benzyl alcohol series where both diastereoisomers are available, the difference is clear (Table 4, entry 5). The relative stereochemistry listed in entry 3 was proved by crystallography. In the other diastereoisomer series, the relative stereochemistry is known from the delivery of the aryl substituent from the organocuprate reagent in the arylation of the 2-methoxycyclohexadienyliron starting material **7**. Thus the assignment of relative stereochemistry in all the

Table 4. Comparison of ^{1}H Chemical Shifts for 5-H in Epimeric 2-Methoxy-5-arylcyclohexadieneiron Complexes

entry	substituent	*exo* 5-H (ppm)	*endo* 5-H (ppm)
1	aldehyde		4.17 (**11**)
2	CH_2OMe		3.46 (**8**)
3	$CH_2OTBDPS$	2.69 (**18b**)	
4	CH_2OTIPS	2.82 (**18c**)	
5	CH_2OH	3.02 (**21**)	3.48 (**9**)

structures prepared in this study is certain. The novel reduction to give the 5-*endo* methoxy complexes forms the expected stereoisomer for a product of *exo* delivery of hydride from the borohydride reducing agent, but the regioisomer formed cannot be accounted for directly by acid catalyzed rearrangement of one of the other reduction products, since this process would deliver hydride on the *endo* face. Equilibration of *exo* and *endo* methoxy products would also be required and although *endo* delivery of methoxy groups is known[17] under thermodynamic control, *exo endo* mixtures would be expected. In none of the examples reported here were any traces of the 5-*exo* methoxy diastereoisomer identified, and the relative stereochemistry of **19b** is clear from the crystallographic results. Furthermore, a characteristic NOESY cross-peak between 3-H of the rearranged 2-aryldiene ligand and one of the hydrogens on the aromatic ring (see the Supporting Information) confirms the structure of all three products **19a−c**.

CONCLUSION

The oxidative cyclization of benzylic and phenolic OH groups in the 5-arylcyclohexadieneiron(0) series appears to require the *exo* relative stereochemistry between the arene and the tricarbonyliron groups, which is consistent with the possibility of an intramolecular nucleophilic addition to the iron-bound ligand. Reduction of 1-aryl-4-methoxycyclohexadienyliron(1+) complexes with sodium borohydride gives 5-*endo* products from hydride addition to the *exo* face, by the *ipso* (*i*) pathway relative to the arene, together with the 1,4-disubstituted product from ω addition, and a novel 2-aryl-5-*endo*-methoxy rearranged product. The hypervalent iodine oxidants PIFA and IBX are compatible with the presence of the tricarbonyliron complex, but show different chemoselectivities. IBX is selective for oxidation of the benzyl alcohol to the aldehyde and PIFA oxidizes the tricarbonyliron group to effect the oxidative cyclization. The $Fe(CO)_3$ group, however, can be retained in the product. Iron(III) chloride was also shown to cause oxidative cyclization in the 5-*exo*-aryl series, but is less effective than PIFA. 2,2,2-Trifluoroethanol is the solvent of choice for PIFA-promoted oxidative cyclizations of tricarbonyl(η^4-diene)-iron(0) complexes with pendant nucleophilic heteroatom side-chain groups.

EXPERIMENTAL SECTION

General Methods. *Features.* See the Supporting Information. HRMS measurements were performed on a high-resolution double-focusing (BE) mass spectrometer.

*(±)-Tricarbonyl[(1,2,3,4-η)-5α-(4′,5′-dimethoxy-2′-methoxymethylphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) (**8**).* 4,5-Dimethoxy-2-methoxymethylbromobenzene[18] (1.48 g, 5.69 mmol) was dissolved in dry THF (80 mL) at −78 °C. *n*-Butyllithium (2.3 M in hexanes; 2.47 mL, 5.69 mmol) was added. After 1 h at −78 °C, copper(I) iodide (541 mg, 2.84 mmol) was added. After 1.5 h at −78 °C, the reaction mixture turned black and cyclohexadienyliron salt **7**[11] (1.60 g, 4.06 mmol) was added, and after a further 1 h at −78 °C, the

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reaction mixture was allowed to warm to rt overnight. The solvent was removed under reduced pressure. Water (100 mL) was added, and the reaction mixture was extracted into Et_2O (1 × 100 mL, 3 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give the crude product (1.84 g) as an orange oil. The crude oil was purified by column chromatography over silica gel (eluting with a gradient of 2:1 to 1:1 hexanes − Et_2O) to give (±)-tricarbonyl[(1,2,3,4-η)-5α-(4′,5′-dimethoxy-2′-methoxymethylphenyl)-2-methoxy-1,3-cyclohexadiene]-iron(0) **8** as a brown oil (1.04 g, 56%): R_f = 0.22 (1:1 Et_2O − hexanes); IR ν_{max}/cm^{-1} ($CDCl_3$) 3008 (ArH), 2955 and 2936 (CH), 2044 and 1972 (C≡O), 1515 (C═C), 1106 (CO); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.75 (s, 1 H, 6′-H), 6.66 (s, 1 H, 3′-H), 5.19 (dd, J = 6.4, 2.2 Hz, 1 H, 3-H), 4.33 (s, 2H, methoxymethyl OCH_2), 3.87 (s, 3 H, 5′-OMe), 3.85 (s, 3 H, 4′-OMe), 3.70 (s, 3 H, 2-OMe), 3.50−3.42 (m, 2 H, 1-H and 5-H), 3.39 (s, 3 H, methoxymethyl OMe), 2.74 (dd, J = 6.4, 3.6 Hz, 1 H, 4-H), 2.37 (ddd, J = 14.9, 11.0, 3.6 Hz, 1 H, 6β-H), 1.66 (dd, J = 14.9, 2.5 Hz, 1 H, 6α-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 212.7 (Fe-CO), 148.7 (4′-C or 5′-C), 146.9 (4′-C or 5′-C), 140.2 (2-C), 137.7 (1′-C), 127.6 (2′-C), 112.5 (6′-C), 109.5 (3′-C), 72.6 (methoxymethyl OCH_2), 66.5 (3-C), 58.1 (methoxymethyl OMe), 56.0 (5′-OMe), 55.9 (4′-OMe), 55.8 (4-C), 54.4 (2-OMe), 53.4 (1-C), 38.5 (5-C), 34.3 (6-C); MS (EI) m/z 430 (2) $[M]^+$, 402 (99) $[M - CO]^+$, 374 (100) $[M - 2CO]^+$, 346 (58) $[M - 3CO]^+$, 223 (86); HRMS (EI) m/z calcd for $C_{20}H_{22}O_7{}^{56}Fe$ 430.0709, found 430.0707 $[M]^+$. A trace of methyl 3,4-dimethoxybenzyl ether derived from the excess nucleophile was visible in the NMR spectrum. The compound was used at this state of purity for the next step to form **9** because chromatographic purification was easier at that stage.

*(±)-Tricarbonyl[(1,2,3,4-η)-5α-(4′,5′-dimethoxy-2′-hydroxymethylphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) (**9**).* Compound **8** (60 mg, 131 μmol) was dissolved in THF (4 mL). Aqueous HCl (2 M, 4 mL) was added to the reaction mixture, which was then heated at reflux overnight. After cooling, water (5 mL) was added and the mixture was extracted into Et_2O (3 × 5 mL). The combined organics were washed with brine (5 mL), dried (K_2CO_3), filtered and evaporated under reduced pressure to give crude product (49 mg) as a yellow oil. The crude oil was purified by column chromatography over silica gel (eluting with a gradient from 2:1 to 1:1 hexanes−EtOAc) to give (±)-tricarbonyl[(1,2,3,4-η)-5α-(4′,5′-dimethoxy-2′-hydroxymethylphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) **9** as a brown oil (26 mg, 48%): R_f = 0.3 (1:1 hexanes−EtOAc); IR ν_{max}/cm^{-1} ($CDCl_3$) 3482 (OH), 3006 (ArH), 2955 and 2937 (CH), 2042 and 1964 (C≡O), 1516 (C═C), 1099 (CO); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (s, 1H, 6′-H), 6.68 (s, 1 H, 3′-H), 5.19 (dd, J = 6.2, 1.5 Hz, 1 H, 3-H), 4.63 (s, 2 H, hydroxymethyl OCH_2), 3.88 (s, 3 H, 5′-OMe), 3.85 (s, 3 H, 4′-OMe), 3.71 (s, 3 H, 2-OMe), 3.51−3.45 (m, 2 H, 1-H and 5-H), 2.73 (dd, J = 6.2, 3.2 Hz, 1 H, 4-H), 2.39 (ddd, J = 14.7, 11.0, 3.2 Hz, 1 H, 6β-H), 1.68 (d, J = 14.7 Hz, 1 H, 6α-H), 1.60 (br s, 1H, OH); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 211.2 (Fe-CO), 148.6 (4′-C or 5′-C), 147.0 (4′-C or 5′-C), 140.2 (2-C), 137.2 (1′-C), 130.1 (2′-C), 111.7 (6′-C), 109.6 (3′-C), 66.2 (3-C), 62.7 (hydroxymethyl OCH_2), 55.9 (5′-OMe), 55.8 (4′-OMe), 55.6 (4-C), 54.4 (2-OMe), 53.3 (1-C), 38.2 (5-C), 34.5 (6-C); MS (EI) m/z 416 (2) $[M]^+$, 388 (4) $[M - CO]^+$, 360 (60) $[M - 2CO]^+$, 332 (45) $[M - 3CO]^+$, 209 (100); HRMS (EI) m/z calcd for $C_{19}H_{20}O_7{}^{56}Fe$ 416.0553, found 416.0550 $[M]^+$.

*(±)-Tricarbonyl[(1,2,3,4-η)-(4a,10b-dihydro-3,8,9-trimethoxy-6H-dibenzo[b,d]pyran)]iron(0) (**10**).* Alcohol **9** (60 mg, 144 μmol) was dissolved in F_3CCH_2OH (2 mL) and cooled to −40 °C. Phenyliodine(III) bis(trifluoroacetate) (62 mg, 144 μmol) was added to the reaction mixture which turned brown. After 25 min of stirring at −40 °C, more phenyliodine(III) bis(trifluoroacetate) (62 mg, 144 μmol) was added. After 1 h, the solvent was removed under reduced pressure. The crude product was purified by column chromatography over silica gel (eluting with a gradient of 2:1 to 1:1 hexanes−Et_2O) to give (±)-tricarbonyl[(1,2,3,4-η)-(4a,10b-dihydro-3,8,9-trimethoxy-6*H*-dibenzo[*b*,*d*]pyran)]iron(0) **10** (25 mg, 42%), which was crystallized from Et_2O−hexanes as colorless needles (8 mg) for X-ray analysis: mp 142−144 °C; R_f = 0.46 (1:1 hexanes−EtOAc); IR ν_{max}/cm^{-1} ($CDCl_3$) 3010 (ArH), 2938 and 2839 (CH), 2050 and 1980 (C≡O), 1512 (C═C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.69 (s, 1 H, 10-H), 6.52 (s, 1 H, 7-H), 5.01 (dd, J = 6.3, 2.2 Hz, 1 H, 2-H), 4.56 (dd, J = 9.3, 3.7 Hz, 1 H, 4a-H), 4.47 (d, J = 14.0 Hz, 1 H, 6-H), 4.30 (d, J = 14.0 Hz, 1H, 6-H), 3.87 (s, 3H, 9-OMe), 3.84 (s, 3H, 8-OMe), 3.64 (s, 3H, 3-OMe), 3.33 (dd, J = 3.7, 2.2 Hz, 1H, 4-H), 3.12 (dd, J = 9.3, 3.9 Hz, 1 H, 10b-H), 2.88 (dd, J = 6.3, 3.9 Hz, 1 H, 1-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 210.7 (Fe-CO), 148.5 (8-C or 9-C), 147.1 (8-C or 9-C), 141.1 (3-C), 131.7 (10a-C), 126.8 (6a-C), 111.2 (10-C), 108.0 (7-C), 75.0 (2-C), 65.8 (4a-C), 62.7 (6-C), 56.0 (9-OMe), 55.9 (8-OMe), 54.7 (3-OMe), 52.0 (4-C), 51.7 (1-C), 35.4 (10b-C); MS (EI) m/z 414 (2) $[M]^+$, 386 (5) $[M - 2CO]^+$, 358 (18) $[M - 3CO]^+$, 300 (46), 42 (100); HRMS (EI) m/z calcd for $C_{19}H_{18}O_7{}^{56}Fe$ 414.0396, found 414.0397 $[M]^+$.

*(±)-Tricarbonyl[(1,2,3,4-η)-5α-(2′-formyl-4′,5′-dimethoxyphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) (**11**).* Alcohol **9** (12 mg, 28.8 μmol) was dissolved in DMSO (0.2 mL). 2-Iodoxybenzoic acid (16 mg, 57.1 μmol) dissolved in DMSO (0.4 mL) was added to the reaction mixture, which turned pink. After 2 h, 5% aqueous sodium bicarbonate (0.5 mL) was added to the reaction mixture, which was then extracted with Et_2O (3 × 1 mL). The combined organics were evaporated under reduced pressure to give crude product (13 mg) as a yellow oil. The crude product was purified by column chromatography over silica gel (eluting with 2:1 hexanes−EtOAc) to (±)-tricarbonyl-[(1,2,3,4-η)-5α-(2′-formyl-4′,5′-dimethoxyphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) **11** as a pale yellow oil (8 mg, 67%): R_f = 0.48 (1:1 hexanes−EtOAc); IR ν_{max}/cm^{-1} ($CDCl_3$) 3011 (ArH), 2964, 2936, and 2856 (CH), 2048 and 1977 (C≡O), 1673 (C═O), 1599 and 1510 (C═C), 1098 (CO); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1 H, formyl CH), 7.28 (s, 1 H, 3′-H), 6.76 (s, 1 H, 6′-H), 5.22 (dd, J = 6.4, 1.7 Hz, 1 H, 3-H), 4.17 (ddd, J = 11.0, 3.5, 3.0 Hz, 1 H, 5-H), 3.96 (s, 3 H, 5′-OMe), 3.90 (s, 3 H, 4′-OMe), 3.71 (s, 3 H, 2-OMe), 3.48 (dd, J = 3.7, 1.7 Hz, 1 H, 1-H), 2.72 (dd, J = 6.4, 3.5 Hz, 1 H, 4-H), 2.48 (ddd, J = 15.0, 11.0, 3.7 Hz, 1 H, 6β-H), 1.73 (dd, J = 15.0, 3.0 Hz, 1H, 6α-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.4 (formyl CH), 153.8 (5′-C), 147.5 (4′-C), 144.2 (1′-C), 140.3 (2-C), 126.4 (2′-C), 111.1 (3′-C), 108.7 (6′-C), 66.1 (3-C), 56.0 (4′-OMe and 5′-OMe), 54.5 (2-OMe), 54.4 (4-C), 53.0 (1-C), 36.7 (5-C), 34.6 (6-C); MS (CI) m/z 432 (18) $[M + NH_4]^+$, 415 (100) $[M + H]^+$, 275 (70) $[M - Fe(CO)_3]^+$, 259 (52); HRMS (CI) m/z calcd for $C_{19}H_{19}O_7{}^{56}Fe$ 415.0475, found 415.0480 $[M + H]^+$.

*(±)-Tricarbonyl[(1,2,3,4-η)-2-methoxy-5α-(3′-methoxy-2′-(2″-trimethylsilanylethoxymethoxy)phenyl)-1,3-cyclohexadiene]iron(0) (**13**).* 3-Methoxy-2-(2′-trimethylsilanylethoxymethoxy)bromobenzene[7] (888 mg, 2.67 mmol) was dissolved in dry THF (25 mL) at −78 °C. *n*-Butyllithium (1.89 M in hexanes; 1.41 mL, 2.67 mmol) was added. After 1 h at −78 °C, copper(I) iodide (254 mg, 1.33 mmol) was added. After 1 h at −78 °C, the reaction mixture had turned dark gray and cyclohexadienyliron salt **7**[11] (525 mg, 1.33 mmol) was added, and after a further 2 h at −78 °C, the reaction mixture was allowed to warm to rt overnight. Water (15 mL) was added, and the mixture was extracted into Et_2O (4 × 20 mL). The combined organics were washed with brine (20 mL), dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give the crude product (972 mg) as a brown oil. The crude oil was purified by column chromatography over silica gel twice (eluting in the first column with 8:1 hexanes−Et_2O, and the second with CH_2Cl_2) to give (±)-tricarbonyl[(1,2,3,4-η)-2-methoxy-5α-(3′-methoxy-2′-(2″-trimethylsilanylethoxymethoxy)phenyl)-1,3-cyclohexadiene]iron(0) **13** as a yellow oil (201 mg, 30%): R_f = 0.38 (4:1 hexanes−Et_2O); IR ν_{max}/cm^{-1} ($CDCl_3$) 3009 (ArH), 2957 and 2898 (CH), 2043 and 1972 (C≡O), 1583 (C═C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (t, J = 8.0 Hz, 1 H, 5′-H), 6.72 (d, J = 8.0 Hz, 2 H, 4′-H and d, J = 8.0 Hz, 6′-H), 5.16 (dd, J = 6.5, 2.3 Hz, 1 H, 3-H), 5.09 (s, 2 H, O−CH_2-O), 3.99−3.78 (m, 2 H, O−CH_2), 3.80 (s, 3 H, 3′-OMe), 3.83−3.74 (m, 1 H, 5-H), 3.70 (s, 3 H, 2-OMe), 3.48 (dt, J = 3.7, 2.3 Hz, 1 H, 1-H), 2.83 (1H, dd, J = 6.5, 3.5 Hz, 4-H), 2.39 (ddd, J = 14.9, 11.2, 3.7 Hz, 1 H, 6β-H), 1.68 (ddd, J = 14.9, 3.3, 2.3 Hz, 1 H, 6α-H), 1.03 (t, J = 8.5 Hz, 2 H, $SiCH_2$), 0.05 (s, 9 H, $SiMe_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.5 (Fe-CO), 152.0 (2′-C), 144.1 (3′-C), 140.8 (2-C or 1′-C), 140.3 (2-C or 1′-C), 124.2 (5′-C), 118.7

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(6′-C), 109.9 (4′-C), 97.4 (OCH_2O), 67.4 (OCH_2), 66.6 (3-C), 55.7 (4-C), 55.6 (3′-OMe), 54.3 (2-OMe), 53.7 (1-C), 35.7 (5-C), 34.0 (6-C), 18.1 ($SiCH_2$), −1.6 ($SiMe_3$); MS (CI) m/z 520 (1) $[M + NH_4]^+$, 445 (1), 249 (4), 118 (14), 90 (100); HRMS (CI) m/z calcd for $C_{23}H_{34}O_7N^{28}Si^{56}Fe$ 520.1448, found 520.1440 $[M + NH_4]^+$.

*(±)-Tricarbonyl[(1,2,3,4-η)-5α-(2′-hydroxy-3′-methoxyphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) (**14**). Method i.* Compound **13** (200 mg, 398 μmol) was dissolved in THF (10 mL) and CH_3OH (10 mL). Concentrated H_2SO_4 (0.3 mL) in CH_3OH (5 mL) was added to the reaction mixture. After 10 min, aqueous Na_2CO_3 (15 mL) was added. Solvent was evaporated from the reaction mixture under reduced pressure, and the residue was extracted into EtOAc (3 × 25 mL). The combined organics were washed with brine (20 mL), dried ($MgSO_4$), filtered and evaporated under reduced pressure to give crude product (157 mg) as a pale yellow oil. The crude oil was purified by column chromatography over silica gel (eluting with 4:1 hexanes/Et_2O) to give (±)-tricarbonyl[(1,2,3,4-η)-5α-(2′-hydroxy-3′-methoxyphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) **14** as a pale yellow oil (128 mg, 86%): R_f = 0.22 (4:1 hexanes−Et_2O); IR ν_{max}/cm^{-1} (film) 3530 (OH), 2932 and 2844 (CH), 2034, 1960, and 1939 (C≡O), 1614 and 1591 (C═C); ^1H NMR (400 MHz, $CDCl_3$) δ 6.82−6.68 (m, 3 H, 4′-H, 5′-H and 6′-H), 5.71 (s, 1 H, OH), 5.18 (dd, J = 6.5, 2.3 Hz, 1 H, 3-H), 3.87 (s, 3 H, 3′-OMe), 3.69 (s, 3 H, 2-OMe), 3.61 (dt, J = 11.1, 3.5 Hz, 1 H, 5-H), 3.46 (dt, J = 3.7, 2.3 Hz, 1 H, 1-H), 2.79 (dd, J = 6.5, 3.5 Hz, 1 H, 4-H), 2.40 (ddd, J = 14.9, 11.1, 3.7 Hz, 1 H, 6β-H), 1.76 (ddd, J = 14.9, 3.5, 2.3 Hz, 1 H, 6α-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.3 (Fe-CO), 146.1 (2′-C or 3′-C), 142.8 (2′-C or 3′-C), 140.1 (2-C), 132.1 (1′-C), 119.3 (5′-C or 6′-C), 119.1 (5′-C or 6′-C), 108.2 (4′-C), 66.6 (3-C), 56.0 (3′-OMe), 54.6 (4-C), 54.3 (2-OMe), 53.6 (1-C), 36.1 (5-C), 33.0 (6-C); MS (CI) m/z 373 (100) $[M + H]^+$, 305 (28), 235 (27), 233 (81); HRMS (CI) m/z calcd for $C_{17}H_{17}O_6{}^{56}Fe$ 373.0369, found 373.0373 $[M + H]^+$.

Method ii. 3-Methoxy-2-(2′-trimethylsilanylethoxymethoxy)-bromobenzene[7] (955 mg, 2.86 mmol) was dissolved in dry THF (20 mL) at −78 °C. *n*-Butyllithium (1.89 M in hexanes; 1.52 mL, 2.86 mmol) was added. After 1 h at −78 °C, copper(I) iodide (273 mg, 1.43 mmol) was added. After 1 h at −78 °C, the reaction mixture had turned black and cyclohexadienyliron salt **7**[11] (564 mg, 1.43 mmol) was added, and after a further 4 h at −78 °C, the reaction mixture was allowed to warm to rt. CH_3OH (15 mL) followed by concentrated H_2SO_4 (0.5 mL) was added, causing the mixture to change from black to green. After 10 min, concentrated sulfuric acid (0.5 mL) was added. After 10 min, the mixture was reduced in volume by evaporation under reduced pressure. Water (20 mL) was added, and the mixture was extracted into EtOAc (4 × 50 mL). The combined organics were washed with brine (25 mL), dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give crude product (869 mg) as a brown oil. The crude oil was purified by column chromatography over silica gel twice (eluting with 4:1 hexanes/Et_2O in the first column and 1:1 hexanes−CH_2Cl_2 in the second column) to give (±)-tricarbonyl-[(1,2,3,4-η)-5α-(2′-hydroxy-3′-methoxyphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) **14** (247 mg, 46%) as a pale yellow oil with identical spectral data to those produced using method *i*.

*(±)-Tricarbonyl[(1,2,3,4-η)-(3,6-dimethoxy-4a,9b-dihydrodibenzofuran)]iron(0) (**15**). Method i.* Iron(III) chloride on silica (10%, 3.08 g) was dried under pressure (0.03 mmHg) at 70 °C for 6 h and then added to the phenol **14** (140 mg, 376 μmol) in dry THF (2 mL) and evaporated under reduced pressure on a rotary evaporator for 1 h at 30 °C. The crude product was partially purified by column chromatography over basic alumina (eluting with Et_2O) to give a colorless solid (13 mg), which was crystallized from Et_2O/hexanes to give (±)-tricarbonyl[(1,2,3,4-η)-(3,6-dimethoxy-4a,9b-dihydrodibenzofuran)]iron(0) **15** as cream plates (5 mg, 4%): mp 206−208 °C (decomposes); R_f = 0.24 (1:1 CH_2Cl_2 − hexanes). IR ν_{max}/cm^{-1} ($CDCl_3$) 3064 and 3012 (ArH), 2929 and 2843 (CH), 2052 and 1965 (C≡O); ^1H NMR (400 MHz, $CDCl_3$) δ 6.77 (dd, J = 8.0, 7.3 Hz, 1 H, 8-H), 6.70 (dd, J = 8.0, $^3J_{7,9}$ 0.9 Hz, 1 H, 9-H), 6.66 (dd, J = 7.3, 0.9 Hz, 1 H, 7-H), 5.31 (dd, J = 10.4, 4.2 Hz, 1 H, 4a-H), 5.17 (dd, J = 6.5, 2.3 Hz, 1 H, 2-H), 3.83 (s, 3 H, 6-OMe), 3.80 (dd, J = 10.4, 4.3 Hz, 1 H, 9b-H), 3.61 (s, 3 H, 3-OMe), 3.60 (dd, J = 4.2, 2.3 Hz, 1 H, 4-H), 2.97 (dd, J = 6.5, 4.3 Hz, 1 H, 1-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.2 (5a-C or 6-C), 144.4 (5a-C or 6-C), 140.1 (3-C), 131.6 (9a-C), 120.8 (8-C), 115.7 (7-C), 111.0 (9-C), 86.9 (4a-C), 67.7 (2-C), 55.8 (6-OMe), 54.8 (3-OMe), 53.2 (4-C), 49.4 (1-C), 45.6 (9b-C); MS (EI) m/z 370 (8) $[M]^+$, 342 (30) $[M - CO]^+$, 286 (100) $[M - 3CO]^+$, 178 (32), 84 (46); HRMS (EI) m/z calcd for $C_{17}H_{15}O_6{}^{56}Fe$ 371.0213, found 371.0211 $[M + H]^+$.

Method ii. The phenol **14** (80 mg, 215 μmol) was dissolved and sonicated in F_3CCH_2OH (4 mL) and cooled to −40 °C. Phenyliodine(III) bis(trifluoroacetate) (111 mg, 258 μmol) in F_3CCH_2OH (3 mL) was added to the reaction mixture, and the mixture turned brown. After 20 min, the solvent was removed under reduced pressure. The crude product was partially purified by multiple column chromatography over silica gel (eluting the first column with a gradient of 1:1 to 3:1 CH_2Cl_2−hexanes and the second column with 4:1 hexanes−Et_2O) to give (±)-tricarbonyl[(1,2,3,4-η)-(3,6-dimethoxy-4a,9b-dihydrodibenzofuran)]iron(0) **15** (12 mg, 15%), data for which matched the spectral data from method *i* except for some inseparable impurities.

*(±)-Tricarbonyl[(1,2,3,4-η)-2-(4′,5′-dimethoxy-2′-methoxymethylphenyl)-5β-methoxy-1,3-cyclohexadiene]iron(0) (**19a**).* (±)-Tricarbonyl-[(1,2,3,4,5-η)-1-(4′,5′-dimethoxy-2′-methoxymethylphenyl)-4-methyoxycyclohexadienyl]iron(1+) tetrafluoroborate(1−) **16a**[1b] (700 mg, 1.36 mmol) was dissolved in dry CH_3CN (10 mL) at 0 °C. Sodium borohydride (2.0 equiv, 103 mg, 2.71 mmol) was added. After 3 h at 0 °C, more sodium borohydride (1.2 equiv, 61 mg, 1.61 mmol) was added, and after 10 min, the solvent was removed under reduced pressure. Water (20 mL) was added, and the reaction mixture was extracted with Et_2O (4 × 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give the crude product (663 mg) as a yellow oil. Column chromatography (silica gel eluted with 3:2 hexanes−CH_2Cl_2) affordedan inseparable mixture of dienes **17a** and **18a** in a ratio of 1.3:1 and a combined yield of 47%. The ^1H NMR spectrum of this mixture confirmed their presence with a doublet of doublets at 5.26 ppm for diene **18a** and two doublets at 5.51 and 5.33 ppm for diene **17a**. An additional product from the first chromatographic separation was further purified by column chromatography over silica gel (eluting with a gradient of 4:1 hexanes−EtOAc to EtOAc) and then was crystallized from Et_2O−hexanes to give (±)-tricarbonyl[(1,2,3,4-η)-2-(4′,5′-dimethoxy-2′-methoxymethylphenyl)-5β-methoxy-1,3-cyclohexadiene]iron(0) **19a** as yellow plates for X-ray analysis (77 mg, 13%): mp 117−119 °C; R_f = 0.25 (2:1 hexanes/EtOAc). IR ν_{max}/cm^{-1} (film) 2936 and 2827 (C−H), 2037 and 1966 (C≡O), 1603 and 1518 (C═C); ^1H NMR (300 MHz, $CDCl_3$) δ 6.95 (s, 1 H, 6′-H), 6.90 (s, 1 H, 3′-H), 5.41 (d, J = 6.8 Hz, 1 H, 3-H), 4.48 (s, 2 H, methoxymethyl OCH_2), 3.91 (s, 3 H, 4′-OMe), 3.87 (s, 3 H, 5′-OMe), 3.45−3.38 (m, 2 H, 1-H, 5-H), 3.41 (s, 3 H, methoxymethyl OMe), 3.31 (s, 3 H, 5β-OMe), 3.26 (dd, J = 6.8, 2.3 Hz, 1 H, 4-H), 2.16 (ddd, J = 15.0, 6.7, 2.1 Hz, 1 H, 6β-H), 1.76 (ddd, J = 15.0, 3.3, 2.4 Hz, 1 H, 6α-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.0 (Fe-CO), 149.1 (4′-C or 5′-C), 148.3 (4′-C or 5′-C), 130.0 (1′-C or 2′-C), 129.2 (1′-C or 2′-C), 114.0 (6′-C), 112.3 (3′-C), 106.5 (2-C), 86.3 (3-C), 75.4 (1-C), 72.4 (methoxymethyl OCH_2), 62.1 (5-C), 61.2 (4-C), 58.2 (5β-OMe), 55.9 (4′-OMe and 5′-OMe), 55.2 (methoxymethyl OMe), 34.6 (6-C); MS (CI) m/z 448 (1) $[M^+ + NH_4]^+$, 399 (22), 246 (34), 227 (100); HRMS (CI) m/z calcd for $C_{20}H_{26}O_7N^{54}Fe$ 446.1100, found 446.1096 $[M + NH_4]^+$.

*(4,5-Dimethoxybiphenyl-2-yl)methanol (**20**).* Compound **19a** (39 mg, 90.7 μmol) was dissolved in THF (2 mL). Aqueous HCl (2 M, 2 mL) was added, and the reaction mixture was heated at reflux for 5 h. After cooling, water (2 mL) was added and the mixture was extracted into Et_2O (4 × 2 mL). The combined organics were dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give crude product (30 mg) as a yellow oil. The crude oil was purified by column chromatography over silica gel (eluting with a gradient from 2:1 to 1:1 hexanes−EtOAc) to give (4,5-dimethoxybiphenyl-2-yl)methanol **20** as a yellow oil (8 mg, 36%): R_f 0.26 (1:1 hexanes/EtOAc); IR ν_{max}/cm^{-1} ($CDCl_3$) 3484 (OH), 3058 and 3003 (ArH), 2960, 2937, and 2848 (CH), 1608 and 1517 (C═C); ^1H NMR (300 MHz, $CDCl_3$) δ 7.46−

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7.32 (m, 5 H, 8-H, 9-H, 10-H, 11-H and 12-H), 7.08 (s, 1 H, 3-H), 6.80 (s, 1 H, 6-H), 4.56 (s, 2 H, hydroxymethyl OCH_2), 3.95 (s, 3 H, 4-OMe), 3.89 (s, 3 H, 5-OMe), 1.58 (s, 1 H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.6 (4-C or 5-C), 148.3 (4-C or 5-C), 140.7 (1′-C), 134.1 (1-C), 130.5 (2-C), 129.4 (3′-C and 5′-C), 128.3 (2′-C and 6′-C), 127.2 (4′-C), 113.3 (3-C), 111.8 (6-C), 62.9 (hydroxymethyl OCH_2), 56.0 (4-OMe and 5-OMe); MS (EI) m/z 244 (100) $[M]^+$, 226 (10) $[M - H_2O]^+$, 215 (17), 141 (20), 115 (16), 77 (12) $[C_6H_5]^+$; HRMS (EI) m/z calcd for $C_{15}H_{16}O_3$ 244.1094, found 244.1092 $[M]^+$.

*(±)-Tricarbonyl[(1,2,3,4-η)-5β-(2′-(tert-butyldiphenylsilanyloxymethyl)-4′,5′-dimethoxyphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) (**18b**) and (±)-Tricarbonyl[(1,2,3,4-η)-2-(2′-(tert-butyldiphenylsilanyloxymethyl)-4′,5′-dimethoxyphenyl)-5β-methoxy-1,3-cyclohexadiene]iron(0) (**19b**).* (±)-Tricarbonyl[(1,2,3,4,5-η)-1-(4′,5′-dimethoxy-2′-(*tert*-butyl-diphenylsilanyloxymethylphenyl)-4-methyoxycyclohexadienyl]iron(1+) tetrafluoroborate(1−) **16b**[1b] (1200 mg, 270 μmol) was dissolved in dry CH_3CN (9 mL) at 0 °C. Sodium borohydride (41 mg, 1.08 mmol) was added. After 2 h at 0 °C, the solvent was removed under reduced pressure. Water (10 mL) was added, and the reaction mixture was extracted with Et_2O (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give the crude product (149 mg) as a pale yellow oil. Column chromatography (silica gel eluted with 3:2 hexanes−CH_2Cl_2) afforded inseparable dienes **17b** and **18b** in a ratio of 1:2.8. The ^1H NMR spectrum of the mixture of **17b** and **18b** confirmed their presence with a doublet of doublets at 5.13 ppm for diene **18b** and two doublets at 5.31 and 5.18 ppm for diene **17b**. The crude product was further purified by column chromatography over silica gel (eluting with a gradient of 3:2 hexanes−CH_2Cl_2 to CH_2Cl_2) and then was crystallized from Et_2O−hexanes to give (±)-tricarbonyl[(1,2,3,4-η)-5β-(2′-(*tert*-butyldiphenylsilanyloxymethyl)-4′,5′-dimethoxyphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) **18b** as a yellow needles for X-ray analysis (35 mg, 20%): mp 97−99 °C; R_f = 0.24 (1:1 hexanes−CH_2Cl_2); IR ν_{max}/cm^{-1} ($CDCl_3$) 3002 (Ar−H), 2934 and 2857 (C−H), 2043 and 1967 (C≡O), 1609, 1589, and 1513 (C═C), 1111 (C−O); ^1H NMR (300 MHz, $CDCl_3$) δ 7.67 (dt, J = 8.0, 8 Hz, 4 H, 2Ph *o*-Hs), 7.48−7.34 (m, 6 H, 3Ph *m*-Hs, *p*-Hs), 7.07 (s, 1 H, 6′-H), 7.04 (s, 1 H, 3′-H), 5.13 (dd, J = 6.7, 1.8 Hz, 1 H, 3-H), 4.67 (d, J = 12.9 Hz, 1 H, silyloxymethyl OCH), 4.57 (d, J = 12.9 Hz, 1 H, silyloxymethyl OCH), 3.95 (s, 3 H, 5′-OMe), 3.83 (s, 3 H, 4′-OMe), 3.63 (s, 3 H, 2-OMe), 3.47 (m, 1 H, 1-H), 2.69 (dd, J = 7.7, 6.4 Hz, 1 H, 5-H), 2.61 (d, J = 6.7 Hz, 1 H, 4-H), 2.11 (ddd, J = 14.8, 7.7, 3.0 Hz, 1 H, 6β-H), 1.50 (ddd, J = 14.8, 6.4, 2.6 Hz, 1 H, 6α-H), 1.07 (s, 9 H, *tert*-butyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.5 (Fe-CO), 147.8 (4′-C or 5′-C), 146.9 (4′-C or 5′-C), 140.4 (2-C), 135.7 (2Ph *o*-Cs), 134.3 (1′-C8-C or 2′-C), 133.6 (2Phs C-Si), 130.5 (1′-C or 2′-C), 129.8 (2Phs *p*-Cs), 127.8 (2 Phs *m*-Cs), 111.0 (3′-C), 109.8 (6′-C), 65.5 (3-C), 63.0 (silyloxymethyl OCH), 55.7 (1-C, 4-C, 4′-OMe and 5′-OMe), 54.3 (2-OMe), 37.1 (6-C), 32.8 (5-C), 26.7 (*t*-Bu Mes), 19.2 (*t*-Bu C); MS (ES) m/z 672 (2) $[M + NH_4]^+$, 591 (2), 315 (65), 64 (100); HRMS (ES) m/z calcd for $C_{35}H_{42}O_7SiNFe$ 672.2074, found 672.2067 $[M + NH_4]^+$. The column chromatography also yielded (±)-tricarbonyl[(1,2,3,4-η)-2-(2′-(*tert*-butyldiphenylsilanyloxymethyl)-4′,5′-dimethoxyphenyl)-5β-methoxy-1,3-cyclohexadiene]iron(0) **19b** as a yellow oil (23 mg, 13%): R_f = 0.2 (1:1 hexanes/CH_2Cl_2); IR ν_{max}/cm^{-1} ($CDCl_3$) 3072 (Ar−H), 2960, 2933, and 2857 (C−H), 2050, 1987, and 1968 (C≡O), 1608 and 1515 (C═C), 1100 (C−O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, J = 8.0, 1.4 Hz, 2H, 2Phs o-Cs), 7.63 (dd, J = 8.0, 1.4 Hz, 2Phs o-Cs), 7.48−7.33 (m, 6H, 2Phs m-Cs and p-Cs), 7.01 (s, 1 H, 3′-H), 6.88 (s, 1 H, 6′-H), 5.27 (dd, J = 6.7, 1.8 Hz, 1 H, 3-H), 4.81 (d, J = 12.8 Hz, 1 H, silyloxymethyl OCH), 4.71 (d, J = 12.8 Hz, 1 H, silyloxymethyl OCH), 3.88 (s, 3 H, 5′-OMe), 3.85 (s, 3 H, 4′-OMe), 3.23 (s, 3 H, 5β-OMe), 3.17−3.10 (m, 3 H, 1-H, 4-H and 5-H), 1.61 (dd, J = 15.1, 6.4 Hz, 1 H, 6β-H), 1.47 (d, J = 15.1 Hz, 1 H, 6α-H), 1.08 (s, 9 H, tert-Bu); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 210.7 (Fe-CO), 148.9 (4′-C or 5′-C), 147.5 (4′-C or 5′-C), 135.6 (2Ph o-Cs), 133.3 (1′-C or 2′-C), 133.0 (1′-C or 2′-C), 129.9 (2Ph p-Cs), 129.8 (2Ph p-Cs), 127.8 (2Ph m-Cs), 127.7 (2Ph m-Cs), 127.3 (2 Ph C−Si), 113.5 (6′-C), 110.4 (3′-C), 106.2 (2-C), 86.2 (3-C), 75.4 (1-C), 63.7 (silyloxymethyl OCH), 62.2 (5-C), 61.0 (4-C), 56.0 (5′-OMe), 55.8 (4′-OMe), 55.1 (5β-OMe), 34.2 (6-C), 26.8 (tert-Bu Mes), 19.3 (tert-Bu C); MS (CI) m/z 672 (1) $[M + NH_4]^+$, 623 (4), 227 (100); HRMS (CI) m/z calcd for $C_{35}H_{42}O_7{}^{28}SiN^{56}Fe$ 672.2074, found 672.2082 $[M + NH_4]^+$.

*(±)-Tricarbonyl[(1,2,3,4-η)-5β-(4′,5′-dimethoxy-2′-triisopropylsilanyloxymethylphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) (**18c**) and (±)-Tricarbonyl[(1,2,3,4-η)-2-(4′,5′-dimethoxy-2′-triisopropylsilanyloxymethylphenyl)-5β-methoxy-1,3-cyclohexadiene]iron(0) (**19c**).* (±)-Tricarbonyl[(1,2,3,4,5-η)-1-(4′,5′-dimethoxy-2′-triisopropylsilanyloxymethylphenyl)-4-methyoxycyclohexadienyl]iron(1+) tetrafluoroborate(1−) **16c**[1b] (150 mg, 228 μmol) was dissolved in dry CH_3CN (5 mL) at 0 °C. Sodium borohydride (17 mg, 456 μmol) was added. After 2 h at 0 °C, the solvent was removed under reduced pressure. Water (10 mL) was added, and the reaction mixture was extracted with Et_2O (4 × 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give the crude product (142 mg) as a pale yellow solid. Column chromatography (silica gel eluted with 3:2 hexanes − CH_2Cl_2) afforded inseparable mixture of dienes **17c** and **18c** in a ratio of 1:2.7. The ^1H NMR spectrum of the mixture of **17c** and **18c** confirmed their presence with a doublet of doublets at 5.25 ppm for diene **18c** and two doublets at 5.47 and 5.32 ppm for diene **17c**. The crude product was further purified by column chromatography over silica gel (eluting with a gradient of 3:2 hexanes−CH_2Cl_2 to 1:4 hexanes−CH_2Cl_2) and then was crystallized from Et_2O − hexanes to give (±)-tricarbonyl-[(1,2,3,4-η)-5β-(4′,5′-dimethoxy-2′-triisopropylsilanyloxymethyl-phenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) **18c** as pale cream flakes-(10 mg, 8%): mp 132−134 °C dec; R_f = 0.21 (1:1 hexanes/CH_2Cl_2). IR ν_{max}/cm^{-1} ($CDCl_3$) 2943 and 2867 (CH), 2045 and 1970 (C≡O), 1510 (C═C), 1116 (CO); ^1H NMR (400 MHz, $CDCl_3$) δ 7.13 (s, 1 H, 3′-H), 7.09 (s, 1 H, 6′-H), 5.25 (d, J = 6.3 Hz, 1 H, 3-H), 4.74 (d, J = 13.0 Hz, 1 H, silyloxymethyl OCH), 4.62 (d, J = 13.0 Hz, 1 H, silyloxymethyl OCH), 3.94 (s, 3 H, 5′-OMe), 3.86 (s, 3 H, 4′-OMe), 3.68 (s, 3 H, 2-OMe), 3.55 (m, 1 H, 1-H), 2.82 (dd, J = 7.6, 5.7 Hz, 1 H, 5-H), 2.72 (d, J = 6.3 Hz, 1 H, 4-H), 2.35 (ddd, J = 14.4, 7.6, 2.0 Hz, 1 H, 6β-H), 1.60 (dd, J = 14.4, 5.7 Hz, 1 H, 6α-H), 1.21−1.05 (m, 3 H, CH-Si), 1.08 (d, J = 6.6 Hz, 18 H, *i*-Pr Me groups); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.2 (4′-C or 5′-C), 146.8 (4′-C or 5′-C), 140.4 (2-C), 133.4 (1′-C or 2′-C), 131.0 (1′-C or 2′-C), 109.9 (3′-C), 109.6 (6′-C), 65.6 (3-C), 62.2 (silyloxymethyl OCH_2C), 55.8 (5′-OMe), 55.7 (4′-OMe and 1-C), 55.5 (4-C), 54.5 (2-OMe), 37.1 (6-C), 32.9 (5-C), 18.1 (*i*-Pr Me groups), 12.0 (CH-Si); MS (FAB) m/z 572 (1) $[M]^+$, 544 (2) $[M - CO]^+$, 516 (16) $[M - 2CO]^+$, 488 (100) $[M - 3CO]^+$, 343 (17), 315 (18), 259 (18), 226 (16), 173 (13); HRMS (FAB) m/z calcd for $C_{26}H_{40}O_5{}^{28}Si^{56}Fe$ 516.1989, found 516.1987 M − 2CO]$^+$.

The column chromatography also yielded (±)-tricarbonyl[(1,2,3,4-η)-2-(4′,5′-dimethoxy-2′-triisopropylsilanyloxymethylphenyl)-5β-methoxy-1,3-cyclohexadiene]iron(0) (**19c**) as a pale yellow oil (27 mg, 21%): R_f = 0.16 (1:1 hexanes−CH_2Cl_2); IR ν_{max}/cm^{-1} ($CDCl_3$) 2944 and 2867 (CH), 2051 and 1988 (C≡O), 1608 and 1514 (C═C), 1100 (CO); ^1H NMR (400 MHz, $CDCl_3$) δ 7.17 (s, 1 H, 3′-H), 6.90 (s, 1 H, 6′-H), 5.36 (d, J = 6.6 Hz, 1 H, 3-H), 4.97 (d, J = 13.0 Hz, 1 H, silyloxymethyl OCH), 4.81 (d, J = 13.0 Hz, 1 H, silyloxymethyl OCH), 3.90 (s, 3 H, 4′-OMe), 3.87 (s, 3 H, 5′-OMe), 3.40 (d, J = 6.1 Hz, 1 H, 1-H), 3.30 (m, 1 H, 5-H), 3.26 (d, J = 6.6 Hz, 1 H, 4-H), 3.22 (s, 3 H, 5β-OMe), 2.12 (dd, J = 14.9, 6.1 Hz, 1 H, 6β-H), 1.74 (d, J = 14.9 Hz, 1 H, 6α-H), 1.21−1.08 (m, 3H, 15-H, 18-H, 21-H), 1.09 (d, ^3J 6.4 Hz, 18H, 16-H_3, 17-H_3, 19-H_3, 20-H_3, 22-H_3, 23-H_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.7 (Fe-CO), 149.0 (4′-C or 5′-C), 147.2 (4′-C or 5′-C), 133.7 (1′-C or 2′-C), 126.6 (1′-C or 2′-C), 113.5 (6′-C), 109.6 (3′-C), 106.5 (2-C), 82.3 (3-C), 75.4 (1-C), 62.9 (silyloxymethyl OCH), 62.1 (5-C), 60.9 (4-C), 56.0 (5′-OMe), 55.8 (4′-OMe), 55.3 (5β-OMe), 34.5 (6-C), 18.0 (iso-Pr Mes), 12.0 (CH-Si); MS (CI) 590 (99) $[M + NH_4]^+$, 573 (100) $[M + H]^+$, 544 (93); HRMS (CI) m/z calcd for $C_{28}H_{40}O_7{}^{28}Si^{54}Fe$ 570.1934, found 570.1936 $[M]^+$.

*(±)-Tricarbonyl[(1,2,3,4-η)-5β-(4′,5′-dimethoxy-2′-hydroxymethylphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) (**21**).* TBAF (1 M

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in THF) (0.02 mL, 18.9 μmol) was added to compound **18c** (9 mg, 15.7 μmol) dissolved in THF (0.5 mL), and the mixture was stirred at rt for 20 min. Water (0.5 mL) was added to the reaction mixture, and it was extracted with Et_2O (3 × 0.5 mL). The combined organic layers were evaporated under reduced pressure to give the crude product (5.2 mg). The crude oil was purified by column chromatography over silica gel (eluting with a gradient from 2:1 to 1:3 hexanes/EtOAc) to give (±)-tricarbonyl[(1,2,3,4-η)-5β-(4′,5′-dimethoxy-2′-hydroxymethylphenyl)-2-methoxy-1,3-cyclohexadiene]iron(0) **21** as a pale yellow oil (5.0 mg, 75%): R_f = 0.13 (1:1 hexanes−EtOAc); ^{1}H IR ν_{max}/cm^{-1} ($CDCl_3$) 3439 (OH), 3008 (ArH), 2963, 2937, and 2854 (CH), 2044 and 1966 (C≡O), 1609 and 1516 (C═C), 1103 (CO); NMR (400 MHz, $CDCl_3$) δ 7.14 (s, 1 H, 6′-H), 6.87 (s, 1 H, 3′-H), 5.27 (dd, *J* = 6.7, 2.0 Hz, 1 H, 3-H), 4.61 (d, *J* = 12.2 Hz, 1 H, hydroxymethyl OCH), 4.52 (d, *J* = 12.2 Hz, 1 H, hydroxymethyl OCH), 3.95 (s, 3 H, 5′-OMe), 3.87 (s, 3 H, 4′-OMe), 3.67 (s, 3 H, 2-OMe), 3.57 (ddd, *J* = 3.1, 2.7, 2.0 Hz, 1 H, 1-H), 3.02 (dd, *J* = 7.9, 6.6 Hz, 1 H, 5-H), 2.70 (d, *J* = 6.7 Hz, 1 H, 4-H), 2.42 (ddd, *J* = 14.8, 7.9, 3.1 Hz, 1 H, 6β-H), 1.66 (ddd, *J* = 14.8, 6.6, 2.7 Hz, 1 H, 6α-H), 1.58 (s, 1H, OH); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.5 (Fe-CO), 148.3 (4′-C or 5′-C), 146.8 (4′-C or 5′-C), 140.5 (2-C), 135.7 (1′-C or 2′-C), 130.1 (1′-C or 2′-C), 111.9 (3′-C), 110.0 (6′-C), 65.5 (3-C), 62.8 (hydroxymethyl OCH), 55.9 (4′-OMe), 55.8 (5′-OMe), 55.7 (1-C), 55.7 (4-C), 54.5 (2-OMe), 38.2 (6-C), 33.1 (5-C); MS (CI) *m*/*z* 417 (15) $[M + H]^+$, 399 (7) $[M - OH]^+$, 371 (18) $[M - OH - CO]^+$, 343 (17) $[M^+ - OH - 2CO]$, 280 (100), 261 (88); HRMS (CI) *m*/*z* calcd for $C_{19}H_{21}O_7{}^{56}Fe$ 417.0631, found 417.0633 $[M + H]^+$.

■ ASSOCIATED CONTENT

Supporting Information

Spectroscopic data for all new compounds and X-ray data for compounds **10**, **18b**, and **19a** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

This paper is dedicated to Professor Philip J. Parsons, Chemistry Department, Imperial College London, to mark his 60th birthday.

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(14) Crystallographic details. **10**: $C_{19}H_{18}FeO_7$, 414.18 g mol^{-1}, monoclinic, $P2_1/c$, a = 7.2560(6) Å, b = 19.1627(17) Å, c = 12.7919(11) Å, β = 96.110(2)°, V = 1768.5(3) Å^3, Z = 4, T = 100 K, ρ_{calc} = 1.556 g cm^{-3}, $F(000)$ = 856, μ(Mo Kα) = 0.893 mm^{-1}; 12262 data, 4034 unique (R_{int} = 0.0287), 316 parameters, final wR_2 = 0.0848, S = 1.033 (all data), R_1 (3498 data with $I > 2\sigma(I)$) = 0.0335. **18b**: $C_{36.5}H_{41.5}FeO_7Si$, 676.14 g mol^{-1}, triclinic, *P-1*, a = 12.145(3) Å, b = 16.906(4) Å, c = 18.104(4) Å, α = 68.923(4)°, β = 84.618(4)°, γ = 78.411(4)°, V = 3396.9(12) Å^3, Z = 4, T = 100 K, ρ_{calc} = 1.322 g cm^{-3}, $F(000)$ = 1426, μ(Mo Kα) = 0.527 mm^{-1}; 18747 data, 12286 unique (R_{int} = 0.0323), 838 parameters, final wR_2 = 0.1568, S = 1.016 (all data), R_1 (9176 data with $I > 2\sigma(I)$) = 0.0601. **19a**: $C_{20}H_{22}FeO_7$, 430.23 g mol^{-1}, monoclinic, $P2_1/c$, a = 21.2199(13) Å, b = 10.4053(7) Å, c = 18.6446(12) Å, β = 108.283(1)°, V = 3908.9(4) Å^3, Z = 8, T = 100 K, ρ_{calc} = 1.462 g cm^{-3}, $F(000)$ = 1792, μ(Mo Kα) = 0.811 mm^{-1}; 25378 data, 8751 unique (R_{int} = 0.0347), 677 parameters, final wR_2 = 0.0937, S = 1.031 (all data), R_1 (6898 data with $I > 2\sigma(I)$) = 0.0372. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 753051−753053. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK: http://www.ccdc.cam.ac.uk/cgi-bin/catreq.cgi, e-mail: data_request@ccdc.cam.ac.uk, or fax: +44 1223 336033.

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