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ORGANOIRON COMPLEXES IN ORGANIC SYNTHESIS

XXXII * SYNTHESIS OF STERICALLY CROWDED SPIROCYCLIC COMPOUNDS USING ORGANOIRON CHEMISTRY: AN APPROACH TO ACORANE AND CEDROL SYNTHESIS

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Summary

Studies on the synthesis and reactivity toward carbon nucleophiles of tricarbonyl(1–5-η-4-isopropoxy-1-isopropylcyclohexa-2,4-dienylium)iron hexafluorophosphate are reported. The preparations of tricarbonyl(3-(1–5-η-4-methoxycyclohexa-2,4-dienylium)butyl malononitrile)iron hexafluorophosphate and tricarbonyl-[methyl-3-(1–5-η-4-methoxycyclohex-2,4-dienylium)butyl cyanoacetate]iron hexafluorophosphate, starting from *p*-methoxyacetophenone are described. Treatment of both these complexes with mild bases results in clean spirocyclization and the products are readily demetallated to give spiro[4.5]decane derivatives which are potential precursors for a variety of acorane or cedrol derivatives. The spirocyclization is illustrative of the power of organoiron intermediates for producing sterically crowded spirocenters.

The presence of spirocenters in a wide range of natural products as diverse as histrionicotoxin (**1**), a unique toxic alkaloid isolated from the skins of the Colombian frog, Dendrobates histrionicus [2], aphidicolin (**2**) a tetracyclic diterpene showing strong in vitro activity against Herpes simplex type 1 virus [3], as well as the more familiar examples of acorenone (**3**) and cedrol (**4**) has led to a considerable amount of effort directed at their construction [4]. The problem is particularly vexing when the spirocenter is flanked by a number of substituents, as in **2**, and current methodology is somewhat limited in this respect. We have been developing methods for the general construction of spirocenters based on the chemistry of cyclohexadienyliumiron complexes of general structure **5**, which show a pronounced tend-

* For part XXXI see ref. 1.

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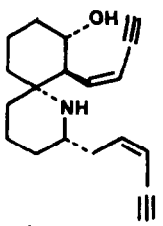

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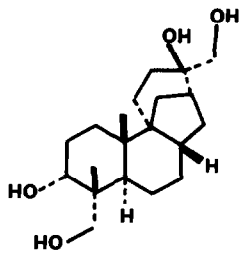

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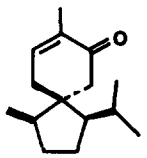

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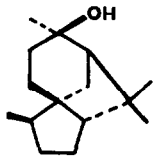

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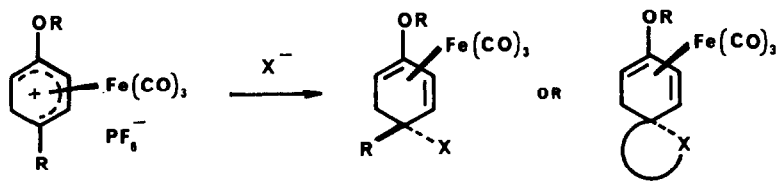
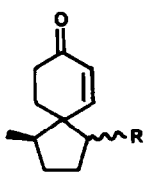
ency to undergo nucleophile addition at the substituted (C(1)) terminus [5], as well as the intramolecular addition of nucleophile already present in the C(1) substituent (R in structure **5**) [6]. The latter annulation is of particular interest when steric crowding is present around the desired dienylium reaction terminus.



5 Intermolecular Intramolecular



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(a) R = β-iso-C_3H_7

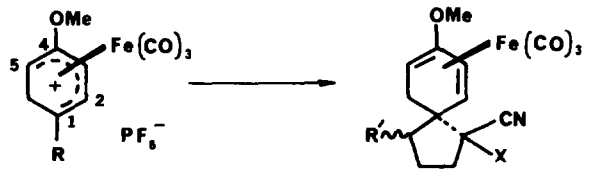
(b) R = α-CO_2Me

In this paper we describe results of our study into the efficacy of this approach when branching of the C(1) substituent is present α to the dienyl moiety. In particular, the chemistry described was initially developed within a potential approach to the synthesis of (±)-acorenone or (±)-cedrol and for this purpose our

target became the enone intermediate **6(a)**, used in the Oppolzer synthesis of acorenone [4], or the intermediate **6(b)** used by Corey in the synthesis of cedrol derivatives [4].

Results and discussion

At the outset, we considered two possible strategies for an approach to enone (**6**) based on organoiron chemistry. The first would use an addition of nucleophile to a complex **7a**, followed by cyclisation to give **8a** or **8b** which we have previously demonstrated for the conversion of **7b** to **8c** [6b], while the second would use a



7 8

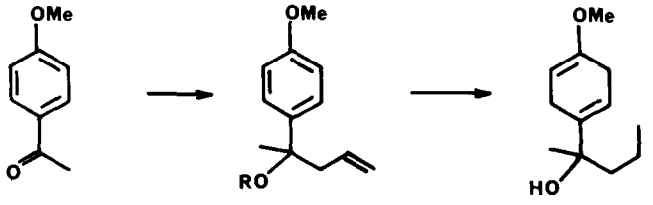
(a) R = $CHMeCH_2CH_2OTs$ (a) R′ = Me, X = CN
(b) R = $CH_2CH_2CH_2OTs$ (b) R′ = Me, X = CO_2Me
(c) R = i-Pr, (4-OPr^i) (c) R′ = H, X = CN or CO_2Me

base-induced cyclisation of a dienylium complex of type **21a** or **21b** to give **8a** or **8b**, also previously shown by us to be successful in the absence of steric congestion at the dienylium terminus [6]. Since the intermolecular nucleophile addition appeared to have less chance of success, we decided to examine a readily accessible model compound **7c** before embarking on a protracted synthesis of **7a**. Accordingly, **7c** was prepared in high yield by the following sequence of reactions.

Conversion of *p*-isopropylphenol to its isopropyl ether (**9**) (NaOEt, i-PrBr, EtOH, reflux), followed by Birch reduction afforded the 1,4-diene **10**, which was treated with a catalytic amount of *p*-toluenesulfonic acid at ca. 80°C to give an 8/1 mixture of conjugated diene **11** and unconjugated diene **10**, in 60% overall yield. Treatment of this mixture with pentacarbonyliron in hot di-n-butyl ether furnished the diene complex **12** (93% yield), which underwent regiospecific hydride abstraction (Ph_3CPF_6, CH_2Cl_2, reflux) to give the desired cyclohexadienylium complex **7c** in 56% overall yield from the aromatic isopropyl ether (Scheme 1).

We have previously shown that regioselectivity problems during the addition of nucleophiles to complexes of general structure, (**5**, R′ = Me) are nicely overcome using (a) an isopropoxy substituent at C(4) (R′ = i-Pr), and (b) the potassium enolates of dicarbonyl compounds such as malonic ester as nucleophile. In the present case, however, the C(1) terminus is sterically encumbered to such an extent that reaction of **7c** with $KCH(CO_2Me)_2$ or $NaCH(CN)_2$ gave exclusively the C(5) addition products **13a** (60%) or **13b** (61%), respectively. Thus, branching of the C(1) side chain α to the dienyl system completely blocks nucleophile attack at C(1). Whilst this result was disappointing for our present purpose, it may be of future interest, since there are now well-established methods [8] for conversion of complexes **13** to cyclohexenones of type **14**, which are not easily prepared by standard techniques. This was not pursued further.

Clearly, our attempts to construct crowded spirocenters would have to make use of an intramolecular nucleophile addition. The desired complexes were prepared as follows. Treatment of *p*-methoxyacetophenone with allylmagnesium chloride in tetrahydrofuran afforded the tertiary alcohol **15a** in 89% yield. Based on the assumption that hydrogenolysis of the benzylic alcohol [9] would occur during Birch reduction of **15a**, we subjected a sample of this material to the usual reaction conditions, and we were surprised to isolate the product 16, arising from reduction of both the aromatic ring and the terminal double bond without loss of the hydroxy group. Consequently, **15a** was converted to the methyl ether **15b**, which was subjected to careful ozonolysis, with reductive work-up to give **17**. Birch reduction of **17** proceeded with concomitant hydrogenolysis of the benzyl ether moiety to afford the diene **18a**, which was immediately acetylated to give **18b** in 52% overall yield from *p*-methoxy acetophenone. Conjugation of the 1,4-diene was accomplished as

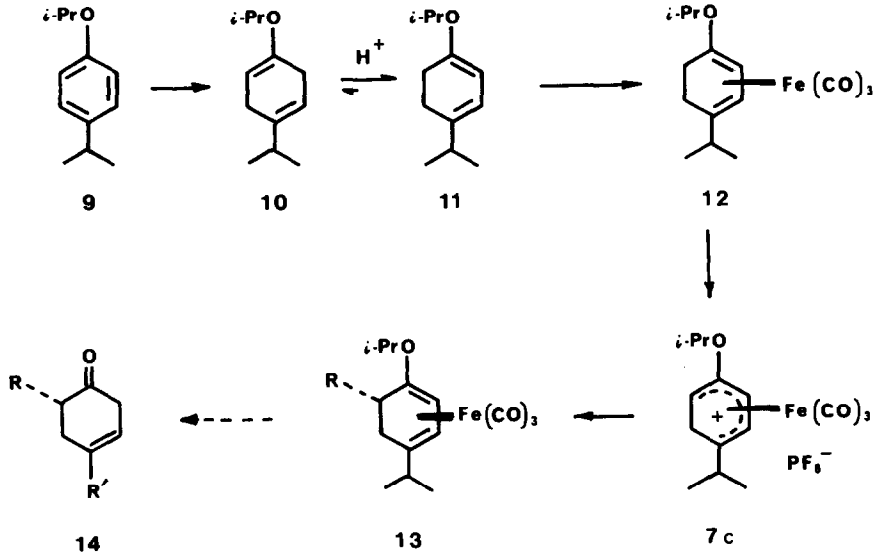


15 16

(a) R = H

(b) R = Me

SCHEME 1



9 10 11 12

14 13 7c

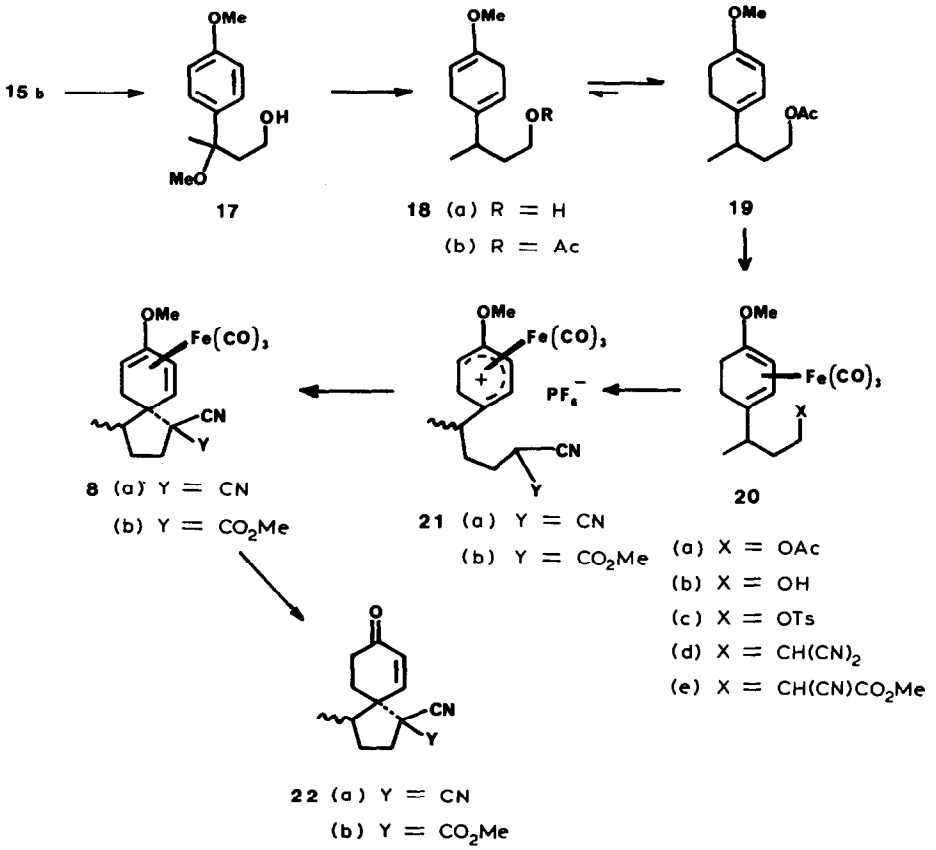
(a) R = $CH(CO_2Me)$

(b) R = $CH(CN)_2$

above (p-TsOH) to give a 6/1 mixture of **19** and **18b** which was treated directly with pentacarbonyliron in di-n-butyl ether at reflux to afford the complex **20a** as an equimolar mixture of diastereomers in 70% yield, revealing that no diastereoselectivity occurs during complexation. Deacetylation of **20a** followed by tosylation produced the tosylate complex **20c** which was easily converted to the malononitrile derivative **20d** or the cyano ester **20e**, although the latter was obtained as a mixture of four diastereomers (and, of course, their enantiomers). In the preceding cases where two diastereomers were obtained, these were separated by preparative TLC on small scale and individually characterized. The overall synthetic scheme was followed through using the mixture.

With the diene complexes **20d** and **20e** in hand we could assess the feasibility of the remaining hydride abstraction/spirocyclisation and, perhaps most important, decomplexation steps. Reaction of the bis-nitrile complex **20d** with trityl hexafluorophosphate was followed by infrared spectroscopy, which showed that no spontaneous cyclisation of the desired cationic dienyl complex **21a** occurred. Consequently, this intermediate was isolated and subjected to mild base treatment (Et_3N, CH_2Cl_2, CH_3CN, $-78°C$) to give the mixture of diastereomers **8a** in 54% overall yield from **20d**. We have previously established that intramolecular nucleophile additions of this type occur *trans* to the $Fe(CO)_3$ group [6]. Mild oxidative removal

SCHEME 2



of the $Fe(CO)_3$ group from **8a** followed by acidic hydrolysis of the resulting dienol ether furnished the spirocyclic enone **22a** in 66% yield. An identical sequence of reactions performed on complex **20e** led to the spirocyclic complexes **8b** which were converted to enones **22b**, although the decomplexation and acid hydrolysis of the cyano ester derivatives proved more troublesome than for the bis-nitrile.

The foregoing results show that intramolecular nucleophile addition to dienyliumiron complexes with branched substituents is a synthetically useful process, particularly for molecules having crowded spirocenters. The enones **2** appear well suited for conversion to the Oppolzer or Corey intermediates [6], though of course the question here is not whether synthesis of acorenone or cedrol is possible using this method, but centers on the more important chemical behavior of dienyliumiron complexes which allow potentially general annulations at crowded reaction centers.

Experimental

IR spectra were recorded with a Perkin–Elmer 1420, and NMR spectra with Varian EM-360, EM-390 or XL-200 spectrometers. Mass spectral services were provided by the Department of Pharmacology, Case Western Reserve University, and combustion analyses were performed by Galbraith Laboratories, Inc. M.p.'s are uncorrected. All synthetic and chromatographic operations with iron complexes were performed under nitrogen atmosphere using standard techniques. Solvents were freshly distilled under nitrogen as follows: tetrahydrofuran (THF) from sodium-benzophenone; dichloromethane from calcium hydride; diethyl ether from lithium aluminum hydride.

1-Isopropoxy-4-isopropylbenzene

p-Isopropylphenol (50 g, 370 mmol) was treated with sodium (9 g, 390 mmol) in ethanol (275 ml) followed by isopropyl bromide (38 ml, 50 g, 400 mmol) (reflux, **6h**) to furnish, after distillation, the isopropyl ether (50.43 g, 77%), b.p. 83°C at 4 mmHg, ν_{max} ($CHCl_3$) 2960, 1610 cm^{-1}; δ ($CDCl_3$, 90 MHz) 7.16 (2H, d, *J* 9 Hz, 2 × ArH), 6.82 (2H, d, *J* 9 Hz, 2 × ArH), 4.48 (1H, hept., *J* 6 Hz, Me_2CHO), 2.86 (1H, hept., *J* 7 Hz, Me_2CH), 1.32 (6H, d, J 6 Hz, Me_2CHO), 1.25 (6H, d, *J* 7 Hz, Me_2CH); *m/e* (%) 178 (23), 136 (20), 121 (100). (Found: C, 80.9; H, 9.95. $C_{12}H_{18}O$ calcd.: C, 80.86; H, 10.15%.)

Tricarbonyl(1-4-η-4-isopropoxy-1-isopropylcyclohexa-1,3-diene)iron (12a)

Birch reduction of the above isopropyl ether (20 g, 112 mmol) with sodium (15 g, 650 mmol) in liquid ammonia (500 ml) containing THF (100 ml) and ethanol (30 ml) according to the usual method, gave the diene **10a** (16.5 g, 80%), ν_{max} (CCl_4) 2970, 1690, 1665 cm^{-1}; δ ($CDCl_3$, 90 MHz) 5.40 (1H, br, 5-H), 4.64 (1H, br, 2-H), 4.30 (1H, hept., *J* 6 Hz, Me_2CHO), 2.70 (4H, br, 2 × CH_2). 2.22 (1H, hept., *J* 7 Hz, Me_2CH), 1.21 (6H, d, *J* 6 Hz, Me_2CHO), 1.02 (6H, d, *J* 7 Hz, Me_2); *m/e* (%) 180 (14), 138 (36), 123 (100). (Found: C, 80.2; H, 11.3. $C_{12}H_{20}O$ calcd.: C, 79.94; H, 11.18%).

Treatment of this compound (neat, 14.53 g) with a catalytic amount of *p*-toluene sulfonic acid at 80°C for 5 h afforded an 8/1 mixture of the 1,3-diene (**11a**) and unchanged (**10a**) (14.1 g, 97%). Compound **11a** was isolated by addition of aqueous sodium carbonate, separation, drying ($MgSO_4$) and distillation of the organic layer,

and showed δ ($CDCl_3$, 90 MHz) 5.62 (1H, d, *J* 6 Hz, 2-H), 4.90 (1H, d, *J* 6 Hz, 3-H), 4.30 (1H, hept., *J* 6 Hz, Me_2CHO), 2.28 (1H, hept. *J* 7 Hz, Me_2CH), 2.21 (4H, s, $2 \times CH_2$), 1.21 (6H, d, *J* 6 Hz, Me_2CHO), 1.01 (6H, d, *J* 7 Hz, Me_2CH). (Found: C, 80.1; H, 11.4. $C_{12}H_{20}O$ calcd.: C, 79.94; H, 11.18%).

This mixture (6 g, 33 mmol) was heated with pentacarbonyliron (20 ml, 30 g, 150 mmol) in refluent di-n-butyl ether (50 ml) for 42 h. Filtration of the cooled mixture through celite (CARE! pyrophoric iron is produced) followed by evaporation of solvent and excess $Fe(CO)_5$, using a rotary evaporator with dry ice/acetone trap, and chromatography on alumina gave the complex as an orange oil (9.5 g, 93%), ν_{max} ($CHCl_3$) 2040, 1960 cm^{-1}; δ ($CDCl_3$), 90 MHz) 5.07 (1H, d, *J* 5 Hz, 3-H), 4.90 (1H, d, *J* 5 Hz, 2-H), 4.05 (1H, hept. *J* 6 Hz, Me_2CHO), 2.2–1.3 (5H, m, Me_2CH and $2 \times CH_2$), 1.3–0.9 (12H, m, $4 \times$ Me); *m/e* (%) 320 (4), 292 (24), 262 (37), 234 (100). (Found: C, 56.37; H, 5.82. $C_{15}H_{20}O_4Fe$ calcd.: C, 56.28; H, 5.66%.)

Tricarbonyl(1–5-η-4-isopropoxy-1-isopropylcyclohexa-2,4-dienylium)iron hexafluorophosphate (7c)

Complex **12a** (9 g, 28 mmol) was treated with trityl hexafluorophosphate (11.6 g, 30 mmol) in refluent dichloromethane (175 ml) for 6 h, to give the dienylium complex **7c**, precipitated with ether as a yellow powder (9.5 g, 73%), ν_{max} (CH_3CN) 2100, 2050 cm^{-1}; δ (CD_3CN, 90 MHz) 6.75 (1H, dd, *J* 6 and 3 Hz, 3-H), 5.60 (1H, d, *J* 6 Hz, 2-H), 4.61 (1H, hept., *J* 6 Hz, Me_2CHO), 3.88 (1H, dd, *J* 6 and 2 Hz, 5-H), 3.00 (1H, dd, *J* 15 and 6 Hz, *endo*-6-H), 2.38 (1H, dd, *J* 15 and 2 Hz, *exo*-6-H), 2.32 (1H, hept., *J* 7 Hz, Me_2CH), 1.33 and 1.29 (6H, $2 \times$ d, *J* 6 Hz), diastereotopic Me_2CHO), 1.05 and 0.94 (6H, $2 \times$ d, *J* 7 Hz, diastereotopic Me_2CH) (Found: C, 38.7; H, 4.1. $C_{15}H_{19}F_6FeO_4P$ calcd.: C, 38.82; H, 4.13%).

Reaction of complex 7c with nucleophiles

These reactions were conducted in THF suspensions according to the previously described procedure [6].

Dimethyl potassiomalonate. Reaction between complex **7c** (200 mg, 0.43 mmol) and dimethyl potassiomalonate (2 eq.) gave tricarbonyl(dimethyl(2-5-η-2-isopropoxy-5-isopropylcyclohexa-2,4-dienyl)malonate)iron (**13a**) as yellow plates (from pentane) (114 mg, 60%) m.p. 107.5–108.5°C, ν_{max} ($CHCl_3$) 2030, 1940, 1735 cm^{-1}, δ ($CDCl_3$, 90 MHz) 5.09 (1H, d, *J* 5 Hz, 3-H), 4.83 (1H, d, *J* 5 Hz, 2-H), 4.01 (1H, hept., *J* 7 Hz, Me_2CHO), 3.74 (1H, d, *J* 4 Hz, $(MeO_2C)_2CH$), 3.70 (6H, s, $(MeO_2C)_2CH$), 2.4–1.4 (4H, m, 5-H, Me_2CH, and CH_2), 1.4–1.0, (12H, m, $4 \times$ Me); *m/e* (%) 450 (3), 422 (10), 394 (34), 366 (100) (Found: C, 53.1; H. 5.8. Calc. for $C_{20}H_{26}FeO_8$: C, 53.35, H. 5.82%).

Sodiomalononitrile. Complex **7c** (200 mg, 0.43 mmol) and sodiomalononitrile (2 eq.) gave tricarbonyl((2-5-η-2-isopropoxy-5-isopropylcyclohexa-2,4-dienyl)malononitrile)iron (**13b**) (100 mg, 61%), ν_{max} ($CHCl_3$) 2260, 2050, 1950 cm^{-1}; δ ($CDCl_3$, 90 MHz), 5.28 (1H, d, *J* 5 Hz, 3-H), 5.05 (1H, d, *J* 5 Hz, 2-H), 4.07 (1H, d, *J* 3 Hz, $(NC)_2CH$), 4.05 (1H, hept., *J* 7 Hz, Me_2CHO), 2.3–1.7 (3H, m, 5-H and CH_2), 1.70 (1H, hept., *J* 7 Hz, Me_2CH), 1.45 and 1.25 (6H, $2 \times$ d, *J* 7 Hz, diastereotopic Me_2CHO), 1.14 and 0.90 (6H, $2 \times$ d, *J* 7 Hz, diastereotopic Me_2CH); *m/e* (%) 384 (5), 356 (27), 328 (10), 300 (92), 234 (100).

4-(4-Methoxyphenyl)-4-hydroxypent-1-ene (15a)

A solution of allyl chloride (63.6 ml, 60 g, 780 mmol) in THF (600 ml) was added

dropwise to a well stirred suspension of magnesium turnings (19 g, 780 mmol) in THF (30 ml) whilst the reaction temperature was maintained at 25°C by means of a water/ice bath. The reaction mixture was stirred for a further 2 h and then a solution of *p*-methoxyacetophenone (60 g, 400 mmol) in THF (300 ml) added over 2 h. After 16 h the reaction was worked up in the usual way (aq. NH_4Cl quench, Et_2O extraction) to afford the alcohol as a colourless liquid (68.4 g, 89%) ν_{max} ($CHCl_3$) 3600, 3500br, 3000, 2900, 1600, 1510 cm^{-1}; δ ($CDCl_3$, 60 MHz) 7.34 (2H, d, *J* 9 Hz, 2 × ArH), 6.83 (2H, d, *J* 9 Hz, 2 × ArH), 5.48 (1H, m, 2-H), 5.17 (1H, br s, *E*-1-H), 4.98 (1H, dd, *J* 12 and 3 Hz, *Z*-1-H), 3.81 (3H, s, OMe), 2.58 (2H, d, *J* 8 Hz, CH_2), 2.30 (1H, br s, exchanges with D_2O, OH), 1.53 (3H, s, Me); *m/e* (%) 175 (3), 148 (11), 135 (100). (Found: C, 74.7; H, 8.5. $C_{12}H_{16}O_2$ calcd.: C, 74.97; H, 8.39%.)

2-(4-Methoxycyclohexa-1,4-dienyl)pentan-2-ol (16)

The alcohol **15a** (6 g, 31 mmol) was subjected to Birch reduction with either lithium or sodium metal according to the usual method (see above) to give **16** (ca. 5.5 g) ν_{max} (CCl_4) 3600, 3500, 2950, 1680, 1650 cm^{-1}; δ ($CDCl_3$, 60 MHz) 5.68 (1H, br s, 2′-H), 4.62 (1H, br s, 5′-H), 3.50 (3H, s, OMe), 2.7–2.5 (5H, m, OH and ring CH_2), 2.3–1.0 (4H, m, 2 × CH_2), 1.27 (3H, s, Me) 0.87 (3H, t, *J* 7 Hz, Me); *m/e* (%) 179 (3), 151 (100). The sensitivity of this compound precluded combustion analysis. It was judged > 95% pure by HPLC.

4-(4-Methoxyphenyl)-4-methoxypent-1-ene (15b)

The alcohol **15a** (60 g, 312 mmol) was treated with sodium hydride (19.4 g of a 50% dispersion in mineral oil, 405 mmol) in THF (500 ml) for 4 h, then methyl iodide (40 ml, 60 g, 650 mmol) added. The mixture was stirred overnight, quenched by careful addition of methanol (50 ml), filtered through celite, and evaporated to one-third of its original volume at aspirator pressure. The residue was poured into water and extracted with ether in the usual way to give the methyl ether **15b** (57.9 g, 90%), ν_{max} ($CHCl_3$) 3090, 2950, 1610, 1510 cm^{-1}, δ ($CDCl_3$, 60 MHz) 7.28 (2H, d, *J* 9 Hz, 2 × ArH), 6.84 (2H, d, *J* 9 Hz, 2 × ArH), 5.44 (1H, m, 2-H), 5.04 (1H, br s, *E*-1-H), 4.98 (1H, d, *J* 12 Hz, *Z*-1-H), 3.80 (3H, s, Ar-OMe), 3.05 (3H, s, OMe), 2.53 (2H, d, *J* 7 Hz, CH_2), 1.50 (3H, s, Me); *m/e* (%) 206 (0.5), 175 (18), 165 (100). (Found: C, 75.8; H, 8.56. $C_{13}H_{18}O_2$ calcd.: C, 75.67; H, 8.78%.)

3-(4-Methoxyphenyl)-3-methoxybutan-1-ol (17)

The olefin **15b** (10 g, 48.5 mmol) was dissolved in a 1/1 mixture of methanol and dichloromethane (100 ml) and cooled to −78°C. A stream of dry ozone in oxygen was bubbled through the solution until a pale mauve colour appeared. The flask was purged with nitrogen, allowed to warm to −20°C, and then sodium borohydride (2 g) added cautiously in small portions. The reaction was worked-up by evaporation of the solvent, taking up the residue in ether, and washing with water. Evaporation of the dried ($MgSO_4$) ether extracts afforded the alcohol **17** (8.2 g, 81%), ν_{max} ($CHCl_3$) 3620, 3500br, 2940, 1610, 1510cm^{-1}; δ ($CDCl_3$, 60 MHz) 7.26 (2H, d, *J* 9 Hz, 2 × ArH), 6.84 (2H, d, *J* 9 Hz, 2 × ArH), 3.79 (3H, s, OMe), 3.63 (2H, t, *J* 6 Hz, C*H*$_2$OH), 3.06 (3H, s, OMe), 2.70 (1H, br, exchanges with D_2O, OH), 1.92 (2H, t, *J* 6 Hz, CH_2), 1.60 (3H, s, Me); (Found: C, 68.3; H, 8.7. $C_{12}H_{18}O_3$ calcd.: C, 68.55; H, 8.63%).

*3-(4-Methoxycyclohexa-1,4-dienyl)butan-1-ol (**18a**)*

The aromatic alcohol **17** (31 g, 148 mmol) was dissolved in liquid ammonia (1.5 l) containing THF (100 ml) and ethanol (80 ml). Sodium was added at intervals to maintain a deep blue colour for 5 h. The reaction was worked-up in the usual way to afford the cyclohexa-1,4-diene derivative (23 g, 85%), ν_{max} ($CHCl_3$) 3620, 3460, 2940, 1690, 1600 cm^{-1}; δ ($CDCl_3$, 60 MHz) 5.44 (1H, br s, 2'-H), 4.63 (1H, br s, 5'-H), 3.59 (2H, t, *J* 7Hz, CH_2OH), 3.55 (3H, s, OMe), 2.73 (4H, br s, ring CH_2), 2.25 (2H, m, CH_2), 1.59 (1H, m, Me(Ar)C*H*), 1.01 (3H, d, *J* 7 Hz, Me); *m/e* (%) 182 (30), 180 (22), 167 (9), 137 (88), 135 (100). The sensitivity of the enol ether group in this compound precluded combustion analysis.

*3-(4-Methoxycyclohexa-1,4-dienyl)butyl acetate (**18b**)*

A solution of the alcohol **18a** (23 g, 126 mmol) in pyridine (120 ml) was cooled to 0°C and acetic anhydride (14.3 ml, 15.5 g, 152 mmol) added. After 16 h at 0°C the mixture was poured into water (500 ml) and extracted with ether (4 × 150 ml). The ether extracts were washed thoroughly with water, brine, dried ($MgSO_4$) and distilled to give the acetate **18b** (25.7 g, 95%), b.p. 124–136°C at 5 mmHg, ν_{max} (CCl_4) 1730, 1690, 1600 cm^{-1}; δ ($CDCl_3$, 60 MHz) 5.38 (1H, br s 2'-H), 4.59 (1H, br s, 5-H), 4.00 (2H, t, *J* 7 Hz, CH_2OAc), 3.52 (3H, s, OMe), 2.70 (4H, br s, ring CH_2), 2.02 (2H, m, CH_2), 2.00 (3H, s, OAc), 1.63 (1H, m, CH), 0.97 (3H, d, *J* 6 Hz, Me); *m/e* (%) 224 (37), 222 (10), 149 (27), 147 (25), 137 (100). (Found: C, 69.8; H, 9.3. $C_{13}H_{20}O_3$ calcd.: C, 69.61; H, 9.04%).

*Tricarbonyl(3-(1-4-η-4-methoxycyclohexa-1,3-dienyl)butylacetate)iron (**20a**).*

The acetate **18b** (25.7 g) was stirred with *p*-toluene sulfonic acid (1.3 g) at 80°C for 2 h to give a 6/1 mixture of conjugated **19** and unconjugated **18b** dienes (23.5 g, 91%). Compound **19** showed δ (CCl_4, 60 MHz) 5.51 (1H, d, *J* 6 Hz, 2'-H), 4.76 (1H, d, *J* 6 Hz, 3'-H), 3.94 (2H, t, *J* 7 Hz, CH_2OAc), 3.50 (3H, s, OMe), 2.14 (4H, br s, ring CH_2), 2.05 (2H, m, CH_2), 1.97 (3H, s, OAc), 1.60 (1H, m, CH), 1.02 (3H, d, *J* 7 Hz, Me).

A portion of this mixture (5 g, 22 mmol) was heated with pentacarbonyliron (15 ml, 22.5 g, 115 mmol) in refluent di-n-butyl ether (60 ml) for 42 h. The usual work-up and chromatography on alumina afforded the complex as an orange oil (5.55 g, 70%), ν_{max} ($CHCl_3$) 2040, 1970, 1720 cm^{-1}; *m/e* (%) 364 (1), 336 (5), 308 (43), 280 (48), 278 (100). The diastereoisomers were resolved by preparative TLC (SiO_2/10% ethyl acetate/benzene), diastereoisomer **A** (faster running): δ ($CDCl_3$, 60 MHz) 5.22 (1H, d, *J* 5 Hz, 3'-H), 4.95 (1H, d, *J* 5 Hz, 2'-H), 3.98 (2H, t, *J* 7 Hz, CH_2OAc), 3.45 (3H, s, OMe), 2.00 (3H, s, OAc) 2.0–1.3 (7H, m, 3 × CH_2 and CH), 1.27 (3H, d, *J* 7 Hz, Me), diastereoisomer **B**: δ ($CDCl_3$, 60 MHz) 5.17 (1H, d, *J* 5 Hz, 3'-H), 4.91 (1H, d, *J* 5 Hz, 2'-H), 4.08 (2H, t, *J* 7 Hz, CH_2OAc), 3.43 (3H, s, OMe), 2.04 (3H, s, OAc), 2.0–1.4 (7H, m, 3 × CH_2 and CH), 1.14 (3H, d, *J* 6 Hz, Me). (Found: mixture: C, 53.0; H, 5.7. $C_{16}H_{20}O_6Fe$ calcd.: C, 52.77; H, 5.54%).

*Tricarbonyl(3-(1-4-η-4-methoxycyclohexa-1,3-dienyl)butanol)iron (**20b**)*

The acetate **20a** (13.8 g, 38 mmol), potassium hydroxide (2.55 g, 45.5 mmol) and methanol (100 ml) were stirred at room temperature for 2 h. Aqueous work-up afforded the alcohol **20b** (11.26 g, 92%), ν_{max} ($CHCl_3$) 3630, 3480, 2040, 1970 cm^{-1}; *m/e* (%) 266 (60), 238 (4), 236 (100). The diastereoisomers, which were separated by

preparative TLC (SiO_2/10% ethyl acetate/benzene) showed the following proton NMR data. Diastereoisomer **A**: δ ($CDCl_3$, 200 MHz) 5.20 (1H, d, *J* 5 Hz, 3'-H), 4.95 (1H, d, *J* 5 Hz, 2'-H), 3.64 (2H, m, CH_2OH), 3.45 (3H, s, OMe), 2.26 (1H, t, exchanges with D_2O, OH), 1.9–1.5 (7H, m, $3 \times CH_2$ and CH), 1.23 (3H, d, *J* 7 Hz, Me); diastereoisomer **B**: δ ($CDCl_3$, 200 MHz) 5.18 (1H, d, *J* 5 Hz, 3'-H), 5.02 (1H, d, *J* 5 Hz, 2'-H), 3.67 (2H, m, CH_2OH), 3.45 (3H, s, OMe), 2.27 (1H, t, exchanges with D_2O, OH), 1.9–1.3 (7H, m, $3 \times CH_2$ and CH), 1.17 (3H, t, *J* 7 Hz, Me). *m/e* M^+ 322. (Found, mixture: C, 52.2; H, 5.71. $C_{14}H_{18}O_5Fe$ calcd.: C, 52.20; H, 5.62%).

*Tricarbonyl(3-(1-4-η-4-methoxycyclohexa-1,3-dienyl)butyl p-toluene sulfonate)iron (**20c**)*

p-Toluene sulfonyl chloride (5.91 g, 31 mmol) was added to a solution of the alcohol **20b** (9.08 g, 28.2 mmol) in pyridine (60 ml) at 0°C. After 24 h at 0°C the reaction mixture was poured into briskly stirred ice-cold 5% hydrochloric acid (400 ml) and extracted with ether (4×150 ml). The organic layer was washed with 5% hydrochloric acid (2×200 ml), brine (300 ml), saturated aqueous sodium carbonate (2×300 ml) and finally dried ($MgSO_4$). Evaporation of the ether afforded the tosylate complex (13 g, 97%), pure by TLC, ν_{max} ($CHCl_3$) 2040, 1970, 1600, 1360, 1175 cm^{-1}; *m/e* (%) 476 (0.5), 448 (1), 420 (17), 392 (32), 235 (100). The separated diastereoisomers (SiO_2/10% ethyl acetate/benzene) showed: diastereoisomer **A**; δ ($CDCl_3$, 200 MHz) 7.77 (2H, d, *J* 9 Hz, $2 \times$ ArH), 7.35 (2H, d, *J* 9 Hz, $2 \times$ ArH), 5.18 (1H, d, *J* 5 Hz, 3'-H), 4.82 (1H, d, *J* 5 Hz, 2'-H), 4.04 (2H, m, CH_2OTs), 3.42 3H, s, OMe), 2.44 (3H, s, ArMe), 1.8–1.5 (7H, m, $3 \times CH_2$ and CH), 0.96 (3H, d, *J* 7 Hz, Me); diastereoisomer **B**: δ ($CDCl_3$, 200 MHz) 7.77 (2H, d, *J* 9 Hz, $2 \times$ ArH), 7.35 (2H, d, *J* 9 Hz, $2 \times$ ArH), 5.12 (1H, d, *J* 5 Hz, 3'-H), 4.92 (1H, d, *J* 5 Hz, 2'-H), 4.04 (2H, m, CH_2OTs), 3.42 (3H, s, OMe), 2.44 (3H, s, ArMe), 1.8–1.5 (7H, m, $3 \times CH_2$ and CH), 1.03 (3H, d, *J* 7 Hz, Me).

*Tricarbonyl(3-(1-4-η-4-methoxycyclohexa-1,3-dienyl)butyl malononitrile)iron (**20d**)*

The tosylate **20c** (3.35 g , 7.04 mmol and sodiomalononitrile (8 equiv.) (from NaH and malononitrile) was stirred for 2 h in refluent THF (75 ml). Aqueous work-up, ether extraction and flash chromatography (30% ethyl acetate/hexane) afforded the complex **20d** (1.87 g, 72%) as a yellow oil, ν_{max} ($CHCl_3$) 2260, 2040, 1970 cm^{-1}; δ ($CDCl_3$, 200 MHz) 5.20 (1H, d, *J* 4 Hz, 3'-H), 4.88 (1H, d, *J* 4 Hz, 2'-H), 3.72 (1H, t, $CH(CN)_2$), 3.43 (3H, s, OMe), 2.4–1.5 (9H, m, $4 \times CH_2$ and CH), 1.20 and 1.13 (3H, $2 \times$ d, *J*, 7 Hz, diastereoisomeric Me); *m/e* (%) 370 (2), 342 (2), 314 (16), 286 (33), 284 (100). (Found: C, 55.4; H, 4.72; N, 7.8. $C_{17}H_{18}N_2O_4Fe$ calcd.: C, 55.16; H, 4.89; N, 7.56%).

*Tricarbonyl(3-(1-5-η-4-methoxycyclohexa-2,4-dienylium)butyl malononitrile)iron hexafluorophosphate (**21a**)*

The complex **20d** (519 mg, 1.4 mmol) was treated with trityl hexafluorophosphate (660 mg, 1.7 mmol) in dichloromethane (4 ml) at 0°C for 2 d. Addition of ether and centrifugation afforded the dienylium complex **21a** as a brown gum (402 mg, 56%), ν_{max} (CH_3CN) 2100, 2040 cm^{-1}; δ (CD_3CN, 60 MHz) 6.86 and 6.77 (1H, $2 \times$ d, *J* 3 Hz, diastereoisomeric 3'-H), 5.60 and 5.54 (1H, $2 \times$ d, *J* 3 Hz, diast. 2'-H), 4.0 (1H, m, 5'-H), 3.8 (1H, obscured, $CH(CN)_2$), 3.80 (3H, s, OMe), 2.90 (1H, m, *endo*-6-H), 2.5–1.4 (6H, m, $2 \times CH_2$, *exo*-6-H and CH), 1.20 and 0.92 (3H, $2 \times$ d, *J* 7 Hz, diast. Me). This material was used without further purification in the next step.

*Tricarbonyl(6-9-η-1,1-dicyano-8-methoxy-4-methylspiro[4.5]deca-6,8-diene)iron (**8a**)*

The salt **21a** (330 mg, 0.64 mmol) was dissolved in a 4/1 mixture of dichloromethane and acetonitrile (20 ml) and cooled to −78°C. Triethylamine (0.098 ml, 71 mg, 0.71 mmol) was added, the mixture stirred for 30 min, and then worked-up in the usual way and chromatographed (SiO_2/10% ethyl acetate/benzene) to give the spirocycle **8a** (225 mg, 96%), ν_{max} ($CHCl_3$) 2260, 2040, 1970, 1490 cm^{-1}; δ ($CDCl_3$, 200 MHz) 5.25 and 5.20 (1H, 2 × dd, *J* 6 and 2.5 Hz, diastereoisomeric 7-H), 3.42 and 3.36 (1H, 2 × dd, *J* 7 and 2.5 Hz, diast. 9-H), 2.64 and 2.40 (1H, 2 × d, *J* 6 Hz, diast. 6-H), 2.5–1.7 (6H, m, 3 × CH_2), 1.21 and 1.10 (3H, 2 × d, *J* 7 Hz, diast. Me); *m/e* (%) 340 (11), 312 (21), 284 (100). (Found: C, 55.7; H, 4.2; N, 7.9. $C_{17}H_{16}N_2O_4Fe$ calcd.: C, 55.46; H, 4.38; N, 7.61%).

*1,1-Dicyano-4-methyl-8-oxospiro[4.5]dec-6-ene (**22a**)*

A solution of the spirocyclic complex **8a** (343 mg, 0.97 mmol) and trimethylamine *N*-oxide (730 mg, 9.7 mmol) in benzene (20 ml) was warmed at 40°C for 3 h and then at 60°C for 8 h. Aqueous work-up and extraction with ether in the usual way afforded the crude dienol ether which was dissolved in methanol (3 ml) and treated with a solution of oxalic acid (120 mg) in water (1 ml). After 1 h the mixture was poured into saturated aqueous sodium hydrogen carbonate (15 ml) and extracted with ether to give the pure enone **22a** (137 mg, 66%) ν_{max} (CCl_4) 2240, 1685 cm^{-1}; δ ($CDCl_3$, 60 MHz) 7.18 (1H, m, 6-H), 6.53 and 6.24 (1H, 2 × d, *J* 10 Hz, diast. 7-H), 2.8–2.0 (9H, m, 4 × CH_2 and CH), 1.13 and 1.02 (3H, 2 × d, *J* 7 Hz, diast. Me); *m/e* (%) 213 (1), 199 (2), 198 (2), 135 (100). (M^+ not observed) (Found: C, 72.4; H, 7.5; N, 13.1. $C_{13}H_{16}N_2O$ calcd.: C, 72.20; H, 7.46; N, 12.95%).

*Tricarbonyl(methyl 3-(1-4-η-4-methoxycyclohexa-1,3-dienyl)butyl cyanoacetate (**20e**)*

Reaction of the tosylate **20c** (4.15 g, 8.7 mmol) with methyl sodiocyanoacetate (8 equiv.) in refluent THF (90 ml) for 2 days, followed by work-up as for **20d** and flash chromatography gave recovered starting material (238 mg) and complex (**20e**) (2.18 g, 66% based on starting material consumed), ν_{max} (CCl_4) 2240, 2040, 1970, 1750 cm^{-1}; δ ($CDCl_3$, 200 MHz) 5.20 (1H, d, *J* 5Hz, 3′-H), 4.94 (1H, d, *J* 5 Hz, 2′-H), 3.85 and 3.83 (3H, 2 × s, diast. CO_2Me), 3.48 (1H, t, *J* 6 Hz, C*H*(CN)CO_2Me), 3.45 (3H, s, OMe), 2.3–1.5 (9H, m, 4 × CH_2 and CH), 1.18 (3H, d, *J* 4.5 Hz, diastereoisomer **A** Me) and 1.12 (3H, d, *J* 6 Hz, diastereoisomer **B** Me); *m/e* (%) 403 (1), 375 (2), 347 (25), 319 (37), 317 (100).

*Tricarbonyl(methyl 3-(1-5-η-4-methoxycyclohexa-2,4-dienylium)butyl cyanoacetate)iron hexafluorophosphate (**21b**)*

The diene complex **20e** (3.05 g, 7.6 mmol) was stirred with trityl hexafluorophosphate (3.82 g, 9.9 mmol) in dichloromethane (40 ml) at room temperature for 7 h. The salt **21b** was isolated as a brown gum by addition of excess ether, decantation, washing with ether by decantation and drying in vacuo (2.97 g, 71%), ν_{max} (CH_2Cl_2) 2240, 2100, 2040, 1745 cm^{-1}; δ (CD_3CN, 60 MHz) 6.91 and 6.83 (1H, 2 × d, *J* 4 Hz, diast. 3′-H), 5.64 and 5.54 (1H, 2 × d, *J* 4 Hz, diast. 2′-H), 3.88 (3H, s, CO_2Me), 3.84 (3H, s, OMe), 3.9–3.8 (2H, m, 5-H and C*H*(CN)CO_2Me), 3.30 (1H, d, *J* 8 Hz, *endo*-6-H), 2.2-1.4 (6H, m, 2 × CH_2, CH and *exo*-6-H), 1.25 and 0.99 (3H, 2 × d, *J* 7 Hz, diast. Me). This material was used in the next step without further purification.

Tricarbonyl(6-9-η-1-cyano-1-methoxycarbonyl-8-methoxy-4-methylspiro[4.5]deca-6,8-diene)iron (8b)

Reaction of **21b** (2.83 g, 5.16 mmol) with triethylamine (0.83 ml, 0.6 g, 5.97 mmol) in 4/1 dichloromethane/acetonitrile (125 ml) at −78°C as above gave the spirocyclic complex (1.87 g, 90%) as a yellow oil, ν_{max} ($CHCl_3$) 2220, 2040, 1970, 1730, 1480 cm^{-1}; δ ($CDCl_3$, 200 MHz) 5.27 and 5.00 (1H, 2 × dd, *J* 7 and 3 Hz, 7-H), 3.86 (3H, s, CO_2Me), 3.67 (3H, s, OMe), 3.40 (1H, dd, *J* 5 and 3 Hz, 9-H), 2.75 and 2.52 (1H, 2 × d, *J* 7 Hz, diast. 6-H), 2.5–1.7 (7H, m, 3 × CH_2 and CH), 1.08 and 1.02 (3H, 2 × d, *J* 7 Hz, diast. Me); *m/e* (%) 401 (0.5), 373 (9), 343 (2), 317 (63), 135 (100). (Found: C, 53.6; H, 4.6; N, 3.8. $C_{18}H_{19}NO_6Fe$ calcd.: C, 53.89, H, 4.77; N, 3.49%).

1-Cyano-1-methoxycarbonyl-4-methyl-8-oxospiro[4.5]dec-6-ene (22b)

Trimethylamine *N*-oxide (970 mg, 13 mmol) was added portionwise to a solution of complex **8b** (1.04 g, 2.6 mmol) in dimethylacetamide (50 ml) at 0°C. When the addition was complete the reaction mixture was allowed to warm to room temperature, stirred overnight, and poured into brine. Extraction with ether in the usual way gave the crude dienol ether which was dissolved in methanol (5 ml) and treated with a solution of oxalic acid (200 mg) in water (1.5 ml) at room temperature for 1 h. After work-up and chromatography as for **22a** (SiO_2/ether) the enone **22b** was obtained as a colourless oil (250 mg, 37%), ν_{max} ($CHCl_3$) 2250, 1740, 1685 cm^{-1}; δ ($CDCl_3$, 200 MHz) 7.26, 7.12, 6.82, 6.70 (1H, 4 × d, *J* 7 Hz, diastereoisomeric 6-H); 6.46, 6.26, 6.08, 5.96 (1H, 4 × d, *J* 7 Hz, diast. 7-H); 3.86 3.80, 3.78, 3.76 (3H, 4 × s, CO_2Me), 2.8–1.6 (9H, m, 4-H and 4 × CH_2), 1.25, 1.14, 1.01, 1.00 (3H, 4 × d, *J* 7 Hz, diast. Me); *m/e* (%) 247 (14), 232 (21), 216 (5), 188 (30), 121 (100). (Found: C, 67.7; H, 7.52; N, 5.83. $C_{14}H_{19}NO_3$ calcd.: C, 68.0; H, 7.74; N, 5.06%).

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