

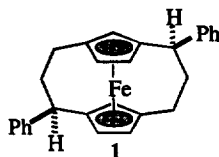
## Synthesis and X-ray crystal structure analysis of a scalemic $C_2$ -symmetric ferrocenophane

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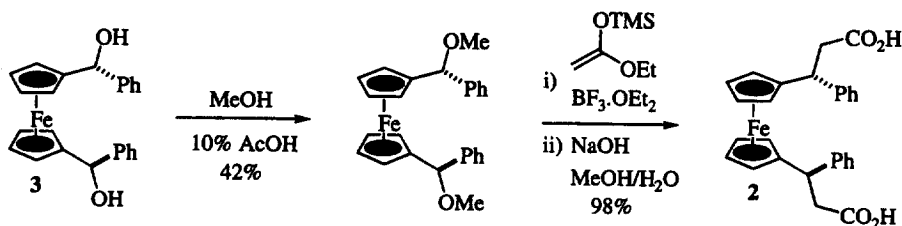
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**Abstract:** (*R,R*)-1,1'-Bis(2-chloroformyl-1-phenylethyl)ferrocene undergoes  $\text{SnCl}_4$  promoted intramolecular Friedel–Crafts cyclisation to give a 1.5:1 ratio of singly bridged ferrocenophane isomers. After separation of their corresponding methyl esters, the major isomer is converted into the novel  $C_2$ -symmetric ferrocenophane (*R,R\_pS\_pS*)-1,1'-(1-phenyltrimethylene)-3,3'-(3-phenyltrimethylene)ferrocene, as determined by an X-ray crystal structure analysis. © 1997 Elsevier Science Ltd

Metallocenes have been widely incorporated as redox responsive functions in supramolecular host systems that have potential applications as chemical sensors, devices for molecular electronics, and metalloenzyme mimetics.<sup>1</sup> These structures are normally constructed from 1,1'-disubstituted metallocenes incorporated into achiral cyclic structures,<sup>2</sup> or alternatively from monosubstituted metallocenes attached to frameworks such as porphyrins and calixarenes.<sup>3</sup> We are interested in the synthesis of novel metallocene building blocks for redox active chiral supramolecular systems, and report here the synthesis and X-ray structure of scalemic  $C_2$ -symmetric ferrocenophane **1**.



Our approach involves a double intramolecular Friedel–Crafts cyclisation/carbonyl reduction on diacid **2**, previously obtained in 92% e.e. from diol **3**<sup>4</sup> by the procedure outlined in Scheme 1.<sup>5</sup>

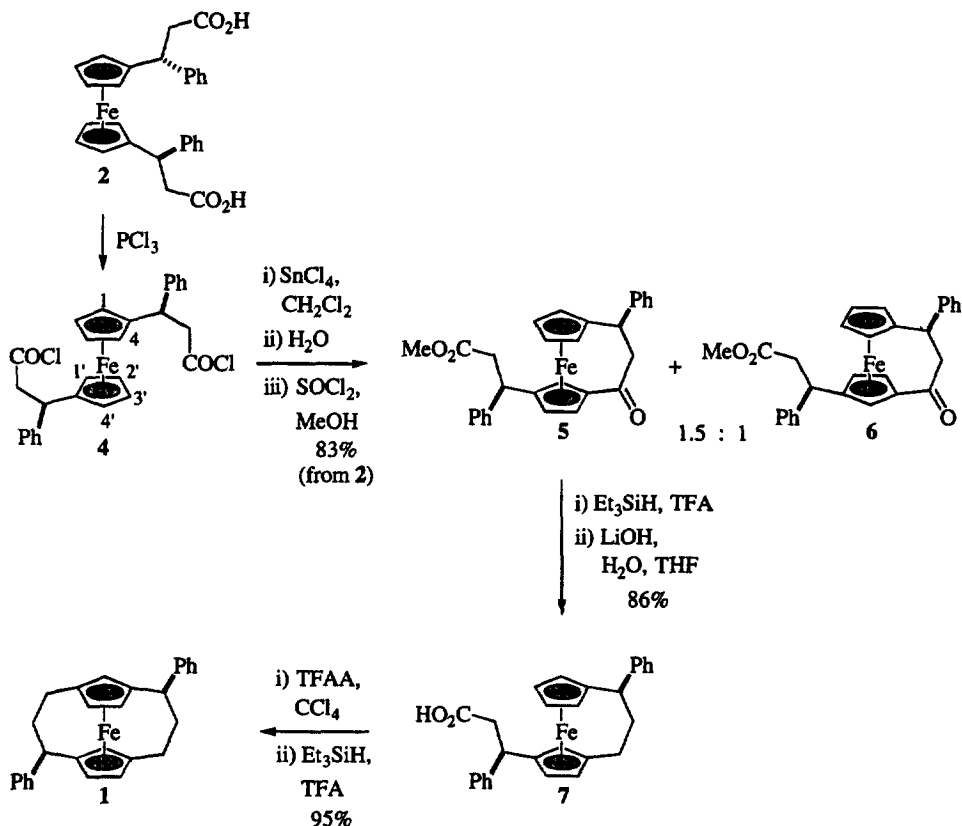


Scheme 1.

Treatment of **2** with neat phosphorus trichloride at 70°C gave clean conversion to the diacid chloride **4** (Scheme 2). Intramolecular Friedel–Crafts cyclisation of one of the two equivalent propanoyl chloride substituents may occur potentially in six different positions: at the two adjacent diastereotopic carbons of the same cyclopentadienyl ring (1, 4), and at the four carbons (two diastereotopic pairs) of the opposite cyclopentadienyl ring (1', 2', 3', 4'). Previous intramolecular cyclisations of 3-ferrocenylpropanoyl chlorides have given products predominantly from cyclisation onto the opposite

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ring.<sup>6</sup> We also anticipated attack at positions 1' and 4' to be disfavoured by the steric block of the other substituent.<sup>7</sup>



Scheme 2.

Slow addition of a solution of 4 to tin(IV) chloride in dichloromethane at room temperature gave, after quenching with dilute HCl, two monocyclised carboxylic acids in a 1.5:1 ratio. After conversion to their corresponding methyl esters, the major isomer<sup>8</sup> was readily separated by a recrystallisation from ethyl acetate/petroleum ether. Use of  $\text{Et}_2\text{AlCl}$  as the Lewis acid for this cyclisation resulted in a 1:1 ratio of isomers, and  $\text{AlCl}_3$ ,  $\text{BF}_3 \cdot \text{OEt}_2$ ,  $\text{TiCl}_4$  and methylaluminium bis(2,6-di-*tert*-butylphenoxide) failed to promote cyclisation. Exhaustive reduction of the ferrocenyl ketone of 5 ( $\text{Et}_3\text{SiH}$ , TFA) and ester hydrolysis gave a new carboxylic acid 7 which was determined to have an e.e. of 98% by coupling with (*S*)-(+)-methyl mandelate.<sup>9</sup> Further cyclisation can now only occur at one position of the opposite conformationally locked cyclopentadienyl ring. Thus treatment with trifluoroacetic anhydride<sup>7b</sup> gave a single product which was further exhaustively reduced to give a novel  $C_2$ -symmetric ferrocenophane.<sup>10</sup> An X-ray crystal structure analysis<sup>11</sup> (Figure 1) confirmed both the structure and absolute configuration as (*R,R,pS,pS*)-1, and thus of the preceding intermediates 5 and 7. The first cyclisation results in the formation of an element of planar chirality, such that (*R,R*)-4 gave (*R,R,pR*)-5 as the major isomer. To date it has not proved possible to isolate a pure sample of the minor isomer, but the similarity of its NMR spectrum to 5 suggests it is the diastereoisomer (*R,R,pS*)-6.

The two views A and B shown in Figure 1 illustrate the difference in the open (*exo* face) and closed (*endo* face) approaches to iron in ferrocenophane 1. This is in part due to the cyclopentadienyl ring–ring tilt angle of  $6.5^\circ$ <sup>12</sup> enhancing the greater distance between the alkyl bridges for orientation

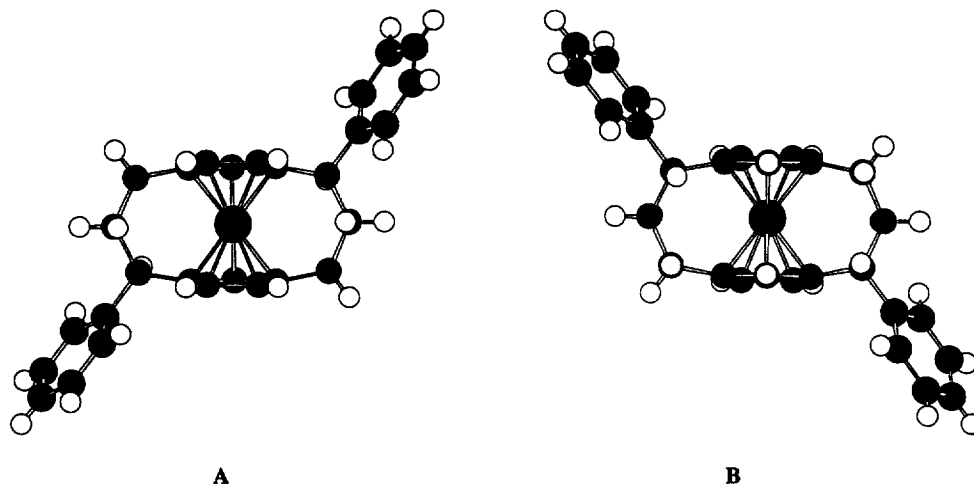


Figure 1. Molecular structures of **1** showing the *exo* face (A) and *endo* face (B).

A compared to B. The *exo* face lies in a  $C_2$ -symmetric environment resulting from the position of the two phenyl groups on this side of the molecule. Both phenyls occupy equatorial positions on the trimethylene bridges, and this conformation is maintained in solution as shown by the coupling constant of 9.8 Hz to the benzylic methine protons ( $H^a$ )<sup>10</sup> at 3.04 ppm.

In summary, we have demonstrated the use of a highly regioselective and partially diastereoselective intramolecular cyclisation method as a key step in the synthesis of a novel  $C_2$ -symmetric scalemic ferrocenophane. We are currently investigating *para*-substituted derivatives of **1** as building blocks for novel supramolecular hosts. It is anticipated that the phenyl groups can be locked by cyclisation into an axial conformation, enhancing the magnitude of the  $C_2$ -environment about the *exo* face of the ferrocenophane.

#### Acknowledgements

We are very grateful to F. C. Brown (Steel Equipment) Ltd for the generous provision of a studentship (AJL).

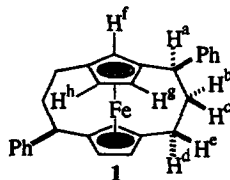
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8. **5**: m.p. 144–148°C;  $[\alpha]_D^{20} = -693$  (c 0.105,  $CHCl_3$ ); (Found: C, 72.59; H, 5.77.  $C_{29}H_{26}FeO_3$  requires C, 72.80; H, 5.49%);  $\nu_{max}$  (nujol) 1731, 1652  $cm^{-1}$ ;  $\delta_H$  (400 MHz,  $CDCl_3$ ) 2.57 (1 H, dd,  $J$  10.3, 3.3,  $-CHPhCH_2CO-$ ), 2.81 (1 H, dd,  $J$  15.5, 9.4,  $-CHHCO_2Me$ ), 2.91 (1 H, dd,  $J$  15.5, 5.9,  $-CHHCO_2Me$ ), 3.52 (3 H, s,  $-OCH_3$ ), 3.67 (1 H, s, Fc), 3.87 (1 H, dd,  $J$  13.0, 10.3,

–CHHCO–), 4.07 (1 H, dd,  $J$  9.5, 5.88, –CHPhCH<sub>2</sub>CO<sub>2</sub>Me), 4.09 (1 H, s, Fc), 4.24 (1 H, dd,  $J$  13.0, 3.1, –CHHCO–), 4.29 (1 H, s, Fc), 4.44 (1 H, s, Fc), 4.55 (1 H, s, Fc), 4.59 (1 H, s, Fc), 4.97 (1 H, s, Fc), 7.10–7.23 (10 H, m, Ph);  $\delta_C$  (100 MHz, CDCl<sub>3</sub>), 41.44 (–CHPh–), 42.28 (–CH<sub>2</sub>–), 49.51 (–CHPh– or –OCH<sub>3</sub>), 50.28 (–CH<sub>2</sub>–), 52.11 (–CHPh– or –OCH<sub>3</sub>), 67.20 (Fc), 68.25 (Fc), 70.80 (Fc), 71.53 (Fc), 72.29 (Fc), 73.21 (Fc), 73.46 (Fc), 76.21 (Fc-*ipso*), 92.30 (Fc-*ipso*), 98.63 (Fc-*ipso*), 126.82 (Ph), 127.16 (Ph), 127.31 (Ph), 127.94 (Ph), 128.84 (Ph), 128.95 (Ph), 143.44 (Ph-*ipso*), 143.88 (Ph-*ipso*), 172.44 (–CO<sub>2</sub>Me), 208.64 (–CO–);  $m/z$  (ES) 479 (MH<sup>+</sup>, 100%), 478 (M<sup>+</sup>, 7%).

9. Major diastereoisomer 5.75 ppm (1 H, s, –OCH(CO<sub>2</sub>CH<sub>3</sub>)Ph), minor diastereoisomer 5.79 ppm.

10. **1**: m.p. 254–256°C,  $[\alpha]_D^{24} = -99$  ( $c$  0.185, CHCl<sub>3</sub>); (Found: C, 80.65; H, 6.02. C<sub>28</sub>H<sub>26</sub>Fe requires C, 80.37; H, 6.28%);  $\delta_H$  (400 MHz, CDCl<sub>3</sub>) 1.79 (2 H, td,  $J$  11.3, 3.5, H<sup>d</sup>), 2.15–2.26 (4 H, m, H<sup>b</sup>, H<sup>c</sup>), 2.37 (2 H, d,  $J$  14.6, H<sup>e</sup>), 3.04 (2 H, d,  $J$  9.8, H<sup>a</sup>), 4.04 (2 H, s, H<sup>g</sup> or H<sup>h</sup>), 4.10 (2 H, s, H<sup>g</sup> or H<sup>h</sup>), 4.25 (2 H, s, H<sup>f</sup>), 7.09 (2 H, t,  $J$  7.2, Ph-*para*), 7.19 (4 H, t,  $J$  7, Ph-*meta*), 7.28 (4 H, d,  $J$  7.5, Ph-*ortho*);  $\delta_C$  (90 MHz, CDCl<sub>3</sub>), 25.98 (–CHPhCH<sub>2</sub>–), 43.87 (–CHPh–), 46.40 (FcCH<sub>2</sub>–), 69.32 (Fc), 70.41 (2×Fc), 86.14 (Fc-*ipso*), 86.99 (Fc-*ipso*), 125.88 (Ph-*para*), 127.33 (Ph), 128.24 (Ph), 145.40 (Ph-*ipso*);  $m/z$  (ES) 419 (MH<sup>+</sup>, 40%), 418 (M<sup>+</sup>, 88), 102 (66), 60 (100).



11. Crystals of **1** (0.12×0.10×0.10 mm) grown from Et<sub>2</sub>O/hexane. C<sub>28</sub>H<sub>26</sub>Fe,  $M = 418.34$ , monoclinic; P2(1),  $a = 12.911(3)$ ,  $b = 5.8400(10)$ ,  $c = 13.436(3)$  Å,  $\beta = 103.72(3)$ ,  $Z = 2$ , Mo-K $\alpha$  radiation  $\lambda = 0.71069$  Å, 4412 reflections were measured giving 2468 unique data. Final  $wR2$  and  $R$  were 0.0831 and 0.0339 for all data [0.0826 and 0.0321 for 2324 with  $I > 2\sigma(I)$ ]. The absolute configuration was confirmed by application of the chirality test using the Flack parameter in SHELXL-93. Atomic coordinates, bond lengths, angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

12. The corresponding value for the X-ray structure of 1,1':3,3'-bis(trimethylene)ferrocene is 9.6°, Hillman, M.; Austin, J. D. *Organometallics*, **1987**, *6*, 1737.

(Received in UK 3 September 1997)