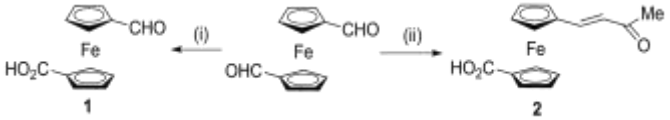
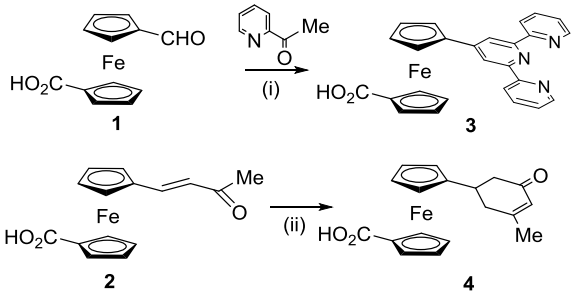
Ferrocene is one of the most widely established compounds in the chemical literature, and it is frequently used as a starting material in both organometallic and organic chemistry transformations.[1] This sandwich-type compound consists of an iron(II) atom bonded in an η^5 fashion to two cyclopentadienide rings (Cp). Redox cycling between the Fe^{2+}/Fe^{3+} states is both chemically and electrochemically reversible.[2] Certainly this final point is one main reason why ferrocene has been so popular as a redox reporter in supramolecular structures.[3] The Cp rings are aromatic and hence it is possible to perform typical electrophilic substitution reactions on one or both of the rings.[4] Selective reactions on a single Cp ring to introduce two disparate functional groups (e.g. PPh_2, dihydrooxazole) is also possible.[5] For this latter case the ferrocene subunit is used as a planar chiral ligand for asymmetric catalysis applications.[6] For each ring to incorporate a different functional group can be complex, often requiring selective BuLi reactions at low temperatures.[7] A long reaction time and a convoluted purification method is possible starting from 1,1′-ferrocenedicarboxaldehyde.[8] A very mild and fast method to achieve a similar outcome would appear to be appealing, provided the two functional groups are useful for further reactions.[9] It turned out that, as part of our research effort into producing ferrocene-based porphyrin and borondipyrromethene (Bodipy) compounds, we discovered such a simple procedure.

The oxidation of ferrocenecarboxaldehyde using aqueous $KMnO_4$ in acetone is well documented to produce the corresponding carboxylic acid.[10] Repeating the literature method afforded ferrocenecarboxylic acid in reasonable yield. However, we found that the same procedure applied to 1,1′-ferrocenedicarboxyaldehyde in acetone or acetonitrile did not produce the corresponding dicarboxylic acid (Scheme 1). The ^1H NMR spectrum for the major product isolated from the acetonitrile reaction showed different resonances for the two Cp rings, confirming the product to be unsymmetrical. Furthermore, two downfield resonances at δ 193.21 and 170.77 for the $^{13}C\{^1H\}$ NMR spectrum were consistent with the presence of aldehyde and carboxylic acid groups. The mass spectrum showed a peak at *m/z* 259, and a broad peak at *ca.* 2939 cm^{-1} in the FT-IR spectrum confirmed production of a carboxylic acid group. The combined evidence verified the product to be compound **1**, in which one aldehyde was oxidized but the other remained untouched. Hence, under these conditions the ferrocene is desymmetrized since it contains two different functional groups. The overall yield for **1** is 49% after a fast and chromatography-free work up, providing material pure enough for further synthetic reactions. A similar reaction performed using an acetone/H_2O mixture (*ca.* 1:1) did not afford a product with a ^1H NMR spectrum consistent with compound **1**. Instead, additional resonances were observed in the olefinic region (δ = 7.35 and 6.30, J = 16.2 Hz), a methyl resonance (δ = 2.25) and a downfield resonance (δ = 197.51) in the ^{13}C NMR spectrum, which is consistent with the existence of a CH_3CO group (see Supporting Information).[11] The mass spectrum showed a peak at *m/z* 299, and once again the FT-IR spectrum corroborated the presence of a carboxylic acid (2934 cm^{-1}).[12] The spectroscopic data are fully consistent with compound **2** with a *trans* double bond. We speculate that oxidation of one aldehyde to the carboxylic acid activates the other carbonyl in **1** to a condensation reaction with the acetone present in solution. Presumably for ferrocenecarboxaldehyde the reaction of the aldehyde with acetone is too slow to compete with oxidation. Rather surprisingly, compounds **1** and **2** could not be found in the literature using popular search tools (i.e., Scifinder, Reaxys). The closest analogue to **2** is the structural isomer ($C_{15}H_{14}FeO_3$) in which one ring has a formyl and the other the (*E*)-β-(methoxycarbonyl)ethenyl subunit.[8] This material was produced by a controlled Wittig reaction with 1,1′-ferrocenedicarboxaldehyde, yielding a mixture of compounds which had to be separated by chromatography. Again for compound **1** the structural analogue ($C_{12}H_{10}FeO_3$) has both the formyl and carboxylic acid substituted on the same Cp ring.[13]



Scheme 1. Reagents and Conditions: (i) $KMnO_4$, CH_3CN/H_2O, 0 °C; (ii) $KMnO_4$, acetone/H_2O, 0 °C.



Scheme 2. Reagents and Conditions: (i) 2-acetylpyridine, aq. $NaOH/NH_4OH$, dark; (ii) (a) diethyl malonate, NaOEt, EtOH; (b) H_2O, H^+.

Having established the simple procedure for desymmetrizing the ferrocene core, we were interested to see if useful chemical transformations could be carried out on compounds **1** and **2**. Noting that the carboxylic acid in **1** may act as an anchoring group to a semiconductor (e.g., TiO_2, NiO), the construction of a ligand from the aldehyde was attempted (Scheme 2). In particular, the established Kröhnke method for synthesizing 2,2′:6′,2″-terpyridine (terpy) is well known.[14] Reaction of **1** with 2-acetylpyridine in aqueous $NaOH/NH_4OH$, in a two-step one-pot reaction, gave after an easy column-free purification the terpy-type ligand **3** in 62% yield. The material is stable in the solid state, but when in a solution of MeOH, DMSO or water, air-equilibrated or N_2-purged, the compound **3** is extremely light-sensitive. Simply leaving a solution exposed to ambient light for several minutes produced a dark purple coloration. When kept in the dark no alteration in color was observed. Interestingly, there is a report that the analogue of **3** without the carboxylic acid very slowly changes its color under light illumination.[15] No further details were given, but it was assumed that oxidation of the ferrocenyl group gave the blue color. Here we report a more thorough study into the instability of the Fc-tpy group in solution. ^{1}H NMR spectra for **3** as the light-driven reaction proceeded are shown in Figure 1. Resonances for the starting material decreased and new peaks appeared with a pattern very similar to authentic $[Fe(Fc\text{-}terpy)_2]^{2+}$ (Figure 1).[15] The conversion yield, estimated from ferrocene integral values, is *ca*. 62%. The reaction could also be followed by UV-Vis spectroscopy in MeOH, and as the reaction proceeded, a new band at λ_{ABS} = 580 nm appeared (see Supporting Information). The new absorption is remarkably similar to the metal-to-ligand charge transfer band observed for $[Fe(terpy)_2]^{2+}$.[16] In addition, the mass spectrum of **3** in methanol left in the light showed peaks at *m/z* 977 and 489 that correspond to the ions $[Fe(\mathbf{3})_2\text{-}H]^+$ and $[Fe(\mathbf{3})_2]^{2+}$.

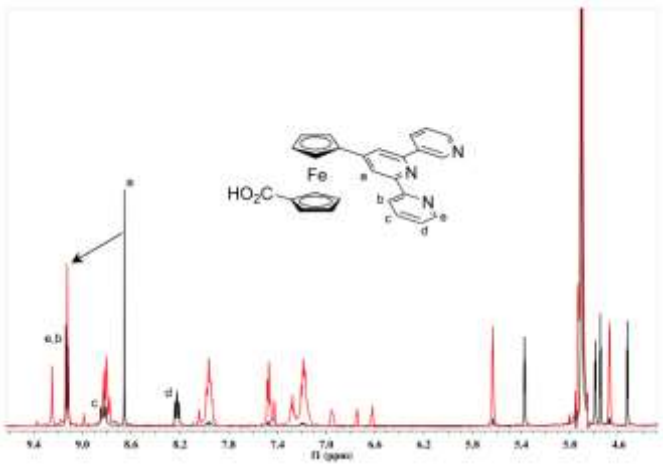


Figure 1. Selected partial 400 MHz ^{1}H-NMR spectra for **3** (black) and light-driven degradation products (red). Assignments of proton resonances for the terpy ligand in **3** are shown.

Hence, the source of the iron(II) must be ferrocene for the light-activated reaction to produce $[Fe(\mathbf{3})_2]^{2+}$. The reaction time is very dependent on the concentration of the starting material and is consistent with a bimolecular mechanism. It is speculated that a terpy ligand from one molecule of ground-state **3** bites onto the ferrocene iron(II) center of another "activated" molecule, leading to degradation of the compound. The identity of the activated ferrocene is not clear. However, the triplet quantum yield for ferrocene is very reasonable (ϕ_T = 0.66), although the lifetime (albeit in DMSO solution) is only 0.6 ns. The triplet energy is around 40 kcal mol^{-1} (14,000 cm^{-1}) and the structure for the triplet state is known to be distorted.[17] The reaction must proceed via the triplet state and the presence of the carboxylic acid appears to promote compound degradation. This idea was tested by reacting under the same conditions a 1:1 mixture of 1,1′-ferrocenedicarboxylic acid and terpyridine in MeOH. When exposed to ambient light the solution became dark purple, with a very distinct absorption pattern suggesting a similar degradation of the ferrocene unit and formation of the $[Fe(terpy)_2]^{2+}$ complex. Non-substituted ferrocene was indefinitely stable in methanol solution in the presence of terpyridine.

Performing all steps, starting from 1,1′-ferrocenedicarboxaldehyde, under ambient light illumination gave after purification by column chromatography (silica gel, MeOH) a deep purple product in 11% yield. Suitable crystals for X-ray crystallographic analysis of the iron complex were obtained, and the obtained structure confirms its identity, although it is of relatively low precision, the marginal-quality crystals giving only weak diffraction. The structure of the cation is illustrated in Figure 2, highlighting the six-coordinate iron(II) center and the two Fe-terpy ligands of compound **3**. The Fe1–N1 [1.876(4) Å] and Fe1–N4 [1.875(4) Å] bond lengths are typically shorter than the remaining Fe–N bond lengths [Fe1–N2 1.974(4), Fe1–N3 1.968(4), Fe1–N5 1.972(4), Fe1–N6 1.971(4) Å]. As observed in previous $[Fe(terpy)_2]^{2+}$ complexes[18] the bite angle of the ligand is not perfectly *trans*, as reflected in the N2–Fe1–N3 and N5–Fe1–N6 bond angles of 161.66(17)° and 162.33(17)°, respectively. A point to note is that each ferrocene group is in its carboxylic acid form and so hexafluorophosphates (not shown) are present as counter-ions.

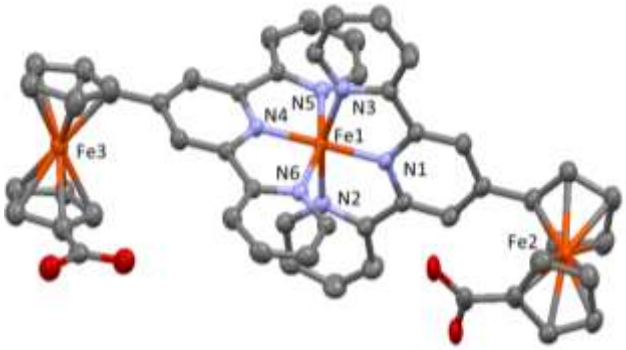


Figure 2. X-ray determined structure of the dication $[Fe(\mathbf{3})_2]^{2+}$. Counter-ions, solvent molecules and hydrogen atoms are omitted for clarity.

The double bond activated by the ketone group in the condensation product **2** is ideally suited for a Michael addition reaction. Thus, reaction of **2** with diethylmalonate in ethanol, catalyzed by sodium ethoxide, gave after quenching with water, acidification and purification by column chromatography (silica gel, CH_2Cl_2/MeOH 9:1) a yellow product in 35% yield. The ^{1}H-, ^{13}C- and DEPT-135° NMR spectra showed resonances typical for a cyclohexenone group (see Supporting Information).[19a-c] The 2-D ^{1}H-^{1}H COSY-45° and heteronuclear (^{1}H/^{13}C HMQC and HMBC) correlation spectra, are consistent with racemic 1′-(5-methylcyclohex-4-en-3-one)ferrocenecarboxylic acid (**4)**. The mass spectrum showed peaks at *m/z* 321, 339 and 677 that match for the $[M–OH]^+$, $[M+H]^+$ and $[2M+H]^+$ ions. After several attempts, crystals of the compound suitable for synchrotron X-ray analysis were obtained. The molecular structure is shown in Figure 3, and confirms unequivocally the identity of the product. The C15–C16 bond length of 1.354(3) Å is consistent with the expected double bond, and other C–C bond lengths in the cyclohexenone ring are typical for C–C single bonds. C12 is a chiral center and both the *R* and *S* enantiomers of **4** are present in the crystal. A centrosymmetric dimer is generated in the crystal structure, as a result of typical hydrogen bonding at the carboxylic acid site (see Supporting Information).

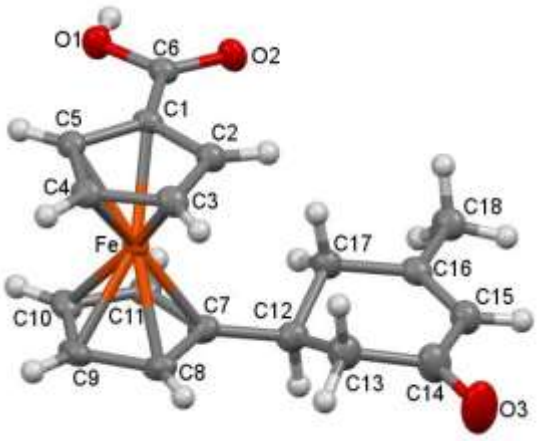
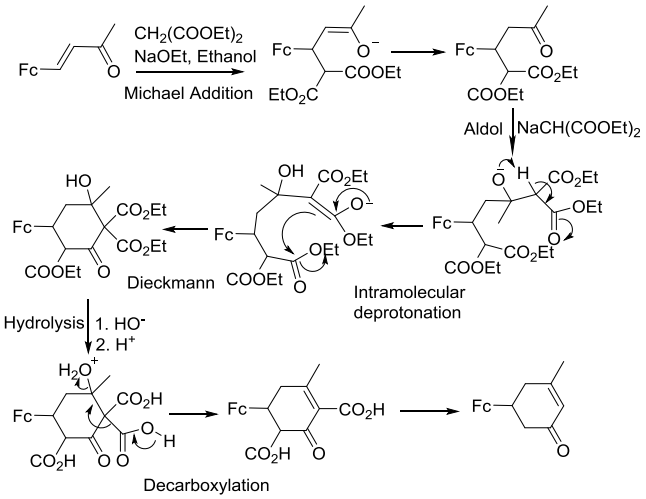


Figure 3. X-ray determined molecular structure for racemic compound **4** showing here the *S* form.

The intriguing conundrum is the mechanism by which compound **2** is converted into **4**, since there is no immediately obvious route. The purity of the diethyl malonate was checked to eliminate any suggestion that the starting material was incorrect. A tentative mechanism is suggested from the initially produced Michael addition product, followed by aldol addition of the second diethyl malonate molecule and cyclohexanone ring closure through a Dieckmann condensation reaction (Scheme 3).[20] Hydrolysis of the esters and acidification is followed by dehydration of the aldol intermediate and a series of decarboxylations to end up eventually with the identified product **4**.

In conclusion, we have demonstrated via simple oxidation that 1,1′-ferrocenedicarboxaldehyde can be converted into desymmetrized compounds. There is clear scope to expand on the chemistry of the two derivatives, especially via the

terpy ligand **3** with its anchoring carboxylic acid site. We expect to produce photoactive systems for semiconductor attachment and dye-sensitized solar cell applications from these products.



Scheme 3. Proposed mechanism to explain the formation of compound **4**.[21] Fc = ferrocenecarboxylic acid.

Acknowledgments

We thank the Engineering and Physical Sciences (EPSRC)-sponsored mass spectrometry service at Swansea for collection of mass spectra, the FP7-PEOPLE-2009-IRSES-246902 grant for the exchange of researchers, EPSRC for a crystallography equipment grant, and Diamond Light Source for access to synchrotron facilities.

References and notes

1. a) Atkinson, R. C. J.; Gibson, V. C.; Long, N. J. *Chem. Soc. Rev.*, **2004**, *33*, 313-328. b) Sutcliffe, O. B.; Bryce, M. R. *Tetrahedron Asymm*., **2003**, *14*, 2297-2325. c) Debroy, P.; Roy, S. *Coord. Chem. Rev.*, **2007**, *251*, 203-221.
2. a) Daeneke, T.; Kwon,T.-H.; Holmes, A.; Duffy, N.; Bach, U.; Spiccia, L. *Nature Chem.*, **2011**, *3*, 211–215. b) Nemykin, V.; Rohde**,** G**.**; Barrett, C.; Hadt, R.; Sabin, J.; Reina**,** G.; Galloni, P.; Floris, B. *Inorg. Chem*., **2010**, *49*, 7497–7509.
3. Bayly, S. R.; Beer P. D. *Struct. Bond.*, **2008**, *129*, 45–94.
4. Buchanan, J. G.; Sable, H. Z. In *Selective Organic Transformations*; Thyagarajan, B. S., Ed.; Wiley-Interscience: New York, 1972; Vol. 2, 1–95.
5. Dong, T.-Y.; Lai, L.-L. *J. Organomet. Chem.*, **1996,** *509***,** 131–134**.** Butler, I. R.; Cullen, W. R. *Can. J. Chem.*, **1983**, *61*, 147–153.
6. Dai, L.-X; Tu, T.; You, S.-L.; Deng, W.-P.; Hou, X.-L. *Acc. Chem. Res.*, **2003**, *36*, 659–667.
7. Zhang, W.; Yoneda,Y.; Kida, T.; Nakatsuji, Y.;Yohji, N.; Ikeda, I. *Tetrahedron Asymm.*, **1998**, *9*, 3371–3380.
8. Argyropoulos, N.; Coutouli-Argyropoulos, E. *J. Organomet. Chem.*, **2002**, *654*, 117–122.
9. In the preparation of neutral receptor systems based on ferrocene the selective hydrolysis of dimethyl 1,1'-ferrocenedicarboxylate was shown to produce the monoester, see Li, C.; Medina, J. C.; Maguire, G. E. M.; Abel, E.; Atwood, J. L.; Gokel, G. W. *J. Am. Chem. Soc*., **1997**, *119*, 1609–1618.
10. Batsanov, A. S.; Hérault, D.; Howard, J. A. K.; Patrick, L. G. F.; Probert, M. R.; Whiting, A. *Organometallics*, **2007**, *26*, 2414–2419.
11. Toma, S.; Sališová, M.; Solčániová, E. *J. Organomet. Chem.*, **1975** *90*, 335–341.
12. a) Kono, H.; Shiga, M.; Motoyama I.; Hata, K. *Bull. Chem. Soc. Jpn.*, **1979**, *43*, 1435–1439; b) Solčániová, E.; Toma, S.; Fiedlerová, A. *Org. Magn. Res.*, **1980**, *14*, 181–185.
13. Gyömöre, Á.; Csámpai, A. *J. Organomet. Chem.*, **2011**, *696*, 1626–1631.
14. Krohnke, F. *Synthesis*, **1976**, 1–24.
15. Constable, E. C.; Edwards, A. J.; Martínez-Máñez, R.; Raithby, P. R.; Cargill Thompson, A. M. W. *J. Chem. Soc., Dalton Trans.*, **1994**, 645–650.
16. Braterman, P.; Song, J.-I.; Peacock, R. *Inorg. Chem.*, **1992**, *31*, 555–559.
17. Maciejewski, A.; Jaworska-Augustyniak, A.; Szeluga, Z.; Wojtczak, J.; Karolczak, *J. Chem. Phys. Lett.*, **1988**, *153*, 227–232.
18. Constable, E. C.; Housecroft, C. E.; Neuburger, M.; Phillips, D.; Raithby, P. R.; Schofield, E.; Sparr, E.; Tocher, D. A.; Zhender, M.; Zimmermann, Y. *J. Chem. Soc., Dalton Trans.*, **2000**, 2219–2228.
19. a) Venkatapuram, P.; Boggu, J. M. R.; Akula, B.; Katta, V. R.; Dandu, B. R. *Molecules*, **2000**, *5*, 1281–1286; b) Hajime, N.; Koichi, T.; Ikua, U. *Chem. Pharm. Bull.*, **1992**, *40*, 858–863; c) Shujian, Q.; Kehui, S.; Hongyin, G.; Qiancai, L.; Hong, W. *Molecules*, **2007**, *12*, 988–996.
20. a) Yamane, H.; Sugawara, J.; Suzuki, Y.; Shimamura, E.;Takahash, N. *Agric. Biol. Chem.*, **1980**, *44*, 2857–2864; b) Xiang, J.-N.; Nambi P.; Ohlstein, E. H.; Elliott, J. D. *Bioorg. Med. Chem.*, **1998**, *6*, 695–700.
21. The alternative ring closure product is from a lactonization of the ketodiester intermediate. There is no obvious mechanism to convert this derivative into the final product.

Supplementary Material

Details of the synthesis of the compounds and their NMR spectra; absorption spectrum for the light-driven reaction; X-ray crystallographic data. Full crystallographic data for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 991073 and 991074. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).