Enantioselective Synthesis of Ferrocenyl Nucleoside Analogs with Apoptosis-Inducing Activity

Philippe James[†], Jörg Neudörfl[†], Moritz Eißmann[‡], Patrick Jesse[‡], Aram Prokop[‡]*, and Hans-Günther Schmalz[†]*

[†]*Institute of Organic Chemistry, University of Cologne, Greinstr. 4, 50939 Köln, Germany*

[‡]*Department of Pediatric Oncology/Hermatology, University Medical Center Charité, Campus Virchow, Humboldt University of Berlin, 13353 Berlin, Germany*

schmalz@uni-koeln.de

Supporting Information

Contents: experimental procedures and full characterization of new compounds (**6-11**, **13-18**); X-ray crystallographic data for compounds **6** and **15**; ^{1}H and ^{13}C NMR spectra.

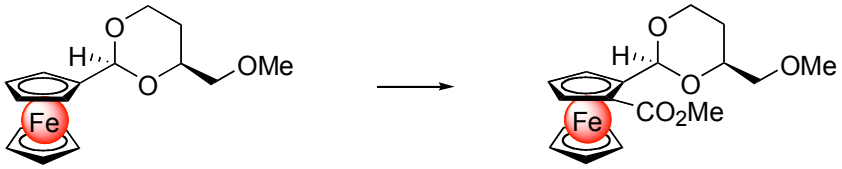
I. General experimental conditions

Reactions were conducted in flame-dried glassware under an atmosphere of argon using freshly distilled anhydrous solvents. NMR spectra were recorded at 300 MHz for protons and at 75 MHz for carbons. Deuterated chloroform was used as solvent unless otherwise indicated. Proton shifts are reported in ppm (δ) downfield from TMS and were determined by reference to the residual solvent peaks ($CDCl_3$: 7.24 ppm, CD_3OD: 3.31 ppm). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), hexet (hex) and multiplet (m)], coupling constants [Hz], integration, assignment). ^{13}C NMR spectra were recorded using an APT sequence with complete proton decoupling. Multiplicities (C, CH_2 or CH, CH_3) were deduced from these spectra. ^{13}C chemical shifts are reported in ppm (δ) relative to solvent resonance as the internal standard ($CDCl_3$: 77 ppm, CD_3OD: 49.05 ppm). Melting points are not corrected. Optical rotations were recorded at the given wavelengths (path length 100 mm).

The TMS-protected nucleobases $(TMS)_2$cytosine and $(TMS)_2$uracil, respectively, were prepared from cytosine or uracil by treatment with an excess of HMDS and TMSCl at 80°C for 2 d and isolation of the product by distillation under reduced pressure (0.1 torr).

II. Synthetic procedures and characterization of the new products

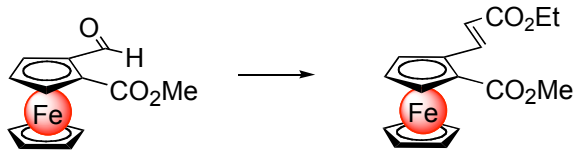
II.1. Synthesis of ester 5 through diastereoselective ortho-deprotonation/alkylation.



4 **5**

To a cooled solution of **4**[1] ($[\alpha]^{20}_{D}$ -32.4, *c* 0.70, $CHCl_3$, $[\alpha]^{20}_{D(lit.)}$[1] -32.5; 4.03 g, 1 equiv., 12.75 mmol) in dry diethyl ether (65 mL) under argon atmosphere was added dropwise at -78°C a 1.5 M solution of *t*-BuLi in hexanes (9.4 mL, 1.1 equiv., 14.02 mmol). After 10 min. at this temperature, the cooling bath was removed and the temperature was allowed to warm to room temperature and stirred 1 h. The suspension was then cannulated to an other apparatus in an additional funnel which was fixed onto a three-necked round-bottom flask (with thermometer and line to argon/vacuum) containing an excess of methyl chloroformate (9.9 mL, 10 equiv., 128 mmol) in ether (10 mL) maintained at a temperature of –50°C. The suspension was then added dropwise slowly to the stirred solution of electrophile. After the addition, the temperature was allowed to warm slowly to room temperature and was stirred overnight at this temperature. The mixture was then quenched with water and the layers were separated. The organic layer was washed with saturated aqueous NH_4Cl solution, brine, dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography (cyclohexane/ethyl acetate 2:1) gave the desired ester **5**[1] as a brown oil (3.27 g, 69 %; $[\alpha]^{20}_{D}$ +19.9, *c* 0.53, $CHCl_3$, $[\alpha]^{20}_{D(lit.)}$[1] +9.0).

II.2. Synthesis of ester 6 through Horner olefination.



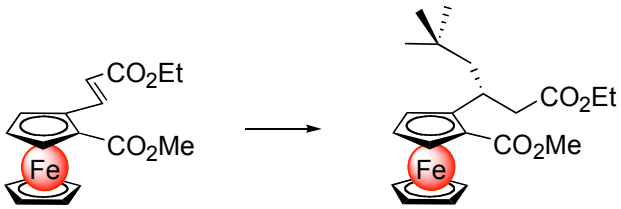
A **6**

The aldehyde **A** was obtained from **5** through acidic acetal cleavage according to Kagan's procedure[1] ($[\alpha]^{20}_{D}$ +935, *c* 0.355, $EtOH_{abs}$, $[\alpha]^{20}_{D(lit.)}$[1] +765, $[\alpha]^{20}_{D(lit.)}$[2] -759, (*R*)-config.). Transformation of **A** into the diester **6** was achieved as follow. To a suspension of NaH (60%

[1] Riant, O.; Samuel, O.; Flessner, T.; Taudien, S .; Kagan, H. B. *J. Org. Chem.* **1997**, *62*, 6733.
[2] Rapic, V.; Schlögl, K.; Steinitz, B. *Monatsh. Chem.* **1977**, *108*, 767.

in mineral oil, washed with dry hexane, 529 mg, 1.5 equiv., 13.21 mmol) in THF (37 mL) under argon atmosphere was added at 0°C, triethylphosphonoacetate (2.6 mL, 1.5 equiv., 13.21 mmol) and the resulting mixture was allowed to warm to room temperature and stirred 1 h. After this period, the aldehyde **A** (2.4 g, 1 equiv., 8.81 mmol) dissolved in THF (16 mL) was added to the mixture. The reaction mixture was stirred at room temperature for another 30 min and the reaction was quenched with a solution of saturated NH_4Cl. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 and filtered. Evaporation of the solvents and purification by flash chromatography (cyclohexane/ethyl acetate 3/1) of the residue afforded a dark red oil which solidifies (2.5 g, 83% yield). **Mp** (CH_2Cl_2) +84°C. **$[\alpha]^{20}_D$** +1297.0 (*c* 0.41, $CHCl_3$). **IR** (neat) ν 3095 (w), 2978 (m), 2948 (m), 2902 (w), 1711 (C=Ost, s), 1694 (C=Ost, s), 1623 (s), 1449 (s), 1419(s), 1367 (s), 1266 (s), 1216 (s), 1170 (s), 1082 (s), 1038 (s), 984 (s), 939 (m), 857 (s), 820 (s), 776 (s), 732 (m), 678 (w) cm^{-1}. **^{1}H NMR** δ 8.26 (d, J = 16.0, 1H, C*H*=CHCO$_2$Et), 6.13 (d, J = 16.0, 1H, CH=C*H*CO$_2$Et), 4.97 (m, 1H, CHCp), 4.77 (m, 1H, CHCp), 4.56 (t, J = 2.7, 1H, CHCp), 4.20 (q, J = 7.1, 2H, C*H*$_2$CH$_3$), 4.17 (s, 5H, Cp), 3.82 (s, 3H, CH$_3$O), 1.31 (t, J = 7.1, 3H, C*H*$_3$CH$_2$). **^{13}C NMR** δ 171.7 (CpC=O), 166.8 (CH=CH*C*=O), 143.7 (*C*H=CHCO$_2$Et), 117.4 (CH=*C*HCO$_2$Et), 80.3 (CCp), 73.6 (CHCp), 72.0 (CHCp), 71.4 (Cp), 71.2 (CCp), 69.3 (CHCp), 60.2 (*C*H$_2$CH$_3$), 51.7 (CH$_3$O), 14.3 (*C*H$_3$CH$_2$). **MS** (EI, 70 eV) *m/z* 343 ([M+1]$^{+\cdot}$, 5), 342 ([M]$^{+\cdot}$, 30), 329 (17), 328 (96), 297 (6), 277 ([M-Cp]$^{+\cdot}$, 3), 263 (13), 245 (12), 233 (16), 231 (67), 201 (20), 152 (23), 145 (78), 122 (60), 117 (85), 89 (100), 56 ([Fe]$^{+\cdot}$, 45). **HRMS** (EI, 70 eV) calcd. for $C_{17}H_{18}FeO_4$ 342.0554. Found 342.055.

II.3. Synthesis of 7 through conjugate cuprate addition

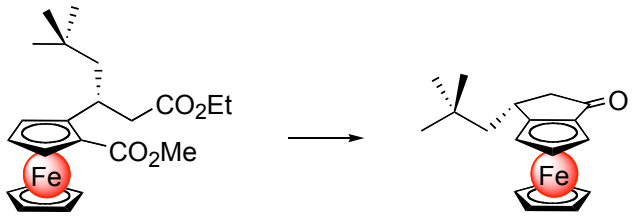


6 **7**

To a mixture of magnesium turnings (988 mg, 1.2 equiv., 40.65 mmol) in dry THF (10 mL) was added under argon atmosphere a small iodine crystal. After activation, 1-bromo-2,2-dimethylpropane (4.3 mL, 1 equiv., 33.88 mmol) in THF (24 mL) was added dropwise so as to maintain a gentle reflux and the mixture was stirred overnight at room temperature. The resulting 1 M solution of 2,2-dimethylpropanemagnesium bromide in THF (12.5 mL, 6

equiv., 12.5 mmol) was added dropwise at –78°C to a mixture of CuBr.Me_2S (257 mg, 0.6 equiv., 1.25 mmol) in THF (3 mL) under argon atmosphere. The temperature was allowed to warm to –30°C for 10 min to give a white slurry and was recooled to –78°C. TMSCl (530 µL, 2 equiv., 4.15 mmol) and then the α,β-unsaturated ferrocenylester **6** (710 mg, 1 equiv., 2.07 mmol) in THF (9.1 mL) were added dropwise successively. The mixture was stirred for 1 h at low temperature (below –60°C) and allowed to warm slowly to –30°C, stirred 1 h at this temperature and finally warm to 0°C. Saturated aqueous NH_4Cl solution was added and the product was extracted with MTBE. The organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography (cyclohexane/ethyl acetate 10/1 then 6/1 and then 3/1) gave **7** as a brown oil (839 mg, 2.03 mmol, 98 % yield). **$[\alpha]^{20}_D$** -24.5 (*c* 0.375, $CHCl_3$). **IR** (neat) *ν* 3095 (w), 2949 (m), 2901 (w), 1731 (C=Ost, s), 1713 (C=Ost, s), 1451 (m), 1365 (m), 1292 (m), 1210 (m), 1189 (m), 1147 (m), 1085 (m), 1033 (m), 818 (w), 776 (w) cm^{-1}. **^{1}H NMR** *δ* 4.64 (dd, *J* = 2.6, 1.5, 1H, C*H*CH_2CO_2Et), 4.21 (t, *J* = 2.6, 1H, CHCp), 4.17 (m, 2H, CHCp), 4.09 (q, *J* = 7.1, 2H, C*H*$_2CH_3$), 4.04 (s, 5H, Cp), 3.70 (s, 3H, CH_3O), 3.04 (dd, *J* = 15.8, 4.4, 1H, C*H*HCO_2Et), 2.60 (dd, *J* = 15.7, 8.7, 1H, CH*H*CO_2Et), 1.42 (dd, *J* = 14.0, 5.4, 1H, C*H*$HC(CH_3)_3$), 1.30 (m, 1H, CH*H*$C(CH_3)_3$), 1.20 (t, *J* = 7.1, 3H, C*H*$_3CH_2$), 0.66 (s, 9H, $(CH_3)_3C$). **^{13}C NMR** *δ* 172.8 (C=O), 172.3 (C=O), 99.9 (*C*CpC=O), 70.6 (CHCp), 70.1 (Cp), 69.4 (CHCp), 69.1 (CHCp), 68.5 (*C*CpCH), 60.3 (CH_2O), 52.2 (CH_2CO_2Et), 51.3 (CH_3O), 44.1 (CH_2*t*-Bu), 31.1 ($C(CH_3)_3$), 30.0 ($C(CH_3)_3$), 29.1 ($CHCH_2CO_2Et$), 14.3 (CH_3CH_2). **MS** (EI, 70 eV) m/z = 415 ($[M+1]^{+\cdot}$, 25), 414 ($[M]^{+\cdot}$, 100), 343 ($[M-(CH_2$*t*-Bu)$]^{+\cdot}$, 2), 297 (8), 257 (11), 239 (8), 175 (13), 121 ($[FeCp]^{+\cdot}$, 22), 105 (14), 91 (14), 57 (32). **HRMS** (EI, 70 eV) calcd. for $C_{22}H_{30}FeO_4$ 414.1493. Found 414.149.

II.4. Synthesis of ketone 8 by Dieckmann cyclization



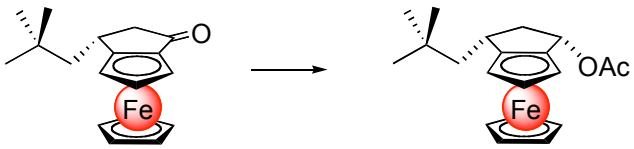
7 **8**

General procedure: To a suspension of NaH (60% in mineral oil, washed with dry hexane, 4 equiv.) in THF (2.5 mL/mmol) under argon atmosphere was added the diester (1 equiv.) in THF (25 mL/mmol) at room temperature. The orange mixture was then stirred under reflux for 7 h. The obtained dark red solution was cooled in an ice bath, MeOH was added slowly,

and then MTBE. The organic layer was washed with a 1 M aqueous solution of HCl then with brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was directly used for the next step without further purification.

Following the general procedure described above, the diester **7** (832 mg, 2.01 mmol) and NaH (321 mg, 8.03 mmol) were reacted. The crude product (2.01 mmol) was dissolved in ethanol (20 mL) and a 1 M solution of NaOH (20 mL) was added. The mixture was heated at +80°C and stirred overnight at this temperature. After cooling to room temperature, MTBE was added and the layers were separated. The aqueous layer was extracted with MTBE and the organic layers were combined. After washing with brine, the solution was dried over Na_2SO_4, filtered, and concentrated under vacuum. Purification by flash chromatography (cyclohexane/ethyl acetate 3/1) afforded **8** as a red oil which then solidified (393 mg, 63% yield, 2 steps). **Mp:** +82.2-82.8°C. **$[\alpha]^{20}_D$** +213.6 (*c* 0.355, $CHCl_3$). **IR** (neat) ν 3095 (w), 2950 (m), 2906 (w), 2863 (w), 1699 (C=Ost, s), 1461 (m), 1363 (m), 1291 (m), 1196 (w), 1106 (m), 1073 (w), 1001 (w), 821 (m) cm^{-1}. **^{1}H NMR** δ 4.58 (m, 1H, CpH), 4.49 (m, 1H, CpH), 4.38 (m, 1H, CpH), 4.18 (s, 5H, Cp), 3.00-2.80 (m, 3H, C*H*C*H*$_2$C=O), 1.93 (dd, *J* = 13.7, 2.4, 1H, CH*H*t-Bu), 1.60 (dd, *J* = 14.0, 8.5, 1H, C*H*Ht-Bu), 0.95 (s, 9H, *t*-Bu). **^{13}C NMR** δ 207.2 (C=O), 111.3 (*C*CpC=O), 79.8 (CCp), 75.2 (CHCp), 70.1 (Cp), 65.2 (CHCp), 61.0 (CHCp), 51.8 (CH_2), 50.8 (CH_2), 30.9 (*C*(CH_3)$_3$), 29.9 (C(*C*H$_3$)$_3$), 29.5 (CH). **MS** (EI, 70 eV) *m/z* 311 ($[M+1]^{+\cdot}$, 22), 310 ($[M]^{+\cdot}$, 100), 282 ($[M-(CO)]^{+\cdot}$, 3), 267 ($[M-(CO)-(CH_3)]^{+\cdot}$, 5), 253 ($[M-(t\text{-}Bu)]^{+\cdot}$, 9), 239 ($[(M-(t\text{-}Bu)-(CH_2)]^{+\cdot}$, 35), 226 (21), 225 ($[M-(CO)-(t\text{-}Bu)]^{+\cdot}$, 43), 211 ($[M-(CO)-(CH_2t\text{-}Bu)]^{+\cdot}$, 22), 186 ($[FeCp_2]^{+\cdot}$, 6), 153 (17), 133 (17), 121 ($[FeCp]^{+\cdot}$, 58), 56 ($[Fe]^{+\cdot}$, 32). **HRMS** (EI, 70 eV) calcd. for $C_{18}H_{22}FeO$ 310.1020. Found 310.102. **Elem. Anal.** calcd. for $C_{18}H_{22}FeO$ C 69.69, H 7.15. Found C 69.54, H 7.11.

II.5. Synthesis of 9 through reduction and acetylation



8 **9**

General Procedure: The α-ferrocenylketone (1 equiv.) was dissolved in a 4:1 mixture of ethanol:dioxane. $NaBH_4$ (5 equiv.) was then added slowly in portions at room temperature. Conversion into the corresponding alcohol was easily observed by the change of the color of the solution, from red to yellow. An aqueous solution of NH_4Cl was then added at 0°C and the alcohol was extracted with MTBE. The organic layer was washed with brine, dried over

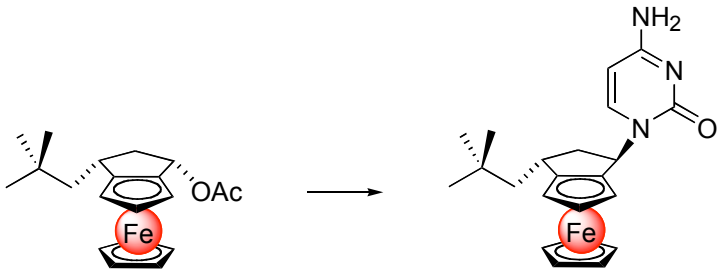
Na_2SO_4, filtered and concentrated under vacuum. Crude products were pure enough to be directly used for the next step without further purification. The obtained α-ferrocenylalcohol (1 equiv.) was dissolved in dry pyridine (6 mL/mmol) under argon atmosphere and acetic anhydride (2.3 mL/mmol) was added dropwise. After stirring overnight at room temperature, a saturated aqueous solution of NH_4Cl was added. The acetate was extracted with CH_2Cl_2 and the organic layer was washed successively with saturated aqueous $NaHCO_3$ and brine. The organic solution was then dried with Na_2SO_4, filtered and concentrated under vacuum. Purification by flash chromatography afforded the corresponding acetate.

Following the general procedure described above, ketone **8** was converted into the acetate **9** using the following amounts of starting materials and reagents: ketone **8** (105 mg, 1 equiv., 0.34 mmol), MeOH:dioxane (2 mL:500 µL), $NaBH_4$ (64 mg, 5 equiv., 1.70 mmol). After 30 min and classical work-up, the alcohol (96 mg, d.r ≥ 92:8) was used without further purification. It was then reacted in pyridine (2mL) with acetic anhydride (780 µL), 5h, rt. Purification by flash chromatography (cyclohexane/ethyl acetate 9/1) afforded **9** as a yellow oil (110 mg, 0.31 mmol, 90% over 2 steps). $\mathbf{[\alpha]^{20}_D}$ -117.5, $[\alpha]^{20}_{365}$ -257.3, $[\alpha]^{20}_{546}$ -148.1 (*c* 0.34, $CHCl_3$). **IR** (neat) ν 3093 (w), 2952 (m), 2865 (w), 1737 (C=Ost, s), 1473 (w), 1365 (m), 1237 (s), 1105 (m), 1037 (m), 816 (m) cm^{-1}. **^{1}H NMR** δ 5.44 (t, *J* = 7.5, 1H, CHOAc), 4.27 (s, 5H, Cp), 4.13 (m, 1H, CHCp), 4.02 (m, 1H, CHCp), 3.92 (m, 1H, CHCp), 2.85 (m, 1H, C*H*HCHOAc), 2.43 (m, 1H, C*H*CH_2*t*-Bu), 2.19 (s, 3H, CH_3CO), 2.10 (m, 1H, CH*H*CHOAc), 1.88 (dd, *J* = 14.0, 3.3, 1H, C*H*H*t*-Bu), 1.58 (dd, *J* = 14.0, 7.6, 1H, CH*Ht*-Bu), 1.00 (s, 9H, *t*-Bu). **^{13}C NMR** δ 201.4 (C=O), 102.6 (CCp), 92.2 (CCp), 73.0 (CHOAc), 69.9 (CHCp), 68.6 (Cp), 60.3 (CHCp), 59.9 (CHCp), 50.1 (CH_2*t*-Bu), 45.0 (*C*H_2CHOAc), 31.5 (*C*HCH_2*t*-Bu), 30.8 (*C*$(CH_3)_3$), 30.0 ($(CH_3)_3$C), 21.1 (*C*H_3CO). **MS** (EI, 70 eV) *m/z* 355 ($[M+1]^{+\cdot}$, 5), 354 ($[M]^{+\cdot}$, 25), 294 (26), 237 (43), 180 (100), 121 ($[FeCp]^{+\cdot}$, 51), 103 (26), 57 (30). **HRMS** (EI, 70 eV) calcd. for $C_{20}H_{26}FeO_2$ 354.1282. Found 354.129.

II.6. General procedure for the synthesis of nucleosides using silylated nucleobases:

To a solution of the α-ferrocenylacetate (1 equiv.) and TMS-protected nucleobase (4 equiv.) in dry CH_2Cl_2 under argon atmosphere was added dropwise at 0°C TMSOTf (6 equiv.). The yellow solution was stirred in an ice bath for 0.5-1.5 h and then treated with a saturated solution of $NaHCO_3$. The phases were separated and the aqueous phase washed with CH_2Cl_2. The combined organic layers were then washed with brine, dried with Na_2SO_4, filtered and the solvent removed under vacuum. Purification was achieved by flash chromatography.

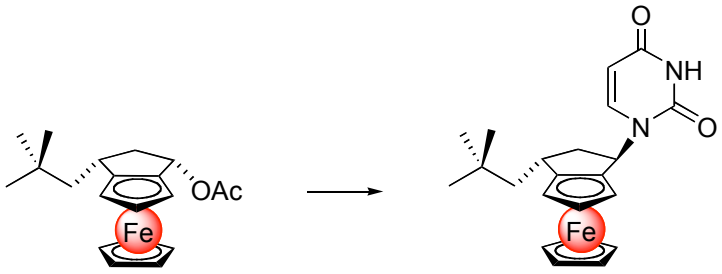
II.7. Synthesis of the cytosine derivative 10.



9 **10**

The general procedure for nucleobase introduction was used (see II.6.). Amounts: acetate **9** (194 mg, 1 equiv., 0.63 mmol), $(TMS)_2$cytosine (643 mg, 4 equiv., 2.50 mmol), in CH_2Cl_2 (14 mL), TMSOTf (685 µL, 6 equiv., 3.78 mmol), stirred for 1.5 h. Flash chromatography (ethyl acetate/methanol 95/5) afforded **10** as a yellow powder (205 mg, 0.51 mmol, 80% yield). **Mp:** decomposition starts at T>200°C. $[\alpha]^{20}_D$ –203 (*c* 0.29, $CHCl_3$). **IR** (neat) ν 3345 (NHst, m), 3201 (NHst, m), 3092 (w), 2949 (m), 2860 (w), 1643 (C=Ost, s), 1522 (m), 1484 (s), 1395 (m), 1275 (m), 1105 (w), 1030 (w), 999 (w), 788 (m), 751 (w) cm^{-1}. **^{1}H NMR** δ 6.73 (d, J = 7.0, 1H, NC*H*=CHC), 5.67 (d, J = 6.2, 1H, NCH=C*H*C), 5.60 (d, J = 6.6, 1H, CHcytosine), 4.20 (m, 1H, CHCp), 4.17 (s, 5H, Cp), 4.85 (m, 1H, CHCp), 4.04 (m, 1H, CHCp), 2.61 (m, 1H, C*H*HCHcytosine), 2.40 (m, 2H, C*H*CH*H*CHcytosine), 1.80 (d, J = 13.7, 1H, C*H*H*t*-Bu), 1.45 (dd, J = 13.4, 6.3, 1H, CH*Ht*-Bu), 0.91 (s, 9H, *t*-Bu). **MS** (EI, 70 eV) *m/z* 406 ($[M+1]^{+\cdot}$, 2), 405 ($[M]^{+\cdot}$, 7), 295 ($[M-(cytosine)]^{+\cdot}$, 22), 294 (100), 238 ($[M-(cytosine)-(t-Bu)]^{+\cdot}$, 19), 237 (62), 232 (13), 231 (51), 172 (11), 137 (21), 121 ($[FeCp]^{+\cdot}$, 52), 103 (18), 69 (12), 57 (16), 56 ($[Fe]^{+\cdot}$, 19). **HRMS** (EI, 70 eV) calcd. for $C_{22}H_{27}FeN_3O$ 405.1503. Found 405.150.

II.8. Synthesis of the uracil derivative 11.

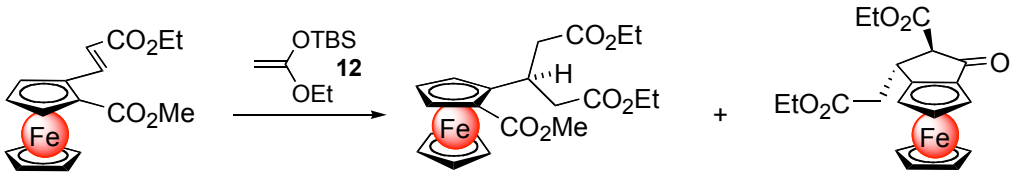


9 **11**

The general procedure for nucleobase introduction was used (see II.6.). Amounts: acetate **9** (64 mg, 0.21 mmol), $(TMS)_2$uracil (213 mg, 0.83 mmol), in CH_2Cl_2 (4.7 mL), TMSOTf (230 µL, 1.26 mmol), stirred for 0.5 h. Flash chromatography (ethyl acetate/methanol 1/1) afforded **11** as a yellow-orange powder (61 mg, 0.15 mmol, 72% yield). **Mp:** decomposition starts when T>220°C. $[\alpha]^{20}_D$ -179, $[\alpha]^{20}_{546}$ –242 (*c* 0.38, $CHCl_3$). **IR** (neat) ν 3263 (NHst, w), 3094

(w), 2951 (w), 2863 (w), 1692 (C=Ost, s), 1680 (C=Ost, s), 1462 (w), 1377 (w), 1364 (w), 1258 (m), 1213 (w), 1175 (w), 1105 (w), 1000 (w), 815 (w), 765 (w) cm^{-1}. **^{1}H NMR** δ 9.40 (br s, 1H, NH), 6.65 (d, J = 8.0, 1H, NC*H*=CHCO), 5.63, (d, J = 6.5, 1H, CHN), 5.49 (d, J = 8.0, 1H, NCH=C*H*CO), 4.23 (br s, 1H, CHCp), 4.19 (s, 5H, Cp), 4.13 (br s, 1H, CHCp), 4.07 (br s, 1H, CHCp), 2.70 (m, 1H, CH*H*CHN), 2.51 (m, 1H, C*H*CH_2*t*-Bu), 2.43 (m, 1H, C*H*HCHN), 1.83 (dd, J = 13.9, 2.5, 1H, C*H*H*t*-Bu), 1.50 (dd, J = 14.0, 7.1, 1H, CH*H*t-Bu), 0.95 (s, 9H, *t*-Bu). **^{13}C NMR** δ 163.5 (C=O), 151.0 (NHC=ON), 140.9 (N*C*H=CHCO), 103.3 (CCp), 101.5 (NCH=*C*HCO), 86.9 (CCp), 71.5 (CHCp), 69.4 (Cp), 61.9 (CHCp), 61.7 (CHCp), 57.3 (CHN), 50.0 (*C*H_2*t*-Bu), 48.0 (*C*H_2CHN), 31.9 (*C*HCH_2*t*-Bu), 30.9 (*C*$(CH_3)_3$), 30.1 (CH_3). **MS** (EI, 70 eV) *m/z* 407 ($[M+1]^{+\cdot}$, 13), 406 ($[M]^{+\cdot}$, 47), 295 ($[M-(uracil)]^{+\cdot}$, 18), 294 (64), 238 ($[M-(uracil)-(t-Bu)]^{+\cdot}$, 32), 237 (72), 172 (21), 121 ($[FeCp]^{+\cdot}$, 100), 103 (48), 57 (16). **HRMS** (EI, 70 eV) calcd. for $C_{22}H_{26}FeN_2O_2$ 406.1343. Found 406.134.

II.9. Synthesis of 13 and 14a through Mukaiyama-Michael addition.



6 **13** **14a**

To a solution of trifluoromethanesulfonic acid (150 µL, 0.57 equiv., 1.66 mmol) in CH_2Cl_2 (15.3 mL) under argon atmosphere was added dropwise at –78°C a 2 M solution of $AlMe_3$ in toluene (290 µL, 0.20 equiv., 0.58 mmol). After 5 min at this temperature, the mixture was stirred 30 min at room temperature. The mixture was then recooled to –78°C and the ester **6** (1 g, 1 equiv., 2.92 mmol) in CH_2Cl_2 (9.5 mL) was added dropwise, followed by the addition of the silylenolether **12**[3] (930 mg, 1.57 equiv., 4.58 mmol) in CH_2Cl_2 (9.5 mL). The solution was stirred for 2.5 h at –78°C[4] and MeOH was then added. After warming to 0°C, saturated NH_4Cl was added and the layers were separated. The aqueous layer was washed with CH_2Cl_2 and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. Purification by flash chromatography (cyclohexane/ethyl acetate 3/1) afforded the addition product **13** as an orange oil (635 mg, 58%) and the cyclized product **14a** as a dark red oil (397 mg, 34%, 92% global yield).[4]

[3] Kita, Y.; Segawa, J.; Haruta, J.-i.; Yasuda, H.; Tamura, Y. *J. Chem. Soc., Prekin Trans. 1* **1982**, 1099.
[4] When the temperature was allowed to warm slowly to room temperature after 30 min. and stirred overnight at r.t., 43% of **14a** was isolated as a single diastereomer besides 47% of **13** (90 % global yield).

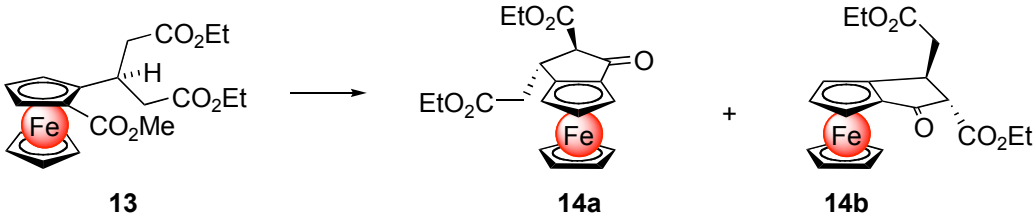
Data for addition product **13**:

[α]$^{20}_{D}$ -42.6, [α]$^{20}_{546}$ -52.4 (*c* 0.385, $CHCl_3$). **IR** (neat) *ν* 3092 (w), 2977 (m), 2948 (m), 1731 (C=Ost, s), 1711 (C=Ost, s), 1445 (m), 1370 (m), 1340 (w), 1293 (m), 1216 (m), 1158 (s), 1090 (m), 818 (w) cm^{-1}. **^{1}H NMR** *δ* 4.65 (s, 1H, CHCp), 4.16 (s, 2 H, CHCp), 4.05 (q, *J* = 7.1, 2H, C*H*$_2$CH$_3$), 4.02 (s, 5H, Cp), 3.90 (m, 1H, C*H*(CH_2CO$_2$Et)$_2$), 3.80 (q, *J* = 7.1, C*H*$_2$CH$_3$), 3.66 (s, 3H, CH_3O), 2.90 (dd, *J* = 15.4, 4.1, 1H, CHC*H*HCO$_2$Et), 2.78 (dd, *J* = 15.3, 9.7, 1H, CHCH*H*CO$_2$Et), 2.43 (m, 2H, CHC*H*$_2$CO$_2$Et), 1.17 (t, *J* = 7.1, 3H, C*H*$_3$CH$_2$), 0.99 (t, *J* = 7.1, 3H, C*H*$_3$CH$_2$). **^{13}C NMR** *δ* 172.0 (C=O), 171.8 (C=O), 171.3 (C=O), 93.5 (CCp), 70.5 (CHCp), 70.3 (CHCp), 69.9 (Cp), 69.0 (CHCp), 68.0 (CCp), 60.1 (CH_2O), 59.6 (CH_2O), 51.0 (CH_3O), 39.9 (*C*H$_2$CO$_2$Et), 37.9 (*C*H$_2$CO$_2$Et), 30.8 (*C*H(CH$_2$CO$_2$Et)$_2$), 13.9 (*C*H$_3$CH$_2$), 13.8 (*C*H$_3$CH$_2$). **MS** (EI, 70 eV) *m/z* 431 ([M+1]$^{+\cdot}$, 25), 430 ([M]$^{+\cdot}$, 100), 319 (17), 121 ([FeCp]$^{+\cdot}$, 24). **HRMS** (EI, 70 eV) calcd. for $C_{21}H_{26}FeO_6$ 430.1078. Found 430.108.

Data for cyclization product **14a**:

[α]$^{20}_{D}$ +309 (*c* 0.085, $CHCl_3$). **IR** (neat) *ν* 3105 (w), 2978 (w), 2928 (w), 1731 (C=Ost, s), 1703 (C=Ost, s), 1462 (w), 1425 (w), 1369 (w), 1327 (w), 1255 (m), 1154 (m), 1106 (w), 1026 (m), 822 (w) cm^{-1}. **^{1}H NMR** *δ* 4.64 (br s, 1H, CHCp), 4.55 (br s, 1H, CHCp), 4.41 (br s, 1H, CHCp), 4.19 (s, 5H, Cp), 4.15 (m, 4H, C*H*$_2$CH$_3$), 3.73 (d, *J* = 6.2, 1H, CHCO), 3.66 (m, 1H, C*H*CHCO), 2.90 (dd, *J* = 15.6, 6.9, 1H, C*H*HCHCHCO), 2.82 (dd, *J* = 15.8, 7.7, 1H, CH*H*CHCHCO), 1.23 (m, 6H, C*H*$_3$CH$_2$). **^{13}C NMR** *δ* 199.0 (C=O), 171.4 (C=O), 168.9 (C=O), 106.5 (CCp), 78.9 (CCp), 76.3 (CHCp), 70.5 (Cp), 66.2 (CHCp), 65.1 (*C*HCO$_2$Et), 61.9 (CHCp), 61.5 (*C*H$_2$CH$_3$), 60.9 (*C*H$_2$CH$_3$), 40.3 (*C*H$_2$CO$_2$Et), 34.0 (*C*HCH$_2$CO$_2$Et), 14.2 (*C*H$_3$CH$_2$). **MS** (EI, 70 eV) *m/z* 399 ([M+1]$^{+\cdot}$, 15), 398 ([M]$^{+\cdot}$, 68), 353 (21), 352 (45), 325 (12), 324 (39), 252 (20), 121 ([FeCp]$^{+\cdot}$, 100), 103 (36), 89 (62), 56 ([Fe]$^{+\cdot}$, 58). **HRMS** (EI, 70 eV) calcd. for $C_{20}H_{22}FeO_5$ 398.0816. Found 398.082.

II.10. Synthesis of 14a and 14b through group-selective Dieckmann cyclization.

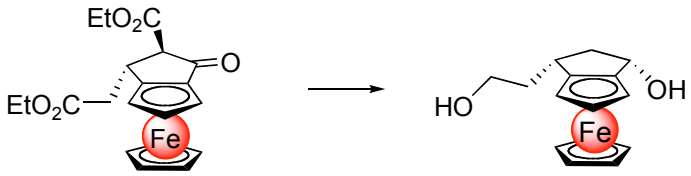


13 **14a** **14b**

Procedure A using LDA: To a solution of triester **13** (1.3 g, 1 equiv., 3.03 mmol) in THF (10 mL) under argon atmosphere was added dropwise at –78°C a solution of LDA in THF (prepared by a dropwise addition at –78°C of a 1.6 M solution of *n*-BuLi (2.1 mL, 1.1 equiv., 3.33 mmol) onto DIPA (515 µL, 1.2 equiv., 3.64 mmol) in THF (33 mL). The solution was then allowed to warm to 0°C for 15 min and used directly.). After the addition, the temperature was allowed to warm slowly to –60°C and was stirred overnight at this temperature. The reaction mixture was quenched at 0°C in an ice bath with a saturated aqueous solution of NH_4Cl. The two phases were separated and the aqueous layer was washed with MTBE. The combined organic layers were then washed with brine, dried over Na_2SO_4, filtered and the solvents were removed under vacuum. Purification by flash chromatography (cyclohexane/ethyl acetate 3/1) gave a 1:1 mixture of the two cyclized diastereoisomers **14a** and **14b** as a red oils (1.18 g, 2.97 mmol, 98%).

Procedure B using KH: To a mixture of KH (30% in oil, washed with dry hexane, 770 mg, 4 equiv., 5.75 mmol) in THF (10 mL) under argon atmosphere was added the diester **13** (620 mg, 1 equiv., 1.44 mmol) in THF (36 mL). The reaction mixture was refluxed for 1 h. The red solution was then cooled to 0°C and water was added slowly and then a 1.0 M solution of aqueous HCl. The layers were separated and the aqueous layer was washed with MTBE. The combined organic layers was washed with $NaHCO_3$, brine, dried over Na_2SO_4, filtered and concentrated under vacuum. Purification by flash chromatography (cyclohexane/ethyl acetate 3/1) gave a 89:11 mixture of the two cyclized diastereoisomers **14a** and **14b** (462 mg, 1.16 mmol, 81%).

II.11. Synthesis of diol 15 from 14a.

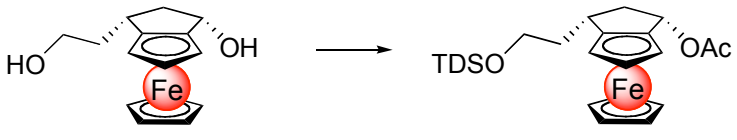


14a **15**

Under argon atmosphere, the diester **14a** (257 mg, 0.65 mmol) was dissolved in ethanol (10 mL) and to this solution was added at room temperature a 1 M aqueous solution of NaOH (10 mL). The mixture was then heated at +80°C overnight. After cooling, MTBE was added and the phases separated. The organic layer was washed with a 1.0 M solution of NaOH (3x). The combined aqueous layers were then acidified with a 2.0 M solution of HCl and the carboxylic

acid extracted with MTBE (3x). The combined MTBE extracts were finally washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford the intermediate mono-carboxylic acid. **MS** (EI, 70 eV) *m/z* 299 ($[M+1]^{+\cdot}$, 15), 298 ($[M]^{+\cdot}$, 100), 121 ($[FeCp]^{+\cdot}$, 23), 56 ($[Fe]^{+\cdot}$, 25). **HRMS** (EI, 70 eV) calcd. for $C_{15}H_{14}FeO_3$ 298.0292. Found 298.029. The crude carboxylic acid (173 mg, 1 equiv., 0.58 mmol) was dissolved in THF (5 mL) under argon atmosphere and the solution was cooled at 0°C. A 1 M solution of $LiAlH_4$ in ether (1.74 mL, 3 equiv., 1.74 mmol) was added dropwise. Temperature was allowed to warm slowly to room temperature and the mixture was stirred overnight at room temperature. An aqueous solution of NaOH 1N was then added carefully. The mixture was then filtered through a pad of celite, rinced many times with CH_2Cl_2 and the filtrate was concentrated under vacuum. Purification by flash chromatography (cyclohexane/ethyl acetate 1/1) afforded a yellow oil which solidifies (68 mg, 0.24 mmol, 41% for 2 steps). An analytical sample of **15** could be prepared by recristallization in 1,2-dichloroethane. **Mp** ($ClCH_2CH_2Cl$): +115-117°C. $\mathbf{[\alpha]^{20}_D}$ +16.5, $[\alpha]^{20}_{546}$ +21.6, (*c* 0.43, $CHCl_3$). **IR** (neat) ν 3327 (OHst, m), 3090 (w), 2922 (m), 2851 (m), 1725 (w), 1673 (w), 1447 (m), 1410 (m), 1327 (m), 1260 (s), 1104 (s), 1079 (s), 1040 (s), 1007 (s), 997 (s), 884 (m), 804 (s), 734 (m) cm^{-1}. **^{1}H NMR** δ 4.52 (q, *J* = 7.0, 1H, C*H*OH), 4.28 (s, 5H, Cp), 4.13 (br t, 1H, CHCp), 4.02 (d, *J* = 2.0, 1H, CHCp), 3.97 (d, *J* = 2.0, 1H, CHCp), 3.77 (t, *J* = 6.8, 2H, CH_2OH), 2.73 (dt, *J* = 12.1, 6.8, 1H, C*H*HCHOH), 2.44 (m, 1H, C*H*CH_2CH_2OH), 2.04 (hex, *J* = 6.8, 1H, C*H*H C H_2OH), 1.86 (m, 3H, CH*H*CHOH + CH*H*CH_2OH+ OH), 1.59 (br s, 1H, OH). **^{13}C NMR** δ 100.3 (CCp), 98.3 (CCp), 70.0 (CHCp), 69.3 (CHOH), 68.3 (Cp), 61.8 (CH_2OH), 60.7 (CHCp), 58.9 (CHCp), 47.1 (*C*H_2CHOH), 38.7 (*C*H_2CH_2OH), 32.2 (*C*HCH_2CH_2OH). **MS** (EI, 70 eV) *m/z* 313 ($[M+1]^{+\cdot}$, 17), 312 ($[M]^{+\cdot}$, 91), 284 (10), 247 ($[M-(Cp)]^{+\cdot}$, 23), 239 ($[M-(CH_2CO_2Me)]^{+\cdot}$, 18), 215 (24), 188 ($[M-(Cp)-(CO_2Me)]^{+\cdot}$, 7), 175 (19), 121 ($[FeCp]^{+\cdot}$, 100), 103 (31), 56 ($[Fe]^{+\cdot}$, 98).

II.12. Synthesis of 16 via selective mono-protection of 15.

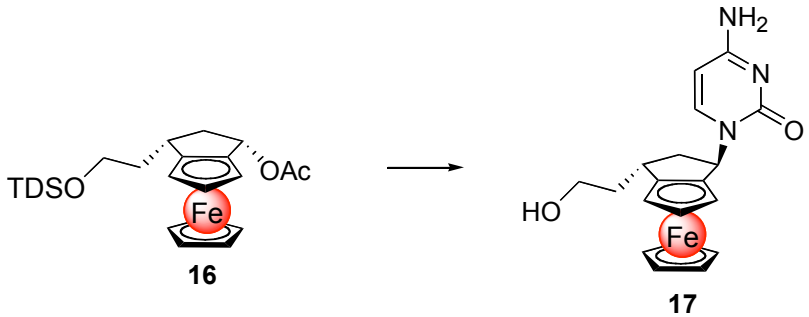


15 **16**

To a solution of diol **15** (80 mg, 1 equiv., 0.28 mmol) and DMAP (3.6 mg, 0.1 equiv., 0.03 mmol) in pyridine (2.8 mL) was added dropwise TDSCl (56 µL, 1 equiv., 0.28 mmol) under argon atmosphere. After 2 h at room temperature, water and then 1 N HCl were added successively. The product was extracted with MTBE and the organic phase was washed with

brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude alcohol was dissolved in dry pyridine (1.7 mL) under argon atmosphere and acetic anhydride (640 µL) was added dropwise. After stirring overnight at room temperature, a saturated aqueous solution of NH_4Cl was added. The acetate was extracted with MTBE and the organic layer was washed successively with saturated aqueous $NaHCO_3$ and brine. The organic solution was then dried with Na_2SO_4, filtered and concentrated under vacuum. Purification by flash chromatography (cyclohexane/ethyl acetate 4/1) afforded **16** as a yellow oil (113 mg, 0.24 mmol, 86% for 2 steps). **$[\alpha]^{20}_D$** -87.4, $[\alpha]^{20}_{546}$ -115.2, $[\alpha]^{20}_{365}$ -156.4 (*c* 0.385, $CHCl_3$). **IR** (neat) *ν* 2955 (m), 2860 (w), 1734 (C=Ost, s), 1463 (w), 1367 (w), 1237 (s), 1094 (s), 1036 (m), 816 (s), 776 (m), 613 (w) cm^{-1}. **^{1}H NMR** *δ* 5.44 (t, *J* = 7.3, 1H, CHOAc), 4.22 (s, 5H, Cp), 4.09 (t, *J* = 2.2, 1H, CHCp), 3.95 (d, *J* = 2.2, 1H, CHCp), 3.74 (d, *J* = 2.1, 1H, CHCp), 3.72 (t, *J* = 6.6, 2H, CH_2O), 2.74 (dt, *J* = 12.2, 7.0, 1H, C*H*HCHOAc), 2.53 (m, 1H, C*H*CH_2CH_2O), 2.15 (s, 3H, CH_3CO), 2.03 (m, 2H, CH*H*CHOAc + CH*H*CH_2O), 1.85 (m, 1H, C*H*HCH_2O), 1.63 (hep, *J* = 6.8, 1H, C*H*$(CH_3)_2$), 0.88 (d, *J* = 6.9, 6H, $(CH_3)_2$CH), 0.85 (s, 6H, $(CH_3)_2$C), 0.11 (s, 6H, CH_3Si). **^{13}C NMR** *δ* 170.9 (C=O), 101.1 (CCp), 93.0 (CCp), 72.6 (CHOAc), 69.9 (CHCp), 68.5 (Cp), 61.7 (CH_2O), 60.4 (CHCp), 60.2 (CHCp), 42.3 (CH_2CHOAc), 38.9 (CH_2CH_2O), 34.2 (CH$(CH_3)_2$), 31.8 (CH$(CH_2)_2O$), 25.1 (C$(CH_3)_2$), 21.0 (CH_3CO), 20.4 ((CH_3)$_2$CH), 18.5 ((CH_3)$_2$C), -3.34 (CH_3Si), -3.37 (CH_3Si). **MS** (EI, 70 eV) *m/z* 470 ($[M]^{+\cdot}$, 26), 410 (100), 250 (39), 133 (20). **HRMS** (EI, 70 eV) calcd. for $C_{25}H_{38}FeO_3Si$ 470.1940. Found 470.194.

II.13. Synthesis of the cytosine derivative 17.



The general procedure for nucleobase introduction was used (see II.6.). Amounts: acetate **16** (85 mg, 1 equiv., 0.18 mmol), $(TMS)_2$cytosine (186 mg, 4 equiv., 0.72 mmol), in CH_2Cl_2 (4 mL), TMSOTf (195 µL, 6 equiv., 1.08 mmol), stirred for 0.5 h. Flash chromatography (ethyl acetate/methanol 4/1) afforded the deprotected alcohol **17** as a major product, yellow solid (48 mg, 0.13 mmol, 75%) and a little amount of the TDS-protected ferrocenyl nucleoside analog

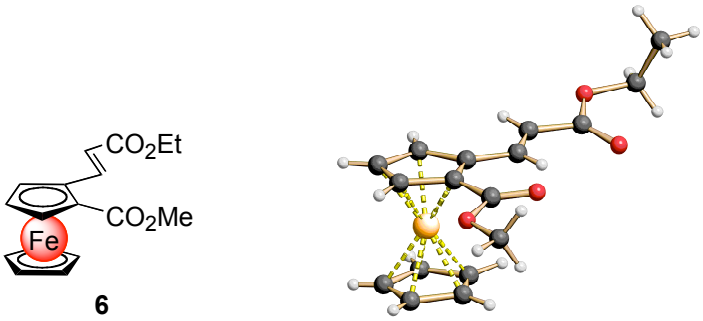
18, yellow solid (3 mg, 0.006 mmol, 3 %). **Mp:** decomposition at 240°C. **$[\alpha]^{20}_{D}$** -196, $[\alpha]^{20}_{546}$ –275 (*c* 0.255, EtOH). **IR** (neat) ν 3328 (OHst, m), 3180 (NHst, m), 2924 (w), 2860 (w), 1635 (C=Ost, s), 1602 (s), 1521 (m), 1482 (s), 1395 (m), 1276 (s), 1184 (w), 1105 (w), 1051 (w), 999 (w), 787 (m) cm^{-1}. **^{1}H NMR** (CD_3OD) δ 6.86 (d, J = 7.4, 1H, NC*H*=CHC), 5.70 (d, J = 7.4, 1H, NCH=C*H*C), 5.66 (d, J = 6.4, 1H, CHN), 4.29 (t, J = 2.2, 1H, CHCp), 4.25 (s, 5H, Cp), 4.20 (d, J = 2.2, 1H, CHCp), 4.18 (d, J = 2.2, 1H, CHCp), 3.73 (br t, 2H, C*H*$_2$OH), 2.72 (m, 2H, C*H*HCHN + C*H*CH_2CH_2OH), 2.35 (m, 1H, CH*H*CHN), 2.13 (hex, J = 6.6, 1H, C*H*HCH_2OH), 1.91 (hex, J = 6.8, 1H, CH*H*CH_2OH). **^{13}C NMR** (CD_3OD) δ 167.2 (NH_2-C=N), 159.0 (C=O), 143.3 (N*C*H=CHC), 103.1 (CCp), 95.7 (NCH=*C*HC), 90.0 (CCp), 76.6 (CHCp), 70.4 (Cp), 63.1 (CHCp), 62.8 (CHCp), 61.8 (CH_2OH), 59.0 (CHN), 46.5 (*C*H_2CHN), 39.4 (*C*$H_2$$CH_2$OH), 33.5 (*C*HC$H_2$$CH_2$OH). **MS** (EI, 70 eV) *m/z* 379 ($[M]^{+\cdot}$, 8), 314 ($[M\text{-}(Cp)]^{+\cdot}$, 2), 269 ($[M\text{-}(cytosine)]^{+\cdot}$ and/or $[M\text{-}(Cp)\text{-}(CH_2CH_2OH)]^{+\cdot}$, 21), 268 ($[M\text{-}(cytosine)\text{-}1]^{+\cdot}$ and/or $[M\text{-}(Cp)\text{-}(CH_2CH_2OH)\text{-}1]^{+\cdot}$, 100), 231 (27), 210 (17), 172 (19), 137 (18), 121 ($[FeCp]^{+\cdot}$, 43), 56 ($[Fe]^{+\cdot}$, 29). **HRMS** (EI, 70 eV) calcd. for $C_{19}H_{21}FeN_3O_2$ 379.0983. Found 379.098.

II.14. Synthesis of the cytosine derivative 18.

Under argon atmosphere, the alcohol **17** (32 mg, 1 equiv., 0.084 mmol), imidazole (14 mg, 2.4 equiv., 0.20 mmol) and DMAP (0.9 mg, 0.09 equiv., 0.008 mmol) were dissolved in dry DMF (800 µL). TDSCl (20 µL, 1.2 equiv., 0.100 mmol) was added dropwise and the mixture was stirred overnight at room temperature. Saturated aqueous NH_4Cl was then added and the product was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated under vacuum. Purification by flash chromatography (ethyl acetate then ethyl acetate/methanol 95/5) afforded **18** as a yellow powder (40 mg, 0.077 mmol, 92%). **Mp:** decomposition starts when T>200°C. **$[\alpha]^{20}_{D}$** -174, $[\alpha]^{20}_{546}$ –241 (*c* 0.30, $CHCl_3$). **IR** (neat) ν 3349 (w), 3146 (w), 3092 (w), 2953 (m), 2860 (m), 1643 (s), 1624 (s), 1517 (m), 1484 (s), 1392 (m), 1277 (m), 1249 (m), 1105 (m), 829 (m), 776 (m) cm^{-1}. **^{1}H**

NMR δ 6.68 (d, J = 7.7, 1H, NC*H*=CHC), 6.60-5.80 (br s, 2H, NH_2), 5.69 (d, J = 6.5, 1H, CHN), 5.52 (d, J = 7.3, 1H, NCH=C*H*C), 4.20 (t, J = 2.3, 1H, CHCp), 4.17 (s, 5H, Cp), 4.08 (d, J = 2.2, 1H, CHCp), 4.05 (d, J = 2.2, 1H, CHCp), 3.68 (t, J = 6.7, 2H, CH_2O), 2.61 (m, 2H, C*H*HCHN + C*H*CH_2CHN), 2.34 (dd, J = 12.3, 5.7, 1H, CH*H*CHN), 2.00 (hex, J = 6.6, 1H, C*H*HCH_2O), 1.82 (hex, J = 6.6, 1H, CH*H*CH_2O), 1.58 (sep, J = 7.0, 1H, C*H*$(CH_3)_2$), 0.83 (d, J = 6.8, 6H, $(CH_3)_2$CH), 0.81 (s, 6H, $(CH_3)_2$C), 0.08 (s, 3H, CH_3Si), 0.07 (s, 3H, CH_3Si). **^{13}C NMR** δ 165.3 (NH_2-C=N), 156.6 (C=O), 142.0 (N*C*H=CHC), 101.8 (CCp), 93.4 (NCH=*C*HC), 88.8 (CCp), 71.1 (CHCp), 69.2 (Cp), 61.7 (2×CHCp), 61.6 (CH_2O), 57.2 (CHN), 45.4 ($C$$H_2$CHN), 38.2 ($C$$H_2CH_2O$), 34.2 ($CH(CH_3)_2$), 32.0 ($CH(CH_2)_2O$), 25.1 ($C$$(CH_3)_2$), 20.4 (($C$$H_3)_2$CH), 18.5 (($C$$H_3)_2$C), -3.4 ($CH_3$Si). **MS** (EI, 70 eV) *m/z* 521 ($[M]^{+\cdot}$, 5), 411 ($[M\text{-(cytosine)}]^{+\cdot}$ and/or $[M\text{-(Cp)-}(CH_2CH_2OH)]^{+\cdot}$, 32), 410 ($[M\text{-(cytosine)-1}]^{+\cdot}$ and/or $[M\text{-(Cp)-}(CH_2CH_2OH)\text{-1}]^{+\cdot}$, 100), 250 (100), 231 (97), 168 (37), 121 ($[FeCp]^{+\cdot}$, 79), 73 (82). **HRMS** (EI, 70 eV) calcd. for $C_{27}H_{39}FeN_3O_2Si$ 521.2161. Found 521.216.

X-ray Crystallographic Data for Compound 6



6

Table 1. Crystal data and structure refinement for **6**.

Identification code	z_pj193
Empirical formula	C17 H18 Fe O4
Formula weight	342.16
Temperature	100(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P21
Unit cell dimensions	a = 9.7914(6) A alpha = 90 deg.
	b = 8.0967(3) A beta = 114.960(2) deg.
	c = 10.6853(7) A gamma = 90 deg.
Volume	767.99(7) A^3
Z, Calculated density	2, 1.480 Mg/m^3
Absorption coefficient	0.997 mm^-1
F(000)	356
Crystal size .	3 x .2 x .2 mm
Theta range for data collection	2.10 to 26.99 deg.
Limiting indices	-10<=h<=12, -8<=k<=10, -11<=l<=13
Reflections collected / unique	3908 / 3053 [R(int) = 0.0270]
Reflection observed [I>2sigma(I)]	2640
Completeness to theta = 26.99	99.6 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3053 / 1 / 249
Goodness-of-fit on F^2	0.967
Final R indices [I>2sigma(I)]	R1 = 0.0365, wR2 = 0.0669
R indices (all data)	R1 = 0.0465, wR2 = 0.0694
Absolute structure parameter	0.004(17)
Largest diff. peak and hole	0.268 and -0.310 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **6**.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Fe(1)	7111(1)	904(1)	2796(1)	18(1)
C(1)	1232(3)	736(4)	33(3)	17(1)
O(3)	793(2)	409(2)	906(2)	22(1)
O(4)	331(2)	1316(2)	-1236(2)	20(1)
O(5)	7519(3)	-2996(3)	4651(2)	26(1)
C(6)	5377(4)	-520(3)	1511(3)	16(1)
C(7)	3820(4)	-233(3)	1266(3)	16(1)
C(8)	6472(4)	-1484(4)	2603(4)	17(1)
C(9)	6225(4)	-2403(4)	3692(3)	20(1)
C(10)	2788(3)	554(4)	190(3)	19(1)
C(11)	7889(4)	-1347(4)	2510(4)	21(1)
O(12)	5024(3)	-2606(3)	3727(2)	32(1)
C(13)	7674(4)	-307(4)	1382(4)	23(1)
C(14)	6152(4)	195(4)	770(3)	20(1)
C(15)	7416(4)	-3924(5)	5762(3)	31(1)
C(16)	-1263(4)	1475(4)	-1547(4)	19(1)
C(1A)	-2054(4)	-159(4)	-1997(4)	29(1)
C(2A)	6207(5)	2757(4)	3499(4)	31(1)
C(3A)	8594(5)	1803(5)	4660(5)	45(1)
C(4A)	7128(5)	1785(4)	4585(4)	34(1)
C(5A)	8551(6)	2825(6)	3577(6)	55(2)
C(6A)	7079(6)	3422(5)	2869(5)	42(1)

Table 3. Anisotropic displacement parameters (A^2 x 10^3) for **6**.

The anisotropic displacement factor exponent takes the form:

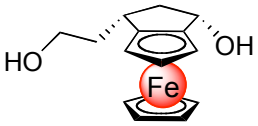
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
Fe(1)	16(1)	19(1)	19(1)	-2(1)	9(1)	-1(1)
C(1)	16(1)	13(2)	21(2)	-3(2)	7(1)	-2(2)
O(3)	18(1)	30(2)	21(1)	3(1)	10(1)	2(1)
O(4)	16(1)	25(1)	20(1)	6(1)	7(1)	2(1)
O(5)	28(1)	25(1)	22(1)	8(1)	8(1)	4(1)
C(6)	17(2)	19(2)	13(2)	-4(1)	7(1)	-4(1)
C(7)	17(2)	19(2)	14(2)	-3(1)	8(2)	-4(1)
C(8)	13(2)	19(2)	18(2)	-1(1)	4(2)	2(1)
C(9)	23(2)	15(2)	21(2)	-2(1)	9(2)	0(1)
C(10)	19(2)	22(2)	18(2)	1(1)	9(1)	-1(1)
C(11)	18(2)	23(2)	23(2)	-1(1)	10(2)	4(2)
O(12)	23(1)	40(1)	33(2)	12(1)	12(1)	-2(1)
C(13)	20(2)	30(2)	24(2)	-4(2)	16(2)	0(1)
C(14)	21(2)	25(2)	17(2)	-1(2)	11(2)	-1(1)
C(15)	43(2)	26(2)	20(2)	3(2)	10(2)	2(2)
C(16)	13(2)	21(2)	22(2)	4(1)	6(2)	3(1)
C(1A)	24(2)	25(2)	28(2)	1(2)	1(2)	-3(2)
C(2A)	28(2)	27(2)	38(2)	-13(2)	12(2)	3(2)
C(3A)	34(3)	35(2)	41(3)	-19(2)	-10(2)	5(2)
C(4A)	54(3)	24(2)	26(2)	-8(2)	20(2)	-6(2)
C(5A)	47(3)	49(3)	89(4)	-42(3)	49(3)	-33(2)
C(6A)	77(4)	15(2)	31(3)	-1(2)	20(3)	-6(2)

Table 4. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for **6**.

	x	y	z	U(eq)
H(15A)	7112	-3187	6327	46
H(15B)	8399	-4412	6336	46
H(15C)	6667	-4804	5377	46
H(1A1)	-1874	-594	-2770	44
H(1A2)	-3138	-7	-2289	44
H(1A3)	-1664	-940	-1225	44
H(1)	2990(30)	980(50)	-520(30)	24(7)
H(2)	5750(30)	880(50)	-20(30)	21(7)
H(3)	8850(40)	-1850(40)	3120(30)	24(9)
H(4)	-1400(30)	1810(30)	-760(30)	15(8)
H(5)	8440(40)	-100(40)	1140(30)	33(10)
H(6)	3590(40)	-670(40)	1900(30)	19(8)
H(7)	9510(50)	1070(70)	5290(40)	80(14)
H(9)	-1650(30)	2360(40)	-2320(30)	12(8)
H(3A)	5050(50)	2920(50)	3100(40)	64(13)
H(7A)	6810(50)	4130(60)	2090(40)	69(14)
H(5A)	6860(40)	1230(50)	5240(40)	46(11)
H(9A)	9240(60)	3050(60)	3400(50)	81(19)

X-ray Crystallographic Data for Compound 15



15

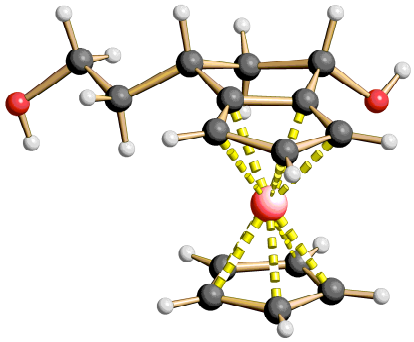


Table 5. Crystal data and structure refinement for **15**.

Identification code	pj213
Empirical formula	C15 H18 Fe O2
Formula weight	286.14
Temperature	100(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P212121
Unit cell dimensions	a = 7.8262(5) A alpha = 90 deg. b = 12.4546(10) A beta = 90 deg. c = 26.589(2) A gamma = 90 deg.
Volume	2591.7(3) A^3
Z, Calculated density	8, 1.467 Mg/m^3
Absorption coefficient	1.154 mm^-1
F(000)	1200
Crystal size	.3 x .1 x .1 mm
Theta range for data collection	2.24 to 26.99 deg.
Limiting indices	-9<=h<=6, -15<=k<=14, -15<=l<=33
Reflections collected / unique	8433 / 5113 [R(int) = 0.0522]
Reflection observed [I>2sigma(I)]	2996
Completeness to theta = 26.99	96.5 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5113 / 0 / 329
Goodness-of-fit on F^2	0.894
Final R indices [I>2sigma(I)]	R1 = 0.0460, wR2 = 0.0759
R indices (all data)	R1 = 0.1063, wR2 = 0.0881
Absolute structure parameter	0.007(19)
Largest diff. peak and hole	0.536 and -0.460 e.A^-3

Table 6. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **15**.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Fe(2)	9034(1)	7602(1)	2028(1)	37(1)
O(1)	7350(4)	8359(3)	3254(1)	38(1)
C(2)	6782(5)	7627(4)	2411(2)	33(1)
C(4)	7321(6)	6560(4)	2336(2)	40(1)
C(9)	5881(5)	9249(3)	1989(2)	35(1)
C(11)	11262(6)	7244(4)	2380(2)	51(2)
C(12)	10856(6)	8326(4)	2457(2)	43(1)
C(18)	6540(5)	8126(4)	1936(2)	37(1)
C(19)	6251(6)	8388(4)	2818(2)	35(1)
C(21)	5969(6)	11194(4)	1670(2)	43(1)
C(22)	10749(5)	8856(4)	1988(2)	46(1)
O(25)	6896(3)	11922(3)	1356(1)	46(1)
C(30)	6982(5)	7372(4)	1558(2)	41(1)
C(31)	7458(6)	6401(4)	1801(2)	44(1)
C(32)	6295(5)	9493(4)	2553(2)	37(1)
C(34)	11447(6)	7080(5)	1850(2)	56(2)
C(38)	11120(6)	8064(5)	1621(2)	54(2)
C(42)	6622(6)	10048(4)	1614(2)	42(1)
Fe(1)	2509(1)	5462(1)	352(1)	36(1)
C(3)	222(6)	5495(5)	-13(2)	50(2)
C(5)	4944(5)	5520(4)	62(2)	33(1)
O(6)	5443(3)	3317(3)	-1490(1)	44(1)
C(10)	4186(6)	6139(4)	846(2)	53(2)
C(13)	4979(5)	5285(4)	585(2)	37(1)
C(14)	4118(6)	6518(4)	-3(2)	50(1)
C(15)	5932(5)	4700(4)	-238(2)	34(1)
C(16)	985(5)	4474(4)	-70(2)	42(1)

C(17)	624(5)	4779(4)	770(2)	44(1)
O(20)	5031(3)	3563(3)	1016(1)	55(1)
C(23)	-10(5)	5676(4)	512(2)	48(2)
C(24)	3622(6)	6899(4)	484(2)	64(2)
C(26)	6344(5)	3787(4)	-1074(2)	41(1)
C(29)	5107(5)	4351(4)	-728(2)	39(1)
C(35)	1228(5)	4037(3)	417(2)	41(1)
C(36)	5904(6)	4264(4)	681(2)	42(1)
C(1A)	6126(6)	3774(4)	152(2)	38(1)

Table 7. Anisotropic displacement parameters (A^2 x 10^3) for **15**.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
Fe(2)	39(1)	48(1)	25(1)	-3(1)	2(1)	2(1)
O(1)	39(2)	56(2)	19(2)	-2(2)	0(2)	8(2)
C(2)	41(3)	34(3)	25(3)	-1(3)	2(2)	-5(2)
C(4)	50(3)	40(3)	31(3)	3(3)	3(3)	-10(3)
C(9)	36(2)	43(3)	27(3)	4(3)	2(2)	1(2)
C(11)	40(3)	63(4)	49(4)	4(3)	-9(2)	11(3)
C(12)	37(3)	58(4)	34(3)	-6(3)	6(2)	-3(3)
C(18)	35(3)	50(3)	25(3)	-3(3)	-1(2)	-7(2)
C(19)	38(3)	42(3)	25(3)	0(2)	5(2)	2(2)
C(21)	37(3)	53(3)	38(3)	8(3)	-2(2)	-8(3)
C(22)	32(3)	56(3)	50(3)	3(4)	-1(3)	-11(2)
O(25)	43(2)	53(2)	42(2)	12(2)	2(2)	6(2)
C(30)	43(3)	53(3)	26(3)	-8(3)	-2(2)	-4(3)
C(31)	56(3)	41(3)	35(3)	-11(3)	7(3)	1(3)
C(32)	41(3)	39(3)	31(3)	-2(3)	-4(2)	6(2)
C(34)	42(3)	73(5)	53(4)	-9(3)	10(3)	7(3)
C(38)	42(3)	89(5)	29(3)	-1(3)	4(3)	-9(3)

C(42)	42(3)	52(3)	31(3)	-2(3)	-4(2)	0(2)
Fe(1)	37(1)	33(1)	39(1)	0(1)	5(1)	-2(1)
C(3)	47(3)	49(4)	55(4)	11(4)	-7(3)	-3(3)
C(5)	37(3)	30(3)	33(3)	-2(3)	4(2)	-9(3)
O(6)	48(2)	60(3)	25(2)	-9(2)	0(2)	14(2)
C(10)	41(3)	61(4)	55(4)	-21(3)	13(3)	-10(3)
C(13)	33(3)	45(4)	33(3)	-12(3)	4(2)	-4(2)
C(14)	53(3)	39(3)	60(4)	11(3)	23(3)	-1(3)
C(15)	34(3)	38(3)	31(3)	2(2)	2(2)	6(2)
C(16)	37(3)	50(3)	39(3)	4(3)	-4(2)	-14(3)
C(17)	36(3)	47(4)	47(3)	5(3)	1(2)	-4(2)
O(20)	42(2)	85(3)	37(2)	28(2)	11(2)	8(2)
C(23)	38(3)	37(3)	69(4)	6(3)	10(3)	9(2)
C(24)	60(4)	29(3)	102(5)	-13(4)	28(3)	-9(3)
C(26)	45(3)	54(3)	24(3)	4(3)	2(2)	3(3)
C(29)	36(3)	61(4)	20(3)	-5(3)	1(2)	8(2)
C(35)	42(3)	26(3)	56(4)	6(3)	5(3)	3(2)
C(36)	34(3)	70(4)	22(3)	7(3)	4(2)	-6(3)
C(1A)	41(3)	35(3)	37(3)	3(2)	1(2)	7(2)

Table 8. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for **15**.

	x	y	z	U(eq)
H(1)	6765	8461	3514	57
H(4)	7551	6043	2590	48
H(9)	4612	9236	1947	42
H(11)	11393	6714	2634	61
H(12)	10679	8653	2775	51
H(19)	5052	8223	2922	42
H(21A)	4742	11218	1580	51
H(21B)	6082	11420	2025	51

H(22)	10483	9590	1931	55
H(25)	7932	11918	1439	69
H(30)	6964	7494	1206	49
H(31)	7807	5758	1638	53
H(32A)	7437	9827	2586	45
H(32B)	5431	9982	2699	45
H(34)	11736	6427	1687	68
H(38)	11143	8187	1269	64
H(42A)	7881	10053	1650	50
H(42B)	6357	9796	1269	50
H(3)	-80	5973	-276	60
H(6)	6040	2828	-1617	66
H(10)	4053	6194	1200	63
H(14)	3925	6873	-314	61
H(15)	7091	4997	-313	41
H(16)	1282	4140	-379	51
H(17)	641	4690	1125	52
H(20)	5696	3072	1109	82
H(23)	-506	6296	661	58
H(24)	3022	7545	553	76
H(26A)	7198	4307	-1201	49
H(26B)	6958	3219	-887	49
H(29A)	4142	3863	-653	47
H(29B)	4640	4990	-901	47
H(35)	1716	3357	491	49
H(36)	7056	4432	823	50
H(1A1)	5247	3216	92	45
H(1A2)	7268	3438	121	45