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Supporting Information

Organometallic Antitumor Compounds: Ferrocifens as Precursors to Quinone Methides

Yong Wang, Pascal Pigeon, Siden Top, Michael J. McGlinchey, and Gérard Jaouen**

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Chemical Synthesis

General Synthetic Methods. Unless otherwise stated, the ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker 300-MHz spectrometer. The data are reported in parts per million relative to the referenced solvent. The mass spectra were obtained on a DSQII and ITQ 1100 Thermo Scientific spectrometer for both electronic ionization (EI) and chemical ionization (CI) methods on API 3000 PE Sciex Applied Biosystems for electrospray ionization (ESI) method. The flash column chromatography was performed on silica gel Merck 60 (40-63 μm). Anhydrous solvents were obtained by standard procedure. The purity of products was more than 95% characterized by elemental analysis or analytical reverse phase HPLC (Shimadzu instrument) with Nucleodur C18 column (4.6 \times 150 mm) using MeOH as eluent, flow rate = 1 mL/min, λ = 254 nm. Elemental analyses were performed by the Laboratory of Microanalysis at ICSN of CNRS at Gif sur Yvette, France.

2-Ferrocenyl-1-(4-hydroxyphenyl)-5-hydroxy-1-phenyl-pent-1-en, 3a

Methyl 4-ferrocenyl-4-oxo-butanoate

Ferrocene (5 g, 26.9 mmol) was dissolved in dry dichloromethane. Aluminum trichloride (3.58 g, 26.9 mmol) was added in small portions. Then methyl 4-chloro-4-oxobutyrate (2.76 mL, 22.4 mmol) was added dropwise. The stirring was continued overnight and then the solution was carefully poured into water. The aqueous layer was extracted with dichloromethane and the combined organic layers were washed with water, dried over MgSO_4 and concentrated under reduced pressure. The crude mixture was separated on a silica gel column with dichloromethane/petroleum ether (50/50), then dichloromethane as an eluent. The second fraction (4.8 g, yield = 71%) corresponded to the desired product. ^1H NMR (300 MHz; CDCl_3): δ = 2.7 (t, J = 6.8 Hz, 2 H, CH_2 ; $\text{CH}_2\text{-COOMe}$), 3.1 (t, J = 6.8 Hz, 2 H, CH_2 ; $\text{CH}_2\text{-CO-Fc}$), 3.7 (s, 3 H, CH_3 ; Me), 4.22 (s, 5 H, 5xCH; Cp), 4.5 (t, J = 1.8 Hz, 2 H, 2xCH; C_5H_4), 4.8 (t, J = 1.8 Hz, 2 H, 2xCH; C_5H_4). ^{13}C NMR (75 MHz; CDCl_3): δ = 27.9 (CH_2 ; $\text{CH}_2\text{-COOMe}$), 34.3 (CH_2 , $\text{CH}_2\text{-$

CO-Fc), 51.8 (CH₃; Me), 69.3 (2 CH; C₅H₄), 70.0 (5 CH; Cp), 72.3 (2 CH; C₅H₄), 78.6 (C; C₅H₄), 173.7 (C; COOMe), 202.1 (C; CO).

Methyl 4-en-4-ferrocenyl-5-(4-hydroxyphenyl)-5-phenyl-pentanoate, 2a

Titanium chloride (2.2 mL, 20 mmol) was added dropwise to a suspension of zinc powder (2.0 g, 30 mmol) in dry THF at 0 °C. The mixture was heated at reflux for 2 hours. A second solution was prepared by dissolving each ketone in dry THF: the ferrocenyl ester ketone (1.5 g, 5 mmol) and the 4-hydroxybenzophenone (2.0 g, 10 mmol). This latter solution was added dropwise to the first solution and then the reflux was continued overnight. After cooling to room temperature, the mixture was stirred with water and dichloromethane. The mixture was acidified with diluted hydrochloric acid until dark color disappeared and was decanted. The aqueous layer was extracted with dichloromethane and the combination of organic layers was dried on MgSO₄. After concentration under reduced pressure, the crude product was chromatographed on silica gel column with a mixture of cyclohexane/ethyl acetate as the eluent. The second fraction (1.05 g, yield = 45%) corresponded to the desired product. ¹H NMR (300 MHz; acetone-*d*₆): δ = 2.43-2.54 (m, 2H; CH₂), 2.87-3.05 (m, 2H ; CH₂), 3.60 and 3.61 (s, 3H, CH₃; OCH₃), 3.92 and 3.99 (t, *J* = 1.9 Hz, 2H, 2xCH; C₅H₄), 4.11 and 4.15 (t, *J* = 1.9 Hz, 2H, 2xCH; C₅H₄), 4.18 and 4.19 (s, 5H, 5xCH; Cp), 6.76 and 6.87 (d, *J* = 8.7 Hz, 2H, 2xCH; C₆H₄), 6.90-7.44 (m, 7H, 7xCH; Ar), 8.34 and 8.39 (bs, 1H; OH). ¹³C NMR (75 MHz; acetone-*d*₆): δ = 31.1 (CH₂), 35.8 and 35.9 (CH₂), 52.3 (OCH₃), 69.7 (2 CH; C₅H₄), 70.7 (7 CH; 5xCH (Cp) + 2xCH (C₅H₄)), 88.1 and 88.2 (Cq; C₅H₄), 116.7 and 116.9 (2 CH; C₆H₄), 127.8 and 127.9 (CH; C₆H₅), 129.7 and 130.0 (2xCH; Ar), 130.7 and 131.3 (2xCH; Ar), 131.9 and 132.4 (2xCH; Ar), 134.9 and 135.3 (C), 136.8 and 137.0 (C), 141.0 (C), 146.3 and 146.7 (C), 157.7 (C; C-OH), 174.3 and 174.4 (C, CO). MS (CI, NH₃) *m/z*: 467 [M+H]⁺, 484 [M+NH₄]⁺. HRMS calcd for C₂₈H₂₆FeO₃: 466.1231, found: 466.1235.

2-Ferrocenyl-1-(4-hydroxyphenyl)-5-hydroxy-1-phenyl-pent-1-ene, 3a

To a stirred suspension of LiAlH₄ (0.114 g, 3 mmol) in diethyl ether (20 mL) at 0 °C was added dropwise a solution of the previous ester **1a** (0.466 g, 1 mmol) in THF (50 mL). The mixture was left stirring at RT for 3 hours then at reflux overnight. After cooling, it was poured into a saturated sodium bicarbonate solution and extracted five times with diethyl ether. The combination of organic layers was washed with water and dried over MgSO₄. After concentration under reduced pressure, the crude product was purified by semi-preparative HPLC using acetonitrile/water (70:30) as an eluent. (0.39 g, yield = 90%) were obtained as an orange oil. ¹H NMR (300 MHz; acetone-*d*₆): δ = 1.65-1.80 (m, 2H; CH₂),

2.65-2.80 (m, 2H ; CH₂), 3.41-3.54 (m, 3 H, CH₂; CH₂-O + OH), 3.97 and 4.05 (t, *J* = 1.9 Hz, 2H, 2xCH; C₅H₄), 4.08 and 4.12 (t, *J* = 1.9 Hz, 2H, 2xCH; C₅H₄), 4.16 and 4.17 (s, 5H, 5xCH; Cp), 6.77 and 6.86 (d, *J* = 8.7 Hz, 2H, 2xCH; C₆H₄), 6.89-7.42 (m, 7H, 7xCH; Ar), 8.32 and 8.34 (bs, 1H; OH). ¹³C NMR (75 MHz; acetone-*d*₆): δ = 32.6 (CH₂), 35.6 (CH₂), 63.2 (CH₂; CH₂-O), 69.5 (2 CH; C₅H₄), 70.7 (5 CH; Cp), 70.9 (2 CH; C₅H₄), 88.7 (Cq; C₅H₄), 116.7 (2 CH; C₆H₄), 127.6 (CH; C₆H₅), 129.7 and 129.8 (2xCH; Ar), 130.9 and 131.4 (2xCH; Ar), 132.0 and 132.4 (2xCH; Ar), 136.7 and 137.0 (C), 137.5 and 137.8 (C), 139.4 and 139.8 (C), 146.8 (C), 157.5 and 157.6 (C; C-OH). MS (CI, NH₃) *m/z*: 439 [M+H]⁺. HRMS calcd for C₂₇H₂₆FeO₂: 438.1282, found: 438.1288.

2-Ferrocenyl-1,1-bis-(4-hydroxyphenyl)-5-hydroxy-pent-1-ene, 3b

Methyl 4-en-4-ferrocenyl-5,5-bis-(4-hydroxyphenyl)-pentanoate, 2b

TiCl₄ (3.8 ml, 33 mmol) was added dropwise to a suspension of zinc powder (4.5 g, 66 mmol) in 40 ml of THF at 0 °C. The dark grey mixture obtained was heated at refluxing for 2 hrs. A solution of THF (20 ml) containing 4,4'-dihydroxybenzophenone (4.91 g, 22 mmol) and 4-oxo-4-ferrocenylbutanoate (3.13 g, 10 mmol) was added dropwise to the first solution and the resulting mixture was heated overnight. After cooling to room temperature, the mixture was acidified by addition of diluted HCl solution. The aqueous layer was extracted with EtOAc for three times. The combined organic layer was dried over MgSO₄ and evaporated. The residue was purified by column chromatography on silica gel eluting with cyclohexane/ethyl acetate (2:1) to give methyl 4-en-4-ferrocenyl-5,5-bis-(4-hydroxyphenyl)-pentanoate as red solid 2.8 g, yield: 58%. ¹H NMR (300 MHz; acetone-*d*₆): δ = 2.46 (t, *J* = 8.2 Hz, 2H, CH₂), 2.98 (t, *J* = 8.2 Hz, 2H, CH₂), 3.43 (s, 3H, OCH₃), 3.98 (t, *J* = 1.9 Hz, 2H, C₅H₄), 4.12 (t, *J* = 1.9 Hz, 2H, C₅H₄), 4.18 (s, 5H, Cp), 6.74 (d, *J* = 8.7 Hz, 2H, C₆H₄), 6.86 (d, *J* = 8.7 Hz, 2H, C₆H₄), 6.89 (d, *J* = 8.7 Hz, 2H, C₆H₄), 7.11 (d, *J* = 8.7 Hz, 2H, C₆H₄), 8.29 (s, 1H, OH), 8.35 (s, 1H, OH). ¹³C NMR (75 MHz; acetone-*d*₆): δ = 31.7 (CH₂), 35.9 (CH₂), 52.3 (OCH₃), 68.6 (2 CH; C₅H₄), 70.6 (5 CH; Cp), 70.7 (2 CH; C₅H₄), 88.8 (Cq; C₅H₄), 116.6 (2 CH; C₆H₄), 116.8 (2 CH; C₆H₄), 131.9 (2 CH; C₆H₄), 132.5 (2 CH; C₆H₄), 134.2 (C), 137.4 (C), 137.9 (C), 141.1 (C), 157.6 (2 C, C-OH), 174.4 (C, CO). MS (EI, 70 eV) *m/z*: 482 [M]⁺. HRMS calcd for C₂₈H₂₆FeO₄: 482.1181, found: 482.1196. Anal. Calcd for C₂₈H₂₆FeO₄: C, 69.72; H, 5.43. Found: C, 69.79; H, 5.56.

2-Ferrocenyl-1,1-bis-(4-hydroxyphenyl)-5-hydroxy-pent-1-ene, 3b

LiAlH₄ (0.16 g, 4.2 mmol) was added slowly to the solution of methyl 5,5-bis(4-hydroxyphenyl)-4-ferrocenylpent-4-enoate (0.4 g, 0.83 mmol) in 10 ml of Et₂O. The mixture obtained was heated at reflux overnight. The reaction was then quenched by water. The aqueous layer was extracted with ethyl acetate for three times. The organic layer was dried over MgSO₄ and evaporated. The residue was purified by column chromatography on silica gel eluting with cyclohexane/ethyl acetate (2:1) to give 2-ferrocenyl-1,1-bis-(4-hydroxyphenyl)-5-hydroxy-pent-1-ene as brown solid 0.29 g, yield: 77%. ¹H NMR (300 MHz; acetone-*d*₆): δ = 1.72-1.85 (m, 2H; CH₂), 2.82 (t, *J* = 8.0 Hz, 2H ; CH₂), 3.51-3.60 (m, 3 H, CH₂; CH₂-O + OH), 4.10 (t, *J* = 1.9 Hz, 2H, 2xCH; C₅H₄), 4.17 (t, *J* = 1.9 Hz, 2H, 2xCH; C₅H₄), 4.23 (s, 5H, 5xCH; Cp), 6.82 (d, *J* = 8.7 Hz, 2H, 2xCH; C₆H₄), 6.93 (d, *J* = 8.7 Hz, 2H, 2xCH; C₆H₄), 6.99 (d, *J* = 8.7 Hz, 2H, 2xCH; C₆H₄), 7.18 (d, *J* = 8.7 Hz, 2H, 2xCH; C₆H₄), 8.32 (bs, 1H; OH), 8.35 (bs, 1H; OH). ¹³C NMR (75 MHz; acetone-*d*₆): δ = 32.7 (CH₂), 35.6 (CH₂), 63.3 (CH₂; CH₂-O), 69.4 (2 CH; C₅H₄), 70.6 (5 CH; Cp), 70.8 (2 CH; C₅H₄), 89.3 (Cq; C₅H₄), 116.5 (2 CH; C₆H₄), 116.6 (2 CH; C₆H₄), 132.0 (2 CH; C₆H₄), 132.5 (2 CH; C₆H₄), 136.0 (C), 138.0 (C), 138.3 (C), 139.9 (C), 157.3 (Cq; C-OH), 157.4 (Cq; C-OH). MS (EI, 70 eV) *m/z*: 454 [M]⁺, 389 [M-Cp]⁺, 121 [CpFe]⁺. HRMS calcd for C₂₇H₂₆FeO₃: 454.1232, found: 454.1237.

2-Ferrocenyl-1-(4-hydroxy-3,5-dimethyl-phenyl)-5-hydroxy-1-phenyl-pent-1-en, 3c

Methyl 4-en-4-ferrocenyl-5-(4-hydroxy-3,5-dimethyl-phenyl)-5-phenyl-pentanoate, 2c

TiCl₄ (1.8 ml, 16 mmol) was added dropwise to a suspension of zinc powder (2.1 g, 32 mmol) in 20 ml of THF at 0 °C. The dark grey mixture obtained was heated at reflux for 2 hrs. A solution of THF (10 ml) containing (4-hydroxy-3,5-dimethylphenyl)(phenyl)methanone (1.2 g, 5 mmol) and methyl 4-oxo-4-ferrocenylbutanoate (1.2 g, 4 mmol) was added dropwise to the first solution and the resulting mixture was heated overnight. After cooling to room temperature, the mixture was acidified by addition of diluted HCl. The aqueous layer was extracted with ethyl acetate for three times. The combined organic layer was dried over MgSO₄ and evaporated. The residue was purified by column chromatography on silica gel eluting with cyclohexane/ethyl acetate (2:1) to give methyl methyl 4-en-4-ferrocenyl-5-(4-hydroxy-3,5-dimethyl-phenyl)-5-phenyl-pentanoate as a light yellow solid 1.5 g, yield 76%. ¹H NMR (300 MHz; acetone-*d*₆): δ = 2.12 and 2.15 (s, 6H, 2xCH₃; CH₃), 2.46 (m, 2H; CH₂), 2.86 and 2.95 (m, 2H; CH₂), 3.56 and 3.58 (s, 3H, OCH₃), 3.87 and 3.95 (t, *J* = 1.9 Hz, 2H, 2xCH; C₅H₄), 4.06 and 4.09 (t, *J* = 1.9 Hz, 2H, 2xCH; C₅H₄), 4.12 and 4.14 (s, 5H, 5xCH; Cp), 6.70 and 6.85 (s, 2H, 2xCH; C₆H₂), 7.06 and 7.08 (t, *J* = 1.9 Hz, 1H, CH; C₆H₅), 7.16 - 7.37 (m, 4H, 4xCH; C₆H₅). ¹³C NMR (75 MHz; acetone-*d*₆): δ

= 16.7 (2xCH₃), 30.9 (CH₂), 35.2 (CH₂), 51.6 (OCH₃), 68.9 (4 CH; C₅H₄), 69.9 (5 CH; Cp), 87.4 (Cq; C₅H₄), 124.5 and 124.7 (CH; C₆H₅), 127.0 (C), 127.1 (C), 128.9 and 129.2 (2 CH; C₆H₅), 129.8 and 129.9 (2 CH; C₆H₅), 130.3 and 130.5 (2 CH; C₆H₂), 133.8 and 134.1 (C), 136.3 and 136.6 (C), 140.5 and 140.6 (C), 145.7 and 146.1 (C), 152.9 (C; C-O), 173.6 and 173.7 (C, CO). MS-CI (NH₃) *m/z*: 495 (M+H)⁺. HRMS calcd for C₃₀H₃₀FeO₃: 494.1544, found: 494.1536.

2-Ferrocenyl-1-(4-hydroxy-3,5-dimethylphenyl)-5-hydroxy-1-phenyl-pent-1-ene, 3c

LiAlH₄ (0.3 g, 5 mmol) was added slowly to the solution of methyl 4-ferrocenyl-5-(4-hydroxy-3,5-dimethylphenyl)-5-phenylpent-4-enoate (0.5 g, 1 mmol) in 10 ml of THF. The mixture obtained was heated at reflux overnight. And then the reaction was quenched by water. The aqueous layer was extracted with ethyl acetate for three times. The organic layer was dried over MgSO₄ and evaporated. The residue was purified by column chromatography on silica gel eluting with cyclohexane/ethyl acetate (2:1) to give 2-ferrocenyl-1-(4-hydroxy-3,5-dimethylphenyl)-5-hydroxy-1-phenyl-pent-1-ene as a light yellow solid 0.4 g, yield 86%. ¹H NMR (300 MHz; acetone-*d*₆): δ = 1.65 and 1.77 (m, 2H; CH₂), 2.15 and 2.21 (s, 6H; 2xCH₃), 2.63 and 2.72 (m, 2H; CH₂), 3.40 – 3.48 (m, 3H; OH and CH₂), 3.91 and 4.01 (t, *J* = 1.9 Hz, 2H, 2xCH; C₅H₄), 4.03 and 4.06 (t, *J* = 1.9 Hz, 2H, 2xCH; C₅H₄), 4.12 (s, 5H, 5xCH; Cp), 6.70 and 6.84 (s, 2H, 2xCH; C₆H₂), 7.06 and 7.08 (t, *J* = 1.9 Hz, 1H, CH; C₆H₅), 7.13 - 7.36 (m, 4H, 4xCH; C₆H₅). ¹³C NMR (75 MHz; acetone-*d*₆): δ = 16.7 (2xCH₃), 31.7 and 31.9 (CH₂), 34.9 and 35.0 (CH₂), 62.6 (OCH₂), 68.7 (2 CH; C₅H₄), 69.9 (5 CH; Cp), 70.1 (2 CH; C₅H₄), 87.7 and 88.0 (Cq; C₅H₄), 124.5 (2C), 126.8 (CH; C₆H₅), 128.9 and 129.0 (2 CH; C₆H₅), 129.9 and 130.0 (2 CH; C₆H₅), 130.4 and 130.6 (2 CH; C₆H₂), 135.5 and 135.8 (C), 136.8 and 137.1 (C), 139.4 and 139.5 (C), 146.2 and 146.5 (C), 152.6 and 152.7 (C; C-O). MS-CI (NH₃) *m/z*: 467 (M+H)⁺. HRMS calcd for C₂₉H₃₀FeO₂: 466.1595, found: 466.1586.

1,1-bis-(4-Hydroxyphenyl)-5-hydroxy-pent-2-phenyl-1-ene, 4b

Methyl 4-en-5,5-bis-(4-hydroxyphenyl)-4-phenyl-pentanoate

TiCl₄ (6.6 ml, 60 mmol) was added dropwise to a suspension of zinc powder (5.9 g, 90 mmol) in 60 ml of THF at 0 °C. The dark grey mixture obtained was heated at refluxing for 2 hrs. A solution of THF (20 ml) containing 4,4'-dihydroxybenzophenone (3.2 g, 15 mmol) and methyl 3-benzoylpropionate (2.9 g, 15 mmol) was added dropwise to the first solution and the resulting mixture was heated overnight. After cooling to room temperature, the mixture was acidified by addition of diluted HCl solution. The aque-

ous layer was extracted with EtOAc for three times. The combined organic layer was dried over MgSO₄ and evaporated. The residue was purified by column chromatography on silica gel eluting with cyclohexane/ethyl acetate (2:1) to give methyl 4-en-5,5-bis-(4-hydroxyphenyl)-4-phenyl-pentanoate as white solid 3.2 g, yield: 57%. ¹H NMR (300 MHz; acetone-*d*₆): δ = 2.32 (t, *J* = 7.9 Hz, 2H, CH₂), 2.82 (t, *J* = 7.9 Hz, 2H, CH₂), 3.55 (s, 3H, OCH₃), 6.53 (d, *J* = 8.5 Hz, 2H, C₆H₄), 6.75 (d, *J* = 8.5 Hz, 2H, C₆H₄), 6.89 (d, *J* = 8.5 Hz, 2H, C₆H₄), 7.14 (d, *J* = 8.5 Hz, 2H, C₆H₄), 7.15 – 7.27 (m, 5H, C₆H₅), 8.16 (s, 1H, OH), 8.41 (s, 1H, OH). ¹³C NMR (75 MHz; acetone-*d*₆): δ = 32.8 (CH₂), 34.5 (CH₂), 52.3 (OCH₃), 115.8 (2 CH; C₆H₄), 116.6 (2 CH; C₆H₄), 127.7 (CH; C₆H₅), 129.5 (2 CH; CH_{arom}), 131.3 (2 CH; CH_{arom}), 132.0 (2 CH; CH_{arom}), 133.4 (2 CH; CH_{arom}), 136.1 (C), 136.4 (C), 138.4 (C), 141.9 (C), 143.8 (C), 157.1 (C, C-OH), 158.0 (C, C-OH), 174.2 (C, CO).

1,1-bis-(4-Hydroxyphenyl)-5-hydroxy-pent-2-phenyl-1-ene, 4b

LiAlH₄ (0.9 g, 24 mmol) was added slowly to the solution of methyl 4-en-5,5-bis-(4-hydroxyphenyl)-4-phenyl-pentanoate (3 g, 8 mmol) in 30 ml of Et₂O. The mixture obtained was heated at reflux overnight. The reaction was then quenched by water. The aqueous layer was extracted with ethyl acetate for three times. The organic layer was dried over MgSO₄ and evaporated. The residue was purified by column chromatography on silica gel eluting with cyclohexane/ethyl acetate (2:1) to give 1,1-bis-(4-hydroxyphenyl)-5-hydroxy-pent-2-phenyl-1-ene as white solid 2.8 g, yield: 98%. ¹H NMR (300 MHz; acetone-*d*₆): δ = 1.49 - 1.64 (m, 2H; CH₂), 2.56 (t, *J* = 8.1 Hz, 2H; CH₂), 3.45 (t, *J* = 6.8 Hz, 2H; CH₂), 6.51 (d, *J* = 8.7 Hz, 2H, 2xCH; C₆H₄), 6.73 (d, *J* = 8.7 Hz, 2H, 2xCH; C₆H₄), 6.86 (d, *J* = 8.7 Hz, 2H, 2xCH; C₆H₄), 7.11 (d, *J* = 8.7 Hz, 2H, 2xCH; C₆H₄), 7.12 – 7.24 (m, 5H, C₆H₅), 8.47 (br s, 2H; OH). ¹³C NMR (75 MHz; acetone-*d*₆): δ = 33.9 (2xCH₂), 63.3 (CH₂; CH₂-O), 115.7 (2 CH; C₆H₄), 116.5 (2 CH; C₆H₄), 127.4 (CH; C₆H₅), 129.4 (2 CH; C₆H₄), 131.2 (2 CH; C₆H₅), 132.1 (2 CH; C₆H₄), 133.4 (2 CH; C₆H₅), 136.3 (C), 136.6 (C), 140.2 (C), 140.7 (C), 144.8 (C), 157.0 (Cq; C-OH), 157.8 (Cq; C-OH). MS (CI, NH₃) *m/z*: 347 [M+H]⁺, 364 [M+NH₄]⁺. HRMS calcd for C₂₃H₂₃O₃ [M+H]⁺: 347.1647, found: 347.1660.

1-(4-Hydroxy-3,5-dimethyl-phenyl)-5-hydroxy-pent-1,2-diphenyl-1-en, 4c

Methyl 4-en-5-(4-hydroxy-3,5-dimethyl-phenyl)-4,5-diphenyl-pentanoate

TiCl₄ (2.3 ml, 20 mmol) was added dropwise to a suspension of zinc powder (2.7 g, 42 mmol) in 30 ml of THF at 0 °C. The dark grey mixture obtained was heated at reflux for 2 hrs. A solution of THF (10

ml) containing (4-hydroxy-3,5-dimethylphenyl)(phenyl)methanone (1.4 g, 6.3 mmol) and methyl 4-oxo-4-phenylbutanoate (0.7 ml, 4.2 mmol) was added dropwise to the first solution and the resulting mixture was heated overnight. After cooling to room temperature, the mixture was acidified by addition of diluted HCl. The aqueous layer was extracted with ethyl acetate for three times. The combined organic layer was dried over MgSO₄ and evaporated. The residue was purified by column chromatography on silica gel eluting with cyclohexane/ethyl acetate (2:1) to give methyl 4-en-5-(4-hydroxy-3,5-dimethylphenyl)-4,5-diphenyl-pentanoate as a white solid 0.9 g, yield 58%. ¹H NMR (300 MHz; acetone-*d*₆): δ = 1.97 and 2.23 (s, 6H, 2xCH₃; CH₃), 2.30 (m, 2H; CH₂), 2.72 and 2.81 (m, 2H; CH₂), 3.50 and 3.52 (s, 3H, OCH₃), 6.50 and 6.88 (s, 2H, CH; C₆H₂), 6.90 - 7.04 (m, 2H), 7.06 - 7.22 (m, 5H), 7.25 - 7.33 (m, 2H), 7.38 (m, 1H). ¹³C NMR (75 MHz; acetone-*d*₆): δ = 16.5 and 16.7 (2xCH₃), 32.0 and 32.2 (CH₂), 33.6 and 33.8 (CH₂), 51.6 (OCH₃), 123.5 (C), 124.6 (C), 126.6 (CH), 127.1 (CH), 127.5 (CH), 128.1 (CH), 128.7 (CH), 129.1 (CH), 130.0 (CH), 130.5 (CH), 130.6 (CH), 131.3 (CH), 131.5 (CH), 134.7 (C), 135.2 (C), 138.0 (C), 138.8 (C), 141.5 (C), 141.7 (C), 142.7 (C), 142.9 (C), 144.2 (C), 144.5 (C), 152.4 (C), 153.2 (C), 173.4 (C, CO).

1-(4-Hydroxy-3,5-dimethylphenyl)-5-hydroxy-1,2-diphenyl-pent-1-ene, 4c

LiAlH₄ (0.2 g, 3.5 mmol) was added slowly to the solution of methyl 4-en-5-(4-hydroxy-3,5-dimethylphenyl)-4,5-diphenyl-pentanoate (0.38 g, 1 mmol) in 10 ml of THF. The mixture obtained was heated at reflux overnight. And then the reaction was quenched by water. The aqueous layer was extracted with ethyl acetate for three times. The organic layer was dried over MgSO₄ and evaporated. The residue was purified by column chromatography on silica gel eluting with cyclohexane/ethyl acetate (2:1) to give 1-(4-hydroxy-3,5-dimethylphenyl)-5-hydroxy-1,2-diphenyl-pent-1-ene as a white solid 0.3 g, yield 84%. ¹H NMR (300 MHz; acetone-*d*₆): δ = 1.54 (m, 2H; CH₂), 1.96 and 2.23 (s, 6H; 2xCH₃), 2.42 - 2.62 (m, 2H; CH₂), 3.38 - 3.47 (m, 3H; OH and CH₂), 6.49 and 6.87 (s, 2H, 2xCH; C₆H₂), 6.89 - 7.39 (m, 10H, CH; 2xC₆H₅). ¹³C NMR (75 MHz; acetone-*d*₆): δ = 16.5 and 16.7 (2xCH₃), 33.1 (CH₂), 33.2 (CH₂), 62.5 (OCH₂), 123.5 (C), 124.4 (C), 126.4 (CH), 126.7 (CH), 127.3 (CH), 128.1 (CH), 128.6 (CH), 128.9 (CH), 130.2 and 130.3 (2 CH), 130.4 and 130.5 (2 CH), 131.4 (CH), 131.6 (CH), 135.1 (C), 135.6 (C), 139.9 (C), 140.3 (C), 140.4 (C), 140.7 (C), 143.7 and 143.8 (C), 144.6 and 144.9 (C), 152.2 and 153.0 (C). MS-CI (NH₃) *m/z*: 359 (M+H)⁺, 376 [M+NH₄]⁺.

Chemical Oxidation of 3a, 3b, 3c and 4c

Quinone 3a-QM. Freshly made Ag_2O^1 (0.25 g, 1.1 mmol) was added to a solution of 2-ferrocenyl-1-(4-hydroxyphenyl)-5-hydroxy-1-phenyl-pent-1-ene (0.08 g, 0.18 mmol) in 8 ml of acetone. The dark grey mixture obtained changed to be dark red suspension about 5 minutes later. The reaction was monitored by TLC until complete conversion of the starting material (40 minutes). Filtration was followed by removal of the solvent under reduced pressure to give **3a-QM** as a dark red solid 65 mg, yield 83%. ^1H NMR (300 MHz, acetone- d_6): δ = 2.08 - 2.21 (m, 2H, CH_2), 2.21 - 2.38 (m, 2H, CH_2), 3.95 - 4.05 (m, 2x1H, CH_2 ; $\text{CH}_2\text{-O}$), 4.14 - 4.20 (m, 2H, 2xCH; C_5H_4), 4.21 (s, 5H, 5xCH; Cp), 4.28 (m, 1H, CH; C_5H_4), 4.33 (m, 1H, CH; C_5H_4), 6.01 (dd, J = 10.2, 2.2 Hz, 1H, CH; C_6H_4), 6.30 (dd, J = 10.4, 2.2 Hz, 1H; C_6H_4), 6.59 (dd, J = 10.2, 2.7 Hz, 1H; C_6H_4), 6.72 (d, J = 7.5 Hz, 1H, CH; C_6H_5), 7.31 (m, 2H, 2xCH; C_6H_5), 7.44 (m, 2H, 2xCH; C_6H_5), 8.83 (dd, J = 10.4, 2.7 Hz, 1H, CH; C_6H_4). ^{13}C NMR (75 MHz, acetone- d_6): δ = 25.6 (CH_2), 39.1 (CH_2), 67.7 (CH, C_5H_4), 68.0 (CH, C_5H_4), 68.1 (CH_2 ; $\text{CH}_2\text{-O}$), 69.2 (CH, C_5H_4), 69.8 (5xCH; Cp), 70.1 (CH; C_5H_4), 88.9 (C; Cq-O), 96.3 (C; C_5H_4), 128.3 (CH; C_6H_4), 128.4 (CH; C_6H_5), 128.5 (CH; C_6H_5), 128.6 (CH; C_6H_4), 128.7 (CH; C_6H_5), 129.4 (CH; C_6H_5), 129.5 (CH; C_6H_5), 130.3 (C), 138.2 (CH; C_6H_4), 139.9 (C; C_6H_5), 140.8 (CH; C_6H_4), 165.4 (C), 186.4 (C, C=O). MS-CI (NH_3) m/z : 437 ($\text{M}+\text{H}$) $^+$. HRMS calcd for $\text{C}_{27}\text{H}_{24}\text{FeO}_2$: 436.1126, found: 436.1135.

Quinone 3b-QM. Freshly made Ag_2O (0.47 g, 2.1 mmol) was added to a solution of 2-ferrocenyl-1,1-bis-(4-hydroxyphenyl)-5-hydroxy-pent-1-ene (0.19 g, 0.41 mmol) in 6 ml of acetone. The dark grey mixture obtained changed to be dark red suspension about 5 minutes later. The reaction was monitored by TLC until complete conversion of the starting material (10 minutes). Filtration was followed by removal of the solvent under reduced pressure to give **3b-QM** as a dark red solid 170 mg, yield 89%. ^1H NMR (300 MHz, acetone- d_6): δ = 1.97 (m, 1H, CH_2), 2.06 - 2.18 (m, 1H, CH_2), 2.28 (m, 2H, CH_2), 3.96 (m, 1H, OCH_2), 4.02 - 4.06 (m, 1H, OCH_2), 4.15 - 4.18 (m, 2H, 2xCH; C_5H_4), 4.19 (s, 5H, 5xCH; Cp), 4.25 (m, 1H, CH; C_5H_4), 4.29 (m, 1H, CH; C_5H_4), 6.02 (dd, J = 10.2, 2.1 Hz, 1H, CH; C_6H_4), 6.26 (dd, J = 10.4, 2.1 Hz, 1H; C_6H_4), 6.56 (br s, 1H; C_6H_4), 6.70 (dd, J = 10.2, 2.7 Hz, 1H; C_6H_4), 6.79 (br s, 1H; C_6H_4), 6.91 (br s, 1H; C_6H_4), 7.09 (br s, 1H; C_6H_4), 8.71 (s, 1H, OH), 8.80 (dd, J = 10.4, 2.7 Hz, 1H, CH; C_6H_4). ^{13}C NMR (75 MHz, acetone- d_6): δ = 25.7 (CH_2), 39.2 (CH_2), 67.7 (CH, C_5H_4), 68.0 (CH, C_5H_4), 68.2 (CH_2 ; $\text{CH}_2\text{-O}$), 69.1 (CH, C_5H_4), 69.8 (5xCH; Cp), 70.0 (CH; C_5H_4), 89.1 (C; Cq-O), 96.4 (C; C_5H_4), 115.3 (2 CH; C_6H_4), 128.2 (CH; C_6H_4), 128.3 (CH; C_6H_4), 130.8 (C; C_6H_4), 131.1 (C; C=C), 138.5 (2 CH; C_6H_4), 141.4 (2 CH; C_6H_4), 158.2 (C; C=C), 166.4 (C; C_6H_4), 186.6 (C, C=O). MS-EI m/z : 452 (M) $^+$; HRMS calcd for $\text{C}_{27}\text{H}_{24}\text{FeO}_3$ (M) $^+$: 452.1075, found: 452.1082.

Quinone 3c-QM. Freshly made Ag₂O (0.25 g, 1.1 mmol) was added to a solution of 2-Ferrocenyl-1-(4-hydroxy-3,5-dimethylphenyl)-5-hydroxy-1-phenyl-pent-1-ene (0.08 g, 0.18 mmol) in 8 ml of acetone. The dark grey mixture obtained changed to be dark red suspension about 5 minutes later. The reaction was monitored by TLC until complete conversion of the starting material (60 minutes). Filtration was followed by removal of the solvent under reduced pressure to give **3c-QM** as a dark red solid 65 mg, yield 83%. ¹H NMR (300 MHz, acetone-*d*₆): δ = 1.68 (d, *J* = 1.3 Hz, 3H, CH₃), 1.94 - 1.97 (m, 1H, CH₂), 1.98 (d, *J* = 1.3 Hz, 3H, CH₃), 2.08 - 2.15 (m, 1H, CH₂), 2.16 - 2.38 (m, 2H, CH₂), 3.91 - 4.00 (m, 2H, CH₂; CH₂-O), 4.02 - 4.07 (m, 1H, CH; C₅H₄), 4.12 - 4.18 (m, 1H, CH; C₅H₄), 4.20 (s, 5H, 5xCH; Cp), 4.25 (m, 1H, CH; C₅H₄), 4.33 (m, 1H, CH; C₅H₄), 6.42 (dd, *J* = 2.7, 1.24 Hz, 1H, CH; C₆H₂), 6.76 (d, *J* = 7.4 Hz, 1H; C₆H₅), 7.23 - 7.56 (m, 4H; C₆H₅), 8.60 (dd, *J* = 2.7, 1.4 Hz, 1H; C₆H₂). ¹³C NMR (75 MHz, acetone-*d*₆): δ = 16.5 (CH₃), 17.2 (CH₃), 25.8 (CH₂), 39.5 (CH₂), 67.6 (CH, C₅H₄), 68.0 (CH₂; CH₂-O), 68.3 (CH, C₅H₄), 68.9 (CH, C₅H₄), 69.8 (5xCH; Cp), 69.9 (CH; C₅H₄), 88.7 (C; Cq-O), 96.9 (C; C₅H₄), 128.3 (CH; C₆H₂), 128.5 (CH; C₆H₂), 129.8 (CH; C₆H₅), 130.5 (C; C₆H₅), 134.5 (2 CH; C₆H₅), 135.0 (C), 130.3 (C), 135.2 (C), 136.9 (2 CH; C₆H₅), 140.4 (C; C₆H₅), 161.7 (C), 186.8 (C, C=O). MS-CI (NH₃) *m/z*: 465 (M+H)⁺. HRMS calcd for C₂₉H₂₈FeO₂: 464.1439, found: 464.1455.

Quinone 4c-QM. Freshly made Ag₂O (0.16 g, 0.7 mmol) was added to a solution of 1-(4-hydroxy-3,5-dimethylphenyl)-5-hydroxy-1,2-diphenyl-pent-1-ene (0.05 g, 0.14 mmol) in 3 ml of acetone-*d*₆. The reaction was monitored by TLC until complete conversion of the starting material (90 minutes). Filtration was followed by ¹H NMR spectra directly. ¹H NMR (300 MHz, acetone-*d*₆): δ = 1.91 (d, *J* = 1.3 Hz, 3H, CH₃), 2.00 (d, *J* = 1.3 Hz, 3H, CH₃), 2.57 - 2.67 (m, 2H, CH₂), 3.79 (dt, *J* = 11.3, 5.0 Hz, 2H, CH₂-O), 3.89 (t, 1H, OH), 6.02 (t, *J* = 7.4 Hz, 1H, CH=C), 6.77 (s, 1H, CH; C₆H₂), 6.80 - 7.38 (m, 10H, 10xCH; C₅H₅), 7.80 (s, 1H, CH; C₆H₂).

Chemical stability profile of 3b-QM

Freshly made Ag₂O (0.22 g, 0.9 mmol) was added to a solution of 2-ferrocenyl-1,1-bis-(4-hydroxyphenyl)-5-hydroxy-pent-1-ene (0.1 g, 0.23 mmol) in 6 ml of acetone. The dark grey mixture obtained changed to be dark red suspension about 5 minutes later. The reaction was monitored by TLC until complete conversion of the starting material (10 minutes). Filtration was followed by removal most of the solvent under reduced pressure. The residue was kept at room temperature for around 1 week, there were four new spots appearing identified by TLC. The residue was purified by column chromatog-

raphy on silica gel eluting with cyclohexane/ethyl acetate (2:1) to give 4 compounds. **3b-A. 4,4'-(3-ferrocenyl-5,6-dihydro-2H-pyran-2,2-diyl)diphenol.** A brown solid 15 mg, yield 15%. ¹H NMR (300 MHz, acetone-*d*₆) δ = 2.38 (q, *J* = 5.4 Hz, 2H; CH₂), 3.50 (t, *J* = 5.7 Hz, 2H; OCH₂), 3.83 (s, 2H; C₅H₄), 3.97 (s, 2H; C₅H₄), 4.03 – 4.08 (m, 5H; Cp), 6.57 (s, 1H; CH=C), 6.75 (d, *J* = 8.7 Hz, 4H; C₆H₄), 7.20 (d, *J* = 8.7 Hz, 4H; C₆H₄), 8.32 (s, 2H; OH). ¹³C NMR (75 MHz, acetone-*d*₆) δ = 26.99 (CH₂), 59.20 (OCH₂), 68.15 (2 CH; C₅H₄), 70.51 (2 CH; C₅H₄), 70.85 (5 CH; Cp), 84.11 (C; C-O), 86.21 (C; C₅H₄), 114.70 (4 CH; C₆H₄), 125.73 (CH; CH=C), 131.94 (4 CH; C₆H₄), 136.18 (2 C; C₆H₄), 141.52 (C; CH=C), 157.41 (2 C; C₆H₄). MS-EI *m/z*: 452 (M)⁺. HRMS calcd for C₂₇H₂₄FeO₃ (M)⁺: 452.1075, found: 452.1090. **3b-B. 5-hydroxy-1,1-bis(4-hydroxyphenyl)-1-ferrocenylpentan-2-one.** A brown solid 30 mg, yield 30%. ¹H NMR (300 MHz, acetone-*d*₆) δ = 1.81 (m, 2H; CH₂), 2.82 – 2.90 (m, 2H; CH₂), 3.55 (m, 3H; OH and OCH₂), 3.85 (s, 2H; C₅H₄), 4.14 (s, 5H; Cp), 4.25 (s, 2H; C₅H₄), 6.77 (d, *J* = 8.8 Hz, 4H; C₆H₄), 6.92 (d, *J* = 8.8 Hz, 4H; C₆H₄), 8.37 (s, 2H; OH). ¹³C NMR (75 MHz, acetone-*d*₆) δ = 28.89 (CH₂), 38.82 (CH₂), 61.90 (OCH₂), 66.26 (C), 68.65 (2 CH; C₅H₄), 70.17 (5 CH; Cp), 71.61 (2 CH; C₅H₄), 92.19 (C; C₅H₄), 114.96 (4 CH; C₆H₄), 131.79 (4 CH; C₆H₄), 135.95 (2 C; C₆H₄), 156.96 (2 C; C₆H₄), 208.61 (C=O). MS-EI *m/z*: 470 (M)⁺. HRMS calcd for C₂₇H₂₆FeO₄ (M)⁺: 470.1180, found: 470.1198. **3b-C. 4-hydroxy-1-ferrocenylbutan-1-one.** ¹H NMR (300 MHz, acetone-*d*₆) δ = 1.81 – 1.93 (m, 2H; CH₂), 2.86 (m, 2H; CH₂), 3.62 (m, 3H; OH and OCH₂), 4.22 (s, 5H; Cp), 4.50 – 4.54 (m, 2H; C₅H₄), 4.78 – 4.82 (m, 2H; C₅H₄). ¹³C NMR (75 MHz, acetone-*d*₆) δ = 28.18 (CH₂), 36.49 (CH₂), 61.94 (OCH₂), 69.97 (2 CH; C₅H₄), 70.46 (5 CH; Cp), 72.68 (2 CH; C₅H₄), 80.56 (C; C₅H₄), 203.75 (C=O). **3b-D. bis(4-hydroxyphenyl)methanone.** A brown solid 16 mg, yield 34%. ¹H NMR (300 MHz, acetone-*d*₆) δ = 6.95 (d, *J* = 8.6 Hz, 4H; C₆H₄), 7.68 (d, *J* = 8.6 Hz, 4H; C₆H₄), 9.17 (s, 2H; OH). ¹³C NMR (75 MHz, acetone-*d*₆) δ = 115.78 (4 CH; C₆H₄), 130.83 (2 C; C₆H₄), 132.97 (4 CH; C₆H₄), 161.95 (2 C; C₆H₄), 193.98 (C=O).

X-ray crystal structure determinations for 3a, 3b, 3c-QM and 3b-A

Crystallographic data were recorded at 200 K on a Bruker APEX-II CCD diffractometer with graphite mono-chromated Mo_{Kα} radiation (λ Mo_{Kα} = 0.71073 Å) and the ω and Φ scan technique. Data were corrected for Lorentz and polarization effects, and semi-empirical absorption correction based on symmetry equivalent reflections was applied by using the SADABS program.² Orientation matrix and lattice parameters were obtained by least-squares refinement of the diffraction data of 9985 reflections within the range of $2^\circ < \Theta < 30^\circ$ (a). 9893 reflections within the range $3^\circ < \Theta < 30^\circ$ (b). and 9712 reflections within

the range of $2^\circ < \Theta < 32^\circ$ (c). The structure was solved by direct methods and refined with full-matrix least-squares technique on F^2 using the CRYSTALS programs.³ All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were either set in calculated positions and isotropically refined. These crystallographic data have been deposited at the Cambridge Crystallographic Data Centre: **3a** (1052066), **3b** (1052065) and **3c-QM** (1052064), **3b-A** (1057305). Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ (Fax: +44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk or <http://www.ccdc.cam.ac.uk>).

Biological studies

Lipophilicity. Measurements of the octanol/water partition coefficient ($\log P_{o/w}$) were made by the HPLC technique according to a method described previously.^{4,5} Measurement of the chromatographic capacity factors (k) for each molecule was done at various concentrations in the range of 95–75% methanol containing 0.25% (v/v) 1-octanol and an aqueous phase consisting of 0.15% (v/v) n-decylamine in the buffering agent MOPS (3-morpholinopropane-1-sulfonic acid, prepared in 1-octanol saturated water) adjusted to pH 7.4. These capacity factors (k') are extrapolated to 100% of the aqueous component given the value of k'/w . The $\log P_{o/w}$ is obtained by the formula $\log P_{o/w} = 0.13418 + 0.98452 \log k'$.

Culture cells. Stock solutions (10 mM) of the compounds to be tested were prepared in DMSO and were kept at -20°C in the dark. Serial dilutions in Dulbecco's modified eagle medium (DMEM) without phenol red/Glutamax I were prepared just prior to use. DMEM without phenol red, Glutamax I and fetal bovine serum were purchased from Gibco; MDA-MB-231 cells were obtained from ATCC (Manassas, VA, USA). Cells were maintained in a monolayer culture in DMEM with phenol red/Glutamax I supplemented with 9% fetal bovine serum at 37°C in a 5% CO_2 /air-humidified incubator. For proliferation assays, MDA-MB-231 cells were plated in 1 mL of DMEM without phenol red, supplemented with 9% decompemented and hormone-depleted fetal bovine serum, 1% kanamycin, 1% Glutamax I and incubated. The following day (D0), 1 mL of the same medium containing the compounds to be tested was added to the plates. After 3 days (D3) the incubation medium was removed and 2 mL of the fresh medium containing the compounds was added. At different days (D4, D5), the protein content of each well was quantified by methylene blue staining as follows: cell monolayers were fixed for 1 h at room temperature with methylene blue (1mg mL⁻¹ in 50:50 water/MeOH mixture), then washed with water. After addition of HCl (0.1 M, 2 mL), the plate was incubated for 1 h at 37°C and then the absorbance of each well (4 wells for each concentration) was measured at 655 nm with a Biorad spectrophotometer. The

results are expressed as the percentage of proteins versus the control. Two independent experiments, run in quadruplicate, were performed.

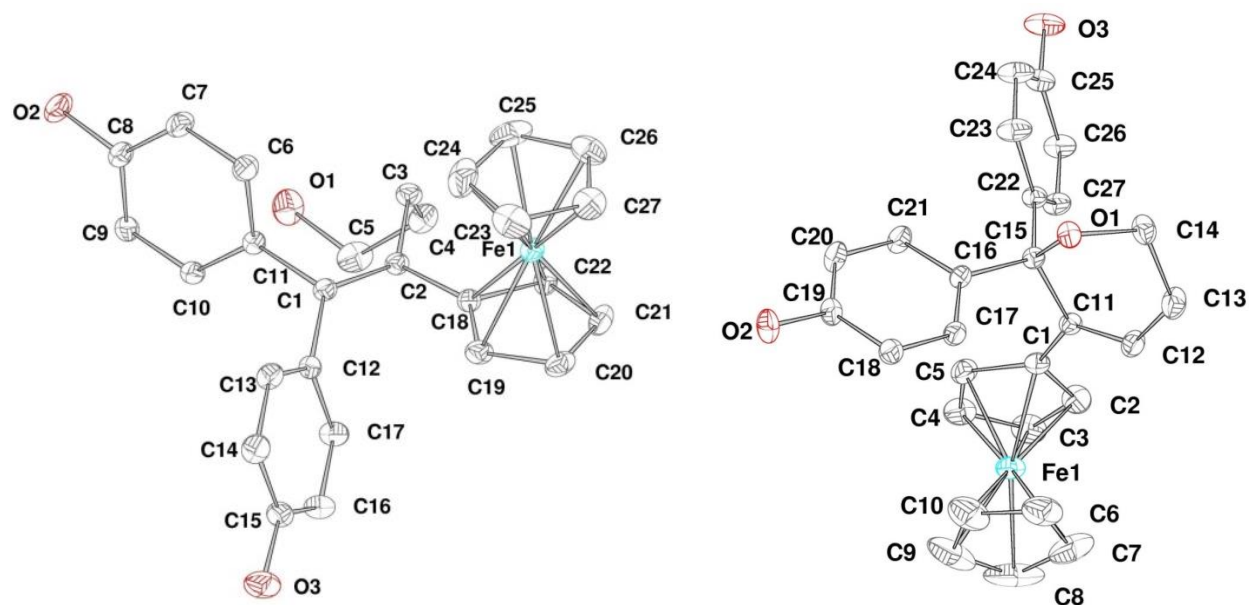


Figure S11. Molecular structure of **3b** (left) and **3b-A** (right), thermal ellipsoids are shown at 50%.

Table S11. IC_{50} values measured for the isolated derivatives of **3b**.

Compound	IC_{50} (μM) ^a MDA-MB-231
3b	0.11 ± 0.02
3b-QM	4.39 ± 1.47
3b-A	2.03 ± 0.79
3b-B	4.14 ± 1.33
3b-C	≈ 150

^a Measured after 5 days of culture (mean of two independent experiments ± SD).

Table SI2. Crystallographic Data for **3a**, **3b**, **3c-QM** and **3b-A**.

Compound	3a	3b	3c-QM	3b-A
Formula	C ₂₇ H ₂₆ FeO ₂	C ₂₇ H ₂₆ FeO ₃	C ₂₉ H ₂₈ FeO ₂	C ₂₇ H ₂₄ FeO ₃
Molecular Weight	438.34	454.35	464.39	452.33
Crystal description	Orange block	Red block	Orange block	Red block
Crystal size (mm)	0.05 x 0.09 x 0.14	0.12 x 0.14 x 0.15	0.10 x 0.12 x 0.14	0.12 x 0.14 x 0.18
λ (Å)	0.710730	0.710730	0.710730	0.71073
Temperature (K)	200(2)	200(2)	200(2)	200(2)
Crystal system	Monoclinic	Monoclinic	Triclinic	Monoclinic
Space group	P 21/c	P 21/c	P -1	P 21/n
a (Å)	9.6118(2)	9.2061(2)	8.6200(3)	12.9618(5)
b (Å)	9.2344(2)	22.7012(5)	10.3366(3)	11.8081(4)
c (Å)	23.8403(6)	10.5180(2)	13.2313(4)	14.6618(6)
α (°)	90	90	77.6250(10)	90
β (°)	100.3440(10)	103.1070(10)	83.9340(10)	103.3520(10)
γ (°)	90	90	77.3890(10)	90
Volume (Å ³)	2081.66(8)	2140.89(8)	1121.61(6)	2183.39(14)
Z	4	4	2	4
R	0.035	0.031	0.037	0.041
Rw	0.084	0.078	0.089	0.101
GOF	1.000	1.001	1.000	0.984

Table SI3. Bond Lengths (Å) and Bond Angles (°) for **3a**, **3b**, **3c-QM** and **3b-A**.

3a		3b		3c-QM		3c-QM	
C(1)-C(2)	1.3480(17)	C(1)-C(2)	1.3591(14)	C(1)-C(2)	1.5503(15)	C(1)-C(2)	1.4350(15)
C(1)-C(6)	1.4953(17)	C(1)-C(11)	1.4918(14)	C(1)-C(6)	1.3730(14)	C(1)-C(11)	1.4818(14)
C(1)-C(12)	1.4918(17)	C(1)-C(12)	1.4885(14)	C(1)-C(12)	1.4980(15)	C(11)-C(12)	1.3404(14)
C(2) - C(3)	1.5200(17)	C(2) - C(3)	1.5182(14)	C(2)-C(3)	1.5355(16)	C(11)-C(15)	1.5333(13)
C(2)-C(18)	1.4811(17)	C(2)-C(18)	1.4791(13)	C(2)-C(18)	1.5011(16)	C(15)-C(16)	1.5269(13)
Fe(1)-C(18)	2.0577(12)	Fe(1)-C(18)	2.0585(10)	C(6)-C(7)	1.4616(15)	C(15)-O(1)	1.4625(12)
Fe(1)-C(23)	2.0478(15)	Fe(1)-C(23)	2.0437(12)	C(7)-C(8)	1.3488(16)	Fe(1)-C(1)	2.0519(10)
				C(8)-C(9)	1.4746(18)		
				C(2)-O(1)	1.4273(13)		
				C(5)-O(1)	1.4334(17)		
				C(9)-O(2)	1.2293(16)		
				Fe(1)-C(18)	2.0476(12)		
				Fe(1)-C(23)	2.0374(16)		
C(18)-C(2)-C(3)	115.43(11)	C(18)-C(2)-C(3)	114.87(8)	C(2)-C(1)-C(6)	126.92(10)	C(1)-C(11)-C(12)	120.70(9)
C(6)-C(1)-C(12)	112.81(10)	C(11)-C(1)-C(12)	114.59(8)	C(2)-C(1)-C(12)	113.45(9)	C(1)-C(11)-C(15)	118.77(8)

C(6)-C(1)- C(12)	119.32(10)	C(15)- C(11)-C(12)	120.48(9)
C(1)-C(2)- C(18)	105.24(9)	C(16)- C(15)-C(11)	110.20(8)
C(2)-O(1)- C(5)	109.41(10)	C(11)- C(15)-O(1)	109.18(7)
C(3)-C(2)- O(1)	102.12(9)	C(14)-O(1)- C(15)	113.85(8)

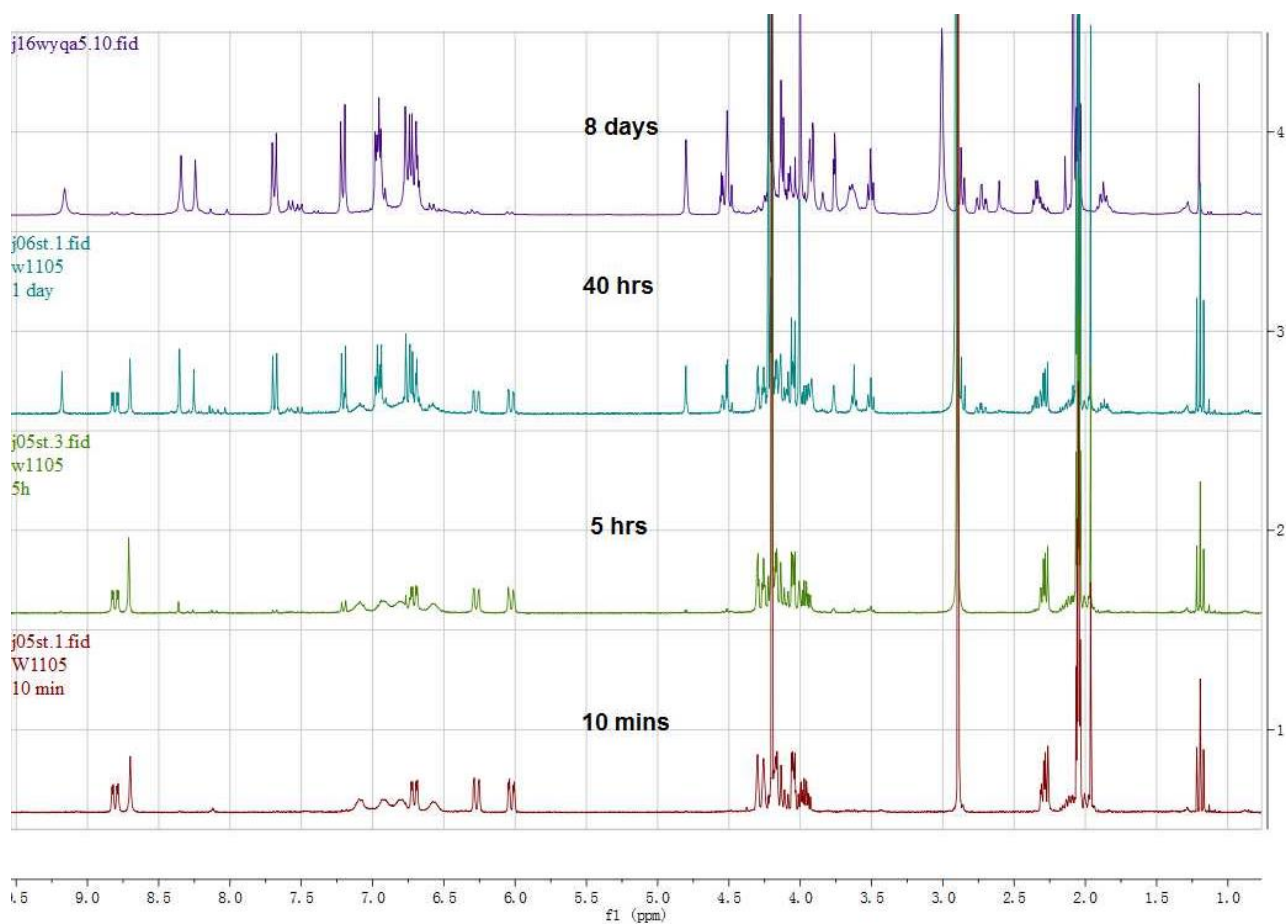


Figure SI2. ¹H NMR spectrum of **3b-QM** in acetone-*d*₆.

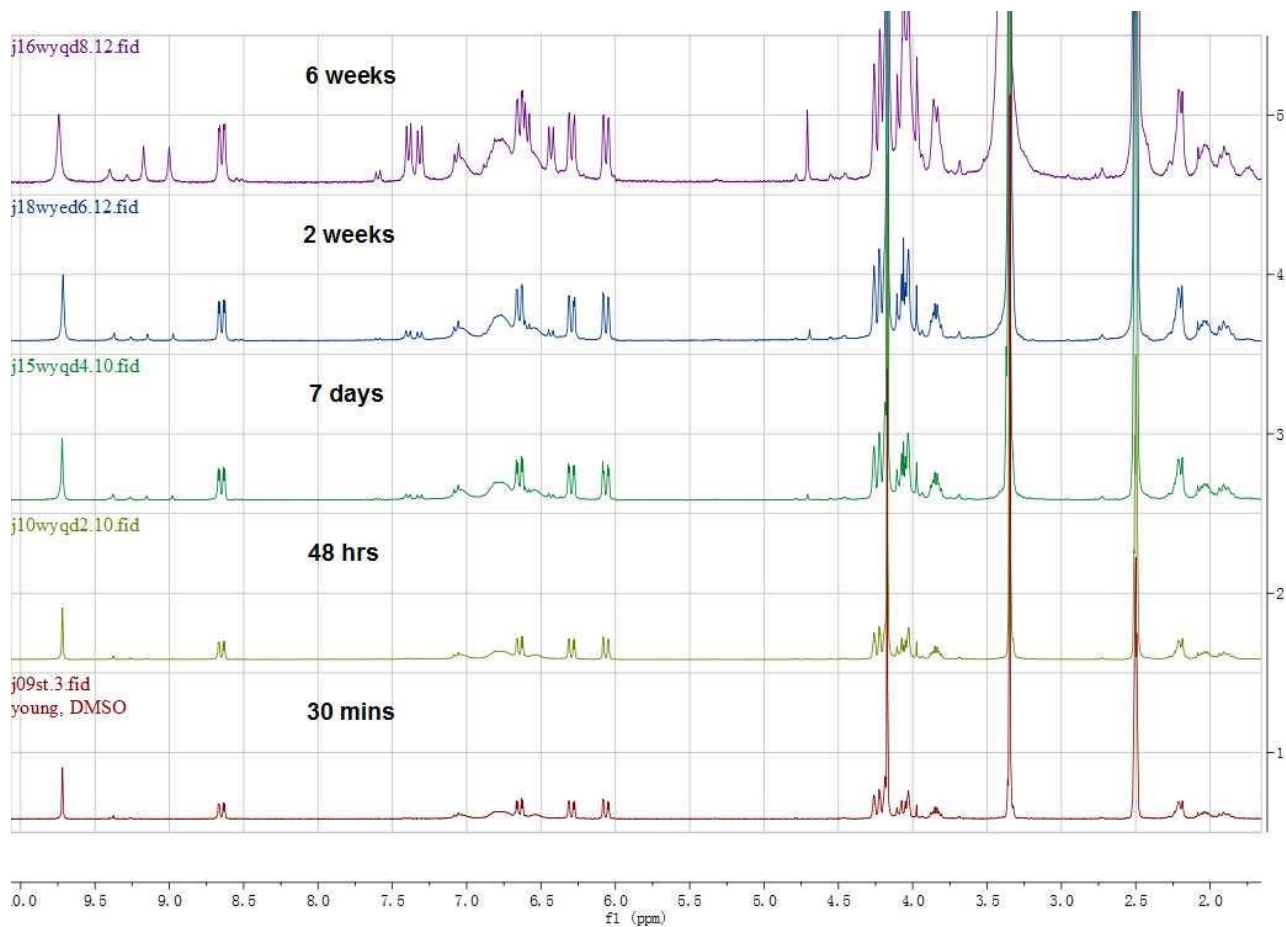


Figure SI3. ^1H NMR spectrum of **3b-QM** in $\text{DMSO-}d_6$.

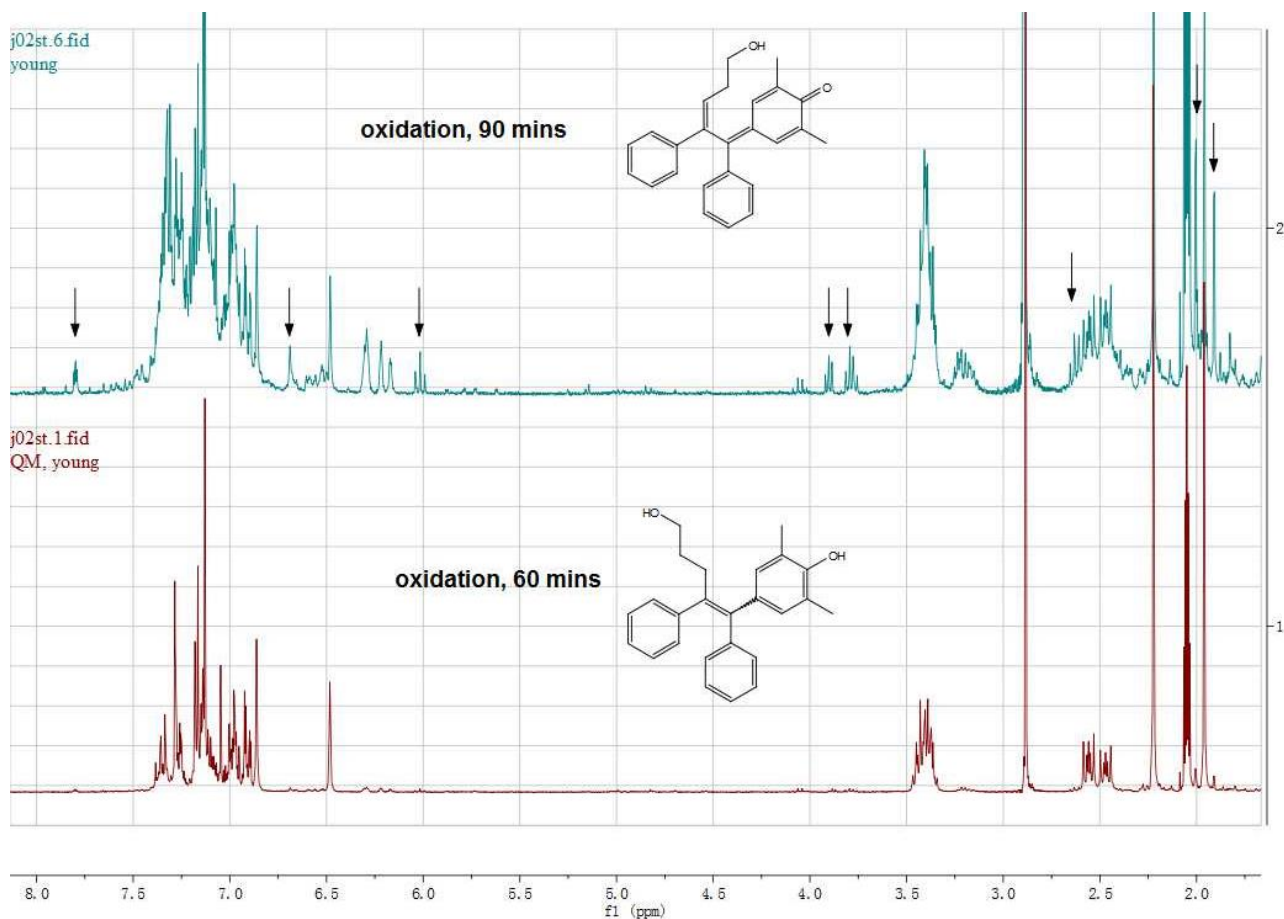
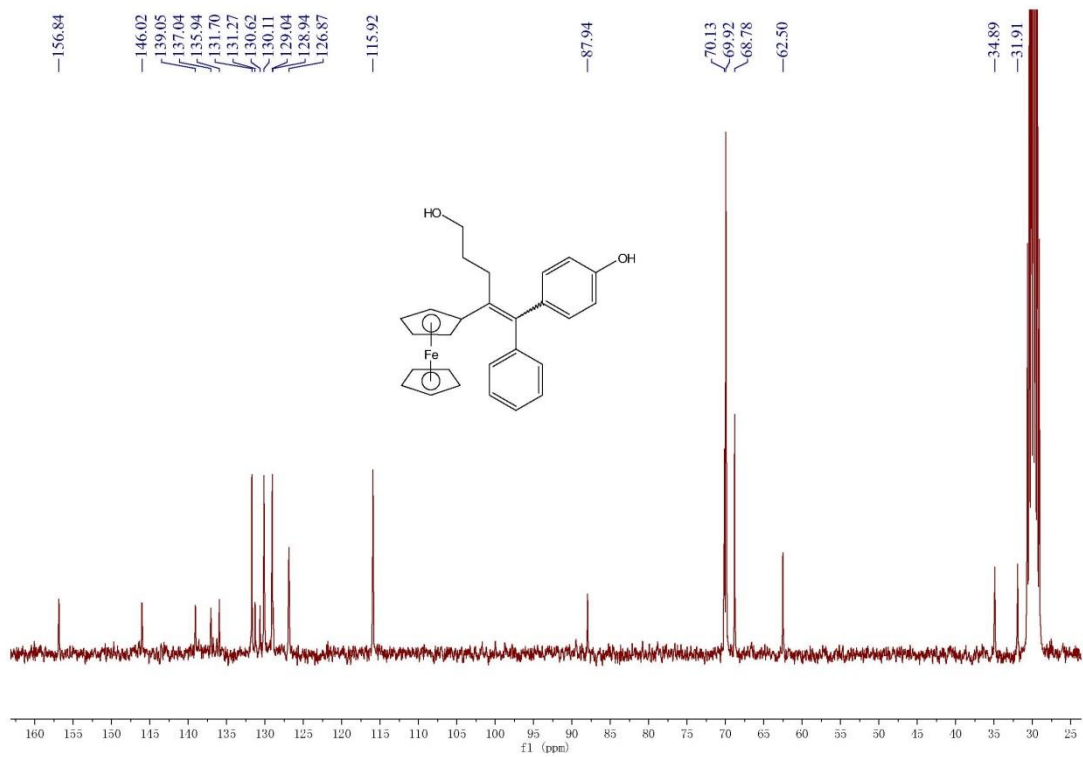
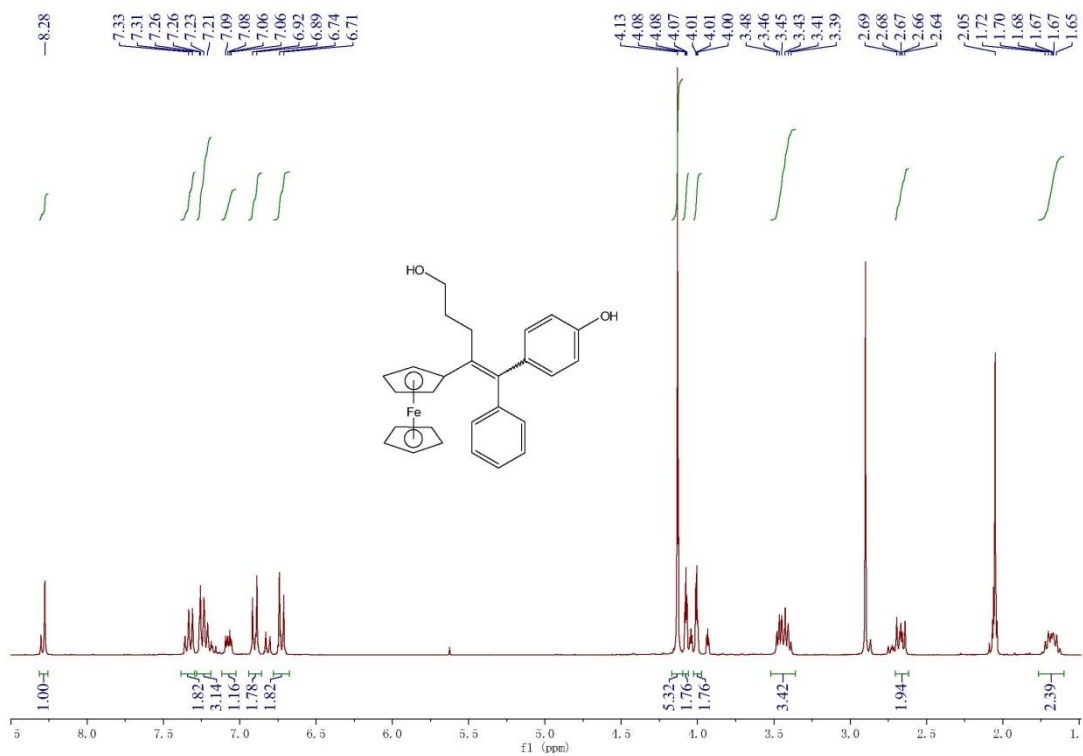


Figure SI4. The oxidation of **4c-QM** in acetone-*d*₆.

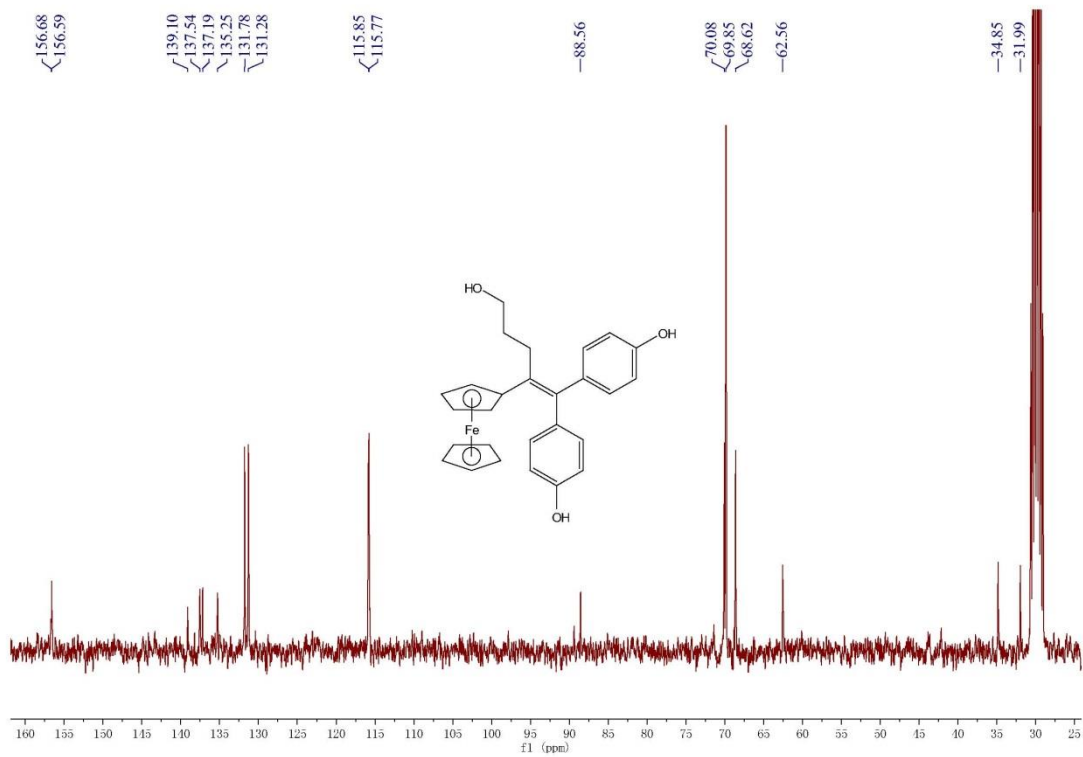
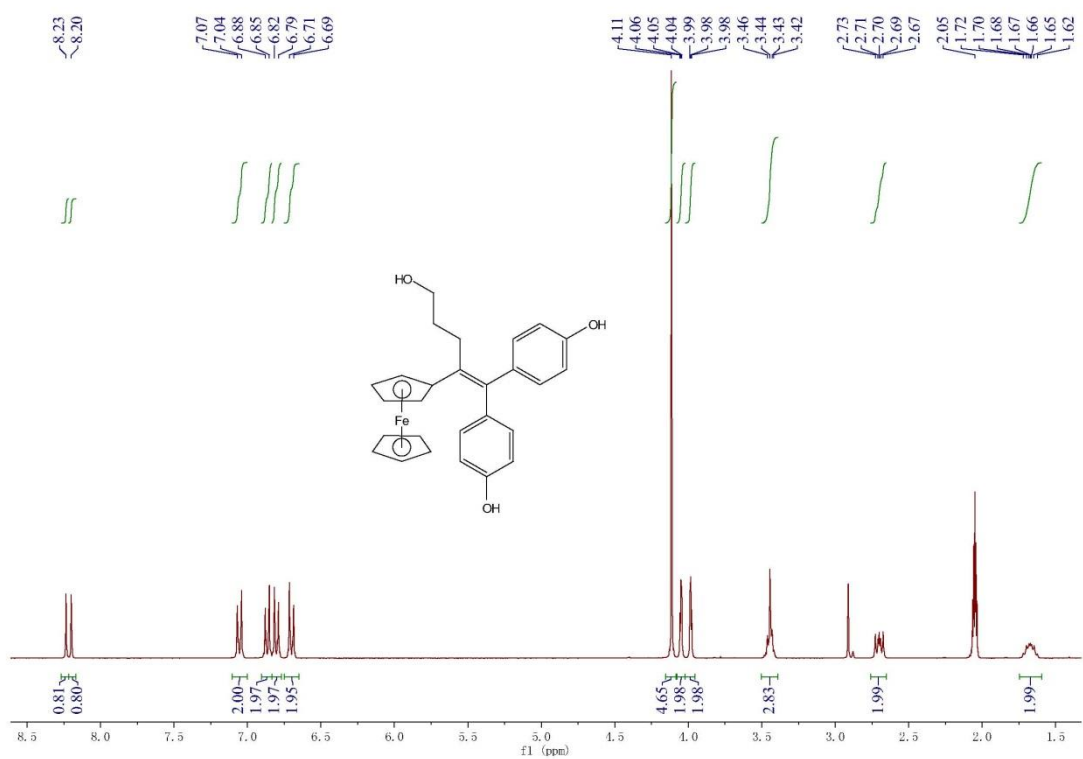
Reference

- (1) Liu, H.; Liu, J.; van Breemen, R. B.; Thatcher, G. R. J.; Bolton, J. L., *Chem. Res. Toxicol.* **2005**, *18*, 162.
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- (5) Pomper, M. G.; Vanbrocklin, H.; Thieme, A. M.; Thomas, R. D.; Kiesewetter, D. O.; Carlson, K. E.; Mathias, C. J.; Welch, M. J.; Katzenellenbogen, J. A. *J. Med. Chem.* **1990**, *33*, 3143.

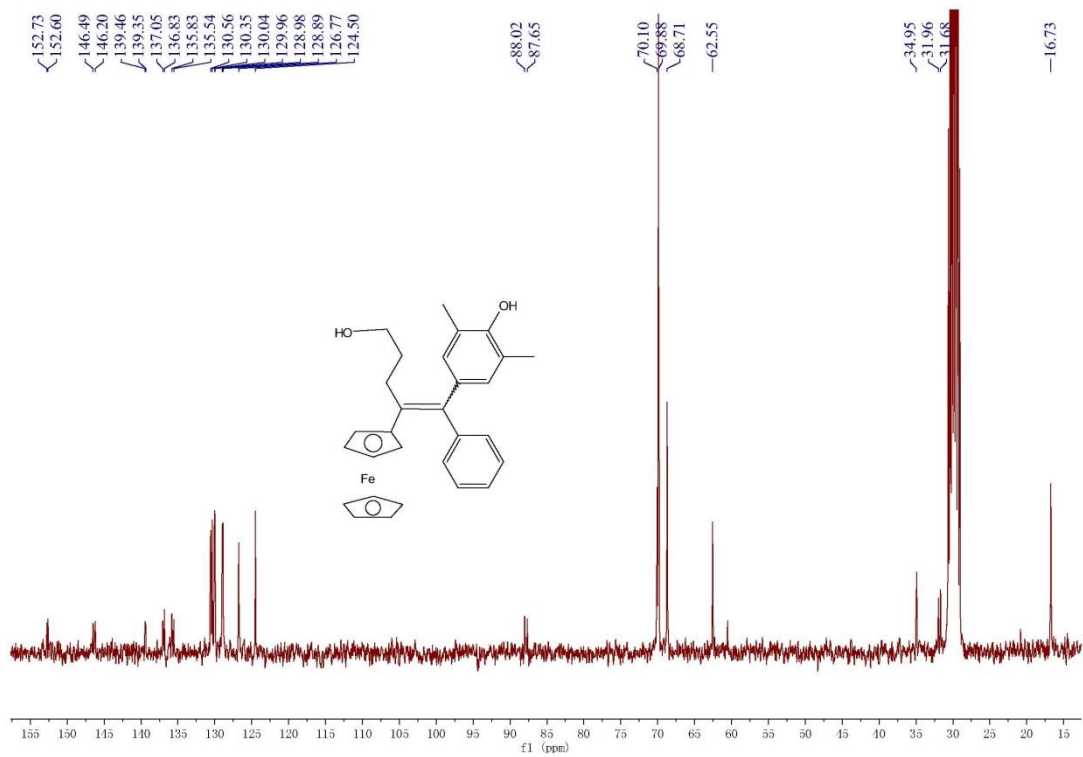
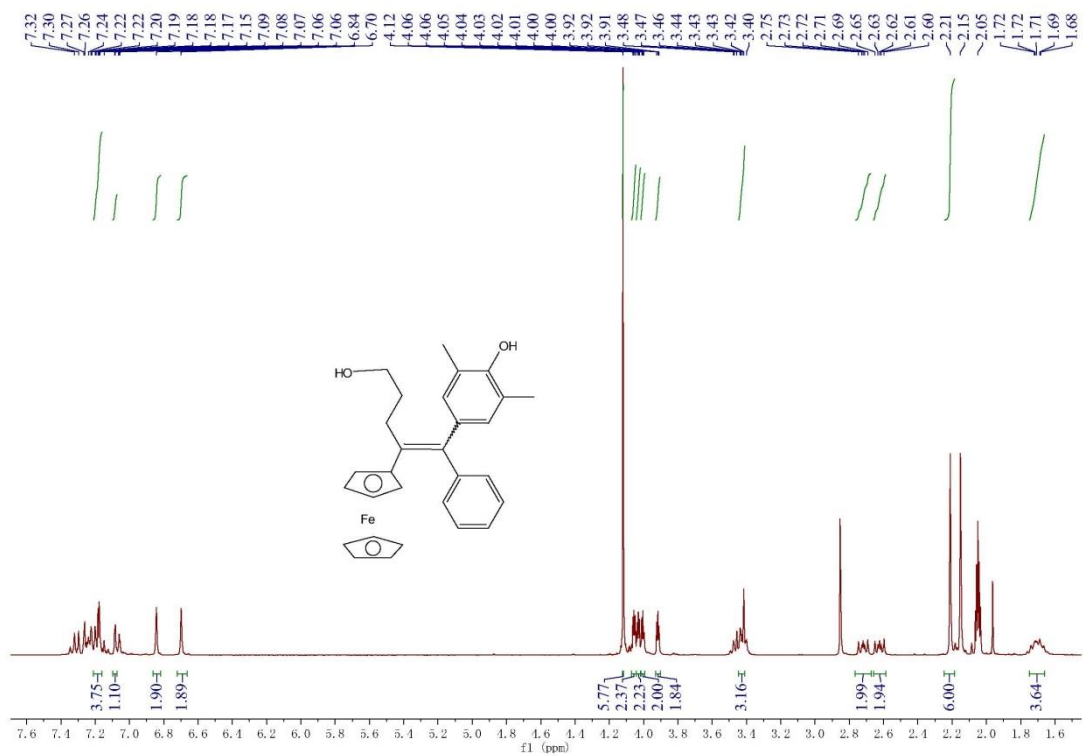
3a



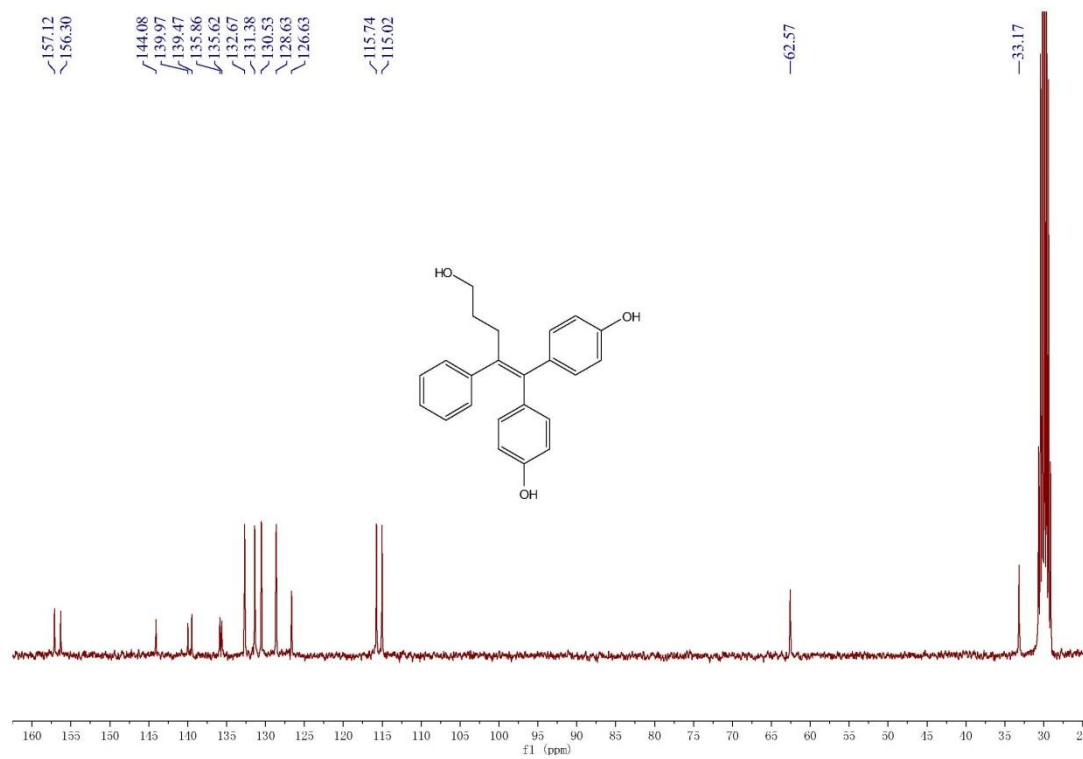
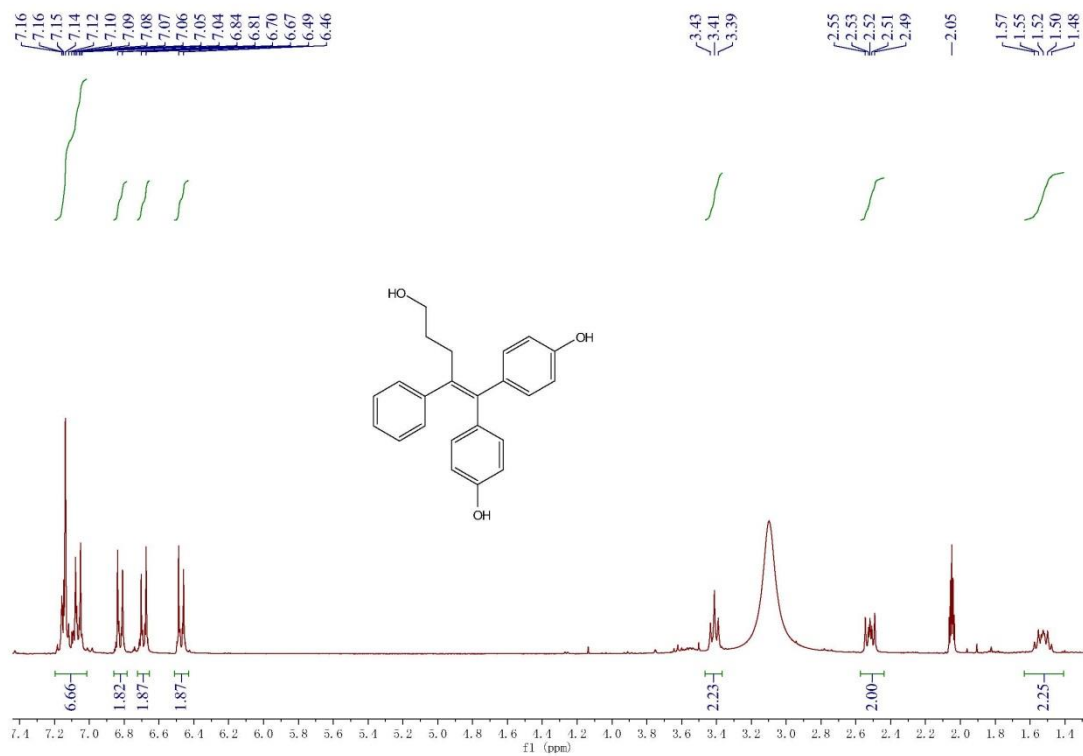
3b



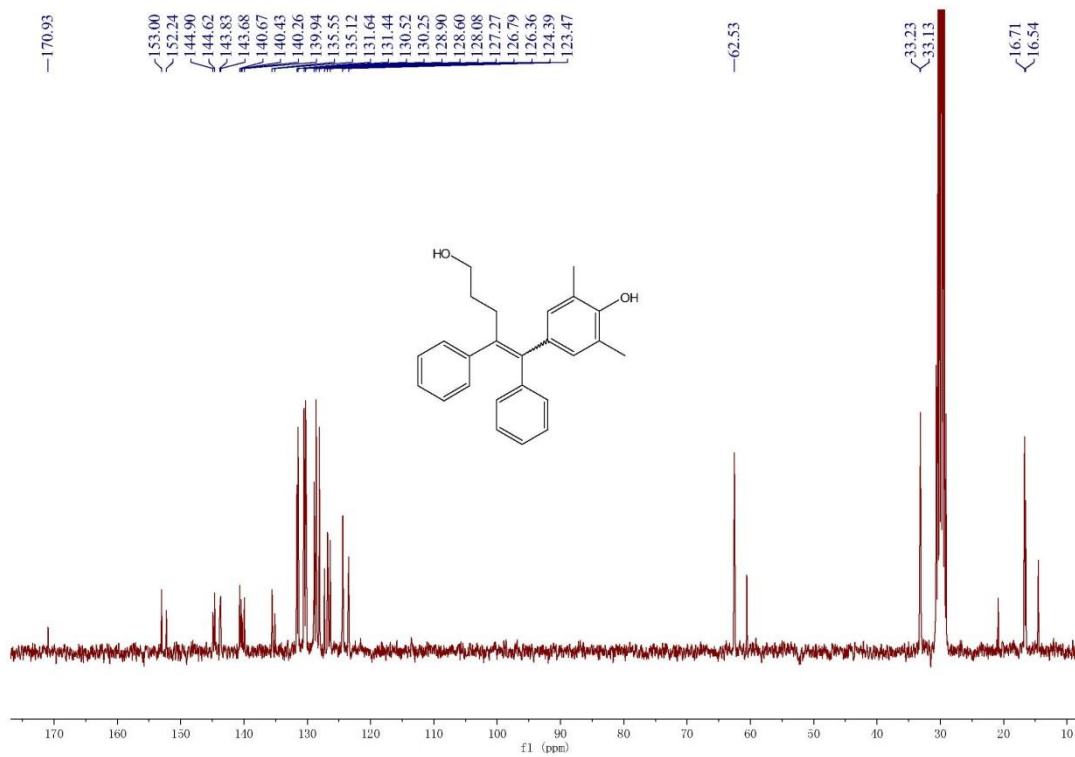
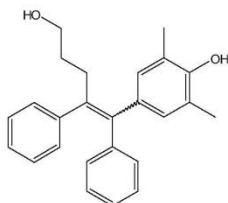
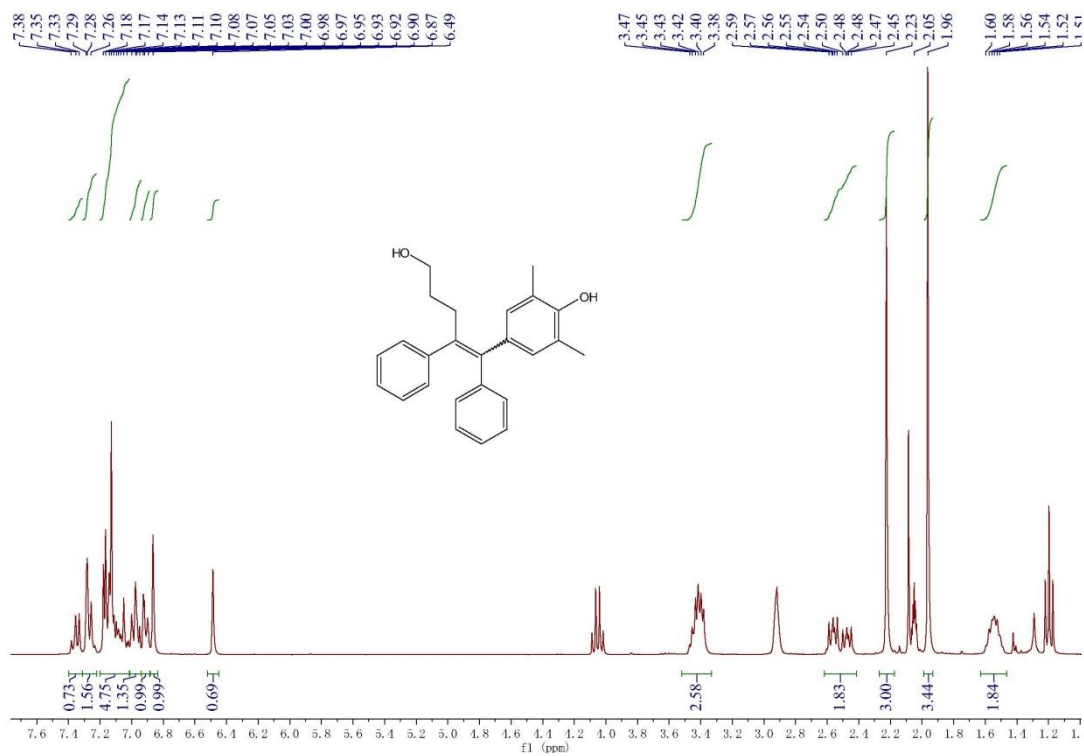
3c



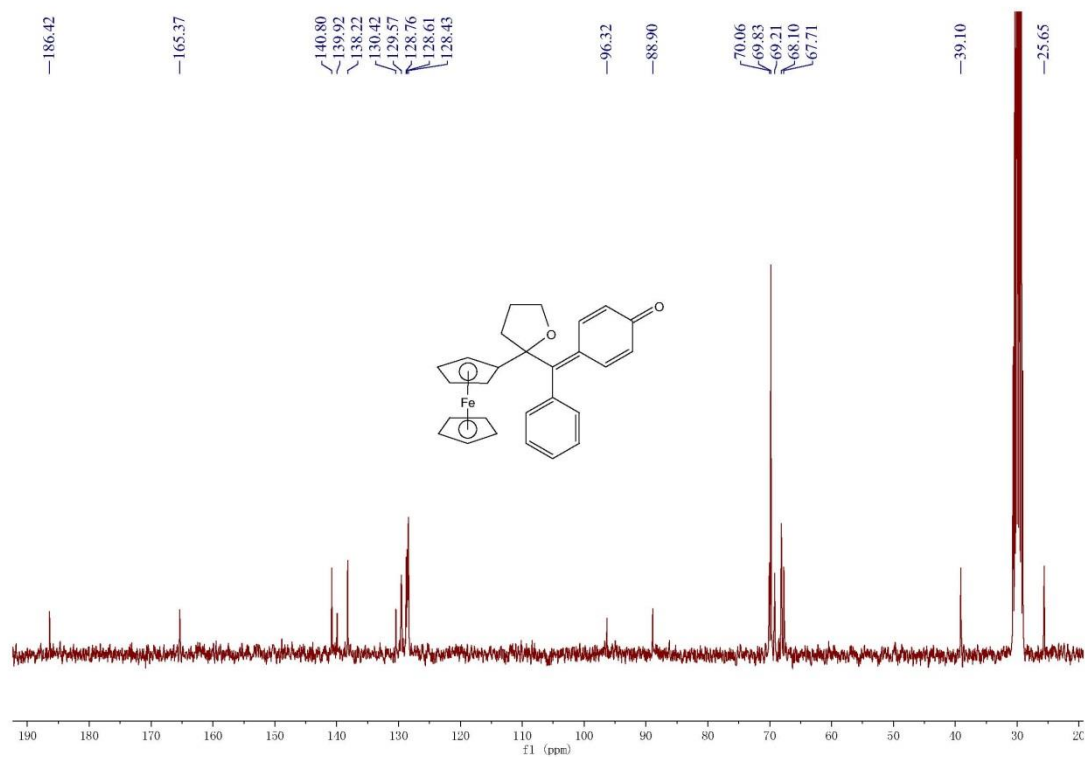
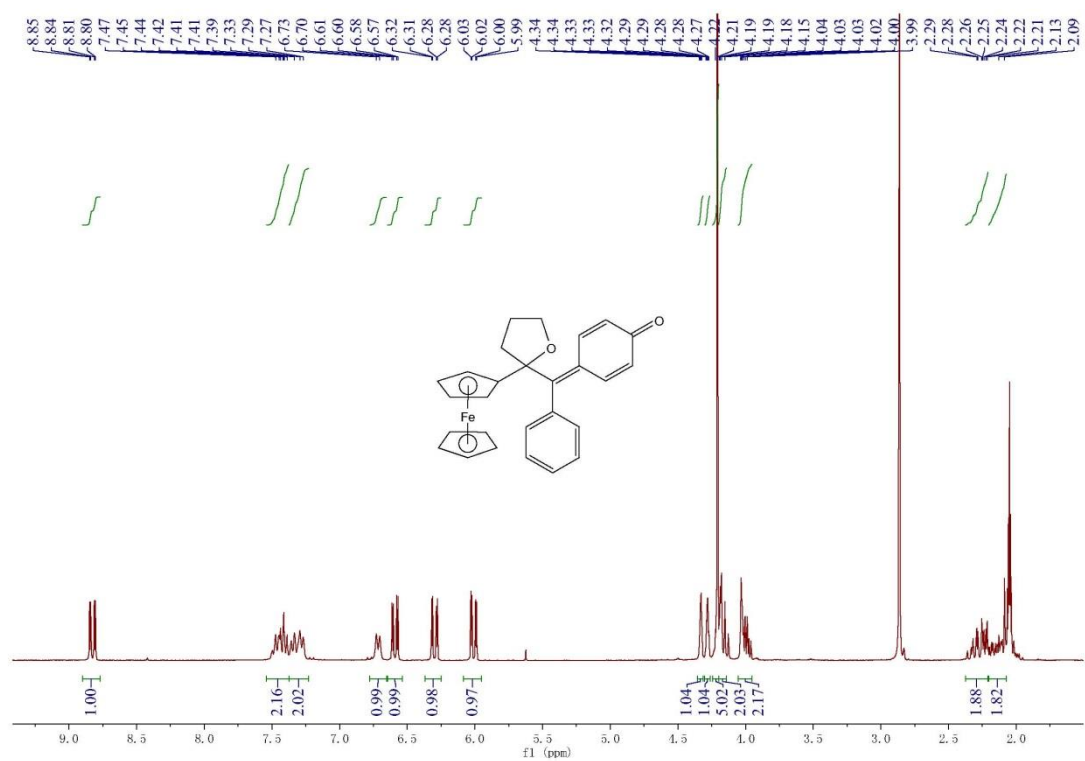
4b



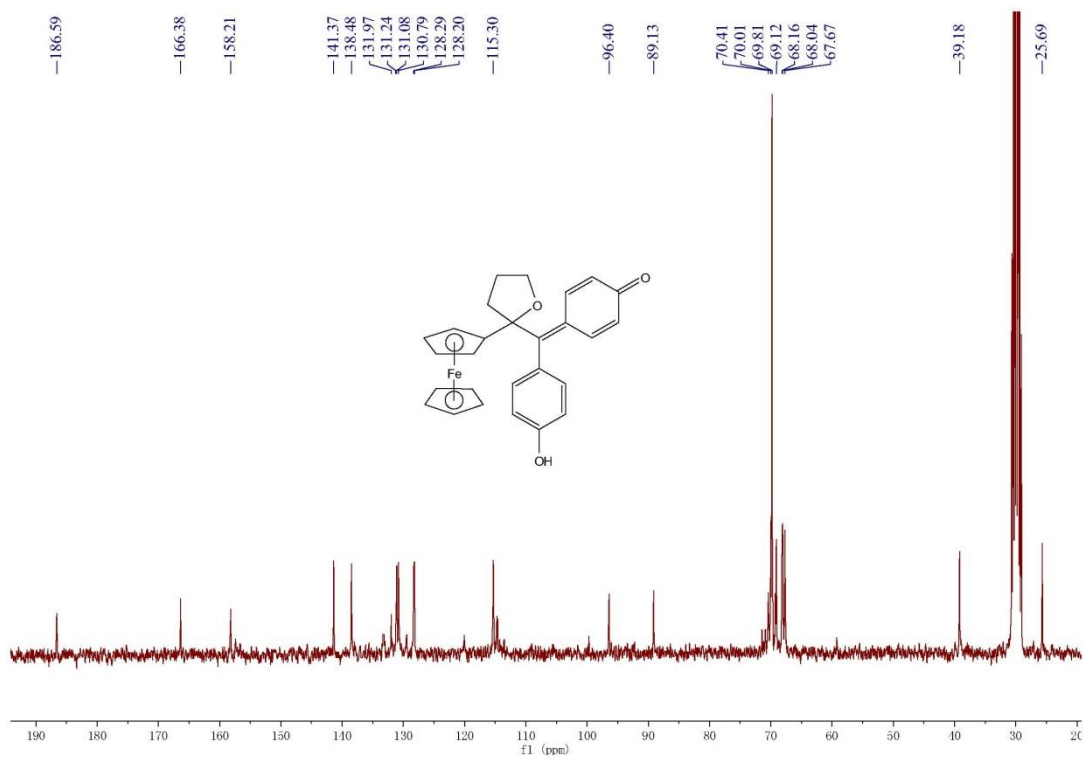
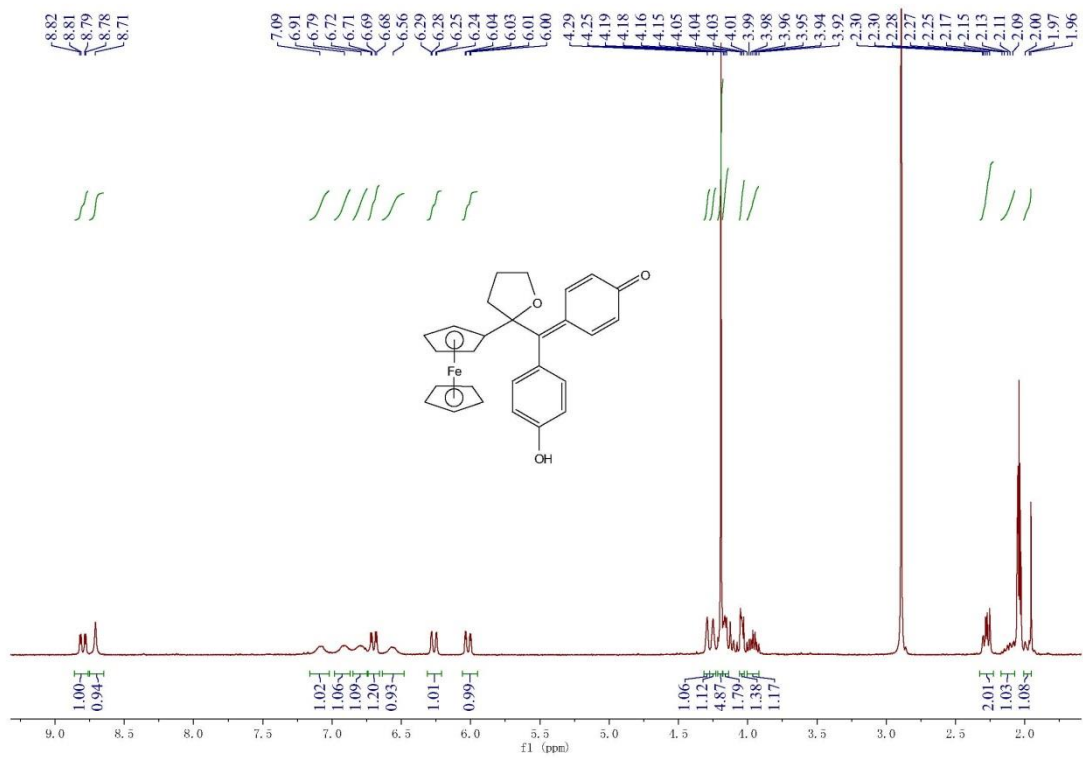
4c



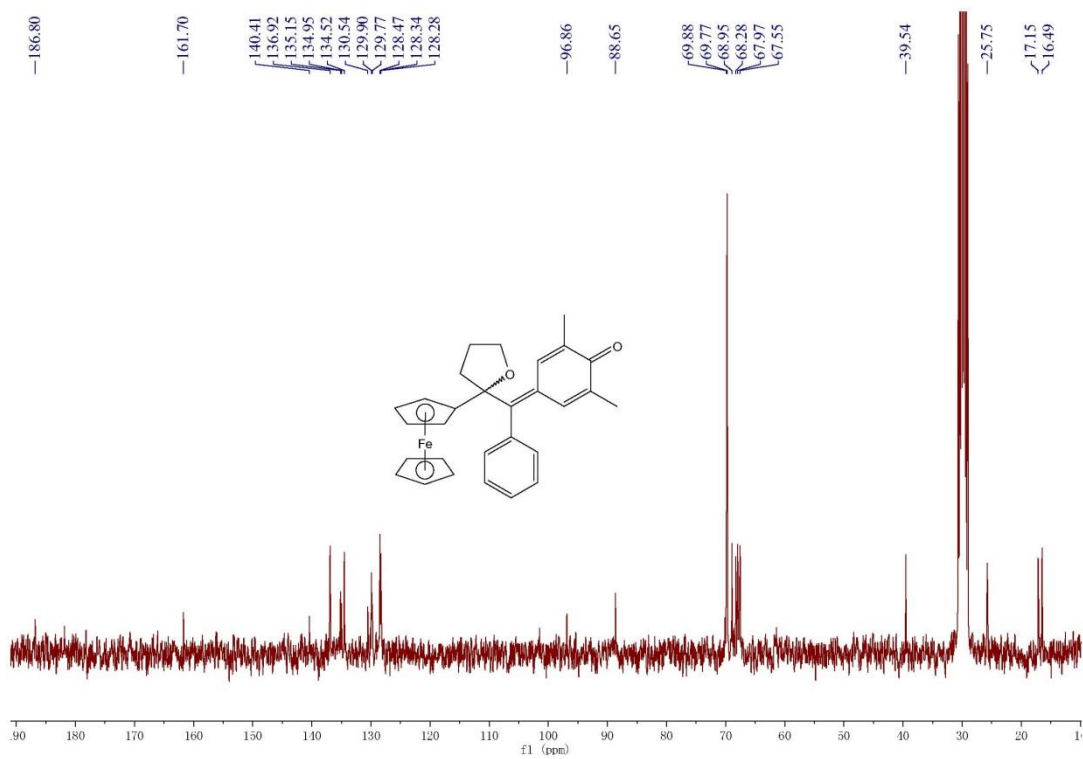
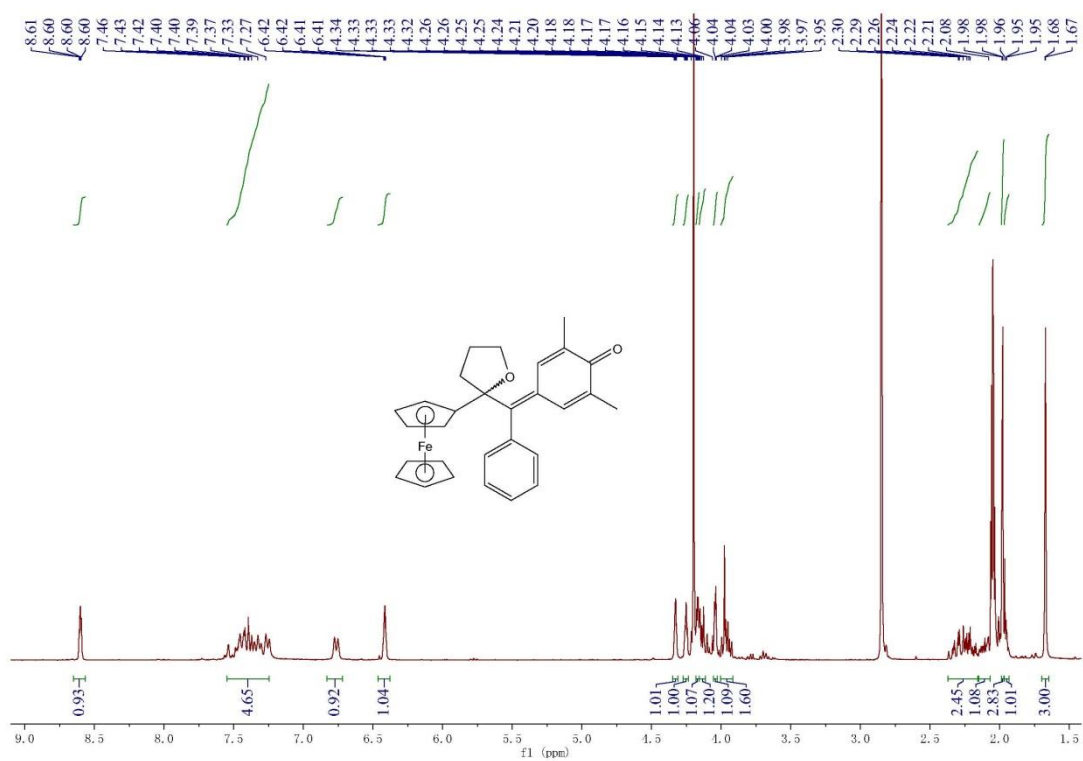
3a-QM



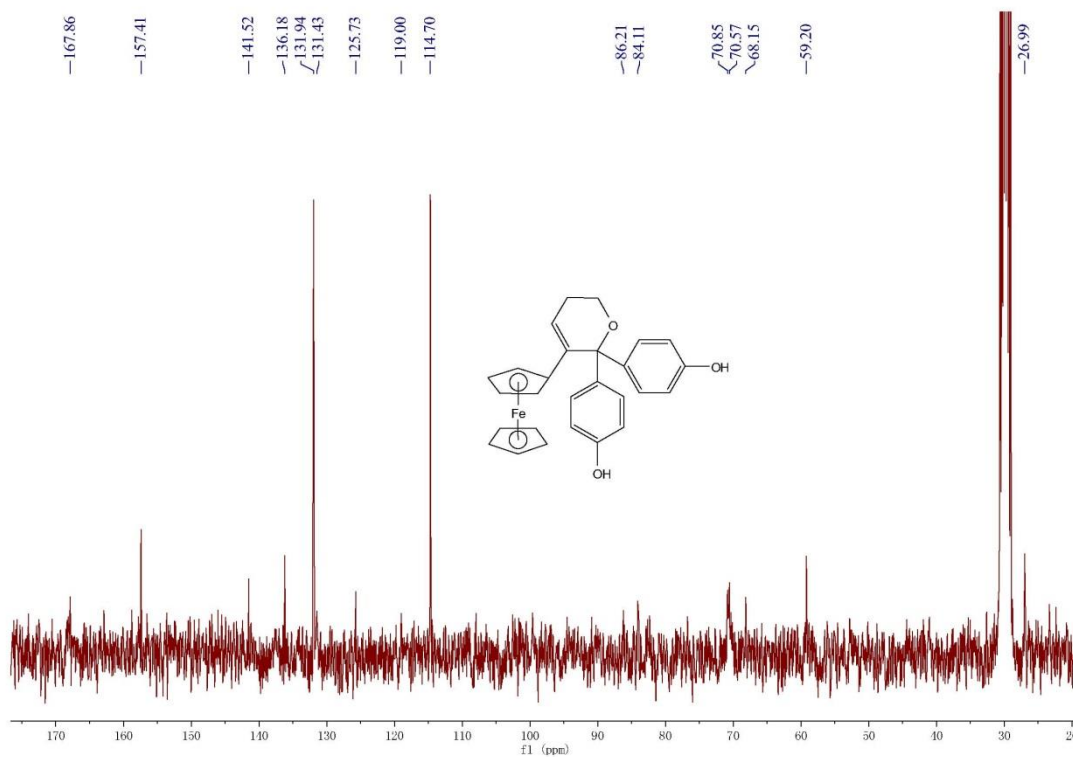
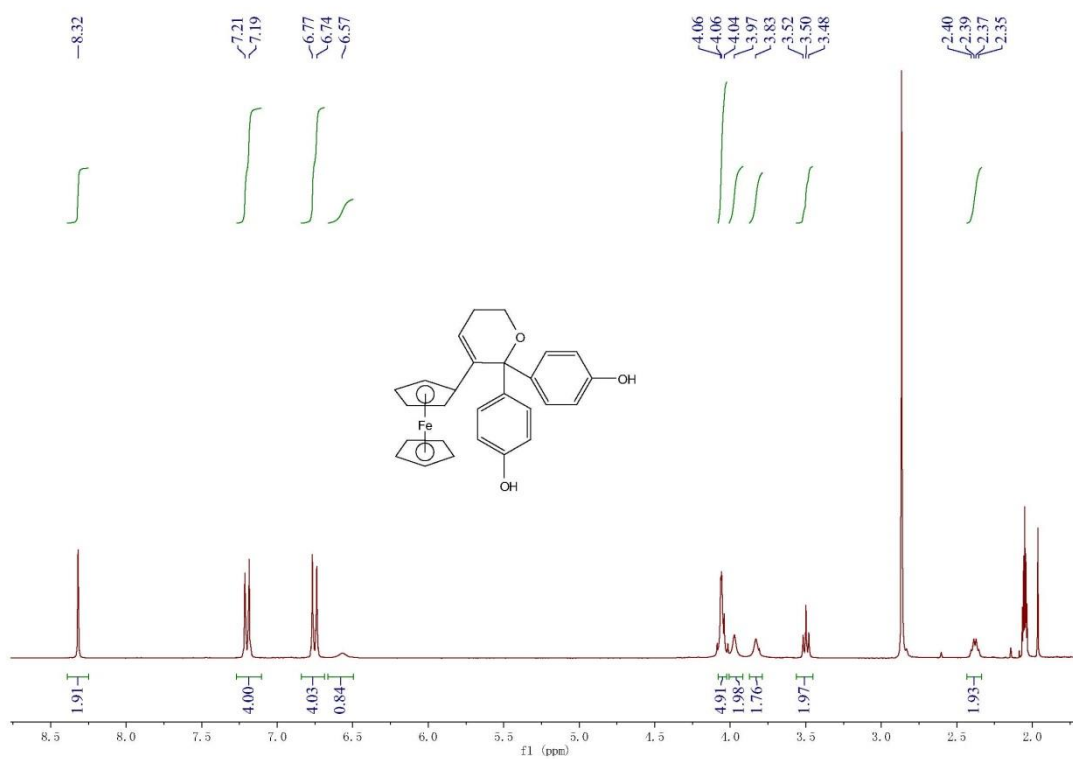
3b-QM



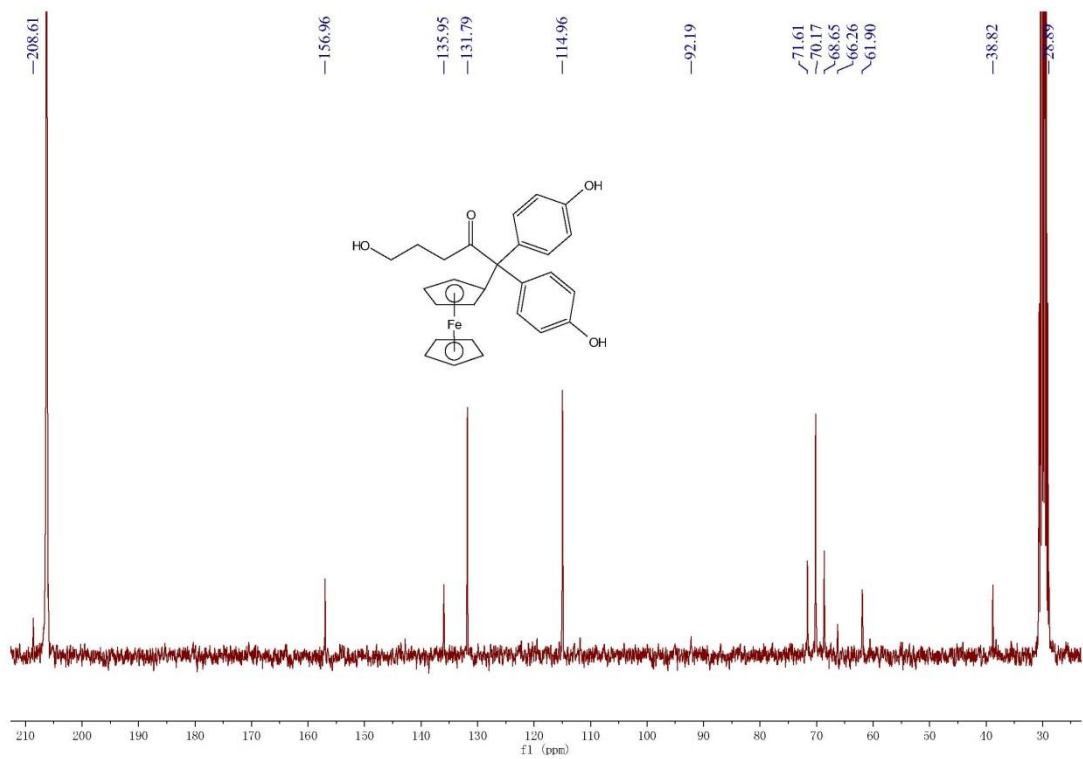
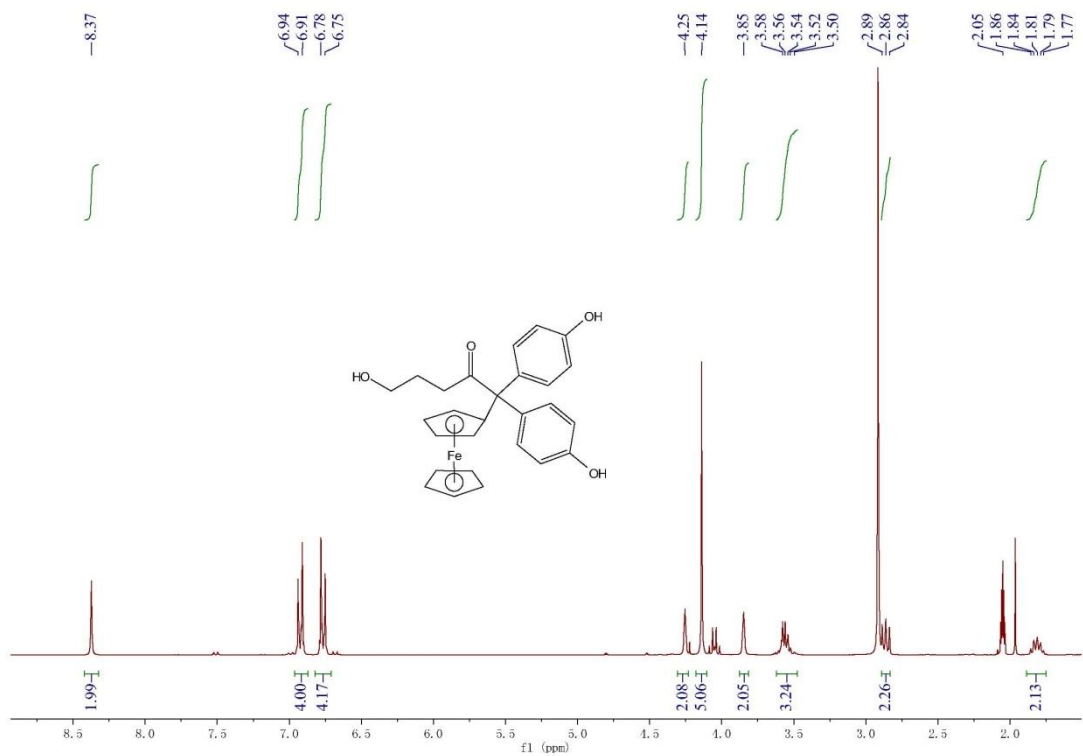
3c-QM



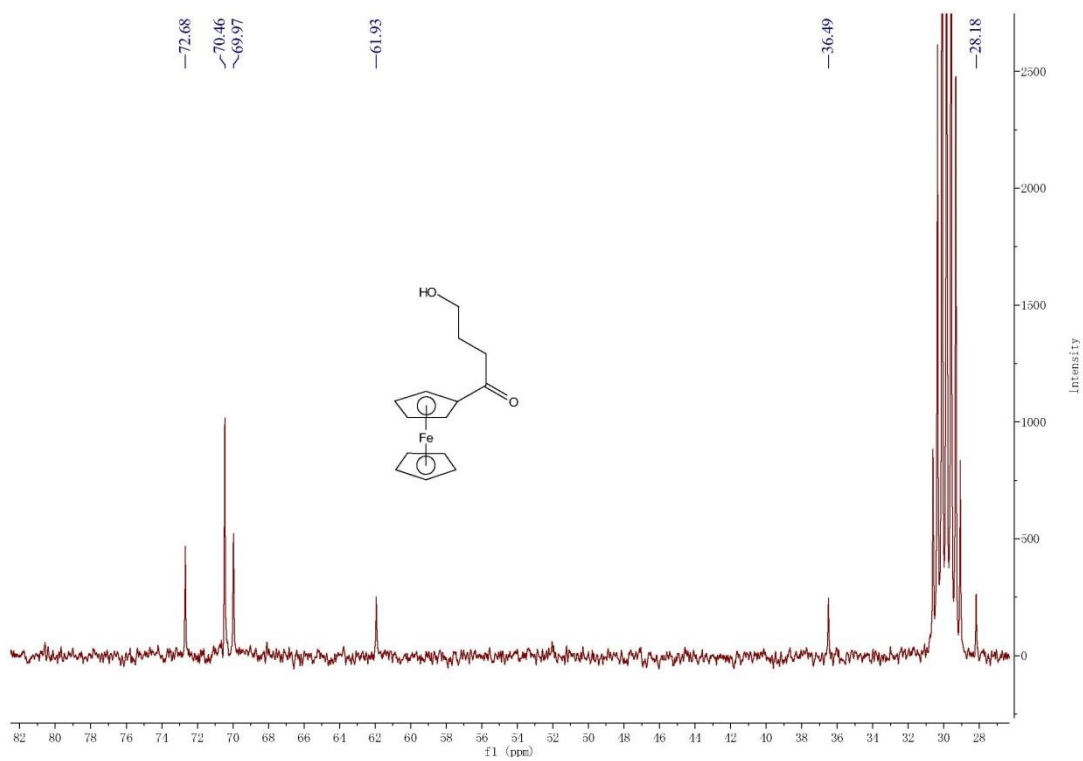
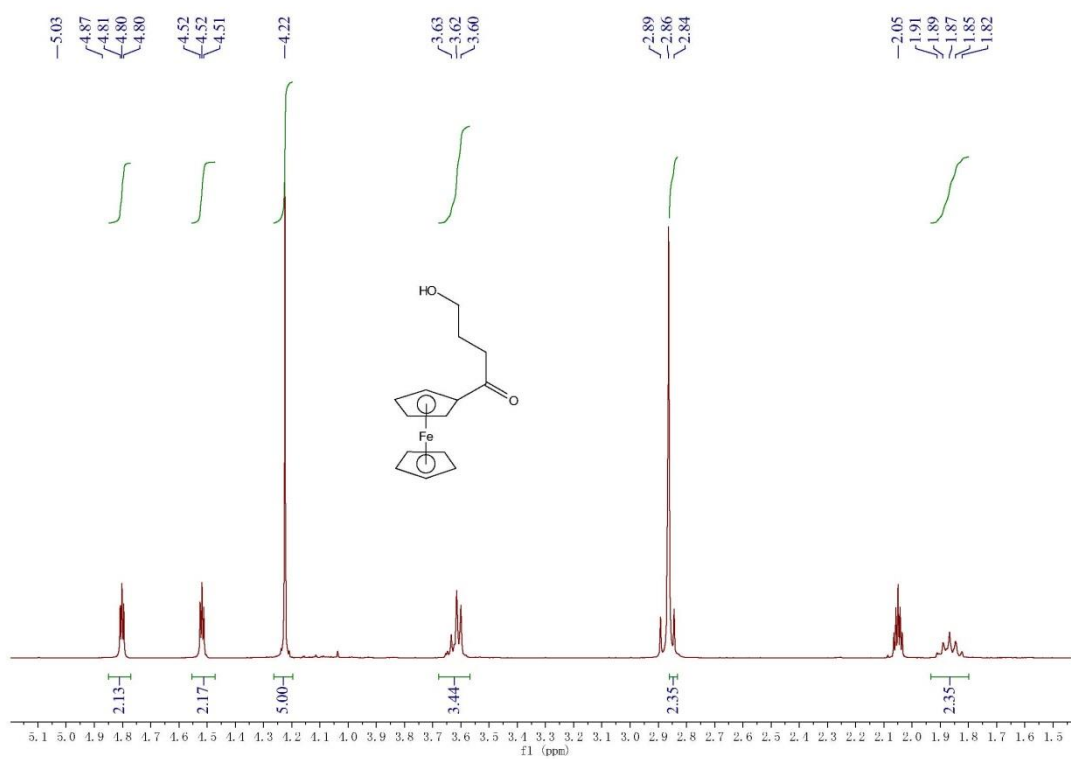
3b-A



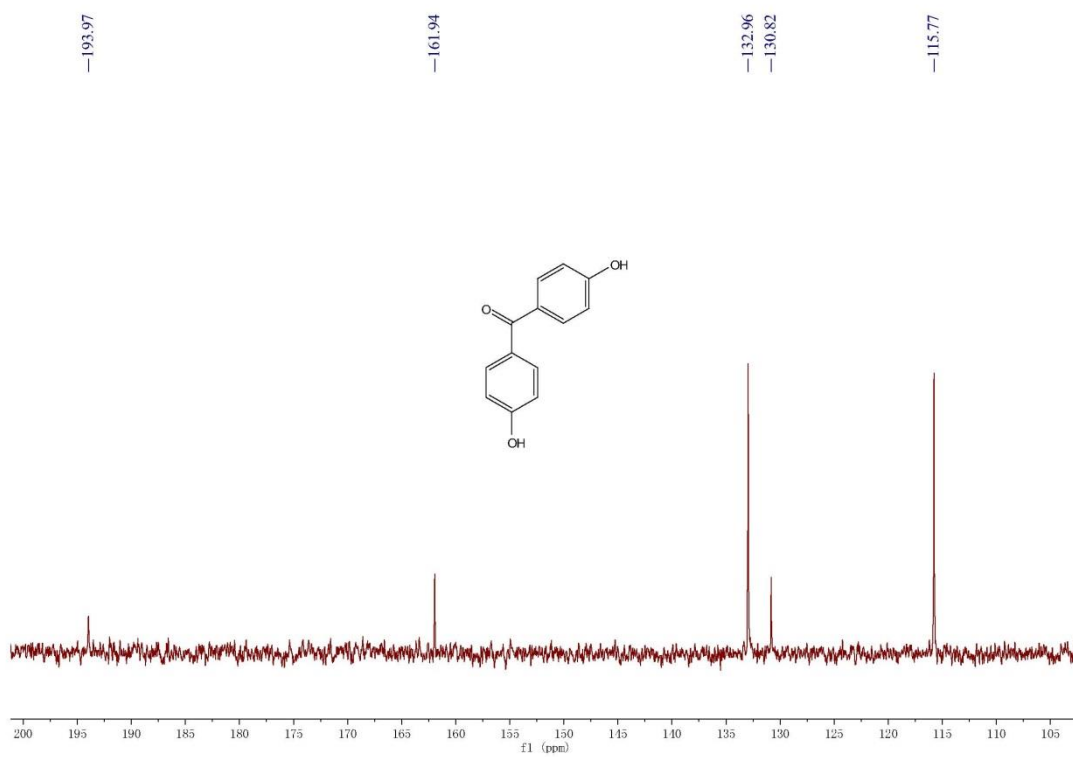
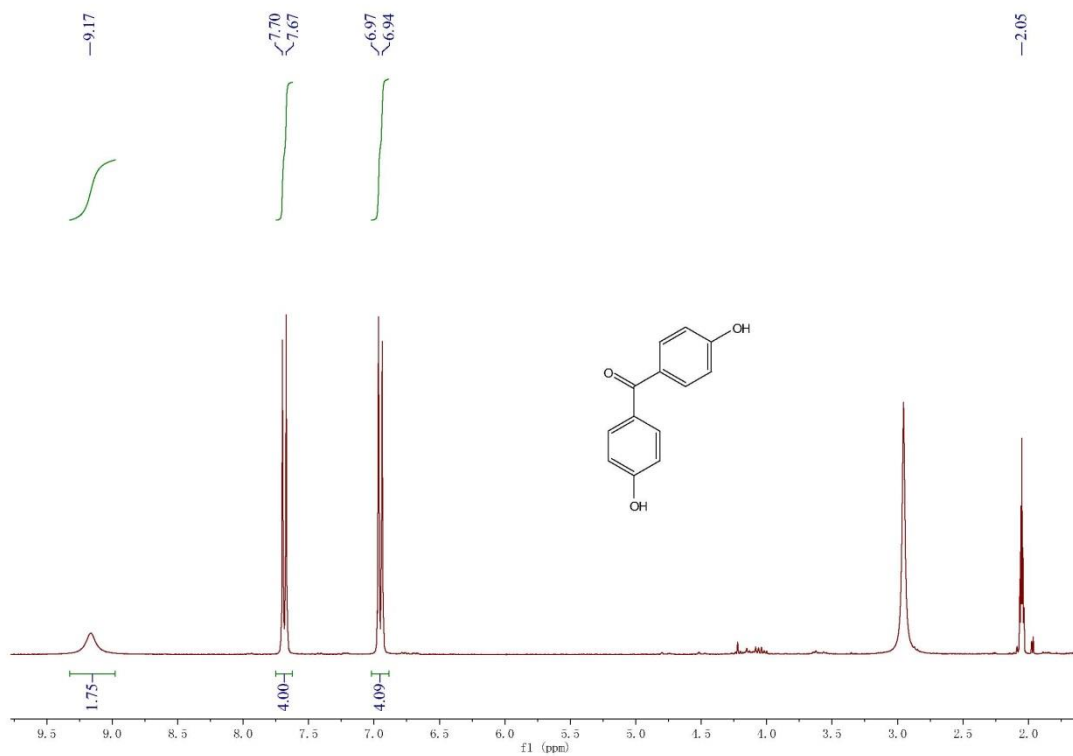
3b-B



3b-C



3b-D



3a

Elemental Composition Report

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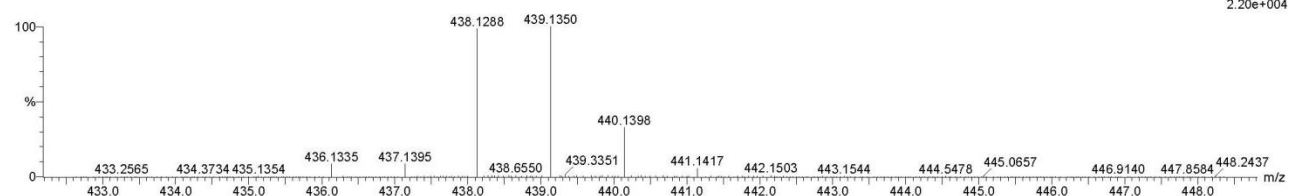
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Odd Electron Ions
422 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-150 N: 0-5 O: 0-20 Fe: 1-1
27-Feb-2013 19:08:24
ENSCP_P681 21 (0.578) Cm (19.26)

MeOH+CH2Cl2

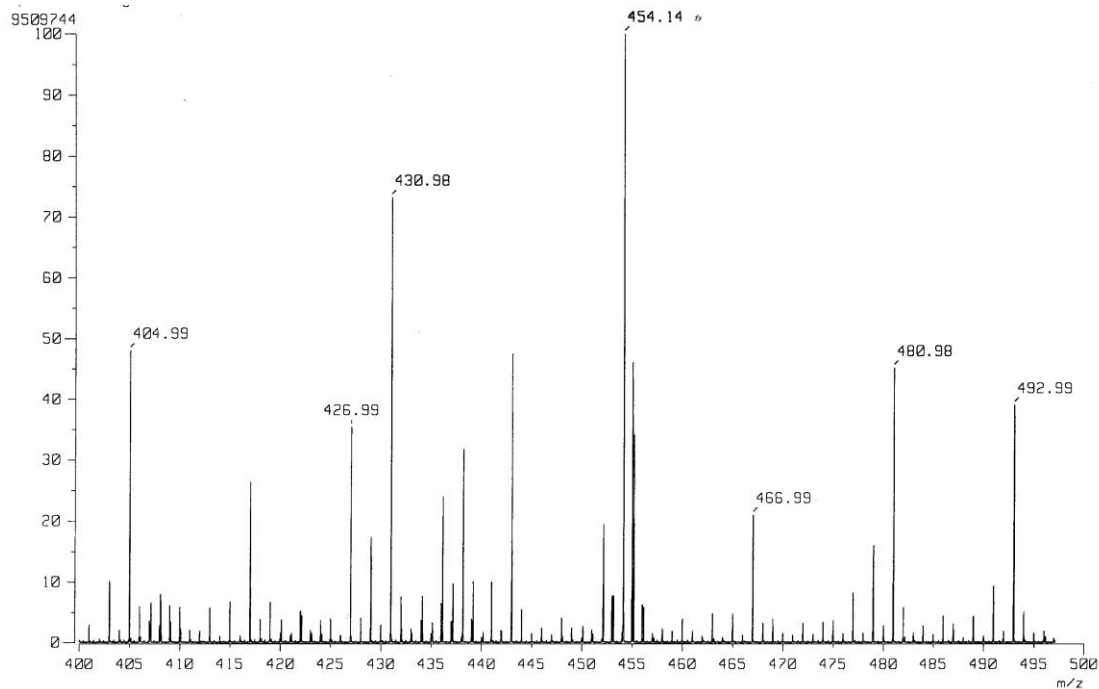
LCT Premier XE KE483
1: TOF MS ES+
2.20e+004



Minimum: -1.5
Maximum: 5.0 5.0 100.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
438.1288	438.1282	0.6	1.4	15.0	778.6	0.1	C27 H26 O2 Fe
	438.1301	-1.3	-3.0	2.0	781.0	2.5	C15 H30 N2 O9 Fe

3b



3c

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Odd Electron Ions

691 formula(e) evaluated with 3 results within limits (all results (up to 1000) for each mass)

Elements Used:

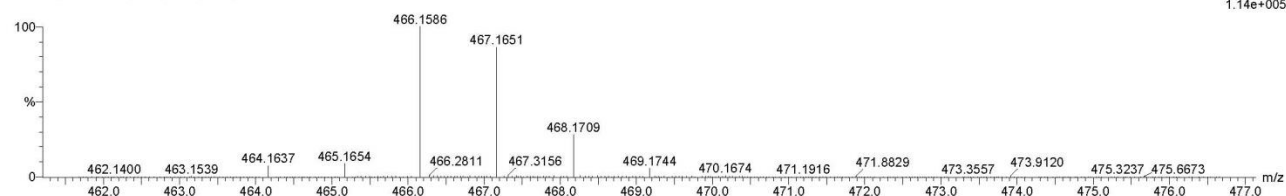
C: 1-100 H: 0-110 N: 0-10 O: 0-15 Fe: 1-1

27-Nov-2014 16:40:34

ENSCP_WS925 21 (0.570) Cm (17:28)

MeOH+CH2Cl2

LCT Premier XE KE483
1: TOF MS ES+
1.14e+005



Minimum: -1.5
Maximum: 10.0 5.0 100.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
466.1586	466.1595	-0.9	-1.9	15.0	1238.8	0.2	C29 H30 O2 Fe
	466.1568	1.8	3.9	16.0	1240.3	1.7	C25 H26 N6 Fe
	466.1587	-0.1	-0.2	3.0	1242.3	3.7	C13 H30 N8 O7 Fe

3a-QM

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Odd Electron Ions

628 formula(e) evaluated with 3 results within limits (all results (up to 1000) for each mass)

Elements Used:

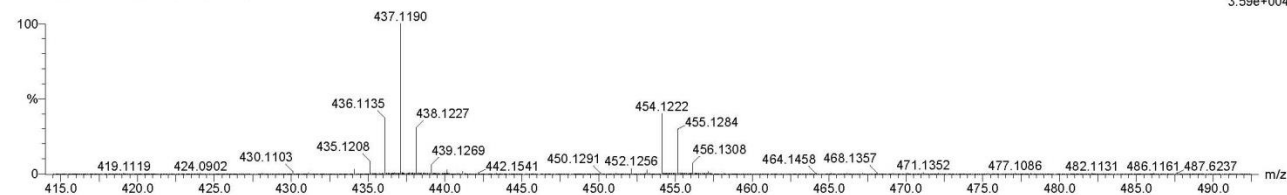
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27-Nov-2014 16:46:31

ENSCP_WY0206 21 (0.570) Cm (18:28)

MeOH+CH2Cl2

LCT Premier XE KE483
1: TOF MS ES+
3.59e+004



Minimum: -1.5
Maximum: 10.0 5.0 100.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
436.1135	436.1126	0.9	2.1	16.0	1097.0	0.4	C27 H24 O2 Fe
	436.1144	-0.9	-2.1	3.0	1098.1	1.5	C15 H28 N2 O9 Fe
	436.1117	1.8	4.1	4.0	1098.9	2.3	C11 H24 N8 O7 Fe

3b-QM

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Odd Electron Ions

53 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

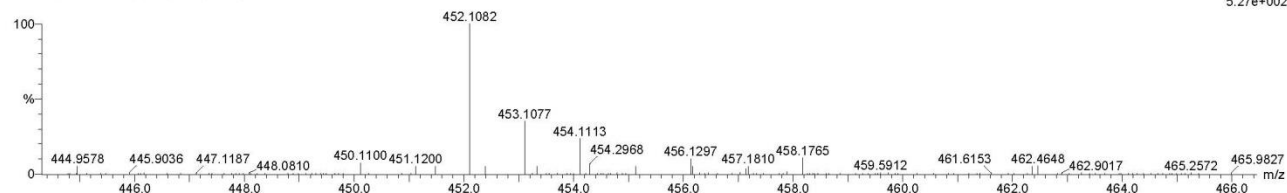
C: 1-110 H: 0-110 O: 0-10 Fe: 1-1

04-Mar-2014 11:19:38

ENSCP_WY1107 17 (0.483) Cm (16:17)

MeOH

LCT Premier XE KE483
1: TOF MS ES+
5.27e+002



Minimum: -1.5
Maximum: 10.0 5.0 100.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
452.1082	452.1075	0.7	1.5	16.0	152.2	0.0	C27 H24 O3 Fe

3c-QM

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Odd Electron Ions

689 formula(e) evaluated with 3 results within limits (all results (up to 1000) for each mass)

Elements Used:

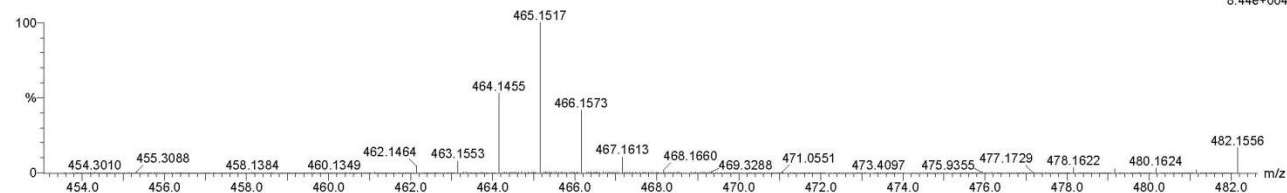
C: 1-100 H: 0-110 N: 0-10 O: 0-15 Fe: 1-1

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ENSCP_WO1009 21 (0.569) Cm (19:28)

MeOH+CH2Cl2

LCT Premier XE KE483
1: TOF MS ES+
8.44e+004



Minimum: -1.5
Maximum: 10.0 5.0 100.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
464.1455	464.1439	1.6	3.4	16.0	1201.2	0.4	C29 H28 O2 Fe
	464.1457	-0.2	-0.4	3.0	1202.5	1.7	C17 H32 N2 O9 Fe
	464.1471	-1.6	-3.4	8.0	1202.6	1.8	C18 H28 N6 O5 Fe

3b-A

Elemental Composition Report

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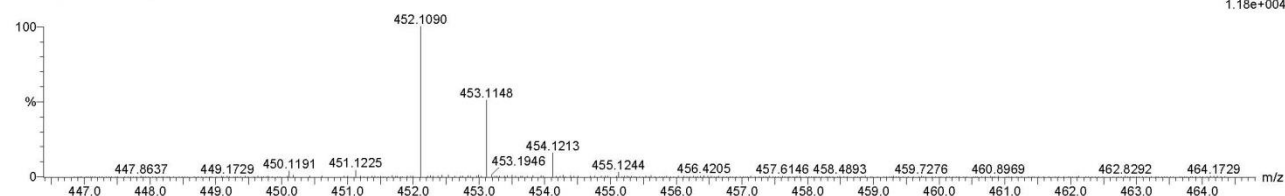
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Odd Electron Ions
53 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
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04-Mar-2014 11:22:40
ENSCP_WY1022-1 21 (0.572) Cm (20:26)

MeOH

LCT Premier XE KE483
1: TOF MS ES+
1.18e+004



Minimum: -1.5
Maximum: 10.0 5.0 100.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
452.1090	452.1075	1.5	3.3	16.0	710.7	0.0	C27 H24 O3 Fe

3b-B

Elemental Composition Report

Page 1

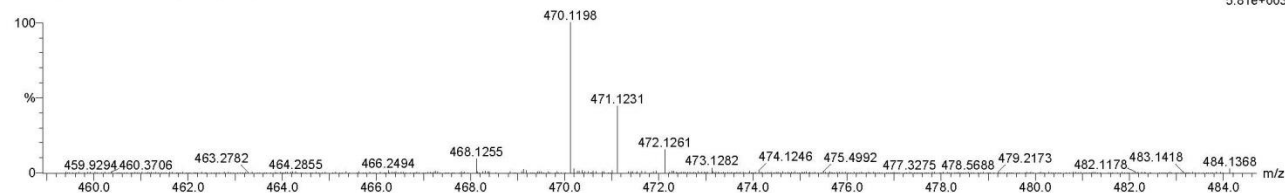
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Odd Electron Ions
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Elements Used:
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04-Mar-2014 11:13:38
ENSCP_WY1022-3 25 (0.663) Cm (25:34)

MeOH

LCT Premier XE KE483
1: TOF MS ES+
5.81e+003



Minimum: -1.5
Maximum: 10.0 5.0 100.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
470.1198	470.1180	1.8	3.8	15.0	569.0	0.0	C27 H26 O4 Fe