

Supplementary Information

Luminescent conjugates between dinuclear rhenium complexes and 17 α -Ethinylestradiol: synthesis, photophysical characterization, and cell imaging

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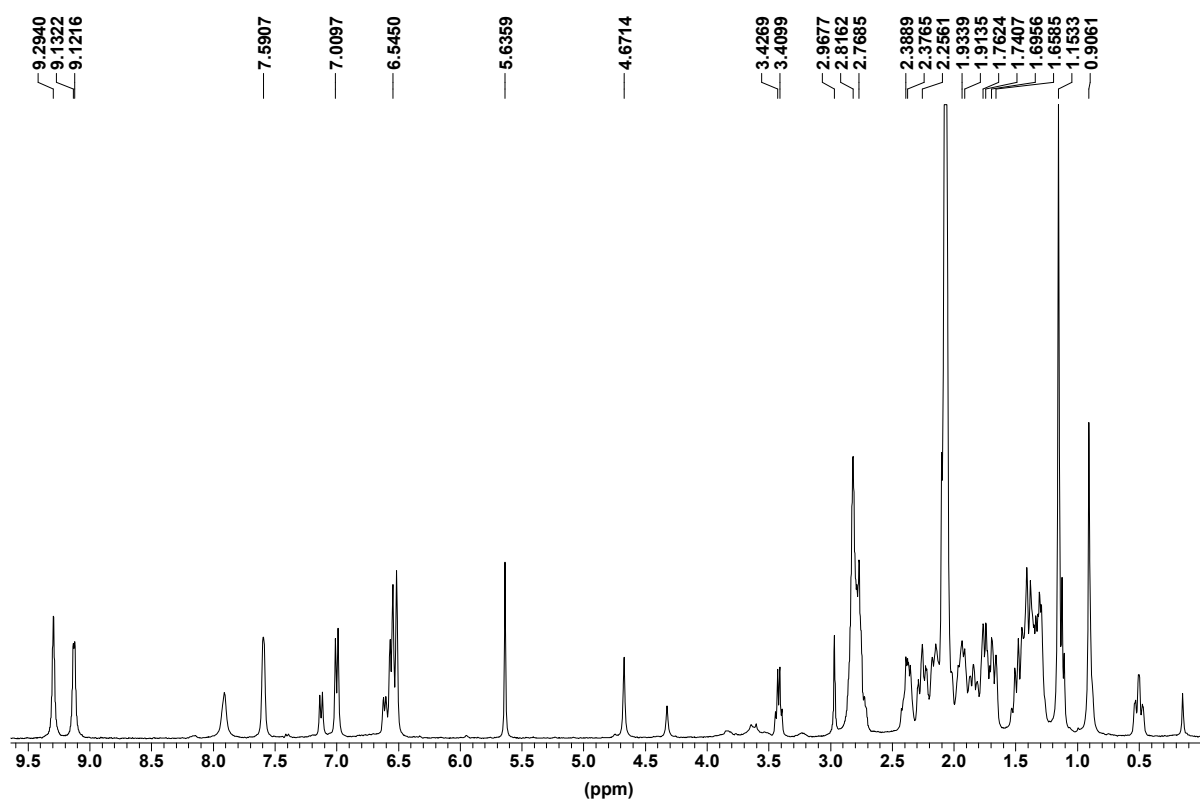
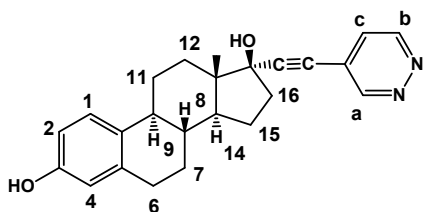
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Content

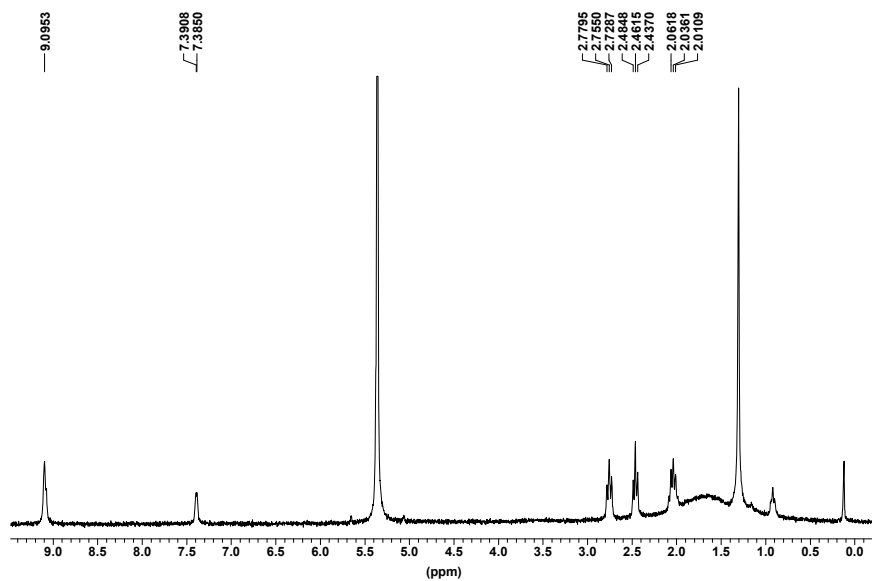
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Compound D1



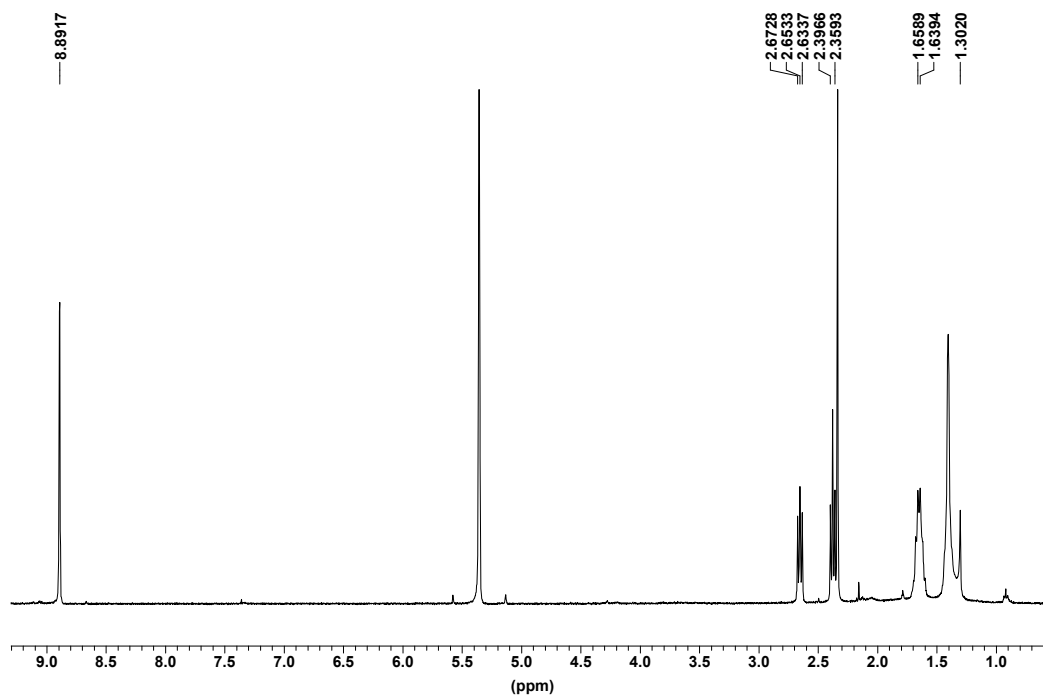
¹H NMR (Acetone-d₆, 298 K): δ = 9.29 (1H, s, H_a pydz), 9.13 (1H, d, H_b pydz), 7.59 (1H, d, H_c pydz), 7.09 (1H, d, H₄), 6.54 (2H, m, H₁, H₂), 4.67 (1H, s, 3-OH), 2.81 (1H, m, H₆), 2.5-2.0 (3H, m, H₁₁ α , H₁₁ β , H₁₂ β), 2.00-1.6 (5H, m, H₉, H₁₅ α , H₁₅ β , H₇ α , H₁₆ α), 1.5-1.3 (4H, m, H₈, H₁₄, H₇ β , H₁₂ α), 1.15 (3H, CH₃), 0.5 (1H, m, H₁₆ β).

Compound D2



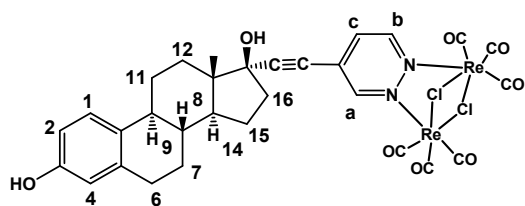
$^1\text{H NMR}$ (CD_2Cl_2 , 298 K): $\delta = 9,09$ (2H, s), 7,39 (1H, s), 2,75 (2H, m), 2,46 (2H, m), 2,06 (2H, m)

Compound D3



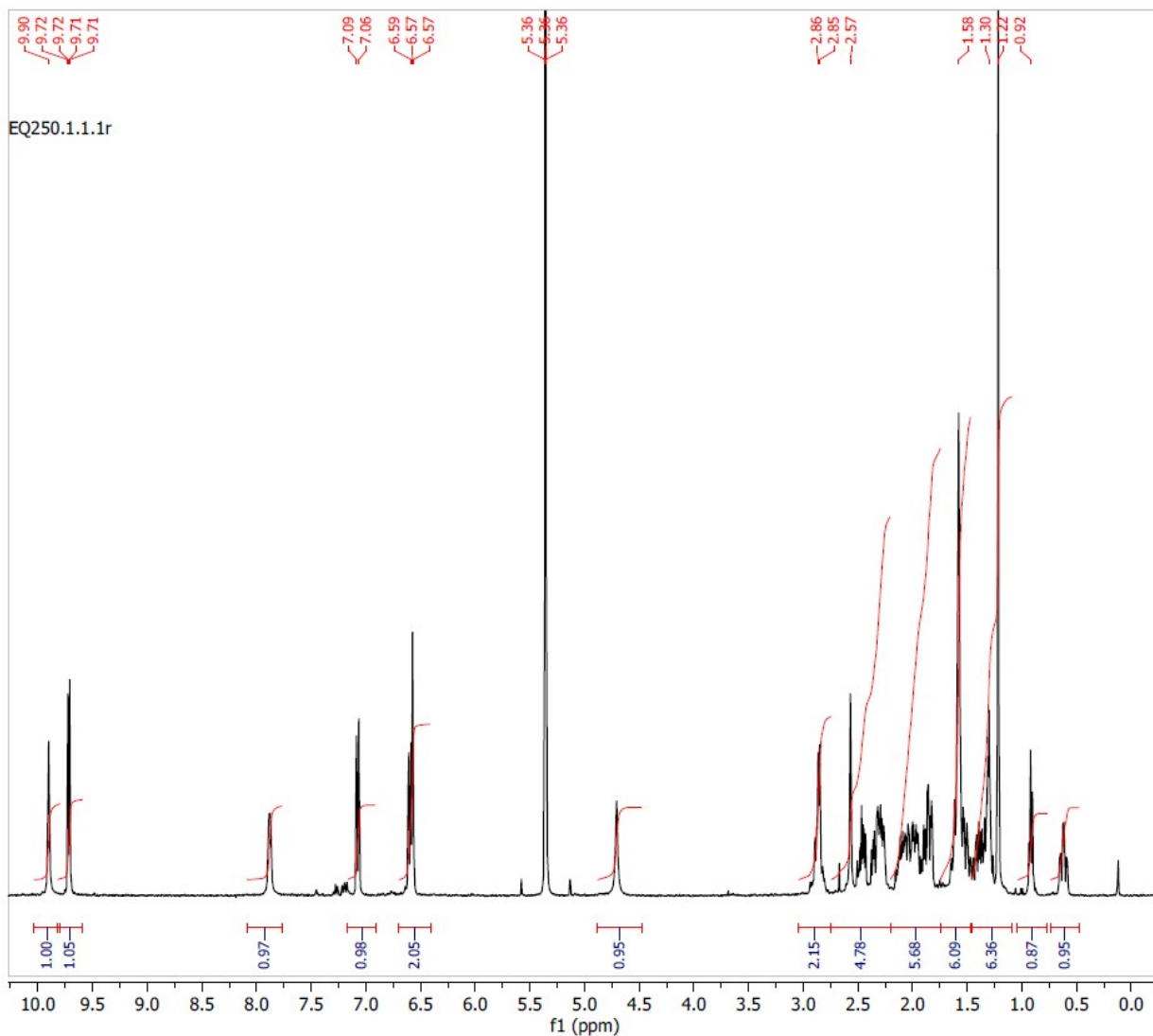
$^1\text{H NMR}$ (CD_2Cl_2 , 298 K): δ 1.76-1.30 (m, 10H, $\text{CH}_2\text{-(CH}_2)_5\text{-CH}_2\text{-COOH}$), 2.40 (t, $J = 7.0$, 2H, $\text{CH}_2\text{-(CH}_2)_5\text{-CH}_2\text{-COOH}$), 2.36 (s, 3H, CH_3), 2.65 (pt, 2H, $\text{CH}_2\text{-(CH}_2)_5\text{-CH}_2\text{-COOH}$), 8.89 (s, 2H, H_{ortho} accidental overlap) ppm.

Complex E2-Re1

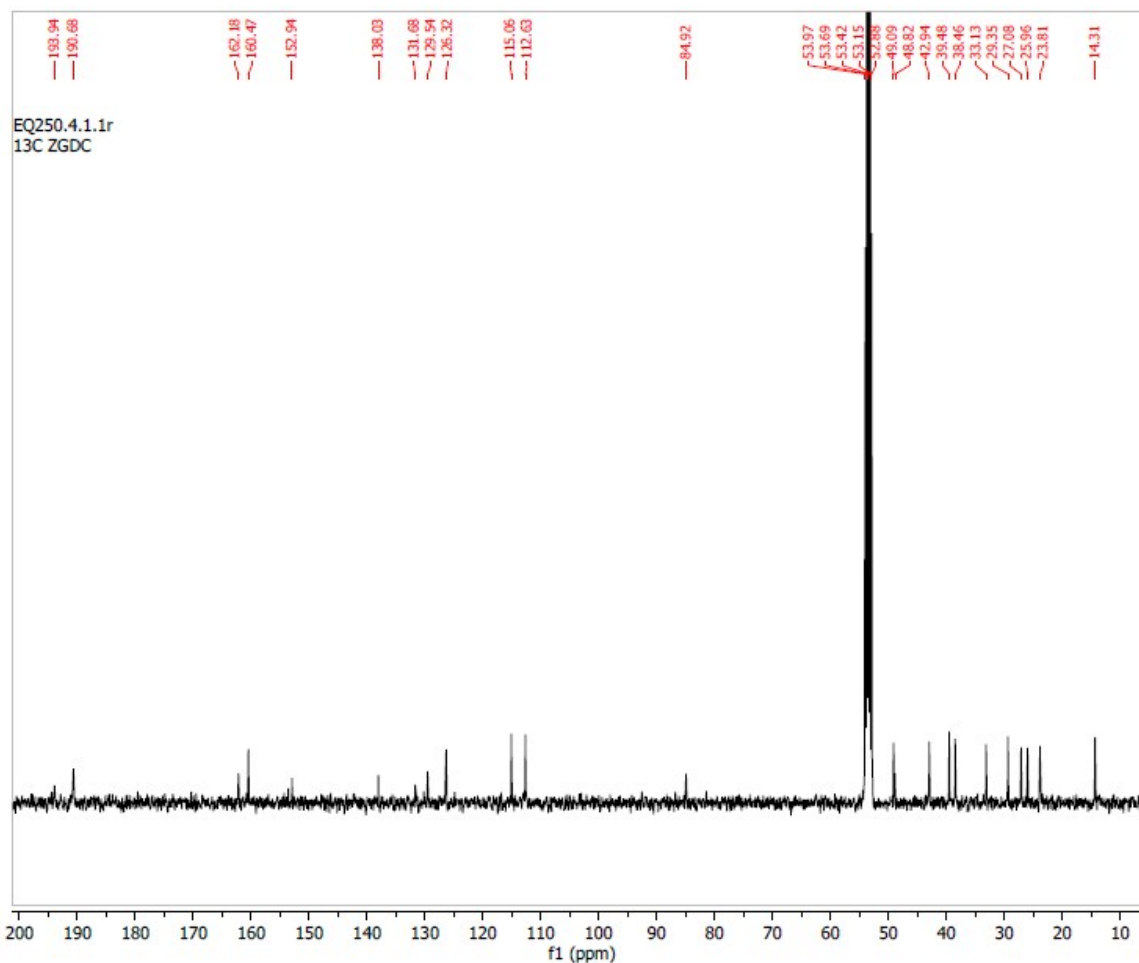


Chemical Formula: $C_{30}H_{26}Cl_2N_2O_8Re_2$

Molecular Weight: 986.02

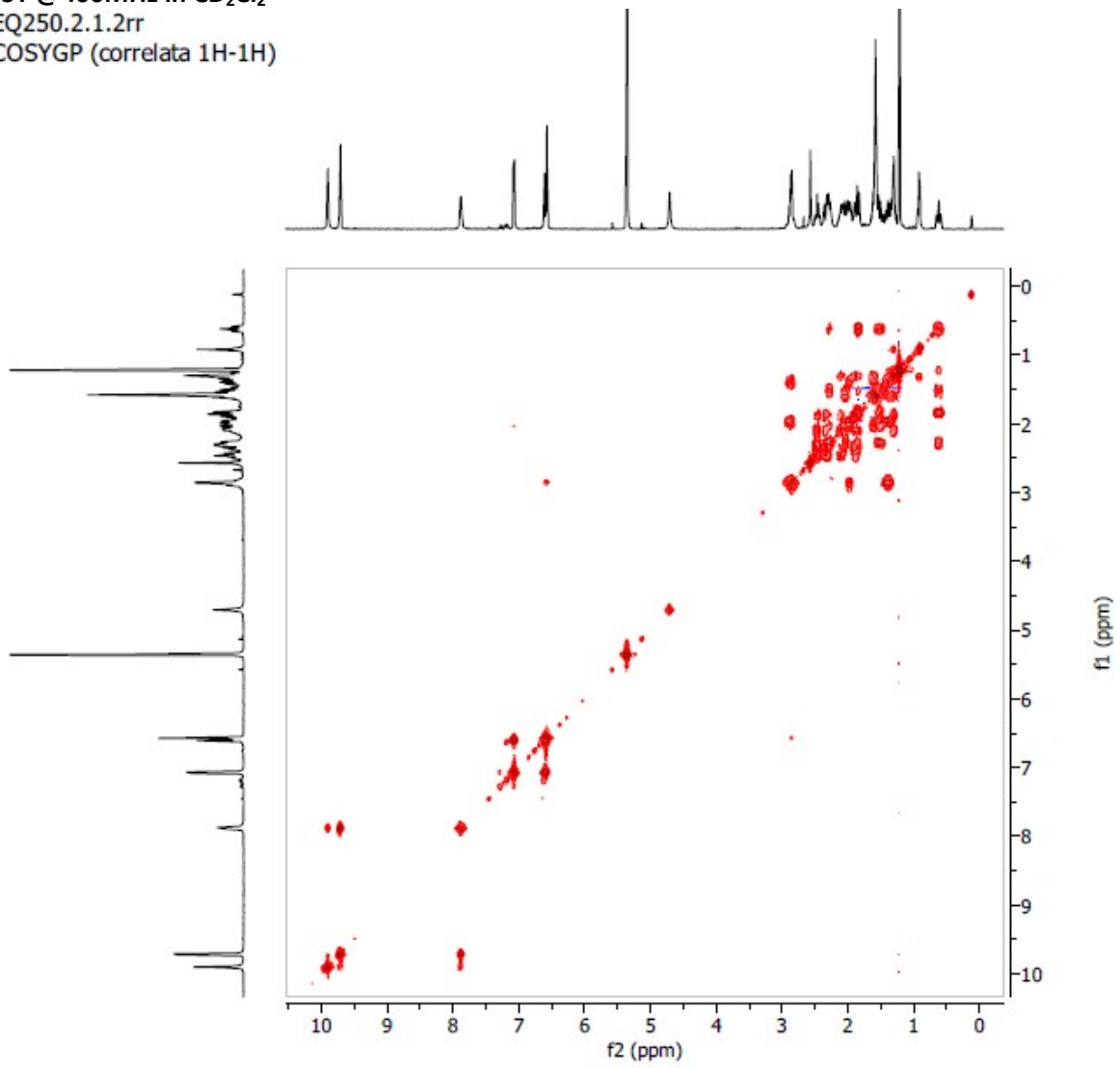


1H NMR (CD_2Cl_2 , 400 MHz, 298 K): δ = 9.90 (1H, s, H_a pydz), 9.72 (1H, d, H_b pydz), 7.87 (1H, d, H_c pydz), 7.09 (1H, d, H1), 6.57 (2H, m, H2, H4), 4.71 (1H, s, 3-OH), 2.86 (2H, m, H6), 2.55-2.2 (3H, m, H11 α , H11 β , H12 β), 2.10-1.75 (5H, m, H9, H15 α , H15 β , H7 α , H16 α), 1.6-1.3 (4H, m, H8, H14, H7 β , H12 α), 1.22 (3H, CH_3), 0.62 (1H, m, H16 β)

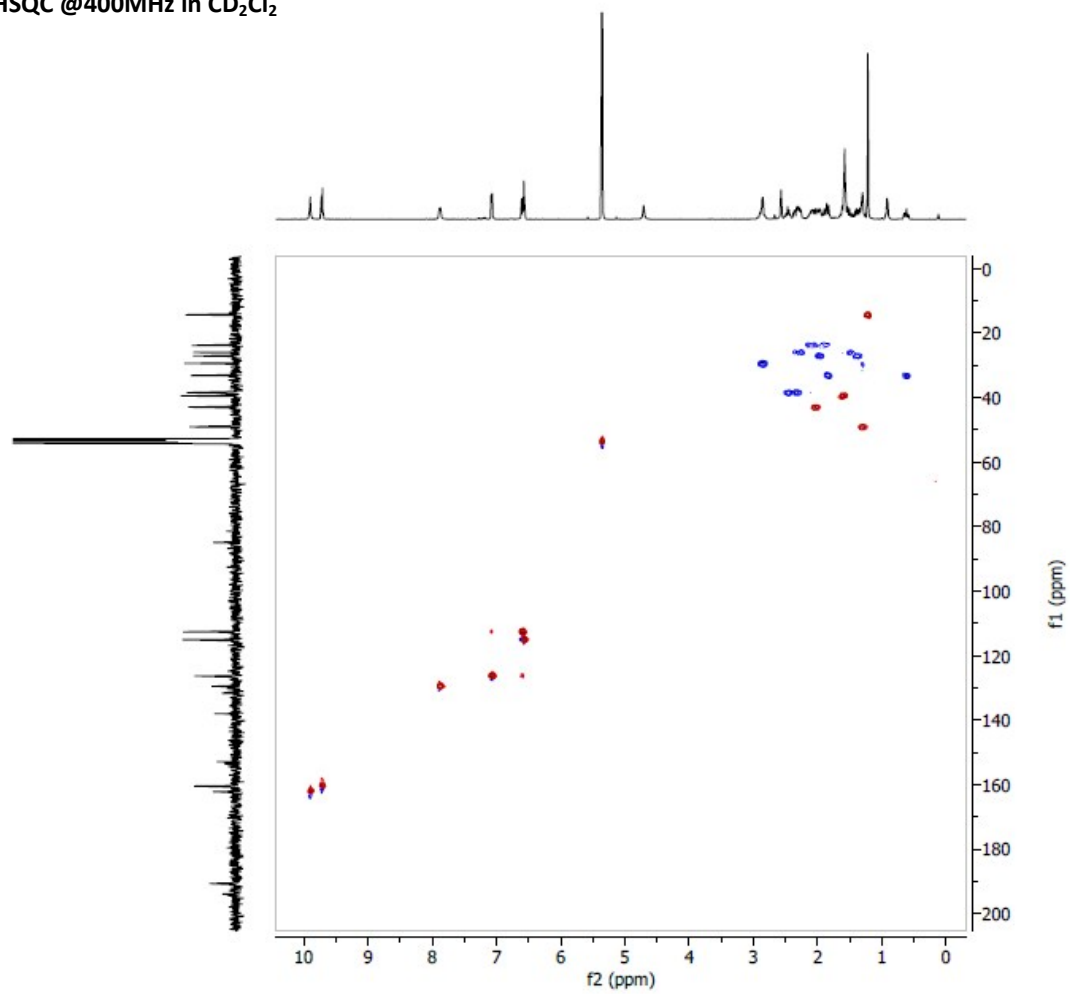


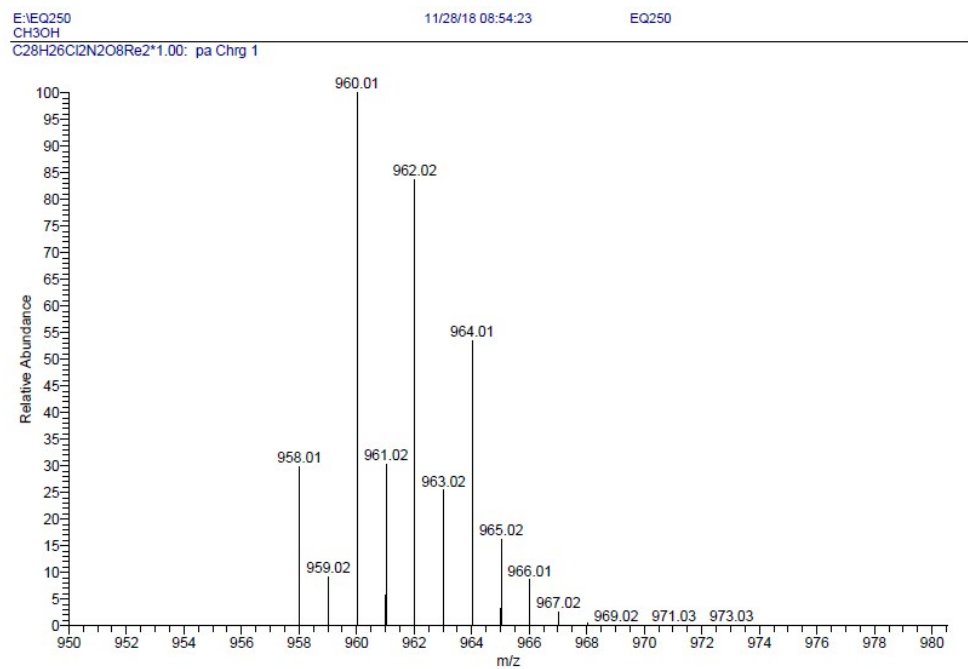
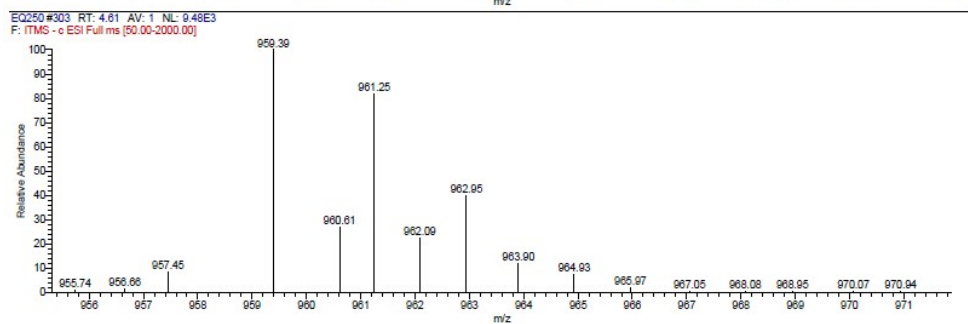
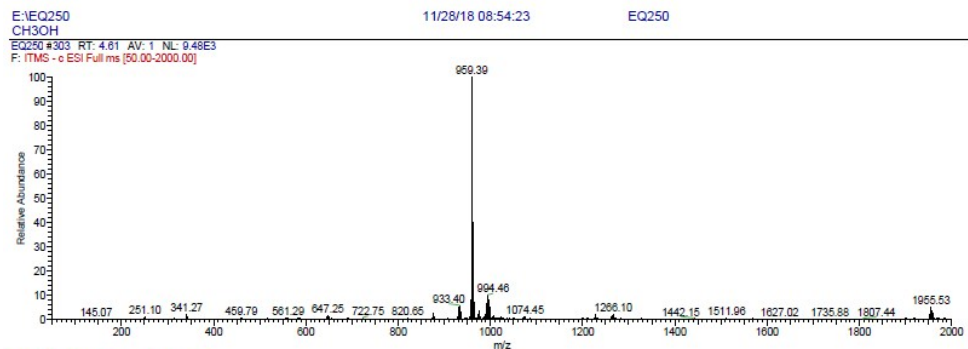
^{13}C NMR (CD_2Cl_2 , 400 MHz, 298 K): δ = 193.95 (1C, CO), 190.08 (1C, CO), 162.18 (1C, C_a pydz), 160.48 (2C, C_b pydz + quater), 153.58 (1C, CO), 152.94 (1C, CO), 138.03 (1C, CO), 131.68 (1C, CO), 129.54 (1C, C_c pydz), 126.33 (1C, C_1 estradiol), 115.06 (1C, C_4 estradiol), 112.63 (1C, C_2 estradiol), 84.92 (1C, quater), 49.09 (1C, C_{14} estradiol), 48.81 (1C, quater), 42.94 (1C, C_9 estradiol), 39.48 (1C, C_8 estradiol), 38.45 (1C, C_{11} estradiol), 33.12 (1C, C_{16} estradiol), 29.35 (1C, C_6 estradiol), 27.98 (1C, C_7 estradiol), 25.96 (1C, C_{12} estradiol), 23.81 (1C, C_{15} estradiol), 14.31 (1C, CH_3 estradiol).

COSY @400MHz in CD₂Cl₂
EQ250.2.1.2rr
COSYGP (correlata 1H-1H)



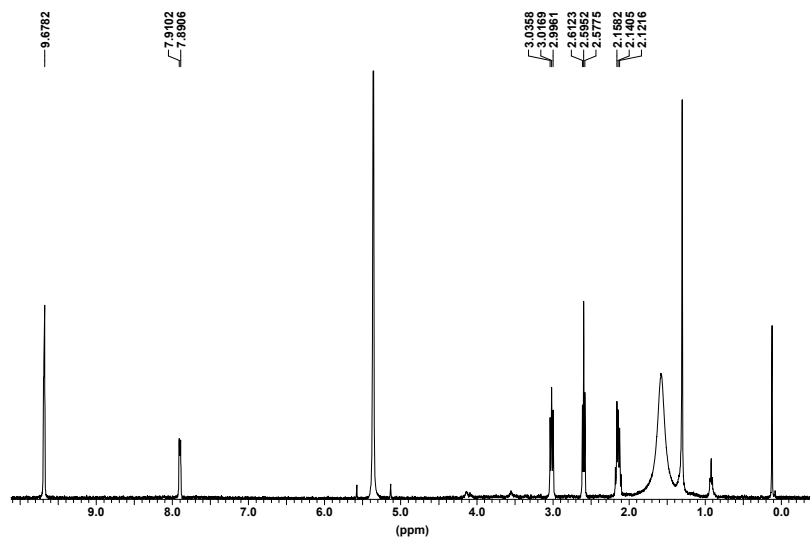
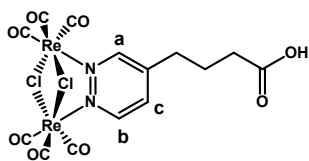
HSQC @400MHz in CD₂Cl₂





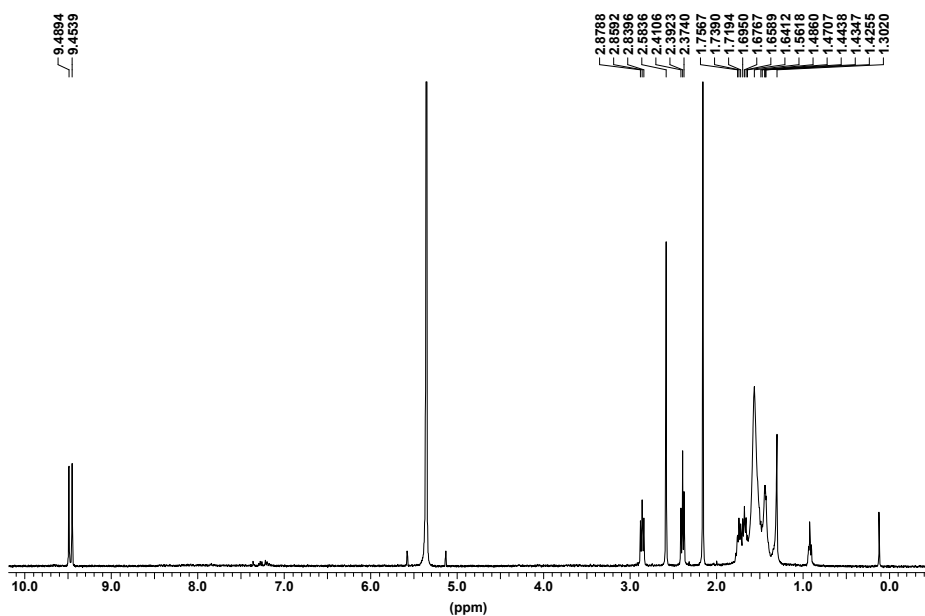
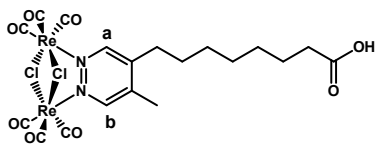
ESI-MS experimental and calculated (right) isotopic distribution for the **E2-Re1**

Complex Re2



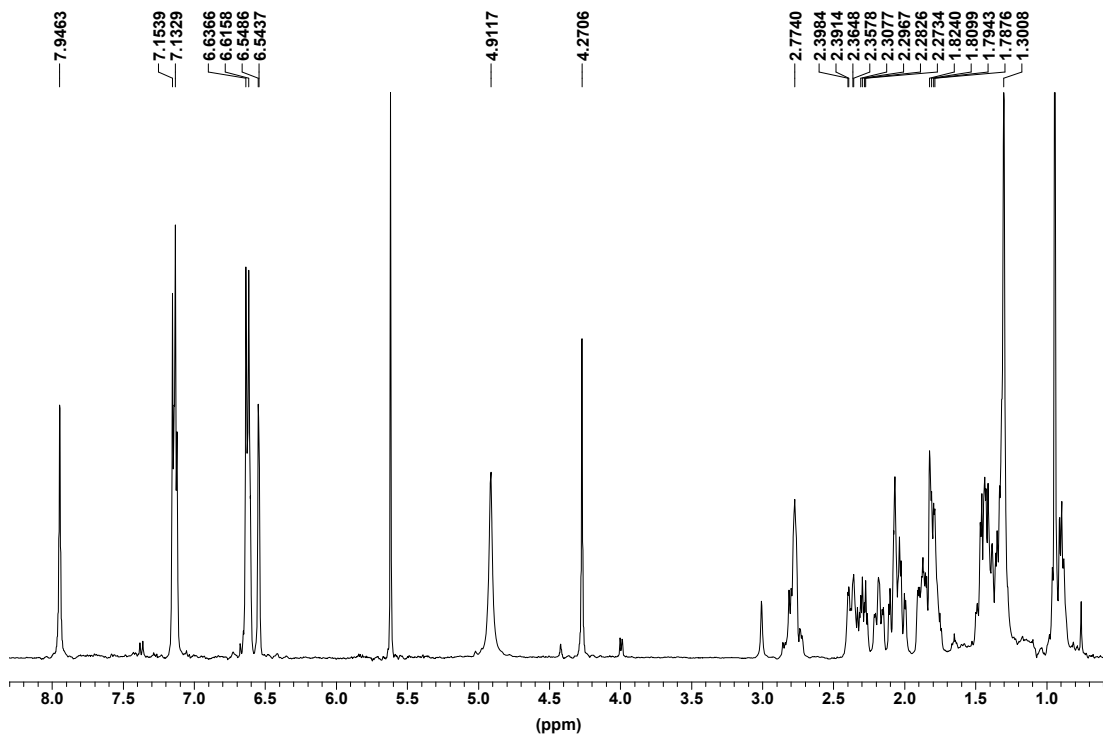
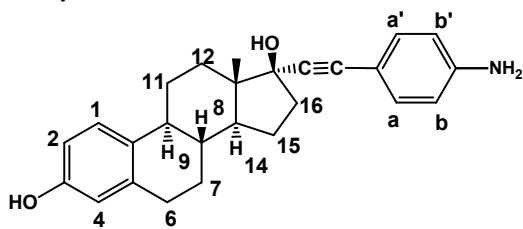
^1H NMR (CD_2Cl_2 , 400 MHz, 298 K): $\delta = 9.68$ (2H, m, $\text{H}_a + \text{H}_b$ pydz), 7.90 (1H, m, H_c pydz), 3.01 (2H, m, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-COOH}$), 2.59 (2H, m, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-COOH}$), 2.14 (2H, m, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-COOH}$).

Complex Re3



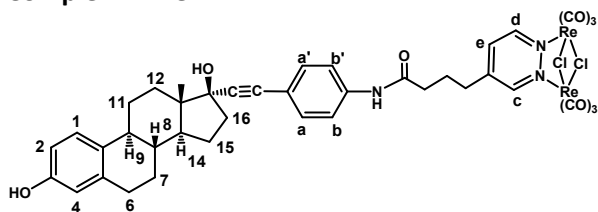
^1H NMR (CD_2Cl_2 , 400 MHz, 298 K): $\delta = 9.49$ (1H, s, H_a), 9.45 (1H, s, H_b pydz), 2.86 (2H, m, $\text{CH}_2\text{-COOH}$), 2.58 (3H, s, CH_3), 2.39 (2H, m, pydz- CH_2), $1.8\text{-}1.4$ (10H, CH_2 aliphatic chain).

Compound E0



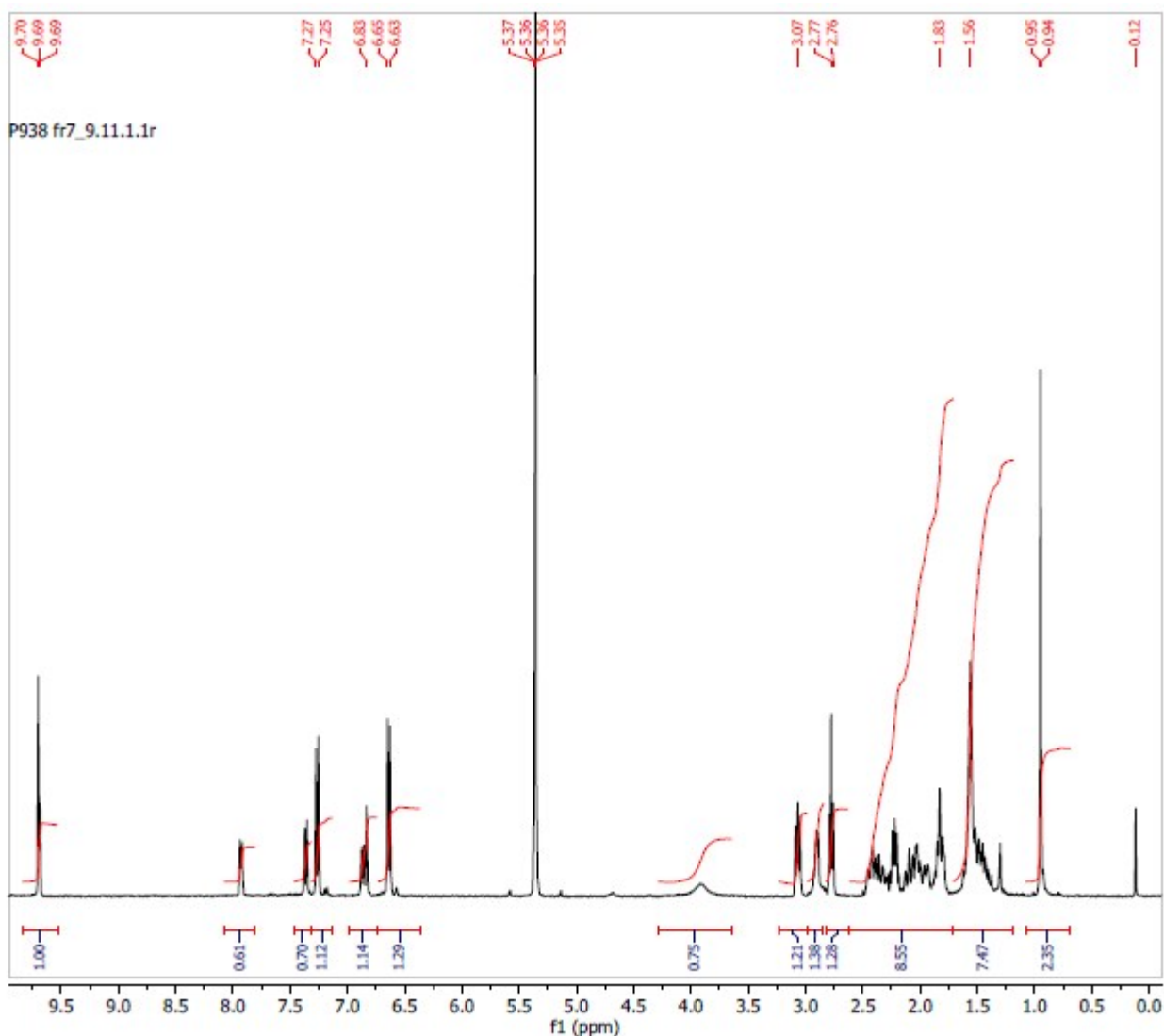
^1H NMR (CD_2Cl_2 , 400 MHz, 298 K): δ = 7.94 (1H, d, H1 estradiol), 7.14 (2H, d, $\text{H}_b + \text{H}_{b'}$), 6.62 (3H, m, $\text{H}_a + \text{H}_{a'}$ and H2 estradiol), 6.54 (1H, H4 estradiol), 4.91 (1H, s, 3-OH), 4.27 (2H, NH_2), 2.77 (2H, m, H6), 2.4-2.15 (3H, m, $\text{H}_{11\alpha}$, H9, $\text{H}_{12\beta}$), 2.10-1.70 (6H, m, H_{14} , $\text{H}_{15\alpha}$, $\text{H}_{7\alpha}$, $\text{H}_{16\beta}$, $\text{H}_{16\alpha}$, $\text{H}_{11\beta}$), 1.5-1.3 (3H, m, H8, $\text{H}_{12\alpha}$, $\text{H}_{7\beta}$), 0.95 (3H, CH_3)

Complex E2-Re2

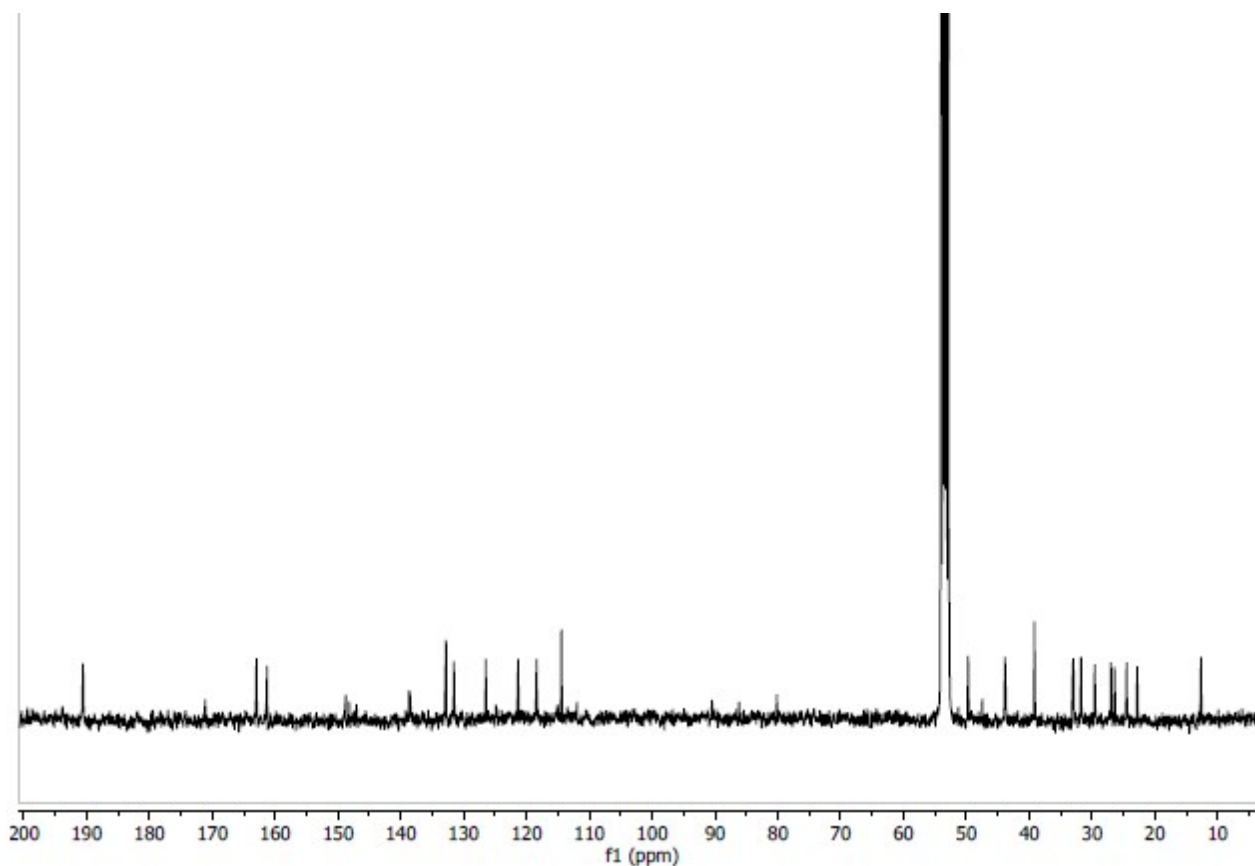


Chemical Formula: $C_{40}H_{37}Cl_2N_3O_9Re_2$

Molecular Weight: 1147.10

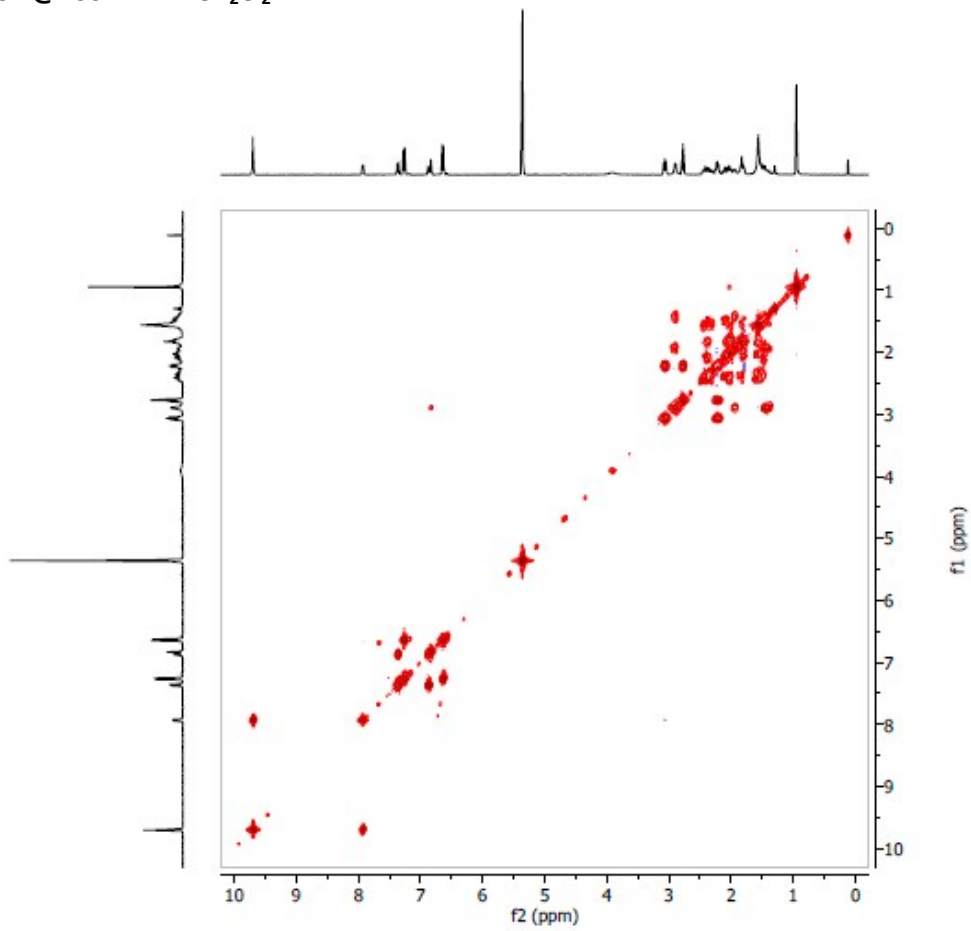


1H NMR (CD_2Cl_2 , 400 MHz, 298 K): δ = 9.70-9.69 (2H, m, H_c+H_d pydz), 7.95 (1H, m, H_e pydz), 7.36 (1H, d, H1 estradiol), 7.26 (2H, dd, $H_b+H_{b'}$), 6.87 (1H, m, H2 estradiol), 6.83 (1H, m, H4 estradiol), 6.64 (2H, dd, $H_a+H_{a'}$), 3.90 (1H, broad, 3-OH), 3.07 (2H, m, $CH_2-CH_2-CH_2-COOH$), 2.90 (2H, m, H6), 2.77 (2H, m, $CH_2-CH_2-CH_2-COOH$), 2.48-2.27 (3H, m, H11 α , H9, H12 β), 2.21 (2H, m, $CH_2-CH_2-CH_2-COOH$), 2.15-1.75 (7H, m, H14, H15 α , H15 β , H7 α , H16 β , H16 α , H11 β), 1.5-1.35 (3H, m, H8, H12 α , H7 β), 0.95 (3H, CH_3)

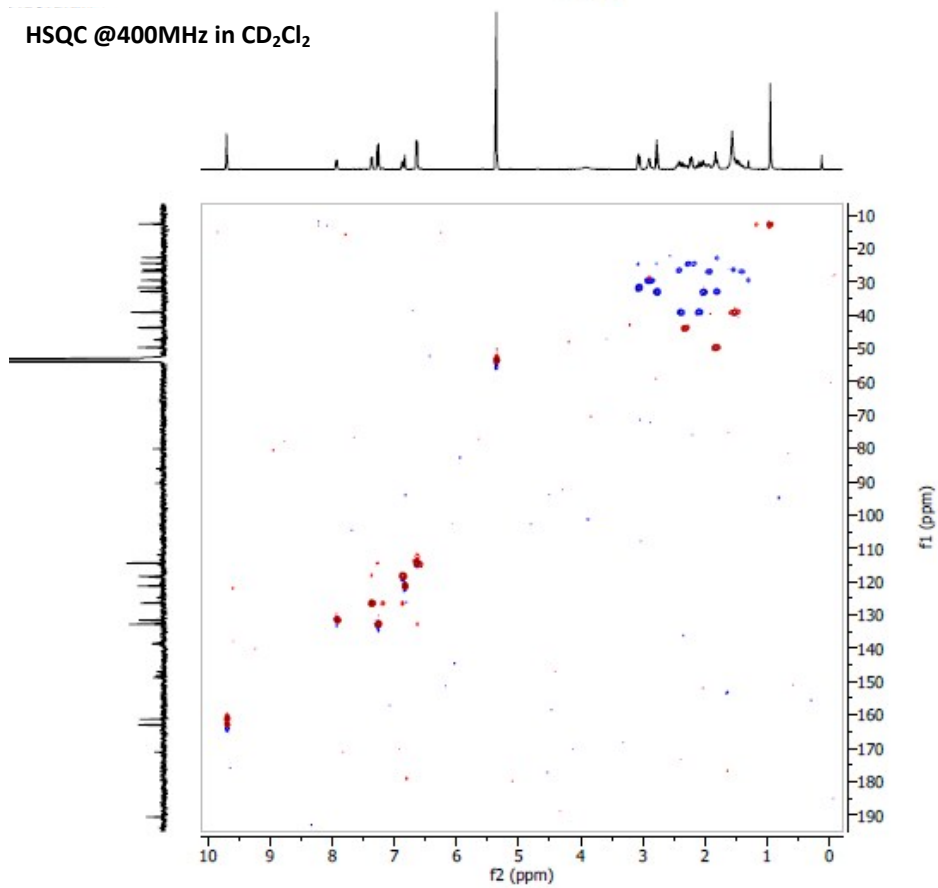


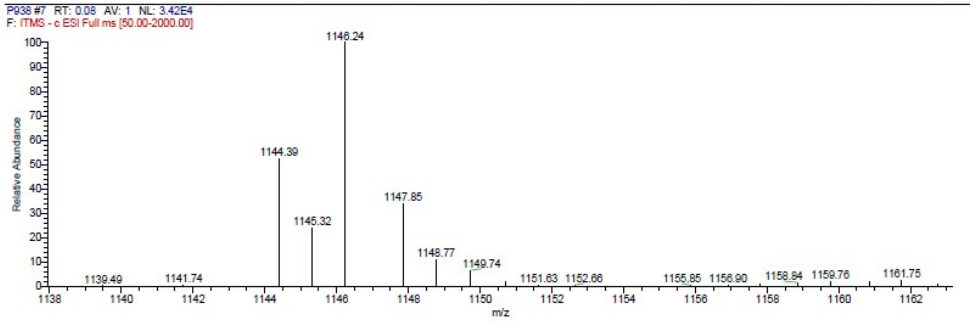
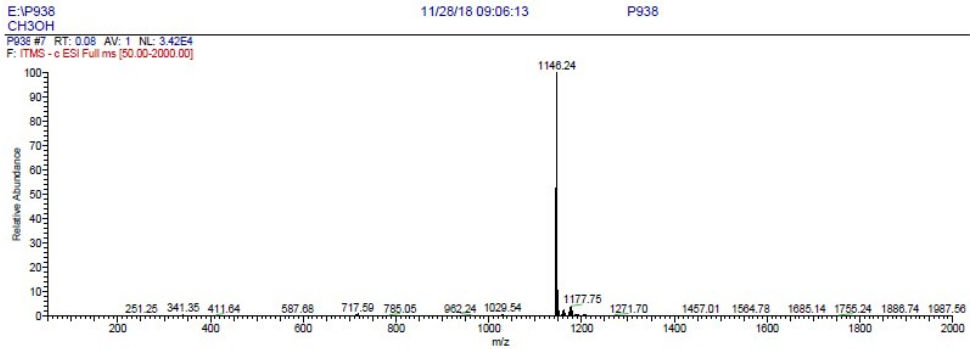
^{13}C NMR (CD_2Cl_2 , 400 MHz, 298 K): $\delta = 190.57$ (1C, CO), 162.97 (1C, C_c pydz), 161.28 (1C, C_d pydz), 132.80 (2C, $\text{C}_b + \text{C}_{b'}$), 131.55 (1C, C_e pydz), 126.46 (1C, C_1 estradiol), 121.32 (1C, C_4 estradiol), 118.38 (1C, C_2 estradiol), 114.44 (2C, $\text{C}_a + \text{C}_{a'}$), 49.70 (1C, C_{14} estradiol), 47.46 (1C, quater), 43.84 (1C, C_9 estradiol), 39.15 (2C, $\text{C}_8 + \text{C}_{11}$ estradiol), 33.05 (1C, C_{16} estradiol), 32.95 (1C, CH_2), 31.74 (1C, CH_2), 29.58 (1C, C_6 estradiol), 27.98 (1C, C_7 estradiol), 26.43 (1C, C_{12} estradiol), 24.49 (1C, CH_2), 22.81 (1C, C_{15} estradiol), 12.65 (1C, CH_3 estradiol).

COSY @400MHz in CD₂Cl₂

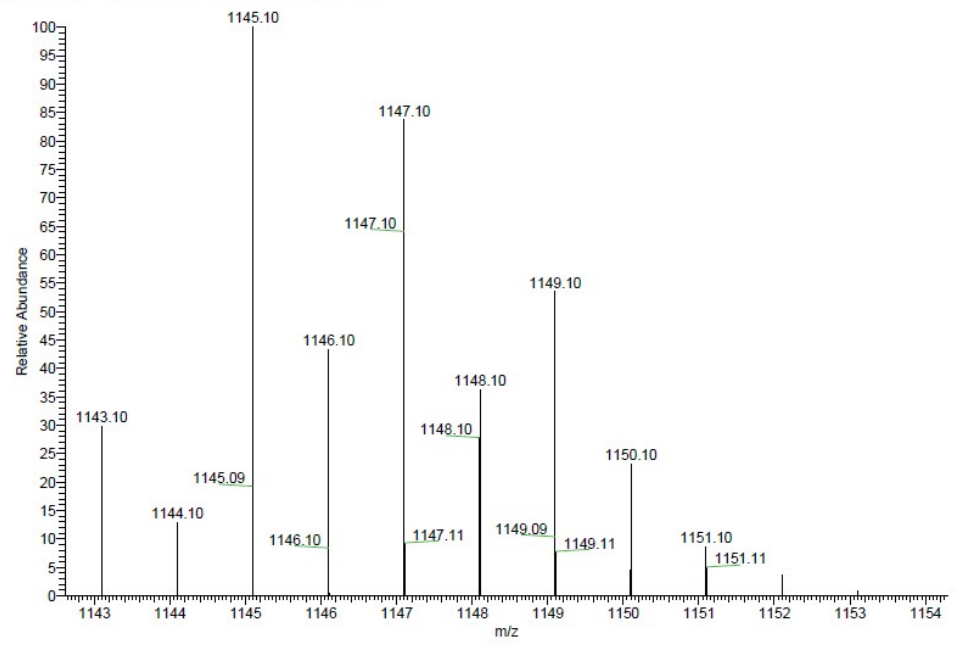


HSQC @400MHz in CD₂Cl₂



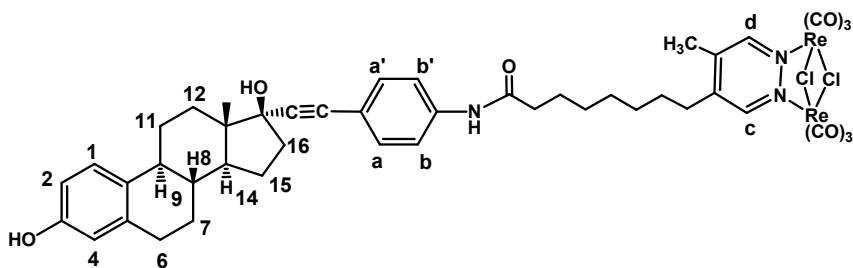


C40H37N3O9Re2Cl2: C40 H37 N3 O9 Re2 Cl2 pa Chrg 1



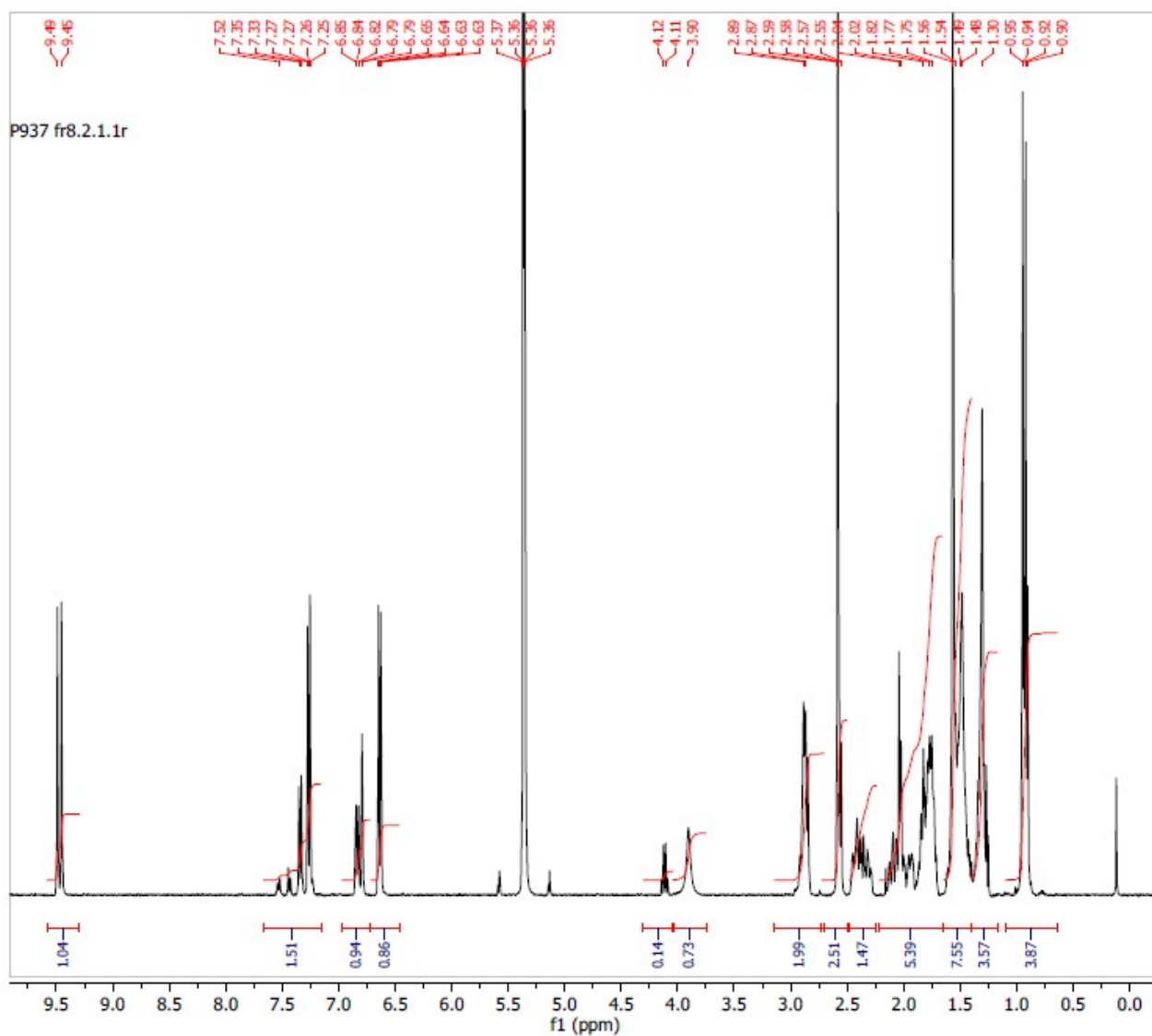
ESI-MS experimental and calculated (right) isotopic distribution for the **E2-Re2**

Complex E2-Re3



Chemical Formula: $C_{45}H_{47}Cl_2N_3O_9Re_2$

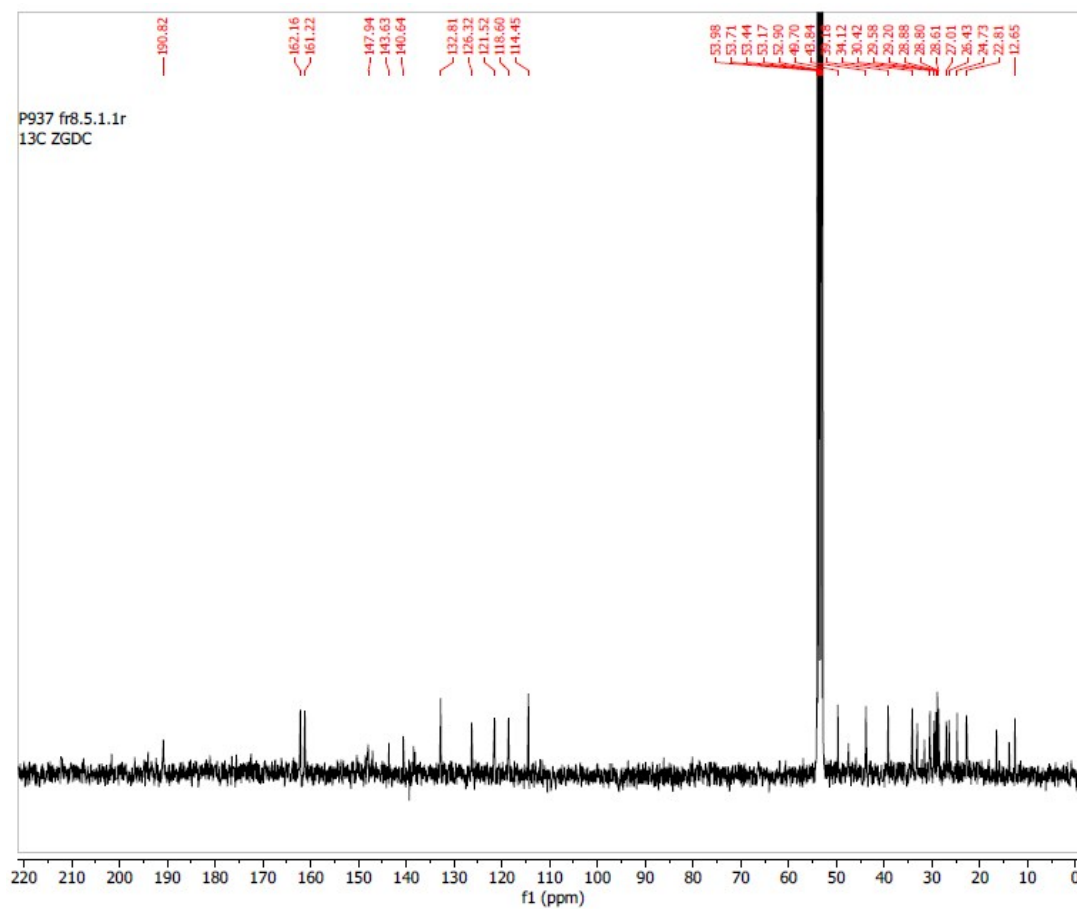
Molecular Weight: 1217.18



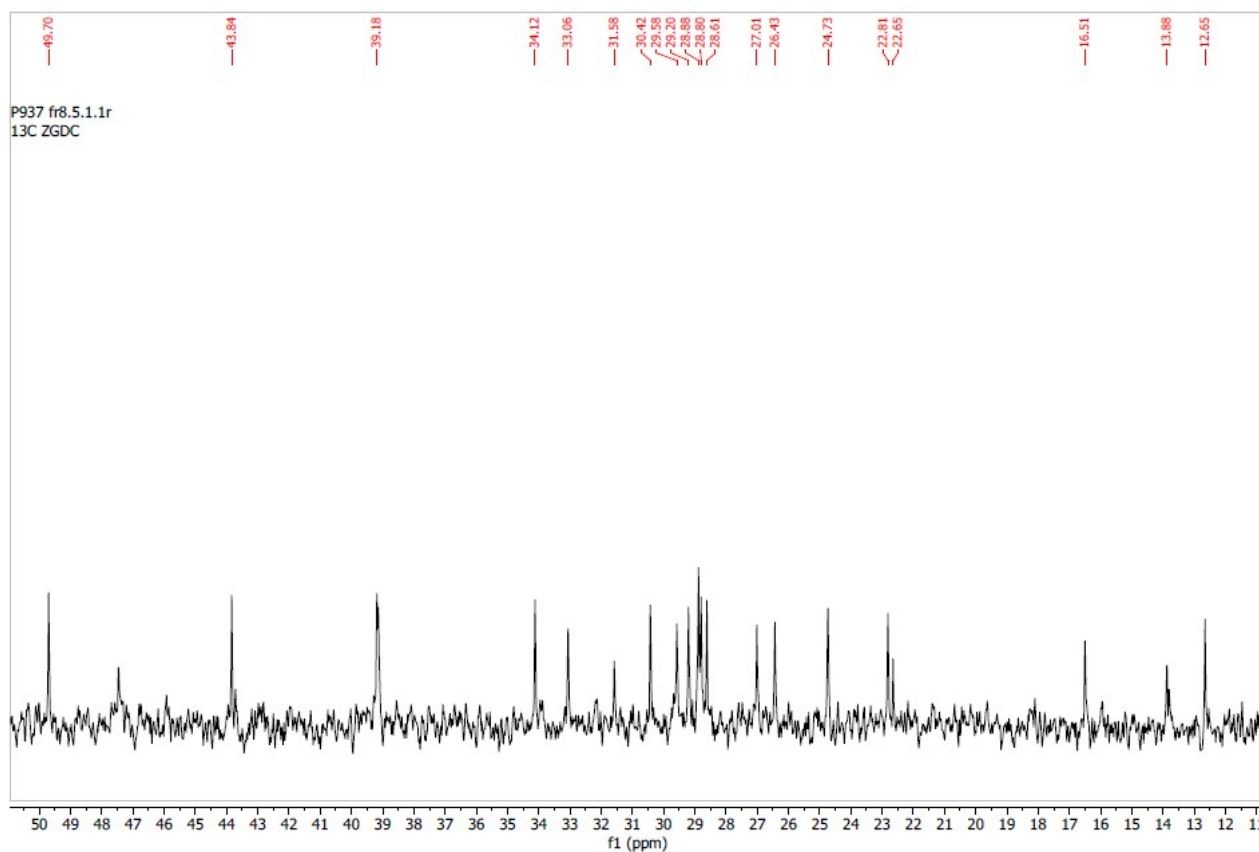
1H NMR (CD_2Cl_2 , 400 MHz, 298 K): δ = 9.49 (1H, s, H_c pydz), 9.45 (1H, s, H_d pydz), 7.34 (1H, d, H1 estradiol), 7.26 (2H, dd, H_b+H_{b'}), 6.83 (1H, m, H2 estradiol), 6.79 (1H, m, H4 estradiol), 6.64 (2H, m, H_a+H_{a'}), 3.90 (1H, broad, 3-OH), 2.87 (4H, m, -CH₂-COOH and H6 estradiol), 2.59-2.57 (5H, m, CH₃ and CH₂ aliphatic chain),

2.50-2.25 (3H, m, H11 α , H9, H12 β), 2.17-1.90 (3H, m, H12 α , H16 α , H11 β), 1.85-1.67 (5H, m, H14, H15 α , H15 β , H16 β , H7 β), 1.6-1.20 (14H, m, H8, H7 α , and 10H of CH₂ aliphatic chain), 0.95 (3H, CH₃)

¹³C-NMR in CD₂Cl₂

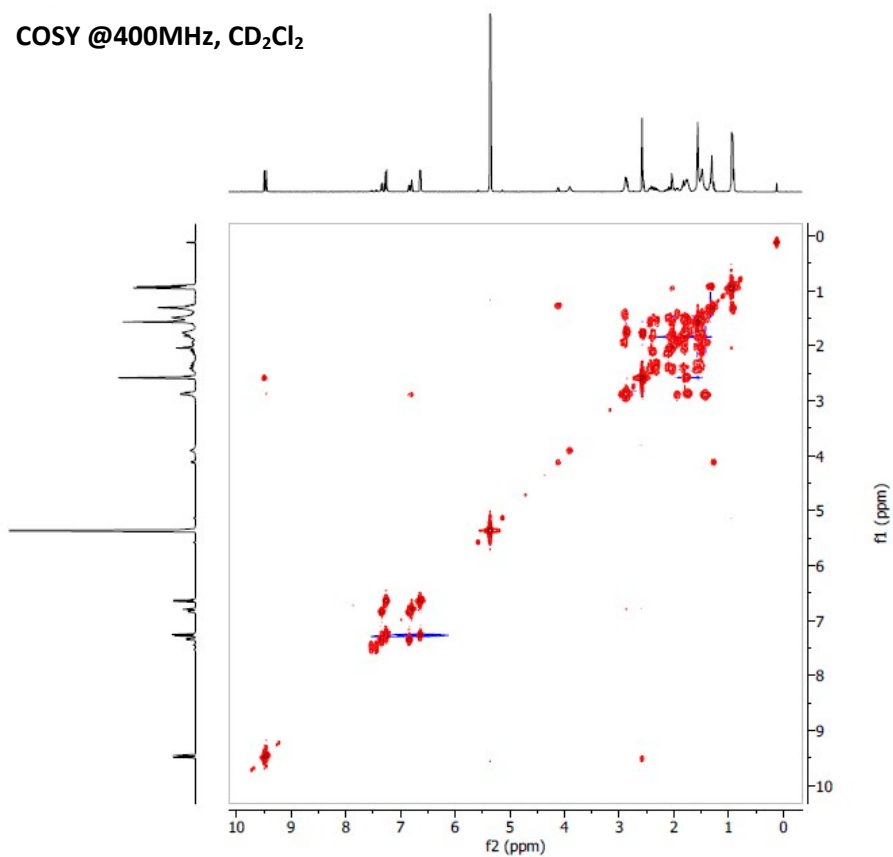


¹³C NMR aliphatic region

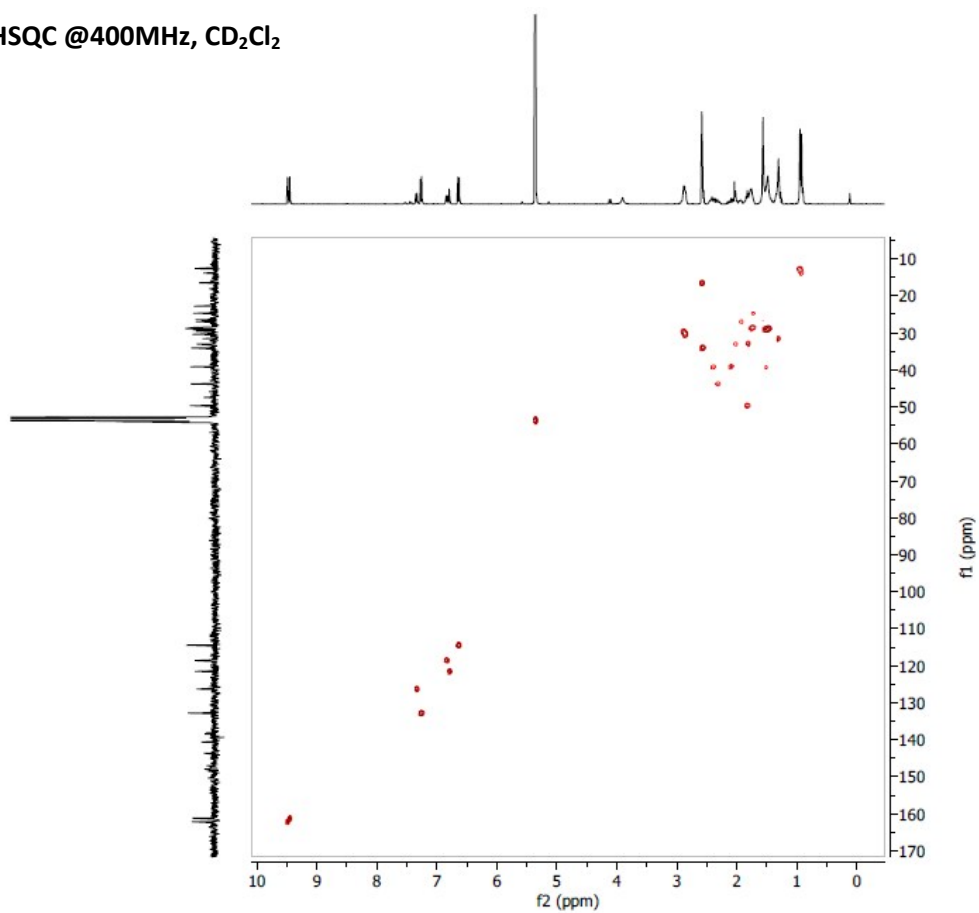


¹³C NMR (CD₂Cl₂, 400 MHz, 298 K): δ = 190.82 (1C, CO), 162.16 (1C, C_c pydz), 161.22 (1C, C_d pydz), 132.81 (2C, C_b+C_{b'}), 126.32 (1C, C₁ estradiol), 121.52 (1C, C₄ estradiol), 118.60 (1C, C₂ estradiol), 114.45 (2C, C_a+C_{a'}), 49.70 (1C, C₁₄, estradiol), 43.84 (1C, C₉ estradiol), 39.18 (2C, C₈+C₁₁ estradiol), 34.12 (1C, CH₂), 33.06 (1C, C₁₆ estradiol), 31.58 (1C, CH₂), 30.42 (1C, CH₂), 29.58 (1C, C₆ estradiol), 29.20 (1C, C₇ estradiol), 28.88 (1C, CH₂), 28.80 (1C, CH₂), 28.61 (1C, CH₂), 27.01 (1C, C₁₂ estradiol), 26.43 (1C, CH₂), 24.73 (1C, C₁₅ estradiol), 16.51 (1C, CH₃ pydz), 12.65 (1C, CH₃ estradiol).

COSY @400MHz, CD₂Cl₂



HSQC @400MHz, CD₂Cl₂

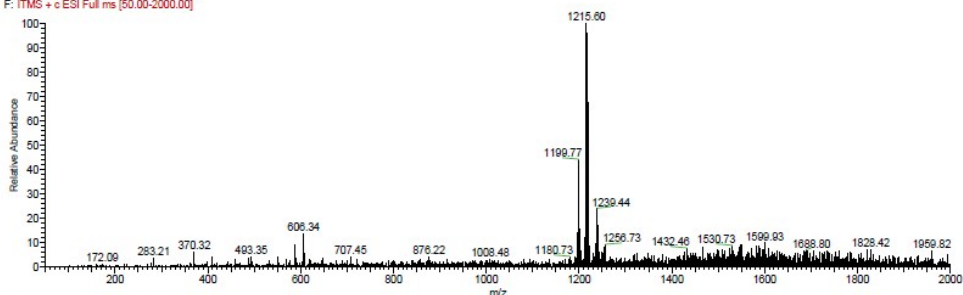


E:\P937
CH3OH

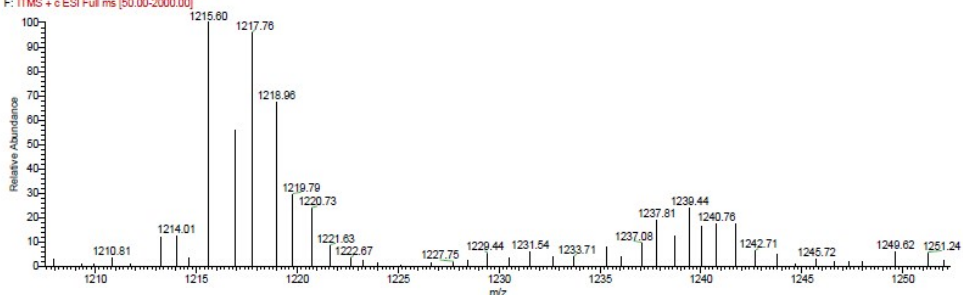
11/28/18 09:18:49

P937

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F: ITMS + c ESI Full ms [50.00-2000.00]



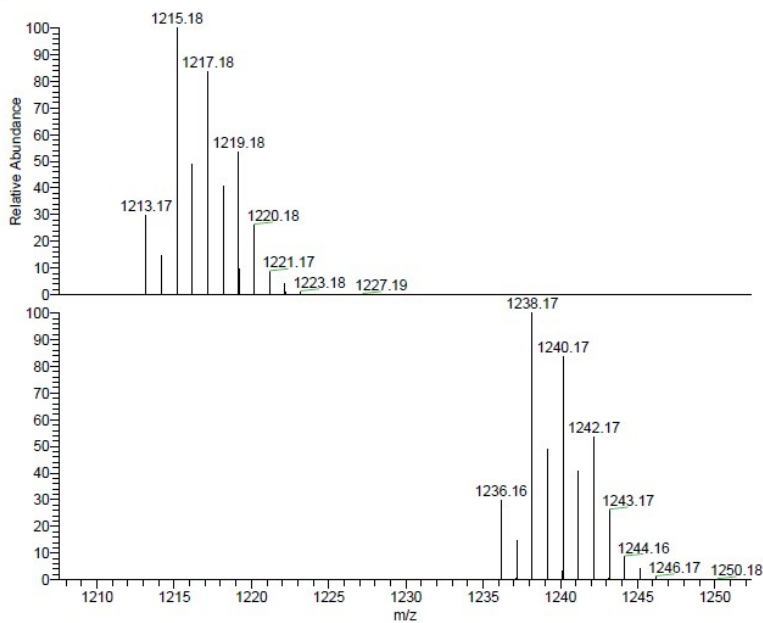
P637 #137 RT: 1.71 AV: 1 NL: 1.15E4
F: ITMS + c ESI Full ms [50.00-2000.00]



E:\P937
CH3OH

11/28/18 09:18:49

P937



NL:
1.59E5
C45 H47 Cl2 N3 O9 Re2
C45 H47 Cl2 N3 O9 Re2
pa Chrg 1

NL:
1.59E5
C45 H47 Cl2 N3 O9 Re2 Na:
C45 H47 Cl2 N3 O9 Re2 Na1
pa Chrg 1

ESI-MS experimental and calculated (right) isotopic distribution for the E2-Re3

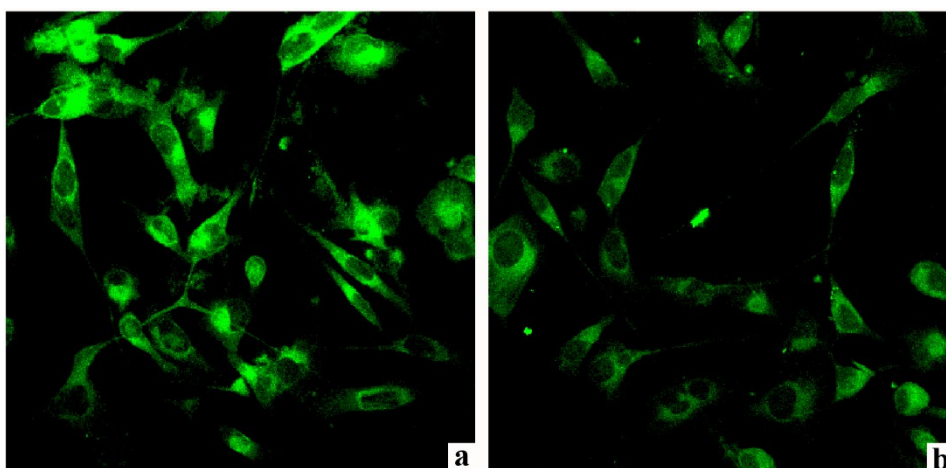


Fig. S1: Complex **E2-Re1** stains the 231 cell lines: a) 50 μM of **E2-Re1** stains 231 cells for 60 min. (B) 50 μM of florescent estradiol-free rhenium complex **Re-4Me** stains 231 cells.

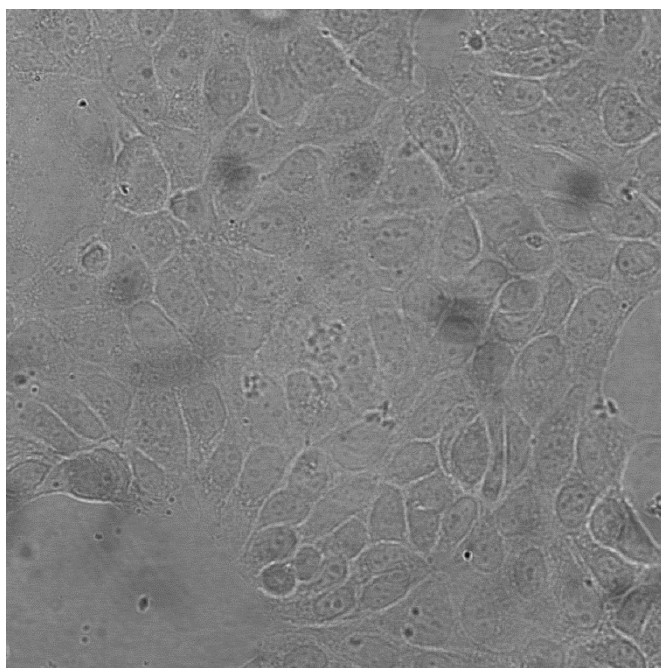


Fig. S2: Bright field image of MCF-7 cells recorded after the addition of **E2-Re1**.