Electronic Supplementary Material (ESI) for Dalton Transactions

Supplementary information

Molecular Interaction Fields vs. Quantum-Mechanical-based descriptors in the modelling of lipophilicity of platinum(IV) complexes

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Content:

Experimental part

General

$K_2[PtCl_4]$ (Johnson Matthey and Co.) and all other chemicals (Aldrich) were used without further purification.

The multinuclear NMR spectra were measured on a JEOL Eclipse Plus operating at 400 MHz (^{1}H), 100.5 MHz (^{13}C) and 85.9 MHz (^{195}Pt), respectively. ^{1}H and ^{13}C NMR chemical shifts were reported in parts per million (ppm) referenced to solvent resonances; for measurements in D_2O 1% methanol was added as internal reference. ^{195}Pt NMR spectra were recorded using a solution of $K_2[PtCl_4]$ in saturated aqueous KCl as the external reference. The shift for $K_2[PtCl_4]$ was adjusted to -1628 ppm from Na_2PtCl_6 ($\delta = 0$ ppm).

RP-HPLC and mass analysis were performed using a Waters HPLC-MS instrument equipped with Alliance 2695 separations module, 2487 dual lambda absorbance detector and 3100 mass detector. Electrospray ionization mass spectra (ESI-MS) were obtained delivering a diluted solution of the compound in methanol directly into the spectrometer source at 0.01 mL min^{-1}. The source and desolvation temperatures were set to 150° and 250° C, respectively, with nitrogen used both as a drying and a nebulizing gas. The cone and the capillary voltages were usually 30 V and 2.70 kV, respectively. Quasi-molecular ion peaks $[M+H]^+$ or sodiated $[M+Na]^+$ peaks were assigned on the basis of the *m/z* values and of the simulated isotope distribution patterns.

Purity of compounds was assessed by analytical RP-HPLC (see below), elemental analysis and determination of Pt content by inductively coupled plasma optical emission spectrometry (ICP-OES). Elemental analyses were carried out with a EA3000 CHN Elemental Analyzer (EuroVector, Milano, Italy). Platinum was quantified by means of a Spectro Genesis ICP-OES spectrometer (Spectro Analytical Instruments, Kleve, Germany) equipped with a crossflow nebulizer. In order to quantify the platinum concentration the Pt 299.797 nm line was selected. A platinum standard stock solution of 1000 mg L^{-1} was diluted in 1.0 % v/v nitric acid to prepare calibration standards.

Synthesis of dihydroxido Pt(IV) complexes

The dihydroxido Pt(IV) complexes **1-22** were obtained by oxidation with hydrogen peroxide of the parent Pt(II) compound. The synthesis are described below, where am = ammonia, methylamine, isopropylamine, ethylenediamine, N-methylethylenediamine, N,N'-dimethylethylenediamine, N,N,N'-trimethylethylenediamine, N,N,N',N'-tetramethylethylenediamine, cyclobutylamine, cyclopentylamine, cyclohexylamine, 1,2-diaminocyclohexane (DACH), (2-isopropyl-carboxyamide)ethylendiamine and X = malonato, oxalato, 1,1'-cyclobutanedicarboxylato (CBDC), 2-(acetylamino)malonato, benzamidomalonato and 2-(3-(2-benzamidoacetamido)propyl)malonato.

Synthesis of cis-[Pt(am)$_2$I$_2$]

$K_2[PtCl_4]$ (0.50 g, 1.20 mmol) was dissolved in water (7 ml) and KI (1.20 g, 7.20 mmol) was added to the solution. The reaction mixture was stirred at RT for 40 min; then a solution of the monodentate (am, 2M, 3.3 mmol) or bidentate amine ($(am)_2$, 1M, 1.7

mmol), was added dropwise to give the *cis*-[Pt(am)$_2$I$_2$] precipitate. After 10 min, the product was isolated by centrifugation and washed with cold water, ethanol and diethyl ether and dried in vacuo.

Synthesis of cis-[Pt(am)$_2$Cl$_2$]

cis-[Pt(am)$_2$I$_2$] (0.96 mmol) was suspended in 10 mL of water and heated at 50°C. To this suspension 0.31 g (1.8 mmol) of $AgNO_3$ was added and the reaction mixture was stirred for 24 h. During this time the corresponding diaqua intermediate was formed. After removal of AgI by filtration, the clear solution was concentrated under reduced pressure and the diacqua species reacted with KCl (0.02 mol) to yield a yellow powder which was washed with cold water, ethanol and diethyl ether and dried in vacuo.

Synthesis of cis-[Pt(am)$_2$X]

To a solution of $AgSO_4$ (0.32 g, 0.98 mmol) in water (30 mL) 1 mmol of *cis*-[Pt(am)$_2$I$_2$] was added. The reaction mixture was stirred at 50°C for 24 h. After removal of AgI by filtration, BaX (pH = 5-6) was added to the filtrate. The resulting solution was stirred at 40°C overnight. After removal of $AgSO_4$ by filtration, the clear solution was reduced under pressure to obtain a white solid that was washed with methanol and finally dried in vacuo.

Synthesis of cis,cis,trans-[Pt(am)$_2$Cl$_2$(OH)$_2$]or cis,trans,cis-[Pt(am)$_2$(OH)$_2$X]

H_2O_2 (35% v/v, 600 μL) was added dropwise to a suspension of *cis*-[Pt(am)$_2$Cl$_2$] or *cis*-[Pt(am)$_2$X] (0.45 mmol) in water (6 mL). The reaction mixture was stirred at RT overnight. The yellow precipitate was isolated by filtration, washed with cold water, ethanol and diethyl ether and dried in vacuo.

1: Yield 0.10 g (0.30 mmol), 62%. ^{195}Pt-NMR (D_2O): δ 860 ppm. ESI-MS (positive-ion mode): 357.5 m/z; 357.3 m/z calcd for $[M+Na]^+$.

2: Yield 0.11 g (0.31 mmol), 70%. ^{1}H-NMR (D_2O): δ 2.28 ppm (s, 6H, 2 CH_3). ^{13}C-NMR (D_2O): δ 29.90 ppm (2 CH_3). ^{195}Pt-NMR (D_2O): δ 838 ppm. ESI-MS (positive-ion mode): 385.4 m/z; 385.2 m/z calcd for $[M+Na]^+$.

3: Yield 0.10 g (0.23 mmol), 51%. ^{1}H-NMR (D_2O): δ 1.86 (d, 12H, 4 CH_3, J = 7.69 Hz), 2.85 (sept, 2H, 2 C*H*, J = 7.69 Hz) ppm. ^{13}C-NMR (D_2O): δ 22.08 (4 CH_3), 47.93 (2 *C*H) ppm. ^{195}Pt-NMR (D_2O): δ 934 ppm. ESI-MS (positive-ion mode): 442.3 m/z; 442.0 m/z calcd for $[M+Na]^+$.

4: Yield 0.12 g (0.35 mmol), 77%. ^{1}H-NMR (D_2O): δ 2.92 ppm (s, 4H, 2 CH_2). ^{13}C-NMR (D_2O): δ 50.33 ppm (2 CH_2). ^{195}Pt-NMR (D_2O): δ 784 ppm. ESI-MS (positive-ion mode): 383.5 m/z; 383.9 m/z calcd for $[M+Na]^+$.

5: Yield 0.15 g (0.40 mmol), 88%. ^{1}H-NMR (D_2O): δ 2.62 (s, 3H, CH_3), 2.92 (m, 4H, 2 CH_2) ppm. ^{13}C-NMR (D_2O): δ 46.00 (CH_3), 58.30 (2 CH_2) ppm. ^{195}Pt-NMR (D_2O): δ 676 ppm. ESI-MS (positive-ion mode): 397.7 m/z; 397.9 m/z calcd for $[M+Na]^+$.

6: Yield 0.13 g (0.34 mmol), 75%. ^{1}H-NMR (D_2O): δ 2.66 (s, 6H, 2 CH_3), 2.91 (m, 4H, 2 CH_2) ppm. ^{13}C-NMR (D_2O): δ 47.10 (2 CH_3), 55.80 (2 CH_2) ppm. ^{195}Pt-NMR (D_2O): δ 658 ppm. ESI-MS (positive-ion mode): 412.4 m/z; 412.0 m/z calcd for $[M+Na]^+$.

7: Yield 0.15 g (0.38 mmol), 85%. ^{1}H-NMR (D_2O): δ 2.45 (s, 3H, -NHCH_3), 2.62 (s, 6H, -NCH_3), 2.87 (m, 4H, 2 CH_2). ^{13}C-NMR (D_2O): δ 47.80 (3 CH_3), 56.40 (2 CH_2) ppm. ^{195}Pt-NMR (D_2O): δ 658 ppm. ESI-MS (positive-ion mode): 426.3 m/z; 426.0 m/z calcd for $[M+Na]^+$.

8: Yield 0.11 g (0.26 mmol), 59%. ^{1}H-NMR (D_2O): δ 2.69 (s, 12H, 4 CH_3), 3.03 (m, 4H, 2 CH_2). ^{13}C-NMR (D_2O): δ 49.28 (4 CH_3), 64.76 (2 CH_2) ppm. ^{195}Pt-NMR (D_2O): δ 698 ppm. ESI-MS (positive-ion mode): 440.3 m/z; 440.1 m/z calcd for $[M+Na]^+$.

9: Yield 0.12 g (0.28 mmol), 63%. ^{1}H-NMR (DMSO-d_6): δ 1.55 (m, 4H, H3, 2 CH_2), 1.86 (m, 4H, H4, 2 CH_2), 2.16 (m, 4H, H2, 2 CH_2), 3.51 (m, 2H, H1, 2 C*H*), 5.04 (m, 4H, 2 NH_2) ppm. ^{13}C-NMR (DMSO-d_6): δ 22.80 (C3, 2 CH_2), 42.00 (C2, 4 CH_2), 58.07 (C1, 2 *C*H) ppm. ^{195}Pt-NMR (DMSO-d_6): δ 965 ppm. ESI-MS (positive-ion mode): 466.6 m/z; 466.3 m/z calcd for $[M+Na]^+$.

10: Yield 0.14 g (0.30 mmol), 67%. ^{1}H-NMR (DMSO-d_6): δ 1.51 (m, 8H, H3-4, 4 CH_2), 1.64 (m, 4H, H2, 2 CH_2), 1.96 (m, 4H, H5, 2 CH_2), 3.33 (m, 2H, H1, 2 C*H*), 4.85 (m, 4H, 2 NH_2) ppm. ^{13}C-NMR (DMSO-d_6): δ 24.01 (C3, 4 CH_2), 33.49 (C2, 4 CH_2), 57.59 (C1, 2 *C*H) ppm. ^{195}Pt-NMR (DMSO-d_6): δ 1360 ppm. ESI-MS (positive-ion mode): 494.4 m/z; 494.2 m/z calcd for $[M+Na]^+$.

11: Yield 0.11 g (0.22 mmol), 51%. ^{1}H-NMR (DMSO-d_6): δ 1.09 (m, 4H, H4, 2 CH_2), 1.19 (m, 4H, H3, 2 CH_2), 1.54 (m, 4H, H5, 2 CH_2), 1.69 (m, 4H, H2, 2 CH_2), 2.30 (m, 4H, H6, 2 CH_2), 2.69 (m, 2H, H1, 2 C*H*), 4.74 (m, 4H, 2 NH_2) ppm. ^{13}C-NMR (DMSO-d_6): δ 23.14 (C4, 2 CH_2), 29.15 (C3, 4 CH_2), 43.51 (C2, 4 CH_2), 60.05 (C1, 2 *C*H) ppm. ^{195}Pt-NMR (DMSO-d_6): δ 1450 ppm. ESI-MS (positive-ion mode): 521.9 m/z; 522.1 m/z calcd for $[M+Na]^+$.

12: Yield 0.13 g (0.35 mmol), 78%. ^{13}C-NMR (D_2O): δ 47.23 (CH_2), δ 179.81 (2 -*C*(O)O) ppm. ^{195}Pt-NMR (D_2O): δ 1550 ppm. ESI-MS (positive-ion mode): 389.3 m/z; 389.0 m/z calcd for $[M+Na]^+$.

13: Yield 0.12 g (0.31 mmol), 70%. ^{1}H-NMR (D_2O): δ 2.23 (s, 6H, 2 C*H*$_3$) ppm. ^{13}C-NMR (D_2O): δ 30.06 (*C*H$_3$), 51.10 (*C*H$_2$), 176.60 (2 -*C*(O)O) ppm. ^{195}Pt-NMR (D_2O): δ 1600 ppm. ESI-MS (positive-ion mode): m/z 416.8; 417.0 m/z calcd for $[M+Na]^+$.

14: Yield 0.088 g (0.2 mmol), 75%. ^{1}H-NMR (D_2O): δ 2.88 (m, 4H, N-C*H*$_2$) ppm. ^{13}C-NMR (D_2O): δ 48.10 (N-*C*H$_2$), 52.97 (*C*H$_2$), 169.10 (2 -*C*(O)O) ppm. ^{195}Pt-NMR (D_2O): δ 961 ppm. ESI-MS (positive-ion mode): 415.5 m/z; 415.3 m/z calcd for $[M+Na]^+$.

15: Yield 0.27 g (0.7 mmol), 73%. ^{1}H-NMR (D_2O): δ 2.01 (q, 2H, H4, C*H*$_2$, J = 8.42 Hz), 2.63 (t, 4H, H3, 2 C*H*$_2$, J = 8.42 Hz) ppm. ^{13}C-NMR (D_2O): δ 16.07 (C4, *C*H$_2$), 32.29 (C3, 2 *C*H$_2$), 55.81 (C2, C_{quat}), 180.90 (C1, 2 -C(O)O) ppm. ^{195}Pt-NMR (D_2O): δ 1297 ppm. ESI-MS (positive-ion mode): 509.4 m/z; 509.1 m/z calcd for $[M+Na]^+$.

16: Yield 0.05 g (0.09 mmol), 45%. ^{1}H-NMR (D_2O): δ 1.11 (m, 2H, C*H*$_2$, DACH), 1.97 (q, 2H, H4, C*H*$_2$, CBDC, J = 8.26 Hz), 2.02 (m, 4H, C*H*$_2$, DACH), 2.43 (t, 4H, H3, 2 CH$_2$, CBDC, J = 8.26 Hz), 2.76 (m, 2H, C*H*$_2$, DACH), 3.13 (m, 2H, 2 C*H*, DACH) ppm. ESI-MS (positive-ion mode): 503.9 m/z; 504.2 m/z calcd for $[M+Na]^+$.

17: Yield 0.02 g (0.09 mmol), 63%. ^{1}H-NMR (D_2O): δ 2.73 (s, 6H, 2 C*H*$_3$), 3.12 (m, 4H, 2 C*H*$_2$) ppm. ^{13}C-NMR (D_2O): δ 45.90 (2 *C*H$_3$), 58.01 (2 *C*H$_2$), 174.3 (2 -*C*(O)O) ppm. ^{195}Pt-NMR (D_2O): δ 1115 ppm. ESI-MS (positive-ion mode): 429.4 m/z; 429.2 m/z calcd for $[M+Na]^+$.

18: Yield 0.11 g (0.28 mmol), 62%. ^{1}H-NMR (D_2O): δ 2.10 (s, 1H, C*H*), 1.97 (s, 3H, C*H*$_3$) ppm. ^{13}C-NMR (D_2O): δ 51.02 (*C*H$_3$), 65.00 (*C*H), 165.90 (N-*C*(O)O), 179.10 (2 -*C*(O)O) ppm. ^{195}Pt-NMR (D_2O): δ 1305 ppm. ESI-MS (positive-ion mode): 432.6 m/z; 432.4 m/z calcd for $[M+Na]^+$.

19: Yield 0.13 g (0.27 mmol), 57%. ^{1}H-NMR (DMSO-d_6): δ 4.66 (m, 1H, C*H*-C(O)O), 5.72 (m, 6H, 2 NH_3), 7.01 (m, 3H, H_o and H_p, 3 C*H*) 7.82 (d, 2H, H_m, 2 C*H*, J = 8.31 Hz), 8.13 (m, 1H, N*H*) ppm. ^{13}C-NMR (DMSO-d_6): δ 52.8 (*C*H-C(O)O), 110.8 (C_m), 121.1 (C_p), 126.3 (C_o), 151.3 (C_{quat}), 168.3 (NH-*C*(O)O), 176.3 (2 *C*(O)O-CH) ppm. ESI-MS (positive-ion mode): 508.3 m/z; 508.0 m/z calcd for $[M+Na]^+$.

20: Yield 0.26 g (0.58 mmol), 60%. ^{1}H-NMR (D_2O): δ 1.15 (m, 6H, 2 CH_3), 3.15 (m, 3H, CH_2, NH_2-C*H*), 3.98 (m, 1H, NH-C*H*) ppm. ^{13}C-NMR (D_2O): δ 23.50 (*C*H_3), 43.60 (NH-*C*H), 54.11 (*C*H_2), 63.12 (NH_2-*C*H), 187.10 (-*C*(O)O) ppm. ^{195}Pt-NMR (DMSO-d_6): δ 1959 ppm. ESI-MS (positive-ion mode): 460.3 m/z; 460.1 m/z calcd for $[M+Na]^+$.

21: Yield 0.16 g (0.31 mmol), 69%. ^{1}H-NMR (DMSO-d_6): δ 2.90 (s, 6H, 2 CH_3), 4.71 (m, 1H, C*H*-C(O)O), 5.68 (m, 4H, 2 NH_2), 6.68 (m, 3H, H_o and H_p, 3 C*H*), 7.71 (d, 2H, H_m, 2 C*H*, J = 8.79 Hz), 8.09 (m, 1H, N*H*) ppm. ^{13}C-NMR (DMSO-d_6): δ 28.1 (*C*H_3), 53.5 (*C*H-C(O)O), 111.4 (C_m), 122.1 (C_p), 128.9 (*Co*), 152.5 (C_q), 166.4 (*C*(O)O-NH), 174.8 (2 *C*(O)O-CH) ppm). ^{195}Pt-NMR (DMSO-d_6): δ 1650 ppm. ESI-MS (positive-ion mode): 536.4 m/z; 536.1 m/z calcd for $[M+Na]^+$.

22: Yield 0.15 g (0.34 mmol), 75%. ^{1}H-NMR (DMSO-d_6): δ 1.41 (m, 2H, C(O)O-CH-CH_2-CH_2), 1.60 (m, 2H, C(O)O-CH-CH_2), 3.03 (m, 2H, C(O)O-CH-CH_2-CH_2-CH_2), 3.83 (d, 2H, C(O)O-CH_2, J = 5.86 Hz), 4.66 (m, 1H, C(O)O-C*H*), 5.77 (m, 6H, NH_3), 7.46 (m, 2H, H_m, 2 C*H*), 7.51 (m, 1H, H_p, C*H*), 7.88 (m, 2H, CH_o, 2 C*H*), 8.70 (m, 1H, N*H*-C(O)O-Ph) ppm. ^{13}C-NMR (DMSO-d_6): δ 25.70 (C(O)O-CH-CH_2-*C*H_2), 28.08 (C(O)O-CH-*C*H_2-), 39.05 (C(O)O-CH-CH_2-CH_2-*C*H_2), 43.16 (C(O)O-*C*H_2), 52.88 (C(O)O-*C*H), 127.7 (C_m, 2 *C*H), 128.8 (C_o, 2 *C*H), 131.8 (C_p, *C*H), 134.6 (C_q-Ph), 166.9 (NH-*C*(O)O), 169.2 (Ph-*C*(O)O), 174.8 (2 -*C*(O)O-CH) ppm. ^{195}Pt-NMR (DMSO-d_6): δ 1649 ppm. ESI-MS (positive-ion mode): 468.9 m/z; 469.1 m/z calcd for $[M+Na]^+$.

Table S1. Values of the MOPAC2009 descriptors for all the Pt(IV) complexes

Compound	**Area (A^2)**	**Volume (A^3)**	**PSA (A^2)**	**E_{HOMO} (eV)**	**E_{LUMO} (eV)**	**Mol Wt (Da)**	**Dipole (D)**	**q(Pt) (e)**	**max q(H) (e)**	**min q (e)**
1	185.25	126.82	118.85	- 9.16	- 1.26	334.06	8.79	0.852	0.348	- 0.802
2	218.41	167.21	82.597	- 9.08	- 1.06	362.12	9.11	0.845	0.348	- 0.829
3	285.45	239.68	78.039	- 8.94	- 0.93	418.22	9.74	0.858	0.347	- 0.836
4	200.85	154.64	84.646	- 9.03	- 1.01	360.10	10.71	0.857	0.350	- 0.809
5	215.40	174.47	71.866	- 8.94	- 0.94	374.13	10.75	0.851	0.350	- 0.815
6	228.63	194.05	56.490	- 8.89	- 0.86	388.15	10.75	0.850	0.349	- 0.815
7	239.87	211.88	47.201	- 8.76	- 0.82	402.18	10.76	0.835	0.349	- 0.822
8	250.45	229.84	37.965	- 8.63	- 0.78	416.21	10.81	0.821	0.346	- 0.810
9	301.71	258.22	73.888	- 8.97	- 0.97	442.25	9.67	0.860	0.350	- 0.817
10	337.44	292.12	78.835	- 8.94	- 0.92	470.30	9.63	0.859	0.348	- 0.811
11	365.42	323.98	77.315	- 8.96	- 0.92	498.35	9.90	0.859	0.348	- 0.836

12	213.68	163.58	165.26	- 9.68	- 1.21	365.20	10.45	1.036	0.349	- 0.823
13	246.36	204.50	127.03	- 9.55	- 1.05	393.25	11.32	1.013	0.350	- 0.824
14	232.25	192.60	136.74	- 9.47	- 1.12	391.24	13.58	1.027	0.353	- 0.829
15	252.88	208.56	160.72	- 9.55	- 1.08	405.27	9.74	1.036	0.346	- 0.840
16	321.18	296.50	127.05	- 9.22	- 0.89	485.40	13.40	1.029	0.352	- 0.838
17	250.24	214.90	111.12	- 9.36	- 1.07	405.27	14.65	0.995	0.347	- 0.824
18	270.26	215.79	188.82	- 9.70	- 1.27	422.25	7.37	1.023	0.355	- 0.834
19	327.11	280.88	188.82	- 9.86	- 1.47	484.32	14.08	1.028	0.351	- 0.824
20	292.89	242.81	109.11	- 8.87	- 0.97	445.21	14.28	0.856	0.351	- 0.817
21	360.50	321.72	150.70	- 9.74	- 1.32	512.38	14.97	1.008	0.351	- 0.826
22	425.10	386.61	211.35	- 9.53	- 1.55	583.46	16.61	1.030	0.349	- 0.821
23	178.17	195.50	66.290	- 9.68	- 2.31	370.96	10.48	0.668	0.260	- 0.414
24	230.45	264.55	112.89	- 9.93	- 1.89	418.15	5.74	0.881	0.278	- 0.742
25	253.21	301.73	110.50	- 10.30	- 2.54	526.09	9.74	0.897	0.273	- 0.705
26	267.24	308.05	112.51	- 9.87	- 1.84	446.20	5.56	0.876	0.279	- 0.754

27	300.85	351.92	96.710	- 9.84	- 1.83	474.25	5.40	0.877	0.279	- 0.756
28	340.79	397.29	112.11	- 9.85	- 1.84	502.31	5.42	0.877	0.279	- 0.756
29	376.10	439.27	112.10	- 9.84	- 1.83	530.36	5.49	0.877	0.279	- 0.756
30	410.15	481.69	112.01	- 9.85	- 1.83	558.41	5.54	0.877	0.279	- 0.757
31	330.87	387.24	181.87	- 10.09	- 2.03	534.22	6.17	0.866	0.343	- 0.738
32	241.92	279.88	149.41	- 9.74	- 1.61	421.28	6.08	1.021	0.268	- 0.741
33	266.82	324.19	142.16	- 10.06	- 2.43	529.22	10.36	1.061	0.269	- 0.697
34	269.71	323.45	151.66	- 9.60	- 1.58	449.33	5.52	1.039	0.265	- 0.766
35	298.62	364.64	150.66	- 9.58	- 1.56	477.38	5.17	1.037	0.265	- 0.760
36	331.54	406.41	149.60	- 9.58	- 1.55	505.44	5.35	1.038	0.267	- 0.763
37	370.73	451.57	149.95	- 9.58	- 1.55	533.49	5.26	1.038	0.267	- 0.761
38	410.42	496.34	149.98	- 9.58	- 1.55	561.54	5.35	1.037	0.267	- 0.761
39	336.10	395.13	201.06	- 9.64	- 1.62	537.35	6.09	1.004	0.347	- 0.764
40	248.93	296.04	37.430	- 9.40	- 2.01	451.09	14.58	0.674	0.267	- 0.422
41	302.80	367.43	82.540	- 9.66	- 1.61	498.28	9.11	0.875	0.275	- 0.739

42	367.51	452.19	80.040	- 9.57	- 1.57	554.38	7.95	0.882	0.276	- 0.749
43	471.30	588.10	79.840	- 9.57	- 1.57	638.54	7.98	0.882	0.276	- 0.750
44	482.06	614.14	112.50	- 9.39	- 1.03	657.67	4.99	1.049	0.293	- 0.761
45	196.24	223.82	38.240	- 9.51	- 2.12	397.00	13.18	0.670	0.267	- 0.421
46	248.06	294.91	83.280	- 9.75	- 1.71	444.18	7.72	0.872	0.276	- 0.741
47	255.62	308.90	46.140	- 9.47	- 2.08	453.11	12.15	0.670	0.265	- 0.426
48	307.87	378.33	89.090	- 9.75	- 1.68	500.29	7.53	0.879	0.276	- 0.745
49	423.10	513.22	88.640	- 9.69	- 1.65	584.45	7.14	0.874	0.277	- 0.755
50	500.45	597.92	88.610	- 9.68	- 1.65	640.56	7.06	0.874	0.276	- 0.755
51	335.17	409.61	82.120	- 9.59	- 1.58	526.33	8.80	0.869	0.275	- 0.749
52	410.44	496.40	80.480	- 9.57	- 1.58	582.44	8.78	0.871	0.275	- 0.751
53	446.75	537.11	80.450	- 9.56	- 1.57	610.49	8.75	0.871	0.274	- 0.751

Figure S1. MIFs generated by the OH2 probe at -1.0 kcal/mol. for compound **15**.

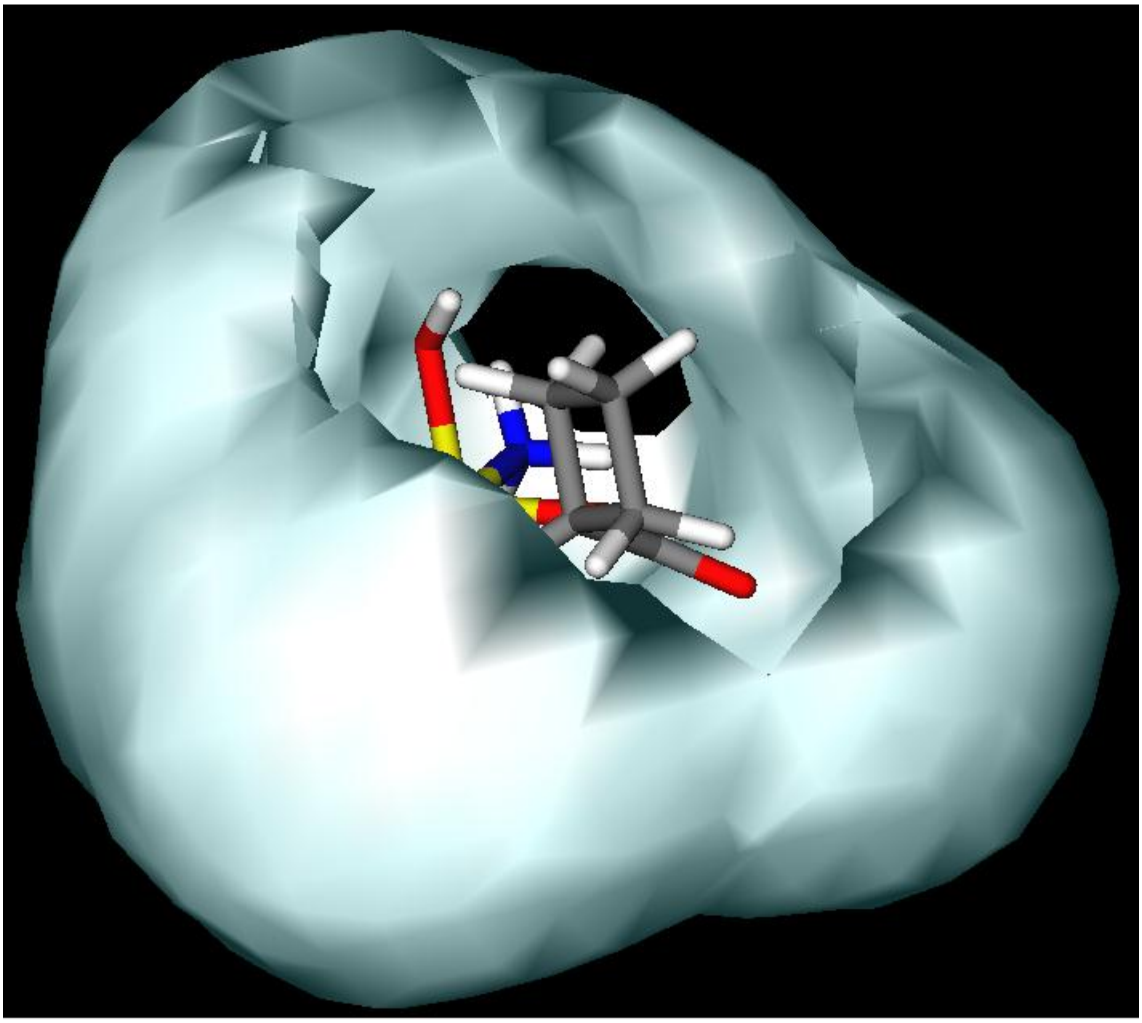

Figure S2. MIFs generated by the OH2 probe at -3.0 kcal/mol. for compound **15**.

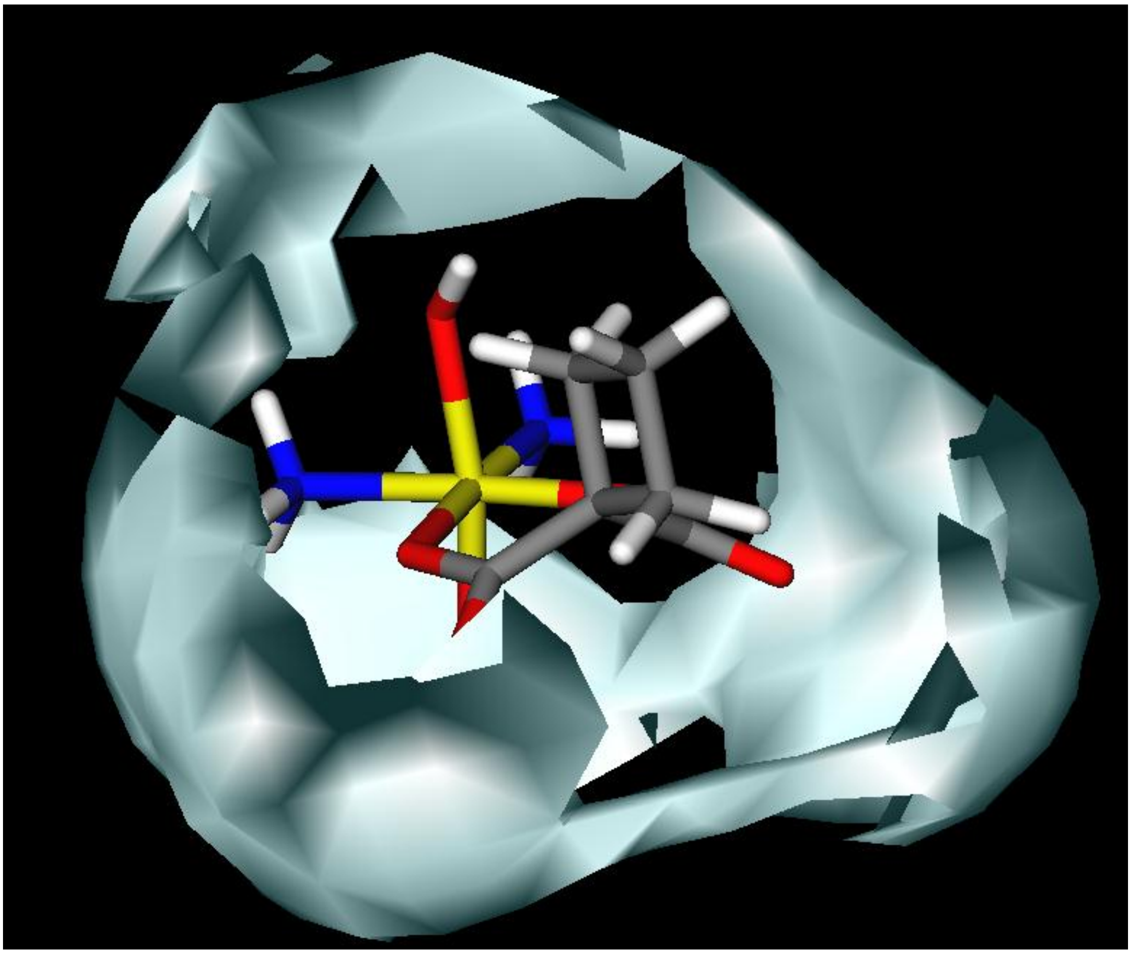

Figure S3. MIFs generated by the OH2 probe at -5.0 kcal/mol. for compound **15**

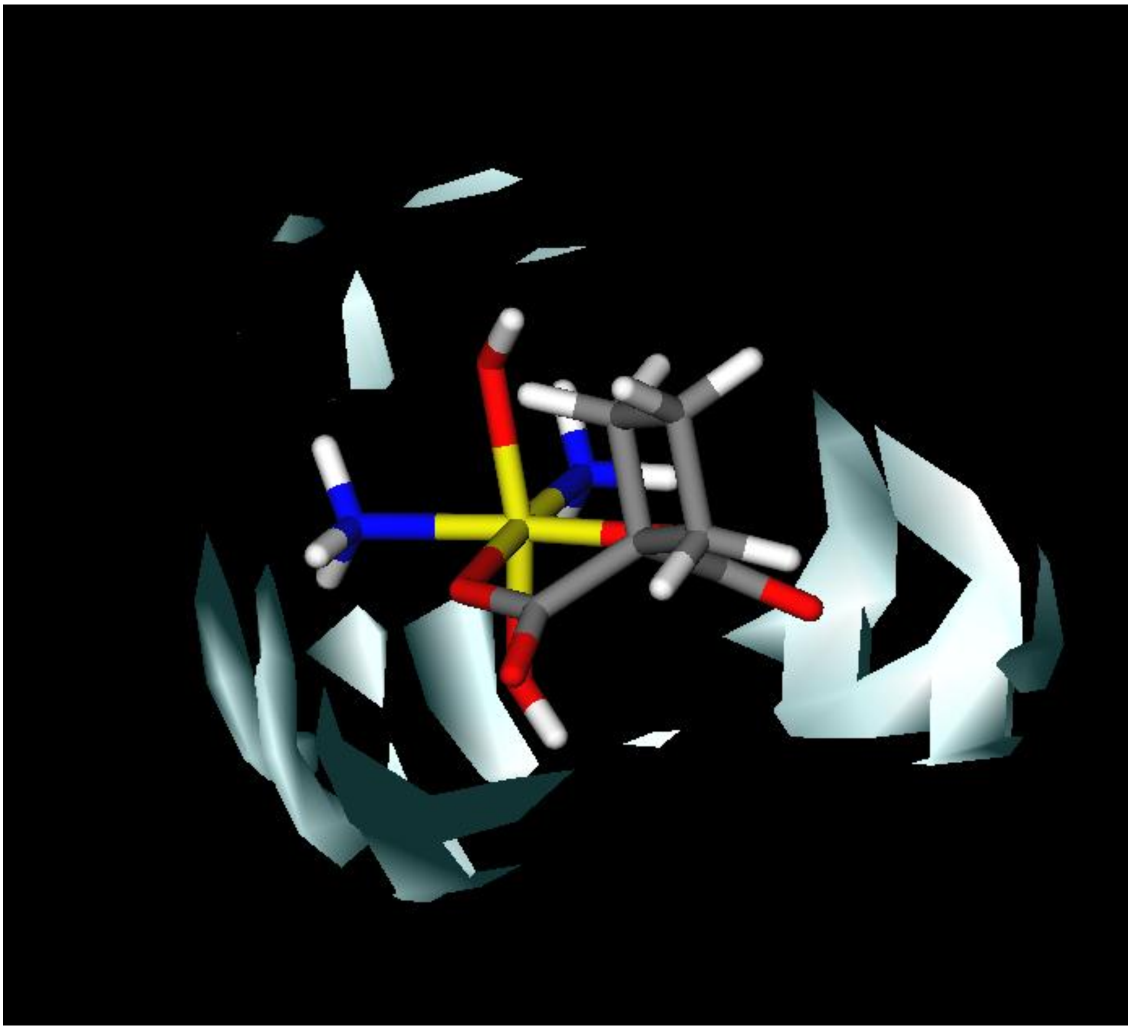

Figure S4. MIFs generated by the DRY probe at -0.2 kcal/mol. for compound **15**.

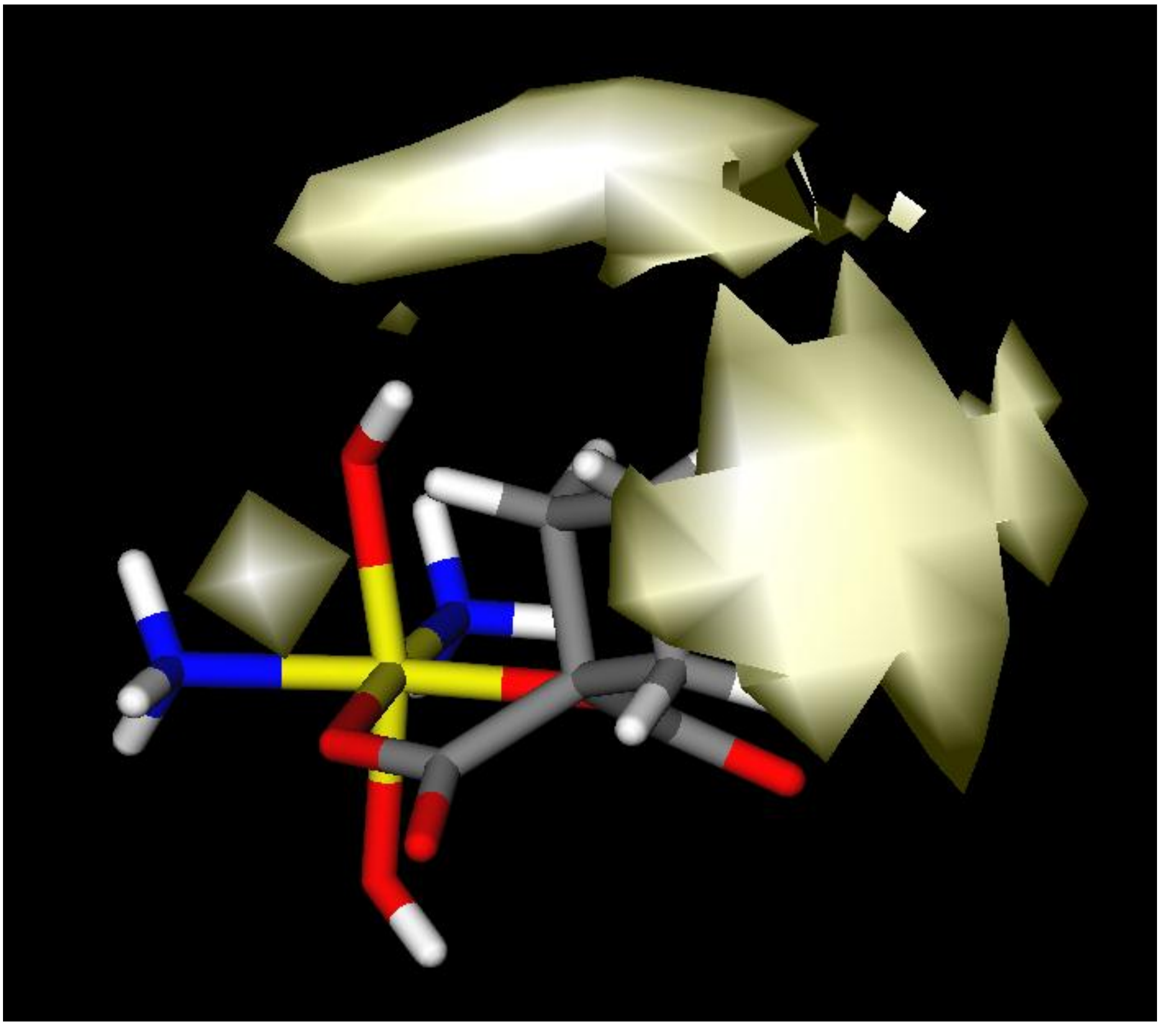

Figure S5. MIFs generated by the DRY probe at -0.4 kcal/mol. for compound **15**.

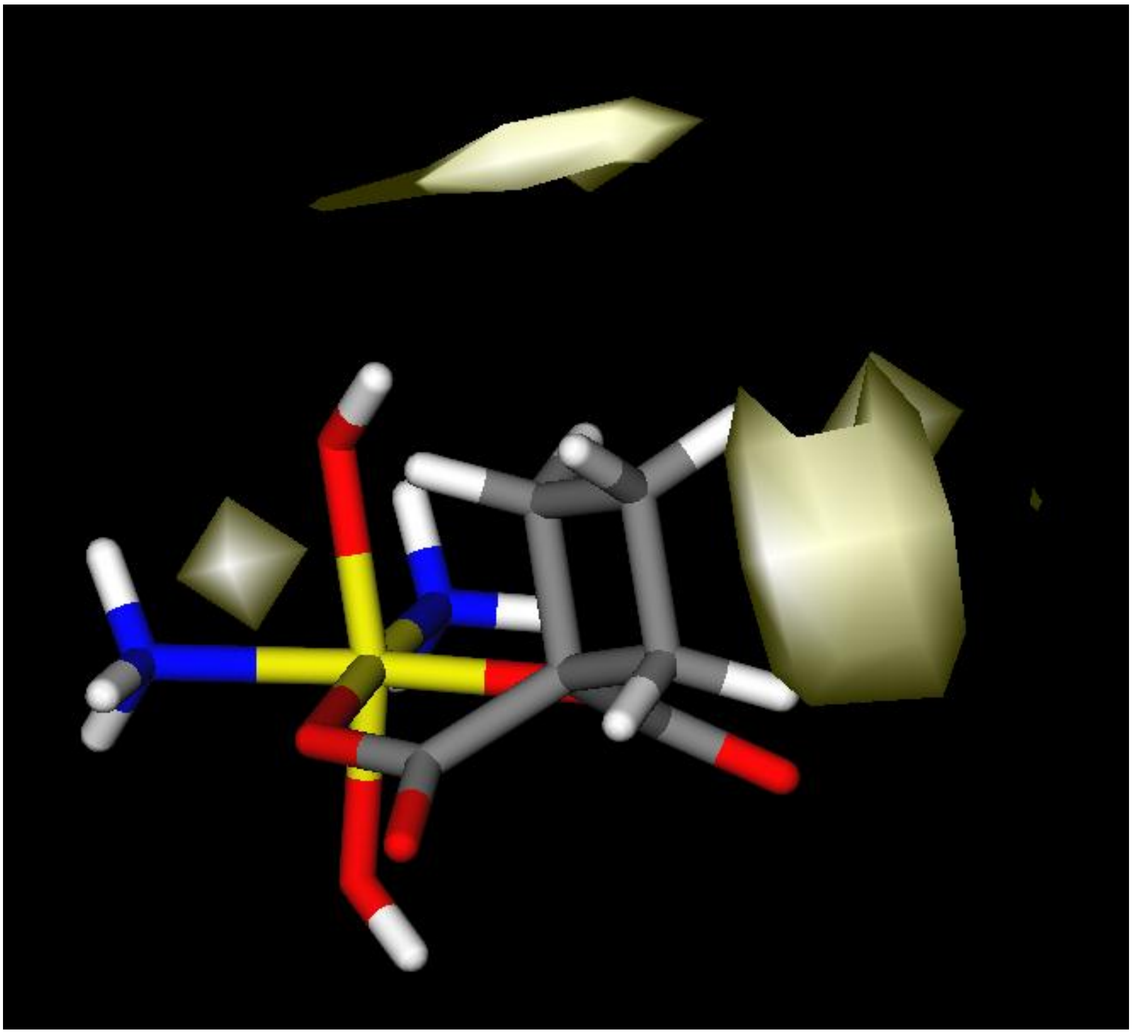

Figure S6. MIFs generated by the DRY probe at -0.6 kcal/mol. for compound **15**.