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SUPPLEMENTARY INFORMATION

Exploiting exo and endo furan-maleimide Diels-Alder linkages for the functionalization of organoruthenium complexes

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Table S1. Optimization of the DA reaction between **3** and each maleimide by ^{1}H NMR spectroscopy.

Ent.	**Maleimide**	**Eq.**	**Solvent**	**Time (day)**	**T (ºC)**	**Conv. (%)**[a]	**Endo/Exo**[a]
1	*N*-Octyl	30 eq	Chloroform	1 d	40	15	7/3
2			MeOH	1 d	40	25	5/2
3			DMSO	1 d	40	n.d[b]	n.d[b]
4			Acetonitrile	1 d	40	37	5/2
5			Acetonitrile-MW[c]	1 d	40	70	2/1
6			Acetone	1 d	40	42	7/3
7			Acetone	1 d	RT	17	3/1
8			Acetone	3 d	RT	40	7/3
9			Acetone	1 d	65	75	4/5
10			Acetone	3 d	40	70	2.1/1
11			Acetone	5 d	40	83	1.7/1
12		5 eq	Acetone	1 d	40	8	2/1
13			Acetone	3 d	40	22	5/3
14	*N*-*p*-nitrophenyl	30 eq	Chloroform	1 d	40	17	1/1
15			MeOH	1 d	40	29	3/2
16			Acetonitrile	1 d	40	56	3/2
17			Acetonitrile-MW[c]	1 d	40	86	1/2
18			Acetone	1 d	40	40	3/2
19			Acetone	1 d	RT	15	5/1
20			Acetone	1 d	65	70	1/3
21			Acetone	3 d	40	69	3/5
22			Acetone	5 d	40	83	1/3.8
23		5 eq	Acetone	1 d	40	20	5/3
24			Acetone	3 d	40	32	5/7

[a] Determined by ^{1}H NMR. Briefly, 5 mg of **3** was dissolved in 0.7 mL of acetone-d_6 with 2 μL of anhydrous DMF as a reference standard. In a 3 mm NMR tube with cap, the final solution of complex **3** was added to each maleimide. The sample was agitated for 5 min, and the NMR tube was sealed with parafilm. The NMR tube was heated in an oil bath at different temperatures. The ^{1}H NMR resonances corresponding to **4a$_{\mathbf{endo}}$** and **4a$_{\mathbf{exo}}$** adducts at 5.24 and 5.12 ppm, respectively and at 5.38 and 5.24 ppm for **4b$_{\mathbf{endo}}$** and **4b$_{\mathbf{exo}}$** adducts, respectively, were used to calculate the %conversion of DA reaction (and isomer ratio). These experiments were done in two to triplicate.

[b] Free benzene was detected in the ^{1}H NMR spectra.

[c] Reaction performed in a microwave (MW) reactor (0 psi, 6.5 W).

Table S2. Crystallographic data and structure refinement for complexes **3** and **4a$_{exo}$**. Complexes were structurally characterized by single-crystal X-ray analysis.[a]

	3	**4a$_{exo}$**
Empirical formula	$C_{20}H_{20}BClF_4N_4O_2Ru$	$C_{36}H_{46}BClF_4N_5O_6Ru$
Formula weight	571.73	868.11
Crystal size [mm^3]	0.38×0.22×0.2	0.2×0.18×0.04
Crystal colour	clear light orange	clear light colourless
Crystal shape	Block	Plate
Crystal system	Triclinic	Monoclinic
Space group (number)	$P\overline{1}$ (2)	$P2_1/c$ (14)
Unit cell dimensions	*a* [Å] = 9.0308(4)	*a* [Å] = 14.619(5)
	b [Å] = 9.5157(4)	*b* [Å] = 14.258(4)
	c [Å] = 14.3909(7)	*c* [Å] = 21.155(7)
	α [°] = 82.575(2)	α [°] = 90
	β [°] = 78.701(2)	β [°] = 106.214(12)
	γ [°] = 63.403(1)	γ [°] = 90
Volume [Å^3]	1083.16(9)	4234(2)
Z	2	4
ρ_{calc} [gcm^{-3}]	1.753	1.362
***F*(000)**	572	1788
μ [mm^{-1}]	5.079	2.770
Temperature [K]	150	150
Radiation	Ga K_α (λ=1.34139 Å)	Ga K_α (λ = 1.34139 Å)
Index ranges	$-11 \le h \le 11$	$-17 \le h \le 16$
	$-11 \le k \le 12$	$-17 \le k \le 15$
	$-18 \le l \le 18$	$-25 \le l \le 20$
2θ range [°]	5.45 to 121.30 (0.77 Å)	6.59 to 110.58 (0.82 Å)
Reflections collected	34010	16543
Independent reflections	4812	7760
	R_{int} = 0.0349	R_{int} = 0.0583
	R_{sigma} = 0.0232	R_{sigma} = 0.0574
Data/parameters/restraints	4812/64/335	7760/300/444
Goodness-of-fit on F^2	1.100	1.051
Final R indices	R_1 = 0.0246	R_1 = 0.0960
[$I \ge 2\sigma(I)$]^{b,c}	wR_2 = 0.0643	wR_2 = 0.2704
Final R indices	R_1 = 0.0247	R_1 = 0.1390
[all data]	wR_2 = 0.0643	wR_2 = 0.3197
Largest diff. peak and hole [eÅ^{-3}]	0.88/-0.56	0.61/-0.49
CCDC deposition no.	2100514	2100515

[a] Single crystals were obtained by slow evaporation of the solutions of complexes **3** and **4a$_{exo}$** in dichloromethane and ethyl acetate, respectively. Structures were solved by direct methods using *XT* and refined by full-matrix least-squares methods against F^2 by *XL*.[1, 2]

[b] $R_1 = \Sigma||F_o| - |F_c|| / \Sigma|F_o|$.

[c] $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma[w(F_o^2)^2]\}^{1/2}$

Table S3. Estimated lipophilicity (LogP) for some of the compounds reported in this study.

Compounds	**LogP (estimated)**[a]
N-octyl maleimide	3.18
N-*p*-nitrophenyl maleimide	0.89
3[b]	1.90
4a[b]	3.26
4b[b]	1.79
5a[b]	3.26

[a] The ALOGSP 2.1[3, 4] software was used to estimate the LogP values presented in this table.

[b] This value represents the estimated LogP of the N,N-donor ligand corresponding to this complex.[5]

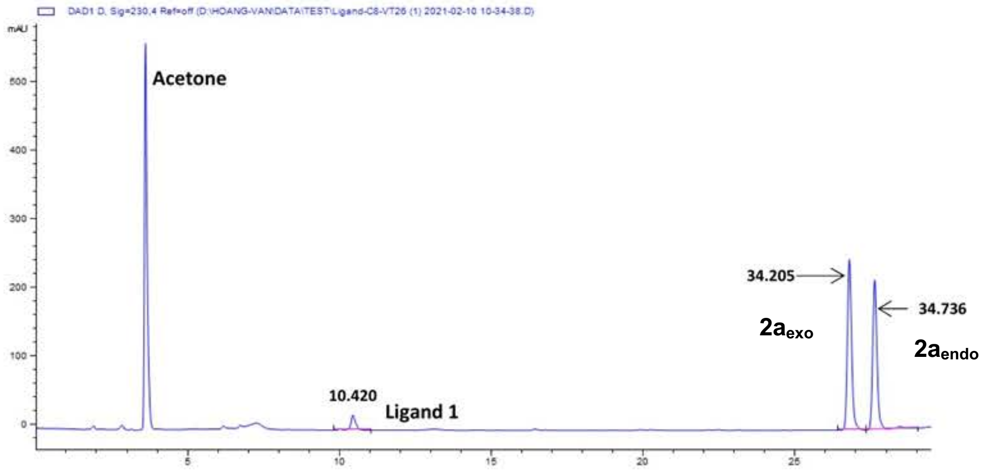


Figure S1. RP-HPLC chromatogram (semi-preparative C18 column, H_2O/acetonitrile) of a mixture of **$2a_{endo}$** and **$2a_{exo}$** (prior to separation).

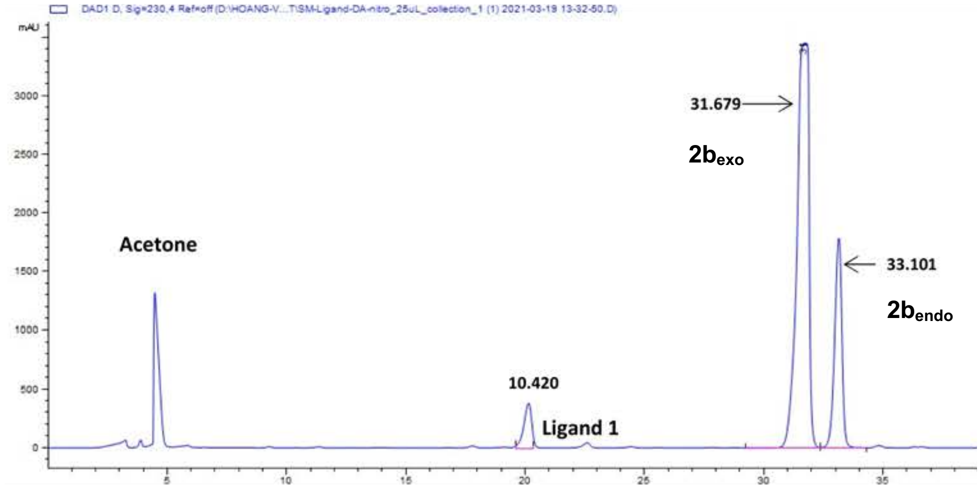


Figure S2. RP-HPLC chromatogram (semi-preparative C18 column, H_2O/acetonitrile) of a mixture of **$2b_{endo}$** and **$2b_{exo}$** (prior to separation).

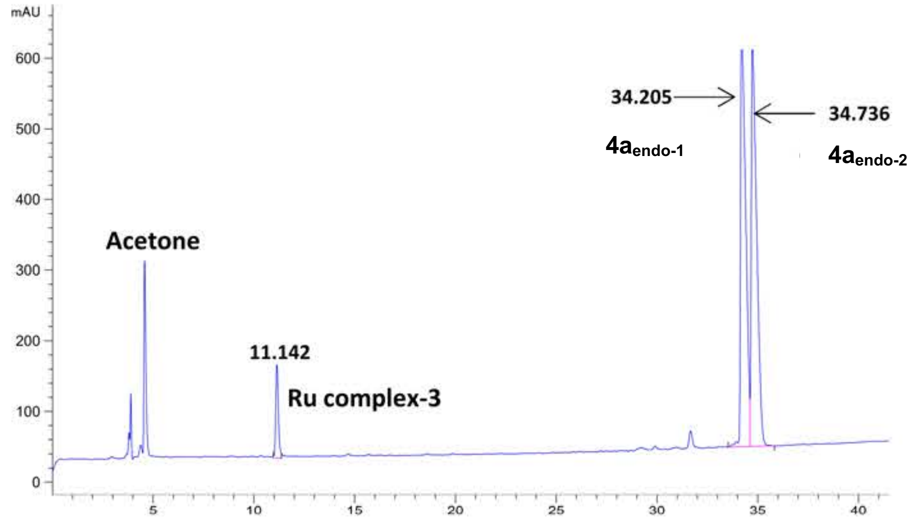


Figure S3. RP-HPLC chromatogram (semi-preparative C18 column, H_2O/acetonitrile/0.1% TFA) of **$4a_{endo}$** (prior to separation).

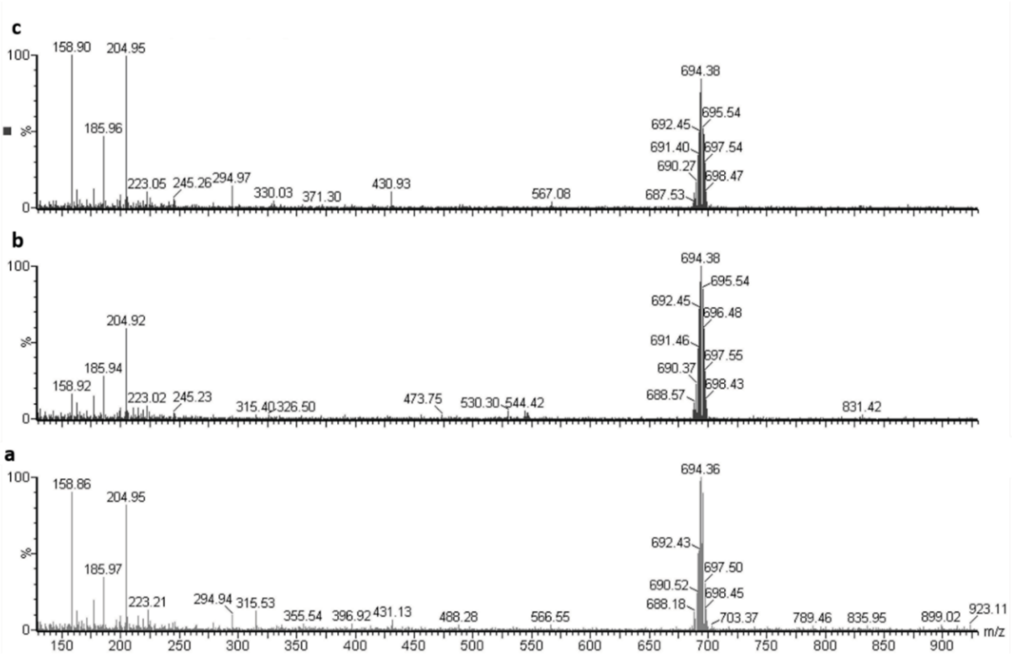


Figure S4. ESI-MS spectra of **4a**$_{endo\text{-}1}$ (a), **4a**$_{endo\text{-}2}$ (b) and **4a**$_{exo}$ (c) (positive mode, H_2O/acetonitrile/0.1% acetic acid).

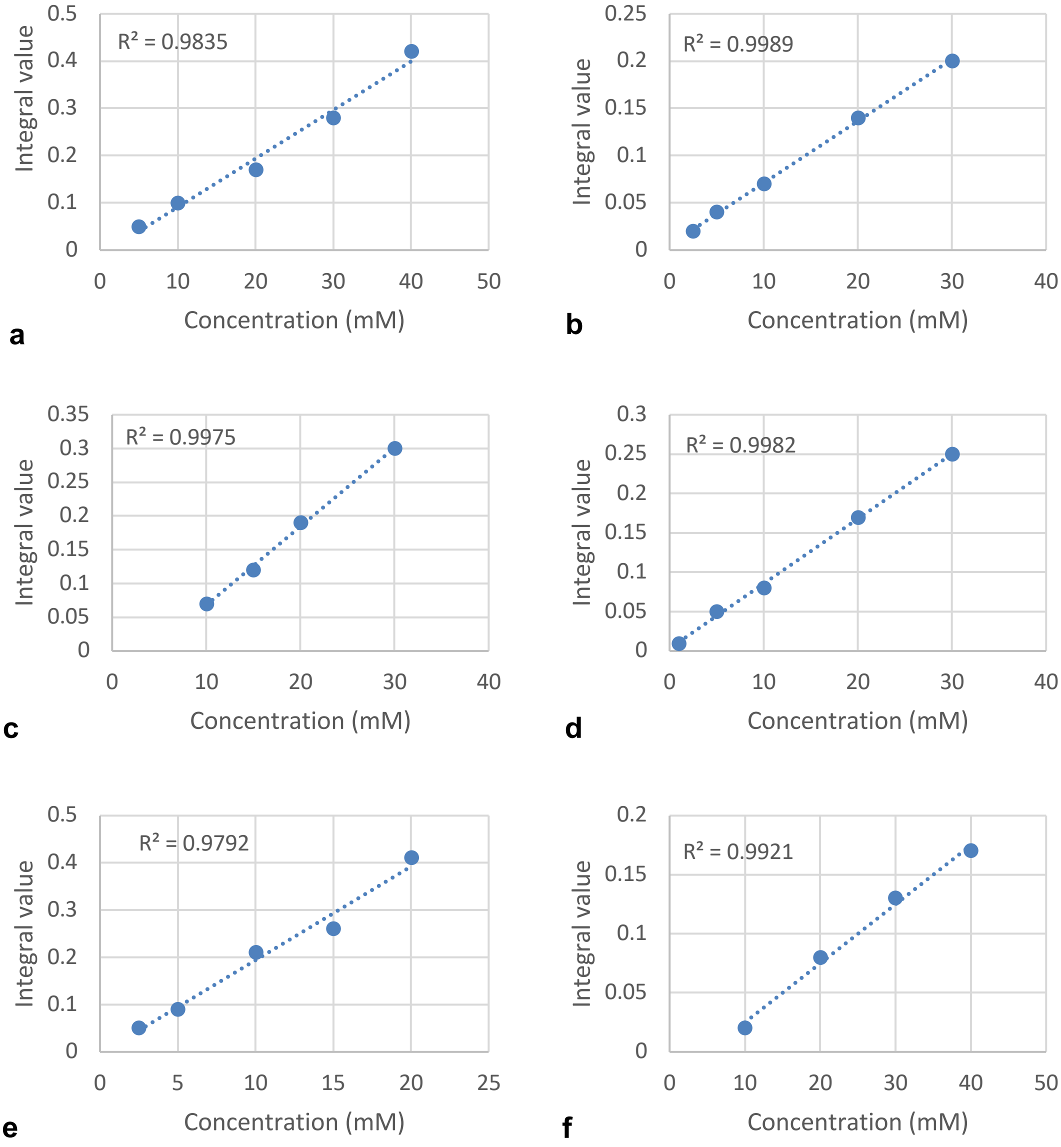


Figure S5. Solubility assessment of complexes **3** (a), **4a** (b), **4b** (c), **5a** (d), *N*-octyl maleimide (e) and *N*-*p*-nitrophenyl maleimide (f) in DMSO-d_6 using ^{1}H NMR spectroscopy at various concentrations. DMSO stock solutions were filtered (0.22 µm) prior to the analysis. The linearity between concentration and the signal intensity of one of the protons resonances for each compound was considered as an indication of the solubility of that compound at the desired concentration.

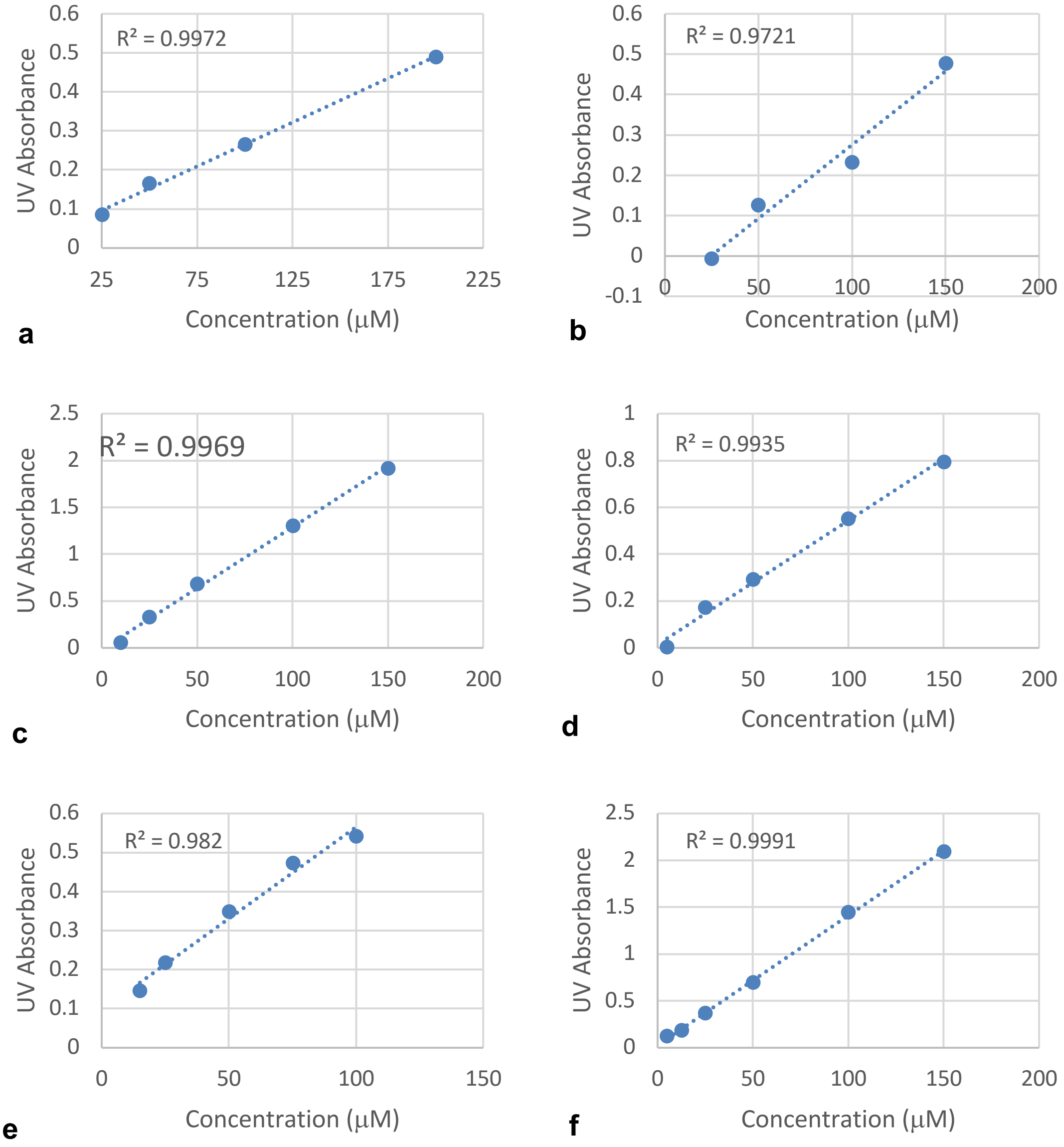


Figure S6. Solubility assessment of complexes **3** (a), **4a** (b), **4b** (c), **5a** (d), *N*-octyl maleimide (e) and *N*-*p*-nitrophenyl maleimide (f) in H_2O/0.5% DMSO using absorbance at 274-278 nm at various concentrations. Stock solutions in DMSO were diluted in miliQ water to reach the concentrations that were used for the *in vitro* cell viability assay (final DMSO concentration = 0.5%). Solutions were filtered (0.22 μm) prior to the analysis. The concentration of saturation of the compounds in this media was assessed by determining the concentration at which the maximum absorbance intensity was observed.

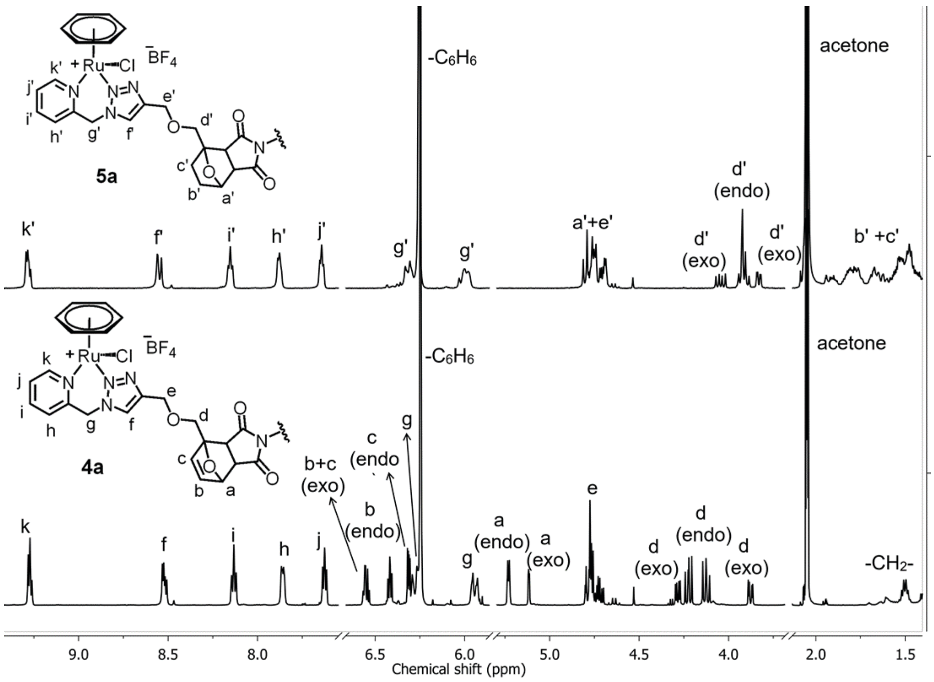


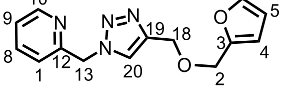
Figure S7. ^{1}H NMR spectra of complex **4a** (bottom) (**4a**$_{\mathbf{endo}}$/**4a**$_{\mathbf{exo}}$: 2/1) and its hydrogenation product **5a** (top) (**5a**$_{\mathbf{endo}}$/**5a**$_{\mathbf{exo}}$: 2/1) in acetone-d_6.

Experimental section

General remarks

All chemicals were purchased from commercial suppliers and used without further purification. Ru(η^6-C_6H_6)Cl_2]$_2$,[6] *N*-octylmaleimide,[7] *N*-*p*-nitrophenylmaleimide,[8] 2-((prop-2-ynyloxy)methyl)furan,[9] and 2-(azidomethyl)pyridine,[10] were synthesized according to literature procedures. All solvents were dried using a solvent purification system (Pure Process Technology). The absorbance of multi-well plates (510 nm) was measured using a Tecan Infinite M1000 PRO microplate reader. NMR spectra (^{1}H, ^{13}C{^{1}H}, COSY, HSQC and HMBC) were recorded on 400 MHz Varian and 600 MHz Bruker Avance III NMR spectrometers. Chemical shifts (δ) and coupling constants (J) are reported in parts per million (ppm) and Hertz (Hz), respectively. ^{1}H and ^{13}C{^{1}H} NMR spectra were referenced to solvent peaks as an internal standard, and spectral assignments were confirmed by 2D experiments. High-resolution and high accuracy mass spectra (HR-ESI-MS) were obtained using an Exactive Orbitrap spectrometer (Department of Chemistry, McGill University) or an LTQ Orbitrap (CQIB-INRS) from ThermoFisher Scientific. Column chromatography was performed using a Biotage Isolera One flash purification system with silica gel KP-Sil SNAP cartridges. Semi-preparative separation was performed using an Agilent 1260 Infinity II HPLC equipped with an Agilent Pursuit 5 C18 150 ×10.0 mm column. Diffraction measurements were performed on a Bruker Venture Metaljet k-geometry diffractometer with a Metal Jet using Helios MX Mirror Optics as monochromator and a Bruker CMOS Photon III detector (Department of Chemistry, Université de Montréal). Elemental analyses of Ru complexes were performed by ThermoFisher Flash 2000 analyzer with Mettler MT5 balance (ANALEST, Department of Chemistry, University of Toronto). All statistical analyses were done using the GraphPad Prism 6.01 software. ANOVA analysis was used for testing the significance of the difference between the means and a p-value <0.05 was considered statistically significant.

Synthesis of 1. Ligand **1** was prepared by reacting 2-((prop-2-ynyloxy)methyl)furan (265 mg, 1.95 mmol) with 2-(azidomethyl)pyridine (313 mg, 2.33 mmol) in a mixture of water/THF (1:1) (2 mL). The reaction was catalyzed by adding drop by drop an aqueous solution of $CuSO_4.5H_2O$ (0.389 mL, 0.5 M) and then an aqueous solution of sodium ascorbate in water (0.778 mL, 0.5 M). The solution mixture was stirred vigorously for 2-4h at room temperature and the completion of reaction was confirmed by GC-MS. The solvent was evaporated, and the crude product was purified by flash chromatography (R_f = 0.24, hexane/ethyl acetate, 50:50). The most intensive band was collected, the solvent was then evaporated under vacuum to give ligand **1** (420 mg, 80%) as a yellowish oil. **^{1}H NMR (600 MHz, CDCl$_3$):** δ_H = 8.56 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H, H10), 7.68 (s, 1H, H20), 7.65 (td, J = 7.7, 1.8 Hz, 1H, H9), 7.36 (dd, J = 1.9, 0.9 Hz, 1H, H6), 7.23 (ddd, J = 7.7, 4.9, 1.1 Hz, 1H, H8), 7.16 (dt, J = 7.8, 1.1 Hz, 1H, H1), 6.31 (dd, J = 3.3, 0.9 Hz, 1H, H4), 6.30 (d, J = 3.3, 1H, H5), 5.62 (s, 2H, H13), 4.65 (s, 2H, H18), 4.51 (s, 2H, H2) ppm. **^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$):** δ_C = 155.4 (C12), 152.3 (C19), 150.7 (C10), 146.2 (C3), 143.9 (C6), 138.3 (C9), 124.4 (C20), 124.4 (C8), 123.4 (C1), 111.3 and 110.8 (C4/5), 65.1 (C2), 64.3 (C18), 56.5 (C13) ppm. **HR-ESI-MS *m/z* (+):** [M + Na]$^+$ calc. for $C_{14}H_{14}N_4NaO_2^+$ 293.1009, found: 293.1008.



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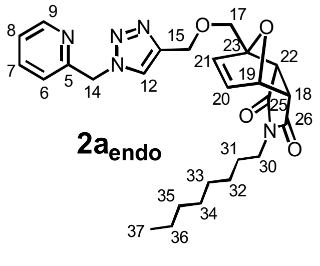
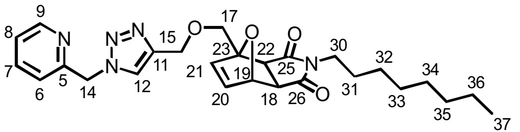
General procedure for the synthesis of 2a and 2b. In a 35 mL pressure vessel sealed with a silicone cap (CEM), acetonitrile (25 mL) was added to ligand furan **1** (1.0 eq) and maleimides (15 eq). The reaction was carried out with a CEM Discover S microwave reactor (T = 40°C, power: 6.5 W, P: 0 psi, hold time: 24h) and was followed by TLC (hexane/ethyl acetate, 1:9). After 24h, the completion of the reaction was confirmed by ^{1}H-NMR (acetone-d_6), then the solvent was evaporated. The crude product was dissolved in minimum amount of dichloromethane and loaded on 50 g KP-Sil column (Biotage SNAP) and eluted with hexane/ethyl acetate to afford the ligand DA **2a** or **2b**.

Synthesis of 2a. Ligand **1** (218 mg, 0.81 mmol) was reacted with *N*-octyl maleimide (2.6 g, 12.42 mmol). After purification by flash chromatography (R_f = 0.19, hexane:ethyl acetate, 15:85), ligand **2a** was obtained (**2a$_{endo}$**/**2a$_{exo}$**: 1.5/1) (358 mg, 93%) as a colorless oil. **2a$_{endo}$** and **2a$_{exo}$** were separated by further purification with 1260 Infinity II LC system (Agilent) using a semi-preparative RP column (Pursuit C18 150×10.0 mm, 5 µm) using a CH_3CN/H_2O gradient (H_2O/acetonitrile, 80:20 to 40:60 in 25 min, flow: 3.0 mL min^{-1}). **2a$_{endo}$**. **^{1}H NMR (600 MHz, acetone-d_6):** δ_H = 8.56 (dt, *J* = 4.9, 1.3 Hz, 1H, H9), 8.05 (s, 1H, H12), 7.80 (td, *J* = 7.7, 1.8 Hz, 1H, H7), 7.32 (dd, *J* = 7.6, 4.9 Hz, 1H, H8), 7.26 (d, *J* = 7.8 Hz, 1H, H6), 6.41 (dd, *J* = 5.8, 1.7 Hz, 1H, H20), 6.32 (d, *J* = 5.8 Hz, 1H, H21), 5.72 (s, 2H, H14), 5.22 (dd, *J* = 5.5, 1.7 Hz, 1H, H19), 4.72 (s, 2H, H15), 4.18 and 4.09 (d, *J* = 12.1 Hz, 2H, H17), 3.61 (dd, *J* = 7.7, 5.5 Hz, 1H, H18), 3.45 (d, *J* = 7.7 Hz, 1H, H22), 3.23 (t, *J* = 7.3 Hz, 2H, H30), 1.39 (m, 2H, H31), 1.32 – 1.19 (m, 10H, -CH$_2$-), 0.87 (t, *J* = 7.0 Hz, 3H, H37) ppm. **^{13}C{^{1}H} NMR (150 MHz, acetone-d_6):** δ_C = 175.8 and 175.5 (C25/26), 156.3 (C5), 150.4 (C9), 145.5 (C11), 138.0 (C7), 135.9 (C21), 135.9 (C20), 124.9 (C12), 124.0 (C8), 122.9 (C6), 92.1 (C23), 80.1 (C19), 68.9 (C17/17'), 65.5 (C15), 55.8 (C14), 48.5 (C18), 46.6 (C22), 38.8 (C30), 32.5 (-CH$_2$-), 29.9 (2C, -CH$_2$-), 28.1 (C31), 27.5 (-CH$_2$-), 23.2 (-CH$_2$-), 14.3 (C37) ppm. **2a$_{exo}$**. **^{1}H NMR (600 MHz, acetone-d_6):** δ_H = 8.56 (dt, *J* = 4.8, 1.4 Hz, 1H, H9), 8.03 (s, 1H, H12), 7.79 (td, *J* = 7.7, 1.8 Hz, 1H, H7), 7.33 (dd, *J* = 7.6, 4.9 Hz, 1H, H8), 7.26 (d, *J* = 7.8 Hz, 1H, H6), 6.55 (dd, *J* = 5.7, 1.7 Hz, 1H, H20), 6.52 (d, *J* = 5.7 Hz, 1H, H21), 5.71 (s, 2H, H14), 5.10 (d, *J* = 1.7 Hz, 1H, H19), 4.73 and 4.68 (d, *J* = 12.1 Hz, 2H, H15), 4.24 and 3.85 (d, *J* = 11.5 Hz, 2H, H17), 3.40 (td, *J* = 7.0, 1.6 Hz, 2H, H30), 3.02 (d, *J* = 6.4 Hz, H18), 2.93 (d, *J* = 6.4 Hz, 1H, H22), 1.50 (m, 2H, H31), 1.33 – 1.20 (m, 10H, -CH$_2$-), 0.87 (t, *J* = 6.9 Hz, 3H, H37) ppm. **^{13}C{^{1}H} NMR (150 MHz, acetone-d_6):** δ_C = 176.8 and 175.5 (C25/26), 156.3 (C5), 150.4 (C9), 145.6 (C11), 138.7 (C21), 138.0 (C7), 137.3 (C20), 124.9 (C12), 124.0 (C8), 122.9 (C6), 91.4 (C23), 81.8 (C19), 68.6 (C17), 65.6 (C15), 55.7 (C14), 50.7 (C18), 49.1 (C22), 38.9 (C30), 32.5 (-CH$_2$-), 29.5 (2C, -CH$_2$-), 28.2 (C31), 27.2 (-CH$_2$-), 23.3 (-CH$_2$-), 14.3 (-CH$_3$, C37) ppm. **HR-ESI-MS *m/z* (+):** $[M + H]^+$ calc. for $C_{26}H_{34}N_5O_4^+$ 480.2605, found: 480.2599; $[M + Na]^+$ calc. for $C_{26}H_{33}N_5NaO_4^+$ 502.2425, found: 502.2415; $[2M+Na]^+$ calc. for $C_{52}H_{66}N_{10}NaO_8^+$ 981.4957, found: 981.4950.

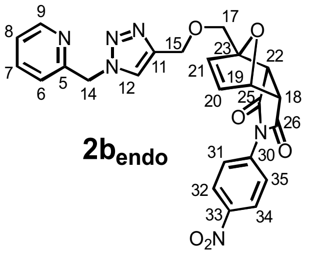


2a$_{endo}$

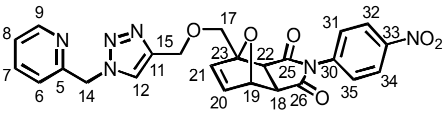


2a$_{exo}$

Synthesis of 2b. Ligand furan **1** (100 mg, 0.37 mmol) was reacted with *N*-*p*-nitrophenylmaleimide (1.21 g, 5.56 mmol). After purification by flask chromatography (R_f = 0.40, hexane/ethyl acetate, 15:85), ligand **2b** was obtained (**2b$_{\mathbf{endo}}$**/**2b$_{\mathbf{exo}}$**: 1/4) (115 mg, 80%) as a colorless foam. **2b$_{\mathbf{endo}}$** and **2b$_{\mathbf{exo}}$** were separated by further purification with 1260 Infinity II LC system (Agilent) using a semi-preparative RP column (Pursuit C18 150×10.0 mm, 5 µm) using a H_2O/acetonitrile gradient (H_2O/acetonitrile, 85:15 to 40:60, flow: 3.0 mL min^{-1}). **2b$_{\mathbf{endo}}$**. **^{1}H NMR (600 MHz, acetone-*d*$_6$):** δ_H = 8.55 (dt, *J* = 4.8, 1.8 Hz, 1H, H9), 8.32 (d, *J* = 9.1 Hz, 1H, H32 and H34), 8.07 (s, 1H, H12), 7.78 (td, *J* = 7.7, 1.8 Hz, 1H, H7), 7.53 (d, *J* = 9.1 Hz, 2H, H31 and H35), 7.31 (ddd, *J* = 7.6, 4.8, 1.1 Hz, 1H, H8), 7.27 (d, *J* = 8.0 Hz, 1H, H6), 6.65 (dd, *J* = 5.8, 1.6 Hz, H20), 6.56 (d, *J* = 5.8 Hz, 1H, H21), 5.72 (s, 2H, H14), 5.38 (dd, *J* = 5.5, 1.6 Hz, 1H, H19), 4.75 (s, 2H, H15), 4.24 and 4.17 (d, *J* = 12.1 Hz, 2H, H17), 3.87 (dd, *J* = 7.8, 5.5 Hz, 1H, H18), 3.72 (d, *J* = 7.8 Hz, 1H, H22) ppm. **^{13}C{^{1}H} NMR (150 MHz, acetone-*d*$_6$):** δ_C = 174.3 and 174.1 (2C, C25/26), 156.3 (2C, C30/33), 105.5 (C9), 147.9 (C5), 145.4 (C11), 138.7 (C7), 138.0 (C20), 136.3 (C21), 128.4 (2C, C31/C35), 125.0 (2C, C32/34), 124.9 (C12), 124.0 (C8), 122.9 (C6), 92.6 (C23), 80.6 (C19), 68.7 (C17), 65.4 (C15), 55.8 (C14), 48.8 (C18), 46.9 (C22) ppm. **2b$_{\mathbf{exo}}$**. **^{1}H NMR (600 MHz, acetone-*d*$_6$):** δ_H = 8.53 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H, H9), 8.33 (d, *J* = 9.0 Hz, 2H, H32 and H34), 8.04 (s, 1H, H12), 7.75 (td, *J* = 7.7, 1.8 Hz, 1H, H7), 7.63 (d, *J* = 9.1 Hz, 2H, H31 and H35), 7.29 (ddd, *J* = 7.7, 4.8, 1.1 Hz, 1H, H6), 7.25 (dd, *J* = 7.9, 1.1 Hz, 1H, H8), 6.62 (dd, *J* = 5.7, 1.7 Hz, 1H, H20), 6.59 (d, *J* = 5.7 Hz, 1H, H21), 5.70 (s, 2H, H14), 5.28 (d, *J* = 1.8 Hz, 1H, H19), 4.72 (q, *J* = 7.0 Hz, 2H, H15), 4.31 and 3.99 (d, *J* = 11.5 Hz, 2H, H17), 3.31 (d, *J* = 6.5 Hz, 1H, H18), 3.18 (d, *J* = 6.5 Hz, 1H, H22) ppm. **^{13}C{^{1}H} NMR (150 MHz, acetone-*d*$_6$):** δ_C = 175.6 and 174.3 (2C, C25/26), 156.2 (2C, C30/33), 150.4 (C9), 147.8 (C5), 145.4 (C11), 139.0 (C7), 138.9 (C20), 137.6 (C21), 128.3 (2C, C31/C35), 125.0 (C12), 124.8 (2C, C32/34), 123.9 (C8), 122.9 (C6), 92.0 (C23), 82.3 (C19), 68.3 (C17), 65.5 (C15), 55.7 (C14), 51.3 (C18), 49.6 (C22) ppm. **HR-ESI-MS *m/z* (+):** [M + H]$^+$ calc. for $C_{24}H_{21}N_6O_6^+$ 489.1517, found: 489.1510; [M + Na]$^+$ calc. for $C_{24}H_{20}N_6NaO_6^+$ 511.1337, found: 511.1328; [2M+Na]$^+$ calc. for $C_{48}H_{40}N_{12}NaO_{12}^+$ 999.2781, found: 999.2774.

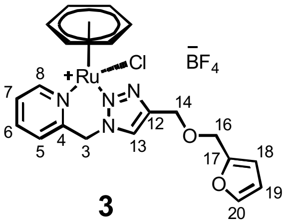


2b$_{\mathbf{endo}}$



2b$_{\mathbf{exo}}$

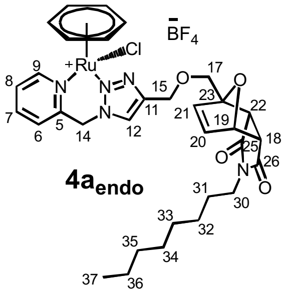
Synthesis of 3. Under N_2 atmosphere, 10 mL of dry ethanol was added to Ru(η^6-C_6H_6)Cl_2]$_2$ (50 mg, 0.1 mmol) and ligand **1** (60 mg, 0.22 mmol) in the presence of 52 mg of NH_4BF_4 (0.497 mmol) in a Schlenk flask. The reaction mixture was refluxed and stirred for 3h. The mixture was cooled down to room temperature and the precipitate was filtered and washed with ethanol/diethyl ether and dried in air to afford the final complex **3** (54 mg, 95%) as a light brown solid. **^{1}H NMR (600 MHz, acetone-*d*$_6$):** δ_H = 9.27 (dd, *J* = 5.8, 1.5 Hz, 1H, H8), 8.48 (s, 1H, H13), 8.13 (td, *J* = 7.7, 1.5 Hz, 1H, H6), 7.86 (dt, *J* = 7.9, 1.1 Hz, 1H, H5), 7.62 (ddd, *J* = 7.3, 5.7, 1.3 Hz, 1H, H7), 7.54 (dd, *J* = 1.9, 0.8 Hz, 1H, H20), 6.43 (dd, *J* = 3.2, 0.8 Hz, 1H, H18), 6.37 (dd, *J* = 3.2, 1.8 Hz, 1H, H19), 6.29 and 5.94 (d, *J* = 15.7 Hz, 2H, H3), 6.24 (s, 6H, C_6H_6), 4.62 (m, 2H, H14), 4.53 (s, 2H, H16) ppm. **^{13}C{^{1}H} NMR (150 MHz, acetone-*d*$_6$):** δ_C = 159.8 (C8), 154.5 (C4), 152.4 (C12), 148.7 (C17), 143.9 (C20), 141.4 (C6), 130.1 (C13), 127.0 (C5), 126.6 (C7), 111.2 (C19), 110.8 (C18), 87.9 (6C, C_6H_6), 64.6 (C16), 63.1 (C14), 55.4 (C3) ppm. **^{19}F{^{1}H} NMR (565 MHz, acetone-*d*$_6$)** δ_F = −151.22 (s, 4F, $^{10}BF_4$), −151.27 (s, 4F, $^{11}BF_4$). Found (%): C, 40.88; H, 3.53; N, 9.69. $C_{20}H_{20}BClF_4N_4O_2Ru_1\cdot H_2O$ requires C, 40.73; H, 3.76; N, 9.50. **HR-ESI-MS *m/z* (+):** [M]$^+$ calc. for $C_{20}H_{20}ClN_4O_2Ru^+$ 485.0313, found: 485.0318; [2M+BF$_4$]$^+$ calc. for $C_{40}H_{40}BCl_2F_4N_8O_4Ru_2^+$ 1057.0660, found: 1057.0703; **HR-ESI-MS *m/z* (−):** [M]$^-$ calc. for BF_4^- 87.0035; found 87.0020.



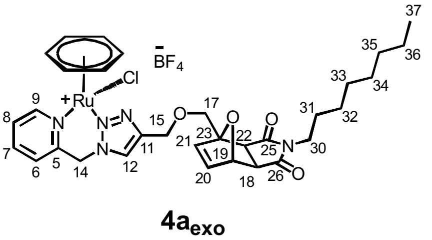
3

General procedures for the synthesis of **4a** and **4b**. *Method 1:* in a 35 mL pressure vessel sealed with a silicone cap (CEM), acetonitrile (25.0 mL) was added to the mixture of **3** (1.0 eq) and maleimides (30 eq). The Diels-Alder reaction was carried out with a CEM Discover S microwave reactor (T = 40ºC, power: 6.5 W, P: 0 PSI, hold time: 24h). After 24h, the completion of the reaction was confirmed by ^{1}H-NMR (acetone-*d*$_6$), then the solvent was evaporated with rotary evaporator. The crude product was dissolved in minimum amount of dichloromethane and loaded on 50 g KP-Sil column (Biotage SNAP) and eluted with CH_2Cl_2/MeOH to afford Ru complex DA **4a** and **4b** correspondent (two consecutively purifications were needed). *Method 2:* in a 15 mL Pyrex® tube, 5 mL of ethanol anhydrous was added to the mixture of ligand DA **2a** or **2b** (1.5 eq), [Ru(η^6-C_6H_6)Cl_2]$_2$ (1.0 eq) and NH_4BF_4 (3.5 eq). The tube was sealed carefully with parafilm to prevent the evaporation of solvent. The reaction was carried out at room temperature for 48h. The completion of the reaction was confirmed by ^{1}H-NMR (acetone-*d*$_6$). The solvent was evaporated then the crude product was re-dissolved in 1-2 mL of dichloromethane and the solution was filtered on a Celite pad. Complexes **4a** and **4b** were obtained by adding 2 mL of Et_2O, scratching the flask with a spatula and then drying the precipitate under vacuum.

Synthesis of 4a. *Method 1:* **3** (100 mg, 0.175 mol) was reacted with *N*-octyl maleimide (1.050 g, 5.02 mmol). After two consecutive purifications by flask chromatography, **4a** was obtained (**4a$_{endo}$**/**4a$_{exo}$**: 1.7/1) (29 mg, 21%) as a yellowish solid. *Method 2:* Ligand **2a** (**2a$_{endo}$**/**2a$_{exo}$**: 2) (27 mg, 0.0346 mmol) was reacted with [Ru(η^6-C_6H_6)Cl_2]$_2$ (19 mg) in the presence of NH_4BF_4 (14 mg, 0.103 mmol) in EtOH anhydrous (5 mL). After purification, **4a** was obtained (**4a$_{endo}$**/**4a$_{exo}$**: 1.5/1) as a yellowish solid (40 mg, 90%). **4a$_{endo}$**. **^{1}H NMR (600 MHz, acetone-*d*$_6$):** δ_H = 9.29 (t, *J* = 6.3 Hz, 1H, H9), 8.53 (s, 1H, H12), 8.15 (t, *J* = 7.5 Hz, 1H, H7), 7.88 (d, *J* = 7.4 Hz, 1H, H6), 7.64 (t, *J* = 6.7 Hz, 1H, H8), 6.42 (dd, *J* = 5.7, 1.6 Hz, 1H, H20), 6.31 (dd, *J* = 5.8, 3.0 Hz, 1H, H21), 6.28 and 5.97 (d, *J* = 15.6 Hz, 2H, H14), 6.26 (m, 6H, C_6H_6), 5.23 (d, *J* = 5.2 Hz, 1H, H19), 4.78 (m, 2H, H15), 4.24 (dd, *J* = 12.2, 9.7 Hz, 1H, H17), 4.14 (dd, *J* = 12.2, 10.7 Hz, 1H, H17), 3.60 (dt, *J* = 13.4, 6.6 Hz, 1H, H18), 3.47 (d, *J* = 7.6 Hz, 1H, H22$_{endo-2}$), 3.42 (d, *J* = 7.6 Hz, 1H, H22$_{endo-1}$), 3.23 (t, *J* = 7.3 Hz, 1H, H30$_{endo-2}$), 3.18 and 3.14 (dt, *J* = 13.2, 7.3 Hz, 1H, H30$_{\text{endo-1}}$), 1.38 (m, 2H, H31), 1.33-1.11 (m, 10H, -CH$_2$-), 0.86 (t, *J* = 7.0 Hz, 3H, H37) ppm. **^{13}C{^{1}H} NMR (150 MHz, acetone-*d*$_6$):** δ_C = 175.9 and 175.5 (2C, C25 and C26), 159.9 (C9), 154.5 (C5), 148.5 (C11), 141.4 (C7), 136.1 (C20), 135.8 (C21), 131.0 (C12), 127.4 (C6), 126.7 (C8), 91.9 (C23), 88.2 (6C, C_6H_6), 80.2 (C19), 69.2 (C17$_{\text{endo-2}}$) and 68.8 (C17$_{\text{endo-1}}$), 64.9 (C15$_{\text{endo-2}}$) and 64.8 (C15$_{\text{endo-1}}$), 56.2 (C14), 48.6 (C18), 46.7 (C22$_{\text{endo-2}}$) and 46.5 (C22$_{\text{endo-1}}$), 38.8 (C30), 27.5 (C31), 32.5, 29.8, 28.1, 27.5, 23.2 (5C, -CH$_2$-), 14.3 (-CH$_3$, C37) ppm. **^{19}F{^{1}H} NMR (565 MHz, acetone-*d*$_6$)** δ_F = −150.69 (s, 4F, $^{10}BF_4$), −150.75 (s, 4F, $^{11}BF_4$). **4a$_{\text{exo}}$. ^{1}H NMR (600 MHz, acetone-*d*$_6$):** δ_H = 9.28 (d, *J* = 5.7 Hz, 1H, H9), 8.51 (d, *J* = 5.7 Hz, 1H, H12), 8.14 (t, *J* = 7.5 Hz, 1H, H7), 7.86 (d, *J* = 7.7 Hz, 1H, H6), 7.63 (t, *J* = 6.6 Hz, 1H, H8), 6.56 (m, 1H, H20), 6.54 (t, *J* = 6.4 Hz, 1H, H21), 6.28 and 5.95 (d, *J* = 15.6 Hz, 2H, H14), 6.25 (s, 6H, C_6H_6), 5.12 (t, *J* = 1.9 Hz, 1H, H19), 4.81 and 4.74 (m, 2H, H15), 4.28 (dd, *J* = 11.4, 4.4 Hz, 1H, H17) and 3.88 (dd, *J* = 11.5, 3.3 Hz, 1H, H17), 3.39 (q, *J* = 6.7 Hz, 2H, H30), 3.03 (dd, *J* = 6.4, 3.8 Hz, 1H, H18), 2.97 (t, *J* = 6.6 Hz, 1H, H22), 1.50 (m, 2H, H31), 1.33-1.11 (m, 10H, -CH$_2$-), 0.86 (t, *J* = 7.0 Hz, 3H, H37) ppm. **^{13}C{^{1}H} NMR (150 MHz, acetone-*d*$_6$):** δ_C = 176.8 and 175.6 (2C, C25 and C26), 159.8 (C9), 154.5 (C5), 148.8 (C11), 141.4 (C7), 138.6 (C20), 137.5 (C21), 130.2 (C12), 127.1 (C6), 126.6 (C8), 91.2 (C23), 88.0 (6C, C_6H_6), 81.9 (C19), 69.0 (C17), 65.1 (C15), 55.7 (C14), 50.7 (C18), 49.1 (C22), 39.0 (C30), 27.3 (C31), 32.5, 29.9, 29.8, 28.3, 23.3 (5C, -CH$_2$-), 14.4 (-CH$_3$, C37) ppm. **^{19}F{^{1}H} NMR (565 MHz, acetone-*d*$_6$):** δ_F = −151.06 (s, 4F, $^{10}BF_4$), −151.11 (s, 4F, $^{11}BF_4$). Found (%): C, 46.70; H, 4.84; N, 8.47. $C_{32}H_{39}BClF_4N_5O_4Ru_1\cdot ½CHCl_3$ requires C, 46.43; H, 4.74; N, 8.33. **HR-ESI-MS *m/z* (+):** [M]$^+$ calc. for $C_{32}H_{39}ClN_5O_4Ru^+$ 694.1729, found: 694.1738; [2M+BF$_4$]$^+$ calc. for $C_{64}H_{78}BCl_2F_4N_{10}O_8Ru_2^+$ 1475.3492, found: 1475.3521; **HR-ESI-MS *m/z* (−):** [M]$^-$ calc. for BF_4^- 87.0035; found 87.0020.



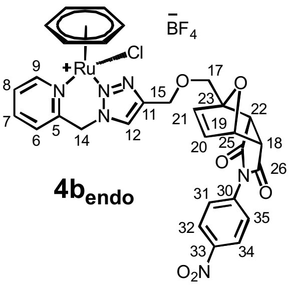
4a$_{\text{endo}}$



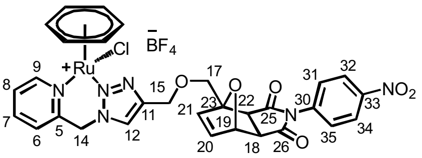
4a$_{\text{exo}}$

NOTE: After purification of **4a$_{\text{endo}}$** by HPLC (H_2O/acetonitrile/0.1% TFA), two different isomers (for which the counterion was replaced by trifluoroacetate during the analysis) were separated. HPLC method: A: H_2O + 0.1% trifluoroacetic acid (TFA), B: acetonitrile + 0.1% TFA; 0-2 min 15% B, 2-40 min 60% B, 40-43 100% B, 43-47 min 100% B, 47-50 min, 15% B, flow: 3.0 mL min^{-1}. **4a$_{\text{endo-1}}$. ^{1}H NMR (600 MHz, acetone-*d*$_6$):** δ_H = 9.27 (d, *J* = 5.7 Hz, 1H, H9), 8.65 (s, 1H, H12), 8.13 (t, *J* = 7.4 Hz, 1H, H7), 7.90 (d, *J* = 7.5 Hz, 1H, H6), 7.63 (t, *J* = 6.6 Hz, 1H, H8), 6.41 (td, *J* = 6.3, 1.6 Hz, 1H, H20), 6.31 (d, *J* = 5.7 Hz, 1H, H21), 6.46 and 6.00 (d, *J* = 15.4 Hz, 1H, 2H, H14), 6.27 (s, 6H, C_6H_6), 5.23 (dd, *J* = 5.5, 1.6 Hz, 1H, H19), 4.77 (m, 2H, H15), 4.21 and 4.13 (d, *J* = 12.1 Hz, 2H, H17), 3.59 (dd, *J* = 7.6, 5.5 Hz, 1H, H18), 3.42 (d, *J* = 7.5 Hz, 1H, H22), 3.20 and 3.13 (dt, *J* = 13.6, 7.3 Hz, 2H, H30), 1.36 (m, 2H, H31), 1.33-1.11 (m, 10H, -CH$_2$-), 0.86 (t, *J* = 6.9 Hz, 3H, H37) ppm. **^{13}C{^{1}H} NMR (150 MHz, acetone-*d*$_6$):** δ_C = 175.9 and 175.5 (2C, C25 and C26), 159.8 (C9), 154.7 (C5), 148.6 (C11), 141.4 (C7), 136.0 (C20), 135.8 (C21), 130.6 (C12), 127.1 (C6), 126.6 (C8), 91.9 (C23), 88.1 (6C, C_6H_6), 80.2 (C19), 68.8 (C17), 64.7 (C15), 55.8 (C14), 48.5 (C18), 46.5 (C22), 38.8 (C30), 27.6 (C31), 32.5, 29.6, 28.1, 28.1, 23.0 (5C, -CH$_2$-), 14.3 (C37) ppm. **^{19}F{^{1}H} NMR (565 MHz, acetone-d$_6$):** δ_F = −75.75 (s, 3F, CF_3COO^-). **HR-ESI-MS *m/z* (+):** [M]$^+$ calc. for $C_{32}H_{39}ClN_5O_4Ru^+$ 694.1729, found: 694.1722; **HR-ESI-MS *m/z* (−):** [M]$^-$ calc. for CF_3COO^- 112.9856, found 112.9857. **4a$_{\text{endo-2}}$. ^{1}H NMR (600 MHz, acetone-*d*$_6$):** δ_H = 9.28 (d, *J* = 5.8 Hz, 1H, H9), 8.53 (d, *J* = 4.7 Hz, 1H, H12), 8.14 (t, *J* = 7.6 Hz, 1H, H7), 7.90 (d, *J* = 7.5 Hz, 1H, H6), 7.63 (t, *J* = 6.6 Hz, 1H, H8), 6.43 (td, *J* = 6.3, 1.6 Hz, 1H, H20), 6.31 (d, *J* = 5.7 Hz, 1H, H21), 6.46 and 6.02 (d, *J* = 15.4 Hz, 2H, H14), 6.26 (s, 6H, C_6H_6), 5.23 (dd, *J* = 5.6, 1.7 Hz, 1H, H19), 4.78 (m, 2H, H15), 4.23 and 4.11 (d, *J* = 12.1 Hz, 2H, H17), 3.62 (dd, *J* = 7.6, 5.5 Hz, 1H, H18), 3.47 (d, *J* = 7.6 Hz, 1H, H22), 3.23 (t, *J* = 7.3 Hz, 1H, H30), 3.18 and 3.14 (dt, *J* = 13.2, 7.3 Hz, 2H, H30), 1.39 (m, 2H, H31), 1.33-1.11 (m, 10H, -CH_2-), 0.86 (t, *J* = 7.0 Hz, 3H, H37) ppm. **$^{13}C\{^1H\}$ NMR (150 MHz, acetone-*d*$_6$):** δ_C = 175.0 and 174.6 (2C, C25 and C26), 159.0 (C9), 153.7 (C5), 147.7 (C11), 140.5 (C7), 135.2 (C20), 134.9 (C21), 129.5 (C12), 126.2 (C6), 125.8 (C8), 91.1 (C23), 87.2 (6C, C_6H_6), 79.3 (C19), 68.3 (C17), 64.0 (C15), 54.7 (C14), 47.6 (C18), 45.8 (C22), 37.9 (C30), 27.3 (C31), 29.4, 28.9, 30.0, 26.7, 22.3 (5C, -CH_2-), 13.4 (C37) ppm. **$^{19}F\{^1H\}$ NMR (565 MHz, acetone-*d*$_6$):** δ_F = −75.87 (s, 3F, CF_3COO^-). **HR-ESI-MS *m/z* (+):** $[M]^+$ calc. for $C_{32}H_{39}ClN_5O_4Ru^+$ 694.1729, found: 694.1721; **HR-ESI-MS *m/z* (−):** $[M]^-$ calc. for CF_3COO^- 112.9856, found 112.9857.

Synthesis of 4b. *Method 1:* **3** (80 mg, 0.14 mol) was reacted with *N*-*p*-nitrophenylmaleimide (920 mg, 4.22 mmol). After two consecutive purifications by flask chromatography, **4b** was obtained (**4b$_{endo}$**/**4b$_{exo}$** : 1/3.8) (27 mg, 25%) as a yellowish solid. *Method 2:* **2b** (**2b$_{endo}$**/**2b$_{exo}$**: 1/2) (50 mg, 0.102 mmol) was reacted with $[Ru(\eta^6\text{-}C_6H_6)Cl_2]_2$ (34 mg) in the presence of NH_4BF_4 (25 mg, 0.238 mmol) in EtOH anhydrous (5 mL). After purification, **4b** was obtained (**4b$_{endo}$**/**4b$_{exo}$**: 1/4) as a yellowish solid (68 mg, 87%). **4b$_{endo}$. ^1H NMR (600 MHz, DMSO-*d*$_6$):** δ_H = 9.11 (d, *J* = 5.7 Hz, 1H, H9), 8.64 (d, *J* = 5.6 Hz, 1H, H12), 8.32 (dd, *J* = 9.0, 7.8 Hz, 1H, 2H, H32/34), 8.14 (t, *J* = 7.6 Hz, 1H, H7), 7.78 (m, 1H, H6), 7.63 (t, *J* = 6.7 Hz, 1H, H8), 7.47 and 7.41 (d, *J* = 9.0 Hz, 2H, H31/35), 6.66 and 6.63 (dd, *J* = 5.8, 1.6 Hz, 1H, H20), 6.55 (m, 1H, H21), 6.22 and 5.73 (d, *J* = 15.6 Hz, 2H, H14), 6.14 (m, 6H, C_6H_6), 5.39 (t, *J* = 6.6 Hz, 1H, H19), 4.70 (m, 2H, H15), 4.19 and 4.10 (m, 2H, H17), 3.84 (ddd, *J* = 13.6, 7.7, 5.5 Hz, 1H, H18), 3.61 and 3.57 (d, *J* = 7.7 Hz, 1H, H22) ppm. **$^{13}C\{^1H\}$ NMR (150 MHz, DMSO-*d*$_6$):** δ_C = 173.5 and 173.4 (2C, C25/26), 158.7 (C9), 153.3 (C5), 146.7 (C11), 143.3 (2C, C30/33), 140.5 (C7), 135.6 (C20), 135.1 (C21), 129.6 (C12), 127.8 and 128.7 (2C, C31/35), 126.0 (C6), 125.7 (C8), 124.3 (2C, C32/34), 91.1 (C23), 86.7 (6C, C_6H_6), 79.2 (C19), 67.7 (C17), 63.6 (C15), 54.1 (C14), 47.7 (C18), 46.2 (C22) ppm. **$^{19}F\{^1H\}$ NMR (565 MHz, acetone-*d*$_6$):** δ_F = −150.91 (s, 4F, $^{10}BF_4$), −150.96 (s, 4F, $^{11}BF_4$). **4b$_{exo}$. ^1H NMR (600 MHz, DMSO-*d*$_6$):** δ_H = 9.13 (d, *J* = 5.3 Hz, 1H, H9), 8.60 (s, 1H, H12), 8.34 (m, 2H, H32/34), 8.13 (tdd, *J* = 7.7, 2.6, 1.6 Hz, 1H, H7), 7.78 (t, *J* = 7.4 Hz, 1H, H6), 7.63 (t, *J* = 6.7 Hz, 1H, H8), 7.58 (m, 2H, H31/35), 6.61 (td, *J* = 5.6, 1.6 Hz, 1H, H20), 6.55 (m, 1H, H21), 6.22 and 5.72 (m, 2H, H14), 6.13 (s, 6H, C_6H_6), 5.24 (dd, *J* = 3.9, 1.6 Hz, 1H, H19), 4.70 (m, 2H, H15), 4.29 and 3.93 (d, *J* = 12.3 Hz, 2H, H17), 3.28 (d, *J* = 6.6 Hz, 1H, H18), 3.13 (dd, *J* = 6.5, 4.9 Hz, 1H, H22) ppm. **$^{13}C\{^1H\}$ NMR (150 MHz, DMSO-*d*$_6$):** δ_C = 175.0 and 173.5 (C25/26), 158.7 (C9), 153.3 (C5), 147.0 (C11), 146.7 (C30/33), 140.5 (C7), 137.5 (C21), 136.9 (C20), 129.4 (C12), 127.7 (2C, C32/34), 126.0 (C6), 125.6 (C8), 124.3 (2C, C31/35), 90.6 (C23), 86.7 (6C, C_6H_6), 80.9 (C19), 67.7 (C17), 63.7 (C15), 54.1 (C14), 50.3 (C18), 48.8 (C22) ppm. **$^{19}F\{^1H\}$ NMR (565 MHz, acetone-*d*$_6$):** δ_F = −151.28 (s, 4F, $^{10}BF_4$), −151.33 (s, 4F, $^{11}BF_4$). Found (%): C, 44.05; H, 3.59; N, 9.40. $C_{30}H_{26}BClF_4N_6O_6Ru_1 \cdot ½CH_2Cl_2$ requires C, 44.01; H, 3.27; N, 9.74. **HR-ESI-MS *m/z* (+):** $[M]^+$ calc. for $C_{30}H_{26}ClN_6O_6Ru^+$ 703.0640, found: 703.0644; **HR-ESI-MS *m/z* (−):** $[M]^-$ calc. for $BF4^-$ 87.0035; found 87.0018.



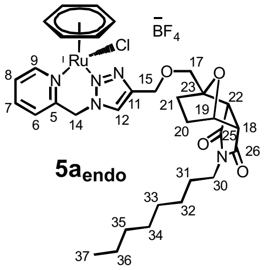
4b$_{endo}$



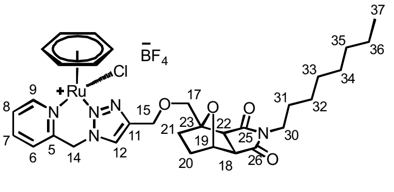
4b$_{exo}$

Synthesis of 5a. The hydrogenation of **4a** (50 mg, 0.064 mmol) was carried out with a H-Cube® reactor (ThalesNano) in 30 min using a catalyst cartridge 10% Pd/C in acetone (20 bar, flow rate: 1.0 mL/min, 23°C). After reaction completion, the solvent was evaporated and **5a** was obtained as a yellowish solid (48 mg, 95%) by adding

Et_2O and scratching the vessel with a spatula. **5a$_{endo}$.** **^{1}H NMR (600 MHz, DMSO-d_6):** δ_H = 9.13 (d, J = 6.0 Hz, 1H, H9), 8.63 (s, 1H, H12), 8.14 (t, J = 7.4 Hz, 1H, H7), 7.79 (t, J = 7.1 Hz, 1H, H6), 7.64 (t, J = 6.7 Hz, 1H, H8), 6.21 (d, J = 15.6 Hz, 1H, H14) and 5.73 (d, J = 15.4 Hz, 1H, H14), 6.14 (s, 6H, C_6H_6), 4.77 (q, J = 6.1 Hz, 1H, H19), 4.71 (m, 2H, H15), 3.85 (m, 2H, H17), 3.48 (m, 1H, H18), 3.34 and 3.28 (m, 1H, H22), 3.32 (m, 2H, H30), 1.74 (m, 2H, H21), 1.62 (m, 2H, H20), 1.45 and 1.40 (m, 2H, H31), 1.28 – 1.14 (m, 10H, -CH_2-), 0.84 (t, J = 7.0 Hz, 3H, H37) ppm. **^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6):** δ_C = 175.7 (2C, C_{25} and C_{26}), 158.7 (C9), 153.3 (C5), 146.8 (C11), 140.4 (C7), 129.5 (C12), 126.0 (C6), 125.6 (C8), 87.6 (C23), 86.7 (6C, C_6H_6), 77.0 (C19), 69.0 (C17), 63.5 (C15), 54.0 (C14), 51.6 (C18), 50.4 (C22), 37.9 (C30), 29.1 (C20), 28.9 (C21), 26.3 (C31), 31.1, 28.5, 28.4 22.0, 27.1 (5C, -CH_2-), 13.9 (-CH_3, C37) ppm. **^{19}F{^{1}H} NMR (565 MHz, acetone-d_6):** δ_F = −148.22 (s, 4F, $^{10}BF_4$), −148.28 (s, 4F, $^{11}BF_4$). **5a$_{exo}$.** **^{1}H NMR (600 MHz, DMSO-d_6):** δ_H = 9.13 (d, J = 6.0 Hz, 1H, H9), 8.60 (s, 1H, H12), 8.14 (t, J = 7.4 Hz, 1H, H7), 7.79 (t, J = 7.1 Hz, 1H, H6), 7.64 (t, J = 6.7 Hz, 1H, H8), 6.21 (d, J = 15.6 Hz, 1H, H14), 5.73 (d, J = 15.4 Hz, 1H, H14), 6.14 (s, 6H, C_6H_6), 4.64 (m, 1H, H19), 4.65 (m, 2H, H15), 3.96 (dd, J = 19.1, 11.1 Hz, 1H, H17), 3.75 (d, J = 11.1 Hz, 1H, H17), 3.12 (d, J = 7.1 Hz, 1H, H22), 3.04 (dd, J = 6.9, 4.2 Hz, 1H, H18), 3.27 and 3.18 (dt, J = 13.6, 7.2 Hz, 2H, H30), 1.41 (m, 2H, H31), 1.76 (m, 2H, H20), 1.62 (m, 2H, H21), 1.28 – 1.14 (m, 10H, -CH_2-), 0.83 (t, J = 7.2 Hz, 3H, H37) ppm. **^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6):** δ_C = 177.4 and 175.5 (2C, C25 and C26), 158.7 (C9), 153.3 (C5), 146.8 (C11), 140.5 (C7), 129.4 (C12), 125.9 (C6), 125.5 (C8), 86.6 (C23), 86.7 (6C, C_6H_6), 78.5 (C19), 68.7 (C17), 63.7 (C15), 54.0 (C14), 50.5 (C18), 50.3 (C22), 37.9 (C30), 28.9 (C31), 25.9 (C20), 26.9 (C21), 31.1, 28.5, 28.4, 22.0, 26.2 (5C, -CH_2-), 13.9 (C37) ppm. **^{19}F{^{1}H} NMR (565 MHz, acetone-d_6):** δ_F = −148.56 (s, 4F, $^{10}BF_4$), −148.61 (s, 4F, $^{11}BF_4$). Found (%): C, 47.45; H, 5.33; N, 8.63. $C_{32}H_{41}BClF_4N_5O_4Ru_1\cdot\frac{1}{2}CH_2Cl_2$ requires C, 47.29; H, 5.13; N, 8.48. **HR-ESI-MS *m/z* (+):** [M]$^+$ calc. for $C_{32}H_{41}ClN_5O_4Ru^+$ 696.1885, found: 696.1860; **HR-ESI-MS *m/z* (−):** [M]$^-$ calc. for $BF4^-$ 87.0035; found 87.0036.



5a$_{endo}$

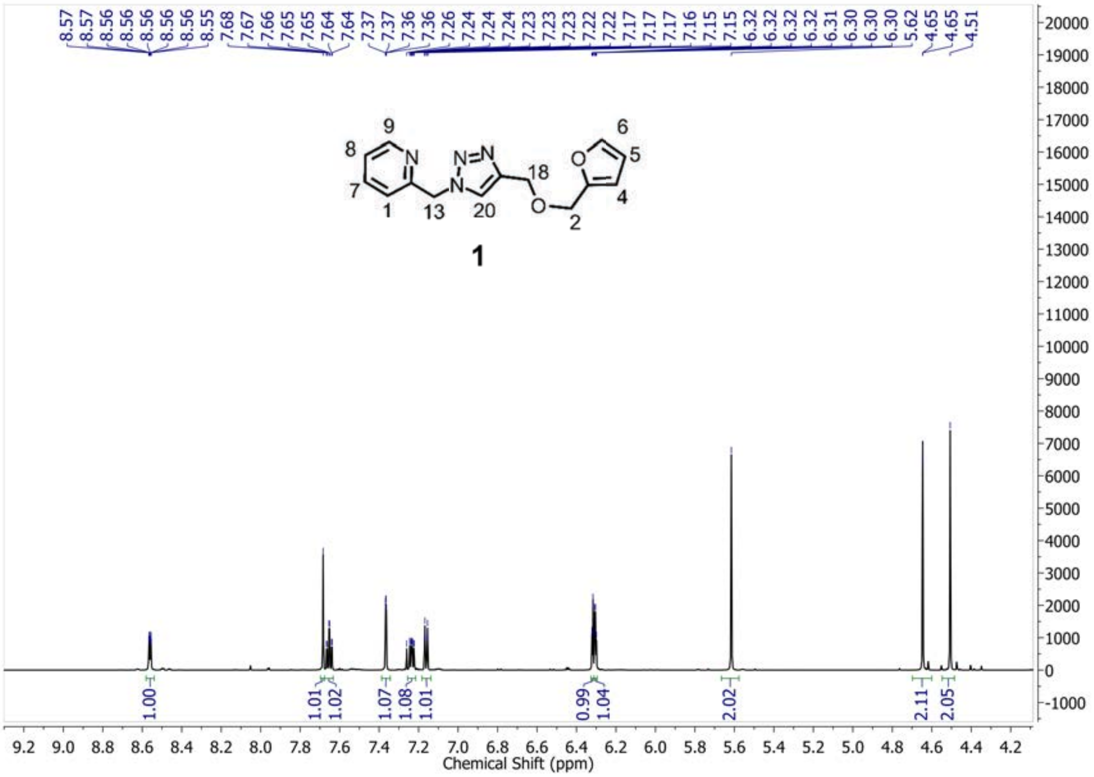


5a$_{exo}$

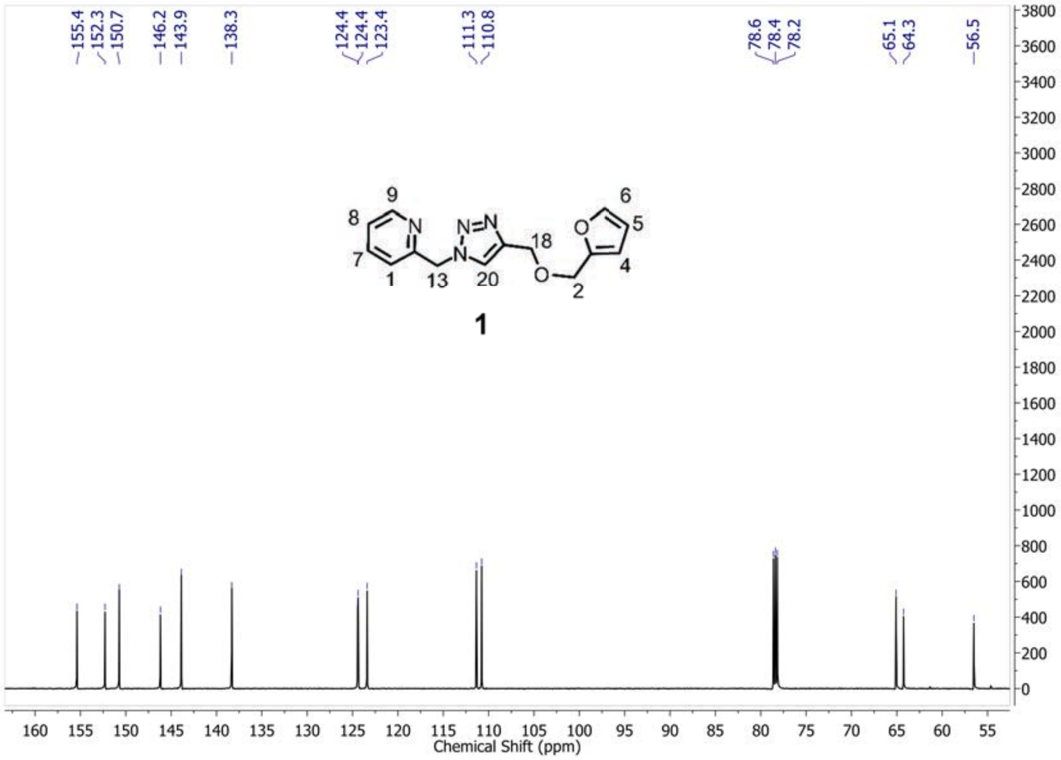
Cell culture. All protocols used for biological studies were approved by the Institutional Research Ethics Committee of INRS-Centre Armand-Frappier Santé Biotechnologie. The human breast cancer cell lines, MCF-7 and T47D were respectively provided by Prof. Chatenet and Prof. Plante (INRS). MCF-7 cells were grown routinely in RPMI-1640 containing fetal bovine serum (FBR, 10%). The growth medium for T47D cells was ATCC-formulated RPMI-1640 Medium supplemented with sodium pyruvate (0.11 g/L), HEPES (2.38 g/L), bovine insulin (10 µg/mL) and 10% fetal bovine serum. All cell growth media were supplemented with 1% penicillin/streptomycin. All cell culture products were purchased from Gibco, Invitrogen and Sigma-Aldrich. The growth of cells was carried out in a humidified atmosphere of 5% CO_2/95% air at 37°C. Passage of cells was performed at 70-80% confluency of cells (verified under microscope) by harvesting with trypsin:EDTA solution and seeding at a 1:4 to 1:10 ratio into 75 mL flasks. Cells were used up to 15 passages after thawing.

***In vitro* cell viability assay.** Cell viability was assessed by the SRB colorimetric assay described by Vichai and Kirtikara with some slightly modifications.[11] Briefly, cell culture treated 96-well plates (Sarstedt) were used to seed cells at a density of 1 × 104 cells/well for MCF-7 and T47D cancer cells and were pre-incubated in a humidified atmosphere at 37°C, 5% CO_2 for 24 h with drug-free complete growth medium. Stock solutions of test compounds were prepared in DMSO and the final concentration of DMSO was kept constant at 0.5% (non-cytotoxic concentration for cells). To achieve final concentration of 1, 4, 12.5, 25, 50, 75, 100 and 150 µM of drug solution, 200 µL of fresh and complete growth medium containing 0.5 µL of each stock solution was added to each well. Cancer cells were exposed also to drug-free complete growth medium, complete growth medium containing 0.5% DMSO as a negative control and complete growth medium containing 25% DMSO as a positive control. After incubation for 48h, 100 µL of cold trichloroacetic acid (TCA, 10% w/v) was added in each well to fix cells without removing the cell culture supernatant. After fixation at 4°C for 1 h, TCA was removed, and each well was washed three to four times with slow-running tap water then air-dried. Afterward, cells were exposed to a SRB solution (0.057% w/v) for 30 min at room temperature, then unbound SRB in each well were removed by washing three times with acetic acid solution (1% v/v) before drying cell-plate in air. To dissolve the protein-bound dye, 200 µL of 10 mM Tris bas solution (pH 10.5) was added to each well and cell-plate was stored in a dark-room for 30 min. Absorbance in each well was recorded with a microplate reader at 510 nm. Cell viability versus different concentration of each compound was reported. IC_{50} values, concentrations that respectively inhibit cell metabolic activity by 50% was also determined from concentration-effect curves by interpolation. This assay was carried out in three independent sets of experiments, each experiment with three or four replicates per concentration level.

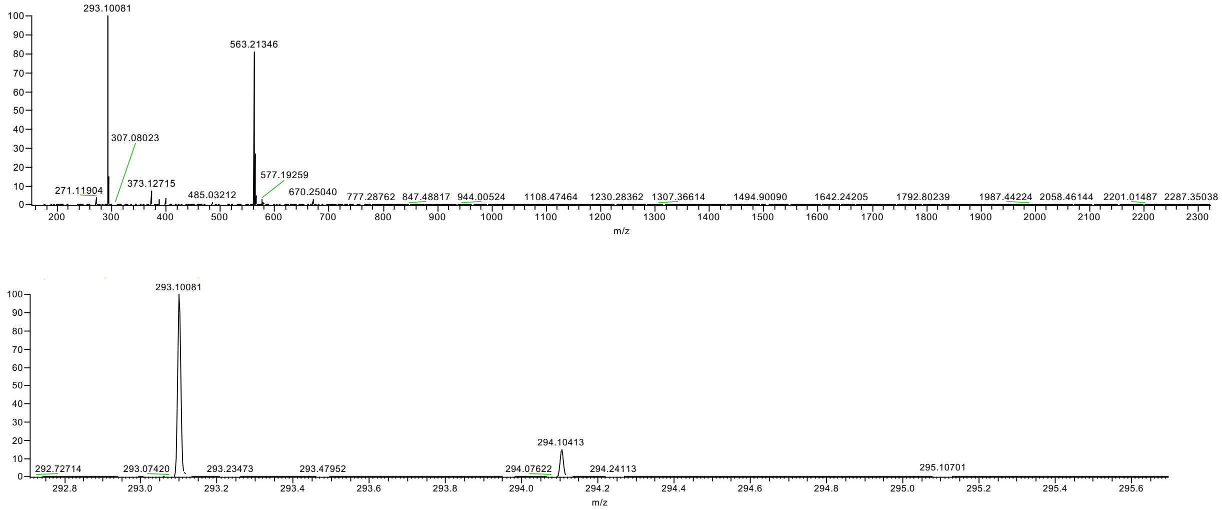
NMR and HR-ESI-MS spectra



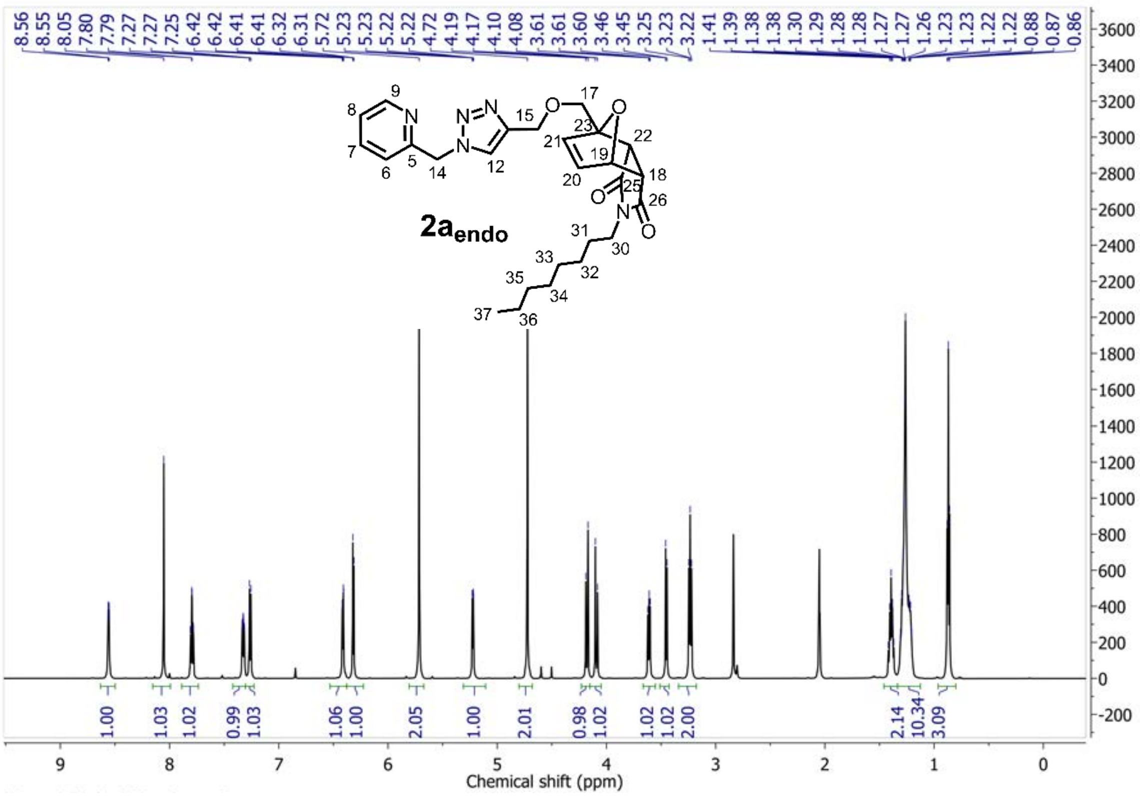
^{1}H NMR spectrum of **1** ($CDCl_3$).



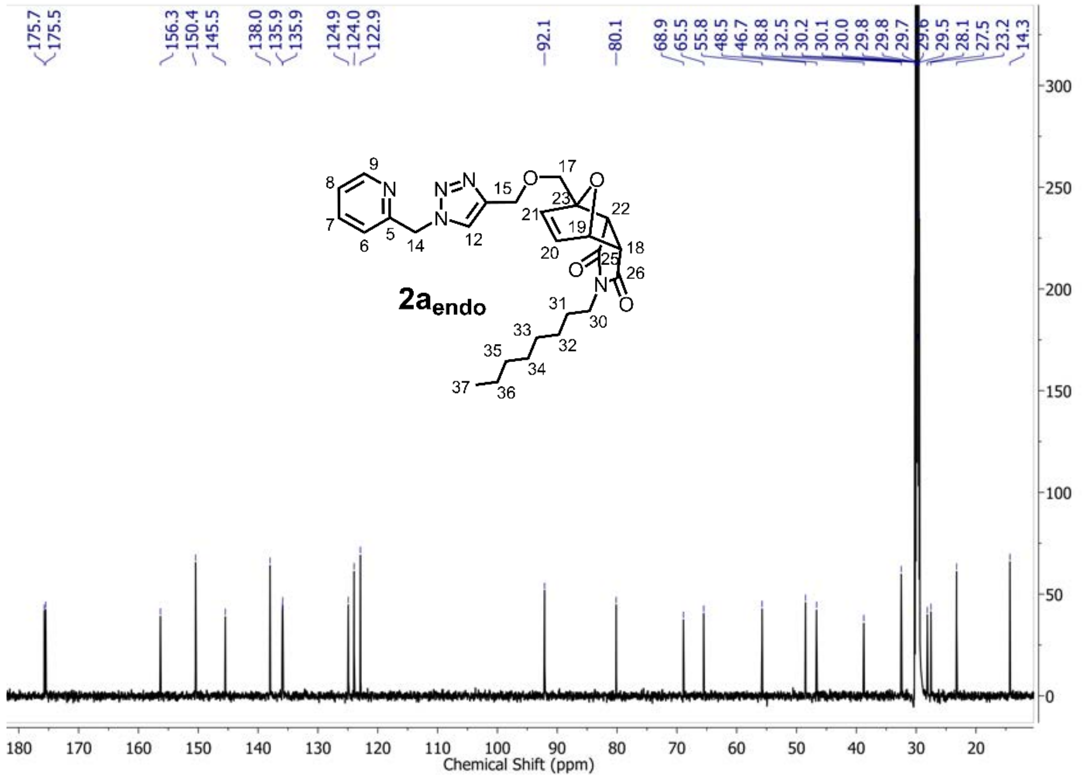
$^{13}C\{^1H\}$ NMR spectrum of **1** ($CDCl_3$).



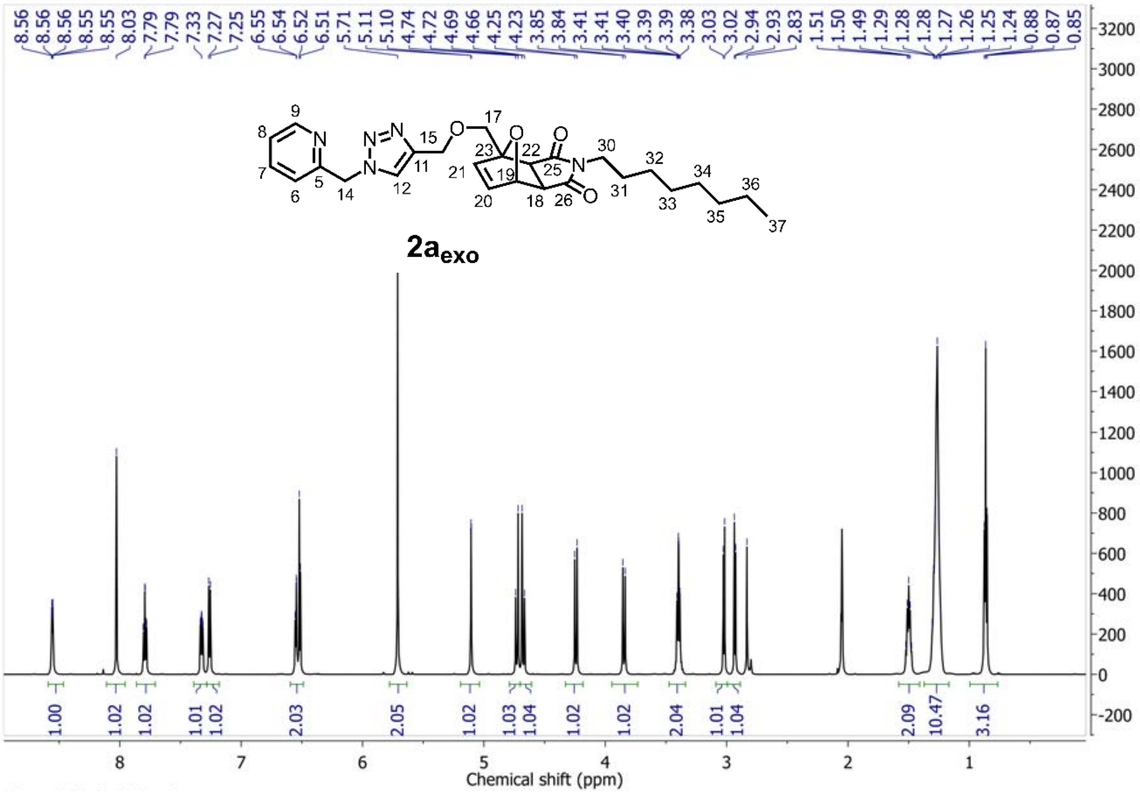
HR-ESI-MS spectrum of **1**, positive mode.



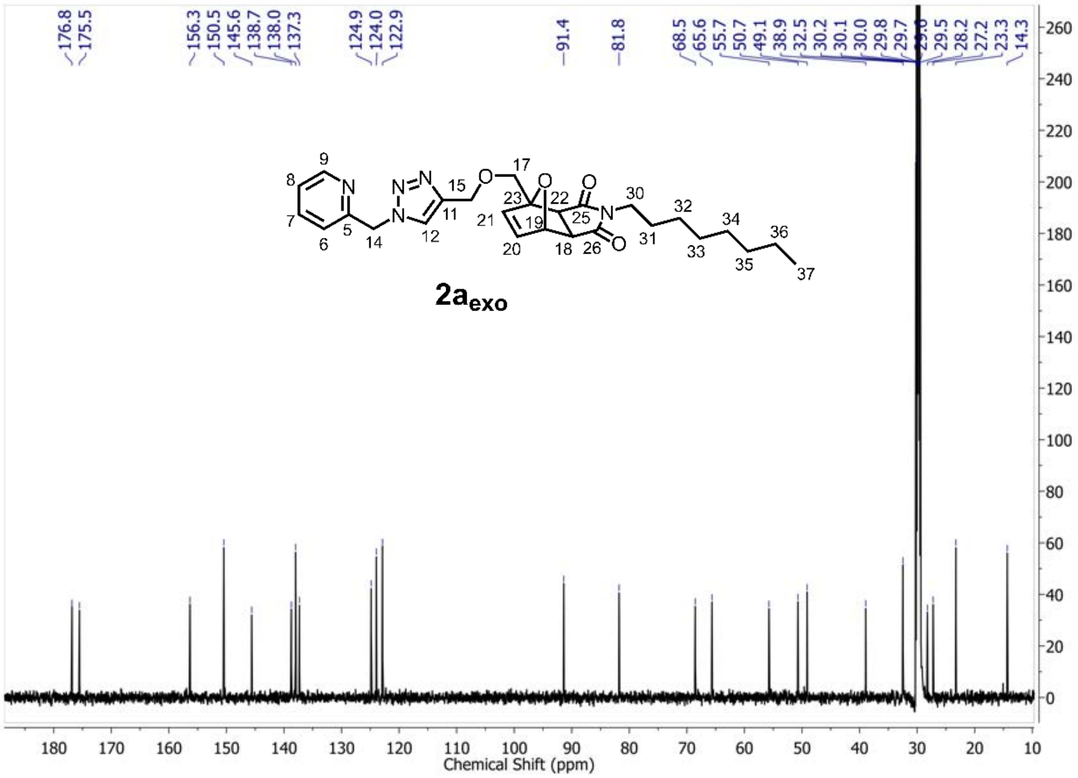
^{1}H NMR spectrum of **2a$_{\mathbf{endo}}$** (acetone-*d*$_6$).



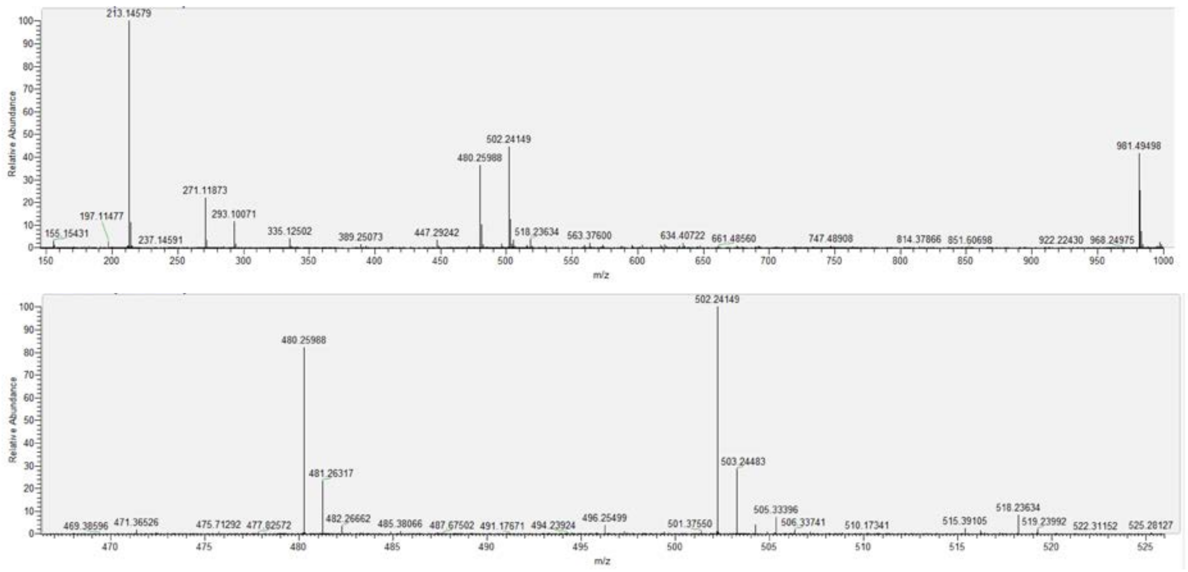
^{13}C{^{1}H} NMR spectrum of **2a$_{\mathbf{endo}}$** (acetone-*d*$_6$).



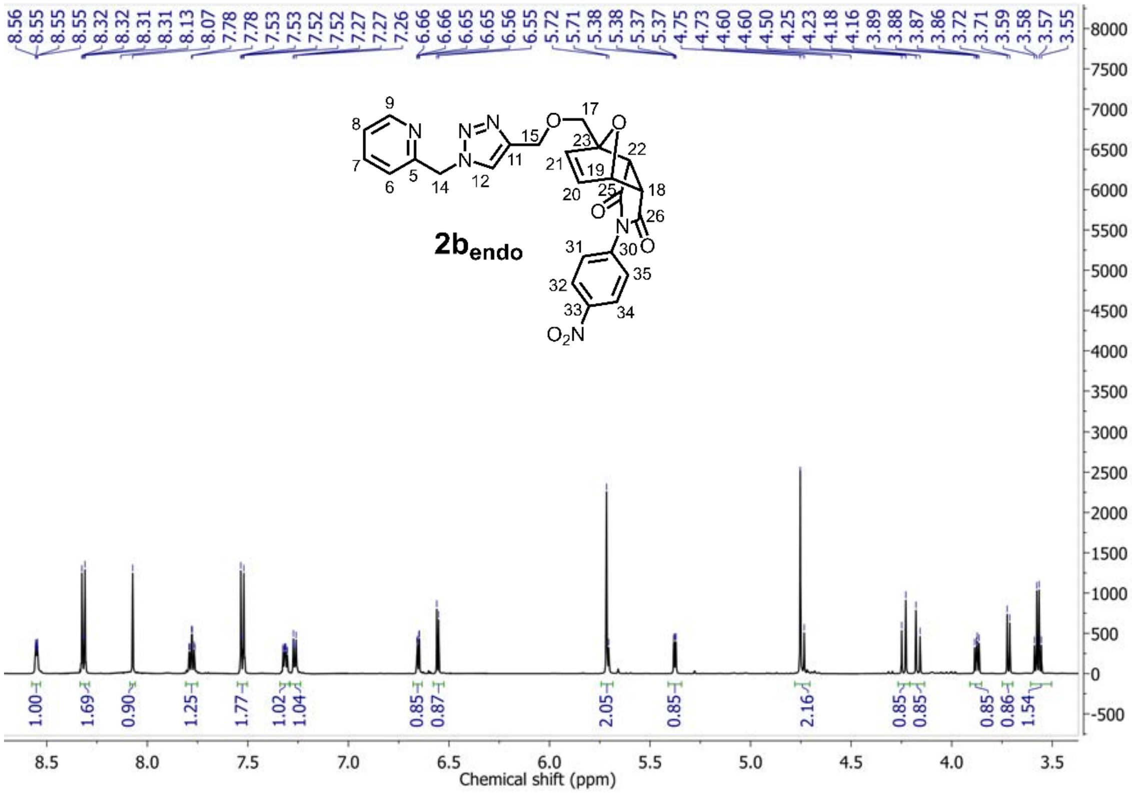
^{1}H NMR spectrum of **2a$_{\text{exo}}$** (acetone-d_6).



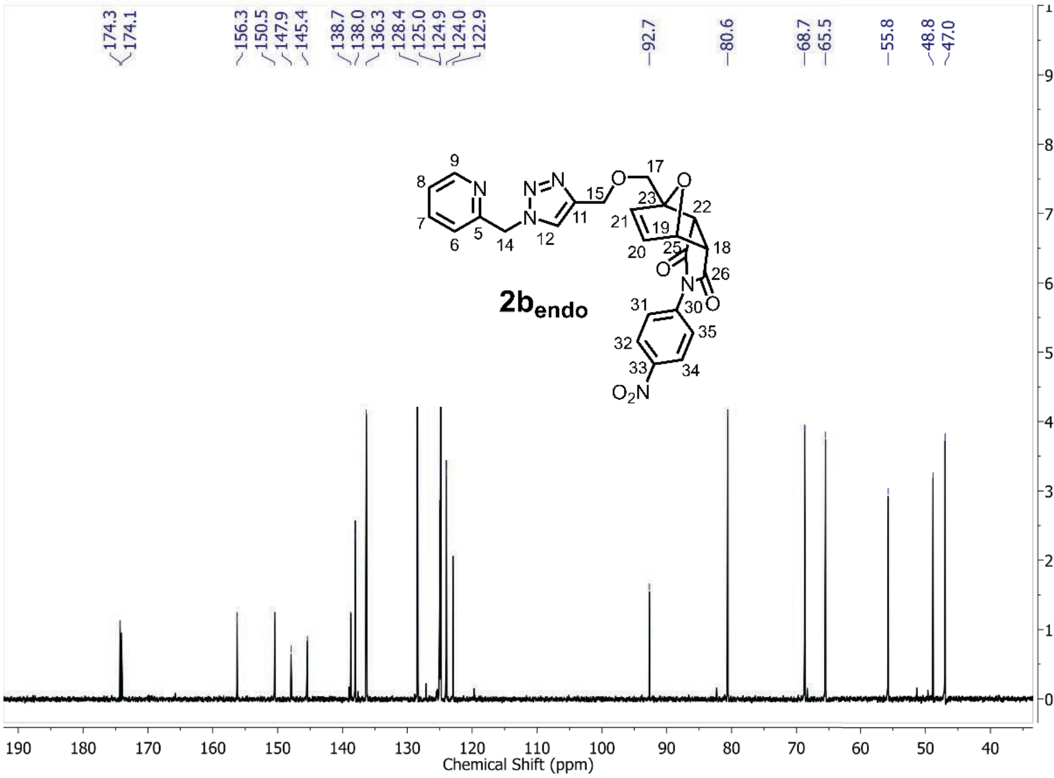
^{13}C{^{1}H} NMR spectrum of **2a$_{\text{exo}}$** (acetone-d_6).



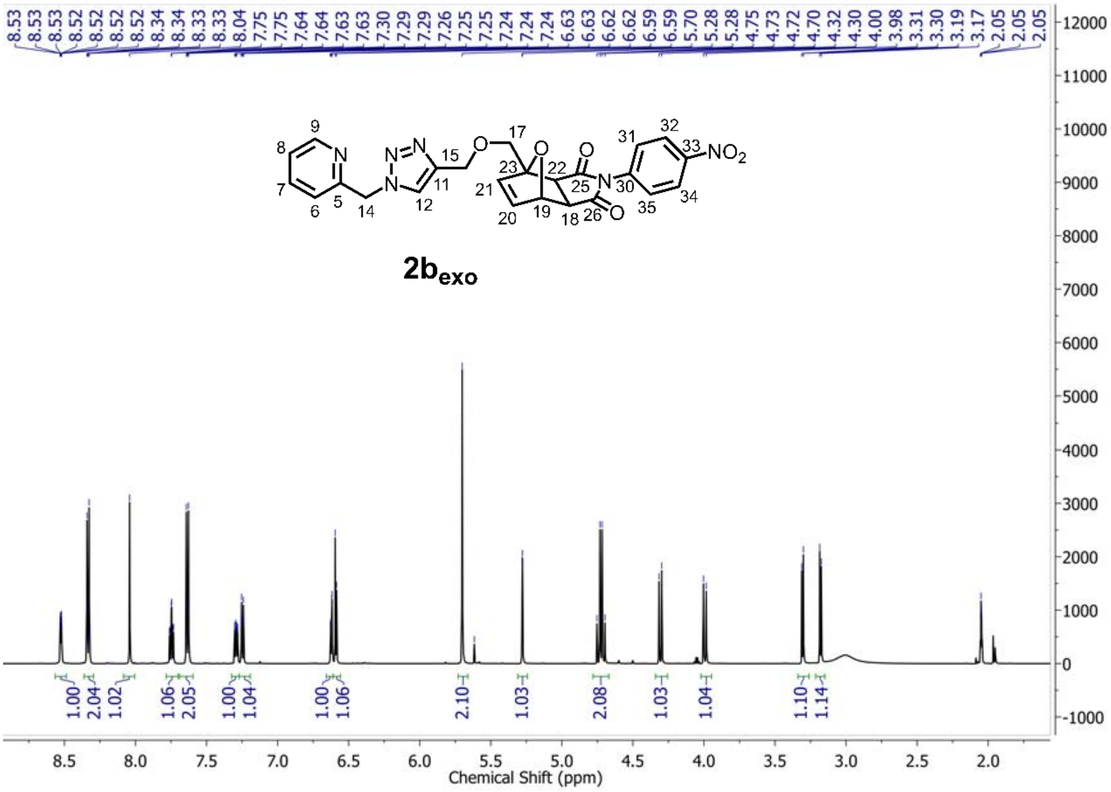
HR-ESI-MS spectrum of **2a** (**$2a_{endo}$**/**$2a_{exo}$**: 1.5/1), positive mode.



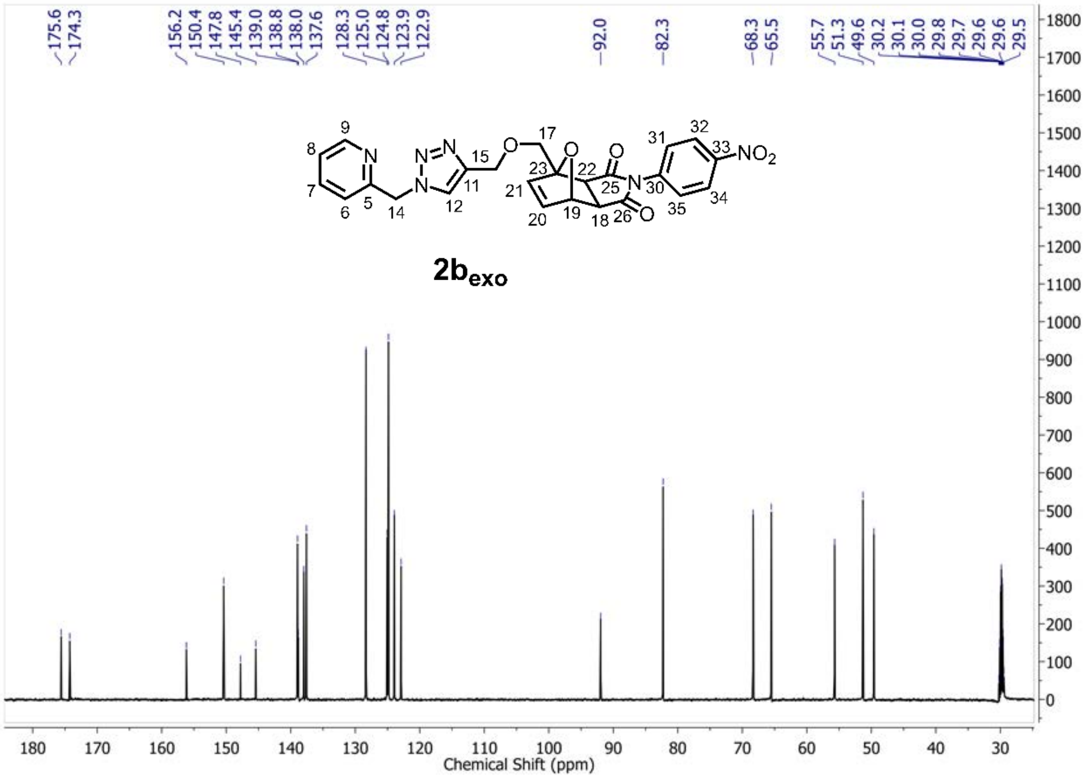
^{1}H NMR spectrum of **2b$_{endo}$** (acetone-*d*$_6$).



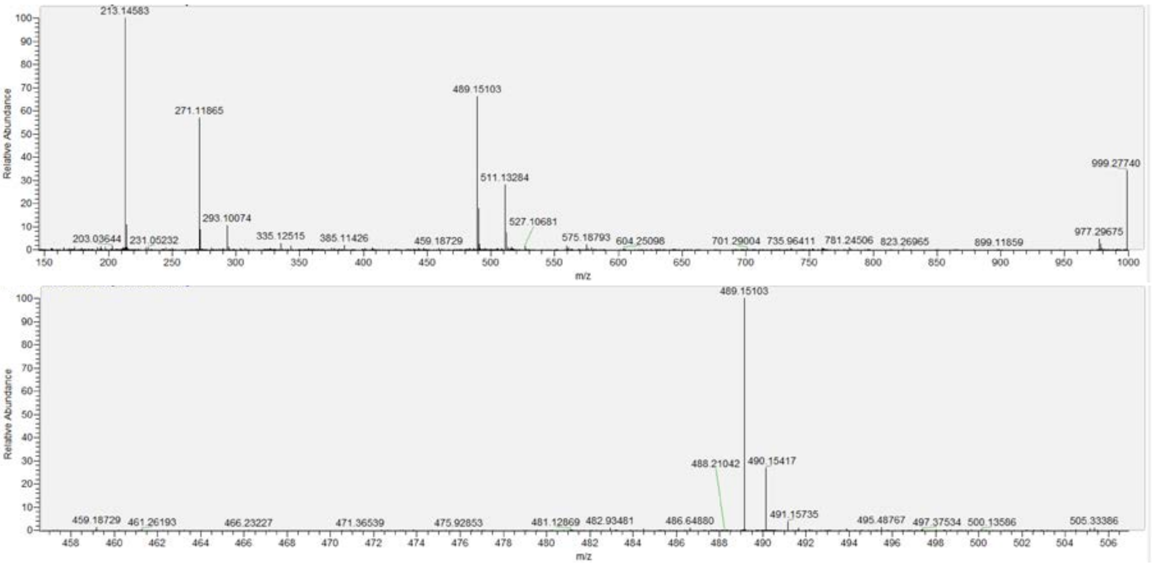
^{13}C{^{1}H} NMR spectrum of **2b$_{endo}$** (acetone-*d*$_6$).



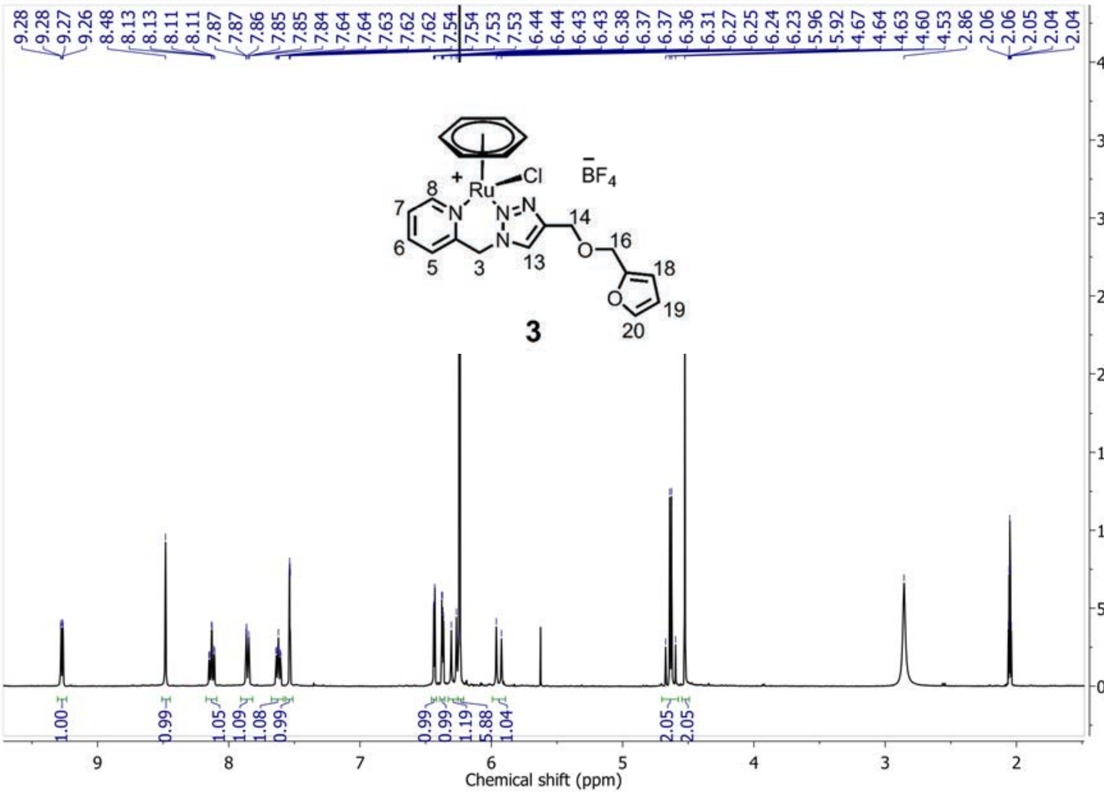
^{1}H NMR spectrum of **2b$_{exo}$** (acetone-d_6).



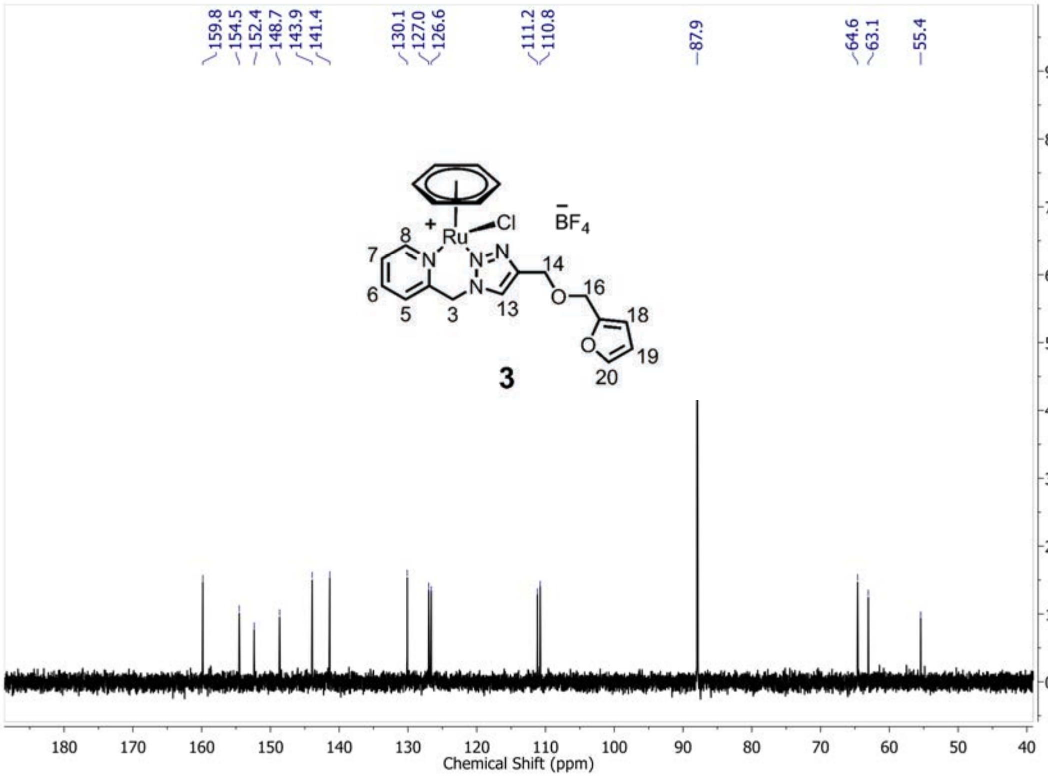
^{13}C{^{1}H} NMR spectrum of **2b$_{exo}$** (acetone-d_6).



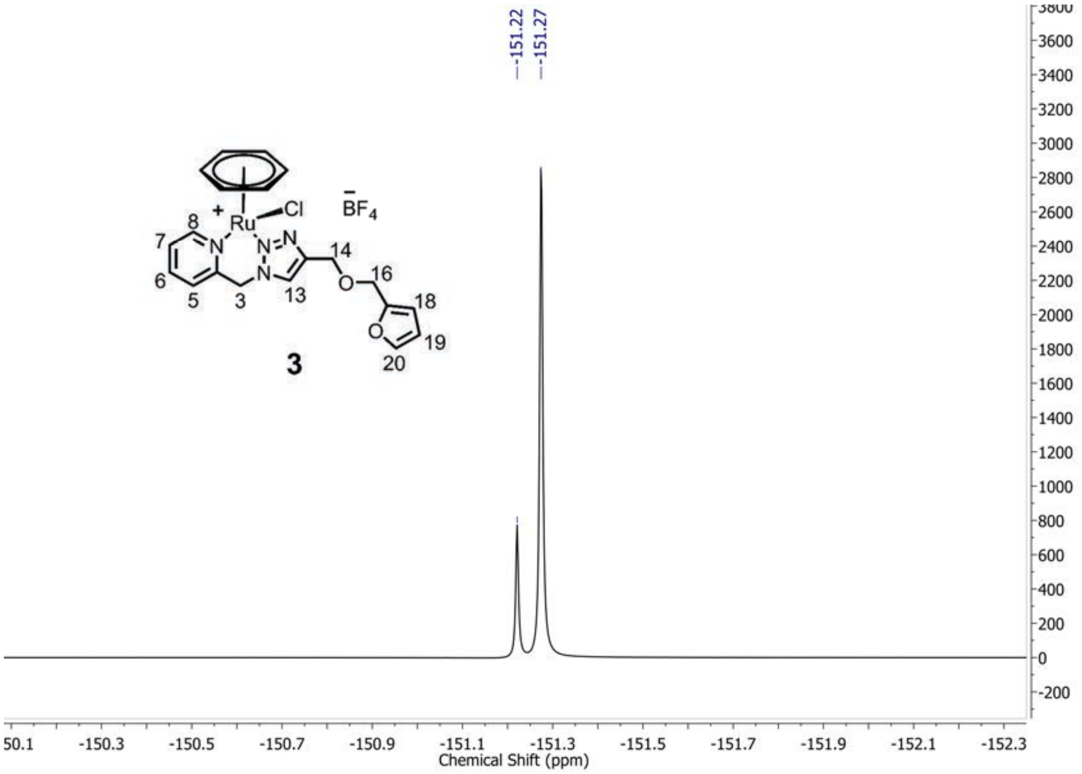
HR-ESI-MS spectrum of **2b** (**2b**$_{\mathbf{endo}}$/**2b**$_{\mathbf{exo}}$: 1/4), positive mode.



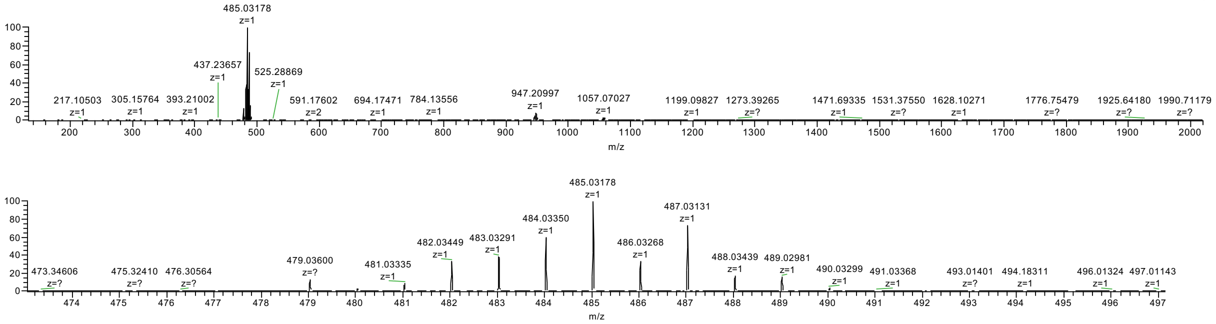
^{1}H NMR spectrum of **3** (acetone-d_6).



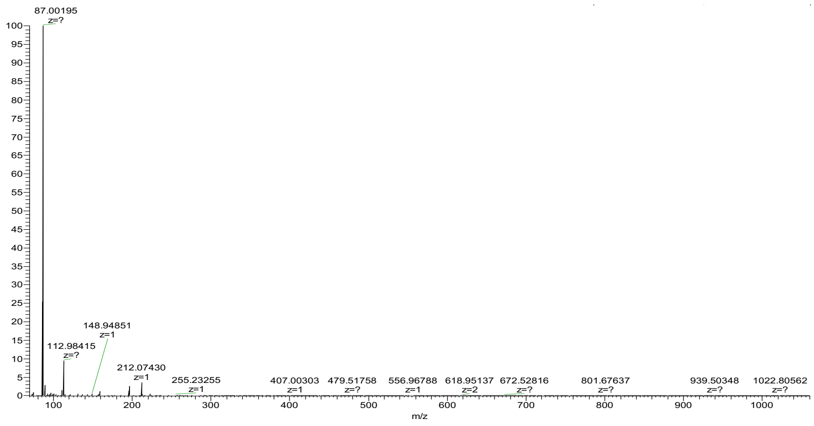
$^{13}C\{^{1}H\}$ NMR spectrum of **3** (acetone-d_6).



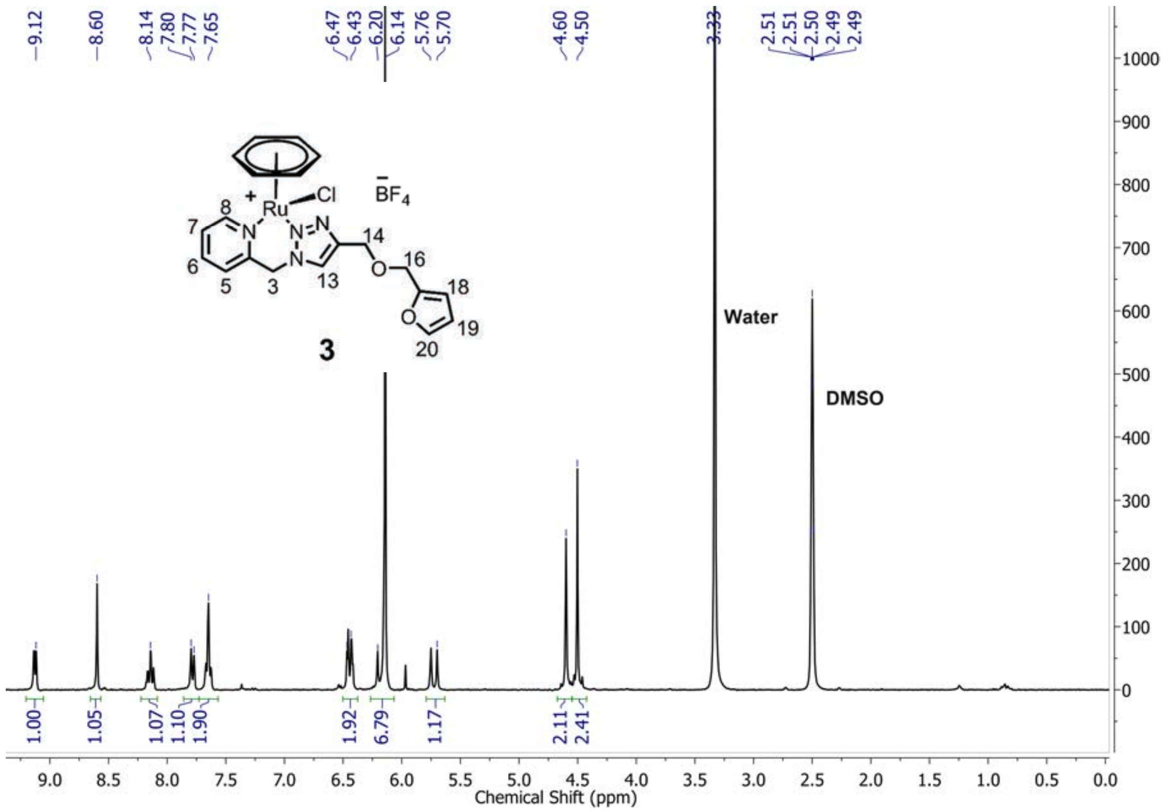
$^{19}F\{^1H\}$ NMR spectrum of **3** (acetone-d_6).



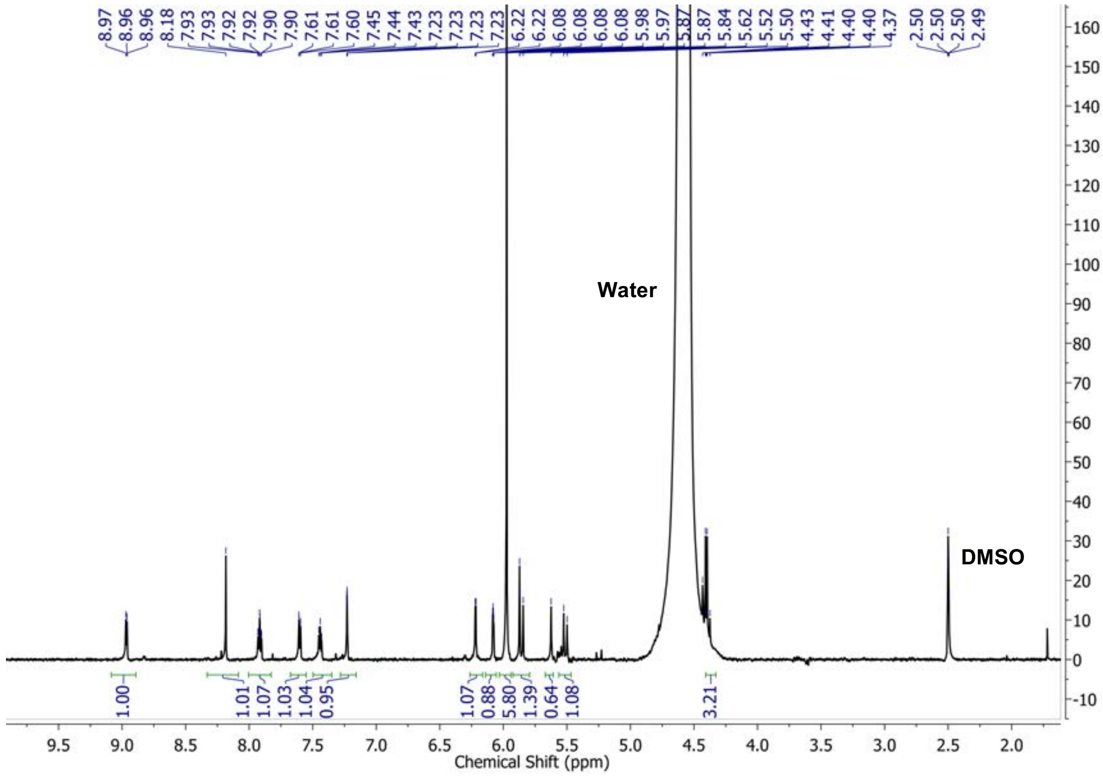
HR-ESI-MS spectrum of **3**, positive mode.



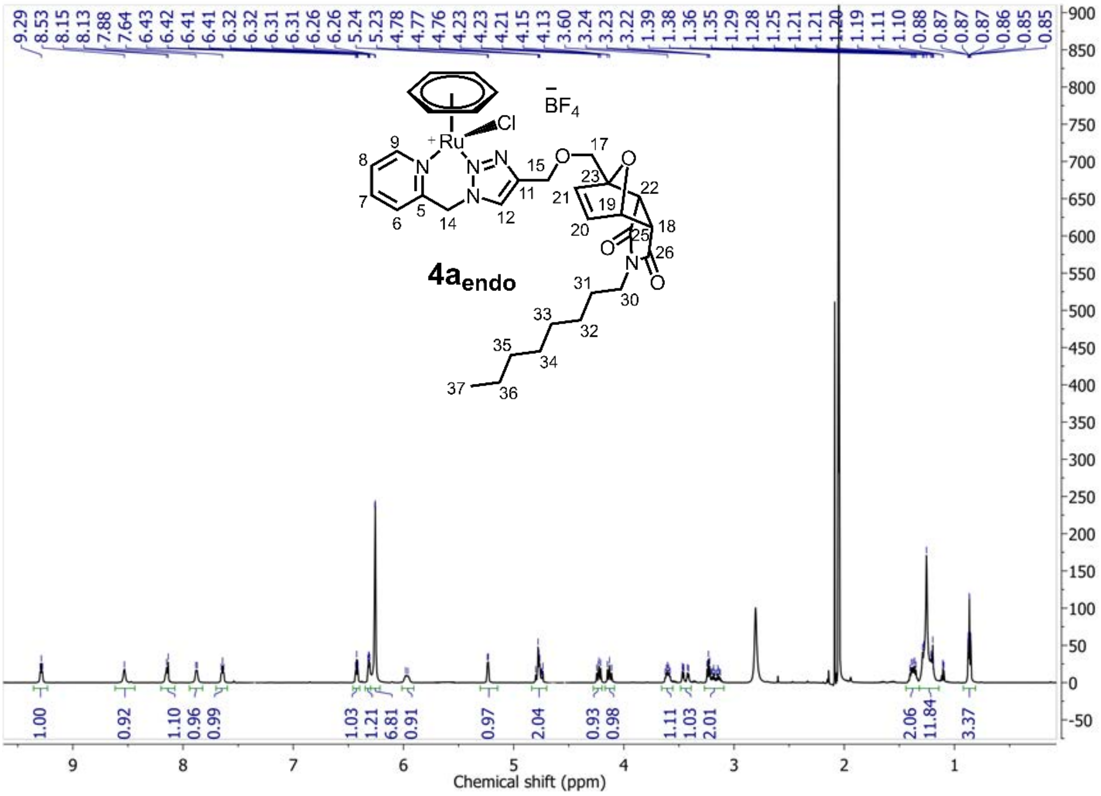
HR-ESI-MS spectrum of **3**, negative mode.



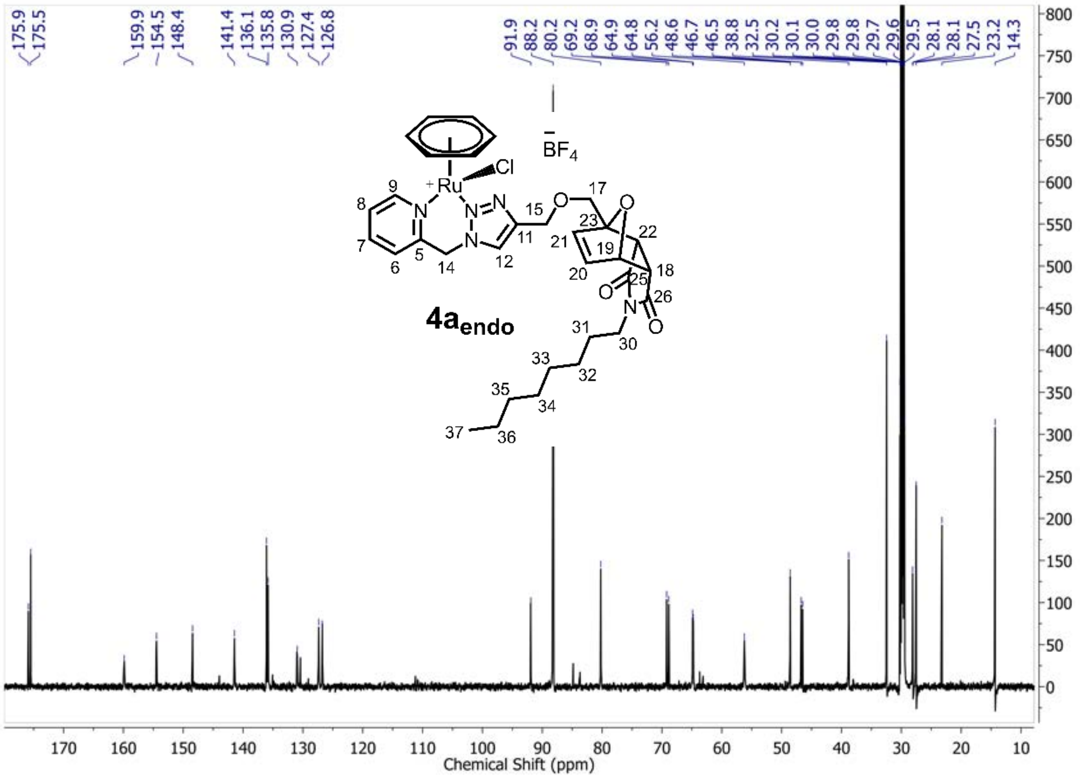
^{1}H NMR spectrum of **3** in DMSO-d_6 after 48h at room temperature.



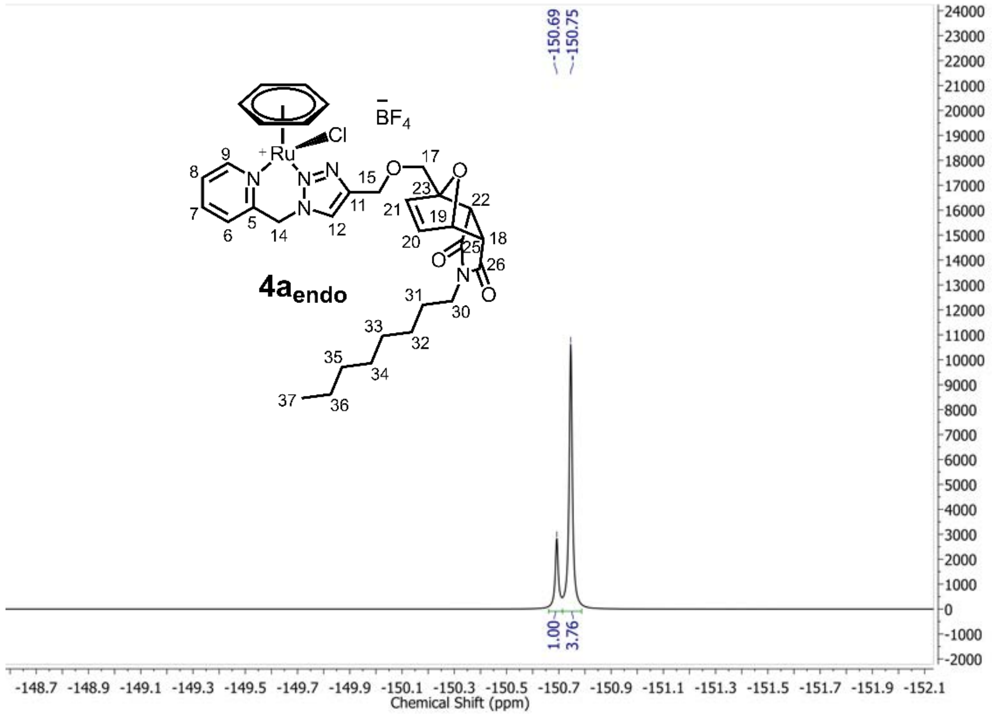
^{1}H NMR spectrum of **3** in D_2O containing 1% DMSO-d_6 (110 mM NaCl) after 2h at room temperature.



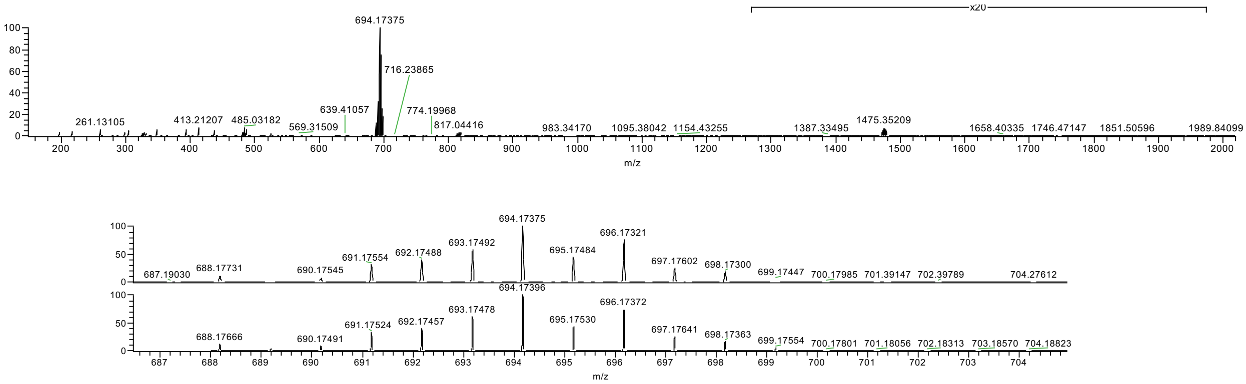
^{1}H NMR spectrum of **4a$_{\mathbf{endo}}$** (acetone-d_6).



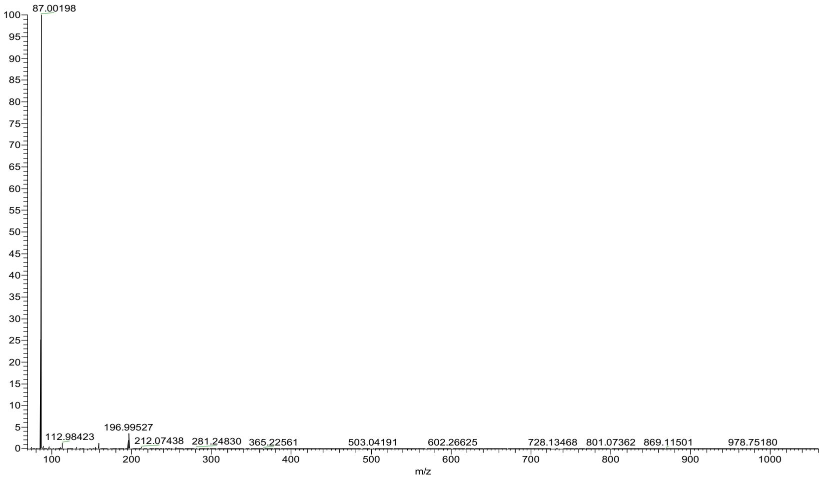
^{13}C{^{1}H} NMR spectrum of **4a$_{\mathbf{endo}}$** (acetone-d_6).



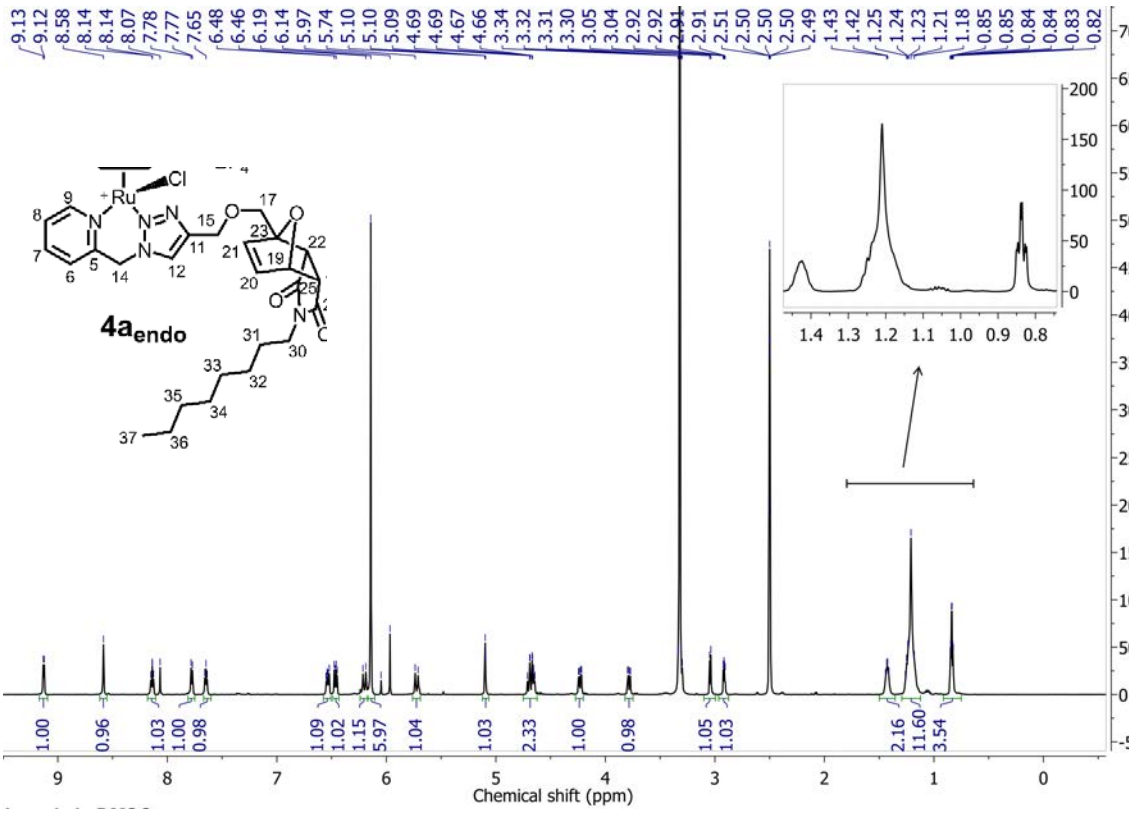
^{19}F{^{1}H} NMR spectrum of **4a$_{\text{endo}}$** (acetone-d_6).



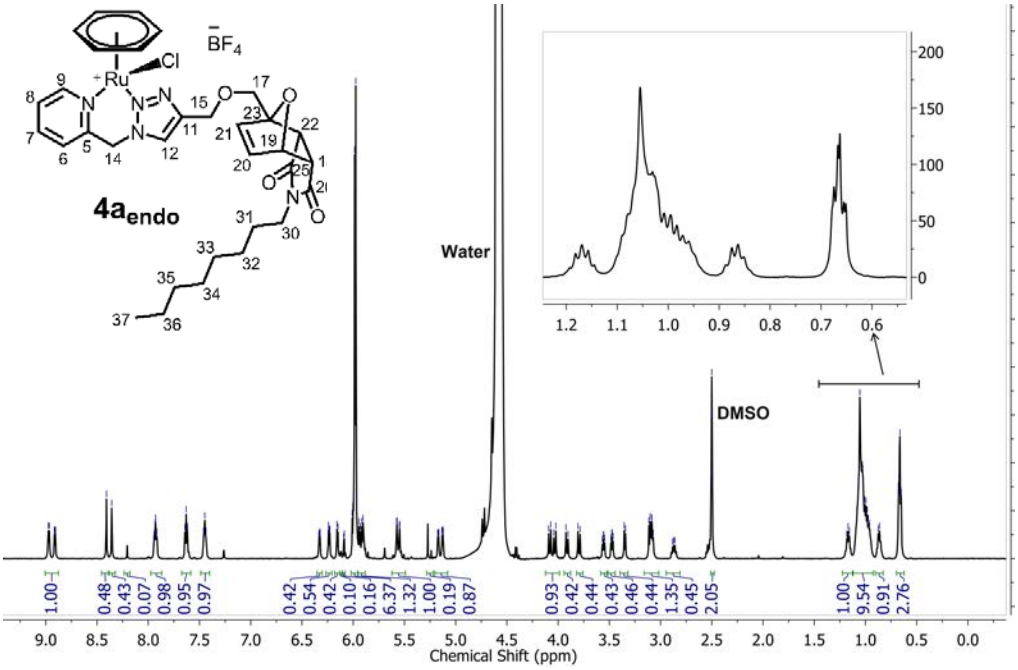
HR-ESI-MS spectrum of **4a** (**4a$_{\text{endo}}$**/**4a$_{\text{exo}}$** : 1.7/1), positive mode



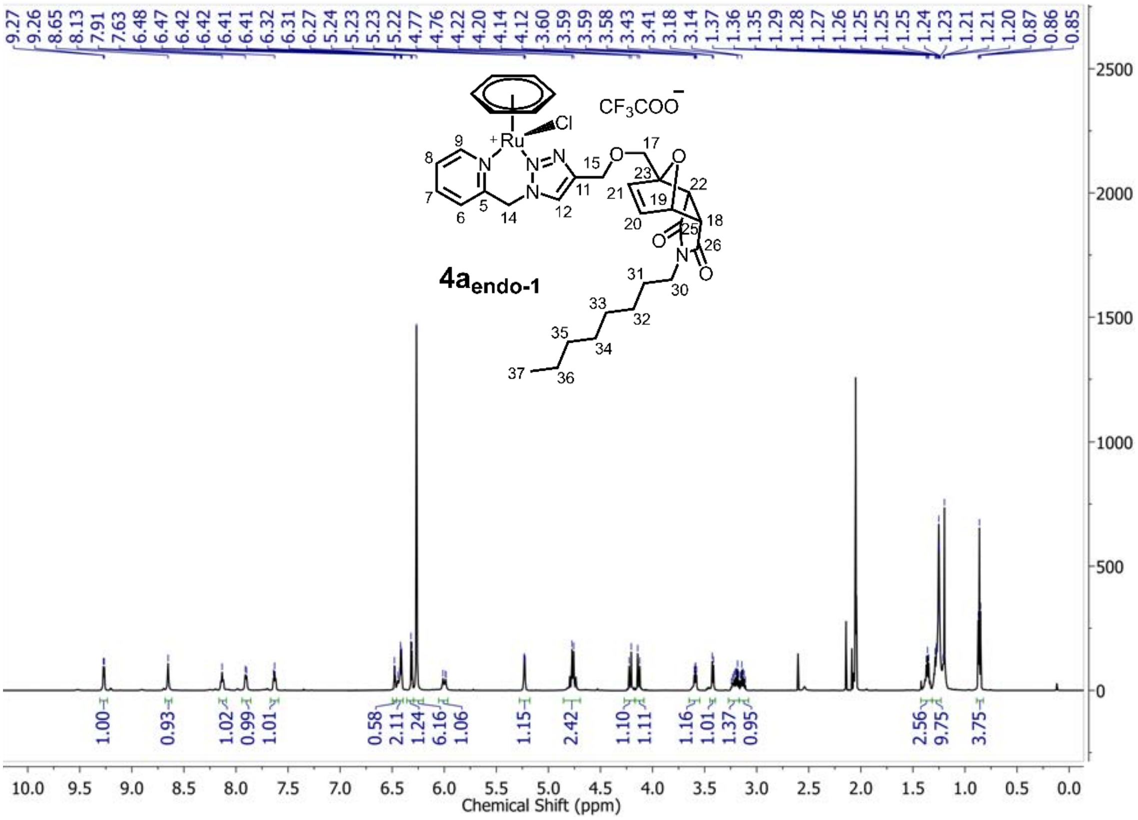
HR-ESI-MS spectrum of **4a** (**4a$_{\text{endo}}$**/**4a$_{\text{exo}}$** : 1.7/1), negative mode.



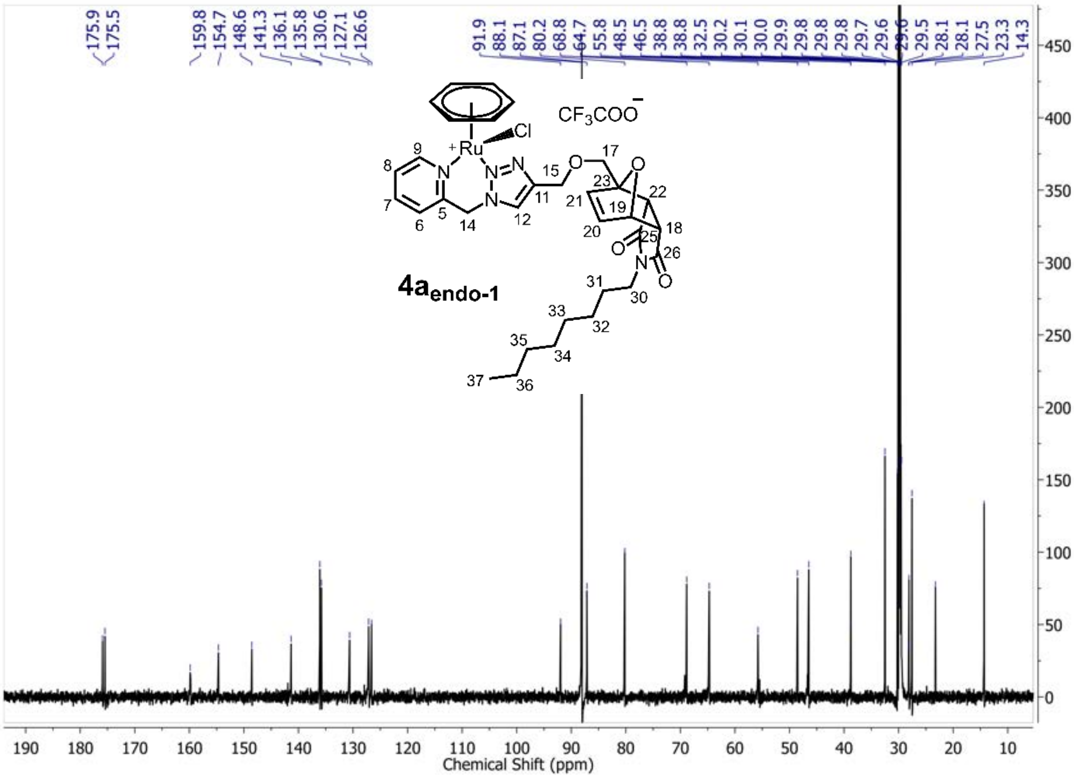
^{1}H NMR spectrum of **4a$_{endo}$** in DMSO-d_6 after 48h at room temperature.



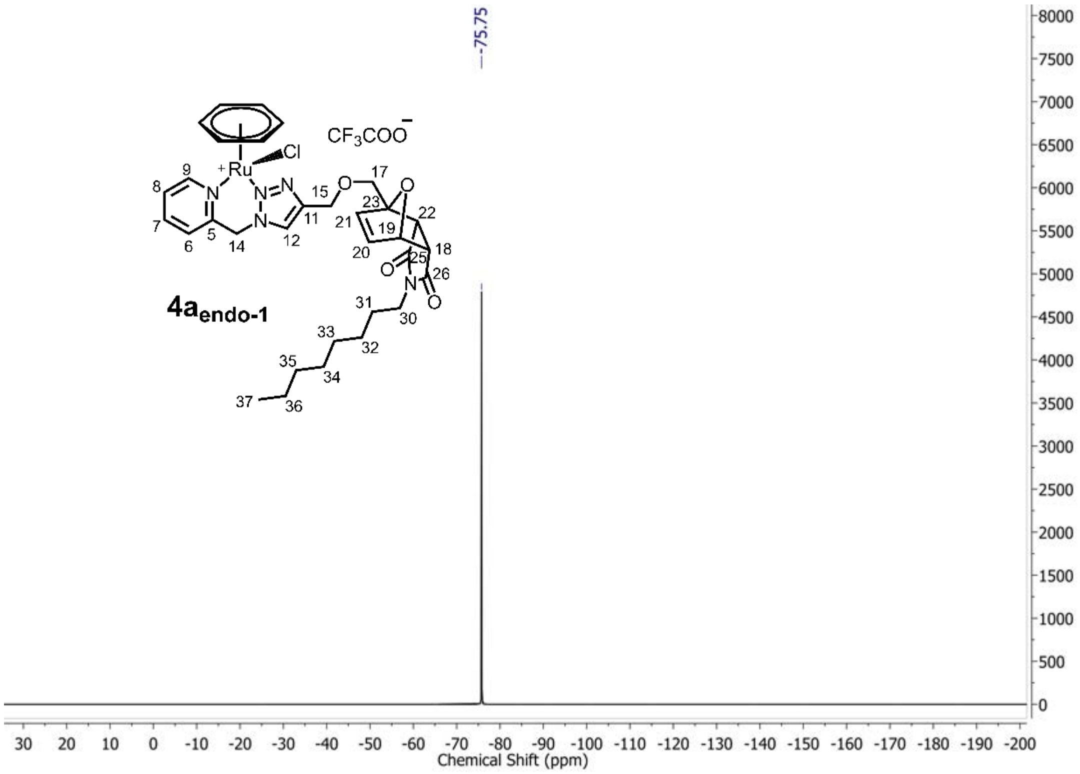
^{1}H NMR spectrum of **4a$_{endo}$** in D_2O containing 1% DMSO-d_6 (110 mM NaCl) after 2h at room temperature.



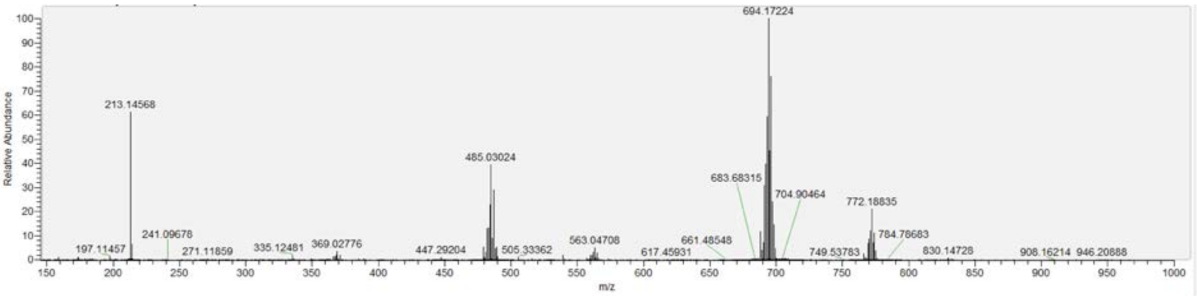
^{1}H NMR spectrum of **4a$_{\text{endo-1}}$** (acetone-d_6) (with trifluoroacetate counterion).



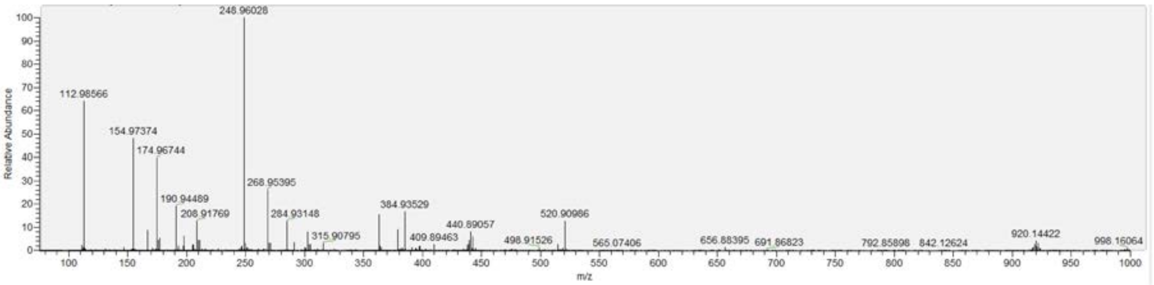
^{13}C{^{1}H} NMR spectrum of **4a$_{\text{endo-1}}$** (acetone-d_6) (with trifluoroacetate counterion).



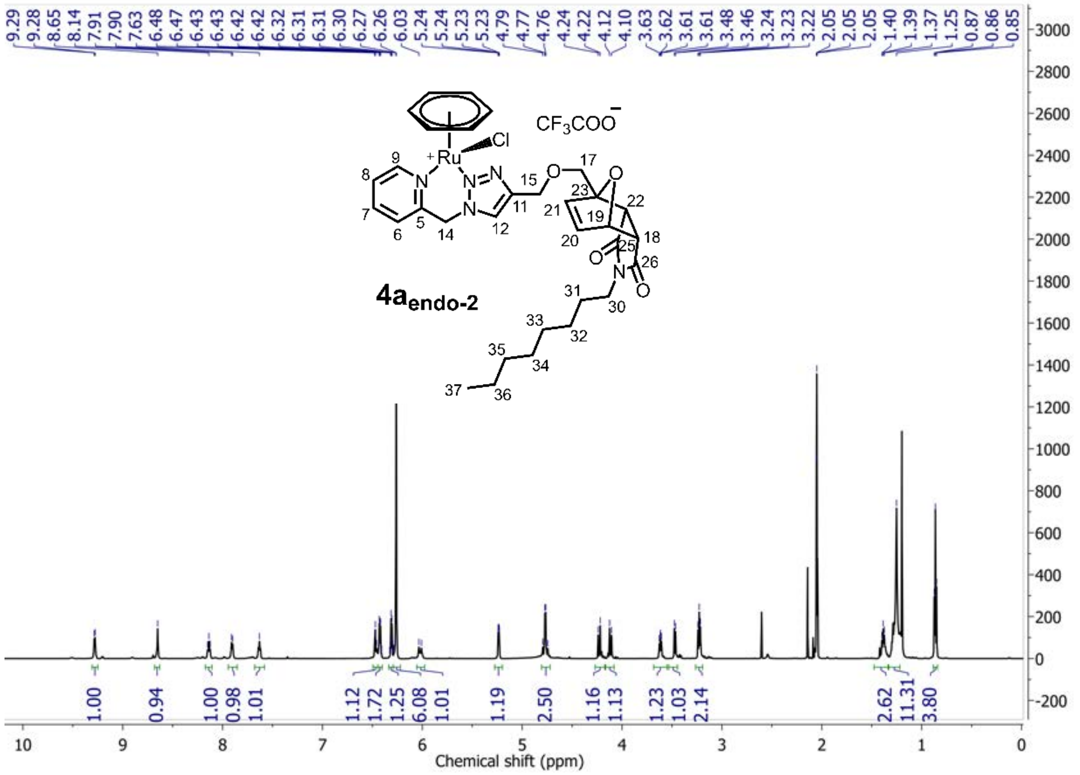
^{19}F{^{1}H} NMR spectrum of **4a$_{endo-1}$** (acetone-*d*$_6$) (with trifluoroacetate counterion).



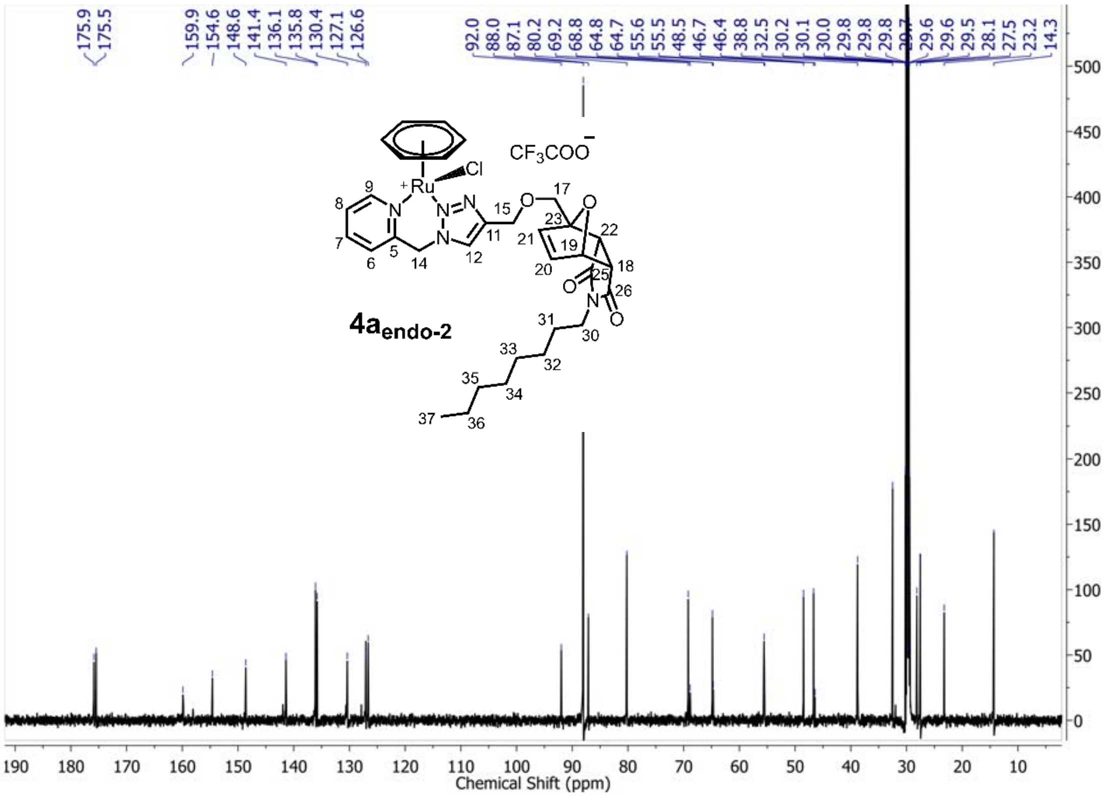
HR-ESI-MS spectrum of **4a$_{endo-1}$**, positive mode (with trifluoroacetate counterion).



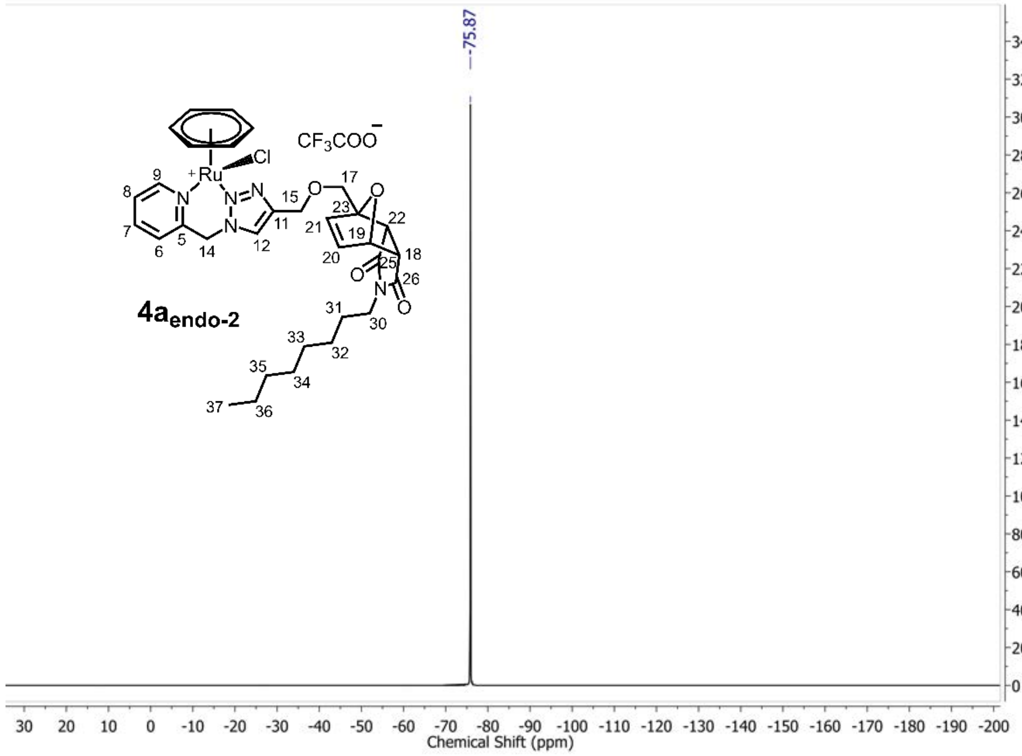
HR-ESI-MS spectrum of **4a$_{endo-1}$**, negative mode (with trifluoroacetate counterion).



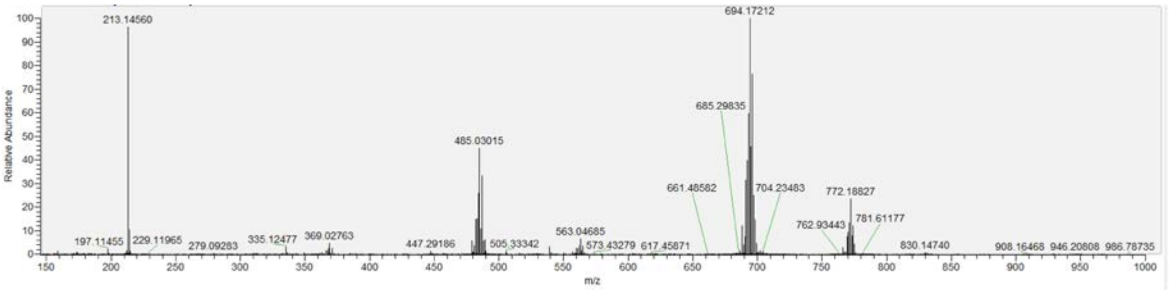
^{1}H NMR spectrum of **4a$_{\text{endo-2}}$** (acetone-d_6) (with trifluoroacetate counterion).



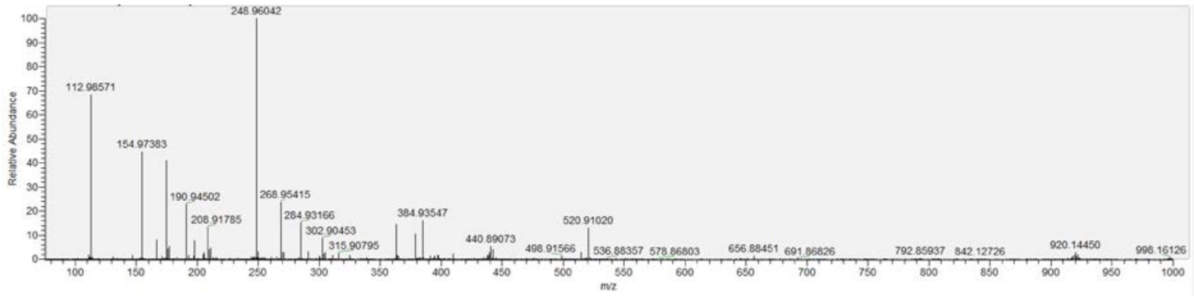
^{13}C{^{1}H} NMR spectrum of **4a$_{\text{endo-2}}$** (acetone-d_6) (with trifluoroacetate counterion).



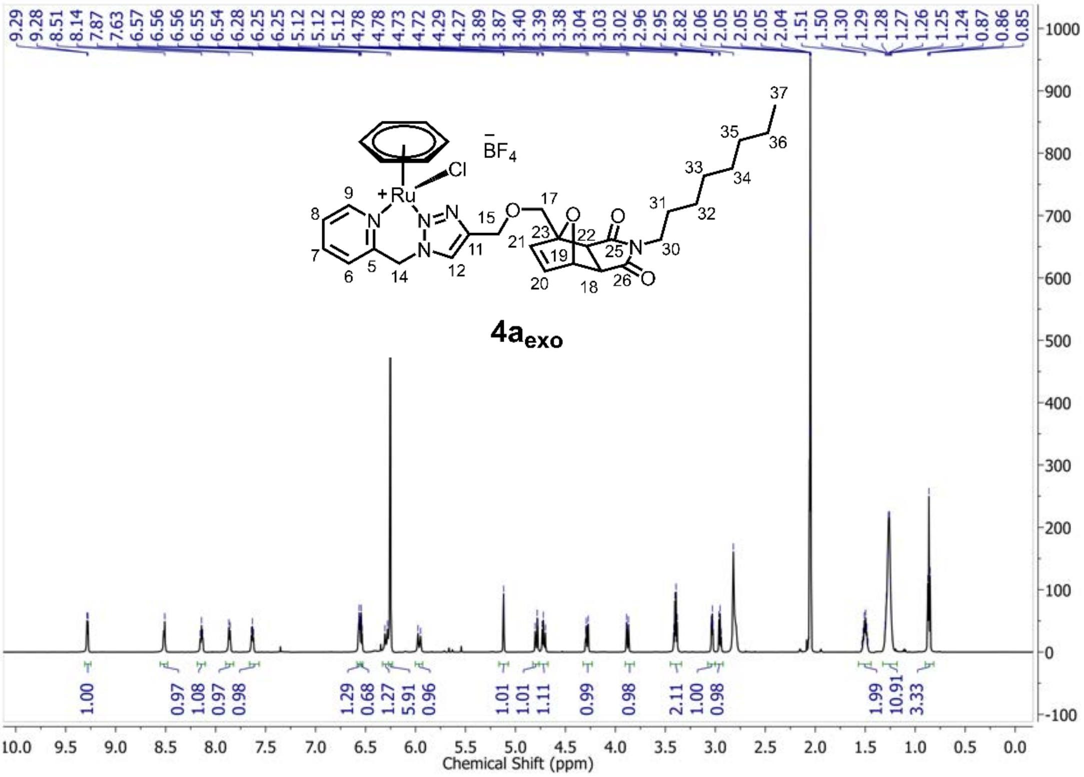
$^{19}F\{^1H\}$ NMR spectrum of **4a**$_{\mathbf{endo-2}}$ (acetone-d_6) (with trifluoroacetate counterion).



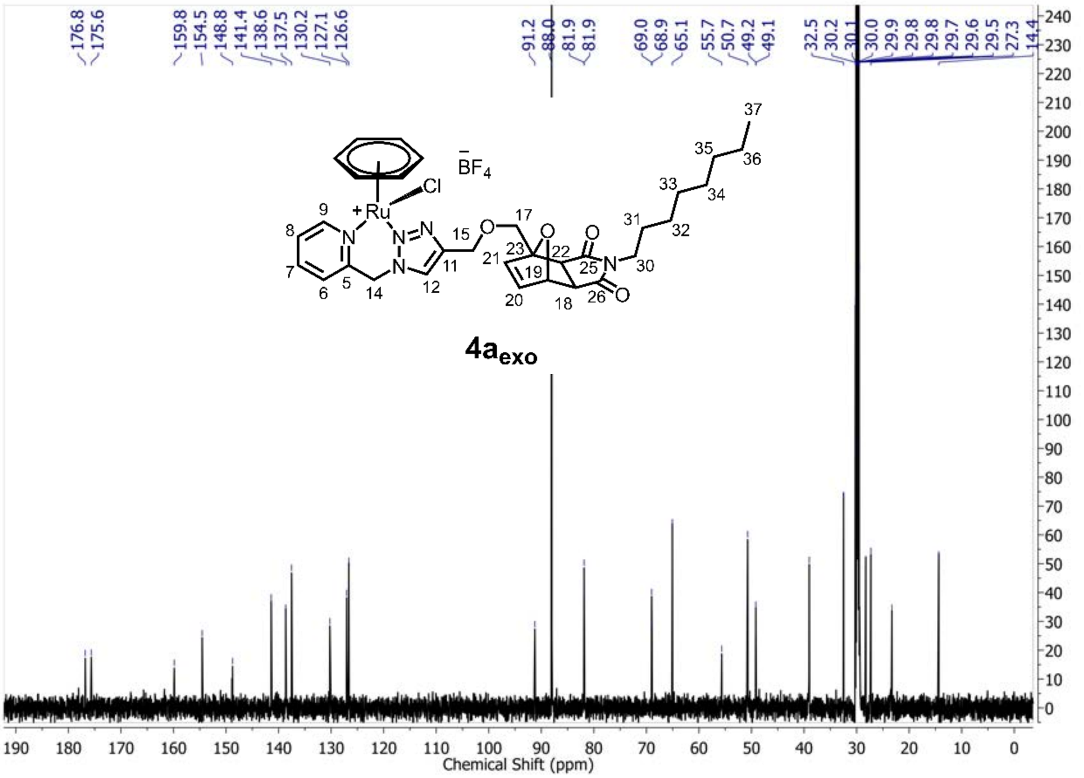
HR-ESI-MS spectrum of **4a**$_{\mathbf{endo-2}}$, positive mode (with trifluoroacetate counterion).



HR-ESI-MS spectrum of **4a**$_{\mathbf{endo-2}}$, negative mode (with trifluoroacetate counterion).



^{1}H NMR spectrum of **4a$_{\mathbf{exo}}$** (acetone-*d*$_6$).



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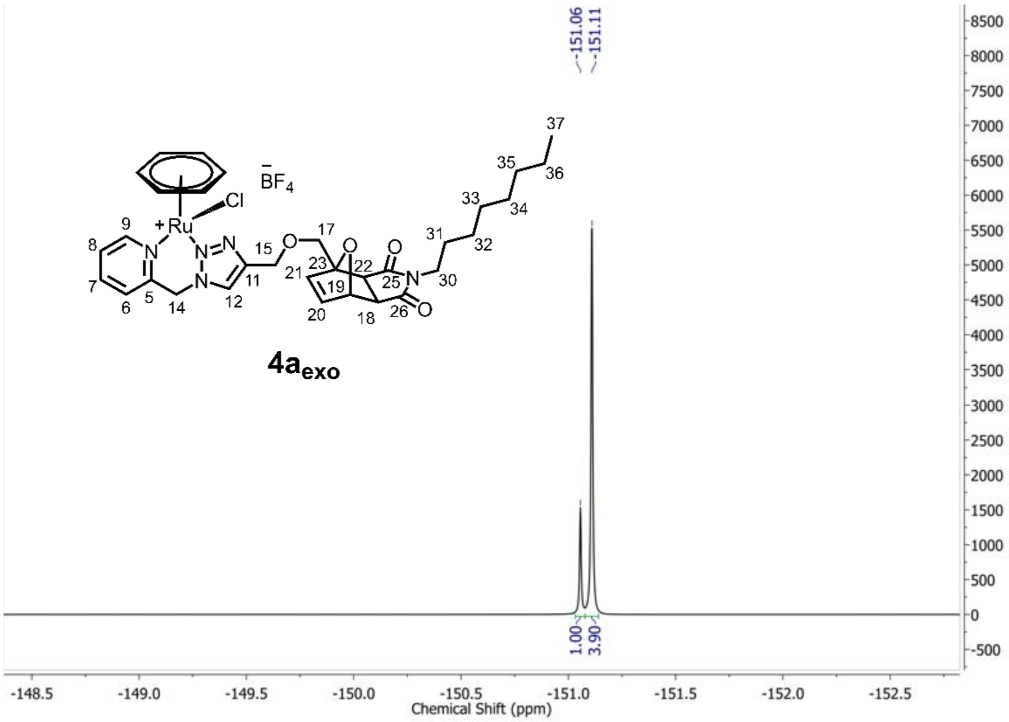

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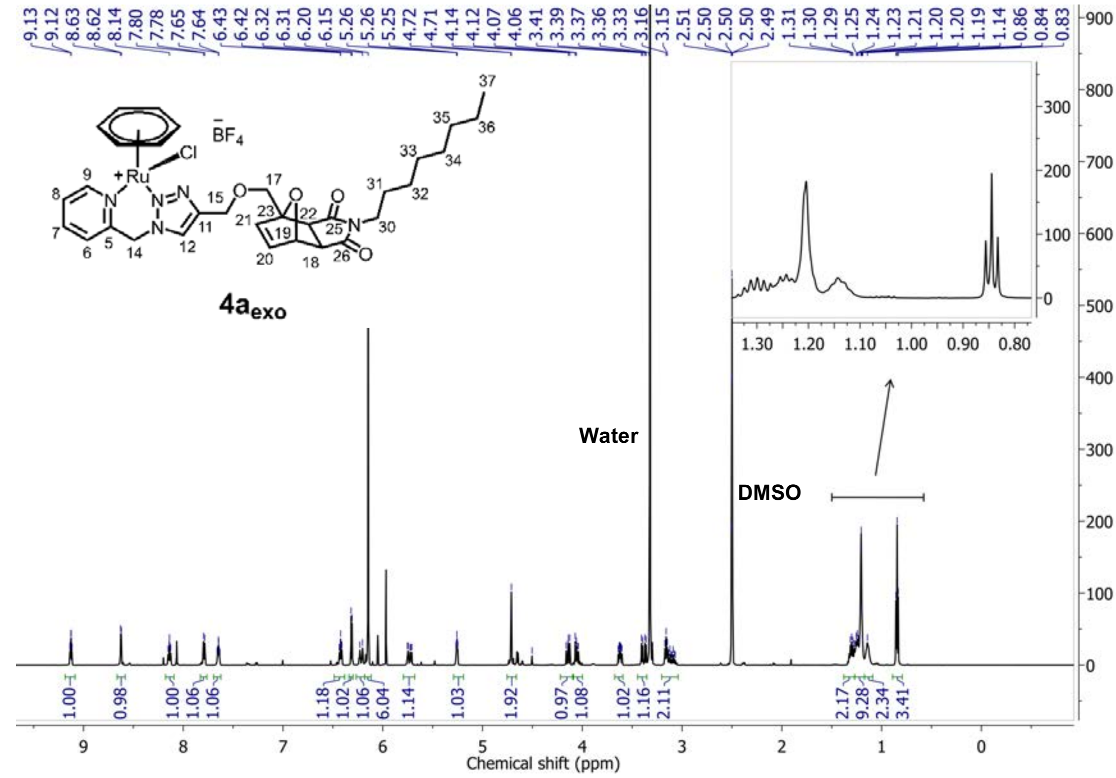
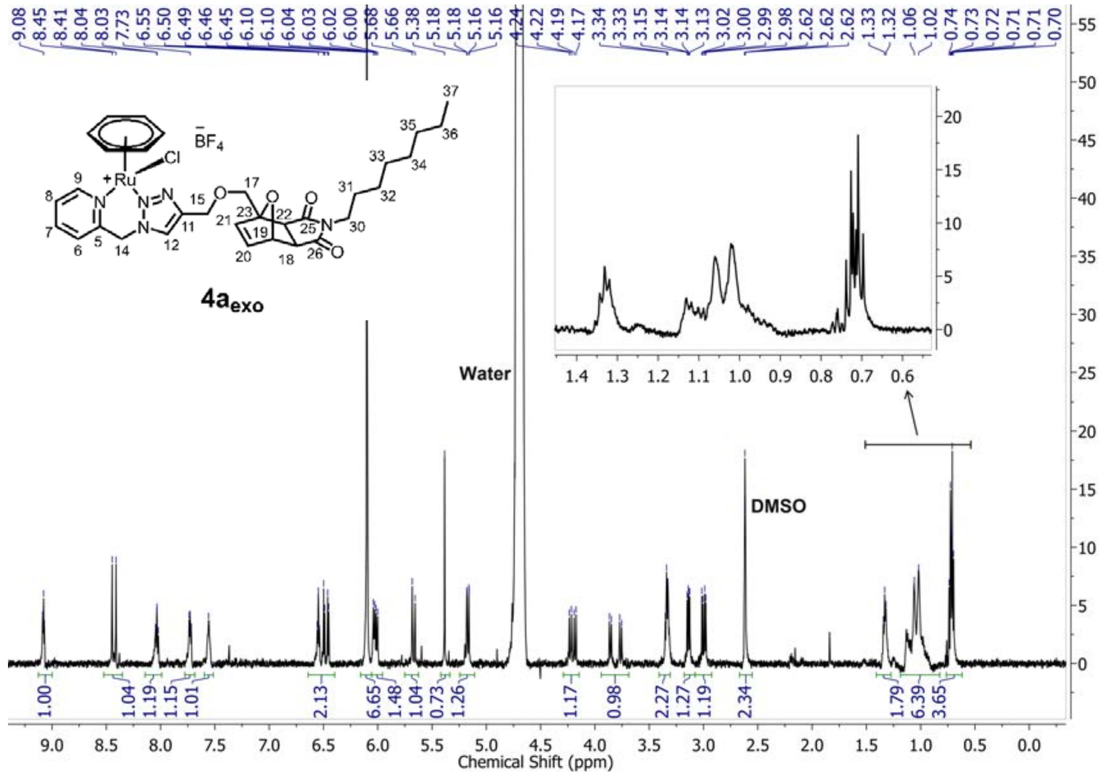
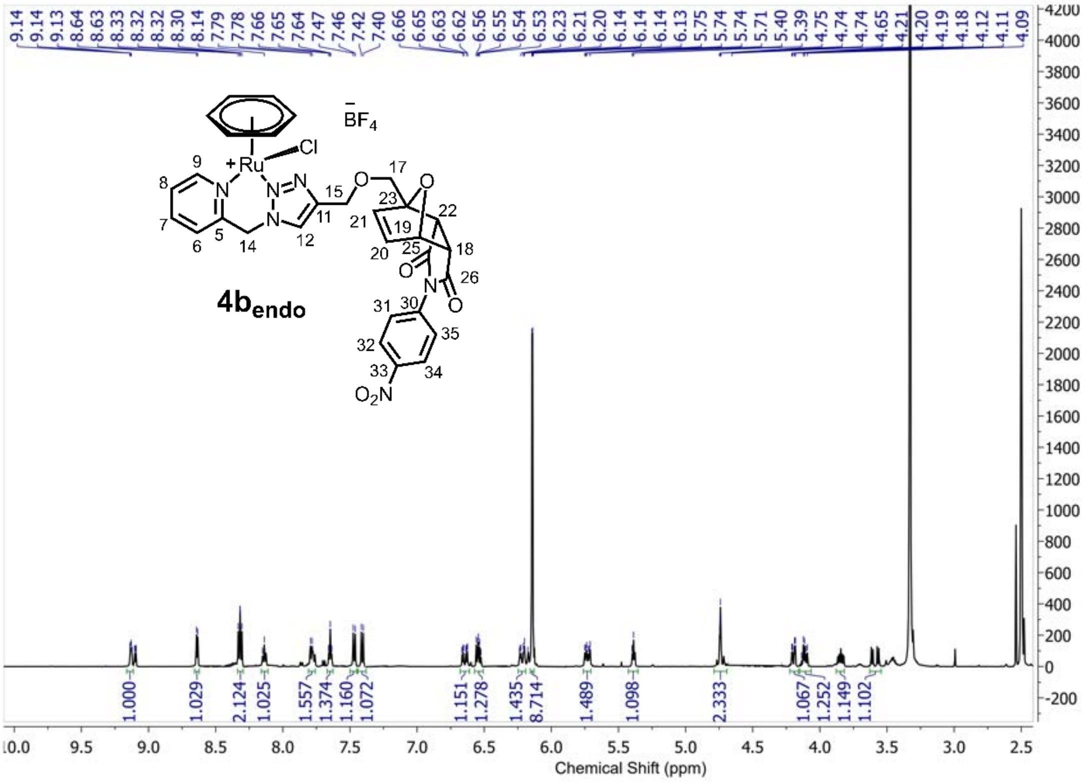


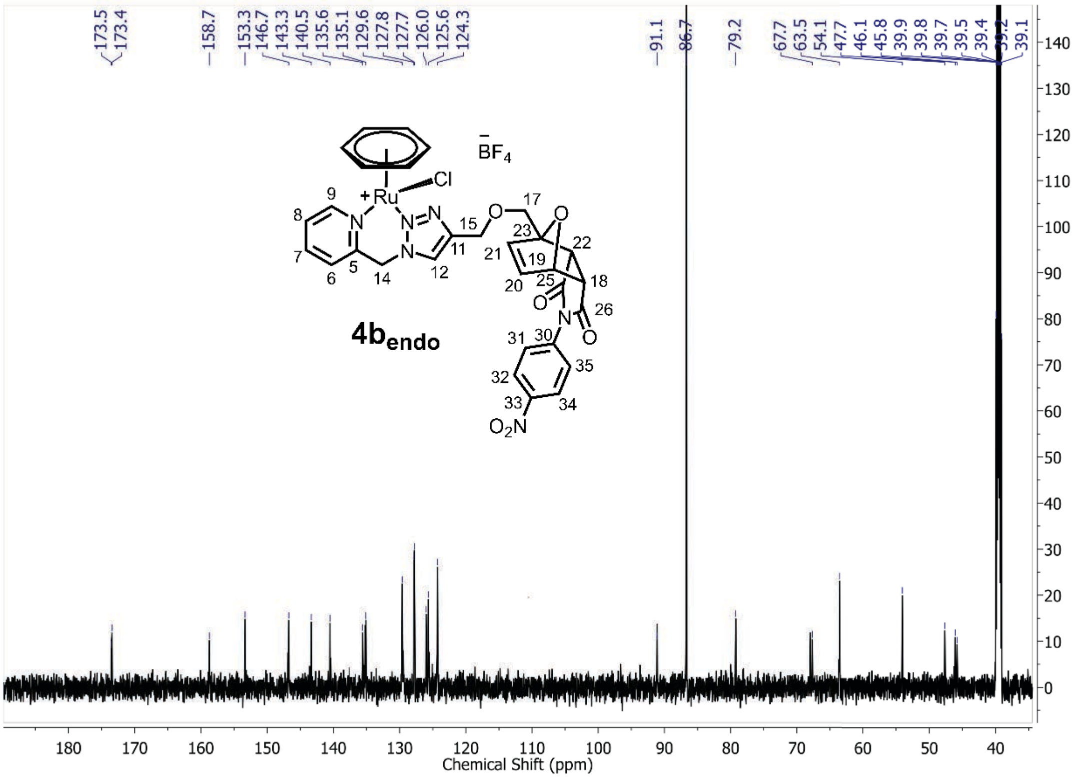
^{1}H-NMR spectrum of **4a$_{exo}$** in DMSO-*d*$_6$ after 48h at room temperature.



^{1}H-NMR spectrum of **4a$_{exo}$** in D$_2$O containing 1% DMSO-*d*$_6$ (110 mM NaCl) after 2h at room temperature.



^{1}H NMR spectrum of **4b$_{\mathbf{endo}}$** (DMSO-d_6).



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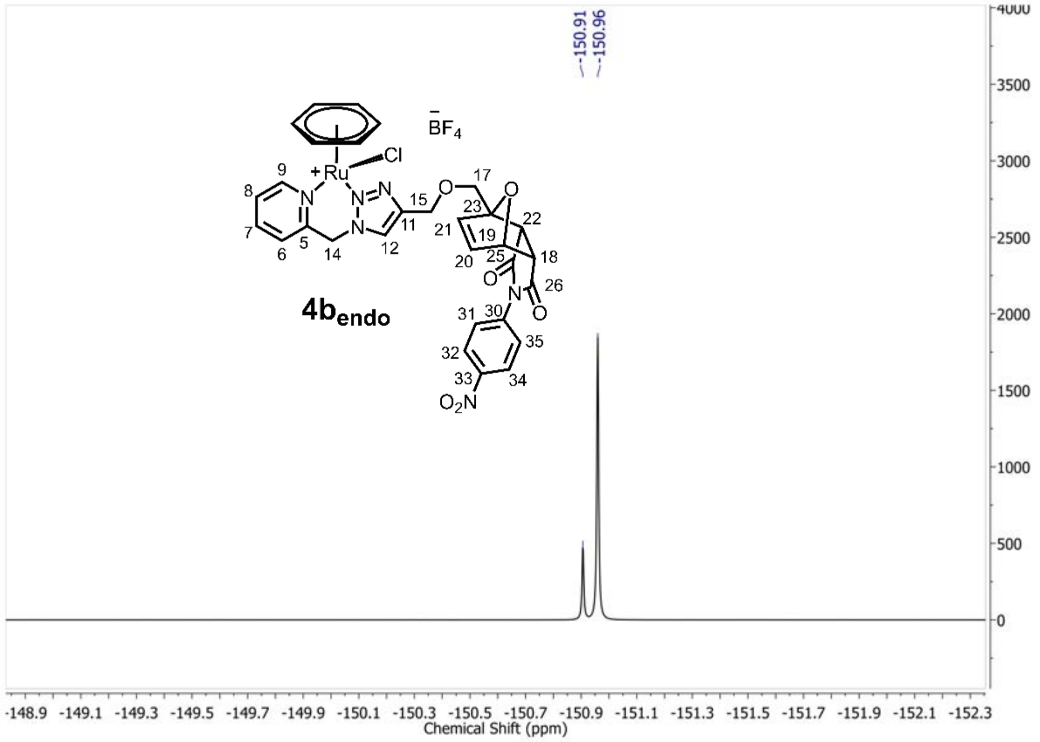
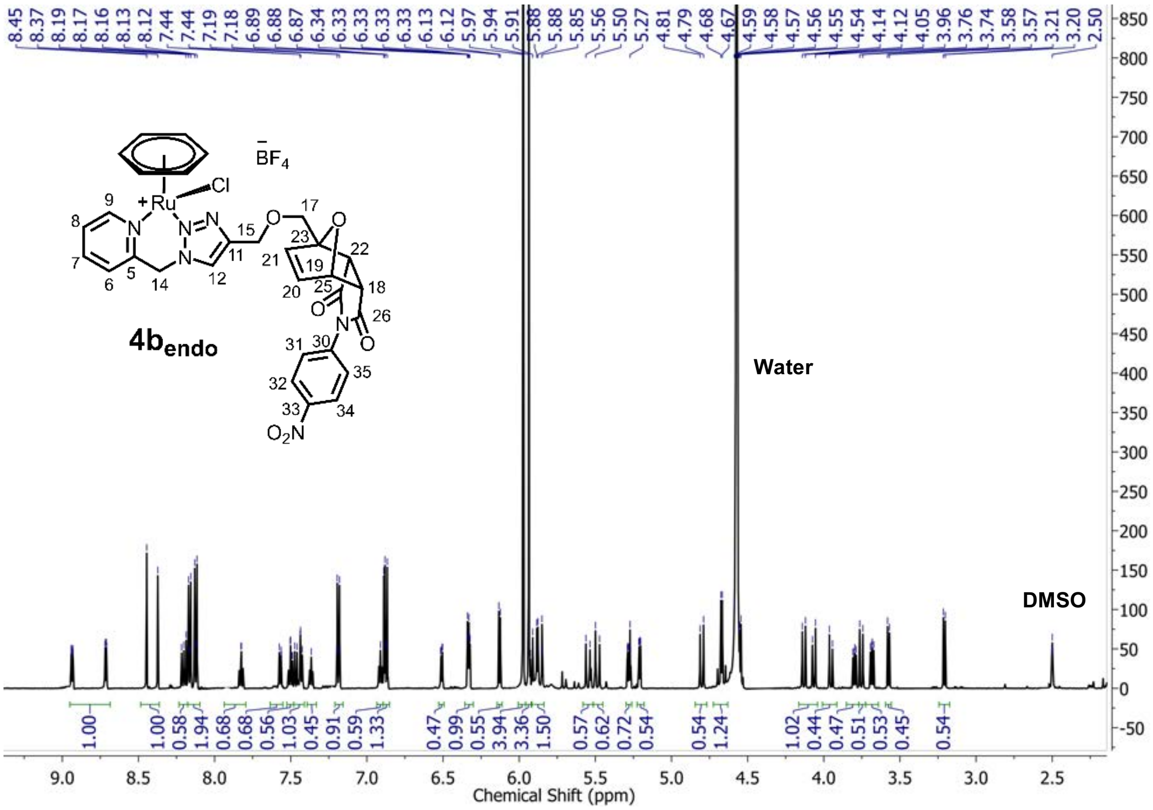
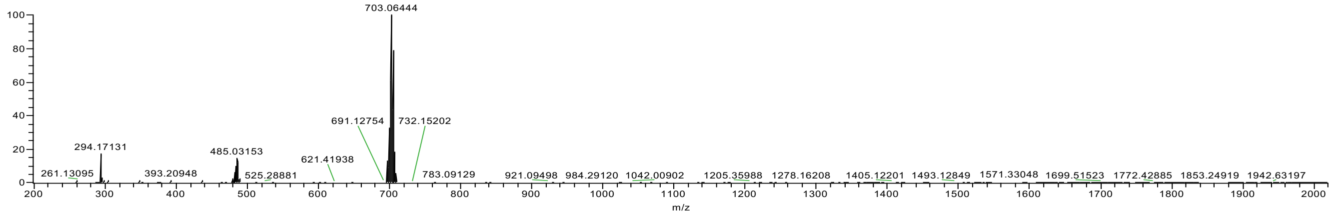


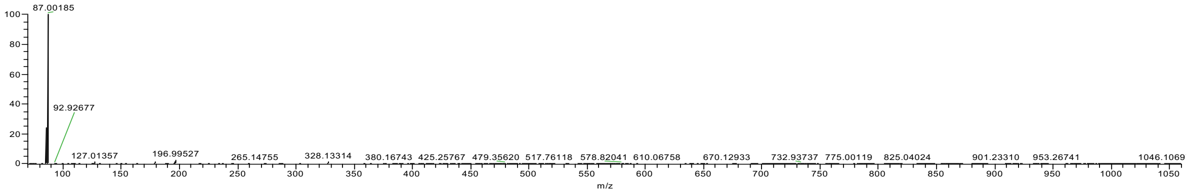
$^{19}F\{^1H\}$ NMR spectrum of **4b$_{endo}$** (acetone-d_6).



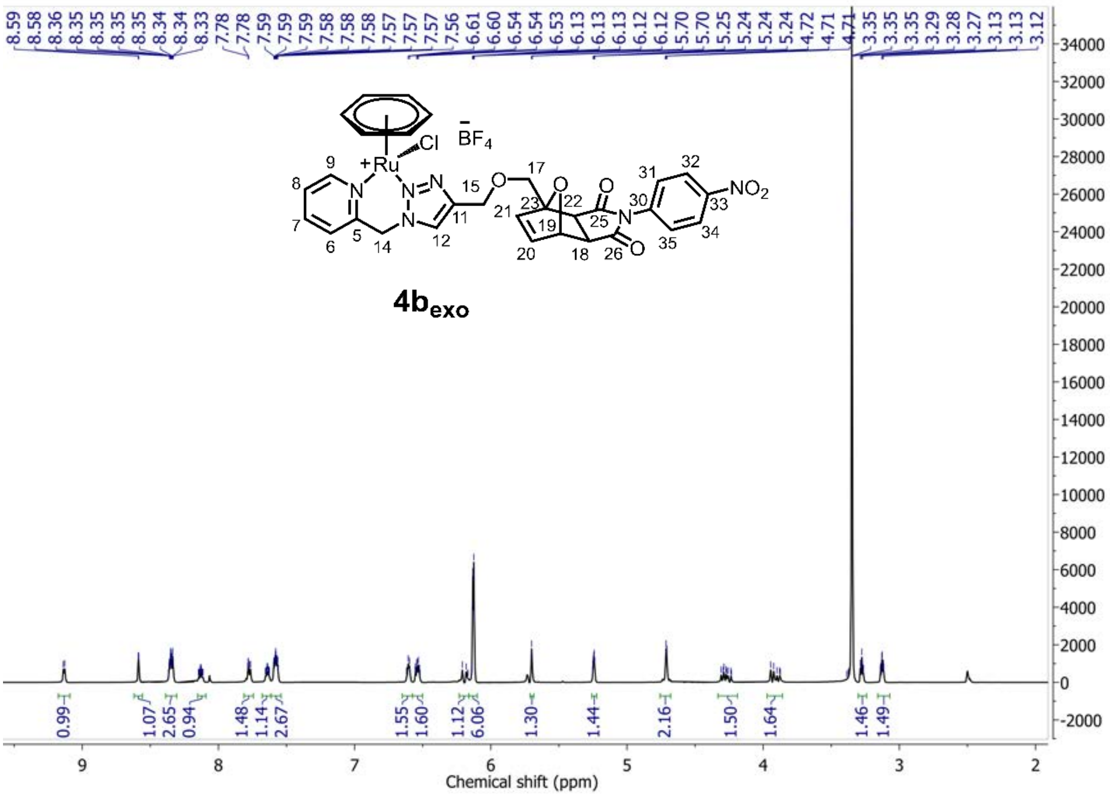
^1H-NMR spectrum of **4b$_{endo}$** in D_2O containing 1% DMSO-d_6 (110 mM NaCl) after 2h at room temperature.



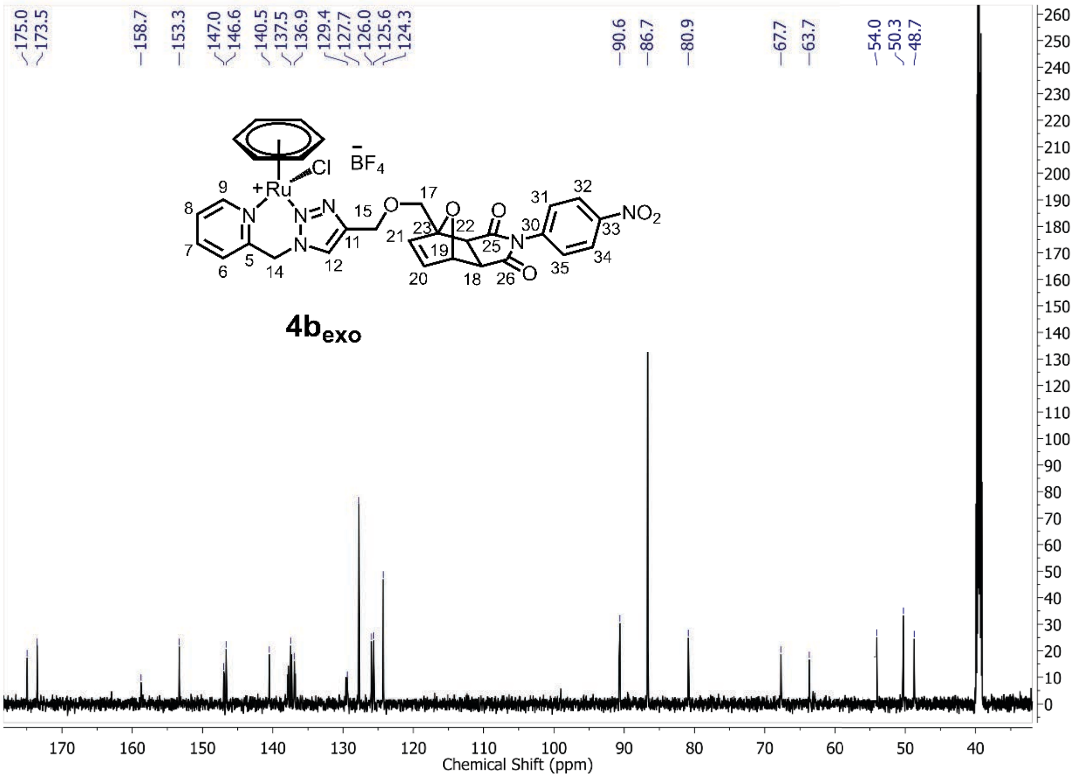
HR-ESI-MS of **4b** (**4b**$_{\mathbf{endo}}$/**4b**$_{\mathbf{exo}}$: 1/3.8), positive modes.



HR-ESI-MS of **4b** (**4b**$_{\mathbf{endo}}$/**4b**$_{\mathbf{exo}}$: 1/3.8), negative modes.



^{1}H NMR spectrum of **4b$_{exo}$** (DMSO-d_6).



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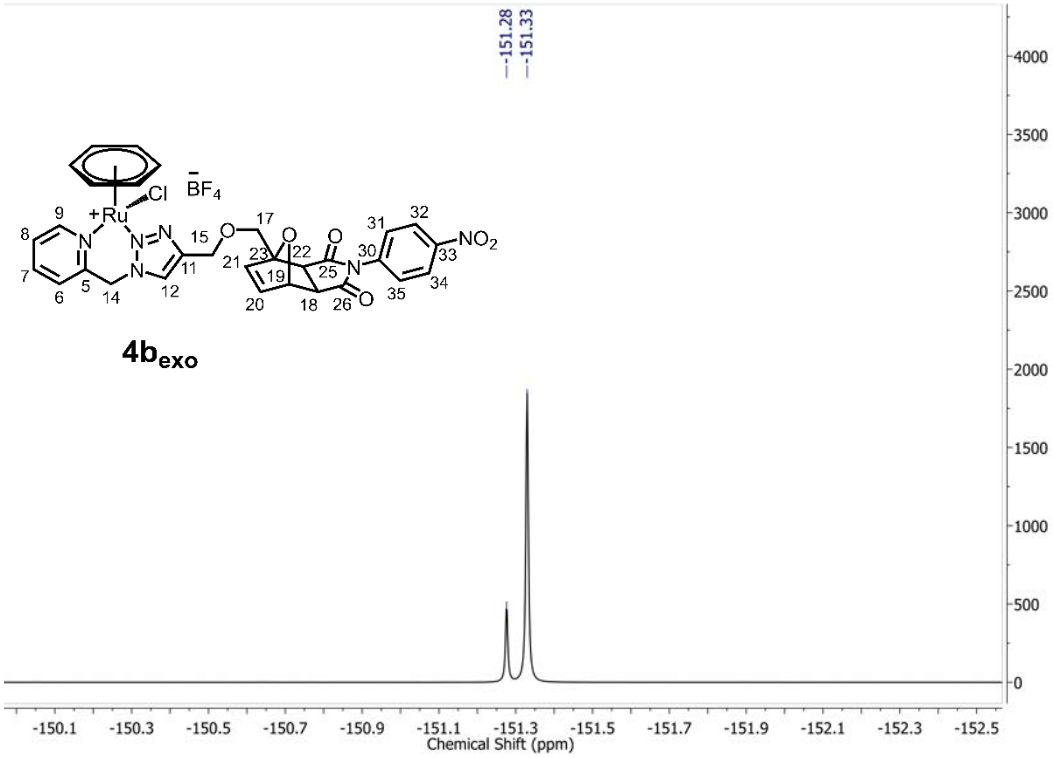
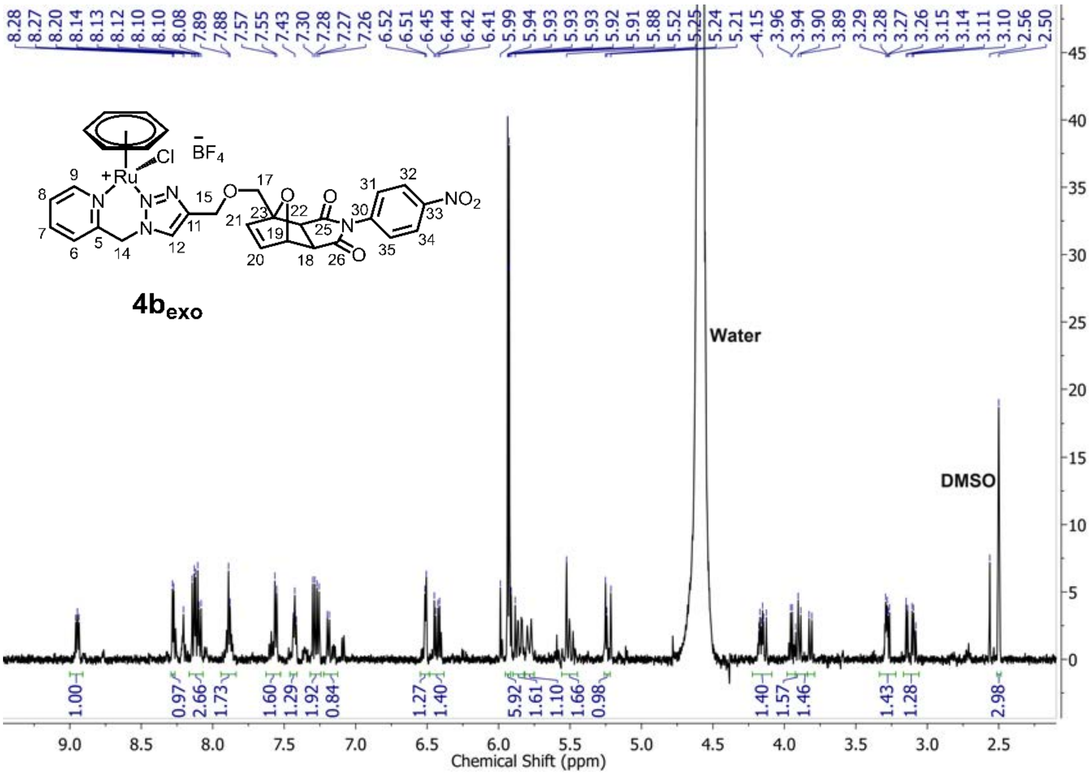
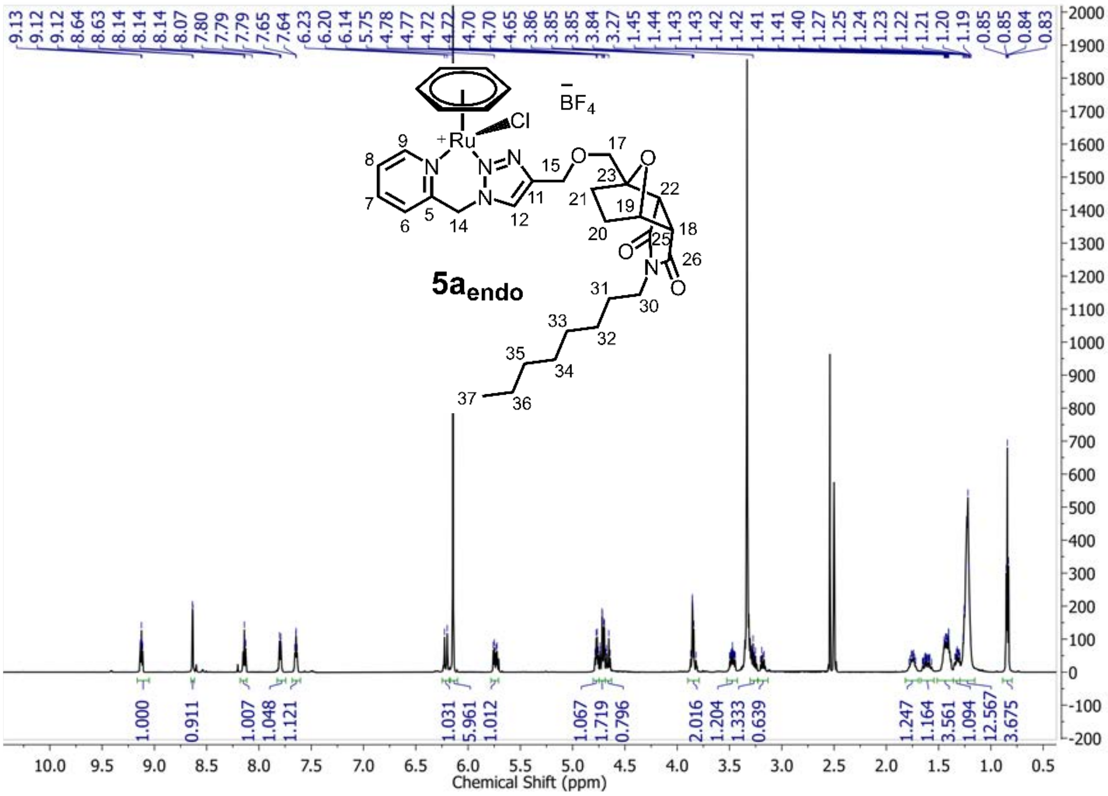


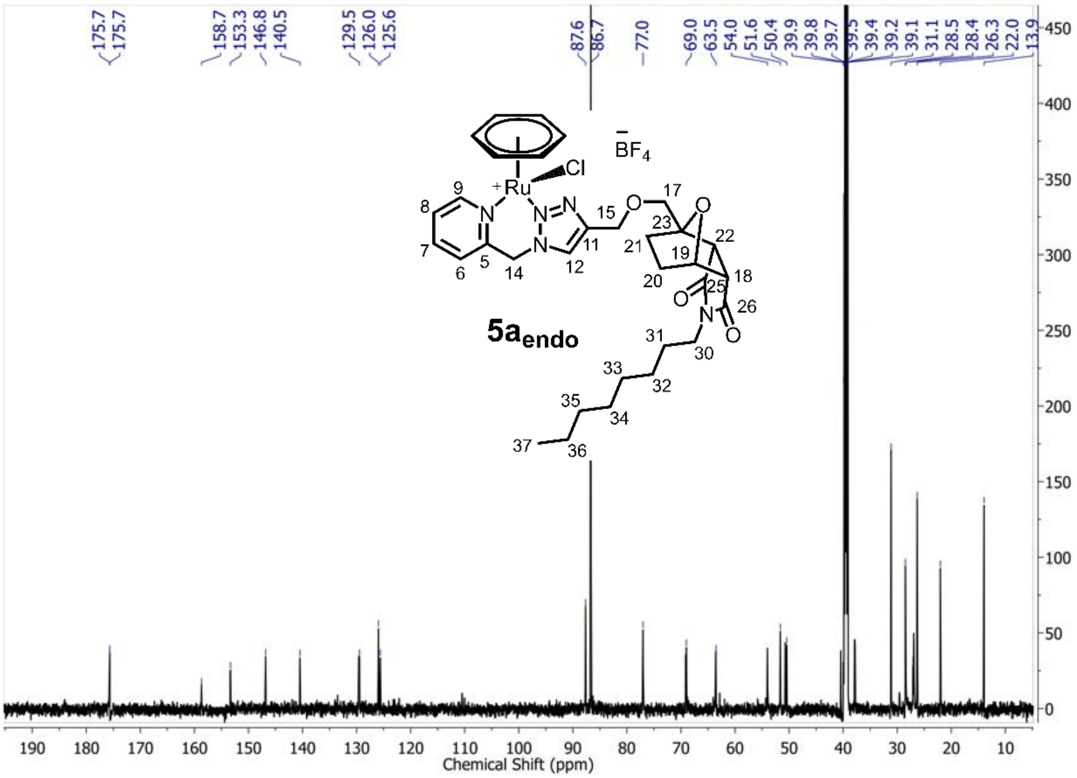
$^{19}F\{^1H\}$ NMR spectrum of **4b$_{exo}$** (acetone-d_6).



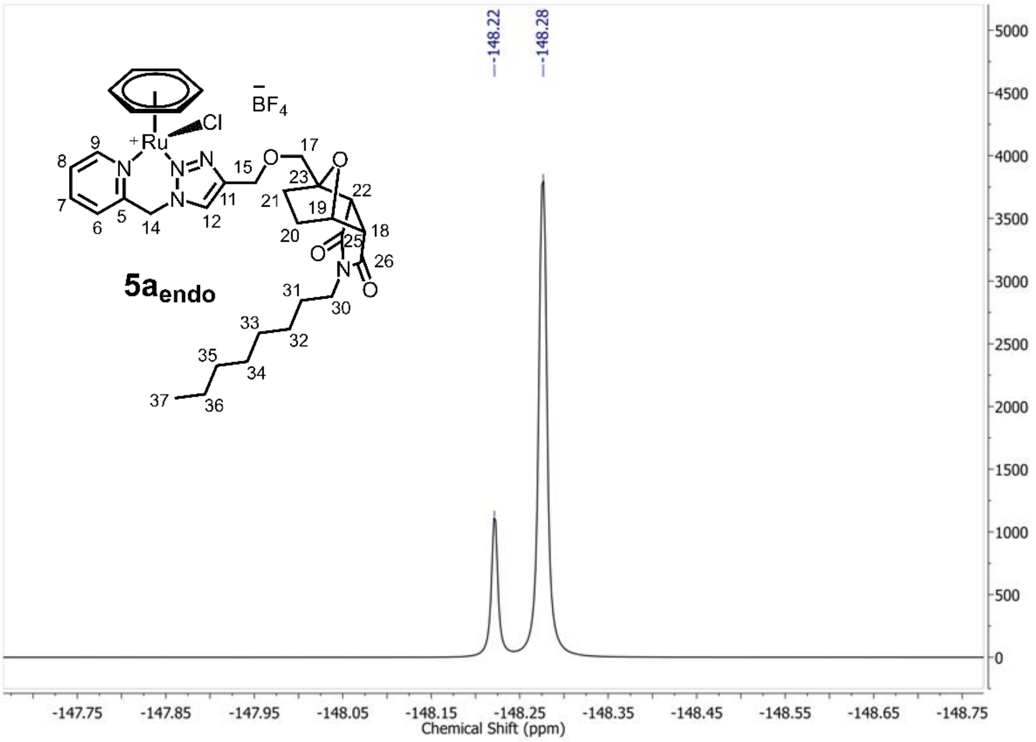
^1H-NMR spectrum of **4b$_{exo}$** in D_2O containing 1% DMSO-d_6 (110 mM NaCl) after 2h at room temperature.



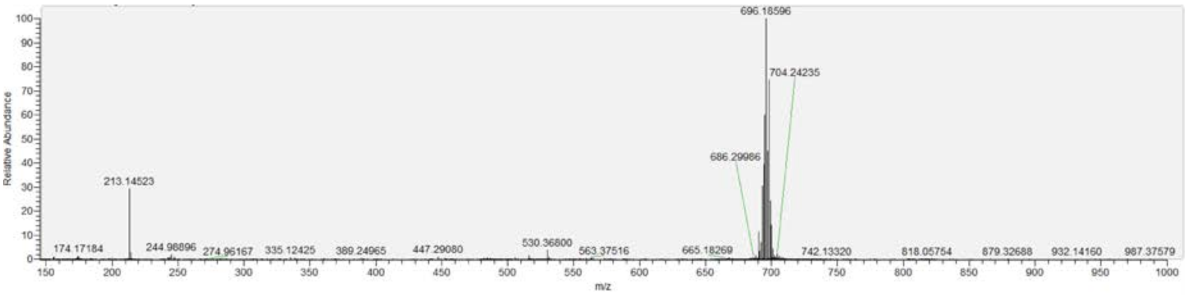
^{1}H NMR spectrum of **5a$_{\mathbf{endo}}$** (DMSO-d_6).



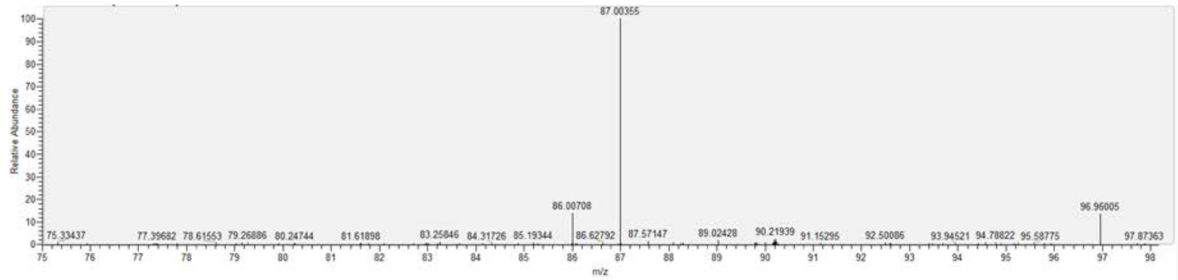
^{13}C{^{1}H} NMR spectrum of **5a$_{\mathbf{endo}}$** (DMSO-d_6).



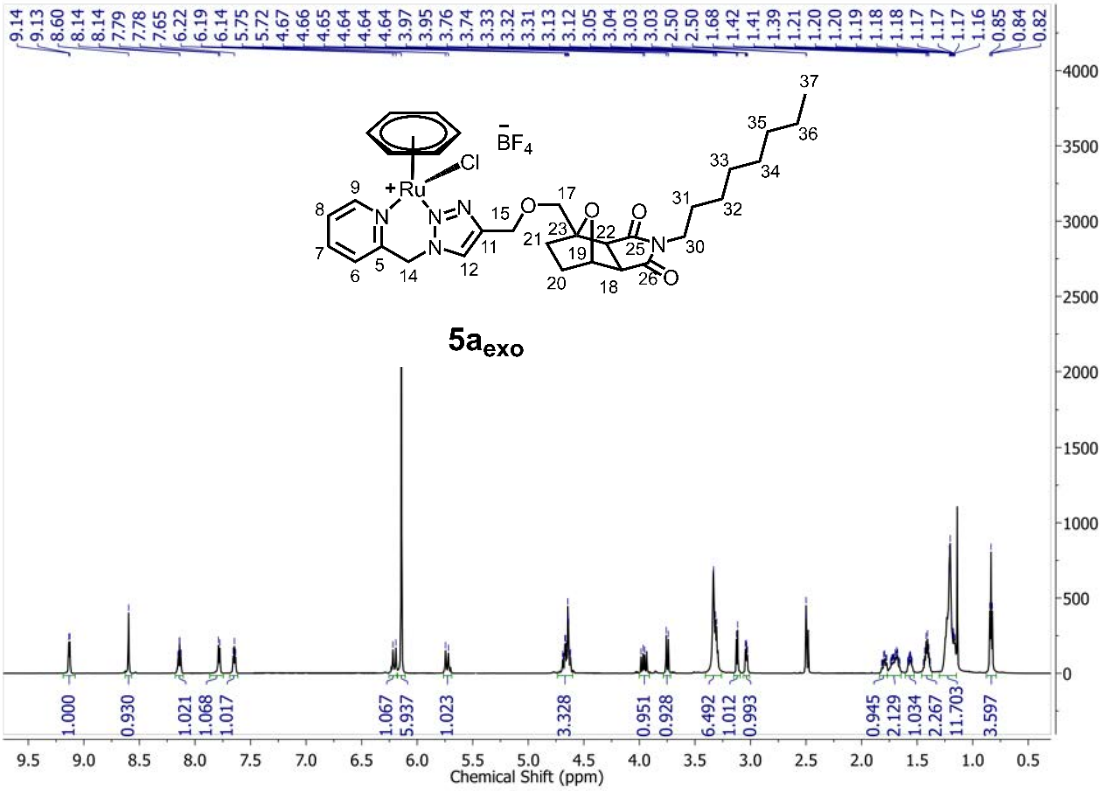
$^{19}F\{^1H\}$ NMR spectrum of **$5a_{endo}$** (DMSO-d_6).



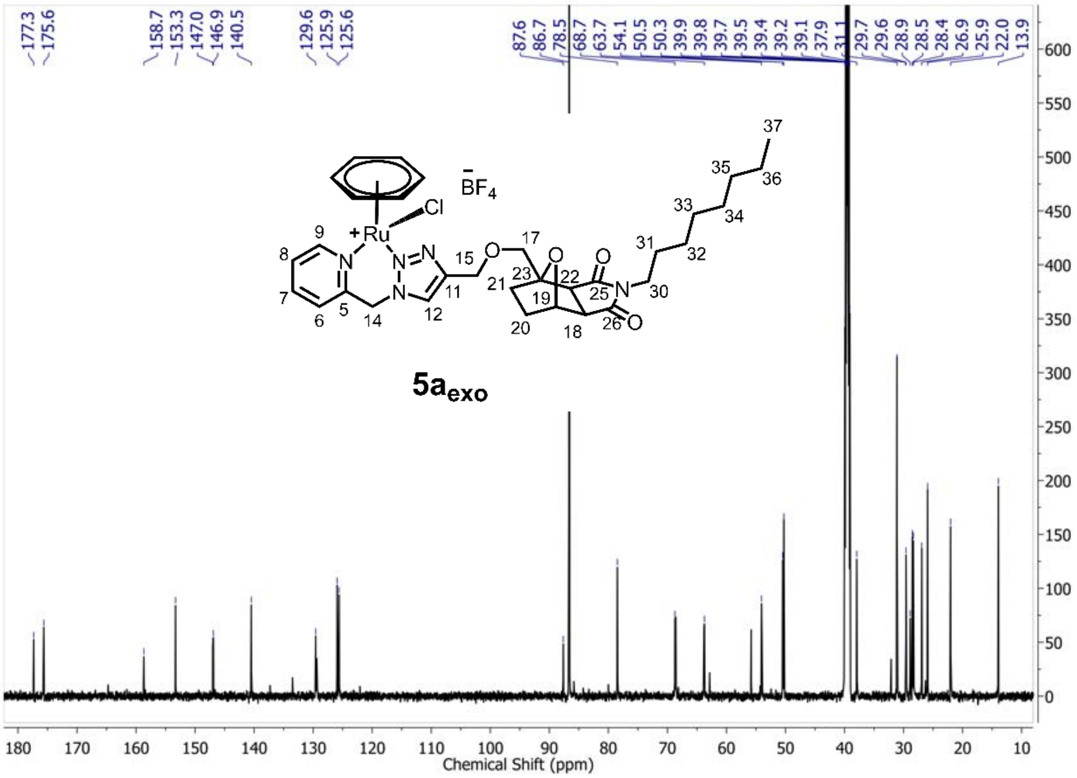
HR-ESI-MS of **5a** (**$5a_{endo}$**/**$5a_{exo}$** : 1.7/1), positive modes.



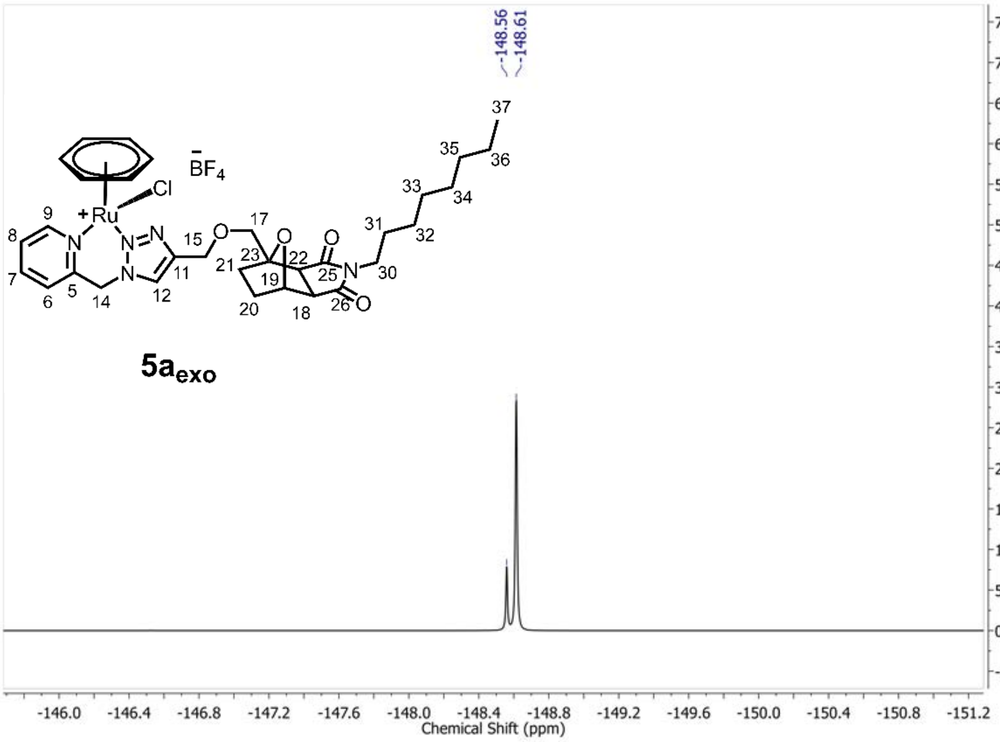
HR-ESI-MS of **5a** (**$5a_{endo}$**/**$5a_{exo}$** : 1.7/1), negative modes.



^{1}H NMR spectrum of **5a$_{\mathbf{exo}}$** (DMSO-d_6).



^{13}C{^{1}H} NMR spectrum of **5a$_{\mathbf{exo}}$** (DMSO-d_6).



$^{19}F\{^1H\}$ NMR spectrum of **5a$_{exo}$** (DMSO-d_6).

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