

Electronic Supplementary Information

N- and *S*-donor leaving groups in triazole-based ruthena(II)cycles: Potent anticancer activity, selective activation, and mode of action studies

Christoph A. Riedl^{a,b}, Michaela Hejl^a, Matthias H.M. Klose^{a,b}, Alexander Roller^a, Michael A. Jakupec^{a,b},
Wolfgang Kandioller^{a,b*}, and Bernhard K. Keppler^{a,b}

(a) Institute of Inorganic Chemistry, Faculty of Chemistry, University of Vienna, and (b) Research Cluster
“Translational Cancer Therapy Research”, Waehringer Str. 42, 1090 Vienna, Austria

(*) wolfgang.kandioller@univie.ac.at, Tel: +43-1-4277-52609; Fax: +43-1-4277-9526

Table of Contents

1. Experimental and calculated pKa values	2
2. NMR investigations	3
3. Single crystal x-ray diffraction analysis	5
4. Stability in aqueous solution	14
5. Oxidation of 3a	18
6. Amino acid binding studies	19
7. Chromatographic lipophilicity index φ_0	23
8. ROS generation	24
9. Methyl green DNA intercalation assay	26
10. Flow cytometric detection of apoptotic cells	27
11. ¹ H and ¹³ C NMR spectra	28

1. Experimental and calculated pK_a values

Table S1 Experimentally measured and calculated (ACD/Labs) pK_a values (conjugated acid) of the metal-coordinating nitrogen donor atom at 25 °C.

Respective Complex	Ligand	pK _a	Reference	calculated pK _a ^b
2a	1 <i>H</i> -Imidazole	6.99	CRC Handbook ³	7.18 ± 0.61
2b	1-Methylimidazole	6.95	CRC Handbook ³	7.01 ± 0.10
2c	4-Phenylimidazole	-	-	6.68 ± 0.10
2d	1 <i>H</i> -Pyrazole	2.49	CRC Handbook ³	2.83 ± 0.10
2e	1 <i>H</i> -Indazole	1.31 ^a	Catalán et al. ⁴	1.26 ± 0.10
2f	Pyridine	5.23	CRC Handbook ³	5.23 ± 0.10
2g	Isoquinoline	5.4	CRC Handbook ³	5.37 ± 0.23
2h	Imidazo[1,2- <i>a</i>]pyridine	6.79 ^a	Catalán et al. ⁴	6.80 ± 0.30
2i	Benzothiazole	1.2	Eicher et al. ⁵	0.85 ± 0.10

a) Corrected to 25 °C

b) Calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02 (© 1994-2017 ACD/Labs)

2. NMR investigations

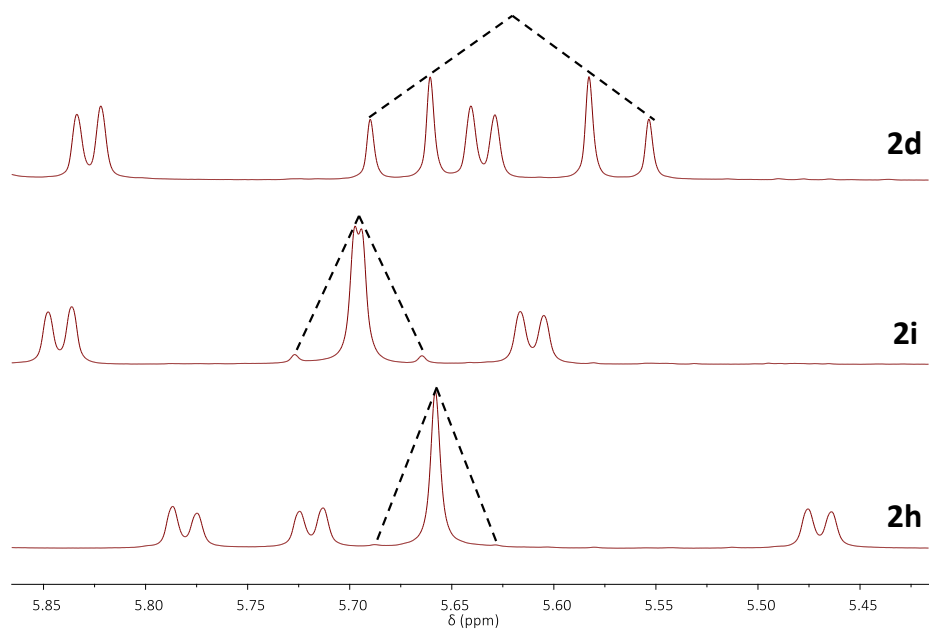


Figure S1 ^1H NMR spectra of **2d** (top), **2i** (middle), and **2h** (bottom) with dashed lines highlighting roof effect.

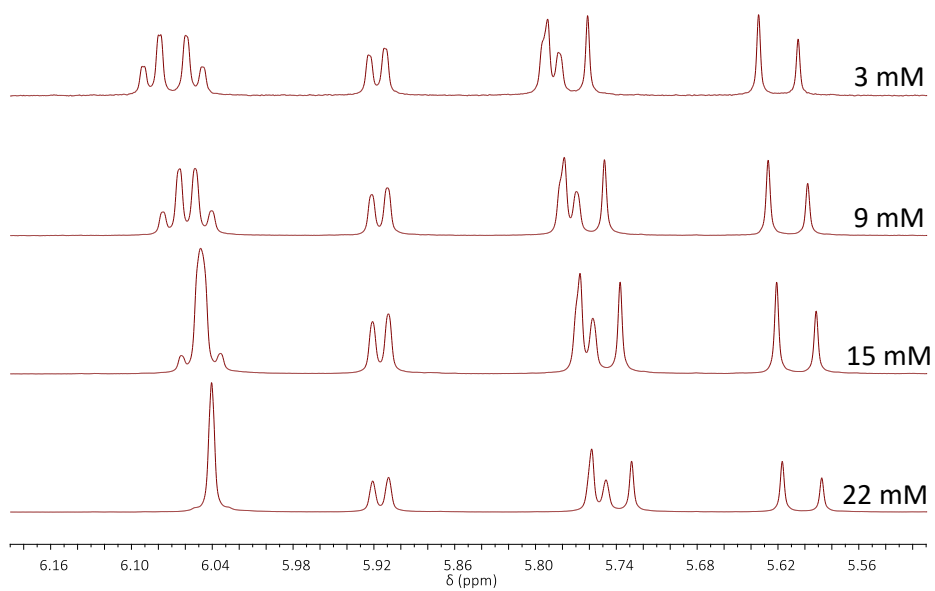


Figure S2 ^1H NMR of **2e** at four different concentrations in CDCl_3 , illustrating the concentration-dependence of aromatic arene and methylene protons.

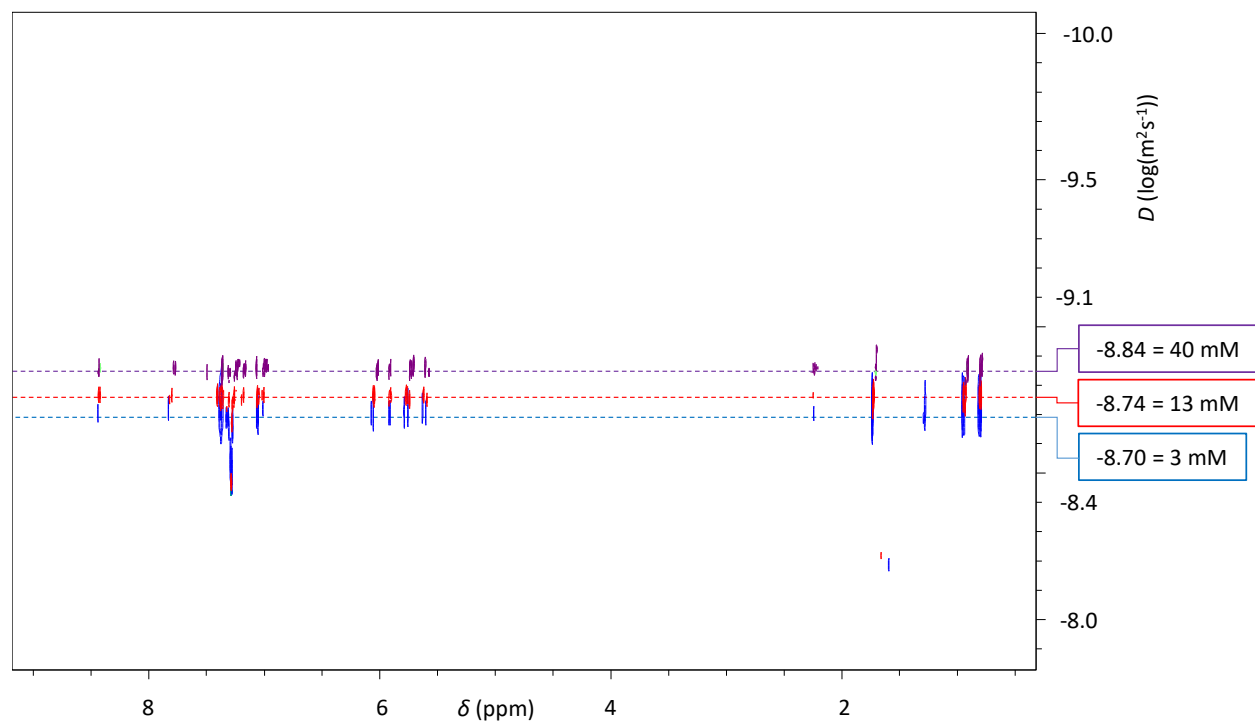


Figure S3 Overlay of ^1H DOSY NMR spectra of **2e** recorded at three different concentrations in CDCl_3 .

3. Single crystal x-ray diffraction analysis

Table S2 Experimental parameters and CCDC codes.

Sample	Diffractometer	Source	Temp. [K]	Detector distance [mm]	Time per frame [s]	No. of frames	Frame width [°]	CCDC
2e	X8	Mo	100	35	50	2835	0.5	1575667
2i	X8	Mo	100	35	30	1773	0.5	1575668
3a	D8	Mo	100	34	24	1419	0.5	1575669

Table S3 Selected bond lengths.

Compound	Bond lengths (Å)								
	Ru–LG	Ru–N3	Ru–PhC2	PhC1–PhC2	PhC2–PhC3	PhC3–PhC4	PhC4–PhC5	PhC5–PhC6	PhC6–PhC1
1_A	2.4280(18)	2.069(6)	2.057(6)	1.429(9)	1.431(9)	1.387(9)	1.394(10)	1.401(10)	1.383(9)
1_B	2.4165(17)	2.067(6)	2.063(6)	1.418(9)	1.416(9)	1.365(8)	1.410(10)	1.383(9)	1.398(9)
2e_A	2.087(4)	2.058(4)	2.077(5)	1.413(8)	1.385(8)	1.408(9)	1.372(11)	1.377(10)	1.394(8)
2e_B	2.088(4)	2.067(4)	2.082(5)	1.398(8)	1.397(7)	1.385(8)	1.376(9)	1.376(9)	1.392(8)
2i_A	2.130(3)	2.068(3)	2.072(4)	1.415(5)	1.401(6)	1.399(6)	1.380(6)	1.392(6)	1.393(5)
2i_B	2.110(3)	2.086(3)	2.083(4)	1.408(6)	1.397(5)	1.401(5)	1.384(6)	1.388(5)	1.390(5)
3a	2.3620(4)	2.0607(13)	2.0761(17)	1.419(2)	1.400(2)	1.396(3)	1.386(4)	1.391(3)	1.393(3)

Table S4 Selected bond lengths.

Compound	Bond lengths [Å]							
	N1–N2	N2–N3	N3–C4	C4–C5	C5–N1	C4–PhC1	N1–BnCH ₂	Ring slippage ^a
1_A	1.338(7)	1.329(8)	1.367(8)	1.372(10)	1.365(8)	1.451(10)	1.451(8)	0.095
1_B	1.351(7)	1.324(7)	1.368(8)	1.382(9)	1.345(8)	1.472(9)	1.470(8)	0.095
2e_A	1.341(7)	1.309(6)	1.376(7)	1.386(8)	1.334(9)	1.441(8)	1.464(7)	0.082
2e_B	1.324(7)	1.318(6)	1.360(7)	1.368(8)	1.345(8)	1.458(7)	1.480(7)	0.077
2i_A	1.339(5)	1.327(4)	1.361(5)	1.379(5)	1.347(5)	1.455(5)	1.480(5)	0.082
2i_B	1.346(4)	1.320(4)	1.369(5)	1.369(5)	1.351(5)	1.456(5)	1.462(5)	0.077
3a	1.342(2)	1.3214(19)	1.366(2)	1.377(2)	1.348(2)	1.450(2)	1.468(2)	0.064

(a) Distance between the perpendicular projection of an heavy atom on the ring l.s.-plane and the arene ring

Table S5 Selected bond angles.

Compound	Bond angles [°]								
	PhC2–Ru–LG	LG–Ru–N3	N3–Ru–PhC2	Ru–PhC2–PhC1	Ru–PhC2–PhC3	PhC1–C4–C5	PhC1–C4–N3	Ru–N3–N2	Ru–N3–C4
1_A	87.29(17)	84.99(15)	77.4(3)	117.4(5)	128.1(5)	138.5(6)	115.5(6)	130.4(4)	117.5(5)
1_B	86.95(16)	86.58(14)	77.5(2)	117.0(5)	115.0(6)	138.9(6)	114.0(6)	131.4(4)	118.3(4)
2e_A	84.53(19)	86.19(17)	77.7(2)	116.1(4)	126.6(4)	139.6(6)	115.1(5)	131.1(4)	117.4(4)
2e_B	85.01(18)	87.77(17)	77.30(18)	116.1(4)	127.3(4)	138.9(5)	114.5(5)	130.8(4)	117.9(3)
2i_A	85.67(13)	90.75(12)	77.24(15)	116.6(3)	127.1(3)	138.5(4)	114.6(3)	130.2(3)	118.1(3)
2i_B	87.26(13)	88.58(12)	77.22(13)	116.5(3)	127.0(3)	138.2(4)	114.8(3)	131.5(2)	117.5(2)
3a	86.90(5)	89.73(4)	77.52(6)	116.17(12)	127.52(14)	138.33(17)	115.01(14)	130.81(11)	117.90(11)

Table S6 Selected torsion angles.

Compound	Torsion angles [°]		
	BnCH ₂ –N1–C5–C4	N3–C4–PhC1–PhC2	C5–N1–BnCH ₂ –BnC1
1_A	177.2(5)	-4.4(8)	82.7(8)
1_B	-179.7(5)	-2.9(7)	90.4(7)
2e_A	-169.6(5)	0.4(7)	83.4(8)
2e_B	168.4(5)	-1.4(6)	-83.9(7)
2i_A	-176.8(3)	-2.7(4)	94.4(5)
2i_B	-179.9(3)	-3.0(5)	-90.9(5)
3a	174.10(16)	-0.5(2)	-71.6(2)

3.1. $[[((2-\kappa N)-1H\text{-indazole})(1\text{-benzyl-4-(2'-}\kappa C\text{)-phenyl-1,2,3-(3-}\kappa N\text{)-triazolato})(\eta^6\text{-}p\text{-cymene) ruthenium(II)] \text{ nitrate (2e)}$

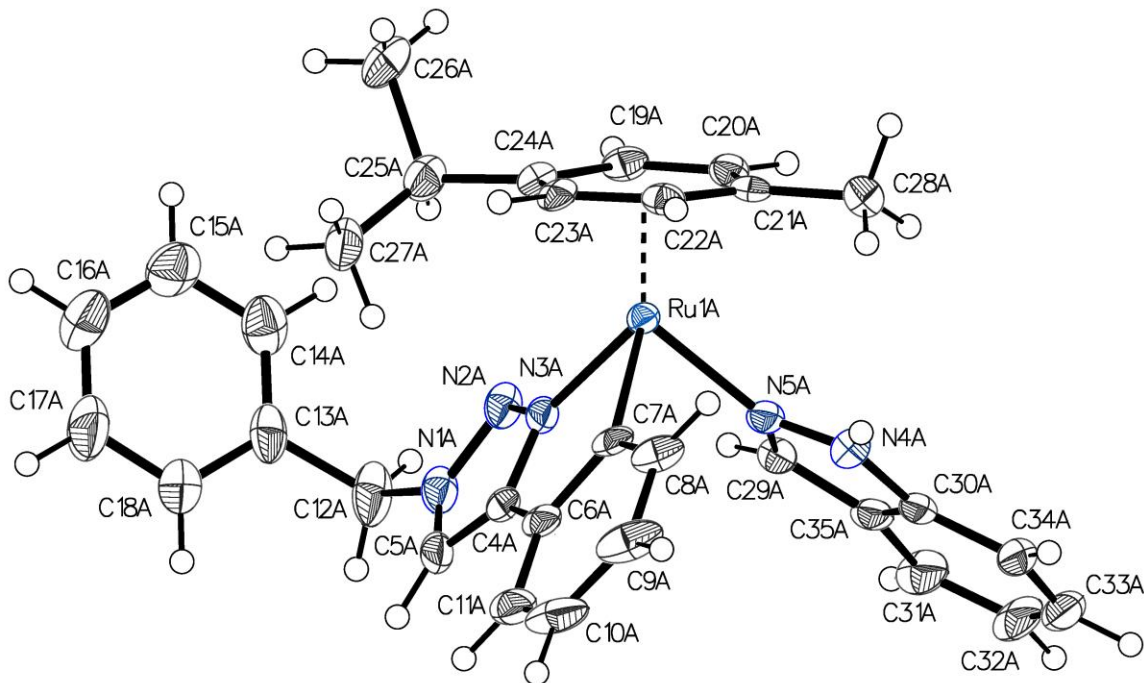


Figure S4 Crystal structure of **2e**, drawn with 50% displacement ellipsoids. The second molecule of the asymmetric unit, solvent molecules and counter ions were omitted for clarity.

Table S7 Sample and crystal data of **2e**.

Chemical formula	$C_{64}H_{66}N_{12}O_7Ru_2$	
Formula weight (g/mol)	1317.42	
Temperature (K)	100	
Measurement method	\f and \w scans	
Radiation wavelength (Å)	MoK α ($\lambda = 0.71073$)	
Crystal size (mm ³)	0.23 $\times$ 0.06 $\times$ 0.025	
Crystal habit		
Density (calculated) (g/cm ³)	1.422	
Abs. correction $T_{\min}$	0.6739	
Abs. correction type	multi-scan	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Z	4	
Volume (Å ³)	6151.8(11)	
Unit cell dimensions (Å) and (°)	10.6875(11)	90
	22.259(2)	90.648(4)
	25.861(3)	90
Absorption coefficient (mm ⁻¹)	0.554	
Abs. correction $T_{\max}$	0.7460	
F(000) (e ⁻)	2712	

Table S8 Data collection and structure refinement parameters of **2e**.

Index ranges	-12 ≤ h ≤ 12, -25 ≤ k ≤ 26 -31 ≤ l ≤ 31	Theta range for data collection (°)	3.642 to 50.7	
Reflections number	166872	Data / restraints / parameters	11203 / 165 / 764	
Refinement method	Least squares	Final R indices	all data	R ₁ = 0.0791 wR ₂ = 0.1627
Function minimized	$\sum w(\text{Fo}^2 - \text{Fc}^2)^2$		I > 2σ(I)	R ₁ = 0.0563 wR ₂ = 0.1492
Goodness-of-fit on F ²	1.042	Weighting scheme	w = 1/[s ² (Fo ²) + (0.0717P) ² + 33.9060P] where P = (Fo ² + 2Fc ²)/3	
Largest diff. peak and hole [e Å ⁻³]	2.06/-2.01			

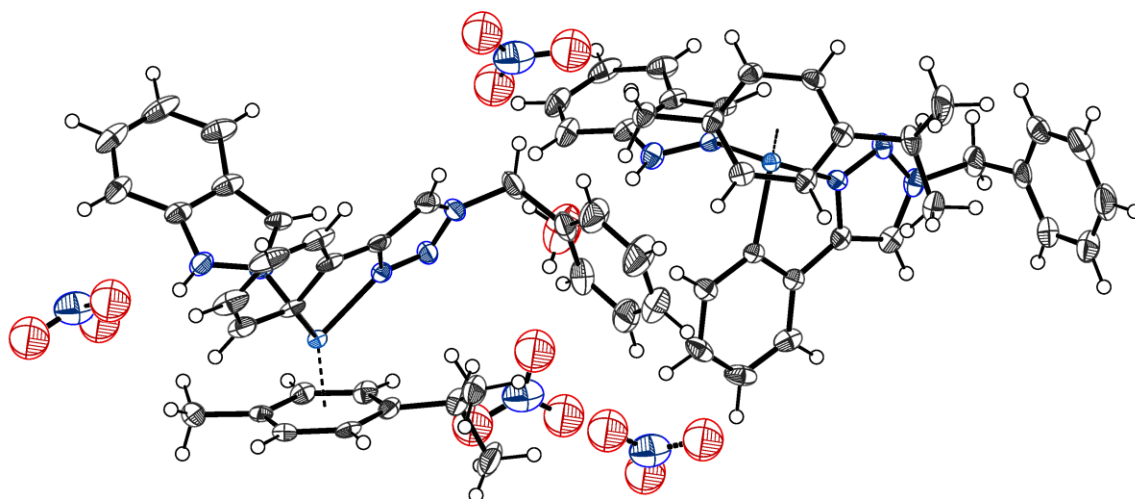


Figure S5 Asymmetric unit of **2e**, drawn with 50% displacement ellipsoids. Four NO₃⁻ must be part of the asymmetric unit as evidenced by other analyses presented herein. Four positions could be characterized, but we believe that there is a fifth position to part for NO₃⁻ as visualized by the displacement ellipsoids and confirmed by the need to cut solvent-available void. Details about the excluded volume are part of the cif (_refine_special_details & _shelx_fab_file).

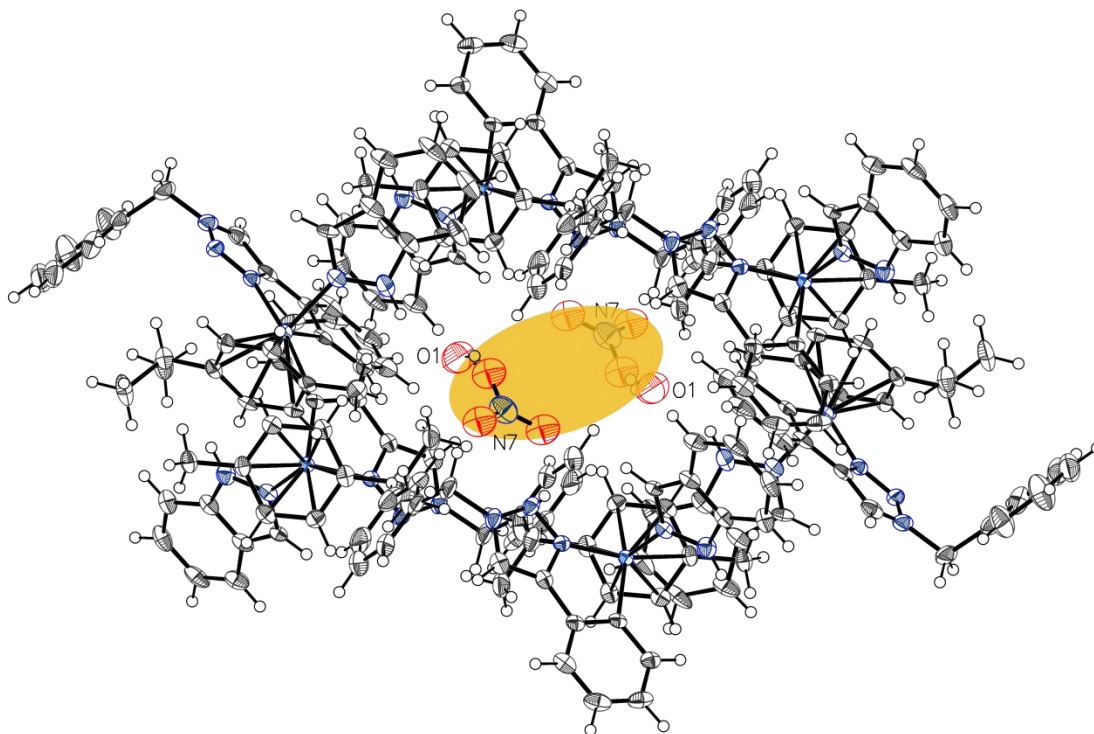


Figure S6 It was not possible to locate approximately 53% of one of two disordered NO_3^- ions in the unit cell. The orange ellipsoid describes the location of the corresponding NO_3^- accessible void. The HKL masked volume is two times $191.2 \text{ \AA}^3$ per unit cell, and the electron content is two times 45.8 per unit cell. This indicates that in addition to the missing nitrate, also some water molecules are present in the available void. NO_3^- was fixed with the help of DFIX and EADP.

3.2. $[(\kappa N-1,3\text{-Benzothiazole})(1\text{-benzyl-4-(2'-}\kappa\text{C)-phenyl-1,2,3-(3-}\kappa\text{N)-triazolato})(\eta^6\text{-}p\text{-cymene})\text{ruthenium(II)}]\text{ nitrate (2i)}$

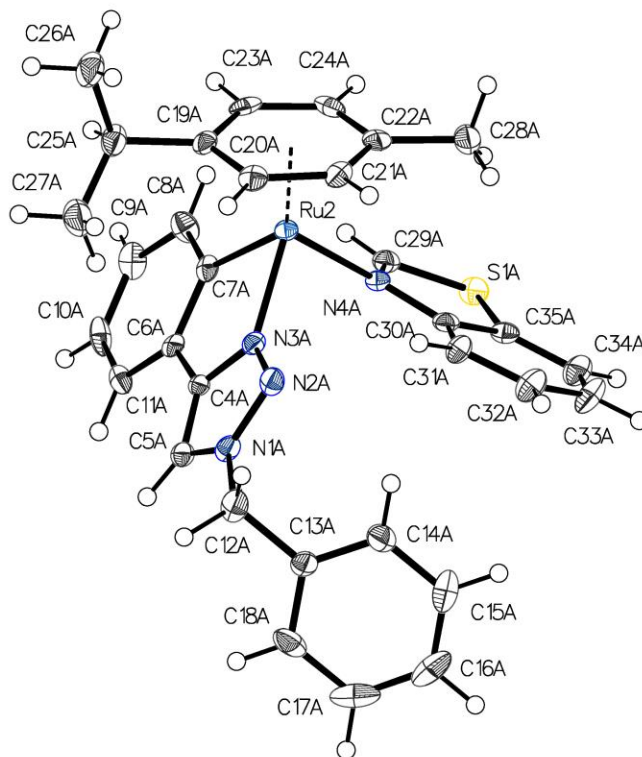


Figure S7 Crystal structure of **2i**, drawn with 50% displacement ellipsoids. The second molecule of the asymmetric unit, solvent molecules and counter ions were omitted for clarity.

Table S9 Sample and crystal data of **2i**.

Chemical formula	$\text{C}_{33}\text{H}_{34}\text{Cl}_2\text{N}_5\text{O}_{3.5}\text{RuS}$	
Formula weight (g/mol)	760.68	
Temperature (K)	100	
Measurement method	\f and \w scans	
Radiation wavelength (Å)	$\text{MoK}\alpha$ ($\lambda = 0.71073$)	
Crystal size (mm ³)	$0.12 \times 0.08 \times 0.03$	
Crystal habit	Clear yellow needle	
Density (calculated) (g/cm ³)	1.538	
Abs. correction $T_{\min}$	0.6935	
Abs. correction type	multi-scan	
Crystal system	triclinic	
Space group	$P-1$	
Z	4	
Volume (Å ³)	3284.4(4)	
Unit cell dimensions (Å) and (°)	12.0373(8)	95.649(2)
	13.4469(8)	95.099(3)
	20.7463(15)	98.748(2)
Absorption coefficient (mm ⁻¹)	0.748	
Abs. correction $T_{\max}$	0.7460	
F(000) (e ⁻)	1556	

Table S10 Data collection and structure refinement parameters of **2i**.

Index ranges	-14 ≤ h ≤ 14 -11 ≤ k ≤ 16 -24 ≤ l ≤ 24	Theta range for data collection (°)	3.968 to 50.698	
Reflections number	57798	Data / restraints / parameters	11970 / 21 / 845	
Refinement method	Least squares	Final R indices	all data	R ₁ = 0.0666 wR ₂ = 0.1197
Function minimized	$\sum w(F_o^2 - F_c^2)^2$		I > 2σ(I)	R ₁ = 0.0469 wR ₂ = 0.1100
Goodness-of-fit on F ²	0.981	Weighting scheme		
Largest diff. peak and hole [e Å ⁻³]	1.21 / -1.38			
		w=1/[s ² (F _o ²)+(0.0596P) ²] where P=(F _o ² +2F _c ²)/3		

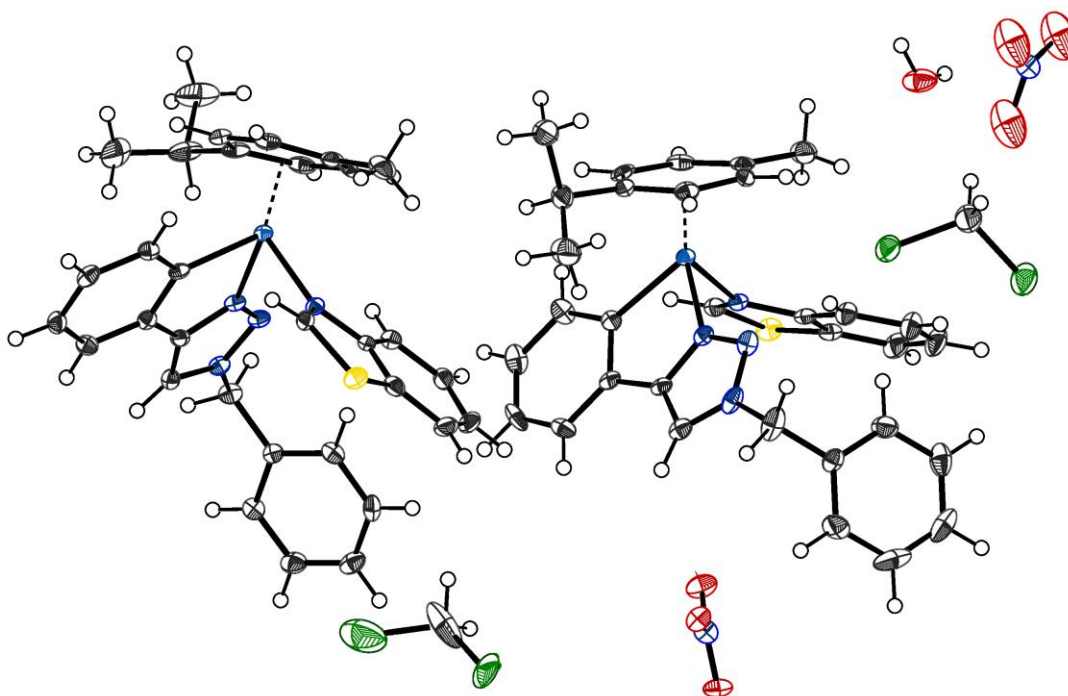


Figure S8 Asymmetric unit of **2i**, drawn with 50% displacement ellipsoids. Disordered solution (DCM) was omitted for clarity.

3.3. $[(\kappa\text{-S-(Methylsulfanyl)methane)}(1\text{-benzyl-4-(2'-}\kappa\text{C)-phenyl-1,2,3-(3-}\kappa\text{N)-triazolato)}](\eta^6\text{-}p\text{-cymene})\text{ruthenium(II)] nitrate (3a)}$

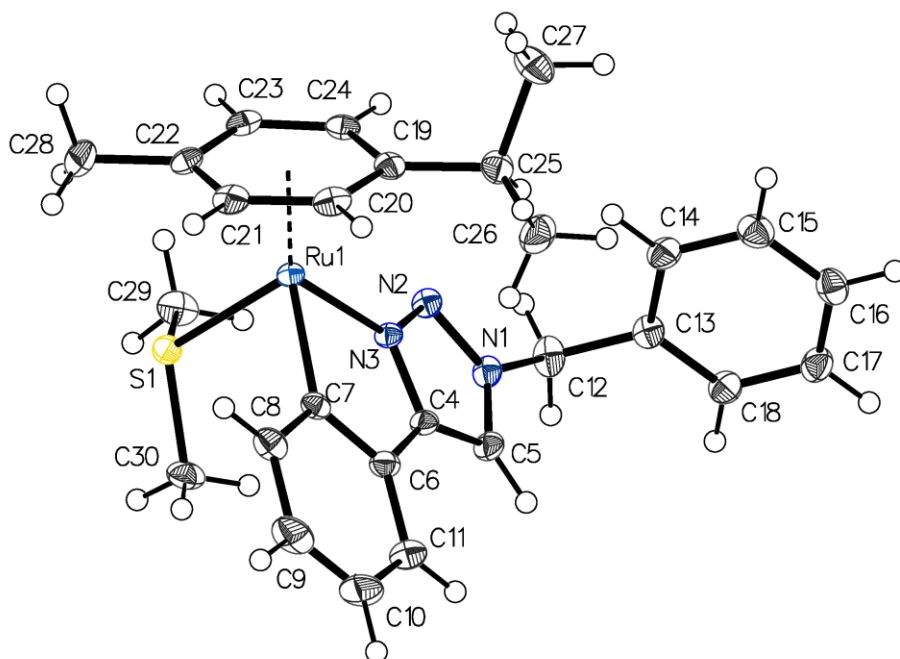


Figure S9 Crystal structure of **3a**, drawn with 50% displacement ellipsoids, the counterion is omitted for clarity.

Table S11 Sample and crystal data of **2e**.

Chemical formula	C ₂₇ H ₃₂ N ₄ O ₃ RuS		Crystal system	triclinic	
Formula weight (g/mol)	593.69		Space group	P-1	
Temperature (K)	100		Z	2	
Measurement method	\f and \w scans		Volume (Å ³)	1427.31(14)	
Radiation wavelength (Å)	MoK _α (λ = 0.71073)		Unit cell dimensions (Å) and (°)	9.8204(5)	98.178(2)
Crystal size (mm ³)	0.12 × 0.08 × 0.03			11.5773(6)	107.253(2)
Crystal habit	Clear yellow block			15.0588(9)	113.792(2)
Density (calculated) (g/cm ³)	1.381		Absorption coefficient (mm ⁻¹)	0.656	
Abs. correction T _{min}	0.6449		Abs. correction T _{max}	0.7460	
Abs. correction type	multi-scan		F(000) (e ⁻)	612	

Table S12 Data collection and structure refinement parameters of **2e**.

Index ranges	-13 ≤ h ≤ 13 -16 ≤ k ≤ 16 -21 ≤ l ≤ 21	Theta range for data collection (°)	4.652 to 60.172	
Reflections number	39743	Data / restraints / parameters	8364 / 0 / 339	
Refinement method	Least squares	Final R indices	all data	R ₁ = 0.0338 wR ₂ = 0.0865
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$		I > 2σ(I)	R ₁ = 0.0319 wR ₂ = 0.0851
Goodness-of-fit on F ²	1.09	Weighting scheme	w = 1/[s ² (F _o ²) + (0.0482P) ² + 1.1984P] where P = (F _o ² + 2F _c ²)/3	
Largest diff. peak and hole [e Å ⁻³]	1.61 / -1.48			

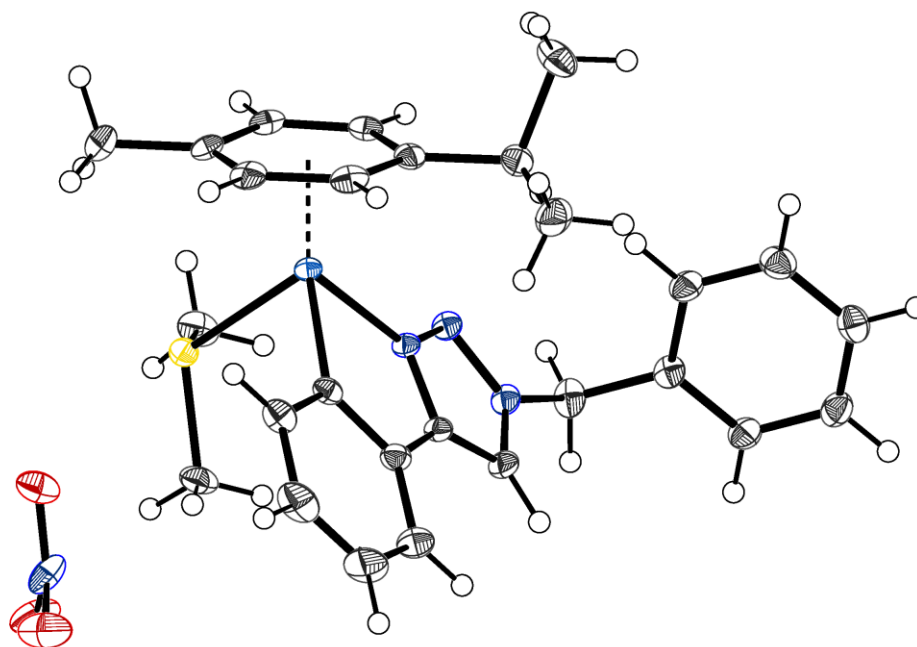


Figure S10 Asymmetric unit of **3a**, drawn with 50% displacement ellipsoids. Disordered solution (nitrate) was omitted for clarity and solvent available void was cut. Details on the excluded volume can be found in the cif code (_refine_special_details & _shelx_fab_file)

4. Stability in aqueous solution

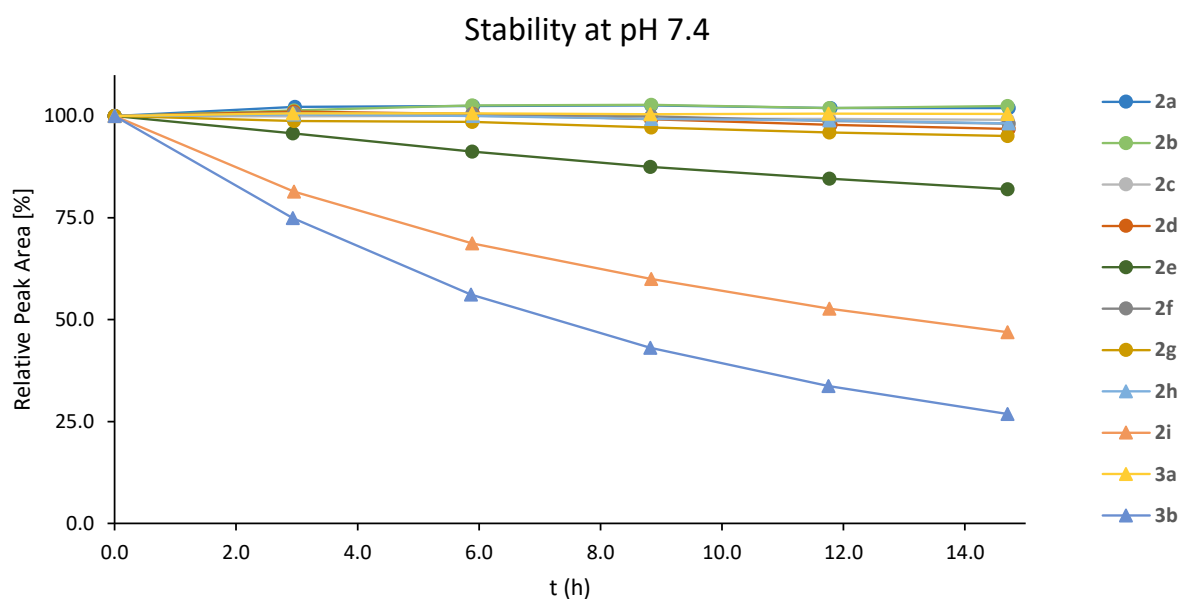


Figure S11 Stability of complexes (50 μ M) in 1% DMF/phosphate buffer (40 mM, pH 7.4), expressed as relative decrease of the analyte peak area over time in uHPLC runs.

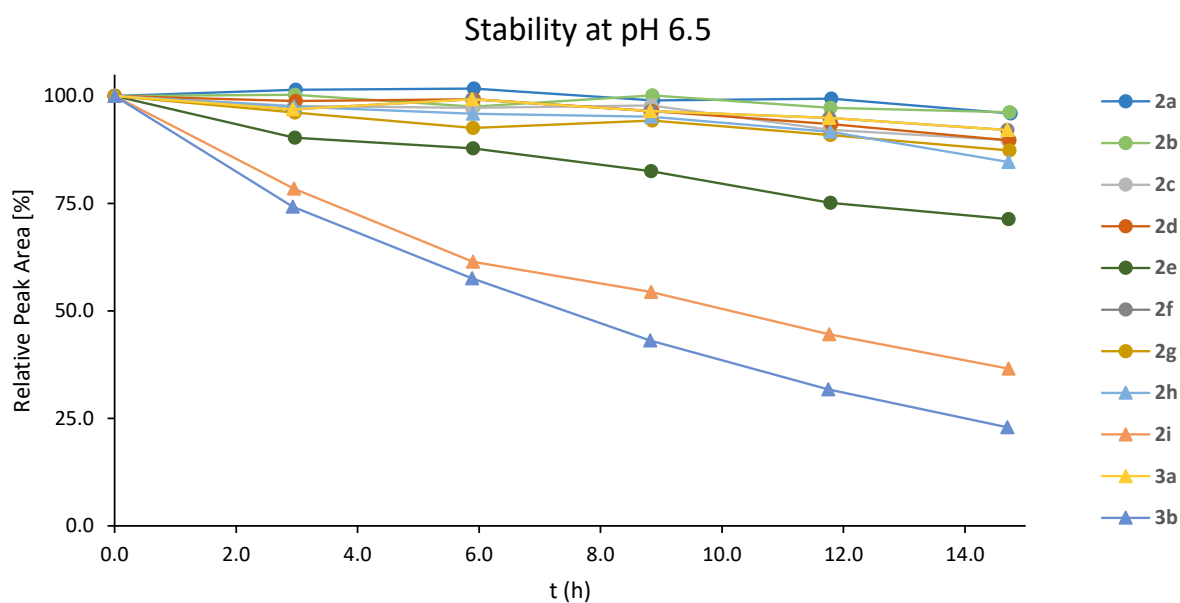


Figure S12 Stability of complexes (50 μ M) in 1% DMF/phosphate buffer (40 mM, pH 6.5), expressed as relative decrease of the analyte peak area over time in uHPLC runs.

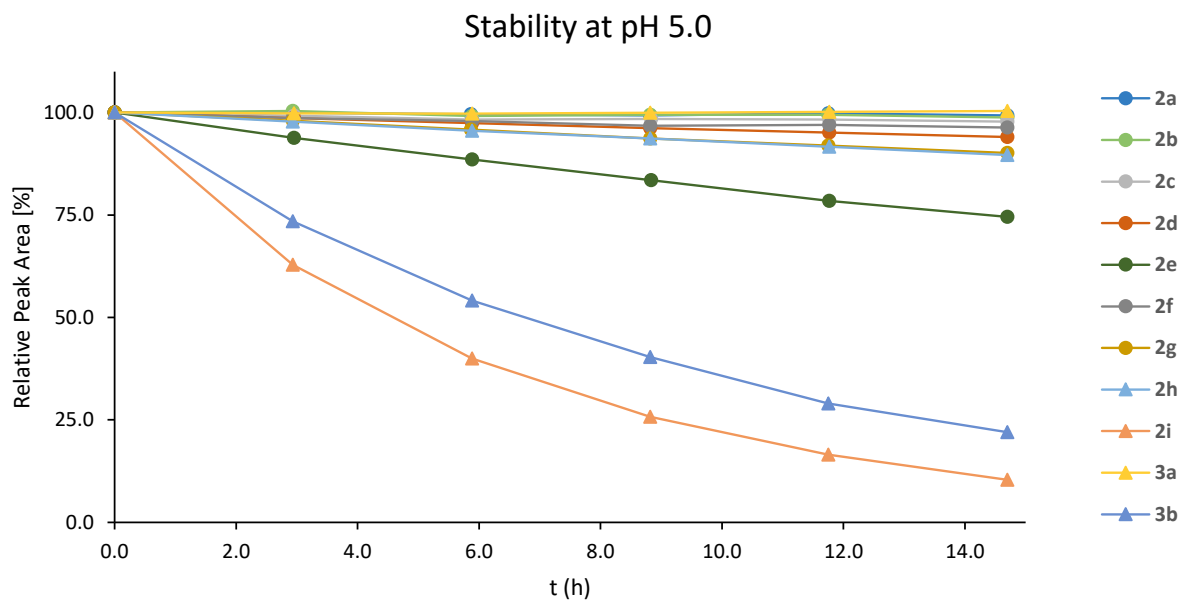


Figure S13 Stability of complexes (50 μ M) in 1% DMF/ammonium acetate buffer (40 mM, pH 5.0), expressed as relative decrease of the analyte peak area over time in uHPLC runs.

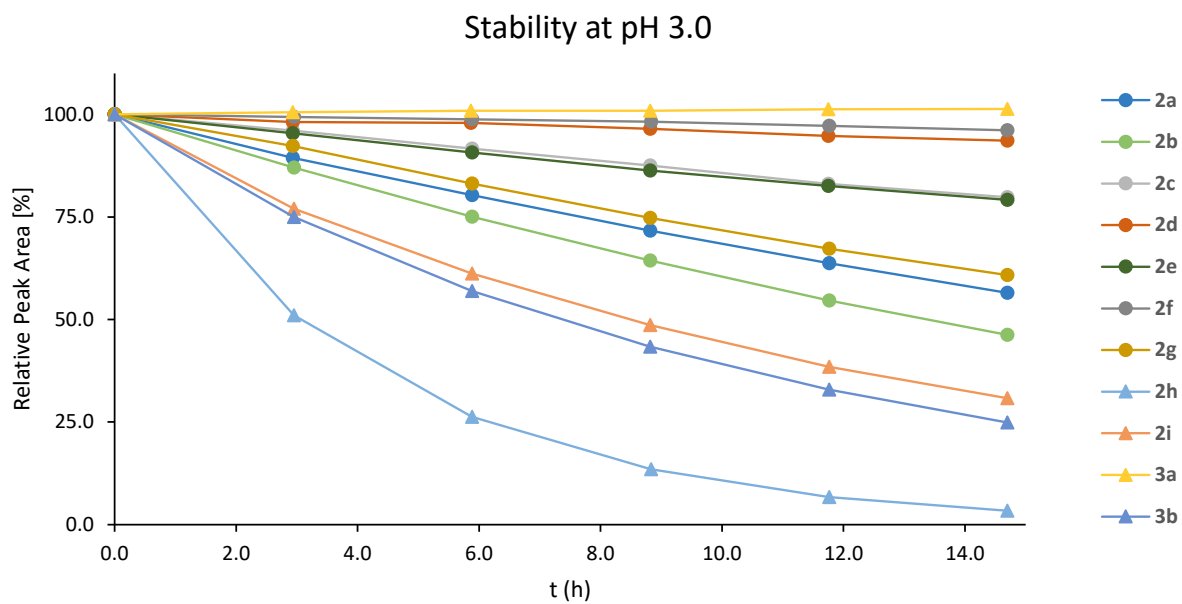


Figure S14 Stability of complexes (50 μ M) in 1% DMF/phosphate buffer (40 mM, pH 3.0), expressed as relative decrease of the analyte peak area over time in uHPLC runs.

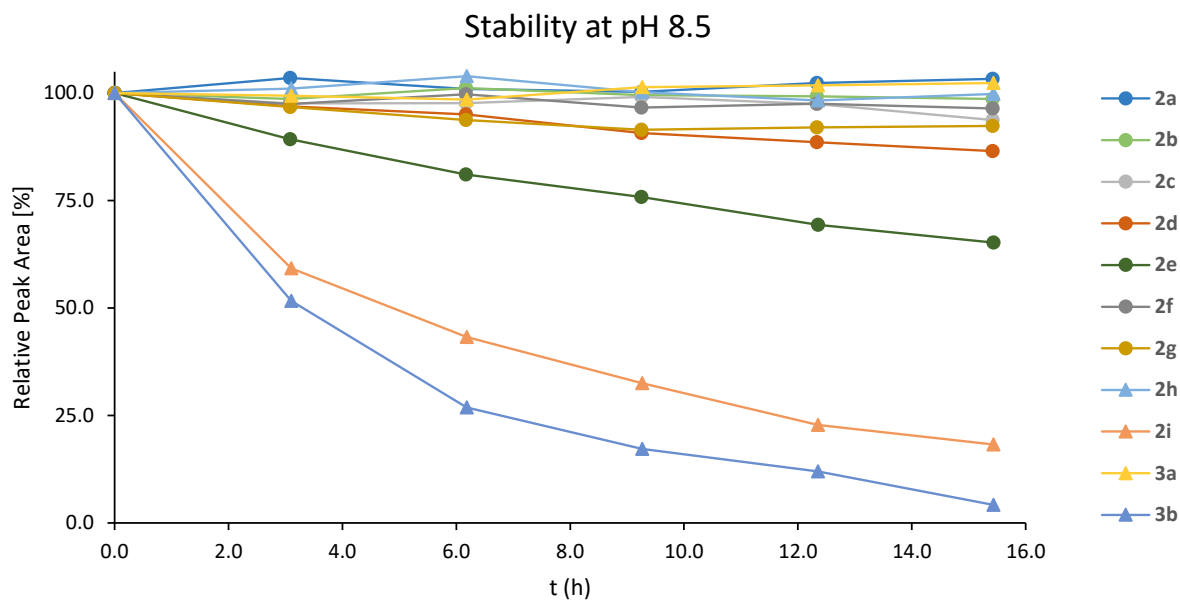


Figure S15 Stability of complexes (50 μ M) in 1% DMF/phosphate buffer (40 mM, pH 8.5), expressed as relative decrease of the analyte peak area over time in HPLC runs.

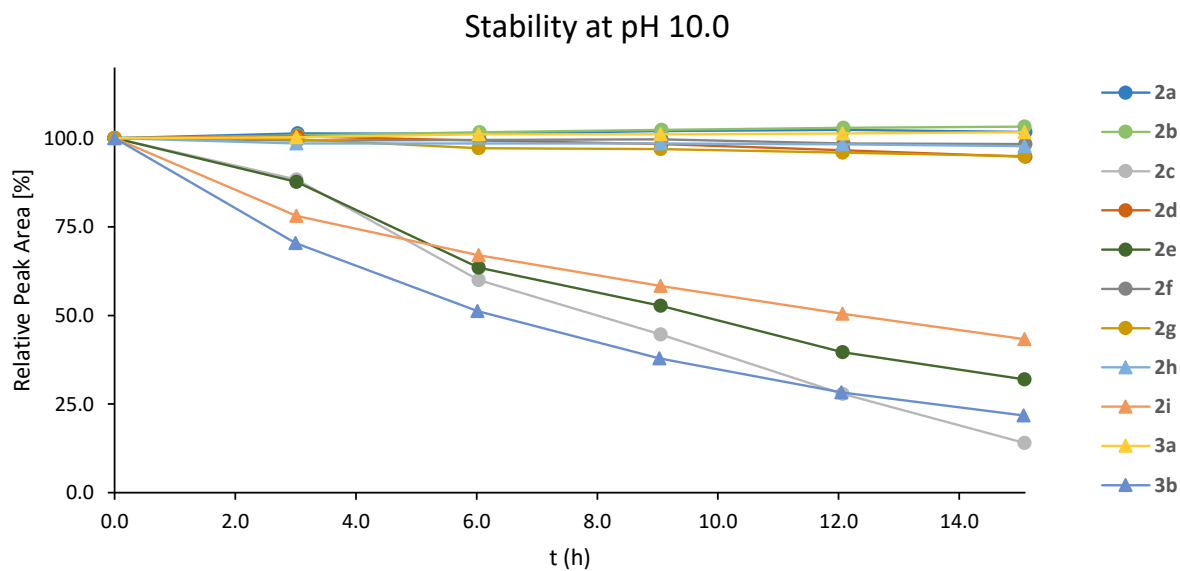


Figure S16 Stability of complexes (50 μ M) in 1% DMF/phosphate buffer (40 mM, pH 10.0), expressed as relative decrease of the analyte peak area over time in uHPLC runs.

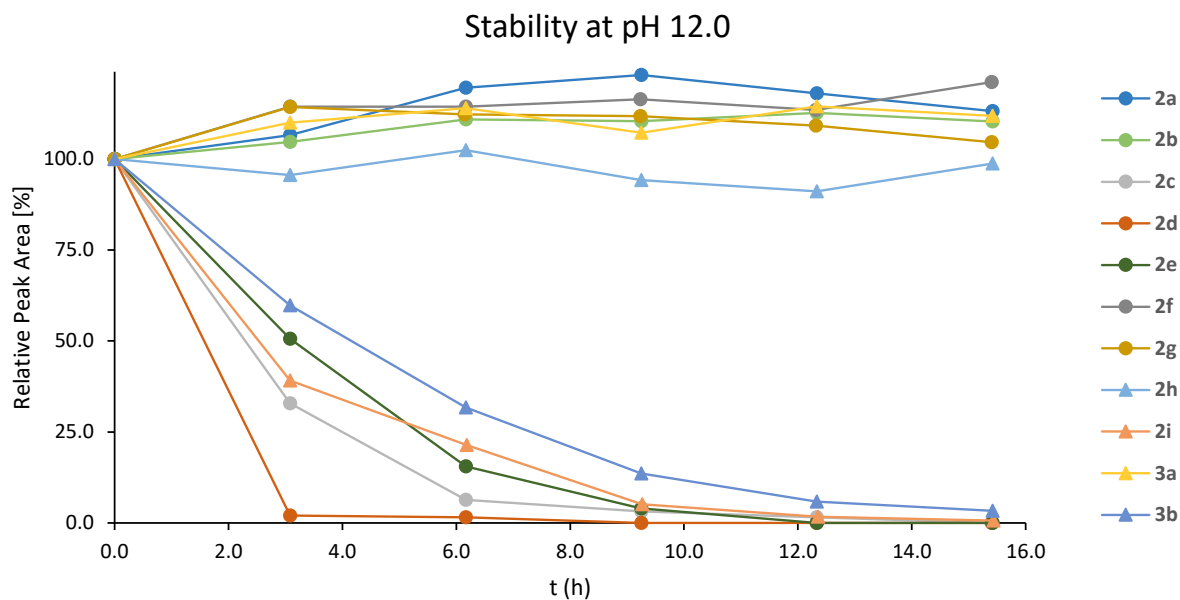


Figure S17 Stability of complexes (50 μ M) in 1% DMF/phosphate buffer (40 mM, pH 12.0), expressed as relative decrease of the analyte peak area over time in HPLC runs.

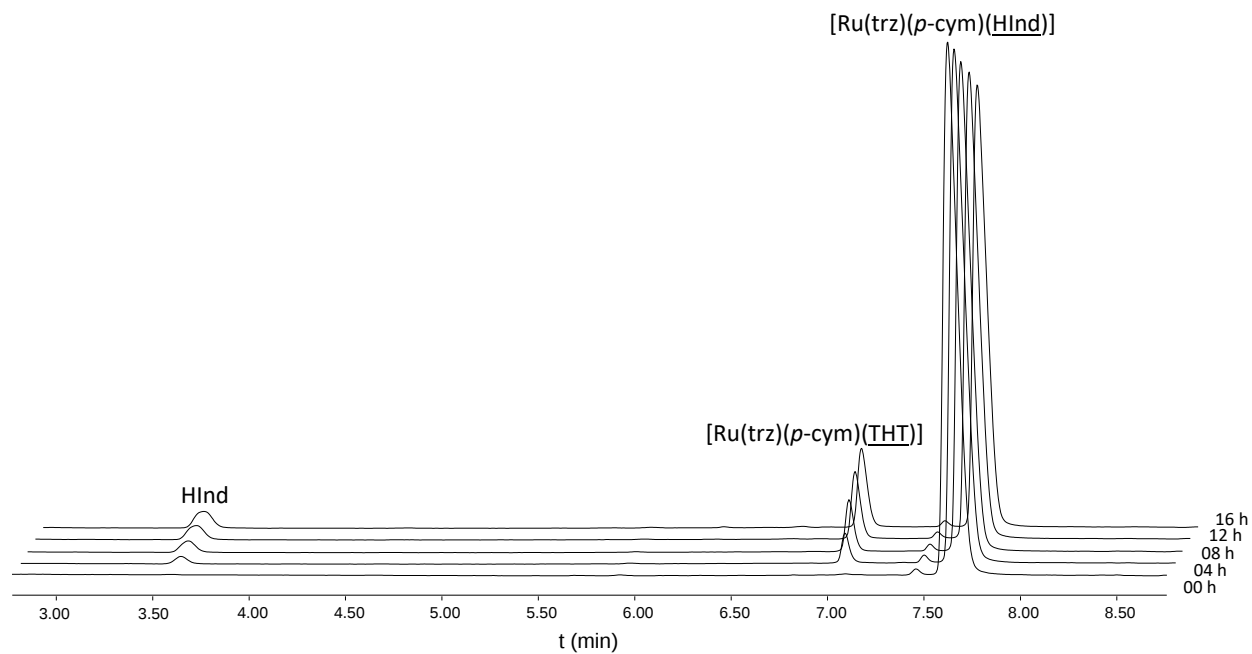


Figure S18 Overlay of HPLC runs of **2e** (50 μ M in 1% DMF / 40 mM phosphate buffer at pH 3.0) incubated with 10 eq THT collected over 16 h in uHPLC runs.

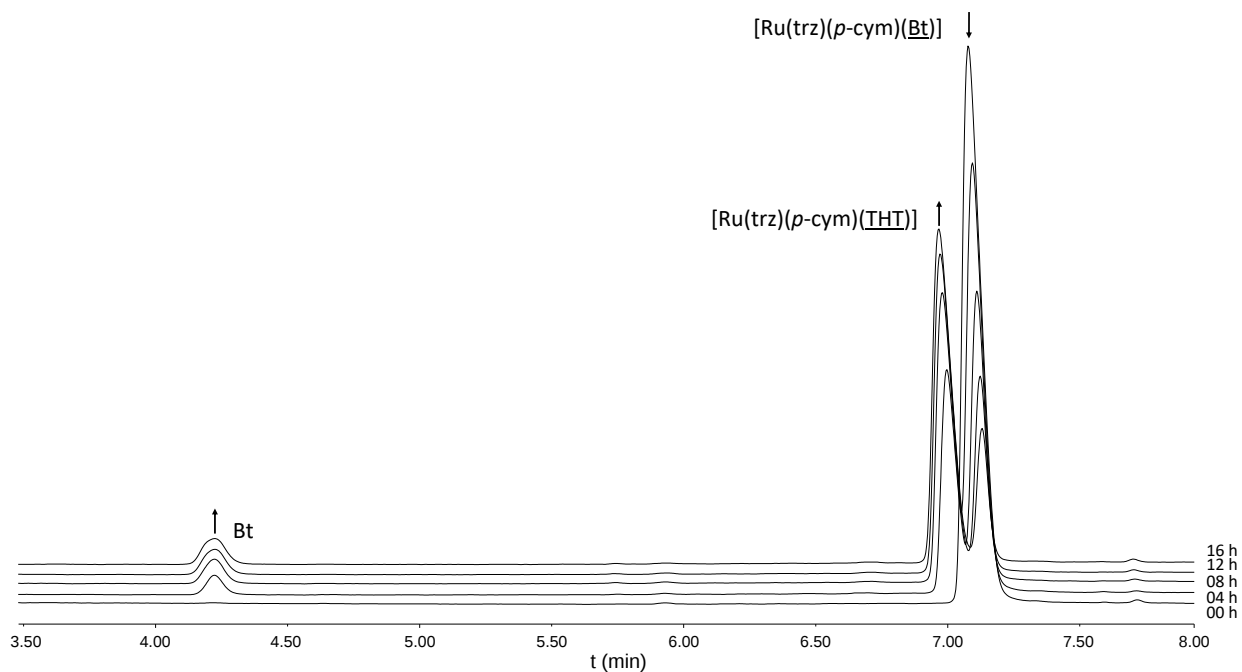


Figure S19 Overlay of uHPLC runs of **2i** (50 μM in 1% DMF / 40 mM phosphate buffer at pH 3.0) incubated with 10 eq THT collected over 16 h.

5. Oxidation of **3a**

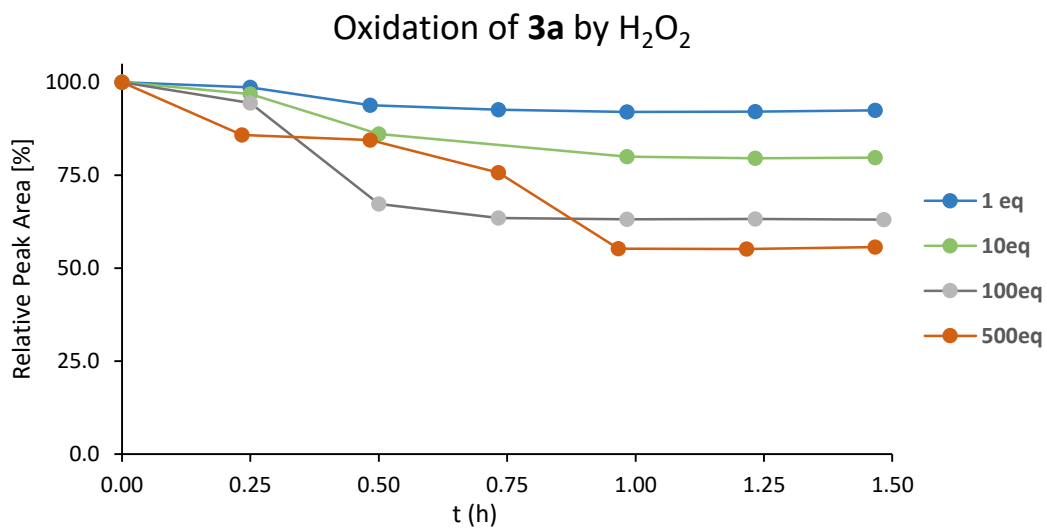


Figure S20 Oxidation of **3a** (50 μM) by hydrogen peroxide in 4 different concentrations to in 1% DMF/phosphate buffer (40 mM, pH 7.4), expressed as relative decrease of the analyte peak area over time in uHPLC runs.

6. Amino acid binding studies

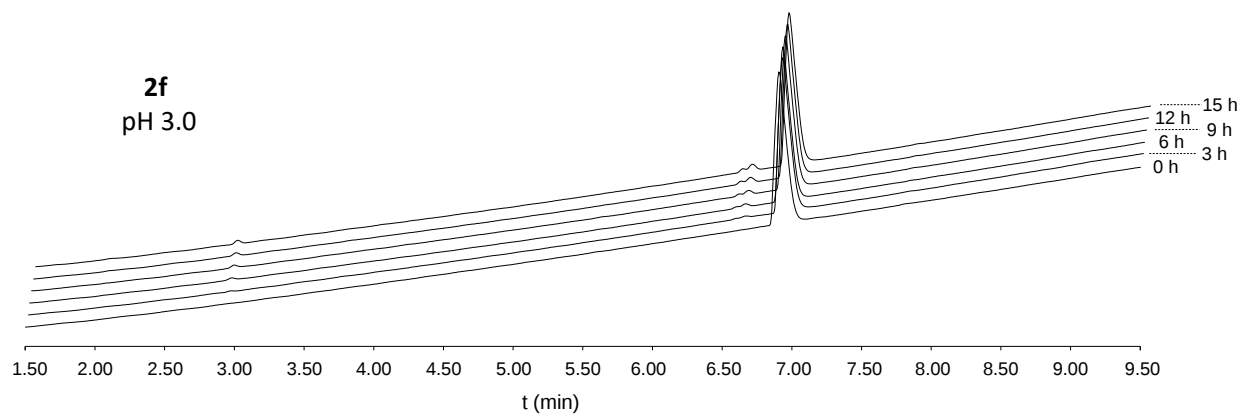


Figure S21 Overlaid uHPLC chromatograms of **2f** (50 μM) incubated with *N*-Ac-His, *N*-Ac-Met, and *N*-Ac-Cys (500 μM each) at pH 3.0 collected over 15 h.

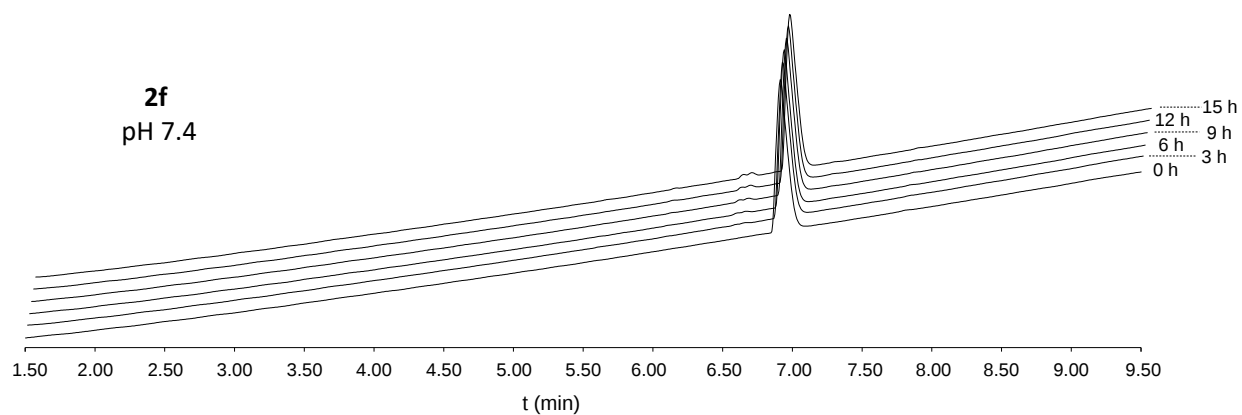


Figure S22 Overlaid uHPLC chromatograms of **2f** (50 μM) incubated with *N*-Ac-His, *N*-Ac-Met, and *N*-Ac-Cys (500 μM each) at pH 7.4 collected over 15 h.

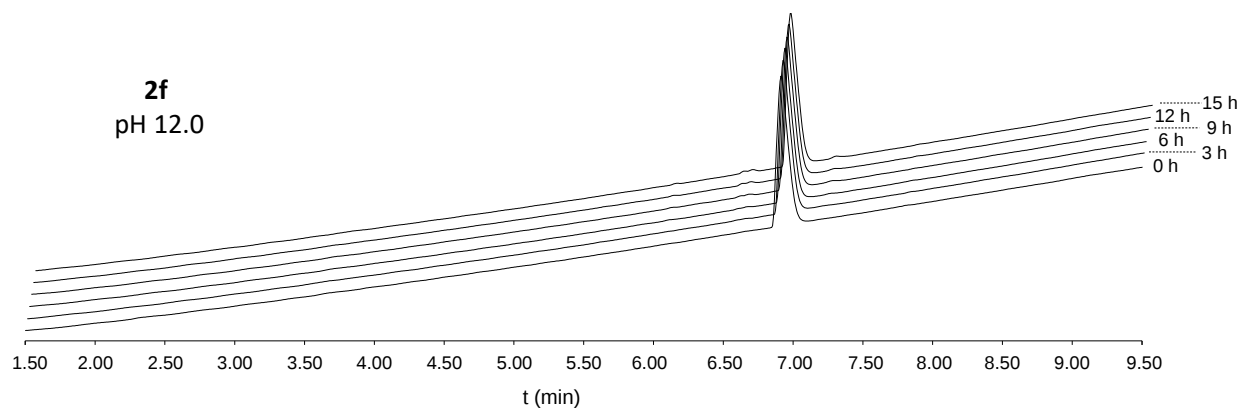


Figure S23 Overlaid uHPLC chromatograms of **2f** (50 μ M) incubated with *N*-Ac-His, *N*-Ac-Met, and *N*-Ac-Cys (500 μ M each) at pH 12.0 collected over 15 h.

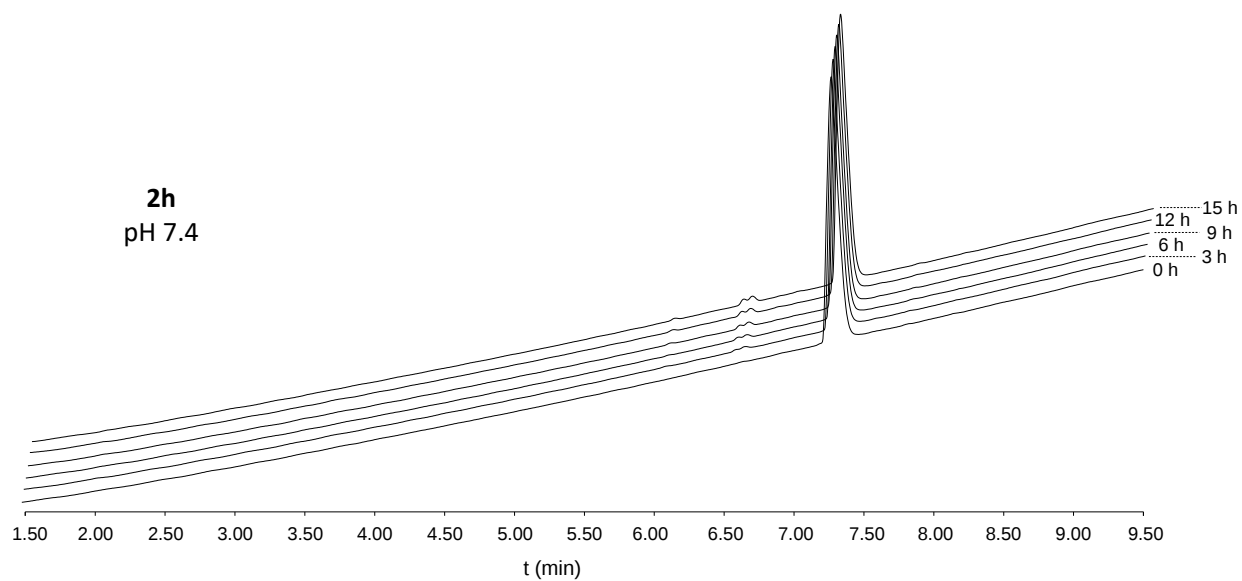


Figure S24 Overlaid uHPLC chromatograms of **2h** (50 μ M) incubated with *N*-Ac-His, *N*-Ac-Met, and *N*-Ac-Cys (500 μ M each) at pH 7.4 collected over 15 h.

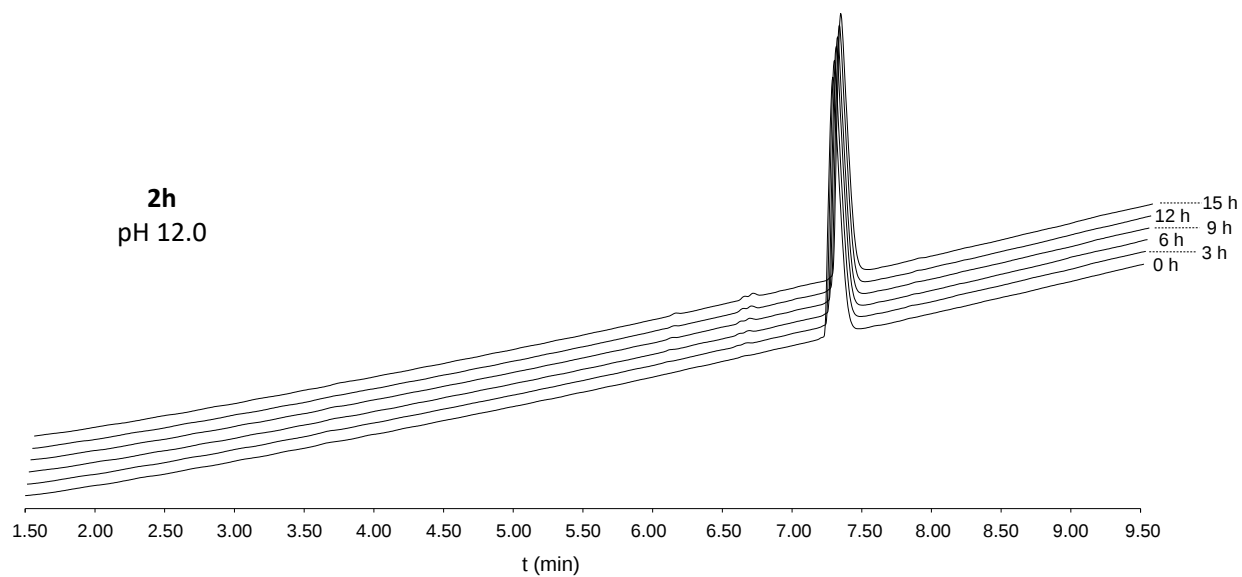


Figure S25 Overlaid uHPLC chromatograms of **2h** (50 μ M) incubated with *N*-Ac-His, *N*-Ac-Met, and *N*-Ac-Cys (500 μ M each) at pH 12.0 collected over 15 h.

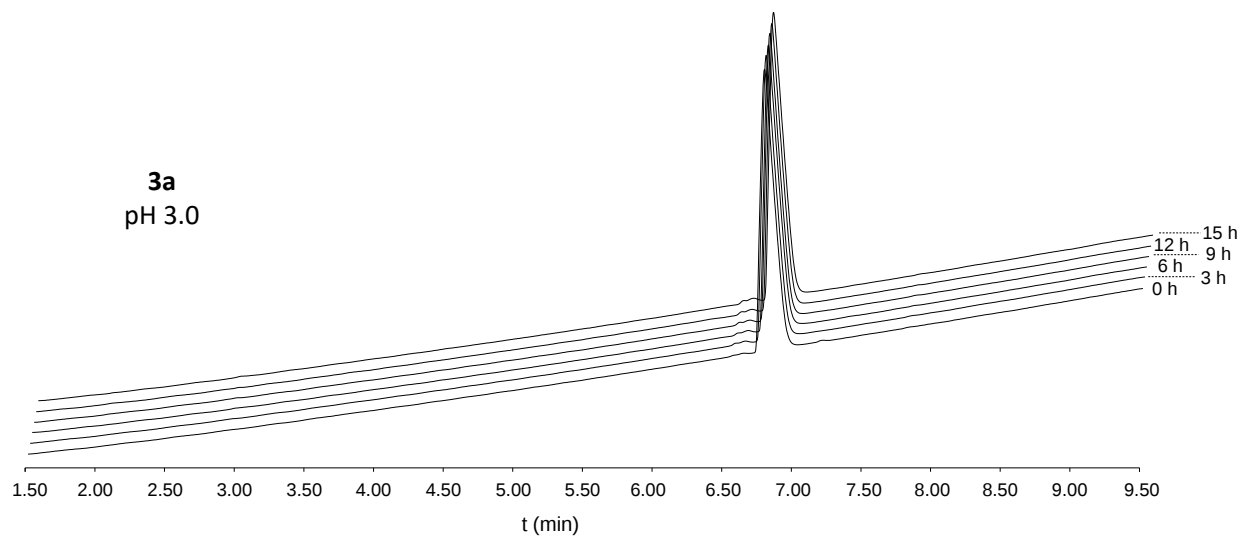


Figure S26 Overlaid uHPLC chromatograms of **3a** (50 μ M) incubated with *N*-Ac-His, *N*-Ac-Met, and *N*-Ac-Cys (500 μ M each) at pH 3.0 collected over 15 h.

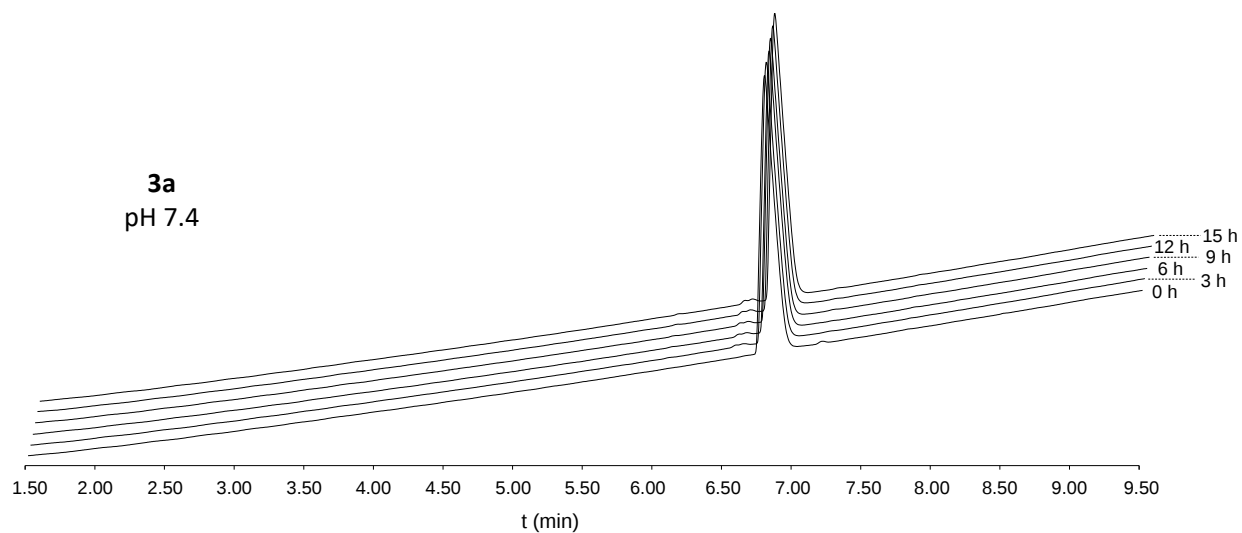


Figure S27 Overlaid uHPLC chromatograms of **3a** (50 μ M) incubated with *N*-Ac-His, *N*-Ac-Met, and *N*-Ac-Cys (500 μ M each) at pH 7.4 collected over 15 h.

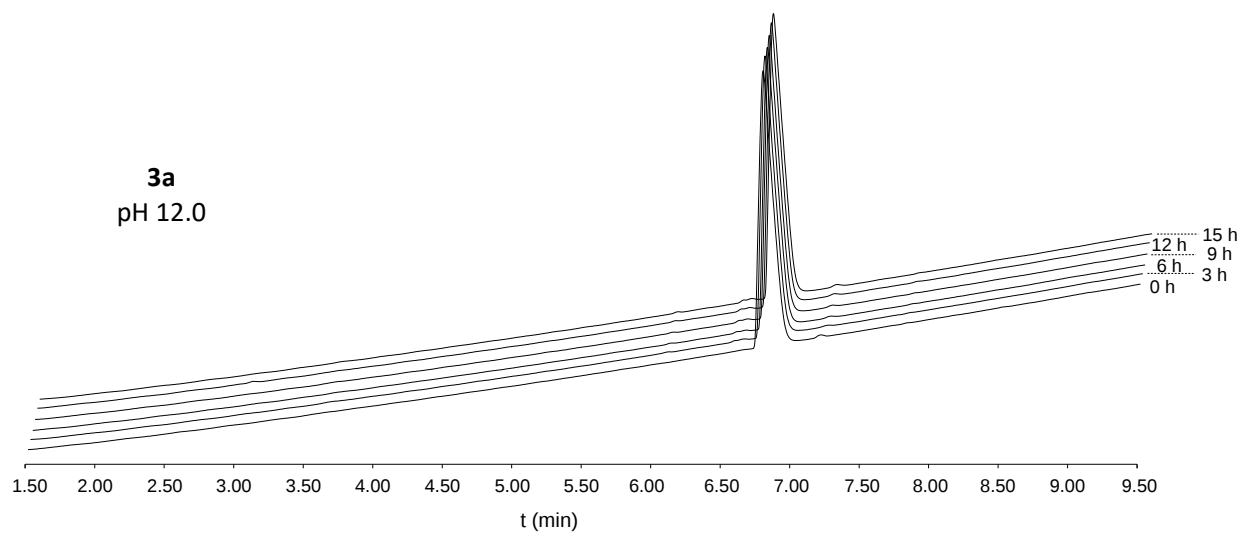


Figure S28 Overlaid uHPLC chromatograms of **3a** (50 μ M) incubated with *N*-Ac-His, *N*-Ac-Met, and *N*-Ac-Cys (500 μ M each) at pH 12.0 collected over 15 h.

7. Chromatographic lipophilicity index φ_0

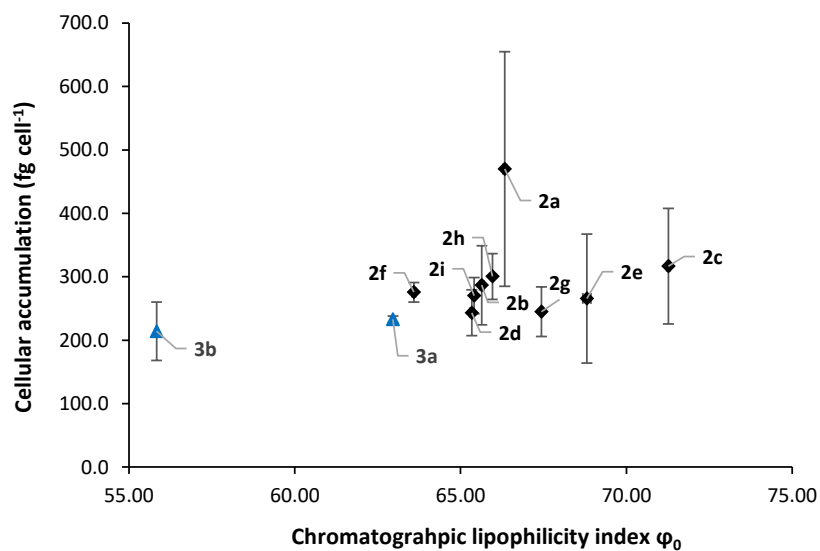


Figure S29 Scatter plot of chromatographic lipophilicity index φ_0 and cellular accumulation in SW480 cells.

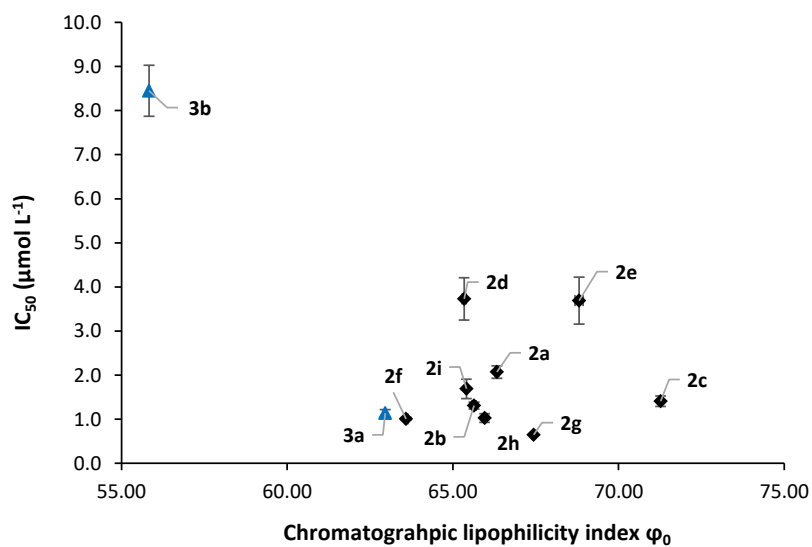


Figure S30 Scatter plot of chromatographic lipophilicity index φ_0 and 50% inhibitory concentration in SW480 cells.

8. ROS generation

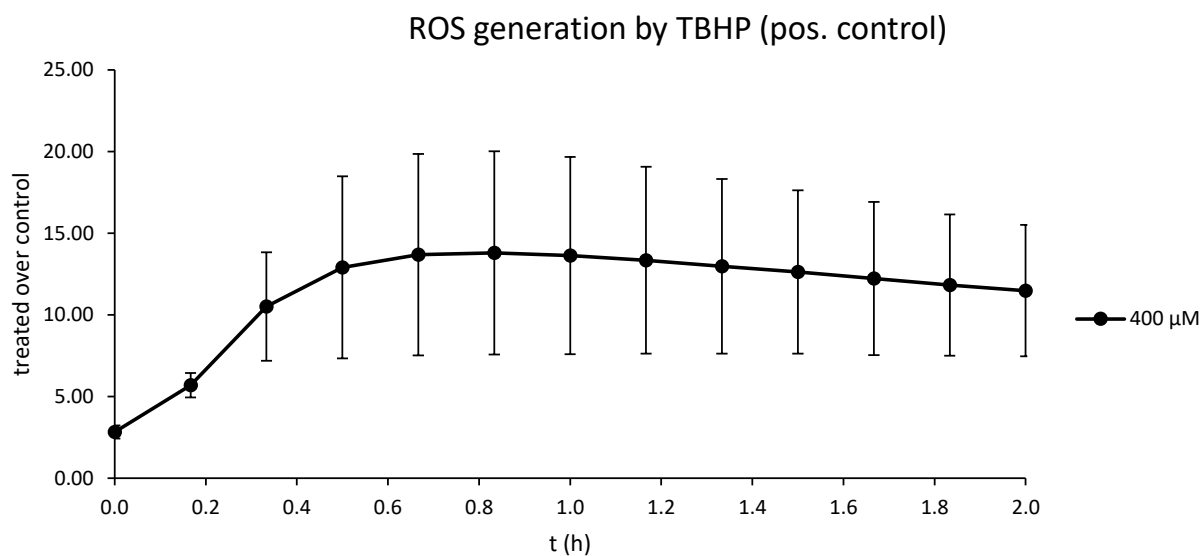


Figure S31 Level of reactive oxygen species (ROS) upon treatment with *tert*-butyl hydroperoxide at 400 μM over 2 h compared to an untreated control.

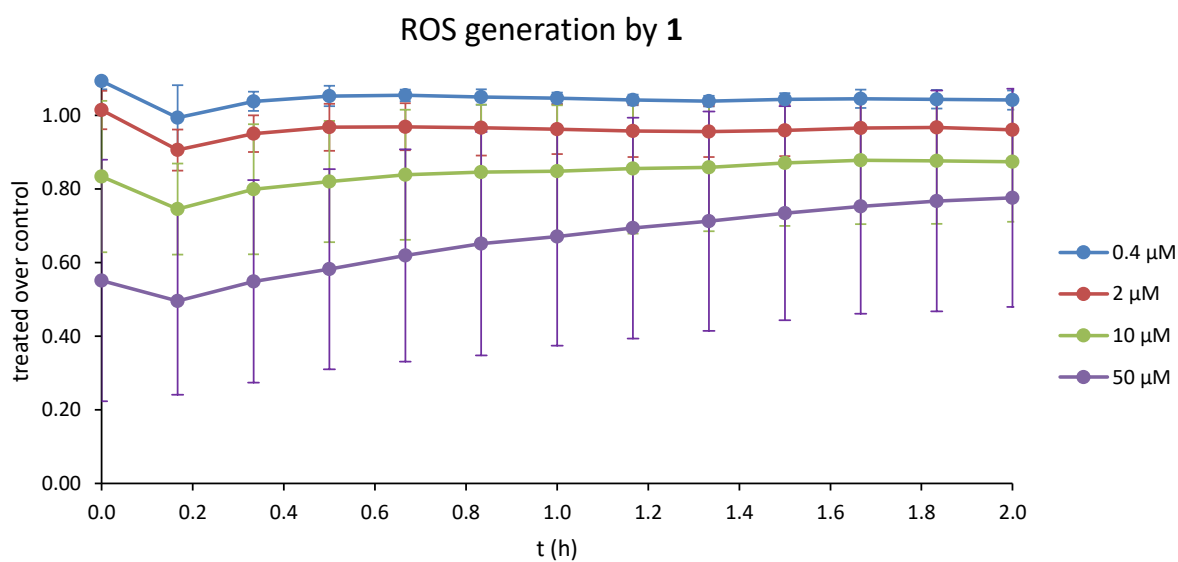


Figure S32 Level of reactive oxygen species (ROS) upon treatment with **1** at different concentrations over 2 h compared to an untreated control.

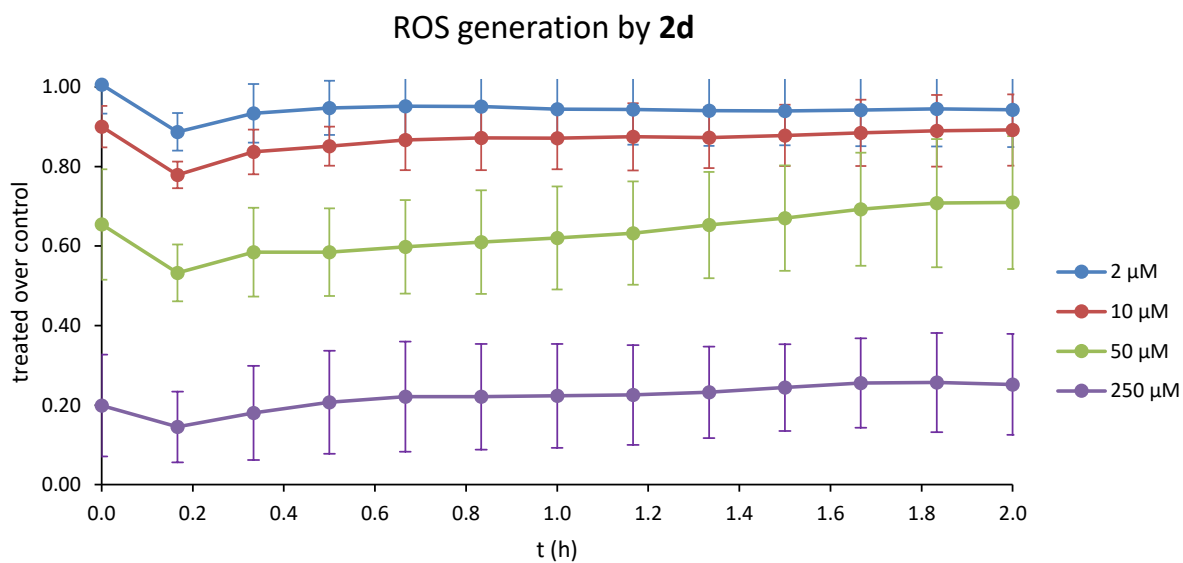


Figure S33 Level of reactive oxygen species (ROS) upon treatment with **2d** at different concentrations over 2 h compared to an untreated control.

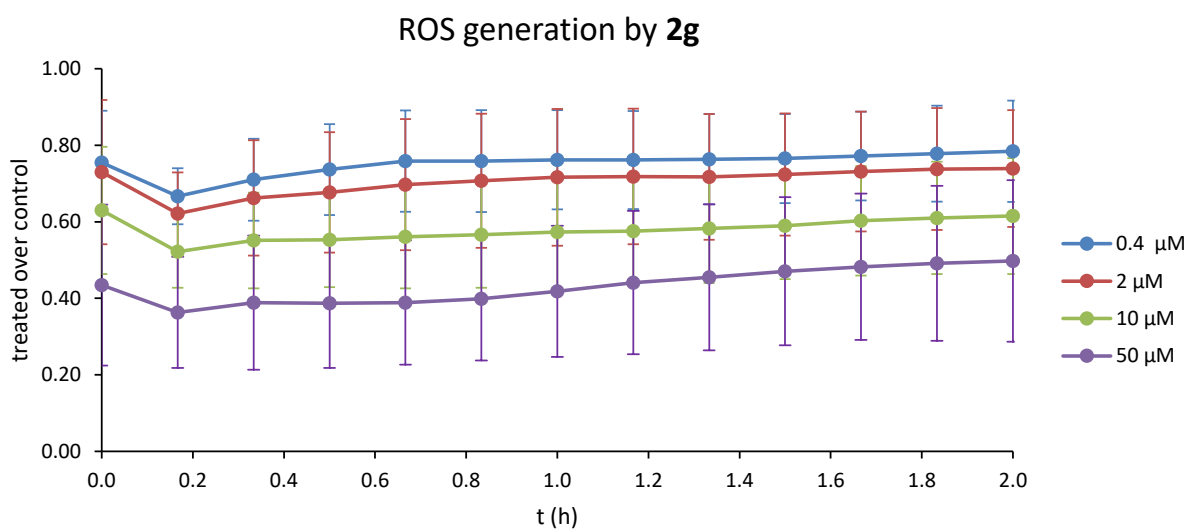


Figure S34 Level of reactive oxygen species (ROS) upon treatment with **2g** at different concentrations over 2 h compared to an untreated control.

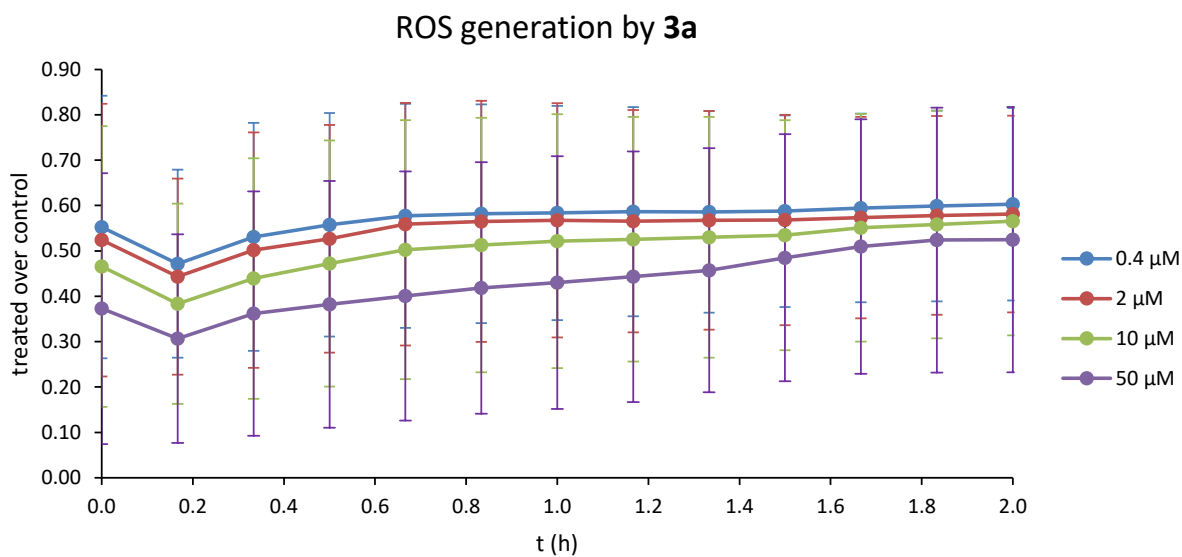


Figure S35 Level of reactive oxygen species (ROS) upon treatment with **3a** at different concentrations over 2 h compared to an untreated control.

9. Methyl green DNA intercalation assay

Table S13 Percentage of methyl green still bound to preincubated DNA after 24 of incubation with compounds **1**, **2d**, **2g**, and **3a**. Positive control doxorubicin hydrochloride: 65.5% (20 μM), 63.4% (50 μM).

Complex	Methyl green retention			
	0.08 μM	0.4 μM	2 μM	10 μM
1	96.1%	98.5%	99.1%	95.1%
2d	100.0%	99.1%	100.4%	99.9%
2g	98.7%	98.1%	100.1%	99.4%
3a	98.5%	98.8%	100.7%	99.8%

10. Flow cytometric detection of apoptotic cells

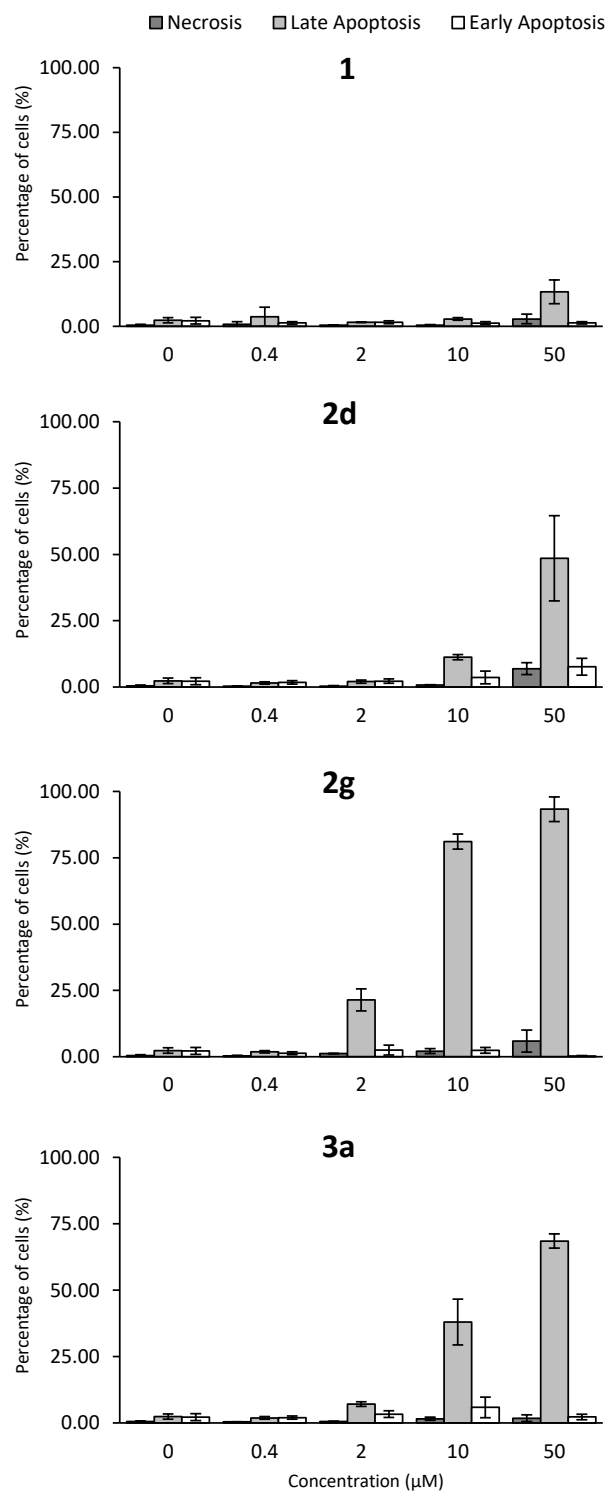


Figure S36 Induction of apoptosis/necrosis (means $\pm$ standard deviations) in SW480 24 h after treatment with **1**, **2d**, **2g**, and **3a** at 3 different concentrations and an untreated control.

11. ^1H and ^{13}C NMR spectra

11.1. $[[((3-\kappa\text{N})\text{-}1H\text{-Imidazole})(1\text{-benzyl-}4\text{-(}2'\text{-}\kappa\text{C})\text{-phenyl-}1,2,3\text{-(}3-\kappa\text{N})\text{-triazolato})(\eta^6\text{-}p\text{-cymene})\text{ruthenium(II)}]\text{ nitrate (2a)}$

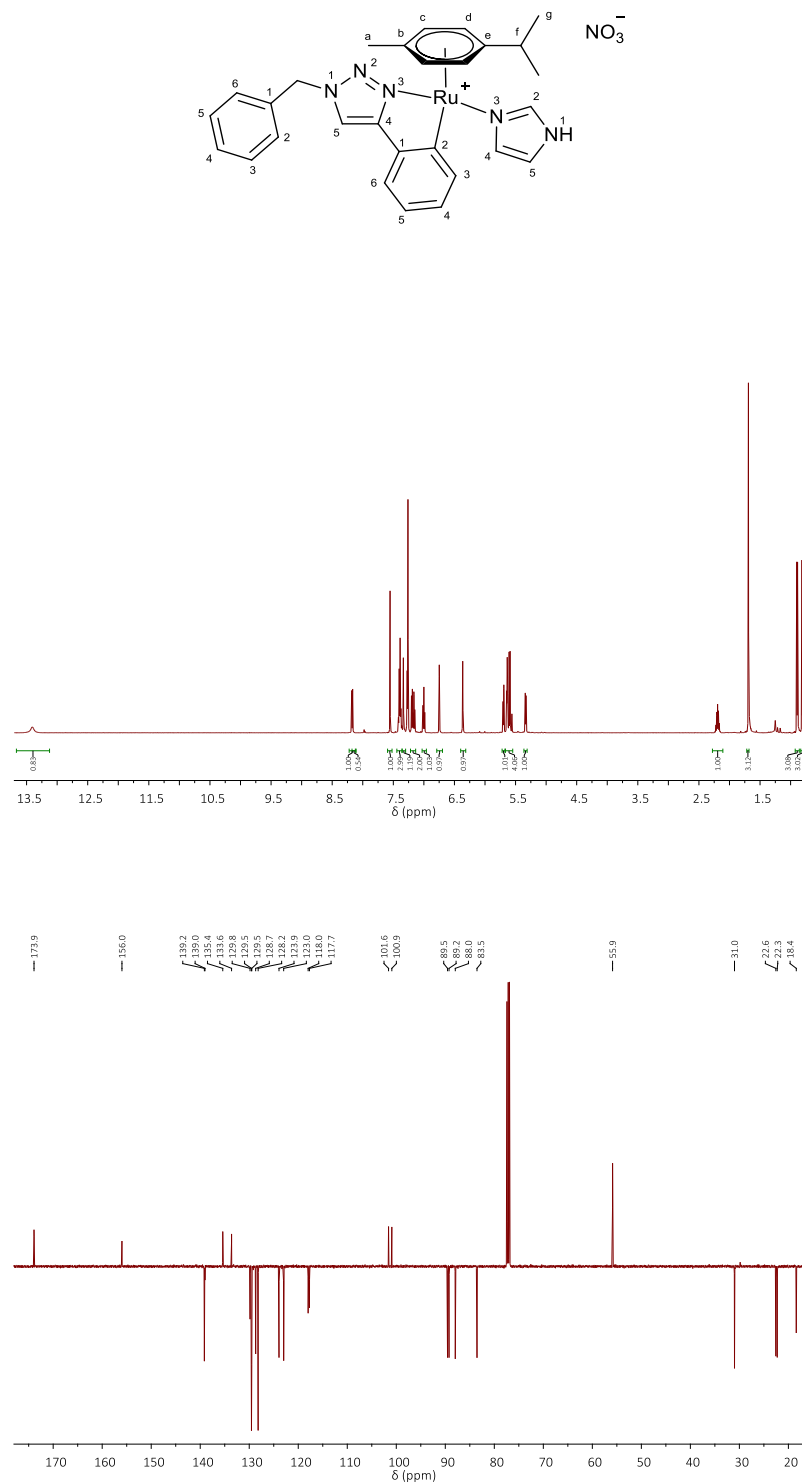


Figure S37 Numbering scheme (top), ^1H NMR (middle), and ^{13}C NMR (bottom) of **2a**.

11.2. $[[((3-\kappa N)\text{-}1\text{-Methylimidazole})(1\text{-benzyl-}4\text{-(}2'\text{-}\kappa C\text{)-phenyl-}1,2,3\text{-(}3-\kappa N\text{)-triazolato})(\eta^6\text{-}p\text{-cymene})\text{ruthenium(II)}]\text{nitrate (2b)}$

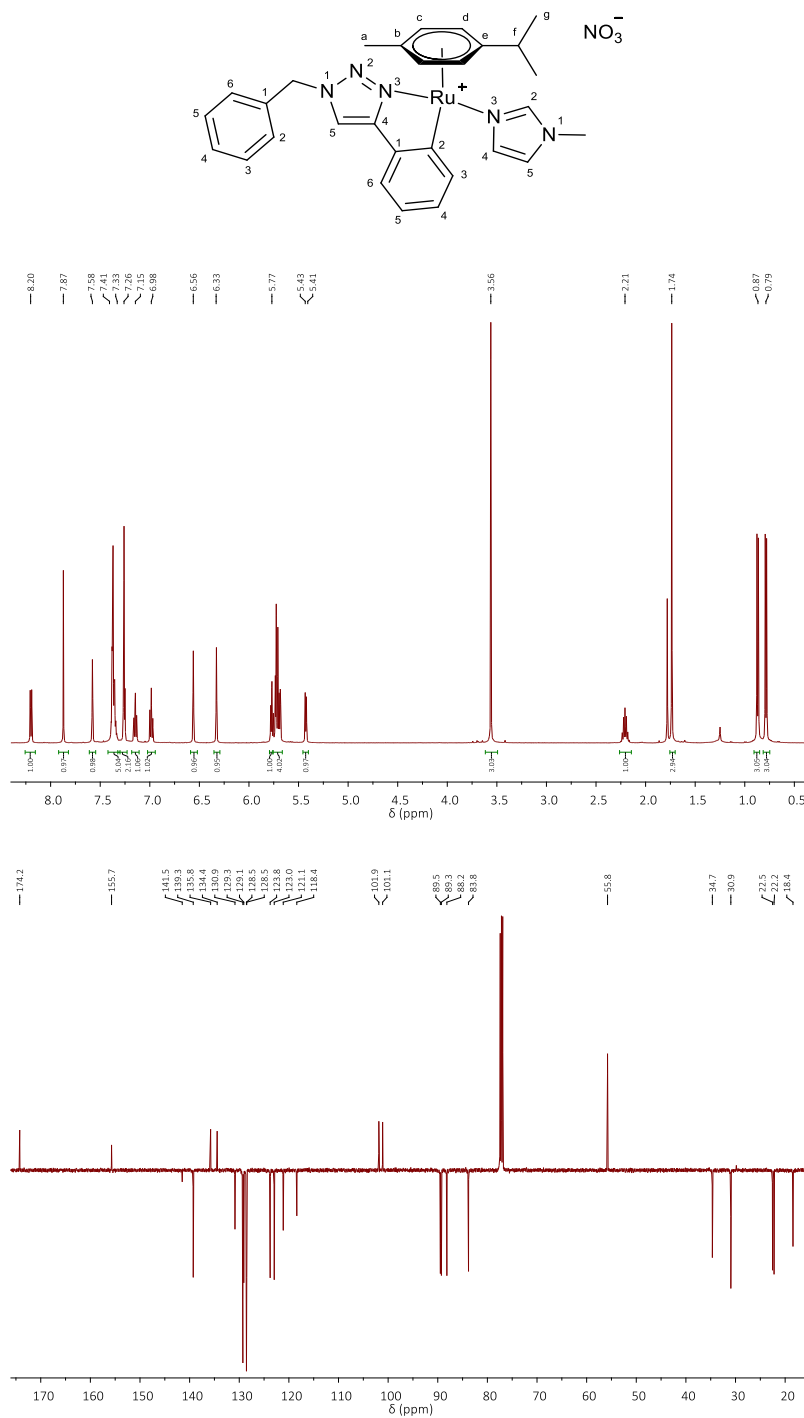


Figure S38 Numbering scheme (top), ^1H NMR (middle), and ^{13}C NMR (bottom) of **2b**.

11.3. [((3- κ N)-4-Phenylimidazole)(1-benzyl-4-(2'- κ C)-phenyl-1,2,3-(3- κ N)-triazolato)(η^6 -*p*-cymene)ruthenium(II)] nitrate (**2c**)

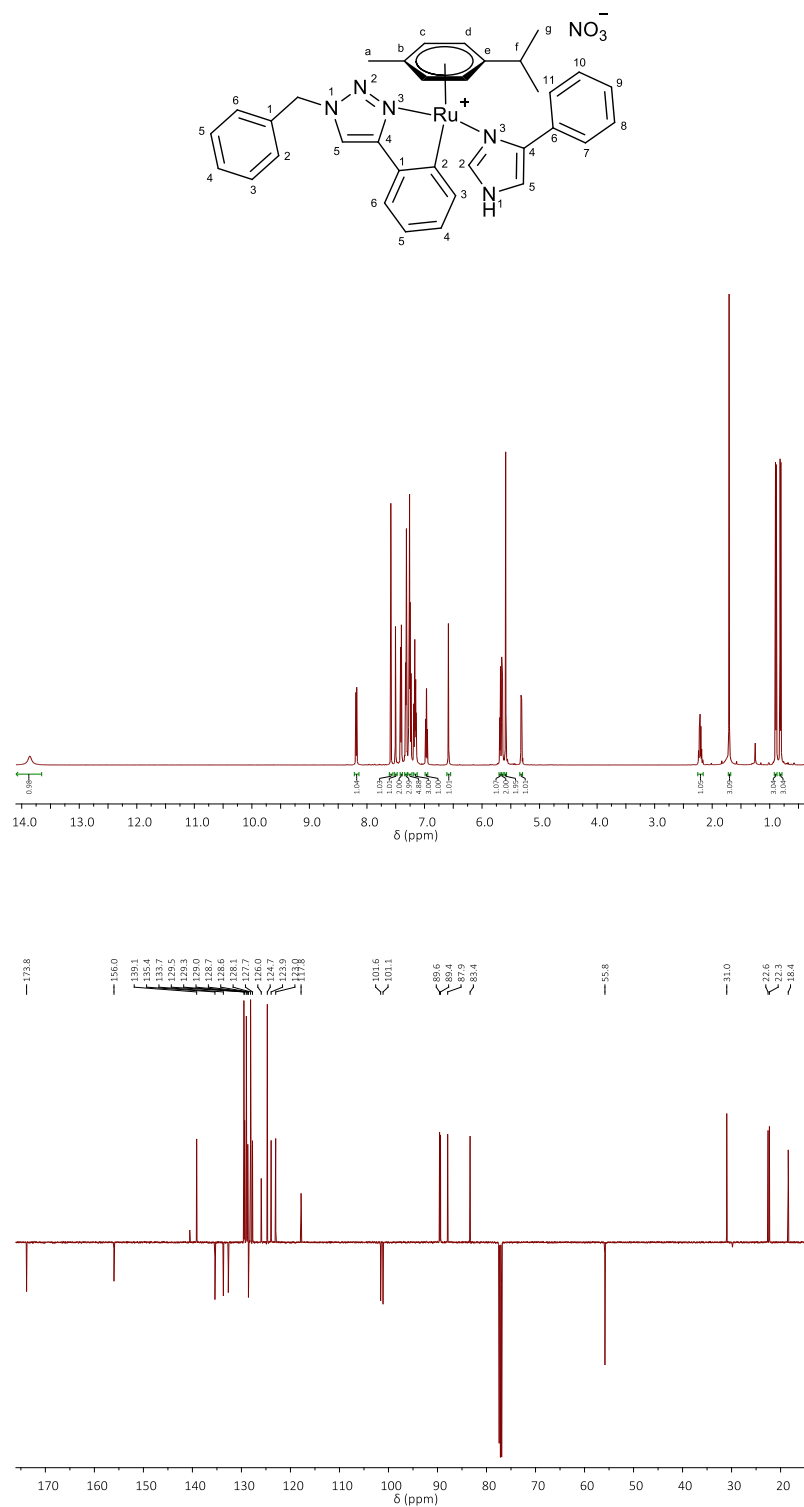


Figure S39 Numbering scheme (top), ^1H NMR (middle), and ^{13}C NMR (bottom) of **2c**.

11.4. $[[((2-\kappa N)\text{-}1H\text{-}Pyrazole)(1\text{-benzyl-}4\text{-(}2'\text{-}\kappa C\text{)-phenyl-}1,2,3\text{-(}3\text{-}\kappa N\text{)-triazolato})(\eta^6\text{-}p\text{-cymene})ruthenium(II)]\text{ nitrate (2d)}$

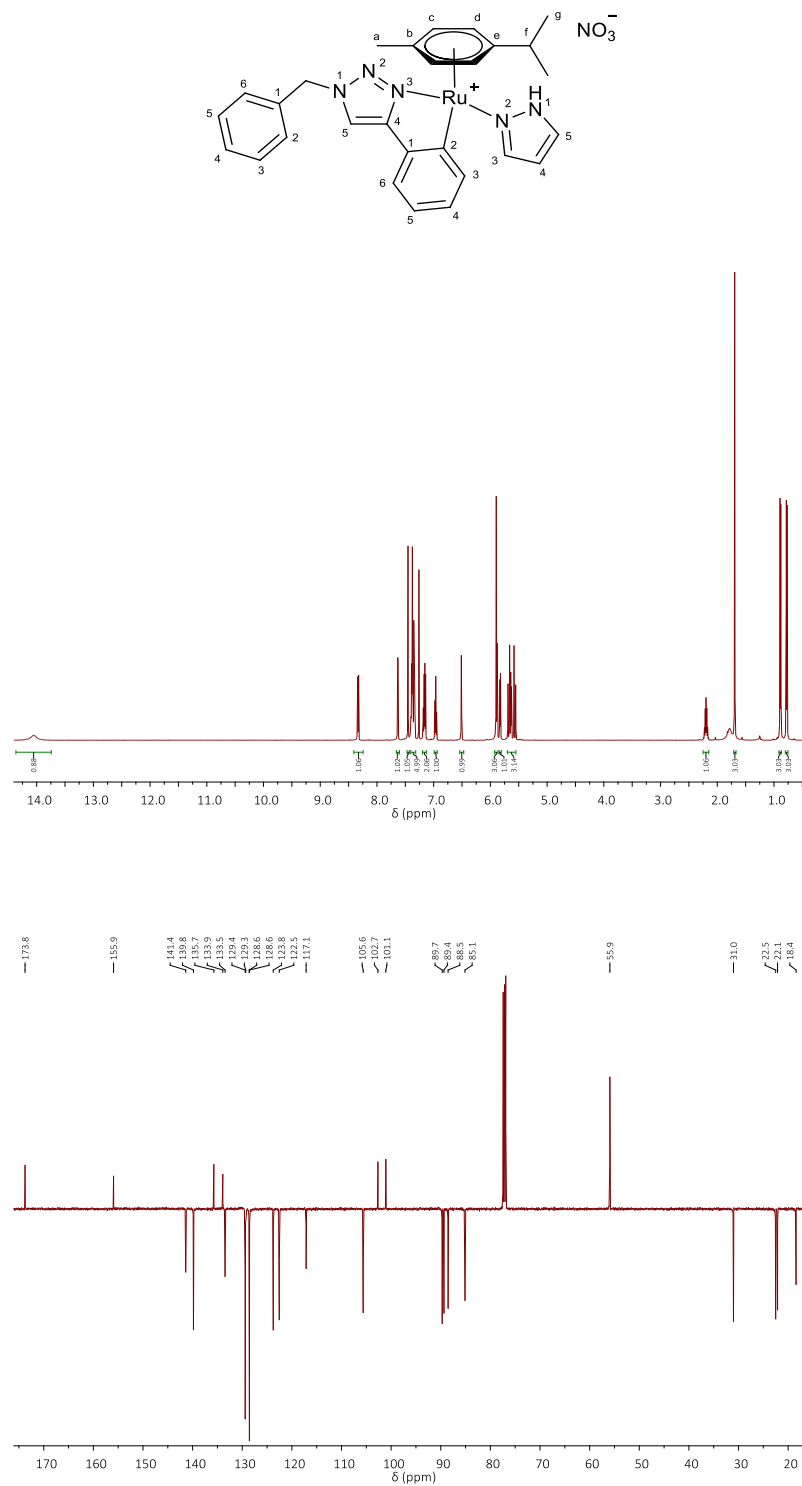


Figure S40 Numbering scheme (top), ^1H NMR (middle), and ^{13}C NMR (bottom) of **2d**.

11.5. $[[((2-\kappa N)-1H\text{-Indazole})(1\text{-benzyl-4-(2'-}\kappa C\text{)-phenyl-1,2,3-(3-}\kappa N\text{)-triazolato})(\eta^6\text{-}p\text{-cymene) ruthenium(II)] \text{ nitrate (2e)}$

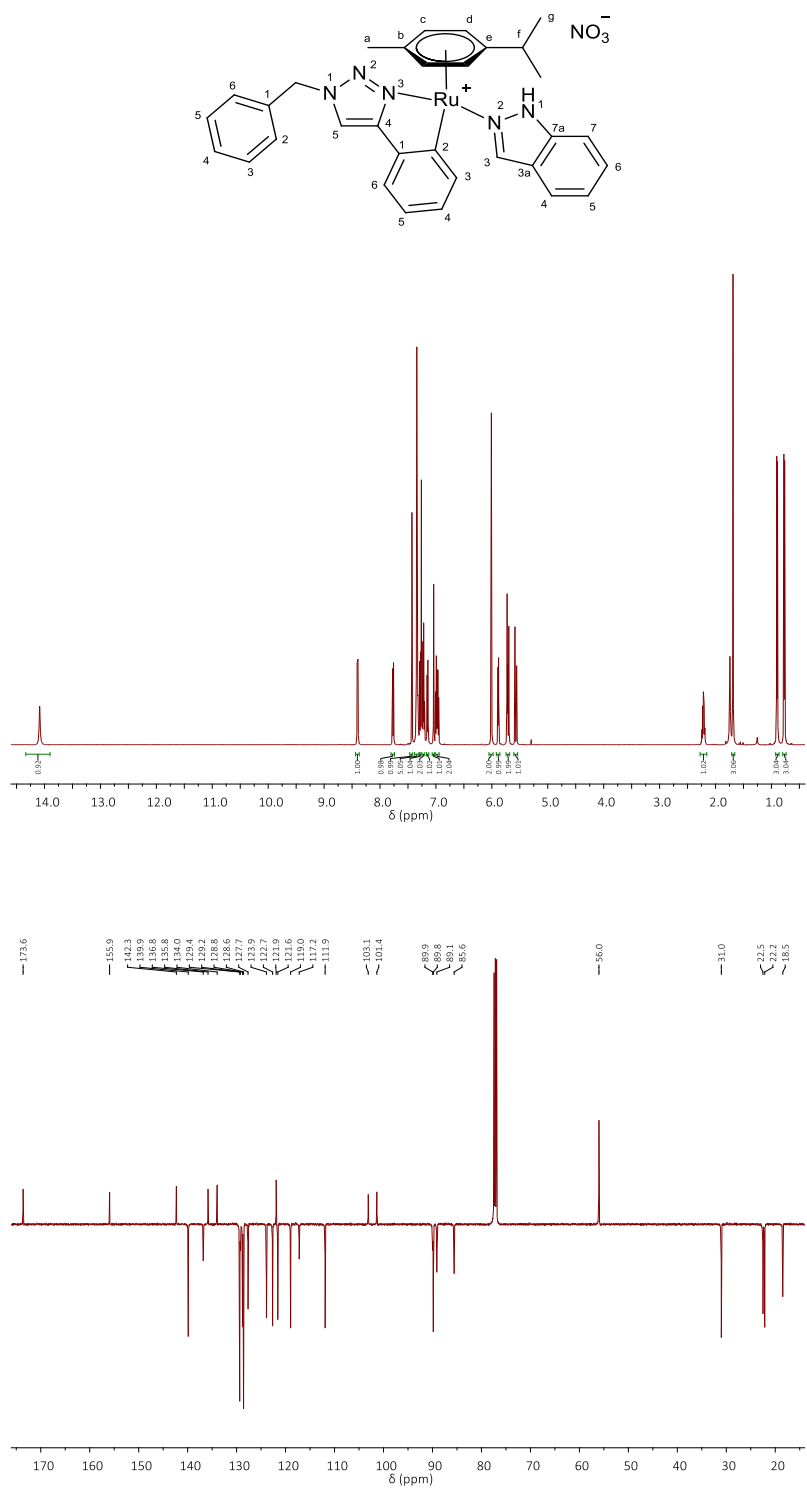


Figure S41 Numbering scheme (top), ^1H NMR (middle), and ^{13}C NMR (bottom) of **2e**.

11.6. $[(\kappa\text{N-Pyridine})(1\text{-benzyl-4-(2'-}\kappa\text{C)-phenyl-1,2,3-(3-}\kappa\text{N)-triazolato})(\eta^6\text{-}p\text{-cymene})\text{ruthenium(II)}]\text{ nitrate (2f)}$

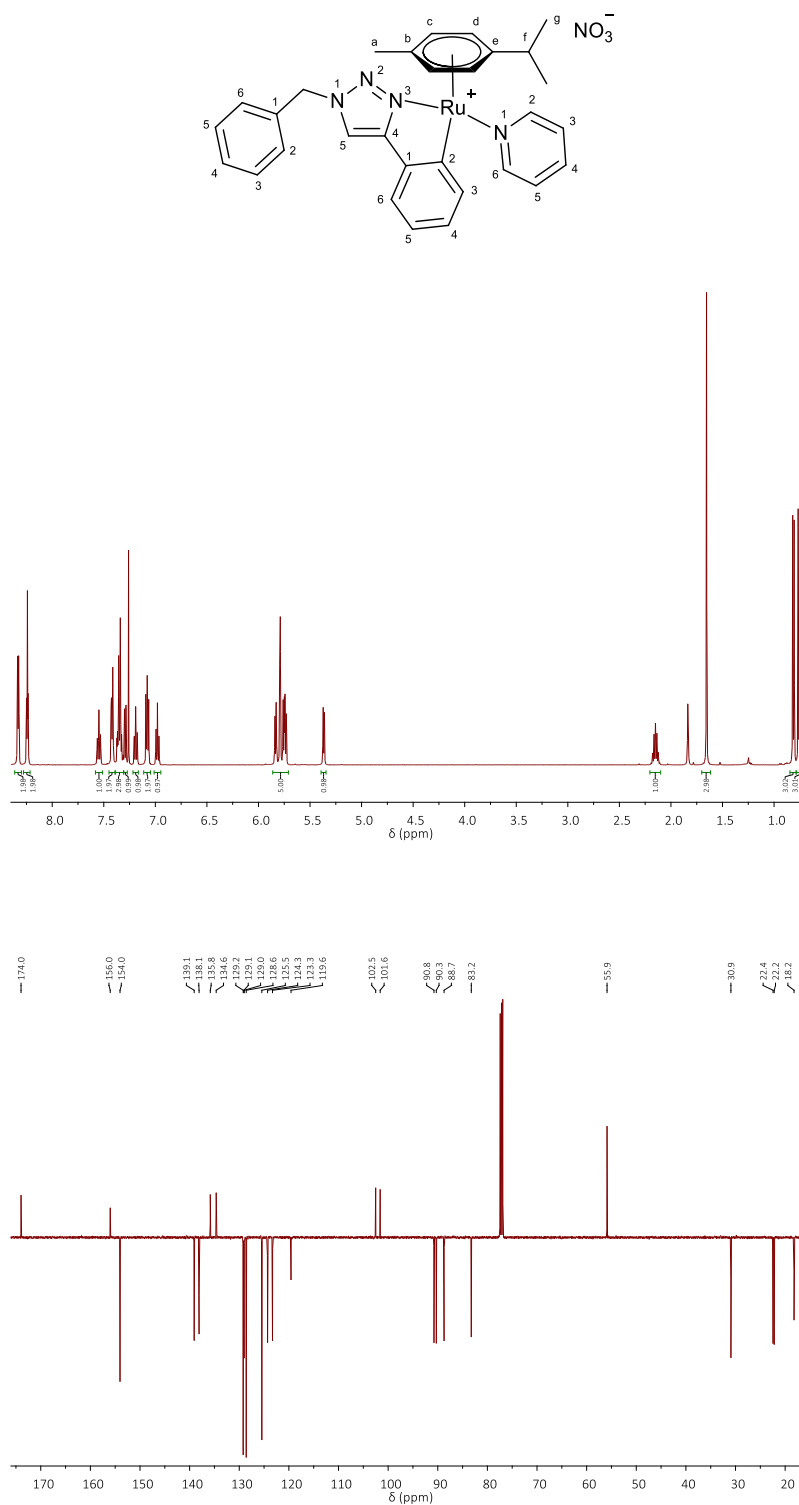


Figure S42 Numbering scheme (top), $^1\text{H NMR}$ (middle), and $^{13}\text{C NMR}$ (bottom) of **2f**.

11.7. [(κ N-Isoquinoline)(1-benzyl-4-(2'- κ C)-phenyl-1,2,3-(3- κ N)-triazolato)(η^6 -*p*-cymene)ruthenium(II)] nitrate (**2g**)

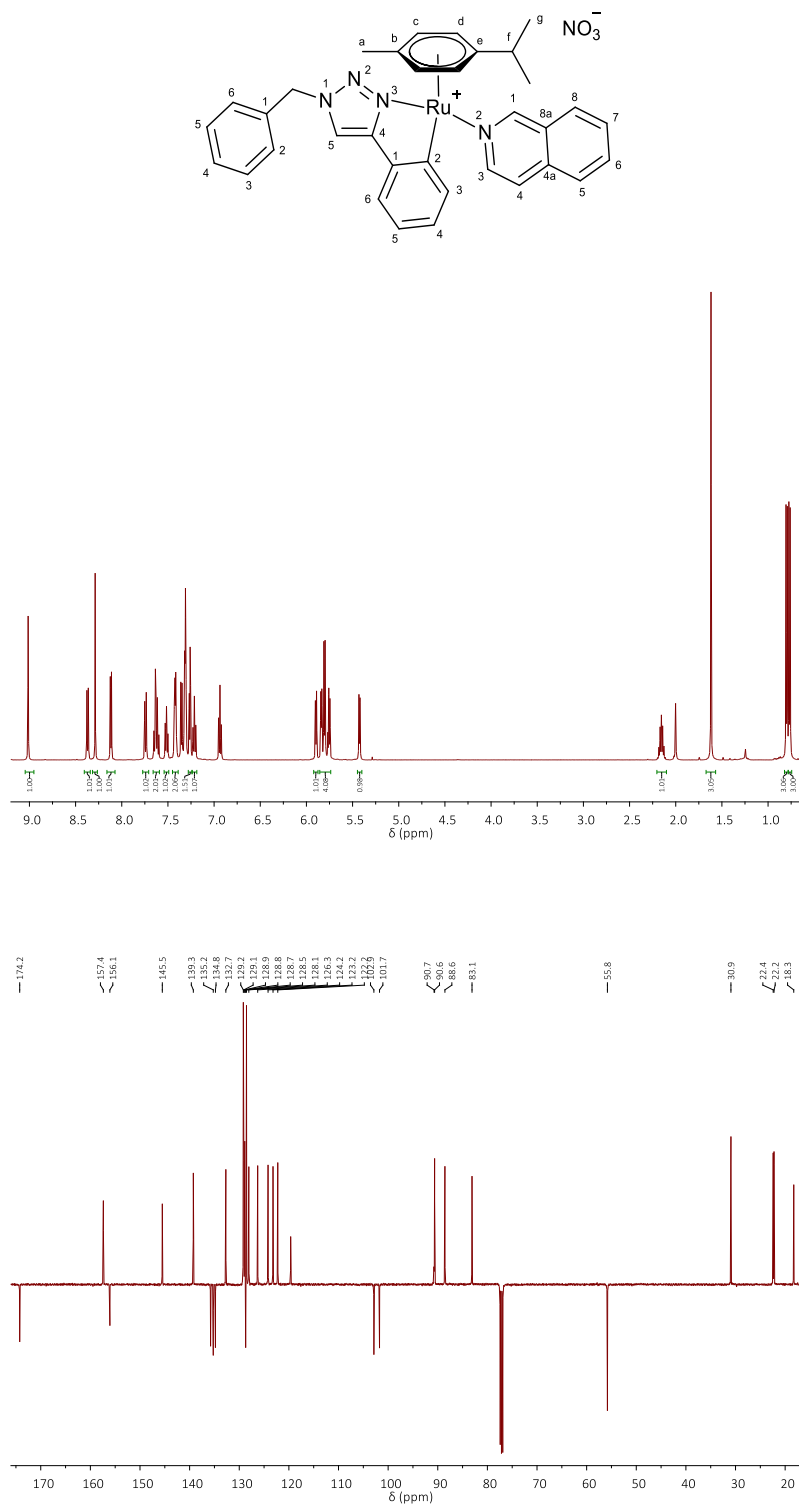


Figure S43 Numbering scheme (top), ^1H NMR (middle), and ^{13}C NMR (bottom) of **2g**.

11.8. [((1- κ N)-Imidazo[1,2-a]pyridine)(1-benzyl-4-(2'- κ C)-phenyl-1,2,3-(3- κ N)-triazolato)(η^6 -*p*-cymene)ruthenium(II)] nitrate (**2h**)

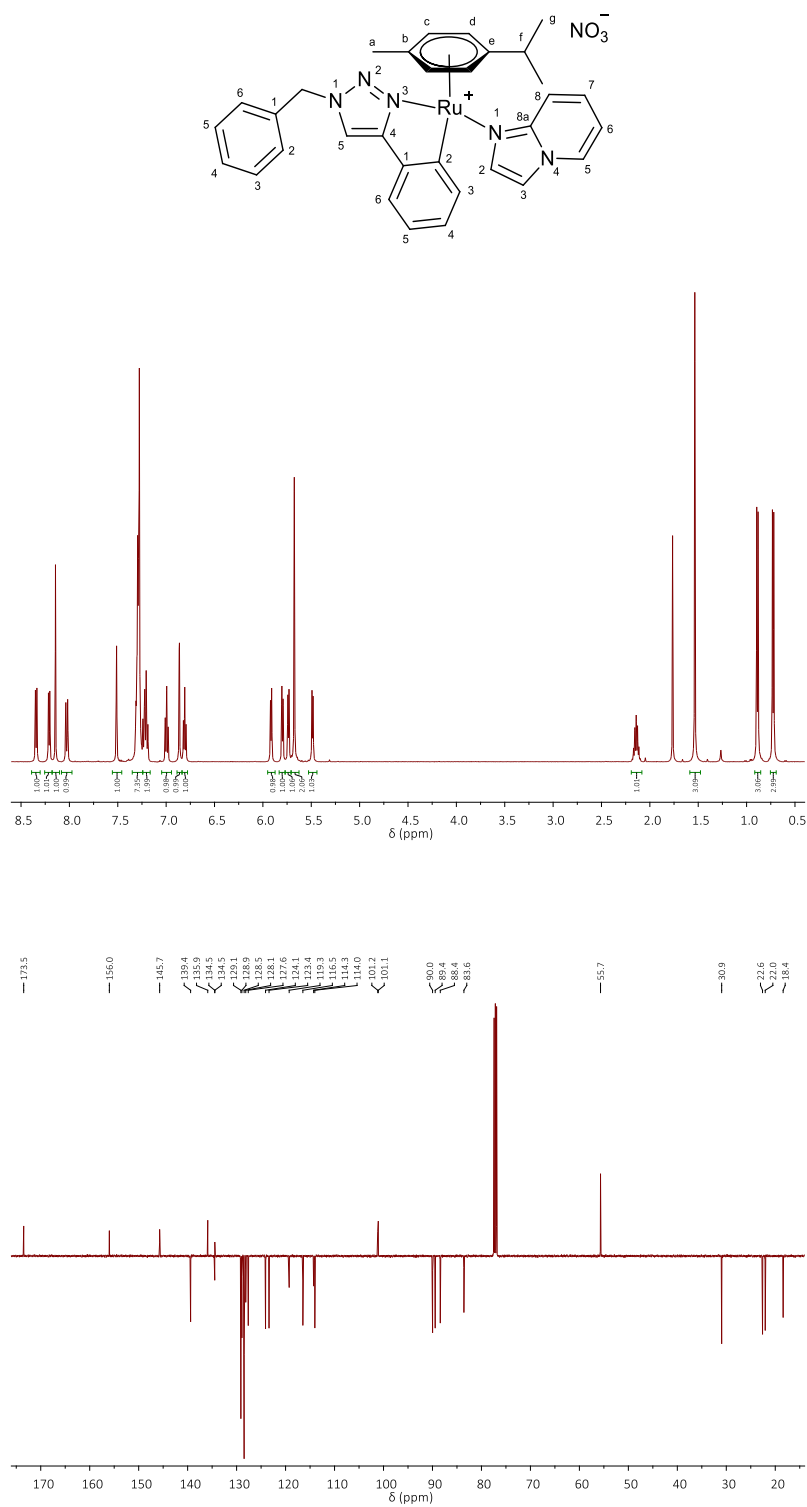


Figure S44 Numbering scheme (top), ^1H NMR (middle), and ^{13}C NMR (bottom) of **2h**.

11.9. $[(\kappa N-1,3\text{-Benzothiazol})(1\text{-benzyl-4-(2'-}\kappa C\text{)-phenyl-1,2,3-(3-}\kappa N\text{)-triazolato})(\eta^6\text{-}p\text{-cymene})\text{ruthenium(II)}]\text{ nitrate (2i)}$

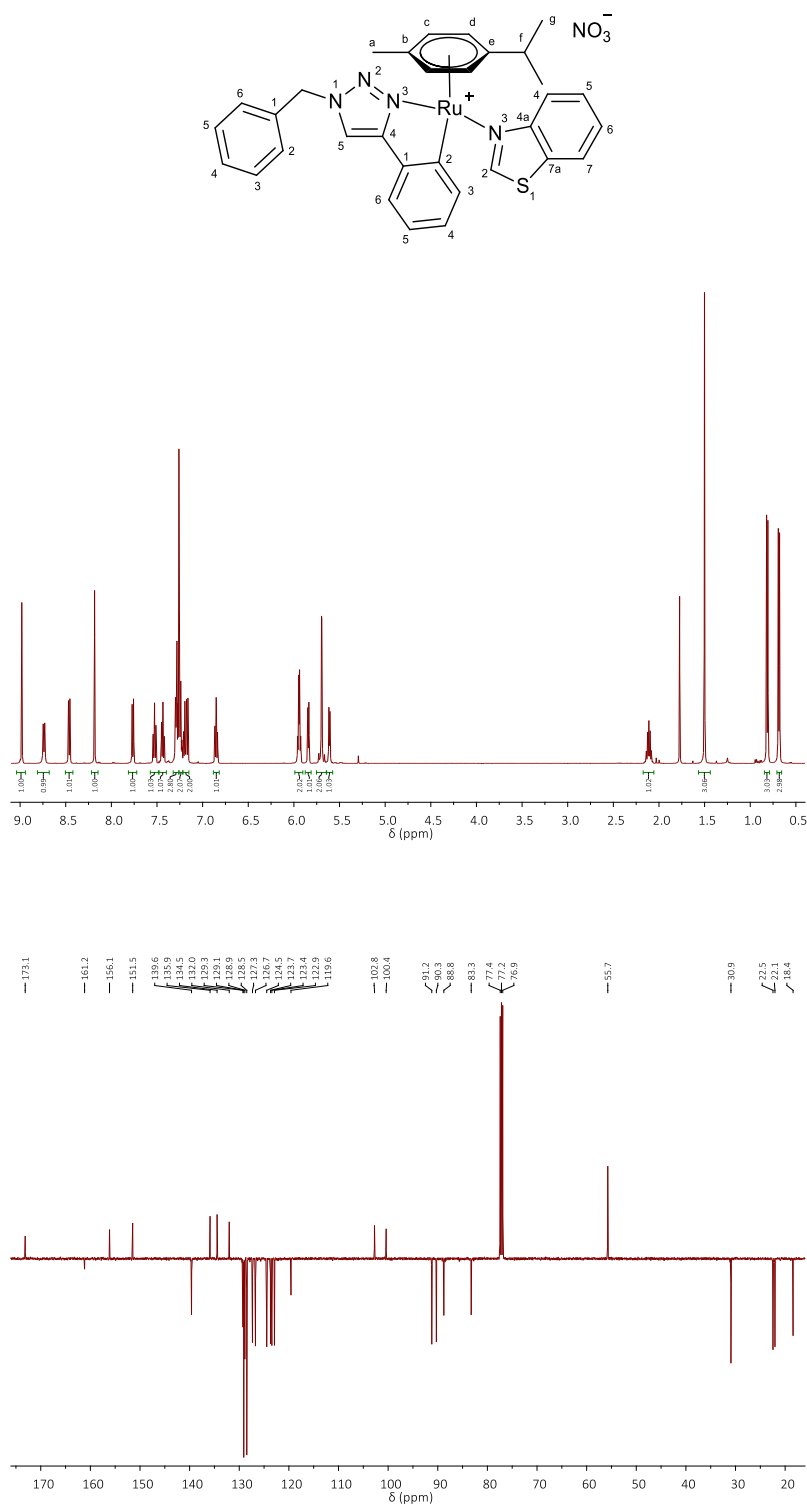


Figure S45 Numbering scheme (top), ^1H NMR (middle), and ^{13}C NMR (bottom) of **2i**.

11.10. $[(\kappa S\text{-(Methylsulfanyl)methan)}(1\text{-benzyl-4-(2'-}\kappa C\text{)-phenyl-1,2,3-(3-}\kappa N\text{)-triazolato})(\eta^6\text{-}p\text{-cymene) ruthenium(II)] \text{ nitrate (3a)}$

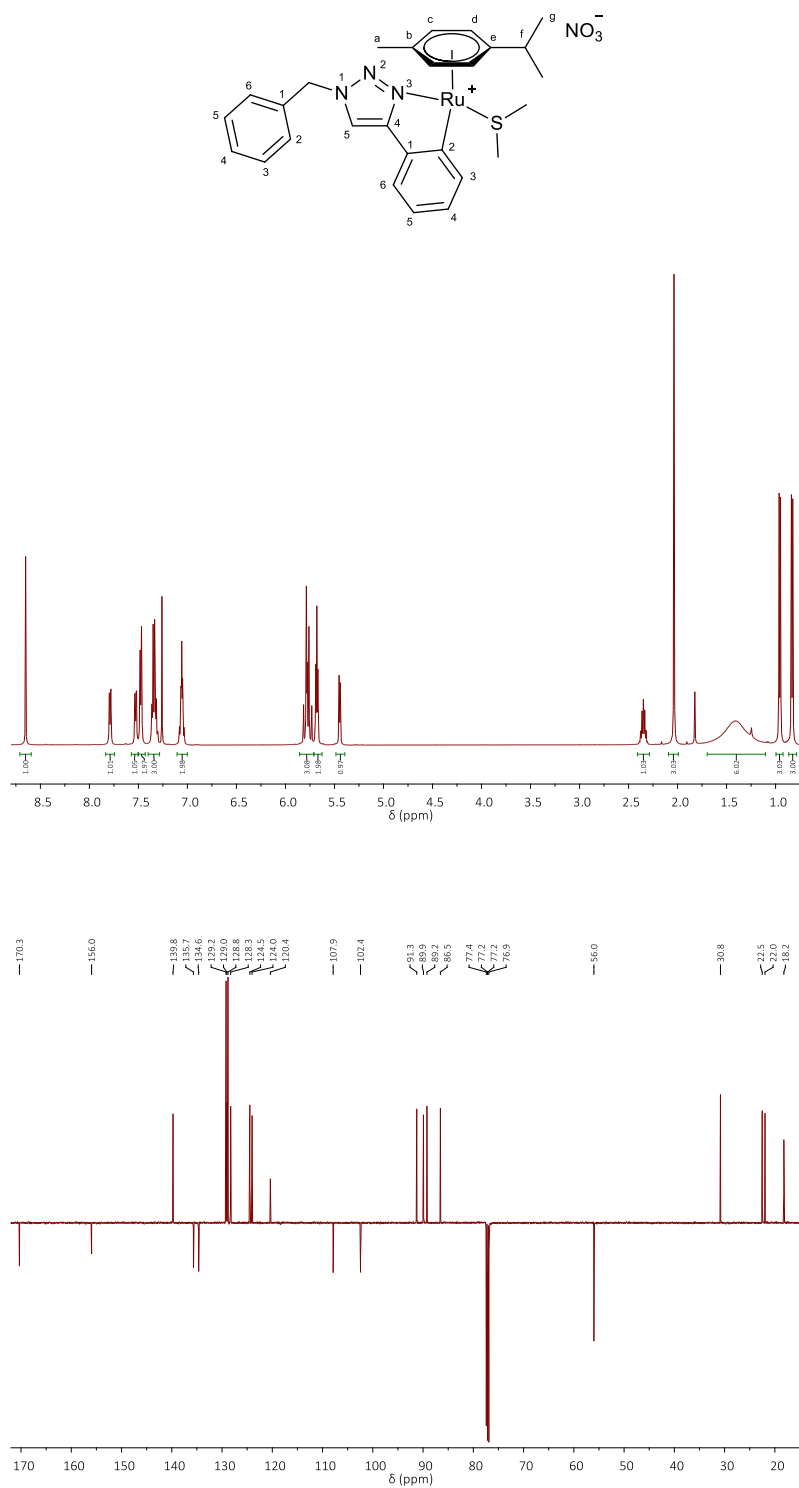


Figure S46 Numbering scheme (top), ^1H NMR (middle), and ^{13}C NMR (bottom) of **3a**.

11.11. [(κ S-Dimethyl sulfoxide)(1-benzyl-4-(2'- κ C)-phenyl-1,2,3-(3- κ N)-triazolato)(η^6 -*p*-cymene)ruthenium(II)] nitrate (**3b**)

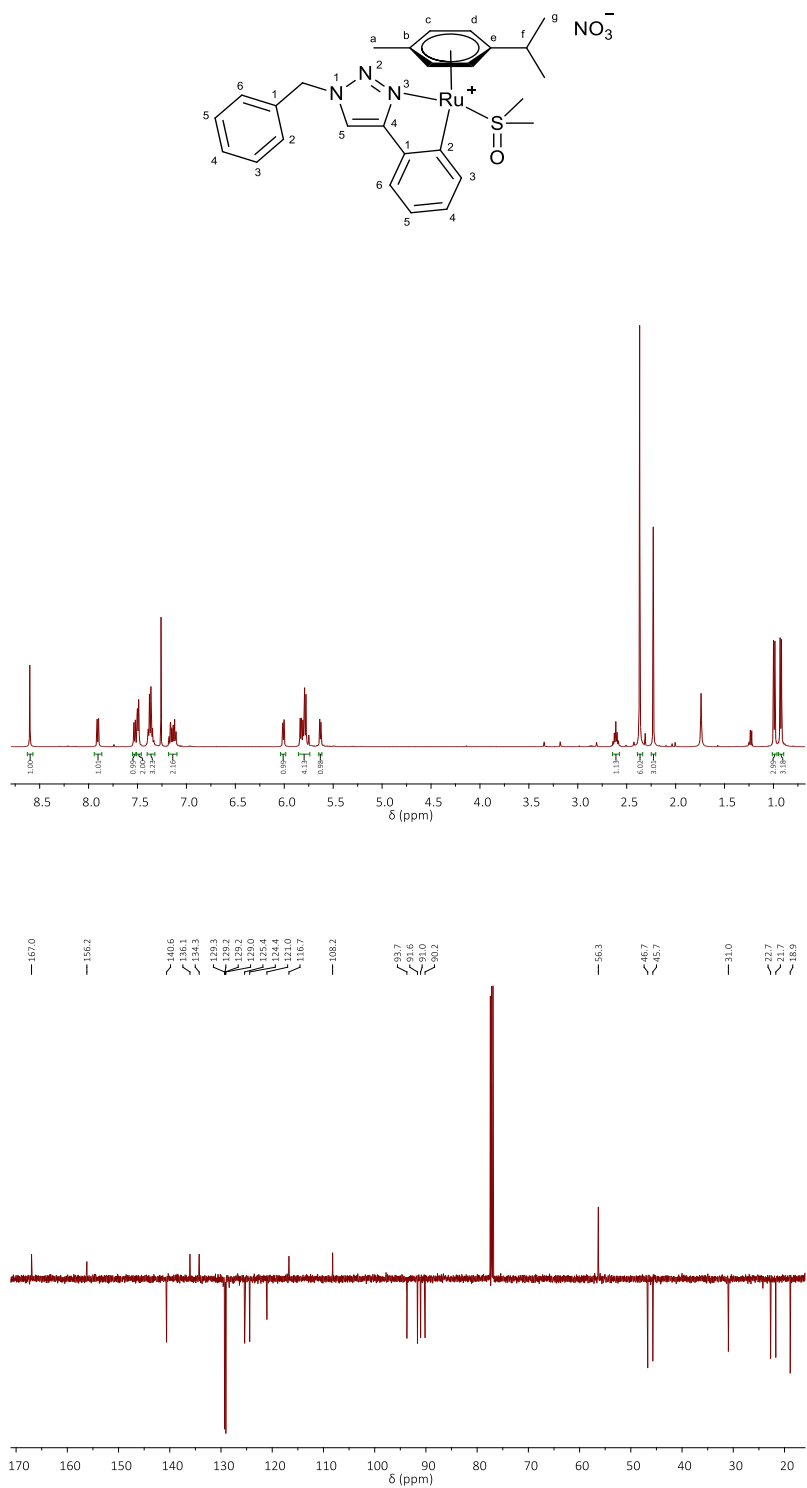


Figure S47 Numbering scheme (top), ^1H NMR (middle), and ^{13}C NMR (bottom) of **3b**.