SUPPORTING INFORMATION

Fine-tuning the activation mode of an 1,3-indandione-based ruthenium(II)-cymene half-sandwich complex by variation of its leaving group

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1 Crystallographic Data

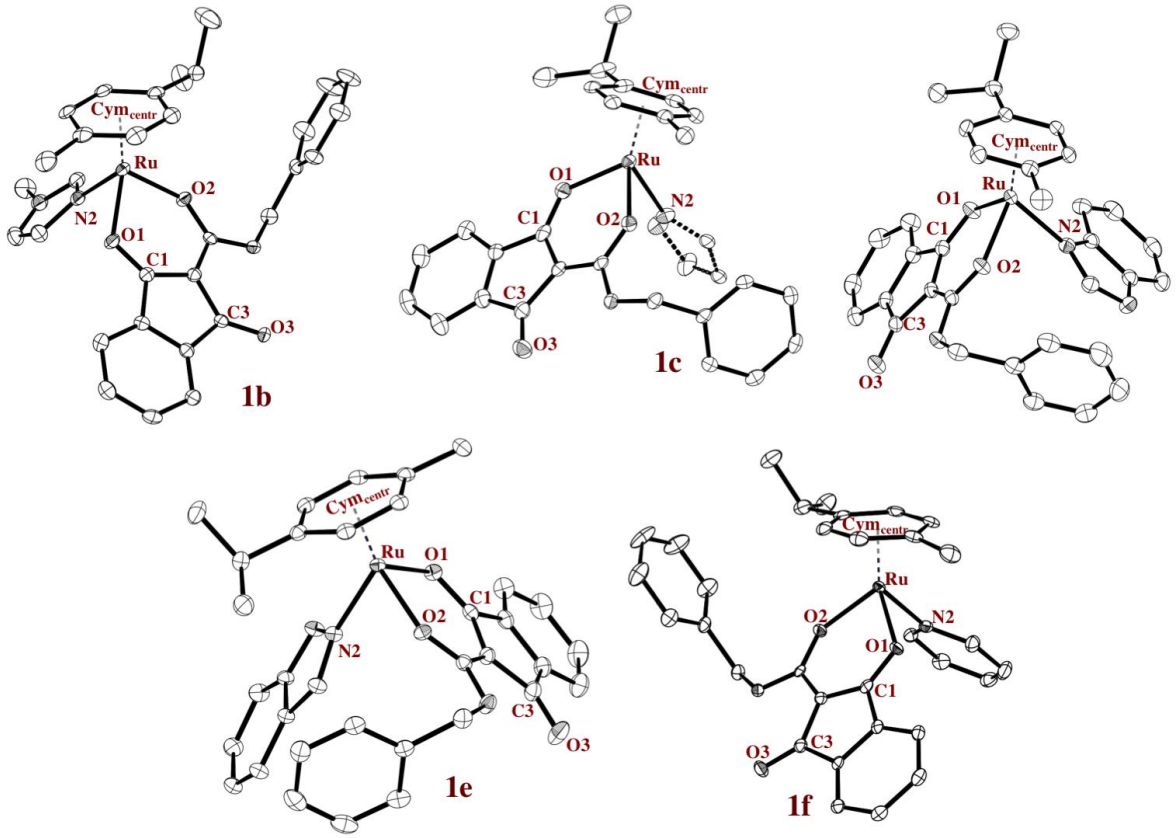


Chart S1. ORTEP-representations of **1b–f**, drawn at the 50% probability level **(**hydrogen atoms and counter ions are omitted for clarity)

Table S1. X-ray data for **1b**

Chemical formula	C31H32F6N3O3PRu	**Crystal system**	triclinic	
Formula weight [g/mol]	740.63	**Space group**	*P-1*	
Temperature [K]	100	**Z**	4	
Measurement method	\f and \w scans	**Volume [Å^3]**	3101.83(17)	
Radiation (Wavelength [Å])	MoKα (λ = 0.71073)	**Unit cell dimensions [Å] and [°]**	11.6359(4)	70.4432(10)
Crystal size / [mm^3]	0.131 × 0.088 × 0.075		15.9779(5)	76.6743(12)
Crystal habit	clear yellow block		18.2130(5)	83.2453(11)
Density (calculated) / [g/cm^3]	1.586	**Absorption coefficient / [mm^{-1}]**	0.631	
Abs. correction Tmin	0.6983	**Abs. correction Tmax**	0.7452	
Abs. correction type	multiscan	**F(000) [e$^-$]**	1504	

Table S2. Data collection and structure refinement of **1b**

Index ranges	-14 ≤ h ≤ 14, -19 ≤ k ≤ 19, -21 ≤ l ≤ 21	**Theta range for data collection [°]**	2.708 to 50.804	
Reflections number	30275	**Data / restraints / parameters**	11390/0/819	
Refinement method	Least squares	**Final R indices**	all data	R1 = 0.0483, wR2 = 0.0900
Function minimized	Σ w(F_o^2 - F_c^2)^2		I>2σ(I)	R1 = 0.0366, wR2 = 0.0844
Goodness-of-fit on F^2	1.033	**Weighting scheme**	w=1/[σ2(Fo2)+(0.0390P)2+5.3443P]	
Largest diff. peak and hole [e Å^{-3}]	1.18/-0.69		where P=(F_o^2+2F_c^2)/3	

Table S3. Sample and crystal data of **1c**

Chemical formula	$C_{30.5}H_{30}F_{4.5}N_3O_{4.5}P_{0.5}RuS_{0.5}$	**Crystal system**	monoclinic	
Formula weight [g/mol]	728.66	**Space group**	*C2/c*	
Temperature [K]	100	**Z**	8	
Measurement method	\f and \w scans	**Volume [Å^3]**	5944.7(7)	
Radiation (Wavelength [Å])	MoKα (λ = 0.71073)	**Unit cell dimensions [Å] and [°]**	18.9427(13)	90
Crystal size / [mm^3]	0.4 × 0.25 × 0.02		7.8912(5)	96.668(5)
Crystal habit	clear yellow plate		40.040(2)	90
Density (calculated) / [g/cm^3]	1.628	**Absorption coefficient / [mm^{-1}]**	0.662	
Abs. correction Tmin	0.573	**Abs. correction Tmax**	0.7452	
Abs. correction type	multiscan	**F(000) [e$^-$]**	2960	

Table S4. Data collection and structure refinement of **1c**

Index ranges	$-22 \le h \le 22$, $-9 \le k \le 9$, $-48 \le l \le 48$	**Theta range for data collection [°]**	5 to 50.698	
Reflections number	30444	**Data / restraints / parameters**	5467/6/444	
Refinement method	Least squares	**Final R indices**	all data	R1 = 0.0450, wR2 = 0.0891
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$		I>2σ(I)	R1 = 0.0426, wR2 = 0.0880
Goodness-of-fit on F^2	1.228	**Weighting scheme**	w=1/[σ2(Fo2)+(0.0061P)2+ 37.0240P]	
Largest diff. peak and hole [e Å^{-3}]	1.65/-1.20		where $P=(F_o^2+2F_c^2)/3$	

Table S5. Sample and crystal data of **1d**

Chemical formula	C34H32F6N3O3PRu	**Crystal system**	monoclinic	
Formula weight [g/mol]	776.66	**Space group**	*P21/n*	
Temperature [K]	100	**Z**	4	
Measurement method	\f and \w scans	**Volume [Å^3]**	3168.46(19)	
Radiation (Wavelength [Å])	MoKα (λ = 0.71073)	**Unit cell dimensions [Å] and [°]**	13.9617(5)	90
Crystal size / [mm^3]	0.2 × 0.13 × 0.03		16.1368(5)	107.5828(15)
Crystal habit	clear yellow plate		14.7527(5)	90
Density (calculated) / [g/cm^3]	1.628	**Absorption coefficient / [mm^{-1}]**	0.622	
Abs. correction Tmin	0.6975	**Abs. correction Tmax**	0.746	
Abs. correction type	multiscan	**F(000) [e$^-$]**	1576	

Table S6. Data collection and structure refinement of **1d**

Index ranges	$-19 \le h \le 19$, $-22 \le k \le 22$, $-20 \le l \le 20$	**Theta range for data collection [°]**	4.808 to 60.174	
Reflections number	113582	**Data / restraints / parameters**	9288/28/430	
Refinement method	Least squares	**Final R indices**	all data	R1 = 0.0588, wR2 = 0.1015
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$		I>2σ(I)	R1 = 0.0408, wR2 = 0.0930
Goodness-of-fit on F^2	1.02	**Weighting scheme**	w=1/[σ2(Fo2)+(0.0396P)2+ 7.7332P]	
Largest diff. peak and hole [e Å^{-3}]	1.42/-1.42		where $P=(F_o^2+2F_c^2)/3$	

Table S7. Sample and crystal data of **1e**

Chemical formula	C35H32F3N3O6RuS	**Crystal system**	monoclinic	
Formula weight [g/mol]	780.76	**Space group**	*P21/n*	
Temperature [K]	100	**Z**	4	
Measurement method	\f and \w scans	**Volume [Å^3]**	3300.7(2)	
Radiation (Wavelength [Å])	MoKα (λ = 0.71073)	**Unit cell dimensions [Å] and [°]**	11.2803(5)	90
Crystal size / [mm^3]	0.24 × 0.155 × 0.122		16.8126(7)	104.2968(15)
Crystal habit	clear yellow block		17.9604(8)	90
Density (calculated) / [g/cm^3]	1.571	**Absorption coefficient / [mm^{-1}]**	0.606	
Abs. correction Tmin	0.6734	**Abs. correction Tmax**	0.746	
Abs. correction type	multiscan	**F(000) [e$^-$]**	1592	

Table S8. Data collection and structure refinement of **1e**

Index ranges	$-15 \le h \le 15$, $-23 \le k \le 23$, $-25 \le l \le 25$	**Theta range for data collection [°]**	3.88 to 60.242	
Reflections number	126357	**Data / restraints / parameters**	9713/0/445	
Refinement method	Least squares	**Final R indices**	all data	R1 = 0.0258, wR2 = 0.0613
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$		I>2σ(I)	R1 = 0.0236, wR2 = 0.0597
Goodness-of-fit on F^2	1.057	**Weighting scheme**	w=1/[σ2(Fo2)+(0.0274P)2+ 2.5680P]	
Largest diff. peak and hole [e Å^{-3}]	0.79/-0.7		where $P=(F_o^2+2F_c^2)/3$	

Table S9. X-ray data for **1f**

Chemical formula	C33H31F3N2O6RuS	**Crystal system**	monoclinic	
Formula weight [g/mol]	741.73	**Space group**	*P21/c*	
Temperature [K]	100	**Z**	12	
Measurement method	\f and \w scans	**Volume [Å^3]**	9532.3(7)	
Radiation (Wavelength [Å])	MoKα (λ = 0.71073)	**Unit cell dimensions [Å] and [°]**	19.4630(8)	90
Crystal size / [mm^3]	0.395 × 0.22 × 0.052		33.1343(14)	95.0087(15)
Crystal habit	clear yellow block		14.8379(7)	90
Density (calculated) / [g/cm^3]	1.551	**Absorption coefficient / [mm^{-1}]**	0.624	
Abs. correction Tmin	0.5728	**Abs. correction Tmax**	0.746	
Abs. correction type	multiscan	**F(000) [e$^-$]**	4536	

Table S10. Data collection and structure refinement of **1f**

Index ranges	$-21 \le h \le 23$, $-39 \le k \le 39$, $-17 \le l \le 17$	**Theta range for data collection [°]**	2.1 to 50.7	
Reflections number	121329	**Data / restraints / parameters**	17439/0/1252	
Refinement method	Least squares	**Final R indices**	all data	R1 = 0.0392, wR2 = 0.0775
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$		I>2σ(I)	R1 = 0.0309, wR2 = 0.0737
Goodness-of-fit on F^2	1.042	**Weighting scheme**	w=1/[σ2(Fo2)+(0.0289P)2+7.9124P]	
Largest diff. peak and hole [e Å^{-3}]	0.88/-0.52		where $P=(F_o^2+2F_c^2)/3$	

Table S11. Experimental parameters and CCDC-Code.

Sample	**Machine**	**Source**	**Temp.**	**Detector Distance**	**Time/ Frame**	**#Frames**	**Frame width**	**CCDC**
	Bruker		[K]	[mm]	[s]		[°]	
1b	D8	Mo	100	34	24	686	0.4	1919571
1c	X8	Mo	100	50	40	1666	0.5	1919572
1d	D8	Mo	100	34	60	2302	0.4	1919573
1e	D8	Mo	100	34	30	1654	0.5	1919574
1f	D8	Mo	100	35	8	1187	0.4	1919575

2 Lipophilicity

Table S12. Death time determination for the relevant MeOH percentages in the eluent

%	t_0-1	t_0-2	t_0-3	mean
45	0.520	0.520	0.523	0.521
47.5	0.528	0.529	0.528	0.528
50	0.537	0.533	0.533	0.534
52.5	0.533	0.533	0.533	0.533
55	0.530	0.537	0.537	0.535
57.5	0.547	0.547	0.543	0.546
60	0.547	0.553	0.550	0.550

Table S13. Determination of logk for **1a** – **1g** in triplicate

	%	t1	t2	t3	t0	logk1	logk2	logk3
1a	52.5	4.837	4.977	4.980	0.533	0.907	0.921	0.921
	50	7.675	7.670	7.650	0.534	1.126	1.126	1.124
	47.5	12.180	12.263	12.160	0.528	1.343	1.347	1.343
1b	50	6.583	6.590	6.593	0.534	1.054	1.054	1.055
	47.5	10.325	10.317	10.333	0.528	1.268	1.268	1.269
	45	16.940	16.953	16.907	0.521	1.499	1.499	1.498
1c	52.5	5.220	5.283	5.220	0.533	0.944	0.950	0.944
	50	8.082	8.080	8.063	0.534	1.150	1.150	1.149
	47.5	12.807	12.847	12.803	0.528	1.366	1.368	1.366
1d	57.5	3.270	3.313	3.277	0.546	0.698	0.705	0.699
	55	5.017	5.080	5.063	0.535	0.923	0.929	0.928
	52.5	7.613	7.600	7.590	0.533	1.123	1.123	1.122
1e	60	3.743	3.787	3.733	0.550	0.764	0.770	0.762
	55	9.000	9.120	8.903	0.535	1.200	1.206	1.195
	52.5	14.307	14.275	14.280	0.533	1.412	1.411	1.411
1f	52.5	4.047	3.950	3.963	0.533	0.819	0.807	0.809
	50	6.047	6.060	6.060	0.534	1.014	1.015	1.015
	47.5	9.587	9.583	9.590	0.528	1.234	1.234	1.234
1g	50	4.197	4.220	4.230	0.534	0.836	0.839	0.840
	47.5	6.427	6.463	6.463	0.528	1.048	1.050	1.050
	45	10.150	10.250	10.150	0.521	1.267	1.271	1.267

3 pH-dependent stability

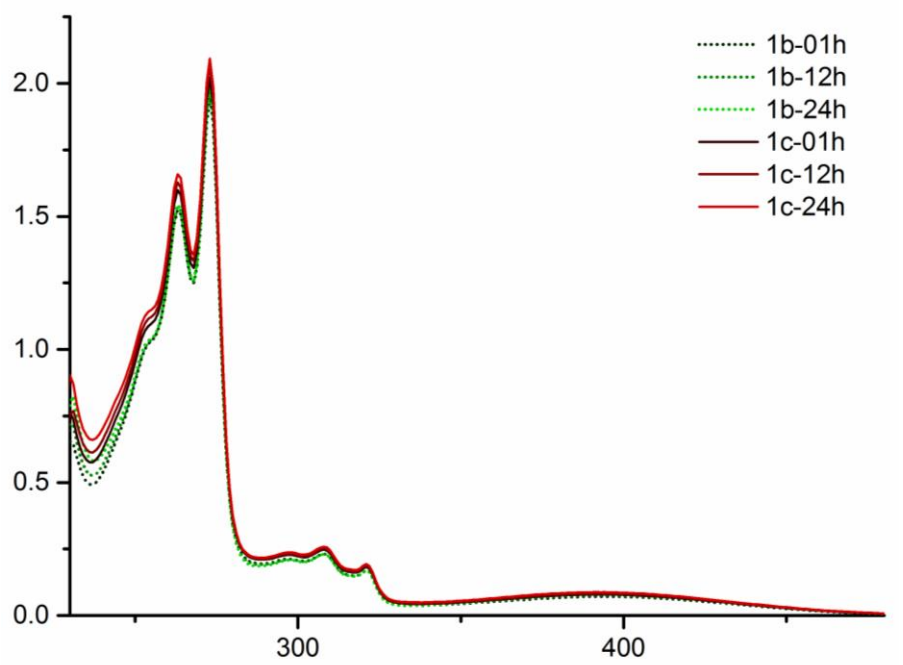


Figure S1. UV-Vis spectra of 40 µM **1b** and **1c** at pH 8.5 in 1% v/v DMSO/H2O (0.9% NaCl, phosphate buffer) at 37 °C

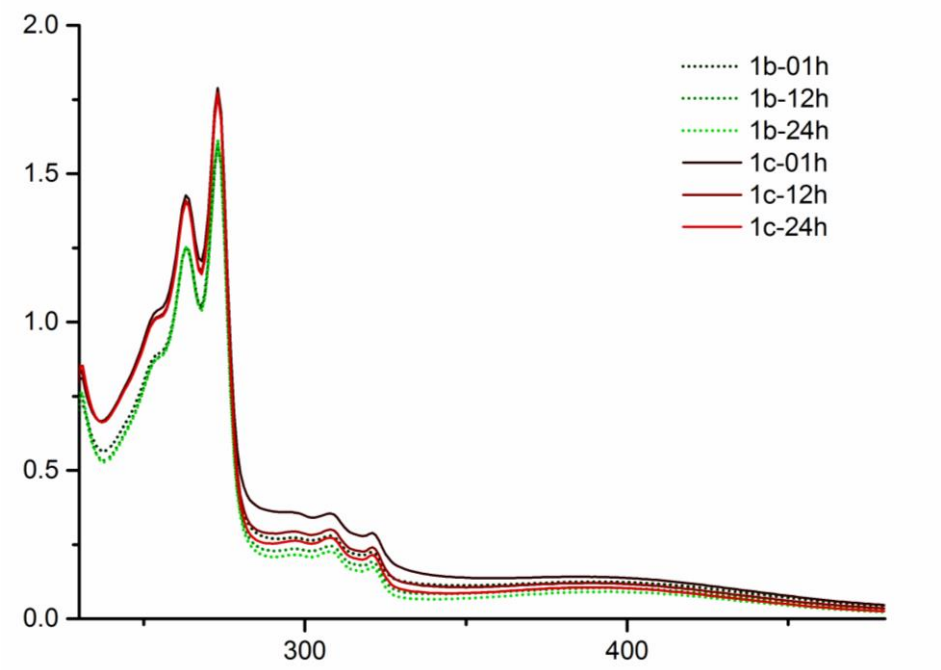


Figure S2. UV-Vis spectra of 40 µM **1b** and **1c** at pH 7.4 in 1% v/v DMSO/PBS at 37 °C

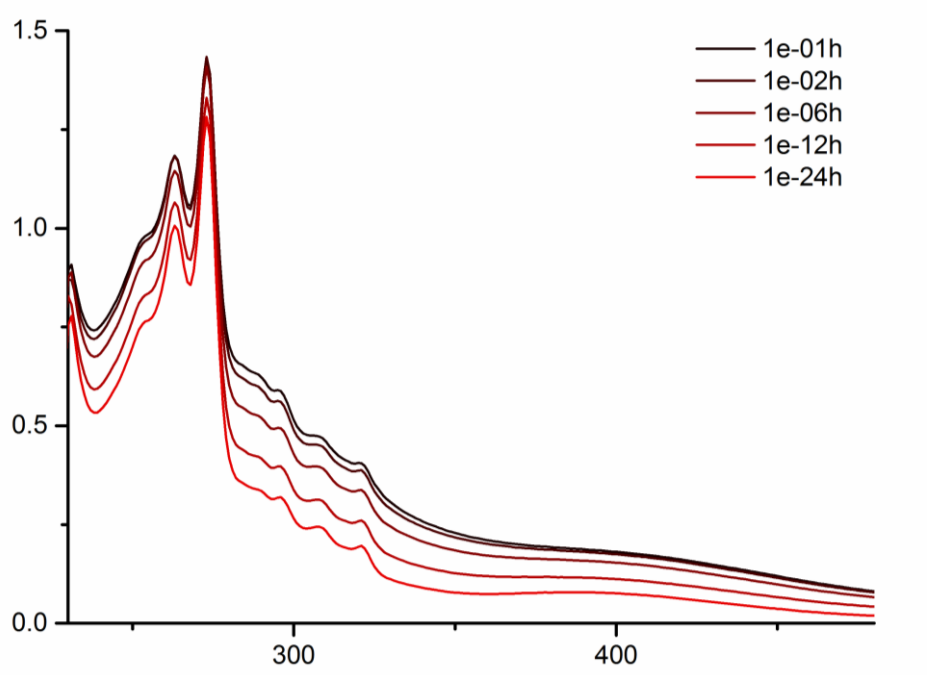


Figure S3. UV-Vis spectra of 40 μM **1e** at pH 7.4 in 1% v/v DMSO/PBS at 37 °C

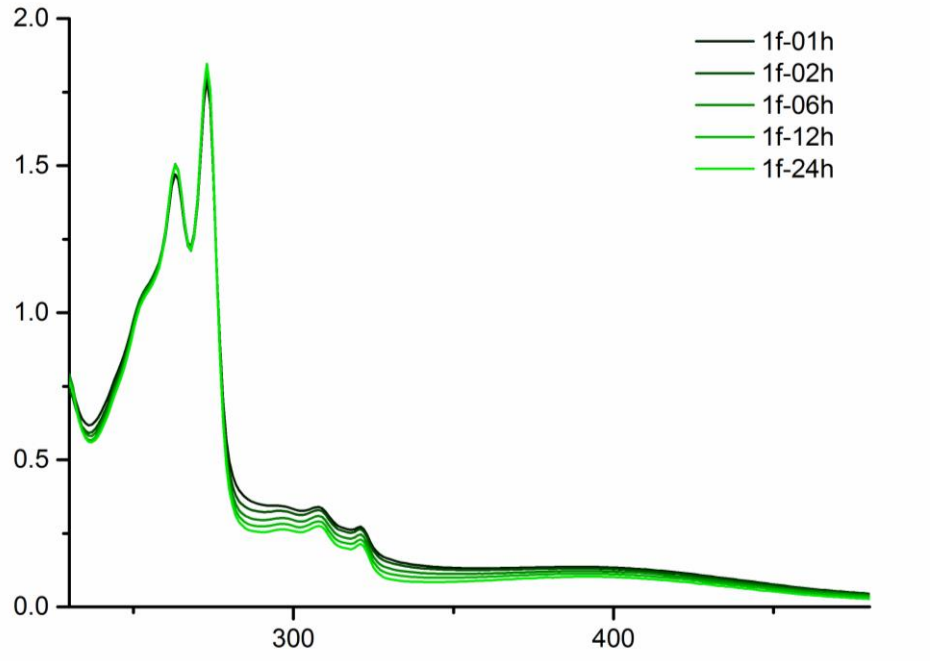


Figure S4. UV-Vis spectra of 40 μM **1f** at pH 6.5 in 1% v/v DMSO/H_2O (acetate buffer) at 37 °C

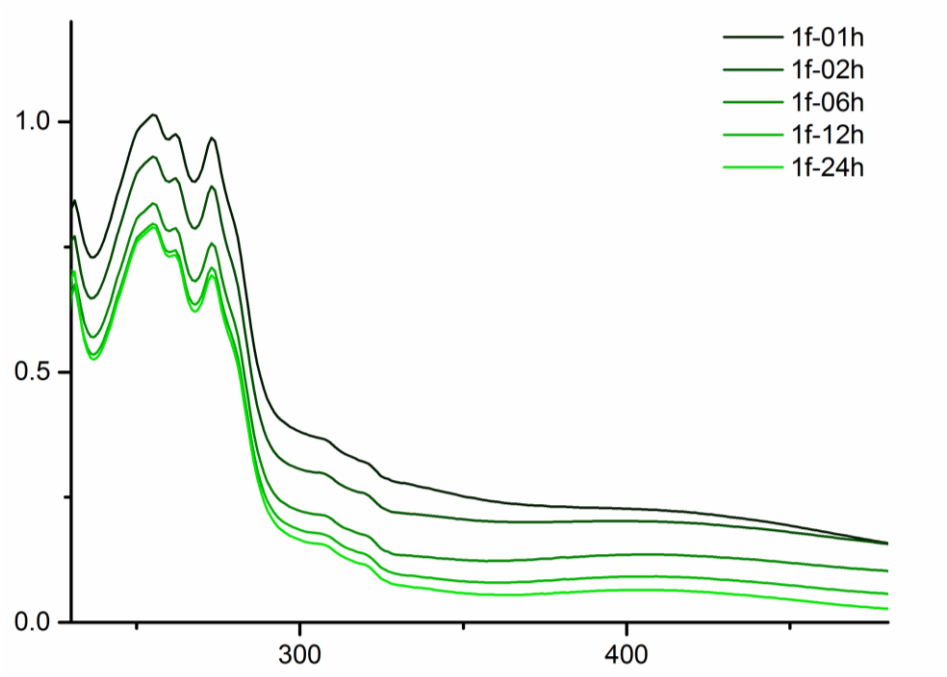


Figure S5. UV-Vis spectra of 40 μM **1f** at pH 5.5 in 1% v/v DMSO/H_2O (0.9 % NaCl, AcOH) at 37 °C

4 Biological experiments

Figure S14. Graphical comparison of IC_{50}-values (complexes are ordered according to their cytotoxicity in the respective cell line)

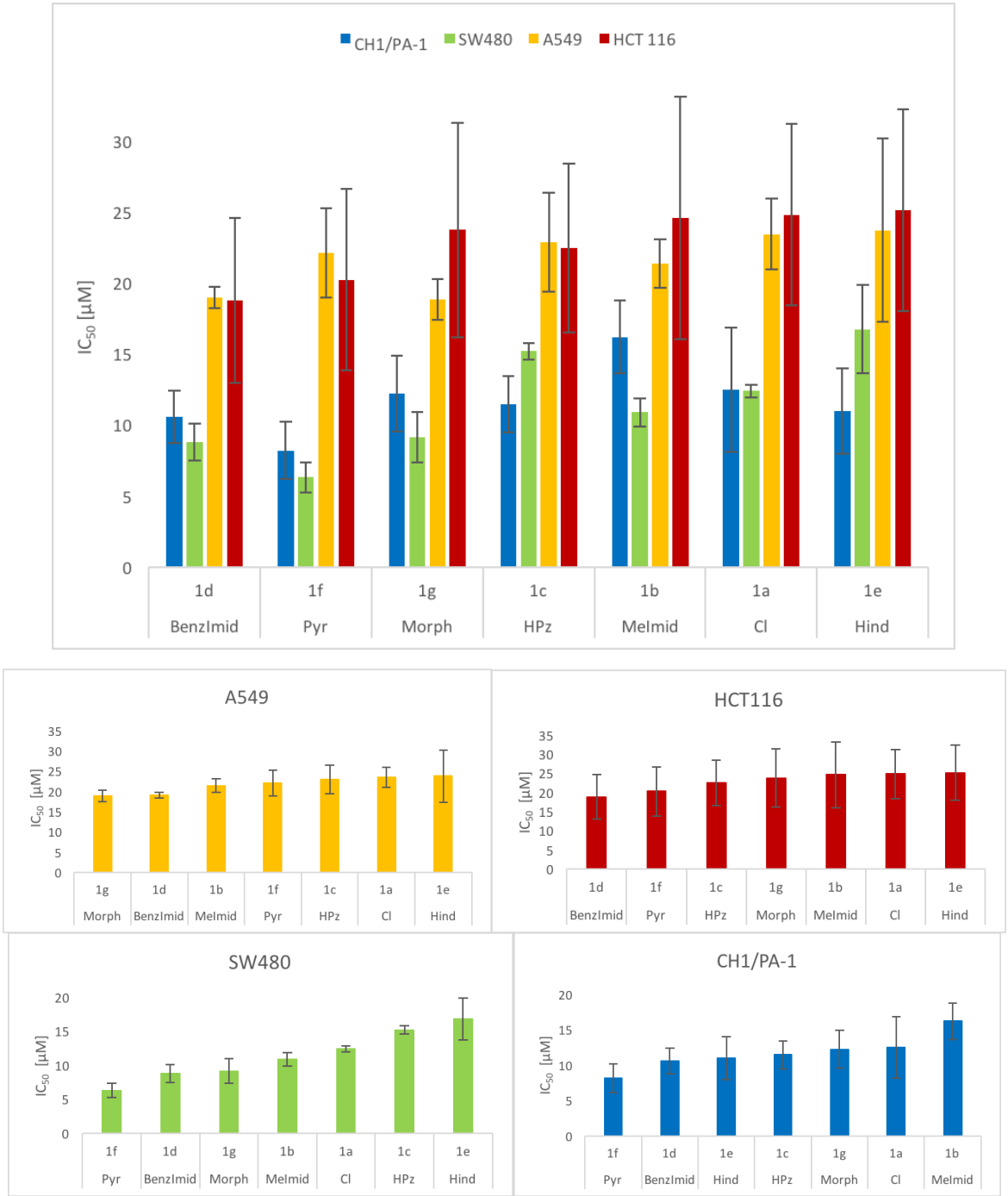
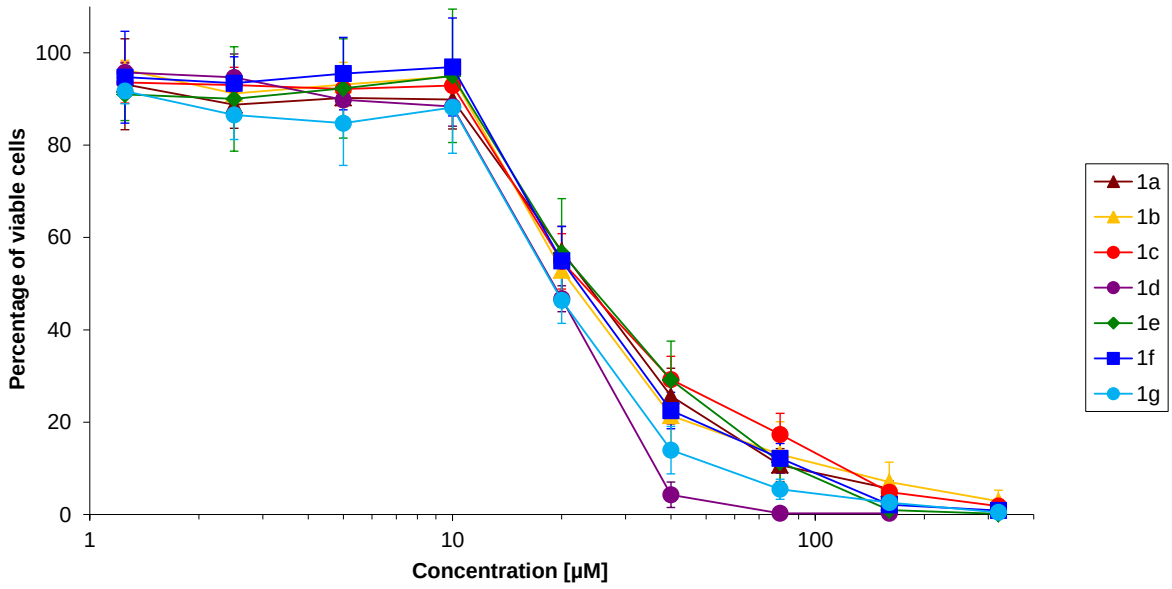


Figure S15. Concentration–effect curves in A549 (top) and CH1/PA-1 (bottom) cells (MTT assay, 96 h exposure)



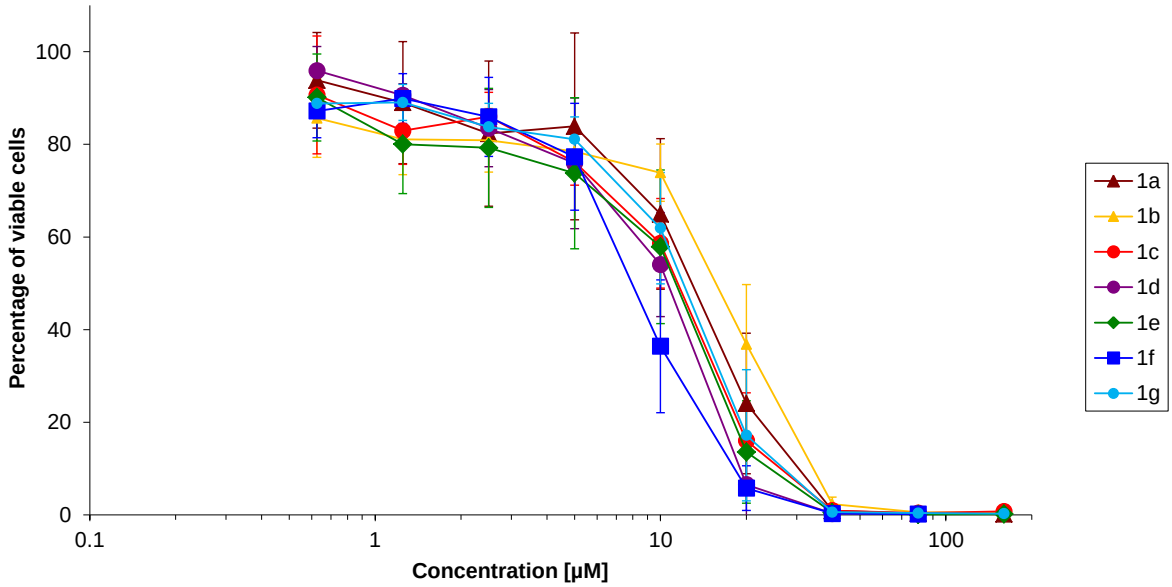


Figure S16. Concentration–effect curves in HCT116 (top) and SW480 (bottom) cells (MTT assay, 96 h exposure)