Supplemental Material

Cationic arene ruthenium(II) complexes with chelating *P*-functionalized alkyl phenyl sulfide and sulfoxide ligands as potent anticancer agents

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Experimental

Materials and methods

All reactions and manipulations were carried out under argon using standard Schlenk techniques. Solvents were dried (diethyl ether/*n*-pentane over Na/benzophenone; methanol over magnesium; methylene chloride over CaH_2) and freshly distilled prior to use. NMR spectra (^1H, ^{13}C, ^{31}P) were recorded at 27 °C on Varian Gemini 200 and VXR 400 spectrometers. Chemical shifts are relative to solvent signals (CD_2Cl_2, δ_H 5.32, δ_C 53.8) as internal references; $\delta(^{31}P)$ is relative to external H_3PO_4 (85%). Microanalyses (C, H) were performed in the Microanalytical Laboratory of the University of Halle using a CHNS-932 (LECO) elemental analyzer. [{$RuCl_2(\eta^6$-*p*-cym)}$_2$] and the ligands were prepared according to literature procedures.[1,2]

Preparation of [Ru(η^6-*p*-cym)Cl{$Ph_2P(CH_2)_nS(O)_xPh$-κ*P*,κ*S*}][PF_6] (1b–5b)

To a methanol solution (30 mL) of [{$RuCl_2(\eta^6$-*p*-cym)}$_2$] (0.10 g, 0.16 mmol) the respective ligand (0.32 mmol) was added while stirring and then the solution was heated under reflux for 3 h. [NH_4][PF_6] (6 equiv.) was added and the precipitate obtained after storage at –70 °C overnight was filtered off, washed with diethyl ether (3 × 2 mL), and dried in vacuum.

1b (*n* = 1; *x* = 0). Yield: 169 mg (73%). Anal. Found: C, 47.74; H, 4.26. Calcd for $C_{29}H_{31}ClF_6P_2RuS$ (724.03): C, 48.10; H, 4.32. ^1H NMR (400 MHz, CD_2Cl_2): δ 1.13 (d, $^3J_{H,H}$ = 6.93 Hz, 3H, CH(CH_3)$_2$), 1.22 (d, $^3J_{H,H}$ = 6.91 Hz, 3H, CH(CH_3)$_2$), 1.96 (s, 3H, CH_3), 2.43–2.57 (m, 1H, C*H*(CH$_3$)$_2$), 4.91–5.02 (m, 1H, SCH_2), 5.56–5.67 (m, 3H, C_{cym}-*H* + SCH_2), 5.83–5.94 (m, 2H, C_{cym}-*H*), 7.46–7.63 (m, 15H, H_{Ph}). ^{13}C NMR (100 MHz, CD_2Cl_2): δ 18.3 (s, C*C*H$_3$), 21.4 (s, CH(*C*H$_3$)$_2$), 22.5 (s, CH(*C*H$_3$)$_2$), 31.5 (s, *C*H(CH$_3$)$_2$), 27.2 (d, $^1J_{P,C}$ = 21.0 Hz, *C*H$_2$PPh$_2$), 86.5 (d, $^2J_{P,C}$ = 5.7 Hz, 2/6-C_{cym}), 88.0 (d, $^2J_{P,C}$ = 5.7 Hz, 2/6-C_{cym}), 89.2 (d, $^2J_{P,C}$ = 4.3 Hz, 3/5-C_{cym}), 91.6 (d, $^2J_{P,C}$ = 4.3 Hz, 3/5-C_{cym}), (s, *C*CH$_3$), 102.9 (s, *C*CH(CH$_3$)$_2$),

114.5 (s, *C*CH$_3$),125.6–136.3 (*C*$_{Ph}$). ^{31}P NMR (80 MHz, CD_2Cl_2): δ 0.35 (s), –142.9 (sept, $^1J_{P,F}$ = 709.0 Hz, PF_6).

2b (*n* = 2; *x* = 0). Yield: 158 mg (67%). Anal. Found: C, 48.49; H, 4.93. Calcd for $C_{29}H_{31}ClF_6P_2RuS$ (738.04): C, 48.82; H, 4.51. ^{1}H NMR (400 MHz, C_5D_5N): δ 0.88 (d, $^3J_{H,H}$ = 6.86 Hz, 3H, CH(C*H*$_3$)$_2$), 1.03 (d, $^3J_{H,H}$ = 6.92 Hz, 3H, CH(C*H*$_3$)$_2$), 1.85 (s, 3H, C*H*$_3$), 2.40 (sept, $^3J_{H,H}$ = 6.92 Hz, 1H, C*H*(CH$_3$)$_2$), 2.87–2.97 (m, 1H, C*H*$_2$PPh$_2$), 3.11–3.20(m, 1H, C*H*$_2$PPh$_2$), 3.45–3.68 (m, 2H, SC*H*$_2$), 5.42–5.43 (m, 1H, C$_{cym}$-*H*), 5.72–5.73 (m, 1H, C$_{cym}$-*H*), 6.19 (br, 1H, C$_{cym}$-*H*), 6.29–6.30 (m, 1H, C$_{cym}$-*H*), 7.40–7.53 (m, 11H, *H*$_{Ph}$), 7.90–7.95 (m, 2H, *H*$_{Ph}$), 8.03–8.05 (m, 2H, *H*$_{Ph}$). ^{13}C NMR (100 MHz, C_5D_5N): δ 17.3 (s, C*C*H$_3$), 21.2 (s, CH(*C*H$_3$)$_2$), 22.2 (s, CH(*C*H$_3$)$_2$), 28.8 (d, $^1J_{P,C}$ = 33.1 Hz, *C*H$_2$PPh$_2$), 30.5 (s, *C*H(CH$_3$)$_2$), 36.6 (s(br), S*C*H$_2$), 89.6 (s(br), 2/6-*C*$_{cym}$), 90.7 (s(br), 2/6-*C*$_{cym}$), 91.1 (d, $^2J_{P,C}$ = 2.3 Hz, 3/5-*C*$_{cym}$), 95.1 (s(br), 3/5-*C*$_{cym}$), 103.4 (s, *C*CH(CH$_3$)$_2$), 127.6–134.8 (*C*$_{Ph}$). ^{31}P NMR (80 MHz, $CDCl_3$): δ 66.5 (s), –142.7 (sept, $^1J_{P,F}$ = 709.3 Hz, PF_6).

3b (*n* = 3; *x* = 0). Yield: 199 mg (83%). Anal. Found: C, 49.84; H, 4.42. Calcd for $C_{29}H_{31}ClF_6P_2RuS$ (752.11): C, 49.50; H, 4.69. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.40 (d, $^3J_{H,H}$ = 6.84 Hz, 3H, CH(C*H*$_3$)$_2$), 1.03 (d, $^3J_{H,H}$ = 7.08 Hz, 3H, CH(C*H*$_3$)$_2$), 1.24–1.35 (m, 1H, CH$_2$C*H*$_2$CH$_2$), 1.79–1.86 (m, 1H, CH$_2$C*H*$_2$CH$_2$), 2.07 (s, 3H, C*H*$_3$), 2.16–2.33 (m, 2H, C*H*(CH$_3$)$_2$+C*H*$_2$PPh$_2$), 2.68–2.72 (m, 1H, SOC*H*$_2$), 3.27–3.34 (m, 1H, C*H*$_2$PPh$_2$), 3.94–3.99 (m, 1H, SOC*H*$_2$), 4.96–4.98 (m, 1H, C$_{cym}$-*H*), 5.11–5.12 (m, 1H, C$_{cym}$-*H*), 5.47–5.48 (m, 1H, C$_{cym}$-*H*), 5.51–5.52 (m, 1H, C$_{cym}$-*H*), 7.51–7.56 (m, 6H, *H*$_{Ph}$), 7.63–7.65 (m, 5H, *H*$_{Ph}$), 7.68–7.72 (m, 2H, *H*$_{Ph}$), 8.18–8.20 (m, 2H, *H*$_{Ph}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.3 (s, C*C*H$_3$), 18.9 (s, CH(*C*H$_3$)$_2$), 21.4 (s, CH(*C*H$_3$)$_2$), 22.7 (s, CH$_2$*C*H$_2$CH$_2$), 23.6 (d, $^1J_{P,C}$ = 31.9 Hz, *C*H$_2$PPh$_2$), 30.3 (s, *C*H(CH$_3$)$_2$), 35.2 (d, $^3J_{P,C}$ = 2.3 Hz, S*C*H$_2$), 89.2 (d, $^2J_{P,C}$ = 8.1 Hz, 2/6-*C*$_{cym}$), 93.2 (d, $^2J_{P,C}$ = 7.4 Hz, 2/6-*C*$_{cym}$), 93.9 (m, 3/5-*C*$_{cym}$), 99.6 (d, $^2J_{P,C}$ = 3.5 Hz, 3/5-*C*$_{cym}$), 116.0 (s, *C*CH(CH$_3$)$_2$), 129.0–137.7 (*C*$_{Ph}$). ^{31}P NMR (80 MHz, $CDCl_3$): δ 20.5 (s), –142.9 (sept, $^1J_{P,F}$ = 710.6 Hz, PF_6).

4b (*n* = 2; *x* = 1). Yield: 188 mg (78%). Anal. Found: C, 47.31; H, 4.25. Calcd for $C_{29}H_{31}ClF_6P_2RuS$ (754.04): C, 47.78; H, 4.41. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.04 (d, $^3J_{H,H}$ = 6.93 Hz, 3H, CH(C*H*$_3$)$_2$), 1.14 (d, $^3J_{H,H}$ = 6.91 Hz, 3H, CH(C*H*$_3$)$_2$), 1.51 (s, 3H, C*H*$_3$), 2.37–2.44 (m, 1H, C*H*(CH$_3$)$_2$), 2.99–3.06 (m, 2H, C*H*$_2$PPh$_2$), 3.52–3.65 (m, 1H, SOC*H*$_2$), 4.00–4.07 (m, 1H, SOC*H*$_2$), 5.62 (d, $^3J_{H,H}$ = 5.95 Hz, 1H, C$_{cym}$-*H*), 5.79 (d, $^3J_{H,H}$ = 5.92 Hz,

2H, C_{cym}-*H*), 6.11 (d, $^{3}J_{H,H}$ = 5.77 Hz, 1H, C_{cym}-*H*), 7.51–7.52 (m, 5H, H_{Ph}), 7.60–7.81 (m, 8H, H_{Ph}), 8.26–8.28 (m, 2H, H_{Ph}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.9 (s, C*C*H$_3$), 21.4 (s, CH(*C*H$_3$)$_2$), 21.5 (s, CH(*C*H$_3$)$_2$), 25.3 (d, $^{1}J_{P,C}$ = 31.4 Hz, *C*H$_2$PPh$_2$), 30.8 (s, *C*H(CH$_3$)$_2$), 59.5 (d, $^{2}J_{P,C}$ = 4.7 Hz, SO*C*H$_2$), 89.9 (d, $^{2}J_{P,C}$ = 1.0 Hz, 2/6-*C*$_{cym}$), 92.8 (d, $^{2}J_{P,C}$ = 6.0 Hz, 2/6-*C*$_{cym}$), 95.4 (d, $^{2}J_{P,C}$ = 1.78 Hz, 3/5-*C*$_{cym}$), 95.4 (d, $^{2}J_{P,C}$ = 1.78 Hz, 3/5-*C*$_{cym}$), 105.7 (s, *C*CH(CH$_3$)$_2$), 124.2–144.7 (*C*$_{Ph}$). ^{31}P NMR (80 MHz, $CDCl_3$): δ 73.0 (s), –142.8 (sept, $^{1}J_{P,F}$ = 711.2 Hz, PF_6).

5b (*n* = 3; *x* = 1). Yield: 181 mg (74%). Anal. Found: C, 47.92; H, 4.34. Calcd for $C_{29}H_{31}ClF_6P_2RuS$ (768.11): C, 48.47; H, 4.59. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.01 (d, $^{3}J_{H,H}$ = 6.79 Hz, 3H, CH(C*H*$_3$)$_2$), 0.75 (d, $^{3}J_{H,H}$ = 7.14 Hz, 3H, CH(C*H*$_3$)$_2$), 1.23 (s, 3H, C*H*$_3$), 1.66–1.88 (m, 3H, CH$_2$C*H*$_2$CH$_2$+C*H*$_2$PPh$_2$), 1.97–2.07 (m, 1H, C*H*(CH$_3$)$_2$), 2.50–2.55 (m, 1H, SOC*H*$_2$), 2.91–3.00 (m, 1H, C*H*$_2$PPh$_2$), 3.79–3.86 (m, 1H, SOC*H*$_2$), 4.79 (d, $^{3}J_{H,H}$ = 6.02 Hz, 1H, C_{cym}-*H*), 5.18 (dd, $^{3}J_{H,H}$ = 6.70 Hz, 2H, C_{cym}-*H*), 5.34 (d, $^{3}J_{H,H}$ = 6.70 Hz, 1H, C_{cym}-*H*), 5.34 (dd, $^{3}J_{H,H}$ = 5.58 Hz, 1H, C_{cym}-*H*), 7.24–7.30 (m, 5H, H_{Ph}), 7.33–7.43 (m, 6H, H_{Ph}), 7.52–7.57 (m, 2H, H_{Ph}), 7.92–7.94 (m, 2H, H_{Ph}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.6 (s, C*C*H$_3$), 17.95 (s, CH(*C*H$_3$)$_2$), 18.0 (s, CH(*C*H$_3$)$_2$), 22.6 (s, CH$_2$*C*H$_2$CH$_2$), 23.2 (d, $^{1}J_{P,C}$ = 32.6 Hz, *C*H$_2$PPh$_2$), 30.8 (s, *C*H(CH$_3$)$_2$), 54.9 (d, $^{3}J_{P,C}$ = 2.3 Hz, SO*C*H$_2$), 92.04 (s, 2/6-*C*$_{cym}$), 92.7 (s, 2/6-*C*$_{cym}$), 93.9 (d, $^{2}J_{P,C}$ = 8.1 Hz, 3/5-*C*$_{cym}$), 102.8 (s, *C*CH(CH$_3$)$_2$), 104.2 (d, $^{2}J_{P,C}$ = 4.9 Hz, 3/5-*C*$_{cym}$), 124.4–149.5 (*C*$_{Ph}$). ^{31}P NMR (80 MHz, $CDCl_3$): δ 25.0 (s), –143.0 (sept, $^{1}J_{P,F}$ = 710.5 Hz, PF_6).

X-ray crystallography

Data for X-ray diffraction analyses of single crystals of **1b**·CH_2Cl_2 were collected on a Stoe-IPDS 2T diffractometer at 200 K and of **4b**·CH_2Cl_2 and **5b**·CH_2Cl_2 on an Oxford Gemini S diffractometer at 110 K using Mo-*K*α radiation (λ = 0.71073 Å, graphite monochromator). Data for X-ray diffraction analyses of single crystals of **2b**·Me_2CO and **3b** were collected on an Oxford Gemini S diffractometer at 116 K using Cu-*K*α radiation (λ = 1.54184 Å, graphite monochromator). A summary of the crystallographic data, the data collection parameters and the refinement parameters are given in Table S3. Multiscan corrections were applied using the PLATON program package (T_{min}/T_{max}: 0.68/0.92, **1b**·CH_2Cl_2) and SCALE3 ABSPACK (0.66/1.00 **2b**·C_3H_6O; 0.58/1.00, **3b**; 0.82/1.00 **4b**·CH_2Cl_2; 0.95/1.00, **5b**), respectively.[3,4] The structures were solved with direct methods using SHELXS-97 and refined using full-matrix least-square routines against F^2 with SHELXL-97.[5,6] All non-hydrogen atoms were refined

with anisotropic displacement parameters and hydrogen atoms with isotropic ones. H atoms were placed in calculated positions according to the riding model. In complex **2b**·C_3H_6O four F atoms of the hexafluorophosphate anion were found to be disordered over two positions with occupancies of 70% and 30%. Furthermore, some restraints had to be used for the refinement of the solvent molecule acetone (DELU, SIMU, ISOR). CCDC 911007–911011 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/-data_request/cif.

In vitro antitumoral studies

Cell lines, culture conditions, and preparation of drug solutions

The cell lines 518A2, 8505C, A253, MCF-7, and SW480 were kindly provided by Dr. Thomas Müller, Department of Hematology/Oncology, Martin Luther University of Halle-Wittenberg, Halle (Saale), Germany. Cultures were maintained as monolayers in RPMI 1640 (PAA Laboratories, Pasching, Austria) supplemented with 10% fetal bovine serum (Biochrom AG, Berlin, Germany) and penicillin/streptomycin (PAA Laboratories) at 37 °C in a humidified atmosphere with 5% of CO_2. Stock solutions of investigated compounds were prepared in dimethylsulfoxide (DMSO, Sigma Aldrich) at a concentration of 20 mM, filtered through Millipore filter, 0.22 μm, before use, and diluted by a nutrient medium to various working concentrations. Nutrient medium was RPMI-1640 (PAA Laboratories) supplemented with 10% fetal bovine serum (Biochrom AG) and penicillin/streptomycin (PAA Laboratories).

Cytotoxicity assay

The cytotoxic activities of the compounds were evaluated using the sulforhodamine-B (SRB) (Sigma Aldrich, Germany) microculture colorimetric assay.[7] The cells were treated with serial dilutions of the compounds (0 to 300 μM) for 96 h and the assay was performed in triplicate. The final concentration of DMSO solvent never exceeded 0.5% at which it was non-toxic to the cells. Absorbance was measured at 570 nm using a 96-well plate reader (Tecan Spectra, Crailsheim, Germany). The IC_{50} values were estimated from the semilogarithmic dose-response curves.

Results

Tables

Table S1 Selected NMR spectroscopic data (δ in ppm, *J* in Hz) of [Ru(η^6-*p*-cym)Cl{$Ph_2P(CH_2)_nS(O)_xPh$-κ*P*,κ*S*}][PF_6] (**1b**–**5b**).

x	(*n* = 1) $Ph_2PC_\alpha H_2S(O)_xPh$			(*n* = 2) $Ph_2PC_\beta H_2C_\alpha H_2S(O)_xPh$				(*n* = 3) $Ph_2PC_\gamma H_2C_\beta H_2C_\alpha H_2S(O)_xPh$			
		$\delta_{\alpha\text{-}C}$ ($^1J_{P,C}$)	δ_P[a]		$\delta_{\alpha\text{-}C}$ ($^2J_{P,C}$)	$\delta_{\beta\text{-}C}$ ($^1J_{P,C}$)	δ_P[a]		$\delta_{\alpha\text{-}C}$ ($^3J_{P,C}$)	$\delta_{\gamma\text{-}C}$ ($^1J_{P,C}$)	δ_P[a]
0	1b	27.2 (21.0)	0.3 (31.3)	2b	36.6	28.8 (33.1)	66.5 (22.6)	3b	35.2 (2.3)	23.6 (31.9)	20.5 (24.5)
1	–	–	–	4b	59.5 (4.7)	25.3 (31.4)	73.0 (23.7)	5b	54.9 (2.3)	23.2 (32.6)	25.0 (24.7)

[a] For comparison, δ_P of the requisite neutral complexes[8] is given in parentheses.

Table S2 For comparison IC_{50} values[a] (in μM) of neutral ruthenium(II) arene complexes of the type [Ru(η^6-*p*-cymene)Cl_2{$Ph_2P(CH_2)_nS(O)_xPh$-κ*P*}] (**1a**–**5a**) having the P^S(O)$_x$ ligands κ*P* coordinated are given, taken from Ref. [8].

Compound	*n*/*x*	**518A2**	**8505C**	**A253**	**MCF-7**	**SW480**
1a	1/0	1.82 ± 0.52	2.85 ± 0.13	1.66 ± 0.28	6.55 ± 0.50	3.47 ± 0.01
2a	2/0	2.55 ± 0.14	3.90 ± 0.37	3.01 ± 0.11	1.37 ± 0.31	2.64 ± 0.07
3a	3/0	3.02 ± 0.06	3.64 ± 0.13	3.94 ± 0.11	1.75 ± 0.45	2.68 ± 0.10
4a	2/1	18.56 ± 0.43	28.59 ± 0.82	26.78 ± 0.35	10.47 ± 1.17	19.53 ± 1.39
5a	3/1	14.31 ± 3.55	12.02 ± 1.04	13.93 ± 1.54	1.79 ± 0.39	11.86 ± 3.26
cisplatin		1.52 ± 0.19	5.02 ± 0.23	0.81 ± 0.02	2.03 ± 0.11	3.24 ± 0.21

[a] Mean values ± SD (standard deviation) from three experiments.

Table S3. Crystallographic data, data collection parameters, and refinement parameters for **1b**·CH_2Cl_2, **2b**·C_3H_6O, **3b**, **4b**·CH_2Cl_2 and **5b**.

	1b·CH_2Cl_2	**2b**·Me_2CO	**3b**	**4b**·CH_2Cl_2	**5b**
Empirical formula	$C_{29}H_{31}ClF_6P_2RuS$ ·CH_2Cl_2	$C_{30}H_{33}ClF_6P_2RuS$·C_3H_6O	$C_{31}H_{35}ClF_6P_2RuS$	$C_{30}H_{33}ClF_6OP_2RuS$ ·CH_2Cl_2	$C_{31}H_{35}ClF_6OP_2RuS$
M_r	808.98	796.16	752.11	796.55	768.11
Crystal System	Triclinic	Orthorhombic	triclinic	monoclinic	triclinic
Space group	*P*–1	$P2_12_12_1$	*P*–1	$P2_1$/c	*P*–1
a / Å	10.148(2)	11.0143(2)	10.2594(5)	11.0122(4)	10.0603(2)
b / Å	10.774(3)	13.0922(2)	11.9436(7)	10.8492(3)	12.0758(3)
c / Å	16.677(6)	23.2592(4)	12.9600(8)	27.1047(9)	13.1404(3)
α / °	81.18(2)		83.578(5)		83.783(2)
β / °	79.32(2)		80.047(5)	99.695(4)	80.719(2)
γ / °	68.398(17)		88.023(5)		87.902(2)
V / $Å^3$	1658.8(8)	3354.01(1)	1554.14(2)	3192.05(2)	1565.92(6)
Z	2	4	2	4	2
D_{cal} / g·cm^{-3}	1.620	1.657	1.607	1.657	1.629
μ(Mo/Cu-Kα) / mm^{-1}	0.928 (Mo)	6.530 (Cu)	6.984 (Cu)	0.885 (Mo)	0.816 (Mo)
F(000)	816	1624	764	1612	780
θ range / °	2.66–25.00	3.80–65.55	3.48–65.25	2.96–25.50	3.04–26.00
Rfln collected	12855	13165	9237	11975	21224
Rfln observed [$I > 2\sigma(I)$]	4584	5267	4559	5144	5707
Rfln independent	5709	5672	5210	5930	6126
	(R_{int} = 0.0476)	(R_{int} = 0.0350)	(R_{int} = 0.0344)	(R_{int} = 0.0286)	(R_{int} = 0.0211)
Data/restraints/parameters	5709/0/391	5672/48/425	5210/0/379	5930/1/397	6126/0/388
Goodness-of-fit on F^2	0.961	1.013	1.026	1.036	1.034
*R*1, *wR*2 [$I > 2\sigma(I)$]	0.0395, 0.0967	0.0377, 0.0898	0.0427, 0.1039	0.0302, 0.0732	0.0207, 0.0491
*R*1, *wR*2 (all data)	0.0502, 0.0997	0.0400, 0.0905	0.0481, 0.1059	0.0371, 0.0766	0.0232, 0.0501
Largest diff. peak and hole/ e $Å^{-3}$	1.054 and –0.911	0.849 and –0.690	1.086 and –0.891	0.523 and –0.758	0.373 and –0.396

Figures

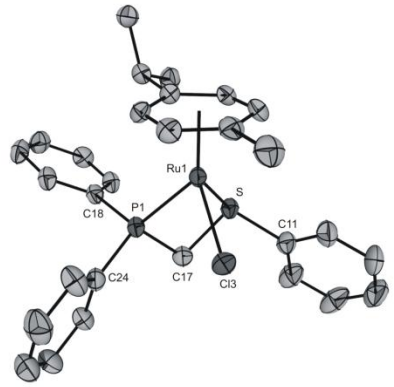

Fig. S1 Molecular structure of the cation in crystals of [Ru(η^6-*p*-cym)Cl{$Ph_2P(CH_2)SPh$-κ*P*,κ*S*}][PF_6]·CH_2Cl_2, **1b**·CH_2Cl_2. The ellipsoids are shown with a probability of 50%. H atoms have been omitted for clarity. Selected structural parameters (distances in Å, angles in °): Ru–Cl 2.381(1), Ru–P 2.314(1), Ru–S 2.390(1), Cl–Ru–P 83.3(4), Cl–Ru–S 88.2(4), S–Ru–P 70.6(4), C17–S–C11 103.1(2).

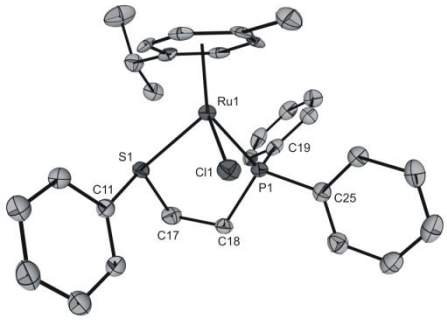

Fig. S2 Molecular structure of the cation in crystals of [Ru(η^6-*p*-cym)Cl{$Ph_2P(CH_2)_2SPh$-κ*P*,κ*S*}][PF_6]·C_3H_6O, **2b**·Me_2CO. The ellipsoids are shown with a probability of 50%. H atoms have been omitted for clarity. Selected structural parameters (distances in Å, angles in °): Ru–Cl 2.386(1), Ru–P 2.318(1), Ru–S 2.354(1), Cl–Ru–P 83.6(4), Cl–Ru–S 90.4(4), S–Ru–P 85.5(4), C11–S–C17 104.8(2).

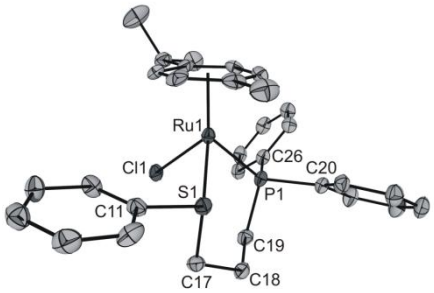

Fig. S3 Molecular structure of the cation in crystals of [Ru(η^6-*p*-cym)Cl{$Ph_2P(CH_2)_3SPh$-κ*P*,κ*S*}][PF_6], **3b**. The ellipsoids are shown with a probability of 50%. H atoms have been omitted for clarity. Selected structural parameters (distances in Å, angles in °): Ru–Cl 2.404(9), Ru–P 2.348(9), Ru–S 2.362(9), Cl–Ru–P 88.2(4), Cl–Ru–S 90.9(3), S–Ru–P 88.1(3), C11–S–C17 99.7(2).

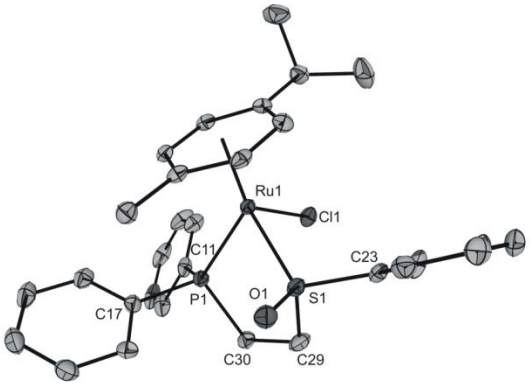

Fig. S4 Molecular structure of the cation in crystals of [Ru(η^6-*p*-cym)Cl{$Ph_2P(CH_2)_2S(O)Ph$-κ*P*,κ*S*}][PF_6]·CH_2Cl_2, **4b**·CH_2Cl_2. The ellipsoids are shown with a probability of 50%. H atoms have been omitted for clarity. Selected structural parameters (distances in Å, angles in °): Ru–Cl 2.398(6), Ru–P 2.312(7), Ru–S 2.262(7), Cl–Ru–P 84.0(2), Cl–Ru–S 88.5(2), S–Ru–P 81.4(2), C29–S–C23 103.1(1)

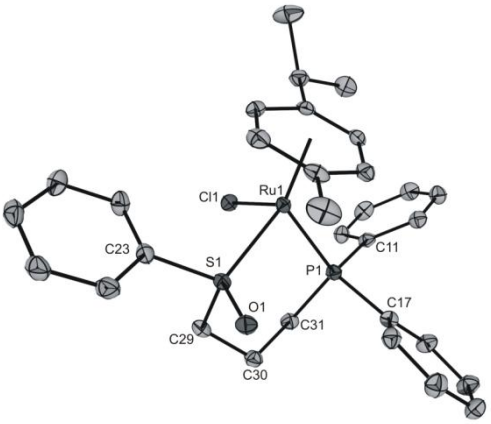

Fig. S5 Molecular structure of the cation in crystals of [Ru(η^6-*p*-cym)Cl{$Ph_2P(CH_2)_3S(O)Ph$-κ*P*,κ*S*}][PF_6], **5b**. The ellipsoids are shown with a probability of 50%. H atoms have been omitted for clarity. Selected structural parameters (distances in Å, angles in °): Ru–Cl 2.400(4), Ru–P 2.349(4), Ru–S 2.285(4), Cl–Ru–P 83.4(2), Cl–Ru–S 89.4(2), S–Ru–P 88.8(2), C29–S–C23 100.6(8).

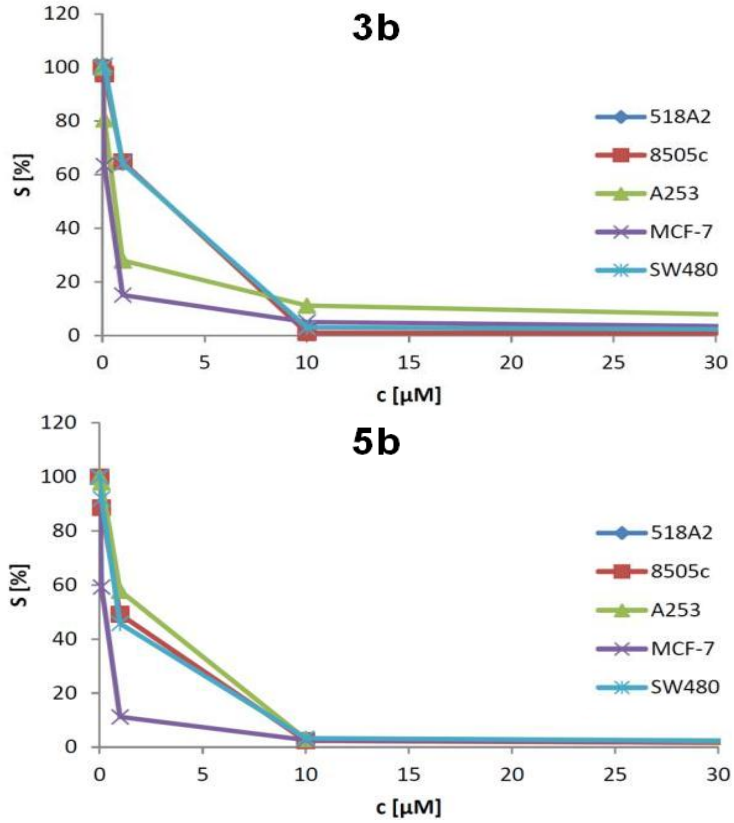

Fig. S6 Representative graphs showing survival (in %) of cells growth for 96 h in the presence of increasing concentrations of compounds **3b** and **5b**.

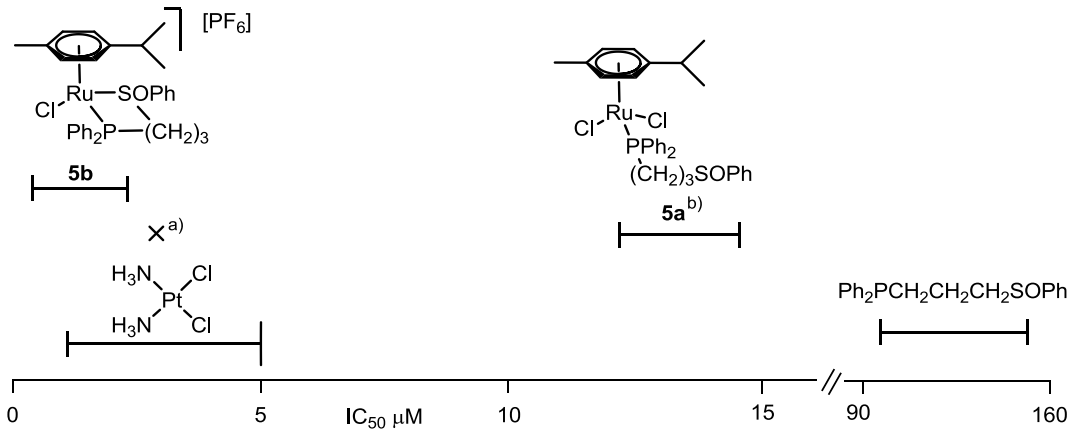

Fig. S7 Range of cytotoxicities of the cationic ruthenium complex **5b** against five cell lines (see Table 2) in comparison with the activities of the corresponding neutral complex **5a**, the noncoordinated ligand, and cisplatin. a) Cytotoxicity of **5a** against one cell line (MCF-7). b) Cytotoxicities of **5a** against four cell lines (518A2, 8505C, A253, SW480).

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