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Ruthenium− and Osmium−Arene Complexes of 2-Substituted Indolo[3,2-*c*]quinolines: Synthesis, Structure, Spectroscopic Properties, and Antiproliferative Activity

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The synthesis of new modified indolo[3,2-*c*]quinoline ligands $\mathbf{L^1}$−$\mathbf{L^8}$ with metal-binding sites is reported. By coordination to ruthenium− and osmium−arene moieties 16 complexes of the type [(η^6-*p*-cymene)M(L)Cl]Cl (**1a**,**b**−**8a**,**b**), where M is Ru^{II} or Os^{II} and L is $\mathbf{L^1}$−$\mathbf{L^8}$, have been prepared. All compounds were comprehensively characterized by elemental analysis, electrospray ionization mass spectrometry, IR, UV−vis, and NMR spectroscopy, thermogravimetric analysis, and single-crystal X-ray diffraction (**2a**, **4a**, **4b**, **5a**, **7a**, and **7b**). The complexes were tested for antiproliferative activity *in vitro* in three human cancer cell lines, namely, CH1 (ovarian carcinoma), SW480 (colon adenocarcinoma), and A549 (non-small-cell lung cancer), yielding IC_{50} values in the submicromolar or low micromolar range.

Introduction

Triggered by the success of flavopiridol, the first cyclin-dependent kinase (cdk) inhibitor under clinical investigation,[1] efforts have been focused on the development of targeted ruthenium complexes,[2−9] among them some with kinase-inhibitory properties.[10,11] Indolo[3,2-*d*]benzazepines, also referred to as paullones, were identified as putative cdk inhibitors by analysis of the National Cancer Institute (NCI) Human Tumor Cell Line Anti-Cancer Drug Screen Database.[12] Experiments with enzyme assays confirmed the assumption, and a larger series of paullones was evaluated for their biological activity.[13−15]

In order to overcome limitations of confined water solubility and bioavailability of these organic compounds, they were complexed with metal ions. As the paullone backbone itself is not suitable for coordination to metals, except for binding via lactam (or thiolactam) groups yielding thermodynamically nonstable four-membered metallocycles, metal-binding sites had to be created at the periphery of the molecule scaffold. By complexation of paullones with gallium(III),[16,17] ruthenium(II),[18−20] osmium(II),[19,20] and copper(II),[21] their physicochemical and biological properties could be altered markedly. Structure−activity relationship studies have shown

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(1) Christian, B. A.; Grever, M. A.; Byrd, J. C.; Lin, T. S. *Clin. Lymphoma Myeloma* **2009**, *9* (Suppl. 3), 179.
(2) Ang, W. H.; Dyson, P. J. *Eur. J. Inorg. Chem.* **2006**, 4003.
(3) Meggers, E.; Atilla-Gokcumen, G. E.; Gründler, K.; Corazon Frias, C.; Prokop, A. *Dalton Trans.* **2009**, 10882.
(4) Ratanaphan, A.; Temboot, P.; Dyson, P. J. *Chem. Biodiversity* **2010**, *7*, 1290.
(5) Grguric-Sipka, S.; Stepanenko, I. N.; Lazic, J. M.; Bartel, C.; Jakupec, M. A.; Arion, V. B.; Keppler, B. K. *Dalton Trans.* **2009**, 3334.
(6) Casini, A.; Karotki, A.; Gabbiani, C.; Rugi, F.; Vašák, M.; Messori, L.; Dyson, P. J. *Metallomics* **2009**, *1*, 434.
(7) Renfrew, A. K.; Phillips, A. D.; Egger, A. E.; Hartinger, C. G.; Bosquain, S. S.; Nazarov, A. A.; Keppler, B. K.; Gonsalvi, L.; Peruzzini, M.; Dyson, P. J. *Organometallics* **2009**, *28*, 1165.
(8) Mendoza-Ferri, M. G.; Hartinger, C. G.; Mendoza, M. A.; Groessl, M.; Egger, A. E.; Eichinger, R. E.; Mangrum, J. B.; Farrell, N. P.; Maruszak, M.; Bednarski, P. J.; Klein, F.; Jakupec, M. A.; Nazarov, A. A.; Severin, K.; Keppler, B. K. *J. Med. Chem.* **2009**, *52*, 916.
(9) Kandioller, W.; Hartinger, C. G.; Nazarov, A. A.; Bartel, C.; Skocic, M.; Jakupec, M. A.; Arion, V. B.; Keppler, B. K. *Chem.—Eur. J.* **2009**, *15*, 12283.
(10) Anand, R.; Maksimoska, J.; Pagano, N.; Wong, E. Y.; Gimotty, P. A.; Diamond, S. L.; Meggers, E.; Marmorstein, R. *J. Med. Chem.* **2009**, *52*, 1602.
(11) Filak, L. K.; Mühlgassner, G.; Jakupec, M. A.; Heffeter, P.; Berger, W.; Arion, V. B.; Keppler, B. K. *J. Biol. Inorg. Chem.* **2010**, *15*, 903.
(12) Zaharevitz, D. W.; Gussio, R.; Leost, M.; Senderowicz, A. M.; Lahusen, T.; Kunick, C.; Sausville, E. A. *Cancer Res.* **1999**, *59*, 2566.
(13) Schultz, C.; Link, A.; Leost, M.; Zaharevitz, D. W.; Gussio, R.; Sausville, E. A.; Meijer, L.; Kunick, C. *J. Med. Chem.* **1999**, *42*, 2909.
(14) Kunick, C.; Zeng, Z.; Gussio, R.; Zaharevitz, D.; Leost, M.; Totzke, F.; Schächtele, C.; Kubbutat, M. H. G.; Meijer, L.; Lemcke, T. *ChemBioChem* **2005**, *6*, 541.
(15) Becker, A.; Kohfeld, S.; Lader, A.; Preu, L.; Pies, T.; Wieking, K.; Ferandin, Y.; Knockaert, M.; Meijer, L.; Kunick, C. *Eur. J. Med. Chem.* **2010**, *45*, 335.
(16) Dobrov, A.; Arion, V. B.; Kandler, N.; Ginzinger, W.; Jakupec, M. A.; Rufińska, A.; G. v. Keyserlingk, N.; Galanski, M.; Kowol, C.; Keppler, B. K. *Inorg. Chem.* **2006**, *45*, 1945.
(17) Ginzinger, W.; Arion, V. B.; Giester, G.; Galanski, M.; Keppler, B. K. *Cent. Eur. J. Chem.* **2008**, *6*, 340.
(18) Schmid, W. F.; Zorbas-Seifried, S.; John, R. O.; Arion, V. B.; Jakupec, M. A.; Roller, A.; Galanski, M.; Chiorescu, I.; Zorbas, H.; Keppler, B. K. *Inorg. Chem.* **2007**, *46*, 3645.
(19) Schmid, W. F.; John, R. O.; Arion, V. B.; Jakupec, M. A.; Keppler, B. K. *Organometallics* **2007**, *26*, 6643.
(20) Schmid, W. F.; John, R. O.; Mühlgassner, G.; Heffeter, P.; Jakupec, M. A.; Galanski, M.; Berger, W.; Arion, V. B.; Keppler, B. K. *J. Med. Chem.* **2007**, *50*, 6343.
(21) Primik, M. F.; Mühlgassner, G.; Jakupec, M. A.; Zava, O.; Dyson, P. J.; Arion, V. B.; Keppler, B. K. *Inorg. Chem.* **2010**, *49*, 302.

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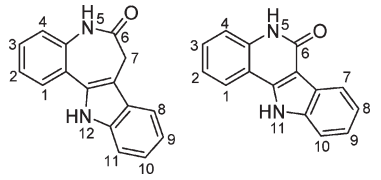
Chart 1. Indolo[3,2-*d*]benzazepine (left) and Indolo[3,2-*c*]quinoline (right) Backbones with Atom-Numbering Schemes



that an intact lactam unit is favorable for cdk inhibition.[13,22,23] *In vitro* cytotoxicity of ruthenium and osmium complexes was, however, found to be higher if complexation occurred via the modified lactam group and not through a chelator group at position 9 of the paullone backbone.[20]

Paullones contain a seven-membered folded azepine ring, which makes the whole molecule nonplanar (Chart 1). Recently, efforts by us were extended to indolo[3,2-*c*]quinolines (Chart 1) that have a framework similar to that of paullones but comprise a flat six-membered ring instead of the folded seven-membered azepine ring, making the whole heteroaromatic system planar. The antiproliferative properties of this class of organic molecules have been reported recently,[24−28] along with convenient synthetic routes.[29] A few ruthenium and osmium complexes showed a significantly higher *in vitro* cytotoxicity compared to that of the related paullone complexes. In addition, the indoloquinolines revealed a high potential for intercalation into DNA and caused concentration-dependent cell cycle perturbations. However, the reported metal complexes of indolo[3,2-*c*]quinolines showed a much lower stability in both organic and aqueous media, in some cases leading to rapid dissociation of the ligands from the metal-arene scaffold.[11]

With the intention to increase the hydrolytic stability of metal complexes by involvement of sp^2-hybridized nitrogen donors, we suggested performing condensation reactions of the indoloquinoline hydrazine with 2-formyl- and/or 2-acetylpyridine and to bind the resulting Schiff base ligands to ruthenium(II)−arene and osmium(II)−arene moieties, taking into account the different kinetics of ligand exchange reactions at ruthenium(II) and osmium(II).[30] Looking for structure−activity relationships to be elucidated in this class of complexes, we intended to study the effect of substitution in position 2 of the parent indoloquinoline on the antiproliferative activity.

Herein we report on the synthesis of 16 novel ruthenium(II)−arene and osmium(II)−arene complexes with modified indolo[3,2-*c*]quinolines **1a**,**b**−**8a**,**b** (Scheme 1, Chart 2), of which six were characterized by X-ray diffraction, their spectroscopic properties (NMR, UV−vis, FT-IR), thermal behavior, and ESI mass spectra. The cytotoxic activity of these metal complexes assayed *in vitro* in three human cancer cell lines, CH1 (ovarian carcinoma), SW480 (colon adenocarcinoma), and A549 (non-small-cell lung carcinoma), is also reported.

Experimental Section

Characterization of the Compounds. One-dimensional ^{1}H and ^{13}C NMR and two-dimensional ^{1}H−^{1}H COSY, ^{1}H−^{1}H TOCSY, ^{1}H−^{1}H ROESY or ^{1}H−^{1}H NOESY, ^{1}H−^{13}C HSQC, and ^{1}H−^{13}C HMBC NMR spectra were recorded on two Bruker Avance III spectrometers at 500.32 or 500.10 (^{1}H), and 125.82 or 125.76 (^{13}C) MHz, respectively, by using as a solvent DMSO-d_6 or MeOD-d_4 at room temperature and standard pulse programs. ^{1}H and ^{13}C shifts are quoted relative to the solvent residual signals. The atom numbering used for assignments is depicted in Chart S1. IR spectra were measured on a Bruker Vertex 70 FT-IR spectrometer by means of attenuated total reflection (ATR) technique, and UV−vis spectra were recorded with a Perkin-Elmer Lambda 650 spectrophotometer equipped with a six-cell changer and a Peltier element for temperature control. Electrospray ionization mass spectrometry (ESI-MS) was carried out with a Bruker Esquire 3000 instrument; the samples were dissolved in methanol. Thermogravimetric analysis (TGA) and differential thermal analysis (DTA) were carried out on a Mettler Toledo TGA/SDTA 851^e instrument. All elemental analyses were performed at the Microanalytical Laboratory of the University of Vienna with a Perkin-Elmer 2400 CHN elemental analyzer.

Synthesis of the Ligands. Ethanol was dried using standard procedures. 2-Aminobenzylamine and substituted indole-2,3-diones were purchased from Aldrich and used as received. Indoloquinolines **A** were synthesized by reaction of 2-aminobenzylamine with indole-2,3-diones in acetic acid and further chlorinated with phosphorus oxychloride to derivatives **B** by following the procedures reported previously (Scheme 1).[24,25,29] Compounds **B** were heated in neat hydrazine hydrate under an Ar atmosphere for 24−29 h, and after cooling, compounds **C** were filtered off, washed with water and diethyl ether, dried *in vacuo*, and used without further purification. Acetylpyridine hydrazone was prepared as described elsewhere.[31]

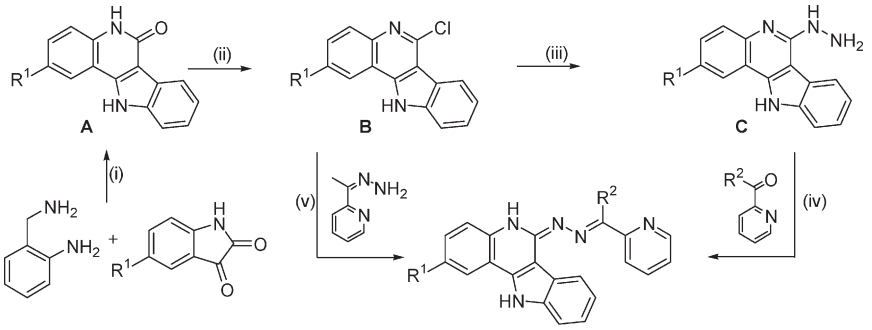
General Procedure A. To the corresponding 11*H*-indolo[3,2-*c*]-quinolin-6-yl)hydrazine (1 equiv) in a 25 mL Schlenk tube was added a solution of 2-formylpyridine (1.1 equiv) or 2-acetylpyridine (1.1 equiv) in ethanol, and the resulting mixture was stirred under an argon atmosphere for 24 h. The mixture was allowed to cool to room temperature; the precipitate formed was filtered off, washed with small amounts of ethanol (2 × 1 mL) and diethyl ether (2 × 2 mL), and dried *in vacuo* at 50 °C.

***N*-(5,11-Dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-methylidene)azine (L^1).** General procedure A: (11*H*-Indolo-[3,2-*c*]quinolin-6-yl)hydrazine (500 mg, 2.01 mmol), ethanol (10 mL), 2-formylpyridine (212 μL, 2.22 mmol). Yield: 607 mg, 89%. Anal. Calcd for $C_{21}H_{15}N_5 \cdot 0.15H_2O$ (M_r 340.08): C, 74.17; H, 4.53; N, 20.59. Found: C, 74.09; H, 4.46; N, 20.72. ESI-MS (methanol), positive: m/z 338 $[M + H]^+$, 360 $[M + Na]^+$. IR (ATR, selected bands, ν_{max}): 3337, 2935, 2830, 1631, 1569, 1528, 1456, 1367, 1216, 1029, 1002, 745, 717, 680, 637 cm^{-1}.

***N*-(5,11-Dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (L^2).** General procedure A: (11*H*-Indolo-[3,2-*c*]quinolin-6-yl)hydrazine (500 mg, 2.01 mmol), ethanol (10 mL), 2-acetylpyridine (248 μL, 2.22 mmol). Yield: 561 mg, 76%.

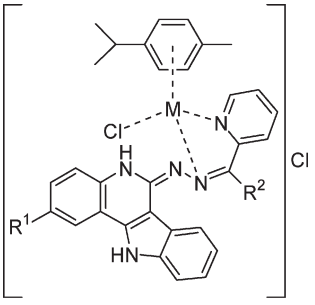
(22) Leost, M.; Schultz, C.; Link, A.; Wu, Y. Z.; Biernat, J.; Mandelkow, E.-M.; Bibb, J. A.; Snyder, G. L.; Greengard, P.; Zaharevitz, D. W.; Gussio, R.; Senderowicz, A. M.; Sausville, E. A.; Kunick, C.; Meijer, L. *Eur. J. Biochem.* **2000**, *267*, 5983.
(23) Kunick, C.; Lauenroth, K.; Wieking, K.; Xie, X.; Schultz, C.; Gussio, R.; Zaharevitz, D.; Leost, M.; Meijer, L.; Weber, A.; Jørgensen, F. S.; Lemcke, T. *J. Med. Chem.* **2004**, *47*, 22.
(24) Chen, Y. L.; Chung, C. H.; Chen, I. L.; Chen, P. H.; Jeng, H. W. *Bioorg. Med. Chem.* **2002**, *10*, 2705.
(25) Hu, X. W.; Chien, C. M.; Yang, S. H.; Lin, Y. H.; Lu, C. M.; Chen, Y. L.; Lin, S. R. *Cell Biol. Toxicol.* **2006**, *22*, 417.
(26) Yang, S. H.; Chien, C. M.; Lu, C. M.; Chen, Y. L.; Chang, L. S.; Lin, S. R. *Leuk. Res.* **2007**, *31*, 1413.
(27) Chien, C. M.; Sheng-Huei Yang, S. H.; Lin, K. L.; Chen, Y. L.; Chang, L. S.; Lin, S. R. *Chem.-Biol. Interact.* **2008**, *176*, 40.
(28) Tzeng, C. C.; Chen, Y. L.; Lin, J. J.; Lu, C. M. U.S. Pat. Appl. US2009/0298846 A1, Dec. 3, 2009.
(29) Bergman, J.; Engqvist, R.; Stalhandske, C.; Wallberg, H. *Tetrahedron* **2003**, *59*, 1033.
(30) Peacock, A. F. A.; Melchart, M.; Habtemariam, A.; Parsons, S.; Sadler, P. J. *Chem.—Eur. J.* **2007**, *13*, 2601.
(31) Kowol, C. R.; Reisner, E.; Chiorescu, I.; Arion, V. B.; Galanski, M.; Deubel, D. V.; Keppler, B. K. *Inorg. Chem.* **2008**, *47*, 11032.

Scheme 1. Synthesis of the Modified Indoloquinoline Ligands[a]



[a] Reagents and conditions: (i) HOAc, Ar, 140 °C, 4 h; (ii) $POCl_3$, Ar, 140 °C, 24−27 h; (iii) $N_2H_4 \cdot H_2O$, Ar, 120 °C, 24−29 h; (iv) EtOH, Ar, 65 °C, 24 h; (v) 1-butanol, Ar, 130 °C, 27 h.

Chart 2. Ruthenium(II)− and Osmium(II)−Arene Complexes with Modified Indoloquinoline Ligands[a]



1a: R^1 = H, R^2 = H, M = Ru
1b: R^1 = H, R^2 = H, M = Os
2a: R^1 = H, R^2 = CH_3, M = Ru
2b: R^1 = H, R^2 = CH_3, M = Os
3a: R^1 = F, R^2 = CH_3, M = Ru
3b: R^1 = F, R^2 = CH_3, M = Os
4a: R^1 = Cl, R^2 = H, M = Ru
4b: R^1 = Cl, R^2 = H, M = Os
5a: R^1 = Cl, R^2 = CH_3, M = Ru
5b: R^1 = Cl, R^2 = CH_3, M = Os
6a: R^1 = Br, R^2 = CH_3, M = Ru
6b: R^1 = Br, R^2 = CH_3, M = Os
7a: R^1 = CH_3, R^2 = CH_3, M = Ru
7b: R^1 = CH_3, R^2 = CH_3, M = Os
8a: R^1 = NO_2, R^2 = CH_3, M = Ru
8b: R^1 = NO_2, R^2 = CH_3, M = Os

[a] Underlined compounds have been characterized by X-ray crystallography.

Anal. Calcd for $C_{22}H_{17}N_5 \cdot 0.15H_2O$ (M_r 354.11): C, 74.62; H, 4.92; N, 19.78. Found: C, 74.44; H, 4.58; N, 19.89. ESI-MS (methanol), positive: m/z 352 $[M + H]^+$, 374 $[M + Na]^+$. IR (ATR, selected bands, ν_{max}): 3353, 3085, 2955, 1627, 1534, 1456, 1372, 1278, 1218, 1032, 1006, 964, 781, 717, 679, 630 cm^{-1}.

***N*-(2-Fluoro-5,11-dihydroindolo[3,2-*c*]quinolin-6-yl)-*N*′-(1-pyridin-2-yl-ethylidene)azine (L^3).** General procedure A: (2-Fluoro-11*H*-indolo[3,2-*c*]quinolin-6-yl)hydrazine (800 mg, 3.01 mmol), ethanol (10 mL), 2-acetylpyridine (371 μL, 3.31 mmol). Yield: 1040 mg, 94%. Anal. Calcd for $C_{22}H_{16}N_5F$ (M_r 369.39): C, 71.53; H, 4.37; N, 18.96. Found: C, 71.37; H, 4.13; N, 18.72. ESI-MS (methanol), positive: m/z 370 $[M + H]^+$, 392 $[M + Na]^+$. IR (ATR, selected bands, ν_{max}): 3349, 3083, 2956, 2919, 2876, 1162, 1589, 1540, 1453, 1277, 1218, 1200, 1015, 873, 856, 807, 748, 679, 613 cm^{-1}.

***N*-(2-Chloro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-methylidene)azine (L^4).** General procedure A: (2-Chloro-11*H*-indolo[3,2-*c*]quinolin-6-yl)hydrazine (700 mg, 2.48 mmol), ethanol (10 mL), 2-formylpyridine (260 μL, 2.72 mmol). Yield: 599 mg, 65%. Anal. Calcd for $C_{21}H_{14}N_5Cl \cdot 0.25H_2O$ (M_r 376.33): C, 67.12; H, 3.88; N, 18.61. Found: C, 67.16; H, 3.81; N, 18.44. ESI-MS (methanol), positive: m/z 372 $[M + H]^+$. IR (ATR, selected bands, ν_{max}): 3339, 3060, 2752, 1631, 1567, 1529, 1217, 1152, 1046, 999, 930, 809, 741, 676, 620 cm^{-1}.

***N*-(2-Chloro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (L^5).** General procedure A: (2-Chloro-11*H*-indolo[3,2-*c*]quinolin-6-yl)hydrazine (700 mg, 2.48 mmol), ethanol (10 mL), 2-acetylpyridine (303 μL, 2.72 mmol). Yield: 640 mg, 67%. Anal. Calcd for $C_{22}H_{16}N_5Cl$ (M_r 385.85): C, 68.48; H, 4.18; N, 18.15. Found: C, 68.21; H, 4.10; N, 18.08. ESI-MS (methanol), positive: m/z 386 $[M + H]^+$, 408 $[M + Na]^+$. IR (ATR, selected bands, ν_{max}): 3335, 3104, 2955, 1629, 1542, 1453, 1429, 1406, 1363, 1277, 1217, 1154, 1015, 809, 747 cm^{-1}.

***N*-(2-Bromo-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (L^6).** General procedure A: (2-Bromo-11*H*-indolo[3,2-*c*]quinolin-6-yl)hydrazine (800 mg, 2.45 mmol), ethanol (10 mL), 2-acetylpyridine (300 μL, 2.72 mmol). Yield: 890 mg, 84%. Anal. Calcd for $C_{22}H_{16}N_5Br \cdot 0.1H_2O$ (M_r 432.10): C, 61.15; H, 3.78; N, 16.21. Found: C, 61.01; H, 3.59; N, 16.29. ESI-MS (methanol), positive: m/z 432 $[M + H]^+$. IR (ATR, selected bands, ν_{max}): 3331, 3076, 2954, 1628, 1538, 1452, 1428, 1405, 1275, 1215, 1152, 1014, 994, 807, 777, 745, 717, 678 cm^{-1}.

***N*-(2-Methyl-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (L^7).** General procedure A: (2-Methyl-11*H*-indolo[3,2-*c*]quinolin-6-yl)hydrazine (800 mg, 3.05 mmol), ethanol (8 mL), 2-acetylpyridine (376 μL, 3.36 mmol). Anal. Calcd for $C_{23}H_{19}N_5 \cdot 0.2H_2O$ (M_r 369.03): C, 74.86; H, 5.30; N, 18.98. Found: C, 74.86; H, 4.95; N, 18.71. Yield: 1016 mg, 91%. ESI-MS (methanol), positive: m/z 366 $[M + H]^+$, 388 $[M + Na]^+$. IR (ATR, selected bands, ν_{max}): 3352, 3037, 2964, 2870, 1630, 1598, 1530, 1459, 1332, 1277, 1218, 1017, 994, 806, 778, 747, 670, 635 cm^{-1}.

***N*-(2-Nitro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (L^8).** A mixture of 6-chloro-2-nitro-11*H*-indolo[3,2-*c*]quinoline (1000 mg, 3.36 mmol), 2-acetylpyridine hydrazone (730 mg, 5.40 mmol), and 1-butanol (10 mL) in a Schlenk tube under argon atmosphere was heated at 130 °C for 27 h. After cooling to room temperature, the solid formed was filtered off, washed with water (4 × 5 mL) and ethanol (2 × 2 mL), and dried *in vacuo*. Further purification was performed by dissolution of the product in ethyl acetate (1.5 L/g) and washing the organic phase with half saturated aqueous $NaHCO_3$ solution (5 × 300 mL) and brine (2 × 300 mL). The solvent was removed under reduced pressure, and the product was dried *in vacuo*.

Yield: 1194 mg, 90%. Anal. Calcd for $C_{22}H_{16}N_6O_2 \cdot 0.25H_2O$ (M_r 400.91): C, 65.91; H, 4.15; N, 20.96. Found: C, 65.95; H, 4.43; N, 20.88. ESI-MS (methanol), positive: m/z 397 $[M + H]^+$, 419 $[M + Na]^+$. IR (ATR, selected bands, ν_{max}): 3316, 2920, 1614, 1541, 1509, 1457, 1408, 1319, 1270, 1146, 1095, 1014, 791, 734, 676, 609, 589 cm^{-1}.

Synthesis of the Complexes. $[Ru^{II}Cl(\mu\text{-}Cl)(\eta^6\text{-}p\text{-cymene})]_2$[32] and its osmium analogue $[Os^{II}Cl(\mu\text{-}Cl)(\eta^6\text{-}p\text{-cymene})]_2$[33] were prepared according to the literature.

General Procedure B. To a mixture of the corresponding ligand (1 equiv) and $[MCl_2(p\text{-cymene})_2]_2$ (0.5 equiv), where M is Ru or Os, in a 25 mL Schlenk tube was added dry ethanol under Ar at room temperature. The resulting solution was protected from light and stirred for 24 h. The precipitate formed was collected under suction, washed with a small amount of ethanol (1−2 mL) and diethyl ether (2 × 5−10 mL), and dried *in vacuo* at 47−50 °C under light protection.

General Procedure C. To a mixture of the corresponding ligand (1 equiv) $[MCl_2(p\text{-cymene})_2]_2$ (0.5 equiv), where M is Ru or Os, in a 25 mL Schlenk tube was added dry ethanol under Ar. The resulting solution was protected from light and stirred at room temperature for 24 h. The precipitate formed was collected under suction, washed with a small amount of ethanol (1−2 mL) and diethyl ether (2 × 5−10 mL), and dried *in vacuo* at 47 °C under light protection. To the mother liquor was added diethyl ether (15−20 mL), whereupon a second crop of product was precipitated. This solid was also collected under suction and dried *in vacuo* at 47−50 °C under light protection. In all cases the NMR spectra of both crops were identical.

(η^6-*p*-Cymene)[*N*-(5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-methylidene)]azinechloridoruthenium(II) Chloride (1a). General procedure B: *N*-(5,11-Dihydroindolo-[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-methylidene)azine (200 mg, 0.59 mmol), $[RuCl_2(p\text{-cymene})_2]_2$ (182 mg, 0.30 mmol), ethanol (5 mL). Yield: 337 mg, 88% (yellow solid). Anal. Calcd for $C_{31}H_{29}N_5Cl_2Ru \cdot 1.5H_2O$ (M_r 670.59): C, 55.52; H, 4.81; N, 10.44. Found: C, 55.54; H, 4.69; N, 10.37. ESI-MS (methanol), positive: m/z 608 $[M - Cl]^+$. IR (ATR, selected bands, ν_{max}): 3655, 3412, 2967, 2868, 1628, 1590, 1527, 1466, 1400, 1228, 1008, 777, 751, 718, 704 cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD): δ 9.44 (d, 1H, ^3J = 5.6 Hz, H^{18}), 8.72 (s, 1H, H^{14}), 8.40 (d, 1H, ^3J = 8.0 Hz, H^7), 8.20−8.15 (m, 2H, H^1+H^{20}), 7.97 (d, 1H, ^3J = 7.9 Hz, H^{21}), 7.81 (d, 1H, ^3J = 8.4 Hz, H^4), 7.73−7.67 (m, 2H, H^{10}+H^{19}), 7.63−7.58 (m, 1H, H^3), 7.51−7.47 (m, 1H, H^9), 7.45−7.41 (m, 1H, H^2), 7.39−7.35 (m, 1H, H^8), 5.87 (d, 1H, ^3J = 6.1 Hz, H^{cy2}), 5.65 (d, 1H, ^3J = 6.1 Hz, H^{cy1}), 5.62 (d, 1H, ^3J = 6.2 Hz, $H^{cy2'}$), 5.21 (d, 1H, ^3J = 6.2 Hz, $H^{cy1'}$), 2.86−2.76 (m, 1H, H^{cy3}), 2.23 (s, 3H, H^{cy5}), 1.16 (d, 3H, ^3J = 6.9 Hz, $H^{cy4'}$), 1.12 (d, 3H, ^3J = 6.9 Hz, H^{cy4}) ppm, H^5+H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 156.4 (*C*H, C^{14}), 155.5 (*C*H, C^{18}), 154.9 (C_q, C^{16}), 149.0 (C_q, C^6), 139.5 (*C*H, C^{20}), 138.9 (C_q, C^{10a}), 136.3 (C_q, C^{4a}), 129.6 (*C*H, C^3), 126.3 (*C*H, C^{19}), 126.3 (*C*H, C^{21}), 124.8 (*C*H, C^9), 123.5 (C_q, C^{6b}), 123.3 (*C*H, C^2), 121.9 (2 *C*H, C^1 + C^7), 121.4 (*C*H, C^8), 117.0 (*C*H, C^4), 113.3 (C_q, C^{11b}), 111.5 (*C*H, C^{10}), 105.1 (C_q, C^{cy2a}), 104.1 (C_q, C^{6a}), 103.7 (C_q, C^{cy1a}), 87.0 (*C*H, $C^{cy2'}$), 85.9 (*C*H, C^{cy2}), 85.7 (*C*H, C^{cy1}), 84.0 (*C*H, $C^{cy1'}$), 31.1 (*C*H, C^{cy3}), 21.0 (CH_3, C^{cy4}), 20.7 (CH_3, $C^{cy4'}$), 17.7 (CH_3, C^{cy5}) ppm, C^{11a} not observed.

(η^6-*p*-Cymene)[*N*-(5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-methylidene)]azinechloridoosmium(II) Chloride (1b). General procedure B: *N*-(5,11-Dihydroindolo-[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-methylidene)azine (170 mg, 0.50 mmol), $[OsCl_2(p\text{-cymene})_2]_2$ (199 mg, 0.25 mmol), ethanol (4.5 mL). Yield: 298 mg, 81% (yellow solid). Anal. Calcd for $C_{31}H_{29}N_5Cl_2Os \cdot 1.5H_2O$ (M_r 759.75): C, 49.01; H, 4.25; N, 9.22. Found: C, 49.05; H, 4.07; N, 9.06. ESI-MS (methanol), positive: m/z 698 $[M - Cl]^+$, 662 $[M - Cl - HCl]^+$. IR (ATR, selected bands, ν_{max}): 3656, 3398, 2963, 2869, 1628, 1591, 1522, 1465, 1398, 1339, 1227, 1033, 1006, 777, 751, 704, 647 cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD): δ 9.38 (d, 1H, ^3J = 5.7 Hz, H^{18}), 9.13 (s, 1H, H^{14}), 8.39 (d, 1H, ^3J = 8.0 Hz, H^7), 8.21−8.12 (m, 3H, H^1+H^{20}+H^{21}), 7.72−7.66 (m, 3H, H^4+H^{10}+H^{19}), 7.62−7.57 (m, 1H, H^3), 7.51−7.47 (m, 1H, H^9), 7.46−7.42 (m, 1H, H^2), 7.40−7.35 (m, 1H, H^8), 6.16 (d, 1H, ^3J = 5.8 Hz, H^{cy2}), 5.92−5.88 (m, 2H, H^{cy1}+$H^{cy2'}$), 5.35 (d, 1H, ^3J = 5.7 Hz, $H^{cy1'}$), 2.75−2.66 (m, 1H, H^{cy3}), 2.29 (s, 3H, H^{cy5}), 1.12 (d, 3H, ^3J = 6.9 Hz, $H^{cy4'}$), 1.08 (d, 3H, ^3J = 6.9 Hz, H^{cy4}) ppm, H^5+H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 157.6 (*C*H, C^{14}), 156.1 (C_q, C^{16}), 155.1 (*C*H, C^{18}), 149.1 (C_q, C^6), 139.7 (*C*H, C^{20}), 139.5 (C_q, C^{11a}), 138.9 (C_q, C^{10a}), 136.2 (C_q, C^{4a}), 129.6 (*C*H, C^3), 127.1 (*C*H, C^{19}), 126.0 (*C*H, C^{21}), 124.8 (*C*H, C^9), 123.5 (C_q, C^{6b}), 123.3 (*C*H, C^2), 121.9 (*C*H, C^1), 121.9 (*C*H, C^7), 121.4 (*C*H, C^8), 116.9 (*C*H, C^4), 113.2 (C_q, C^{11b}), 111.5 (*C*H, C^{10}), 103.8 (C_q, C^{6a}), 97.1 (C_q, C^{cy1a}), 96.3 (C_q, C^{cy2a}), 79.0 (*C*H, $C^{cy2'}$), 77.6 (*C*H, C^{cy2}), 76.4 (*C*H, C^{cy1}), 74.5 (*C*H, $C^{cy1'}$), 31.3 (*C*H, C^{cy3}), 21.2 (CH_3, C^{cy4}), 20.9 (CH_3, $C^{cy4'}$), 17.6 (CH_3, C^{cy5}) ppm.

(η^6-*p*-Cymene)[*N*-(5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-ethylidene)]azinechloridoruthenium(II) Chloride (2a). General procedure B: *N*-(5,11-Dihydroindolo-[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (200 mg, 0.57 mmol), $[RuCl_2(p\text{-cymene})_2]_2$ (175 mg, 0.29 mmol), ethanol (5 mL). Yield: 282 mg, 75% (orange solid). Anal. Calcd for $C_{32}H_{31}N_5Cl_2Ru \cdot 1.5H_2O$ (M_r 684.62): C, 56.14; H, 5.01; N, 10.23. Found: C, 56.22; H, 4.98; N, 10.22. ESI-MS (methanol), positive: m/z 622 $[M - Cl]^+$. IR (ATR, selected bands, ν_{max}): 3650, 3345, 3149, 2965, 1630, 1587, 1528, 1462, 1397, 1340, 1223, 745, 702, 702, 638 cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD): δ 10.59 (br s, 1H, H^5), 9.50 (d, 1H, ^3J = 5.4 Hz, H^{18}), 8.50 (d, 1H, ^3J = 8.0 Hz, H^7), 8.26−8.22 (m, 1H, H^{20}), 8.20 (d, 1H, ^3J = 7.9 Hz, H^1), 8.13 (d, 1H, ^3J = 7.9 Hz, H^{21}), 7.77−7.73 (m, 2H, H^4+H^{19}), 7.71 (d, 1H, ^3J = 8.2 Hz, H^{10}), 7.60−7.55 (m, 1H, H^3), 7.52−7.47 (m, 1H, H^9), 7.44−7.38 (m, 2H, H^2+H^8), 5.89 (d, 1H, ^3J = 6.2 Hz, H^{cy2}), 5.66 (d, 1H, ^3J = 6.2 Hz, H^{cy1}), 5.64 (d, 1H, ^3J = 6.2 Hz, $H^{cy2'}$), 5.18 (d, 1H, ^3J = 6.2 Hz, $H^{cy1'}$), 2.86−2.76 (s, 3H, H^{15}+m, 1H, H^{cy3}), 2.22 (s, 3H, H^{cy5}), 1.15 (d, 3H, ^3J = 6.9 Hz, $H^{cy4'}$), 1.11 (d, 3H, ^3J = 6.9 Hz, H^{cy4}) ppm, H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 165.5 (C_q, C^{14}). 155.6 (C_q, C^{16}), 155.4 (C_q, C^{18}), 147.9 (C_q, C^6), 139.5 (*C*H, C^{20}), 139.2 (C_q, C^{11a}), 138.8 (C_q, C^{10a}), 136.5 (C_q, C^{4a}), 129.5 (*C*H, C^3), 126.5 (*C*H, C^{19}), 125.7 (*C*H, C^{21}), 124.7 (*C*H, C^9), 123.7 (C_q, C^{6b}), 123.0 (*C*H, C^2), 121.9 (*C*H, C^1), 121.8 (*C*H, C^7), 121.4 (*C*H, C^8), 116.9 (*C*H, C^4), 113.2 (C_q, C^{11b}), 111.5 (*C*H, C^{10}), 104.5 (C_q, C^{cy2a}), 104.2 (C_q, C^{6a}), 103.8 (C_q, C^{cy1a}), 87.6 (*C*H, $C^{cy2'}$), 86.0 (*C*H, C^{cy2}), 85.6 (*C*H, C^{cy1}), 84.0 (*C*H, $C^{cy1'}$), 31.0 (*C*H, C^{cy3}), 21.0 (CH_3, C^{cy4}), 20.7 (CH_3, $C^{cy4'}$), 17.8 (CH_3, C^{cy5}), 14.5 (CH_3, C^{15}) ppm.

(η^6-*p*-Cymene)[*N*-(5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-ethylidene)]azinechloridoosmium(II) Chloride (2b). General procedure C: *N*-(5,11-Dihydroindolo[3,2-*c*]-quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (188 mg, 0.57 mmol), $[OsCl_2(p\text{-cymene})_2]_2$ (212 mg, 0.27 mmol, ethanol (4.8 mL). Yield: 269 mg +66 mg, 84% (orange solid). Anal. Calcd for $C_{32}H_{31}N_5Cl_2Os \cdot 2H_2O$ (M_r 782.79): C, 49.10; H, 4.51; N, 8.95. Found: C, 49.19; H, 4.44; N, 8.78. ESI-MS (methanol), positive: m/z 712 $[M - Cl]^+$, 676 $[M - Cl - HCl]^+$. IR (ATR, selected bands, ν_{max}): 3642, 3338, 3069, 2965, 2875, 1630, 1587, 1525, 1463, 1400, 1223, 1035, 1011, 745, 698, 637 cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD): δ 9.43 (d, 1H, ^3J = 5.4 Hz, H^{18}), 8.46 (d, 1H, ^3J = 7.9 Hz, H^7), 8.26−8.21 (m, 2H, H^{20}+H^{21}), 8.19 (dd, 1H, ^3J = 8.1 Hz, ^4J = 0.9 Hz, H^1), 7.76−7.72 (m, 1H, H^{19}), 7.71 (d, 1H, ^3J = 8.2 Hz, H^{10}), 7.62 (d, 1H, ^3J = 8.3 Hz, H^4), 7.59−7.54 (m, 1H, H^3), 7.51−7.47 (m, 1H, H^9), 7.44−7.37 (m, 2H, H^2+H^8), 6.17 (d, 1H, ^3J = 5.8 Hz, H^{cy2}), 5.92 (d, 1H, ^3J = 5.8 Hz, $H^{cy2'}$), 5.87 (d, 1H, ^3J = 5.8 Hz, H^{cy1}), 5.32 (d, 1H, ^3J = 5.8 Hz, $H^{cy1'}$), 2.86 (s, 3H, H^{15}) 2.75−2.66 (m, 1H, H^{cy3}), 2.28 (s, 3H, H^{cy5}), 1.11 (d, 3H,

(32) Bennett, M. A.; Smith, A. K. *J. Chem. Soc., Dalton Trans.* **1974**, 233.

(33) Kiel, W. A.; Ball, R. G.; Graham, W. A. G. *J. Organomet. Chem.* **1990**, *383*, 481.

^3J = 7.0 Hz, $H^{cy4'}$), 1.07 (d, 3H, ^3J = 7.0 Hz, H^{cy4}) ppm, H^5+H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 166.5 (C_q, C^{14}). 156.6 (C_q, C^{16}), 155.3 (*C*H, C^{18}), 148.0 (C_q, C^6), 139.5 (*C*H, C^{20}), 139.2 (C_q, C^{11a}), 138.8 (C_q, C^{10a}), 136.3 (C_q, C^{4a}), 129.5 (*C*H, C^3), 127.3 (*C*H, C^{19}), 125.8 (*C*H, C^{21}), 124.7 (*C*H, C^9), 123.7 (C_q, C^{6b}), 123.0 (*C*H, C^2), 121.9 (*C*H, C^1), 121.7 (*C*H, C^7), 121.4 (*C*H, C^8), 116.8 (*C*H, C^4), 113.2 (C_q, C^{11b}), 111.5 (*C*H, C^{10}), 103.9 (C_q, C^{6a}), 97.0 (C_q, C^{cy1a}), 95.6 (C_q, C^{cy2a}), 79.3 (*C*H, $C^{cy2'}$), 77.7 (*C*H, C^{cy2}), 76.1 (*C*H, C^{cy1}), 74.4 (*C*H, $C^{cy1'}$), 31.2 (*C*H, C^{cy3}), 21.3 (CH_3, C^{cy4}), 20.9 (CH_3, $C^{cy4'}$), 17.7 (CH_3, C^{cy5}), 14.2 (CH_3, C^{15}) ppm.

(η^6-*p*-Cymene)[*N*-(2-fluoro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-ethylidene)]azinechloridoruthenium(II) Chloride (3a). General procedure B: *N*-(2-Fluoro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (180 mg, 0.49 mmol), $[RuCl_2(p\text{-cymene})_2]_2$ (149 mg, 0.24 mmol), ethanol (4 mL). Yield: 287 mg, 87% (orange solid). Anal. Calcd for $C_{32}H_{30}N_5FCl_2Ru\cdot 1.25H_2O$ (M_r 698.11): C, 55.05; H, 4.69; N, 10.03. Found: C, 55.04; H, 4.38; N, 9.94. ESI-MS (methanol), positive: m/z 640 $[M - Cl]^+$. IR (ATR, selected bands, ν_{max}): 3656, 3350, 3069, 2967, 1638, 1596, 1532, 1461, 1395, 1339, 1226, 1202, 1016, 873, 811, 779, 742, 707, 644 cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD): δ 9.51 (d, 1H, ^3J = 5.7 Hz, H^{18}), 8.51 (d, 1H, ^3J = 7.8 Hz, H^7), 8.27−8.22 (m, 1H, H^{20}), 8.14 (d, 1H, ^3J = 8.0 Hz, H^{21}), 7.93 (dd, 1H, J = 8.9, 2.1 Hz, H^1), 7.78−7.73 (m, 2H, H^4+H^{19}), 7.71 (d, 1H, ^3J = 8.2 Hz, H^{10}), 7.54−7.50 (m, 1H, H^9), 7.44−7.40 (m, 1H, H^8), 7.39−7.34 (m, 1H, H^3), 5.90 (d, 1H, ^3J = 6.2 Hz, H^{cy2}), 5.67 (d, 1H, ^3J = 6.2 Hz, H^{cy1}), 5.65 (d, 1H, ^3J = 6.2 Hz, $H^{cy2'}$), 5.22 (d, 1H, ^3J = 6.2 Hz, $H^{cy1'}$), 2.87−2.79 (m, 1H, H^{cy3}), 2.78 (s, 3H, H^{15}), 2.22 (s, 3H, H^{cy5}), 1.15 (d, 3H, ^3J = 6.9 Hz, $H^{cy4'}$), 1.11 (d, 3H, ^3J = 6.9 Hz, H^{cy4}) ppm, H^5 and H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 165.8 (C_q, C^{14}). 158.7 (d, C_q, ^1J = 240 Hz, C^2), 155.5 (C_q, C^{16}), 155.4 (*C*H, C^{18}), 147.6 (C_q, C^6), 139.5 (*C*H, C^{20}), 138.9 (C_q, C^{10a}), 138.3 (d, C_q, ^4J = 2.5 Hz, C^{11a}), 133.1 (d, C_q, ^4J = 1.5 Hz, C^{4a}), 126.6 (*C*H, C^{19}), 125.7 (*C*H, C^{21}), 125.0 (*C*H, C^9), 123.5 (C_q, C^{6b}), 121.9 (*C*H, C^7), 121.6 (*C*H, C^8), 118.7 (d, *C*H, ^3J = 8 Hz, C^4), 117.1 (d, *C*H, ^2J = 25 Hz, C^3), 114.2 (d, C_q, ^3J = 9 Hz, C^{11b}), 111.6 (*C*H, C^{10}), 107.3 (d, *C*H, ^2J = 25 Hz, C^1), 104.8 (C_q, C^{6a}), 104.6 (C_q, C^{cy2a}), 103.7 (C_q, C^{cy1a}), 87.6 (*C*H, $C^{cy2'}$), 86.0 (*C*H, C^{cy2}), 85.7 (*C*H, C^{cy1}), 84.1 (*C*H, $C^{cy1'}$), 31.0 (*C*H, C^{cy3}), 21.0 (CH_3, C^{cy4}), 20.7 (CH_3, $C^{cy4'}$), 17.8 (CH_3, C^{cy5}), 14.4 (CH_3, C^{15}) ppm.

(η^6-*p*-Cymene)[*N*-(2-fluoro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-ethylidene)]azinechloridoosmium(II) Chloride (3b). General procedure B: *N*-(2-Fluoro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (180 mg, 0.49 mmol), $[OsCl_2(p\text{-cymene})_2]_2$ (193 mg, 0.24 mmol), ethanol (4 mL). Yield: 333 mg, 90% (orange solid). Anal. Calcd for $C_{32}H_{30}N_5FCl_2Os\cdot 1.5H_2O$ (M_r 791.77): C, 48.54; H, 4.20; N, 8.85. Found: C, 48.62; H, 3.99; N, 8.66. ESI-MS (methanol), positive: m/z 730 $[M - Cl]^+$, 694 $[M - Cl - HCl]^+$. IR (ATR, selected bands, ν_{max}): 3648, 3350, 3163, 3067, 2966, 1638, 1598, 1528, 1461, 1396, 1225, 1202, 810, 778, 742, 694, 643 cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD): δ 9.44 (d, 1H, ^3J = 5.6 Hz, H^{18}), 8.47 (d, 1H, ^3J = 7.9 Hz, H^7), 8.26−8.20 (m, 2H, H^{20}+H^{21}), 7.92 (dd, 1H, J = 8.9, 2.8 Hz, H^1), 7.77−7.73 (m, 1H, H^{19}), 7.71 (d, 1H, ^3J = 8.2 Hz, H^{10}), 7.61 (dd, 1H, J = 8.2 + 4.6 Hz, H^4), 7.53−7.49 (m, 1H, H^9), 7.42−7.38 (m, 1H, H^8), 7.37−7.32 (m, 1H, H^3), 6.18 (d, 1H, ^3J = 5.8 Hz, H^{cy2}), 5.93 (d, 1H, ^3J = 5.8 Hz, $H^{cy2'}$), 5.88 (d, 1H, ^3J = 5.8 Hz, H^{cy1}), 5.34 (d, 1H, ^3J = 5.8 Hz, $H^{cy1'}$), 2.86 (s, 3H, H^{15}), 2.75−2.66 (m, 1H, H^{cy3}), 2.28 (s, 3H, H^{cy5}), 1.10 (d, 3H, ^3J = 7.0 Hz, $H^{cy4'}$), 1.07 (d, 3H, ^3J = 7.0 Hz, H^{cy4}) ppm, H^5 and H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 166.7 (C_q, C^{14}), 158.7 (d, C_q, ^1J = 242 Hz, C^2), 156.5 (C_q, C^{16}), 155.3 (*C*H, C^{18}), 147.3 (C_q, C^6), 139.6 (*C*H, C^{20}), 138.9 (C_q, C^{10a}), 138.3 (d, C_q, ^4J = 2.7 Hz, C^{11a}), 132.9 (d, C_q, ^4J = 1.8 Hz, C^{4a}), 127.4 (*C*H, C^{19}), 125.9 (*C*H, C^{21}), 125.0 (*C*H, C^9), 123.5 (C_q, C^{6b}), 121.9 (*C*H, C^7), 121.6 (*C*H, C^8), 118.6 (d, *C*H, ^3J = 9 Hz, C^4), 117.1 (d, *C*H, ^2J = 25 Hz, C^3), 114.1 (d, C_q, ^3J = 9 Hz, C^{11b}), 111.6 (*C*H, C^{10}), 107.3 (d, *C*H, ^2J = 25 Hz, C^1), 104.5 (C_q, C^{6a}), 96.9 (C_q, C^{cy1a}), 95.7 (C_q, C^{cy2a}), 79.3 (*C*H, $C^{cy2'}$), 77.7 (*C*H, C^{cy2}), 76.2 (*C*H, C^{cy1}), 74.5 (*C*H, $C^{cy1'}$), 31.2 (*C*H, C^{cy3}), 21.3 (CH_3, C^{cy4}), 20.9 (CH_3, $C^{cy4'}$), 17.7 (CH_3, C^{cy5}), 14.2 (CH_3, C^{15}) ppm.

(η^6-*p*-Cymene)[*N*-(2-chloro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-methylidene)]azinechloridoruthenium(II) Chloride (4a). General procedure B: *N*-(2-Chloro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-methylidene)azine (200 mg, 0.54 mmol), $[RuCl_2(p\text{-cymene})_2]_2$ (188 mg, 0.27 mmol), ethanol (4.5 mL). Yield: 344 mg, 94% (orange-yellow solid). Anal. Calcd for $C_{31}H_{28}N_5Cl_3Ru\cdot 0.5H_2O$ (M_r 687.02): C, 54.19; H, 4.25; N, 10.19. Found: C, 54.17; H, 4.28; N, 9.96. ESI-MS (methanol), positive: m/z 642 $[M - Cl]^+$. IR (ATR, selected bands, ν_{max}): 3665, 3382, 3025, 2963, 2867, 2648, 1629, 1589, 1530, 1458, 1403, 1331, 1295, 1228, 1085, 1011, 938, 825, 772, 748, 695 cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD): δ 9.44 (d, 1H, ^3J = 5.6 Hz, H^{18}), 8.72 (s, 1H, H^{14}), 8.33 (d, 1H, ^3J = 7.8 Hz, H^7), 8.17−8.12 (m, 1H, H^{20}), 8.11 (d, 1H, ^4J = 2.3 Hz, H^1), 7.92 (d, 1H, ^3J = 7.6 Hz, H^{21}), 7.75 (d, 1H, ^3J = 8.8 Hz, H^4), 7.73−7.67 (m, 2H, H^{10}+H^{19}), 7.54 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.3 Hz, H^3), 7.53−7.49 (m, 1H, H^9), 7.37−7.33 (m, 1H, H^8), 5.87 (d, 1H, ^3J = 6.2 Hz, H^{cy2}), 5.65 (d, 1H, ^3J = 6.2 Hz, H^{cy1}), 5.61 (d, 1H, ^3J = 6.2 Hz, $H^{cy2'}$), 5.22 (d, 1H, ^3J = 6.2 Hz, $H^{cy1'}$), 2.83−2.74 (m, 1H, H^{cy3}), 2.22 (s, 3H, H^{cy5}), 1.15 (d, 3H, ^3J = 7.0 Hz, $H^{cy4'}$), 1.11 (d, 3H, ^3J = 7.0 Hz, H^{cy4}) ppm, H^5 and H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 157.0 (*C*H, C^{14}). 155.5 (*C*H, C^{18}), 154.7 (C_q, C^{16}), 148.6 (C_q, C^6), 139.7 (*C*H, C^{20}), 138.9 (C_q, C^{10a}), 138.1 (C_q, C^{11a}), 134.8 (C_q, C^{4a}), 129.4 (*C*H, C^3), 128.6 (C_q, C^2), 126.5 (2C_q, C^{19}+C^{21}), 125.1 (*C*H, C^9), 123.2 (C_q, C^{6b}), 122.0 (*C*H, C^7), 121.6 (*C*H, C^8), 121.4 (*C*H, C^1), 118.4 (*C*H, C^4), 114.5 (C_q, C^{11b}), 111.6 (*C*H, C^{10}), 105.3 (C_q, C^{cy2a}), 104.7 (C_q, C^{6a}), 103.7 (C_q, C^{cy1a}), 86.9 (*C*H, $C^{cy2'}$), 85.8 (2*C*H, C^{cy1}+C^{cy2}), 84.1 (*C*H, $C^{cy1'}$), 31.1 (*C*H, C^{cy3}), 21.0 (CH_3, C^{cy4}), 20.7 (CH_3, $C^{cy4'}$), 17.7 (CH_3, C^{cy5}) ppm.

(η^6-*p*-Cymene)[*N*-(2-chloro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-methylidene)]azinechloridoosmium(II) Chloride (4b). General procedure B: *N*-(2-Chloro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-methylidene)azine (200 mg, 0.54 mmol), $[OsCl_2(p\text{-cymene})_2]_2$ (213 mg, 0.27 mmol), ethanol (4.5 mL). Yield: 347 mg, 84% (orange-red solid). Anal. Calcd for $C_{31}H_{28}N_5Cl_3Os\cdot H_2O$ (M_r 785.19): C, 47.42; H, 3.85; N, 8.92. Found: C, 47.31; H, 3.81; N, 8.67. ESI-MS (methanol), positive: m/z 732 $[M - Cl]^+$, 696 $[M - Cl - HCl]^+$. IR (ATR, selected bands, ν_{max}): 3654, 2965, 2872, 1630, 1588, 1518, 1454, 1397, 1371, 1333, 1224, 1011, 773, 745, 693, 651 cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD): δ 9.38 (d, 1H, ^3J = 5.7 Hz, H^{18}), 9.12 (s, 1H, H^{14}), 8.36 (d, 1H, ^3J = 7.9 Hz, H^7), 8.18−8.11 (m, 3H, H^1+H^{20}+H^{21}), 7.72−7.67 (m, 2H, H^{10}+H^{19}), 7.63 (d, 1H, ^3J = 8.8 Hz, H^4), 7.54 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.3 Hz, H^3), 7.53−7.49 (m, 1H, H^9), 7.40−7.36 (m, 1H, H^8), 6.17 (d, 1H, ^3J = 5.9 Hz, H^{cy2}), 5.92−5.88 (m, 2H, H^{cy1}+$H^{cy2'}$), 5.38 (d, 1H, ^3J = 5.9 Hz, $H^{cy1'}$), 2.74−2.65 (m, 1H, H^{cy3}), 2.29 (s, 3H, H^{cy5}), 1.12 (d, 3H, ^3J = 6.9 Hz, $H^{cy4'}$), 1.07 (d, 3H, ^3J = 6.9 Hz, H^{cy4}) ppm, H^5 and H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 158.2 (*C*H, C^{14}), 156.0 (C_q, C^{16}), 155.1 (*C*H, C^{18}), 148.8 (C_q, C^6), 139.7 (*C*H, C^{20}), 138.9 (C_q, C^{10a}), 138.1 (C_q, C^{11a}), 134.6 (C_q, C^{4a}), 129.4 (*C*H, C^3), 128.5 (C_q, C^2), 127.2 (*C*H, C^{19}), 126.1 (*C*H, C^{21}), 125.1 (*C*H, C^9), 123.3 (C_q, C^{6b}), 122.0 (*C*H, C^7), 121.6 (*C*H, C^8), 121.4 (*C*H, C^1), 118.3 (*C*H, C^4), 114.4 (C_q, C^{11b}), 111.6 (*C*H, C^{10}), 104.5 (C_q, C^{6a}), 97.1 (C_q, C^{cy1a}), 96.6 (C_q, C^{cy2a}), 79.0 (*C*H, $C^{cy2'}$), 77.6 (*C*H, C^{cy2}), 76.5 (*C*H, C^{cy1}), 74.7 (*C*H, $C^{cy1'}$), 31.3 (*C*H, C^{cy3}), 21.2 (CH_3, C^{cy4}), 20.9 (CH_3, $C^{cy4'}$), 17.6 (CH_3, C^{cy5}) ppm.

(η^6-*p*-Cymene)[*N*-(2-chloro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-ethylidene)]azinechloridoruthenium(II) Chloride (5a). General procedure B: *N*-(2-Chloro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)-hydrazine (200 mg, 0.52 mmol), $[RuCl_2(p\text{-cymene})_2]_2$ (174 mg, 0.28 mmol), ethanol (4.7 mL). Yield: 262 mg, 73% (yellow solid). Anal. Calcd for $C_{32}H_{30}N_5Cl_3Ru\cdot 1.5H_2O$ (M_r 719.07): C, 53.45; H, 4.63; N, 9.74. Found: C, 53.28; H, 4.51; N, 9.65. ESI-MS

(methanol), positive: m/z 656 $[M - Cl]^+$. IR (ATR, selected bands, ν_{max}): 3656, 3357, 3146, 3063, 2966, 1628, 1589, 1536, 1457, 1434, 1395, 1332, 1224, 1016, 813, 784, 744, 713, 696, 640 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ 9.50 (d, 1H, ^3J = 5.6 Hz, H^{18}), 8.50 (d, 1H, ^3J = 7.9 Hz, H^7), 8.26−8.19 (d, 1H, ^4J = 2.1 Hz, H^1+m, 1H, H^{20}), 8.13 (d, 1H, ^3J = 8.0 Hz, H^{21}), 7.78−7.74 (m, 1H, H^{19}), 7.71 (d, 1H, ^3J = 8.4 Hz, H^{10}), 7.68 (d, 1H, ^3J = 8.8 Hz, H^4), 7.53−7.49 (m, 2H, H^3+H^9), 7.43−7.39 (m, 1H, H^8), 5.90 (d, 1H, ^3J = 6.2 Hz, H^{cy2}), 5.67 (d, 1H, ^3J = 6.2 Hz, H^{cy1}), 5.65 (d, 1H, ^3J = 6.2 Hz, $H^{cy2'}$), 5.22 (d, 1H, ^3J = 6.2 Hz, $H^{cy1'}$), 2.86−2.76 (m, 1H, H^{cy3}+s, 3H, H^{15}), 2.21 (s, 3H, H^{cy5}), 1.15 (d, 3H, ^3J = 6.9 Hz, $H^{cy4'}$), 1.11 (d, 3H, ^3J = 6.9 Hz, H^{cy4}) ppm, H^5 and H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 166.0 (C_q, C^{14}), 155.5 (CH, C^{18}), 155.4 (C_q, C^{16}), 147.5 (C_q, C^6), 139.5 (CH, C^{20}), 138.9 (C_q, C^{10a}), 137.8 (C_q, C^{11a}), 135.0 (C_q, C^{4a}), 129.3 (CH, C^3), 128.2 (C_q, C^2), 126.6 (CH, C^{19}), 125.8 (CH, C^{21}), 125.0 (CH, C^9), 123.5 (C_q, C^{6b}), 121.9 (CH, C^7), 121.6 (CH, C^8), 121.3 (CH, C^1), 118.4 (CH, C^4), 114.5 (C_q, C^{11b}), 111.6 (CH, C^{10}), 104.8 (C_q, C^{6a}), 104.6 (C_q, C^{cy2a}), 103.7 (C_q, C^{cy1a}), 87.5 (CH, $C^{cy2'}$), 86.0 (CH, C^{cy2}), 85.7 (CH, C^{cy1}), 84.1 (CH, $C^{cy1'}$), 31.0 (CH, C^{cy3}), 21.0 (CH_3, C^{cy4}), 20.7 (CH_3, $C^{cy4'}$), 17.7 (CH_3, C^{cy5}), 14.5 (CH_3, C^{15}) ppm.

(η^6-*p*-Cymene)[*N*-(2-chloro-5,11dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-ethylidene)]azinechloridoosmium-(II) Chloride (5b). General procedure B: *N*-(2-Chloro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (200 mg, 0.52 mmol), $[OsCl_2(p\text{-cymene})_2]_2$ (205 mg, 0.27 mmol), ethanol (4.5 mL). Yield: 320 mg, 79% (orange-yellow solid). Anal. Calcd for $C_{32}H_{30}N_5Cl_3Os \cdot 2H_2O$ (M_r 817.23): C, 47.03; H, 4.19; N, 8.57. Found: C, 46.81; H, 4.06; N, 8.39. ESI-MS (methanol), positive: m/z 746 $[M - Cl]^+$, 710 $[M - Cl - HCl]^+$. IR (ATR, selected bands, ν_{max}): 3656, 3360, 3161, 2965, 1629, 1590, 1532, 1457, 1395, 1331, 1256, 1016, 812, 783, 743, 694, 640 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ 9.43 (d, 1H, ^3J = 5.6 Hz, H^{18}), 8.46 (d, 1H, ^3J = 7.9 Hz, H^7), 8.27−8.20 (m, 3H, H^1+H^{20}+H^{21}), 7.77−7.73 (m, 1H, H^{19}), 7.71 (d, 1H, ^3J = 8.2 Hz, H^{10}), 7.58 (d, 1H, ^3J = 8.8 Hz, H^4), 7.55−7.49 (m, 2H, H^3+H^9), 7.42−7.38 (m, 1H, H^8), 6.19 (d, 1H, ^3J = 5.8 Hz, H^{cy2}), 5.94 (d, 1H, ^3J = 5.7 Hz, $H^{cy2'}$), 5.88 (d, 1H, ^3J = 5.8 Hz, H^{cy1}), 5.36 (d, 1H, ^3J = 5.7 Hz, $H^{cy1'}$), 2.86 (s, 3H, H^{15}), 2.75−2.66 (m, 1H, H^{cy3}), 2.28 (s, 3H, H^{cy5}), 1.11 (d, 3H, ^3J = 6.9 Hz, $H^{cy4'}$), 1.07 (d, 3H, ^3J = 6.9 Hz, H^{cy4}) ppm, H^5 and H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 166.9 (C_q, C^{14}), 156.4 (C_q, C^{16}), 155.3 (CH, C^{18}), 147.7 (C_q, C^6), 139.6 (CH, C^{20}), 138.9 (C_q, C^{10a}), 137.8 (C_q, C^{11a}), 134.8 (C_q, C^{4a}), 129.3 (CH, C^3), 128.2 (C_q, C^2), 127.5 (CH, C^{19}), 125.9 (CH, C^{21}), 125.0 (CH, C^9), 123.5 (C_q, C^{6b}), 121.8 (CH, C^7), 121.6 (CH, C^8), 121.3 (CH, C^1), 118.3 (CH, C^4), 114.4 (C_q, C^{11b}), 111.6 (CH, C^{10}), 104.5 (C_q, C^{6a}), 96.9 (C_q, C^{cy1a}), 95.8 (C_q, C^{cy2a}), 79.2 (CH, $C^{cy2'}$), 77.7 (CH, C^{cy2}), 76.2 (CH, C^{cy1}), 74.5 (CH, $C^{cy1'}$), 31.2 (CH, C^{cy3}), 21.3 (CH_3, C^{cy4}), 20.8 (CH_3, $C^{cy4'}$), 17.7 (CH_3, C^{cy5}), 14.2 (CH_3, C^{15}) ppm.

(η^6-*p*-Cymene)[*N*-(2-bromo-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-ethylidene)]azinechloridoruthenium-(II) Chloride (6a). General procedure B: *N*-(2-Bromo-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (200 mg, 0.47 mmol), $[RuCl_2(p\text{-cymene})_2]_2$ (142 mg, 0.23 mmol), ethanol (4.2 mL). Yield: 234 mg, 68% (yellow solid). Anal. Calcd for $C_{32}H_{30}N_5Cl_2BrRu \cdot 1.5H_2O$ (M_r 763.52): C, 50.34; H, 4.36; N, 9.17. Found: C, 50.16; H, 4.18; N, 9.08. ESI-MS (methanol), positive: m/z 702 $[M - Cl]^+$. IR (ATR, selected bands, ν_{max}): 3652, 3359, 3217, 3142, 2966, 1626, 1586, 1534, 1455, 1393, 1331, 1222, 1014, 812, 744, 712, 693, 642, 577 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ 9.50 (d, 1H, ^3J = 5.6 Hz, H^{18}), 8.50 (d, 1H, ^3J = 7.8 Hz, H^7), 8.37 (d, 1H, ^4J = 1.9 Hz, H^1), 8.24 (ddd, ^3J = 7.9, 7.8 Hz, ^4J = 1.4 Hz, H^{20}), 8.13 (d, 1H, ^3J = 7.9 Hz, H^{21}), 7.76 (ddd, 1H, ^3J = 7.9, 5.6 Hz, ^4J = 1.3 Hz, H^{19}), 7.71 (d, 1H, ^3J = 8.2 Hz, H^{10}), 7.66−7.62 (m, 2H, H^3+H^4), 7.51 (ddd, 1H, ^3J = 8.2, 7.1 Hz, ^4J = 1.2 Hz, H^9), 7.43−7.39 (m, 1H, H^8), 5.90 (d, 1H, ^3J = 6.2 Hz, H^{cy2}), 5.67 (d, 1H, ^3J = 6.2 Hz, H^{cy1}), 5.65 (d, 1H, ^3J = 6.1 Hz, $H^{cy2'}$), 5.22 (d, 1H, ^3J = 6.1 Hz, $H^{cy1'}$), 2.86−2.76 (s, 3H, H^{15} + m, 1H, H^{cy3}), 2.22 (s, 3H, H^{cy5}), 1.15 (d, 3H, ^3J = 7.0 Hz, $H^{cy4'}$), 1.11 (d, 3H, ^3J = 6.9 Hz, H^{cy4}) ppm, H^5 and H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 166.1 (C_q, C^{14}), 155.5 (CH, C^{18}), 155.4 (C_q, C^{16}), 147.5 (C_q, C^6), 139.5 (CH, C^{20}), 138.9 (C_q, C^{10a}), 137.7 (C_q, C^{11a}), 135.4 (C_q, C^{4a}), 132.1 (CH, C^3), 126.6 (CH, C^{19}), 125.8 (CH, C^{21}), 125.1 (CH, C^9), 124.4 (CH, C^1), 123.5 (C_q, C^{6b}), 121.9 (CH, C^7), 121.6 (CH, C^8), 118.6 (CH, C^4), 115.4 (C_q, C^2), 114.9 (C_q, C^{11b}), 111.6 (CH, C^{10}), 104.8 (C_q, C^{6a}), 104.6 (C_q, C^{cy2a}), 103.7 (C_q, C^{cy1a}), 87.5 (CH, $C^{cy2'}$), 86.0 (CH, C^{cy2}), 85.7 (CH, C^{cy1}), 84.2 (CH, $C^{cy1'}$), 31.1 (CH, C^{cy3}), 21.0 (CH_3, C^{cy4}), 20.7 (CH_3, $C^{cy4'}$), 17.8 (CH_3, C^{cy5}), 14.5 (CH_3, C^{15}) ppm.

(η^6-*p*-Cymene)[(*N*-(2-bromo-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-ethylidene)]azinechloridoosmium-(II) Chloride (6b). General procedure C: *N*-(2-Bromo-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)-azine (200 mg, 0.47 mmol), $[OsCl_2(p\text{-cymene})_2]_2$ (184 mg, 0.23 mmol), ethanol (4 mL). Yield: 231 + 106 mg, 88% (red solid). Elemental analysis of pure product was obtained by dissolution of the first crop in methanol and filtration through a GF3-filter, followed by evaporation of the solvent under reduced pressure and drying *in vacuo* at 45 °C. Anal. Calcd for $C_{32}H_{30}N_5BrCl_2Os$ (M_r 825.65): C, 46.55; H, 3.66; N, 8.48. Found: C, 46.40; H, 3.62; N, 8.41. ESI-MS (methanol), positive: m/z 790 $[M - Cl]^+$, 754 $[M - Cl - HCl]^+$. IR (ATR, selected bands, ν_{max}): 3615, 3232, 2965, 2748, 1625, 1585, 1454, 1402, 1332, 1222, 1155, 1023, 811, 784, 749, 695, 641, 617, 576 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ 9.43 (d, 1H, ^3J = 5.5 Hz, H^{18}), 8.45 (d, 1H, ^3J = 7.9 Hz, H^7), 8.36 (d, 1H, ^4J = 1.9 Hz, H^1), 8.26−8.19 (m, 2H, H^{20}+H^{21}), 7.77−7.72 (m, 1H, H^{19}), 7.70 (d, 1H, ^3J = 8.0 Hz, H^{10}), 7.64 (dd, 1H, ^3J = 8.7 Hz, ^4J = 1.9 Hz, H^3), 7.53−7.47 (m, 2H, H^4+H^9), 7.42−7.37 (m, 1H, H^8), 6.18 (d, 1H, ^3J = 5.6 Hz, H^{cy2}), 5.92 (d, 1H, ^3J = 5.7 Hz, $H^{cy2'}$), 5.87 (d, 1H, ^3J = 5.6 Hz, H^{cy1}), 5.34 (d, 1H, ^3J = 5.7 Hz, $H^{cy1'}$), 2.86 (s, 3H, H^{15}), 2.74−2.65 (m, 1H, H^{cy3}), 2.27 (s, 3H, H^{cy5}), 1.10 (d, 3H, ^3J = 6.8 Hz, $H^{cy4'}$), 1.06 (d, 3H, ^3J = 6.9 Hz, H^{cy4}) ppm, H^5 and H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 166.9 (C_q, C^{14}), 156.4 (C_q, C^{16}), 155.4 (CH, C^{18}), 147.6 (C_q, C^6), 139.6 (CH, C^{20}), 138.9 (C_q, C^{10a}), 137.6 (C_q, C^{11a}), 135.2 (C_q, C^{4a}), 132.1 (CH, C^3), 127.5 (CH, C^{19}), 125.9 (CH, C^{21}), 125.0 (CH, C^9), 124.4 (CH, C^1), 123.5 (C_q, C^{6b}), 121.8 (CH, C^7), 121.6 (CH, C^8), 118.5 (CH, C^4), 115.4 (C_q, C^2), 114.9 (C_q, C^{11b}), 111.6 (CH, C^{10}), 104.5 (C_q, C^{6a}), 96.9 (C_q, C^{cy1a}), 95.8 (C_q, C^{cy2a}), 79.2 (CH, $C^{cy2'}$), 77.8 (CH, C^{cy2}), 76.2 (CH, C^{cy1}), 74.5 (CH, $C^{cy1'}$), 31.2 (CH, C^{cy3}), 21.3 (CH_3, C^{cy4}), 20.8 (CH_3, $C^{cy4'}$), 17.7 (CH_3, C^{cy5}), 14.3 (CH_3, C^{15}) ppm.

(η^6-*p*-Cymene)[*N*-(2-methyl-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-$\kappa N'$-(1-κN-pyridin-2-yl-ethylidene)]azinechloridoruthenium-(II) Chloride (7a). General procedure C: *N*-(2-Methyl-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)-azine (180 mg, 0.49 mmol), $[RuCl_2(p\text{-cymene})_2]_2$ (151 mg, 0.25 mmol), ethanol (4 mL). Yield: 173 + 133 mg, 92% (bright orange solid). Anal. Calcd for $C_{33}H_{33}N_5Cl_2Ru \cdot H_2O$ (M_r 689.64): C, 57.47; H, 5.12; N, 10.16. Found: C, 57.45; H, 4.89; N, 10.16. ESI-MS (methanol), positive: m/z 636 $[M - Cl]^+$. IR (ATR, selected bands, ν_{max}): 3655, 3336, 3155, 3064, 2964, 1638, 1586, 1528, 1460, 1427, 1392, 1335, 1223, 812, 780, 744, 706, 643 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ 10.54 (br s, 1H, H^5), 9.49 (d, 1H, ^3J = 5.5 Hz, H^{18}), 8.49 (d, 1H, ^3J = 7.9 Hz, H^7), 8.24−8.20 (m, 1H, H^{20}), 8.11 (d, 1H, ^3J = 7.9 Hz, H^{21}), 8.00 (s, 1H, H^1), 7.75−7.71 (m, 1H, H^{19}), 7.70 (d, 1H, ^3J = 8.2 Hz, H^{10}), 7.63 (d, 1H, ^3J = 8.4 Hz, H^4), 7.50−7.46 (m, 1H, H^9), 7.41−7.37 (m, 2H, H^3+H^8), 5.87 (d, 1H, ^3J = 6.0 Hz, H^{cy2}), 5.63 (d, 1H, ^3J = 6.0 Hz, H^{cy1}), 5.60 (d, 1H, ^3J = 6.0 Hz, $H^{cy2'}$), 5.13 (d, 1H, ^3J = 6.0 Hz, $H^{cy1'}$), 2.85−2.75 (s, 3H, H^{15}+m, 1H, H^{cy3}), 2.52 (s, 3H, $H^{2'}$), 2.20 (s, 3H, H^{cy5}), 1.14 (d, 3H, ^3J = 6.9 Hz, $H^{cy4'}$), 1.10 (d, 3H, ^3J = 6.9 Hz, H^{cy4}) ppm, H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 165.1 (C_q, C^{14}). 155.7 (C_q, C^{16}), 155.4 (CH, C^{18}), 147.8 (C_q, C^6), 139.4 (CH, C^{20}), 139.2 (C_q, C^{11a}), 138.8 (C_q, C^{10a}), 134.4 (C_q, C^{4a}), 133.1 (C_q, C^2), 130.7 (CH, C^3), 126.3 (CH, C^{19}), 125.5 (CH, C^{21}), 124.6 (CH, C^9), 123.7 (C_q, C^{6b}), 121.8 (CH, C^7), 121.5 (CH, C^1), 121.3 (CH, C^8),

116.8 (CH, C^{4}), 113.1 (C_q, C^{11b}), 111.5 (CH, C^{10}), 104.3 (C_q, C^{cy2a}), 104.2 (C_q, C^{6a}), 103.8 (C_q, C^{cy1a}), 87.6 (CH, $C^{cy2'}$), 86.0 (CH, C^{cy2}), 85.5 (CH, C^{cy1}), 84.0 (CH, $C^{cy1'}$), 31.0 (CH, C^{cy3}), 21.0 (CH_3, C^{cy4}), 20.7 (CH_3, $C^{cy4'}$), 19.8 (CH_3, $C^{2'}$), 17.8 (CH_3, C^{cy5}), 14.5 (CH_3, C^{15}) ppm.

(η^6-*p*-Cymene)[(*N*-(2-methyl-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-κ*N*′-(1-κ*N*-pyridin-2-yl-ethylidene)]azinechloridoosmium(II) Chloride (7b). General procedure C: *N*-(2-Methyl-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (180 mg, 0.49 mmol), $[OsCl_2(p\text{-cymene})_2]_2$ (195 mg, 0.25 mmol), ethanol (4 mL). Yield: 244 + 82 mg, 87% (red solid). Elemental analysis of pure product was obtained by dissolution of the first crop in methanol and filtration through a GF3-filter, followed by evaporation of the solvent under reduced pressure and drying *in vacuo* at 47 °C. Anal. Calcd for $C_{33}H_{33}N_5Cl_2Os \cdot 0.75H_2O$ (M_r 774.30): C, 51.19; H, 4.49; N, 9.04. Found: C, 51.23; H, 4.51; N, 8.93. ESI-MS (methanol), positive: m/z 726 $[M - Cl]^+$, 690 $[M - Cl - HCl]^+$. IR (ATR, selected bands, ν_{max}): 3656, 3336, 3173, 3059, 2965, 2869, 1636, 1586, 1460, 1396, 1334, 1222, 1147, 1123, 1023, 812, 784, 744, 700, 639 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ 10.20 (br s, 1H, H^5), 9.42 (d, 1H, ^3J = 5.6 Hz, H^{18}), 8.45 (d, 1H, ^3J = 7.8 Hz, H^7), 8.24−8.19 (m, 2H, H^{20}+H^{21}), 7.99 (br s, 1H, H^1), 7.75−7.71 (m, 1H, H^{19}), 7.69 (d, 1H, ^3J = 8.1 Hz, H^{10}), 7.52−7.46 (m, 2H, H^4+ H^9), 7.41−7.35 (m, 2H, H^3+H^8), 6.15 (d, 1H, ^3J = 5.8 Hz, H^{cy2}), 5.89 (d, 1H, ^3J = 5.8 Hz, $H^{cy2'}$), 5.85 (d, 1H, ^3J = 5.8 Hz, H^{cy1}), 5.26 (d, 1H, ^3J = 5.8 Hz, $H^{cy1'}$), 2.86 (s, 3H, H^{15}), 2.72−2.65 (m, 1H, H^{cy3}), 2.52 (s, 3H, $H^{2'}$), 2.27 (s, 3H, H^{cy5}), 1.10 (d, 3H, ^3J = 7.0 Hz, $H^{cy4'}$), 1.06 (d, 3H, ^3J = 7.1 Hz, H^{cy4}) ppm, H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 166.1 (C_q, C^{14}). 156.6 (C_q, C^{16}), 155.3 (CH, C^{18}), 148.0 (C_q, C^6), 139.5 (CH, C^{20}), 139.1 (C_q, C^{11a}), 138.8 (C_q, C^{10a}), 134.2 (C_q, C^{4a}), 133.1 (C_q, C^2), 130.7 (CH, C^3), 127.2 (CH, C^{19}), 125.7 (CH, C^{21}), 124.6 (CH, C^9), 123.7 (C_q, C^{6b}), 121.7 (CH, C^7), 121.5 (CH, C^1), 121.3 (CH, C^8), 116.7 (CH, C^4), 113.0 (C_q, C^{11b}), 111.4 (CH, C^{10}), 103.9 (C_q, C^{6a}), 97.1 (C_q, C^{cy1a}), 95.5 (C_q, C^{cy2a}), 79.3 (CH, $C^{cy2'}$), 77.7 (CH, C^{cy2}), 75.9 (CH, C^{cy1}), 74.3 (CH, $C^{cy1'}$), 31.2 (CH, C^{cy3}), 21.3 (CH_3, C^{cy4}), 20.8 (CH_3, $C^{cy4'}$), 19.8 (CH_3, $C^{2'}$), 17.7 (CH_3, C^{cy5}), 14.2 (CH_3, C^{15}) ppm.

(η^6-*p*-Cymene)[(*N*-(2-nitro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-κ*N*′-(1-κ*N*-pyridin-2-yl-ethylidene)]azinechloridoruthenium(II) Chloride (8a). General procedure B: *N*-(2-Nitro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (153 mg, 0.39 mmol), $[RuCl_2(p\text{-cymene})_2]_2$ (118 mg, 0.19 mmol), ethanol (3.8 mL). Yield: 207 mg, 77% (brown solid). Anal. Calcd for $C_{32}H_{30}N_6O_2Cl_2Ru \cdot 0.5H_2O$ (M_r 711.60): C, 54.01; H, 4.39; N, 11.81. Found: C, 53.75; H, 4.17; N, 11.61. ESI-MS (methanol), positive: m/z 667 $[M - Cl]^+$. IR (ATR, selected bands, ν_{max}): 3330, 3036, 2964, 1627, 1594, 1520, 1459, 1402, 1331, 1282, 1221, 1156, 1091, 1019, 826, 771, 743, 695 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ 9.53 (d, 1H, ^3J = 5.7 Hz, H^{18}), 9.17 (d, 1H, ^4J = 2.3 Hz, H^1), 8.51 (d, 1H, ^3J = 7.8 Hz, H^7), 8.38 (dd, 1H, ^3J = 9.1 Hz, ^4J = 2.5 Hz, H^3), 8.29−8.25 (m, 1H, H^{20}) 8.18 (d, 1H, ^3J = 8.1 Hz, H^{21}), 7.82 (d, 1H, ^3J = 9.1 Hz, H^4), 7.81−7.78 (m, 1H, H^{19}), 7.74 (d, 1H, ^3J = 8.2 Hz, H^{10}), 7.57−7.52 (m, 1H, H^9) 7.46−7.42 (m, 1H, H^8), 5.95 (d, 1H, ^3J = 6.3 Hz, H^{cy2}), 5.74−5.70 (m, 2H, H^{cy1}+$H^{cy2'}$), 5.33 (d, 1H, ^3J = 6.1 Hz, $H^{cy1'}$), 2.89−2.81 (m, 1H, H^{cy3}), 2.79 (s, 3H, H^{15}), 2.24 (s, 3H, H^{cy5}), 1.17 (d, 3H, ^3J = 6.9 Hz, $H^{cy4'}$), 1.13 (d, 3H, ^3J = 6.9 Hz, H^{cy4}) ppm, H^5 and H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 167.9 (C_q, C^{14}), 156.2 (C_q, C^{16}), 155.4 (CH, C^{18}), 147.3 (C_q, C^6), 142.9 (C_q, C^2), 140.2 (C_q, C^{4a}), 139.7 (CH, C^{20}), 139.0 (C_q, C^{10a}), 137.8 (C_q, C^{11a}), 127.8 (CH, C^{19}), 126.3 (CH, C^{21}), 125.4 (CH, C^9), 123.9 (CH, C^3), 123.4 (C_q, C^{6b}), 121.9 (CH, C^8), 121.8 (CH, C^7), 118.2 (CH, C^1), 113.3 (C_q, C^{11b}), 111.8 (CH, C^{10}), 104.8 (C_q, C^{6a}), 96.9 (C_q, C^{cy1a}), 96.2 (C_q, C^{cy2a}), 79.2 (CH, $C^{cy2'}$), 77.8 (CH, C^{cy2}), 76.4 (CH, C^{cy1}), 74.7 (CH, $C^{cy1'}$), 31.3 (CH, C^{cy3}), 21.3 (CH_3, C^{cy4}), 20.9 (CH_3, $C^{cy4'}$), 17.7 (CH_3, C^{cy5}), 14.3 (CH_3, C^{15}) ppm.

(η^6-*p*-Cymene)[(*N*-(2-nitro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-κ*N*′-(1-κ*N*-pyridin-2-yl-ethylidene)]azinechloridoosmium(II) Chloride (8b). General procedure C: *N*-(2-Nitro-5,11-dihydroindolo[3,2-*c*]quinolin-6-ylidene)-*N*′-(1-pyridin-2-yl-ethylidene)azine (152 mg, 0.38 mmol), $[OsCl_2(p\text{-cymene})_2]_2$ (152 mg, 0.19 mmol), ethanol (3.8 mL). Yield: 234 mg, 77% (brown solid). Elemental analysis of pure product was obtained by dissolution of the first crop in methanol (60 mL) and filtration through a GF3-filter, followed by evaporation of the solvent under reduced pressure and drying *in vacuo* at 47 °C. Anal. Calcd for $C_{32}H_{30}N_6O_2Cl_2Os \cdot H_2O$ (M_r 809.77): C, 47.46; H, 3.98; N, 10.38. Found: C, 47.41; H, 3.81; N, 10.14. ESI-MS (methanol), positive: m/z 757 $[M - Cl]^+$, 721 $[M - Cl - HCl]^+$. IR (ATR, selected bands, ν_{max}): 3337, 3038, 2964, 1627, 1600, 1521, 1459, 1404, 1331, 1282, 1220, 1156, 1140, 1018, 827, 772, 742, 700 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ 9.46 (d, 1H, ^3J = 5.6 Hz, H^{18}), 9.17 (d, 1H, ^4J = 2.5 Hz, H^1), 8.47 (d, 1H, ^3J = 7.9 Hz, H^7), 8.38 (dd, 1H, ^3J = 9.1 Hz, ^4J = 2.5 Hz, H^3), 8.30−8.23 (m, 2H, H^{20}+H^{21}), 7.80−7.76 (m, 1H, H^{19}), 7.74 (d, 1H, ^3J = 8.3 Hz, H^{10}), 7.71 (d, 1H, ^3J = 9.1 Hz, H^4), 7.56−7.52 (m, 1H, H^9), 7.45−7.41 (m, 1H, H^8), 6.23 (d, 1H, ^3J = 5.8 Hz, H^{cy2}), 6.01 (d, 1H, ^3J = 5.7 Hz, $H^{cy2'}$), 5.96 (d, 1H, ^3J = 5.8 Hz, H^{cy1}), 5.47 (d, 1H, ^3J = 5.7 Hz, $H^{cy1'}$), 2.87 (s, 3H, H^{15}), 2.78−2.69 (m, 1H, H^{cy3}), 2.30 (s, 3H, H^{cy5}), 1.13 (d, 3H, ^3J = 7.0 Hz, $H^{cy4'}$), 1.09 (d, 3H, ^3J = 7.0 Hz, H^{cy4}) ppm, H^5 and H^{11} not obsd. ^{13}C NMR (125 MHz, CD_3OD): δ 167.9 (C_q, C^{14}). 156.2 (C_q, C^{16}), 155.4 (CH, C^{18}), 147.3 (C_q, C^6), 142.9 (C_q, C^2), 140.2 (C_q, C^{4a}), 139.7 (CH, C^{20}), 139.0 (C_q, C^{10a}), 137.8 (C_q, C^{11a}), 127.8 (CH, C^{19}), 126.3 (CH, C^{21}), 125.4 (CH, C^9), 123.9 (CH, C^3), 123.4 (C_q, C^{6b}), 121.9 (CH, C^8), 121.8 (CH, C^7), 118.2 (CH, C^1), 113.3 (C_q, C^{11b}), 111.8 (CH, C^{10}), 104.8 (C_q, C^{6a}), 96.9 (C_q, C^{cy1a}), 96.2 (C_q, C^{cy2a}), 79.2 (CH, $C^{cy2'}$), 77.8 (CH, C^{cy2}), 76.4 (CH, C^{cy1}), 74.7 (CH, $C^{cy1'}$), 31.3 (CH, C^{cy3}), 21.3 (CH_3, C^{cy4}), 20.9 (CH_3, $C^{cy4'}$), 17.7 (CH_3, C^{cy5}), 14.3 (CH_3, C^{15}) ppm.

Crystallographic Structure Determination. X-ray diffraction measurements were performed on a Bruker X8 APEXII CCD diffractometer. Single crystals were positioned at 40, 40, 40, 40, 40, and 35 mm from the detector, and 1304, 1131, 1919, 1565, 1936, and 1059 frames were measured, each for 40, 60, 20, 30, 30, and 90 s over 1°, 1°, 1°, 1°, 1°, and 0.5° scan width for **2a**, **4a**, **4b**, **5a**, **7a**, and **7b**, correspondingly. The data were processed using SAINT software.[34] Crystal data, data collection parameters, and structure refinement details are given in Table 2. The structures were solved by direct methods and refined by full-matrix least-squares techniques. Non-H atoms for **2a**, **4a**, **4b**, **5a**, **7a**, and **7b** were refined with anisotropic displacement parameters (except those of cocrystallized disordered solvent molecules). H atoms were inserted in calculated positions and refined with a riding model. Refinement of the structure of **2a** revealed that the arene occupies two statistically disordered positions (rotational disorder around the Ru−$arene_{centroid}$). The disorder was resolved with constrained isotropic displacement parameters and restrained bond distances using EADP and SADI instructions of SHELX97, respectively. The site occupation factors (sof) were refined to about 0.60:0.40. The Cl2 counterion was also found disordered over two positions with sof 0.55:0.45. The following software programs and computer were used: structure solution and refinement, SHELXS-97 and SHELXL-97;[35] molecular diagrams, ORTEP-3;[36] computer, Intel CoreDuo.

Cell Lines and Culture Conditions. CH1 (ovarian carcinoma, human) cells were donated by Lloyd R. Kelland (CRC Centre for Cancer Therapeutics, Institute of Cancer Research, Sutton, U.K.). SW480 (colon adenocarcinoma, human) cells and A549 (non-small-cell lung cancer, human) cells were kindly provided

(34) *SAINT-Plus*, version 7.06a, and *APEX2*; Bruker-Nonius AXS Inc.: Madison, WI, 2004.
(35) Sheldrick, G. M. *Acta Crystallogr.* **2008**, *A64*, 112.
(36) Johnson, G. K. *Report ORNL-5138*; OAK Ridge National Laboratory: Oak Ridge, TN, 1976.

Table 1. Selected Bond Distances (Å) and Angles (deg) for Complexes 2a, 4a, 4b, 5a, 7a, and 7b

	2a	4a	4b	5a	7a	7b
M−Cl	2.4121(9)	2.405(2)	2.4085(18)	2.4149(11)	2.4137(16)	2.421(5)
M−N4	2.100(3)	2.111(6)	2.108(6)	2.078(4)	2.075(5)	2.092(14)
M−N5	2.073(3)	2.101(7)	2.082(5)	2.086(4)	2.075(5)	2.067(14)
$M-C_{arene}$ av	2.188(5)[a]	2.204(16)	2.202(12)	2.201(9)	2.202(10)	2.21(1)
$C_{arene}-C_{arene}$ av	1.390	1.419(8)	1.425(5)	1.415(5)	1.409(6)	1.43(1)
N4−M−N5	76.73(12)	76.9(3)	76.4(2)	76.51(14)	76.55(19)	75.8(5)
N4−M−Cl	88.18(9)	88.0(2)	86.10(17)	87.06(11)	87.41(15)	85.5(4)
N5−M−Cl	82.82(9)	84.61(19)	81.53(17)	83.20(11)	83.70(14)	81.9(4)

[a] The mean value was calculated only for the first disordered component.

Table 2. Crystal Data and Details of Data Collection for 2a, 4a, 4b, 5a, 7a, and 7b

	2a·1.7H_2O	4a	4b·0.25Et_2O·1.5H_2O	5a·EtOH	7a·0.5EtOH·0.2H_2O	7b·H_2O
empirical formula	$C_{32}H_{34.4}Cl_2N_5O_{1.7}Ru$	$C_{31}H_{28}Cl_3N_5Ru$	$C_{32}H_{33.5}Cl_3N_5O_{1.75}Os\ Ru$	$C_{34}H_{36}Cl_3N_5ORu$	$C_{34}H_{36.4}Cl_2N_5O_{0.7}Ru$	$C_{33}H_{35}Cl_2N_5OOs$
fw	688.22	678.00	812.69	738.10	699.26	778.76
space group	$P2_1/n$	$I\bar{4}$	$C2/c$	$P2_1/n$	$P2_1/n$	$C2/c$
a [Å]	10.4899(3)	26.5354(10)	17.2834(5)	10.7350(4)	10.6834(11)	11.690(2)
b [Å]	11.8881(3)	26.5354(10)	14.0348(5)	12.0515(4)	12.0598(12)	21.276(4)
c [Å]	25.1390(8)	9.0872(4)	29.4680(11)	25.1678(9)	25.482(3)	25.898(4)
α [deg]						
β [deg]	95.195(2)		106.416(4)	94.293(2)	93.080(7)	102.712(9)
γ [deg]						
V [Å^3]	3122.08(16)	6398.5(4)	6856.6(4)	3246.9(2)	3278.3(6)	6283.4(19)
Z	4	8	8	4	4	8
λ [Å]	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073
ρ_{calcd} [g cm^{-3}]	1.464	1.408	1.575	1.510	1.417	1.646
cryst size [mm^3]	0.25 × 0.25 × 0.15	0.30 × 0.05 × 0.05	0.50 × 0.25 × 0.03	0.30 × 0.15 × 0.10	0.15 × 0.15 × 0.03	0.35 × 0.20 × 0.10
T [K]	100	100	100	100	100	100
μ [mm^{-1}]	0.710	0.768	3.988	0.766	0.675	4.264
R_1[a]	0.0504	0.0593	0.0546	0.0542	0.0637	0.0915
wR_2[b]	0.1363	0.1646	0.1388	0.1581	0.1836	0.2343
GOF[c]	1.041	1.034	1.084	1.092	1.041	1.012

[a] $R_1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $wR_2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$. [c] $\mathrm{GOF} = \{\sum[w(F_o^2 - F_c^2)^2]/(n-p)\}^{1/2}$, where n is the number of reflections and p is the total number of parameters refined.

by Brigitte Marian (Institute of Cancer Research, Department of Medicine I, Medical University of Vienna, Austria). All cell culture media and reagents were purchased from Sigma-Aldrich Austria. Cells were grown without antibiotics in 75 cm^2 culture flasks (Iwaki/Asahi Technoglass) as adherent monolayer cultures in Minimal Essential Medium (MEM) supplemented with 10% heat-inactivated fetal bovine serum, 1 mM sodium pyruvate, and 2 mM L-glutamine. Cultures were maintained at 37 °C in a humidified atmosphere containing 5% CO_2 and 95% air.

Cytotoxicity in Cancer Cell Lines. Cytotoxicity in the cell lines mentioned above was determined by the colorimetric MTT assay (MTT = 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2*H*-tetrazolium bromide). For this purpose, cells were harvested from culture flasks by trypsinization and seeded in aliquots of 100 μL/well into 96-well microculture plates (Iwaki/Asahi Technoglass) in the following densities, in order to ensure exponential growth of untreated controls throughout the experiment: 1.5 × 10^3 (CH1), 2.5 × 10^3 (SW480), and 4.0 × 10^3 (A549) viable cells per well. Cells were allowed to settle and resume exponential growth in drug-free MEM supplemented with 10% heat-inactivated fetal bovine serum, 1 mM sodium pyruvate, 4 mM L-glutamine, and 1% nonessential amino acids (100× stock) for 24 h. DMSO stocks of the test compounds were serially diluted in the same medium and added to the plates in aliquots of 100 μL/well such that the maximum DMSO content did not exceed 0.5%. After continuous exposure for 96 h, medium was replaced by 100 μL/well RPMI 1640 medium (supplemented with 10% heat-inactivated fetal bovine serum and 4 mM L-glutamine) plus 20 μL/well MTT in phosphate-buffered saline (5 mg/mL). After incubation for 4 h, medium/MTT mixtures were removed, and the formazan product formed by viable cells was dissolved in DMSO (150 μL/well). Optical densities at 550 nm were measured with a microplate reader (Tecan Spectra Classic), using a reference wavelength of 690 nm to correct for unspecific absorption. The quantity of viable cells was expressed as percentage of untreated controls, and 50% inhibitory concentrations (IC_{50}) were calculated from concentration−effect curves by interpolation. Evaluation is based on at least three independent experiments, each comprising three replicates per concentration level.

Results and Discussion

Synthesis and Characterization of the Ligands and Complexes. The modified indoloquinoline ligands $\mathbf{L^1}-\mathbf{L^7}$ and $\mathbf{L^8}$ were prepared in four and three steps, correspondingly, as shown in Scheme 1. First, by reaction of 2-aminobenzylamine with indole-2,3-diones in acetic acid the indoloquinolines **A** were prepared, which were further chlorinated with phosphorus oxychloride to derivatives **B** (Scheme 1).[24,25,29] In the third step species **B** were allowed to react with excess hydrazine hydrate to yield indoloquinoline-hydrazines **C**. Finally the ligands $\mathbf{L^1}-\mathbf{L^7}$ were prepared by condensation reaction of compounds **C** with 2-formyl- or 2-acetylpyridine (Experimental Section, General Procedure A). This reaction pathway proved to be unsuited for $\mathbf{L^8}$, since upon reaction with hydrazine, both the nitro group and the imidoyl chloride were reduced. Therefore $\mathbf{L^8}$ was prepared by direct coupling of 2-acetylpyridine hydrazone with the imidoyl chloride species B. Complexation was realized following a conventional

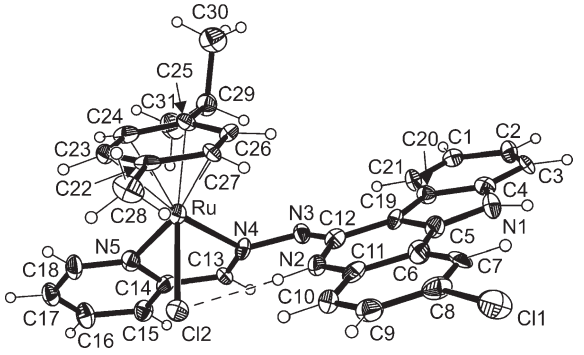


Figure 1. ORTEP view of the cation in **4a** with thermal ellipsoids drawn at the 50% probability level with an intramolecular hydrogen bonding N2−H···Cl2 [N2−H 0.88, H···Cl2 2.304, N2···Cl2 3.180 Å, N2−H···Cl2 174.1°].

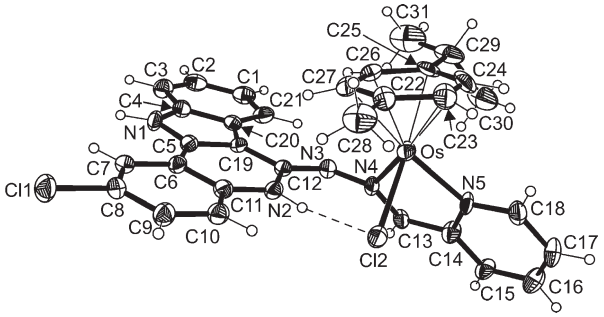


Figure 2. ORTEP view of the cation in **4b**·0.25$(C_2H_5)_2O$·1.5H_2O with thermal ellipsoids drawn at the 50% probability level with an intramolecular hydrogen bonding N2−H···Cl2 [N2−H 0.88, H···Cl2 2.313, N2···Cl2 3.177 Å, N2−H···Cl2 167.3°].

μ-chlorido bridge splitting reaction of the dimeric starting materials [(η^6-*p*-cymene)M^{II}(μ-Cl)Cl]$_2$, where M = Ru, Os, with modified indoloquinolines $\mathbf{L^1}$−$\mathbf{L^8}$ in dry ethanol, affording compounds **1a**,**b**−**8a**,**b** in 68−94% yield. With the exception of **6b**, all complexes were hydrated. Thermogravimetric analysis showed that hydrated samples lose water upon heating with a rate of 10 °C/min to 120 °C under nitrogen and take up water again on cooling and contact with air within 1 h (see Figure S3 for **5a**).

The ESI-MS spectra of ligands $\mathbf{L^1}$−$\mathbf{L^8}$ in methanol showed the molecular peak ions $[M + H]^+$. Additional peaks were assigned to $[M + Na]^+$ for $\mathbf{L^1}$−$\mathbf{L^3}$, $\mathbf{L^5}$, $\mathbf{L^7}$, and $\mathbf{L^8}$. For complexes **1a**,**b**−**8a**,**b**, the peak due to $[M - Cl]^+$ (where M = [(η^6-*p*-cymene)M^{II}(L)Cl]Cl) was observed. Further, osmium complexes **1b**−**8b** showed a small signal that was assigned to $[M - Cl - HCl]^+$. The fact that the $[M - Cl]^+$ peak was the base peak in all spectra measured indicates the higher stability of this family of complexes compared to the quite recently reported metal−arene-based indoloquinolines.[11] Further evidence was provided by UV−vis measurements of **1a**,**b**−**8a**,**b** in 1% DMSO/H_2O over 24 h (see Figures S4 and S5 for details). The observed changes in the optical spectra of the ruthenium complexes were significant, but smaller than those of the complexes reported previously. DMSO (1%) did not influence the spectra, as could be shown by a comparative 24 h run of complex **1a** in pure water (data shown in Figure S4). Attempts to suppress the hydrolysis of the Ru−Cl bond by addition of sodium chloride resulted in slow precipitation of the complexes. No precipitation occurred in the presence of media for the MTT assay (MEM supplemented with 10% heat-inactivated fetal bovine serum, 1 mM sodium pyruvate, 4 mM L-glutamine, and 1% nonessential amino acids (100×)). The osmium compounds remained practically intact in solution over 24 h, as depicted in Figure S5. The higher stability of osmium than ruthenium compounds is, however, well documented in the literature.[30,37−40]

The ^{1}H and ^{13}C NMR spectra of the ligands and ruthenium(II)− and osmium(II)−arene complexes indicate their C_1 molecular symmetry in solution. Whereas the NMR shifts of the indoloquinoline backbone remained almost unaffected by complexation, the resonances of protons and carbon atoms forming the five-membered chelate ring were markedly shifted, along with the ones neighboring the binding site. The signal of C^{18}, for example, was shifted downfield by about 6−7 ppm (ca. 155 ppm, compared to 149 ppm in the metal free ligand), and that of its proton H^{18} was shifted from 8.6 ppm in the ligand to 9.4−9.5 ppm in the complex. As expected for protons neighboring a stereogenic metal center, four distinct signals were observed for the aromatic protons of the *p*-cymene ligands.

Crystal Structures. The results of the X-ray diffraction studies of [(η^6-*p*-cymene)Ru($\mathbf{L^2}$)Cl]Cl·1.7H_2O (**2a**·1.7H_2O), [(η^6-*p*-cymene)Ru($\mathbf{L^4}$)Cl]Cl (**4a**), [(η^6-*p*-cymene)Os($\mathbf{L^4}$)Cl]Cl·0.25Et_2O·1.5H_2O (**4b**·0.25Et_2O·1.5H_2O), [(η^6-*p*-cymene)Ru($\mathbf{L^5}$)Cl]Cl·C_2H_5OH (**5a**·C_2H_5OH), [(η^6-*p*-cymene)Ru($\mathbf{L^7}$)Cl]Cl·0.5C_2H_5OH·0.2H_2O (**7a**·0.5C_2H_5OH·0.2H_2O), and [(η^6-*p*-cymene)Os($\mathbf{L^7}$)Cl]Cl·H_2O (**7b**·H_2O) are shown in Figures S1, 1−4, and S2, respectively. All complexes have a typical "three-leg piano-stool" geometry of ruthenium(II) and osmium(II) arene complexes,[41−44] with an η^6 π-bound *p*-cymene ring forming the seat and three other donor atoms (two nitrogens, N4 and N5, of indolo[3,2-*c*]quinoline and one chlorido ligand) as the legs of the stool. Selected bond distances and angles are quoted in Table 1. All complexes with the exception of **4a** crystallize as racemates owing to the presence of the stereogenic metal center.

Upon binding to ruthenium(II) or osmium(II), the ligands form a five-membered chelate ring, N4C13C14N5M (M = Ru, Os). The torsion angle $\Theta_{N4-C13-C14-N5}$, which serves as a measure of the distortion of the chelate ring from planarity, is −7.6(5)°, 0.8(11)°, −6.5(10)°, −4.4(6)°, −4.0°, and −6(2)° for **2a**, **4a**, **4b**, **5a**, **7a**, and **7b**, respectively.

Cytotoxicity in Cancer Cell Lines. Cytotoxicity of the ruthenium complexes **1a**−**7a** and analogous osmium complexes

(37) Reedijk, J. *Platinum Met. Rev.* **2008**, *52*, 2.
(38) Hanif, M.; Henke, H.; Meier, S. M.; Martic, S.; Labib, M.; Kandioller, W.; Jakupec, M. A.; Arion, V. B.; Kraatz, H.-B.; Keppler, B. K.; Hartinger, C. G. *Inorg. Chem.* **2010**, *49*, 7953.
(39) van Rijt, S. H.; Hebden, A. J.; Amaresekera, T.; Deeth, R. J.; Clarkson, G. J.; Parsons, S.; McGowan, P. C.; Sadler, P. J. *J. Med. Chem.* **2009**, *52*, 7753.
(40) Hanif, M.; Nazarov, A. A.; Hartinger, C. G.; Kandioller, W.; Jakupec, M. A.; Arion, V. B.; Dyson, P. J.; Keppler, B. K. *Dalton Trans.* **2009**, *39*, 7345.
(41) El-khateeb, M.; Damer, K.; Görls, H.; Weigand, W. *J. Organomet. Chem.* **2007**, *692*, 2227.
(42) Kandioller, W.; Hartinger, C. G.; Nazarov, A. A.; Kuznetsov, M. L.; John, R. O.; Bartel, C.; Jakupec, M. A.; Arion, V. B.; Keppler, B. K. *Organometallics* **2009**, *28*, 4249.
(43) Zagermann, J.; Kuchta, M. C.; Merz, K.; Metzler-Nolte, N. *J. Organomet. Chem.* **2009**, *694*, 862.
(44) Albrecht, C.; Gauthier, S.; Wolf, J.; Scopelliti, R.; Severin, K. *Eur. J. Inorg. Chem.* **2009**, 1003.

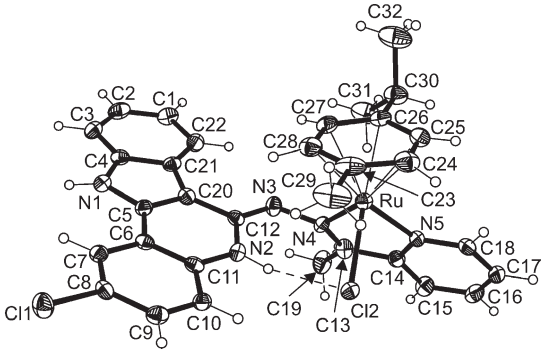


Figure 3. ORTEP view of the cation in **5a**·C_2H_5OH with thermal ellipsoids drawn at the 50% probability level with an intramolecular hydrogen bonding N2−H···Cl2 [N2−H 0.88, H···Cl2 2.340, N2···Cl2 3.176 Å, N2−H···Cl2 158.8°].

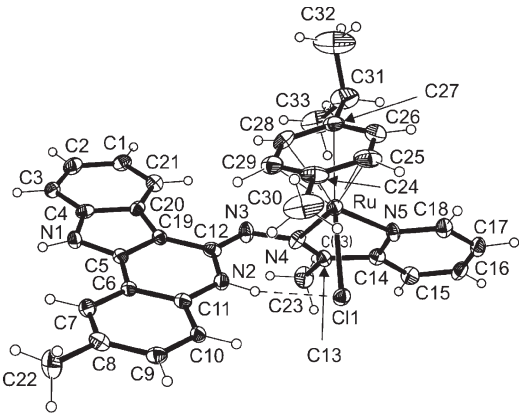


Figure 4. ORTEP view of the cation in **7a**·0.5C_2H_5OH·0.2H_2O with thermal ellipsoids drawn at the 40% probability level with an intramolecular hydrogen bonding N2−H···Cl2 [N2−H 0.88, H···Cl2 2.363, N2···Cl2 3.207 Å, N2−H···Cl2 160.9°].

1b−**7b** was assessed by means of a colorimetric microculture assay (MTT assay) in three human cancer cell lines, yielding the IC_{50} values listed in Table 3. The uncomplexed indoloquinoline derivatives $\mathbf{L^1}$−$\mathbf{L^8}$ as well as complexes **8a** and **8b** could not be tested because of insufficient solubility. Hence, binding to a ruthenium−arene or osmium−arene moiety makes this class of potentially pharmacologically active indoloquinoline derivatives applicable for biological testing in solution, whatever role the metal may play in the mechanism of action, in particular in interactions with biological targets.

All compounds tested are potent inhibitors of cancer cell proliferation *in vitro*, with IC_{50} values in the submicromolar to low micromolar range: 0.19−3.8 μM in the rather chemosensitive ovarian cancer cell line CH1, 0.26−5.0 μM in the colon carcinoma cell line SW480, and 0.83−14 μM in the rather chemoresistant non-small-cell lung cancer cell line A549. **1b** is consistently the most active of these compounds, with IC_{50} values comparable to those of three related indoloquinoline complexes reported previously.[11] A comparison with simple cymene complexes of ruthenium(II) with coordination to one chlorido ligand and two N-donors, such as NH_3 or ethylenediamine (en), shows that the presence of an indoloquinoline ligand is mostly advantageous. All of the ruthenium complexes **1a**−**7a** are much more cytotoxic than [(η^6-*p*-cymene)$Ru^{II}(NH_3)_2Cl$](PF_6) (IC_{50} values >200 μM), and in the majority of cases they are at least as cytotoxic (up to 10 times more potent in a few cases) as [(η^6-*p*-cymene)Ru^{II}(en)Cl](PF_6) (IC_{50} values: 4.4, 3.5, and 7.1 μM in CH1, SW480, and A549 cells, respectively).[5]

Table 3. Cytotoxicity of Ruthenium and Osmium Arene-Based Indoloquinoline Complexes in Three Human Cancer Cell Lines

	IC_{50} (μM)[a]		
compound	CH1	SW480	A549
1a	2.2 ± 0.6	2.1 ± 0.4	6.0 ± 1.5
1b	0.19 ± 0.06	0.26 ± 0.03	0.83 ± 0.19
2a	0.70 ± 0.06	1.0 ± 0.2	4.6 ± 0.8
2b	0.24 ± 0.02	1.0 ± 0.2	1.8 ± 0.3
3a	2.8 ± 0.9	2.3 ± 1.0	14 ± 3
3b	1.2 ± 0.5	2.9 ± 0.6	10 ± 3
4a	0.32 ± 0.13	0.76 ± 0.03	5.1 ± 1.8
4b	0.42 ± 0.05	0.51 ± 0.04	1.8 ± 0.2
5a	3.8 ± 0.6	5.0 ± 1.0	9.3 ± 3.4
5b	0.55 ± 0.14	1.2 ± 0.3	3.9 ± 0.5
6a	1.3 ± 0.2	1.5 ± 0.6	7.2 ± 1.7
6b	1.0 ± 0.4	2.3 ± 0.4	7.8 ± 2.1
7a	0.19 ± 0.02	0.28 ± 0.02	2.0 ± 0.4
7b	0.19 ± 0.08	0.57 ± 0.20	3.2 ± 0.4

[a] 50% inhibitory concentrations (means ± standard derivations), as obtained by the MTT assay (continuous exposure for 96 h).

Generally, the impact of most structural modifications on cytotoxicity is not dramatic, and structure−activity relationships are blurred by overlapping ranges of variation. Mostly, the complexes of the formylpyridine series tend to be at least as cytotoxic as their analogues of the acetylpyridine series, and most osmium complexes show cytotoxic potencies either somewhat higher than or at least similar to those of the corresponding ruthenium complexes.

Variation of the substituent R^1 in the complexes of the acetylpyridine series yields the following pattern, which is illustrated by the concentration−effect curves depicted in Figure S6: The presence of a halogen atom in complexes **3a**, **3b**, **5a**, **5b**, **6a**, and **6b** in position 2 results in an up to 5.4-fold lowered impact on cell viability compared to complexes **2a** and **2b**, lacking a substituent in this position. In contrast, the presence of a methyl substituent results in either comparable cytotoxicity (osmium complex **7b**) or 2- to 4-fold enhanced cytotoxicity (ruthenium complex **7a**) compared to the corresponding unsubstituted analogues and 3−15 times higher cytotoxicity compared to the corresponding fluoro analogues **3a** and **3b**, containing the most electronegative substituent. Even though variation of the halogen group (F, Cl, or Br) does not yield a uniform pattern, these observations suggest that electron-withdrawing substituents tend to be disadvantageous for cytotoxic potency, whereas an electron-donating methyl substituent is not.

Final Remarks. The reported results establish synthetic access to a new family of ruthenium(II)− and osmium(II)−arene complexes with 2-substituted indoloquinolines. The metal-free modified indoloquinolines could not be tested for antiproliferative activity because of their insufficient solubility in biological media. Binding to ruthenium(II)− and osmium(II)−arene moieties resulted in complexes with improved solubility, enabling most of them to be tested as potential antitumor agents. The use of iminopyridines as chelating moieties instead of ethylenediamine ones afforded complexes that are markedly more stable in aqueous solution containing 1% DMSO. As expected, the osmium(II)

complexes were more stable than the ruthenium(II) congeners and practically remained intact over 24 h according to optical spectra measurements. All complexes show remarkably high antiproliferative activities in human cancer cell lines with IC_{50} values in the 10^{-7} to 10^{-5} M concentration range, depending on the cell line. Like in the case of paullones, the electronic properties of substituents in position 2 have no distinct effect on cytotoxicity,[45,46] although electron-withdrawing substituents tend to be disadvantageous for cytotoxic activity, whereas an electron-donating methyl group is not. The formylpyridine series was at least as active as the acetylpyridine analogues. Clear-cut structure−activity relationships were often hindered by overlapping ranges of variation.

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Supporting Information Available: The atom-numbering scheme used for the NMR characterization, NMR data of the ligands $\mathbf{L^1}$−$\mathbf{L^8}$, ORTEP views of the cations of **2a** and **7b**, concentration−effect curves of substances **1a**, **1b**, **4a**, and **4b**, and CIF files of **2a**, **4a**, **4b**, **5a**, **7a**, and **7b**. This material is available free of charge via the Internet at http://pubs.acs.org.

(45) Kunick, C.; Schultz, C.; Lemcke, T.; Zaharevitz, D. W.; Gussio, R.; Jalluri, R. K.; Sausville, E. A.; Leost, M.; Meijer, L. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 567.

(46) Xie, X.; Lemcke, T.; Gussio, R.; Zaharevitz, D. W.; Leost, M.; Meijer, L.; Kunick, C. *Eur. J. Med. Chem.* **2005**, *40*, 655.