Supporting Information to

Quinoline-para-quinones and Metals: Coordination-assisted Formation of Quinoline-ortho-quinones

Mario Kubanik,[a] Nelson Lam,[a] Hannah U. Holtkamp,[a] Tilo Söhnel,[a] Robert F. Anderson,[a],[b] Stephen M. F. Jamieson[b] and Christian G. Hartinger*[a]

[a] University of Auckland, School of Chemical Sciences, Private Bag 92019, Auckland 1142, New Zealand. E-mail: c.hartinger@auckland.ac.nz.
[b] Auckland Cancer Society Research Centre, Faculty of Medical and Health Sciences, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand.

* Corresponding author. E-mail address: c.hartinger@auckland.ac.nz (C. G. Hartinger).

Table of Contents:

Experimental Section

Materials and Methods

All reactions were carried out under standard Schlenk conditions in dry solvents unless otherwise stated. Chemicals obtained from commercial suppliers were used without prior purification. Solvents were dried according to literature procedures.[1] Ruthenium(III) chloride hydrate (99%), iridium(III) chloride hydrate and rhodium(III) chloride hydrate were purchased from Precious Metals Online, osmium tetroxide from Johnson Matthey, 8-hydroxyquinoline (99%) from AK Scientific, α-terpinene, from Sigma-Aldrich. Bis[dichlorido(η^6-*p*-cymene)ruthenium(II)],[2] bis[dichlorido(η^6-*p*-cymene)osmium(II)],[3] bis[dichlorido(η^6-biphenyl)ruthenium(II)], bis[dichlorido(η^5-pentamethylcyclopentadienyl)rhodium(III)][4] and bis[dichlorido(η^5-pentamethylcyclopentadienyl)iridium(III)][5] were prepared as described in the literature.

Elemental analyses for the synthesized compounds were performed at the Campbell Microanalytical Laboratory, The University of Otago.

NMR spectra were recorded on Bruker Avance AVIII 400 MHz, at ambient temperature at 400.13 (^{1}H) or 100.6 MHz (^{13}C{^{1}H}). Chemical shifts are reported versus $SiMe_4$ and were determined by reference to the residual ^{1}H and ^{13}C{^{1}H} NMR solvent peaks. For an unambiguous assignment of the characteristic resonances, multinuclear 2D (^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, and HMBC) NMR spectroscopic experiments were conducted.

Melting points were measured in capillary tubes using an SMP30 Stuart Scientific Melting Point Apparatus. High resolution mass spectra were recorded on a Bruker microOTOF-Q II mass spectrometer in positive ion electrospray ionization (ESI) mode.

X-ray diffraction measurements of single crystals of **1**, **2**, **4** and **5** as well as of ^{Me}**HQ$_{Cl}$** were carried out on a Siemens/Bruker SMART APEX II Single Crystal Diffractometer with a CCD area detector using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). The data were processed using the SHELX2013 software packages.[6] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were inserted at calculated positions and refined with a riding model or without restrictions. Molecular structures were visualized using Mercury 3.5.1.

Crystal structures were deposited at the Cambridge Crystallographic Data Centre with deposition numbers 1571651 (**1**), 1571652 (2), 1571653 (**4**), 1571654 (**5**), and 1571650 (^{Me}**HQ$_{Cl}$**).

6,7-Dichloro-5,8-quinolinedione (**DQQ**) and **HQ_{Cl}**

The synthesis of **DQQ** was carried out according to a procedure reported by Mulchin *et al*.[7] Sodium chlorate (53 g, 500 mmol) was added portionwise over a period of 1 h into a stirred mixture of 8-hydroxyquinoline (14.5 g, 100 mmol) in HCl (38%, *ca.* 600 mL) at 40 °C and the reaction mixture was stirred for 2 h. The reaction mixture was then diluted, filtered to remove the white precipitate and the filtrate was extracted with CH_2Cl_2 (6 × 250 mL). The organic layers were combined, dried with Na_2SO_4 and concentrated in reduced pressure to afford the crude product as a yellow-orange solid. Recrystallization in various alkyl alcohols (MeOH, EtOH, *i*-PrOH or *n*-BuOH) afforded **DQQ** as a bright yellow powder (3.89 g, 17%) and **HQ_{Cl}** side products. Mp. 218–219 °C (Lit.[7] 219–221 °C). R_f = 0.63 (EtOAc). IR: 1692, 1676, 1585, 1557, 1431, 1288, 1275, 1193, 1136, 1043, 893 cm^{-1}. ^1H NMR (400.13 MHz, [d^6]-DMSO): δ = 7.90 (dd, $^4J(H,H)$ = 4Hz, $^3J(H,H)$ = 8Hz, 1H, H3), 8.46 (dd, $^4J(H,H)$ = 2Hz, $^3J(H,H)$ = 8Hz, 1H, H4), 9.06 (dd, $^4J(H,H)$ = 2Hz, $^3J(H,H)$ = 4Hz, 1H, H2) ppm. $^{13}C\{^1H\}$ NMR (100.62 MHz, [d^6]-DMSO) δ = 128.2 (C3), 128.5 (C4a), 134.9 (C4), 141.5 (C7), 143.1 (C6), 147.0 (C8a), 154.4 (C2), 174.2 (C8), 176.50 (C5) ppm.

General procedures for the synthesis of the metal complexes **1**–**5**

The dimeric metal precursors $[M(\eta^6\text{-arene})Cl_2]_2$ (M = Ru, Os; 0.45 eq) or $[M(\eta^5\text{-Cp*})Cl_2]_2$ (M = Rh, Ir; 0.45 eq) were added to a solution of 6,7-dichloro-5,8-quinolinedione (**DQQ**, 1 eq) in methanol and stirred under reflux and nitrogen atmosphere for 1 h. After cooling to room temperature the formed precipitate was collected by filtration, washed several times with methanol and *n*-hexane und dried in vacuum.

Chlorido(7-chloro-8-hydroxyquinolinolato-5,6-dione-κ*N*1,κ*O*8)(η^6-*p*-cymene)ruthenium(II), **1**.

The synthesis was performed according to the general procedure using **DQQ** (200 mg, 1.377 mmol) and bis[dichlorido(η^6-*p*-cymene)ruthenium(II)] (380 mg, 0.62 mmol) to afford a purple solid (393 mg, 76%). Elemental Analysis calculated for $C_{19}H_{17}NO_3Cl_2Ru\cdot 0.75H_2O$: C 46.31, H 3.78, N 2.84%. Found: C 46.01, H 3.46, N 2.99. MS (ESI+): m/z 501.9507 $[M + Na]^+$ (m_{calc} = 501.9520). ^1H NMR (400.13 MHz, [d^6]-DMSO): δ = 1.17–1.22 (m, 6H, Hg), 2.20 (s, 3H, Ha), 2.74–2.81 (m, 1H, Hf), 5.81 (d, $^3J(H,H)$ = 6 Hz, 1H, Hc), 5.84 (d, $^3J(H,H)$ = 6 Hz, 1H, Hc), 6.01 (d, $^3J(H,H)$ = 6 Hz, 1H, Hd), 6.06 (d, $^3J(H,H)$ = 6 Hz, 1H, Hd), 7.82 (dd, $^3J(H,H)$ = 5 Hz, $^4J(H,H)$ = 3 Hz, 1H, H3), 8.32 (d, $^3J(H,H)$ = 5 Hz, 1H, H4), 9.44 (d, $^3J(H,H)$ = 5 Hz, 1H , H2) ppm. $^{13}C\{^1H\}$ NMR (100.62 MHz, [d^6]-DMSO): δ = 18.0 (Ca), 21.7 (Cg), 21.9 (Cg), 30.6 (Cf), 80.2 (Cc), 82.2 (Cd), 82.7 (Cc), 98.3 (Cb), 102.3 (Ce), 113.9 (C7), 126.9 (C4a), 127.8 (C3), 136.1 (C4), 153.7 (C8a), 157.2 (C2), 168.4 (C5), 174.1 (C6), 177.0 (C8) ppm.

Chlorido(7-chloro-8-hydroxyquinolinolato-5,6-dione-κ*N*1,κ*O*8)(η^6-*p*-cymene)osmium(II), **2**.
The synthesis was performed according to the general procedure using **DQQ** (100 mg, 0.438 mmol) and bis[dichlorido(η^6-*p*-cymene)osmium(II)] (156 mg, 0.197 mmol) to afford a purple solid (187 mg, 83%). Elemental Analysis calculated for $C_{19}H_{17}NO_3Cl_2Os \cdot 0.5\ H_2O$: C 39.52, H 3.14, N 2.43%. Found: C 39.60, H 3.14, N 2.42. MS (ESI$^+$): m/z 592.0085 [M + Na]$^+$ (m_{calc} = 592.0073). ^{1}H NMR (400.13 MHz, [d^6]-DMSO): δ = 1.13–1.18 (m, 6H, Hg), 2.25 (s, 3H, Ha), 2.61–2.68 (m, 1H, Hf), 6.11 (d, ^{3}J(H,H) = 6 Hz, 1H, Hc), 5.15 (d, ^{3}J(H,H) = 6 Hz, 1H, Hc), 6.34 (d, ^{3}J(H,H) = 5 Hz, 1H, Hd), 6.41 (d, ^{3}J(H,H) = 6 Hz, 1H, Hd), 7.78 (dd, ^{4}J(H,H) = 2 Hz, ^{3}J(H,H) = 6 Hz, 1H, H3), 8.34 (dd, ^{4}J(H,H) = 2 Hz, ^{3}J(H,H) = 8 Hz, 1H, H4), 8.34 (dd, ^{4}J(H,H) = 2 Hz, ^{3}J(H,H) = 6 Hz, 1H, H5) ppm. ^{13}C{^{1}H} NMR (100.62 MHz, [d^6]-DMSO): δ = 18.1 (Ca), 22.1 (Cg), 22.3 (Cg), 30.9 (Cf), 70.5 (Cc), 72.9 (Cd), 74.0 (Cd), 74.4 (Cc), 90.1 (Cb), 92.7 (Ce), 113.5 (C7), 127.0 (C4a), 128.4 (C3), 136.2 (C4), 154.8 (C8a), 156.9 (C2), 168.7 (C5), 175.9 (C6), 176.5 (C8) ppm.

Chlorido(7-chloro-8-hydroxyquinolinolato-5,6-dione-κ*N*1,κ*O*8)(η^6-biphenyl)ruthenium(II), **3**.
The synthesis was performed according to the general procedure using **DQQ** (75 mg, 0.329 mmol) and bis[dichlorido(η^6-biphenyl)ruthenium(II)] (96 mg, 0.148 mmol) to afford a purple solid (111 mg, 75%). Elemental Analysis calculated for $C_{21}H_{13}NO_3Cl_2Ru \cdot 0.5H_2O$: C 49.62, H 2.78, N 2.76%. Found: C 49.63, H 2.59, N 3.08. MS (ESI$^+$): m/z 521.9224 [M + Na]$^+$ (m_{calc} = 521.9208). ^{1}H NMR (400.13 MHz, [d^6]-DMSO): δ = 6.14 (t, ^{3}J(H,H) = 6 Hz, 1H, Ha), 6.30 (d, ^{3}J(H,H) = 7 Hz, 1H, Hb), 6.34 (d, ^{3}J(H,H) = 7 Hz, 1H, Hb), 6.43 (d, ^{3}J(H,H) = 7 Hz, 1H, Hc), 6.48 (d, ^{3}J(H,H) = 7 Hz, 1H, Hc),7.46–7.52 (m, 3H, Hg, Hh), 7.74 (dd, ^{4}J(H,H) = 2 Hz, ^{3}J(H,H) = 6 Hz, 1H, H3), 7.81–7.84 (m, 2H, Hf), 8.28 (dd, ^{4}J(H,H) = 2 Hz, ^{3}J(H,H) = 8 Hz, 1H, H4), 9.37 (dd, ^{4}J(H,H) = 1 Hz, ^{3}J(H,H) = 8 Hz, 1H, H2) ppm. ^{13}C{^{1}H} NMR (100.62 MHz, [d^6]-DMSO): δ = 80.4 (Cb), 80.6 (Cb), 81.3 (Ca), 84.8 (Cc), 86.3 (Cc), 98.7 (Cd), 113.9 (C7), 126.7 (Cg), 126.8 (Cg) 127.4 (C4a), 127.6 (C3), 128.7 (Cf), 129.0 (Cf), 129.9 (Ch), 133.8 (Ce), 136.1 (C4), 153.9 (C8a), 157.3 (C2), 168.4 (C5), 173.9 (C6), 176.8 (C8) ppm.

Chlorido(7-chloro-8-hydroxyquinolinolato-5,6-dione-κ*N*1,κ*O*8)(η^5-pentamethylcyclopentadienyl)iridium(III), **4**.
The synthesis was performed according to the general procedure using **DQQ** (81 mg, 0.357 mmol) and bis[dichlorido(η^5-pentamethylcyclopentadienyl)iridium(III)] (128 mg, 0.16 mmol) to afford a purple solid (114 mg, 62%). Elemental Analysis calculated for $C_{19}H_{18}NO_3Cl_2Ir$: C 39.93, H 3.17, N 2.45%. Found: C 40.09, H 3.15, N 2.41. MS (ESI$^+$): m/z 594.0166 [M + Na]$^+$ (m_{calc} = 594.0171). ^{1}H NMR (400.13 MHz, [d^6]-DMSO): δ = 1.66 (s, 15H, Cp*), 7.84 (dd,

$^{4}J(H,H)$ = 2 Hz, $^{3}J(H,H)$ = 7 Hz, 1H, H3), 8.38 (dd, $^{4}J(H,H)$ = 1 Hz, $^{3}J(H,H)$ = 8 Hz, 1H, H4), 9.01 (dd, $^{4}J(H,H)$ = 1 Hz, $^{3}J(H,H)$ = 6 Hz, 1H, H2) ppm. $^{13}C\{^{1}H\}$ NMR (100.62 MHz, [d^{6}]-DMSO): δ = 8.4 C(Cp*-CH_3), 86.0 (Cp*), 113.9 (C7), 127.6 (C4a), 129.0 (C3), 136.0 (C4), 153.9 (C8a), 155.5 (C2), 169.0 (C5), 174.1 (C6), 176.8 (C8) ppm.

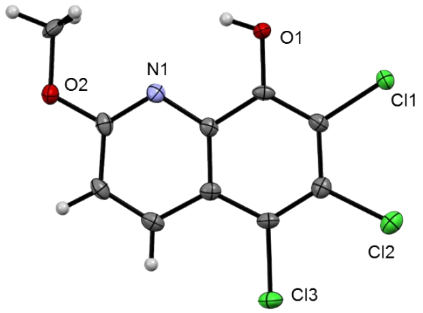
Chlorido(7-chloro-8-hydroxyquinolinolato-5,6-dione-κ*N*1,κ*O*8)(η^{5}-pentamethylcyclopentadienyl)rhodium(III), **5**.

The synthesis was performed according to the general procedure using **DQQ** (104 mg, 0.456 mmol) and bis[dichlorido(η^{5}-pentamethylcyclopentadienyl)rhodium(III)] (100 mg, 0.205 mmol) to afford a purple solid (120 mg, 60%). Elemental Analysis calculated for $C_{19}H_{18}NO_3Cl_2Ir$: C 47.33, H 3.76, N 2.90%. Found: C 47.14, H 3.49, N 2.58. MS (ESI^{+}): m/z 503.9627 $[M + Na]^{+}$ (m_{calc} = 503.9611). ^{1}H NMR (400.13 MHz, [d^{6}]-DMSO): δ = 1.67 (s, 15H, Cp*), 7.87 (dd, $^{4}J(H,H)$ = 2 Hz, $^{3}J(H,H)$ = 8 Hz, 1H, H3), 8.37 (dd, $^{4}J(H,H)$ = 1 Hz, $^{3}J(H,H)$ = 8 Hz, 1H, H4), 9.00 (dd, $^{4}J(H,H)$ = 1 Hz, $^{3}J(H,H)$ = 6 Hz, 1H, H2) ppm. $^{13}C\{^{1}H\}$ NMR (100.62 MHz, [d^{6}]-DMSO): δ = 8.5 C(Cp*-CH_3), 94.5 (Cp*), 113.8 (C7), 127.2 (C4a), 128.5 (C3), 136.2 (C4), 154.1 (C8a), 154.4 (C2), 168.6 (C5), 172.5 (C6), 177.6 (C8) ppm.

Studies on the impact of the solvent and reaction conditions on the formation of the *ortho*-quinone

In order to verify the source of the incorporated oxygen atom, all reactions were performed using dry solvents and inert atmosphere. The solvents where furthermore degassed by bubbling N_2 through the solution for several minutes, or by using the freeze-pump-thaw technique prior to the use.

.



$^{Me}HQ_{Cl}$

Figure S1. Molecular structure of $^{Me}HQ_{Cl}$ drawn at 50% probability level.

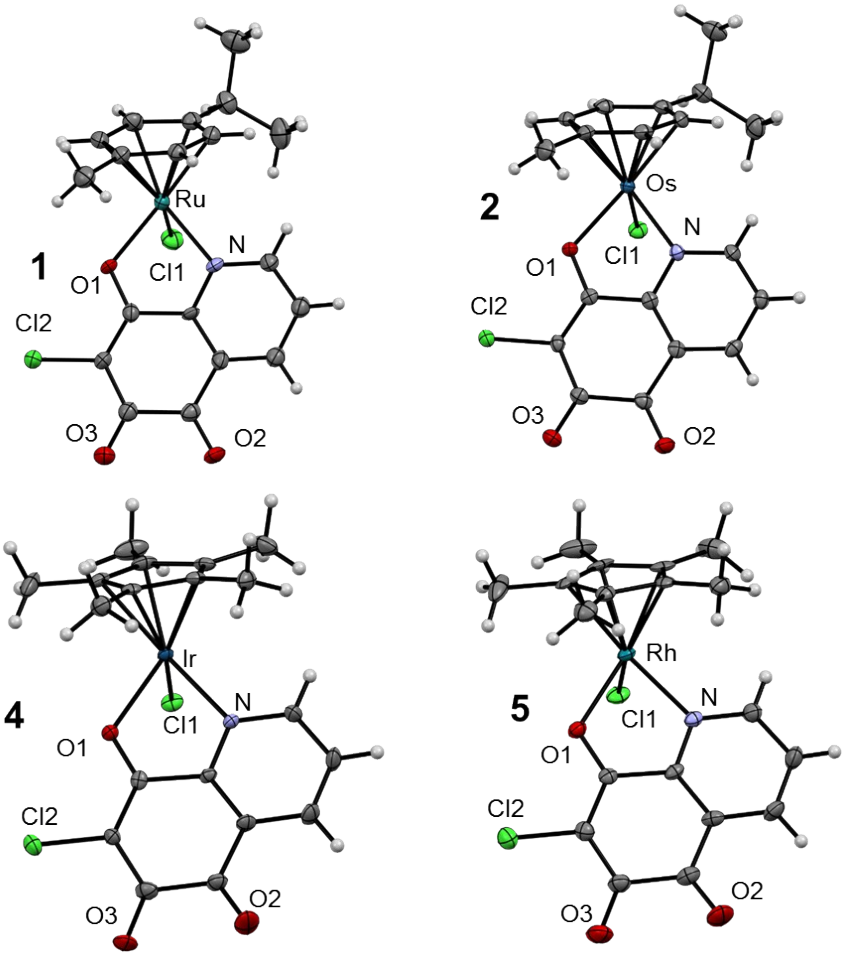


Figure S2. Molecular structures of **1**, **2**, **4** and **5** drawn at 50% probability level. Co-crystallized solvent molecules have been omitted for clarity.

Table S1. Details of collected X-ray data for ^{Me}**HQ$_{Cl}$** in comparison to a literature structure.

	^{Me}**HQ$_{Cl}$**	^{Me}**HQ$_{Cl}$** [8]
Formula	$C_{10}H_6Cl_3NO_2$	$C_{10}H_6Cl_3NO_2$
CCDC Nr.	1571650	819924
Molecular weight (g mol^{-1})	278.51	278.51
Temperature (K)	100(2)	150(2)
Wavelength (Å)	0.71073	1.54178
Crystal system	monoclinic	monoclinic
Space group	$P2_1/c$	$P2_1/c$
a (Å)	21.1155(9)	10.0782(3)
b (Å)	4.9816(2)	4.9979(1)
c (Å)	21.6442(8)	21.5827(6)
α (°)	90	90
β (°)	111.532(3)	99.287(2)
γ (°)	90	90
Volume (Å^3)	2117.84(15)	1072.87(5)
Z	8	4
Calculated density (g cm^{-3})	1.747	1.724
Absorption coefficient (mm^{-1})	0.845	7.607
F(000)	1120	560
Crystal size (mm × mm × mm)	0.42 × 0.10 × 0.08	0.40 × 0.21 × 0.20
2θ (min, max) (°)	3.221, 25.128	4.15, 71.38
Limiting indices	-25 ≤ h ≤ 25 -5 ≤ k ≤ 5 -25 ≤ l ≤ 25	-11 ≤ h ≤ 12 -6 ≤ k ≤ 5 -17 ≤ l ≤ 25
Reflections collected / unique	21650 / 3794 [R(int) = 0.0685]	4752 / 2035 [R(int) = 0.024]
Data / restraints / parameters	3794 / 0 / 291	2035 / 0 / 147
Goodness-of-fit on F^2	1.039	1.044
Final R indices [I>2σ(I)]	R_1 = 0.0402, wR_2 = 0.0944	R_1 = 0.0391, wR_2 = 0.1045
R indices (all data)	R_1 = 0.0724, wR_2 = 0.1081	R_1 = 0.0441, wR_2 = 0.1096
Largest diff. peak and hole (eÅ^{-3})	0.340 and -0.501	0.976 and -0.257

Table S2. Details of collected X-ray data for **1**, **2**, **4** and **5**.

	1	**2**	**4**	**5**
Formula	$C_{19}H_{17}Cl_2NO_3Ru$-CH_2Cl_2	$C_{19}H_{17}Cl_2NO_3Os$-$CHCl_3$	$C_{19}H_{18}Cl_2NO_3Ir$	$C_{19}H_{18}Cl_2NO_3Rh$
CCDC Nr.	1571651	1571652	1571653	1571654
Molecular weight (g mol^{-1})	564.23	687.80	571.44	482.15
Temperature (K)	100(2)	100(2)	100(2)	100(2)
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073
Crystal system	monoclinic	monoclinic	monoclinic	monoclinic
Space group	$P2_1/c$	$P2_1/c$	$P2_1/c$	$P2_1/c$
a (Å)	10.6343(5)	10.3571(6)	14.4492(8)	14.4730(7)
b (Å)	21.1270(9)	21.0903(12)	7.3746(4)	7.3041(3)
c (Å)	19.5934(10)	10.7050(6)	17.1873(9)	17.2691(8)
β (°)	100.782(3)	108.136(3)	92.400(2)	92.709(3)
Volume ($Å^3$)	4324.4(4)	2222.2(2)	1829.82(17)	1823.5(15)
Z	8	4	4	4
Calculated density (g cm^{-3})	1.733	2.056	2.074	1.756
Absorption coefficient (mm^{-1})	1.242	6.363	7.608	1.249
F(000)	2256	1320	1096	968
Crystal size (mm × mm × mm)	0.35 x 0.35 x 0.30	0.30 x 0.18 x 0.16	0.28 x 0.22 x 0.14	0.20 x 0.12 x 0.10
2θ (min, max) (°)	3.215, 25.112	1.931, 27.876	2.71, 27.50	2.36, 27.75
Limiting indices	-13 ≤ h ≤ 12 -26 ≤ k ≤ 26 -24 ≤ l ≤ 23	-13 ≤ h ≤ 13 -27 ≤ k ≤ 27 -13 ≤ l ≤ 14	-18 ≤ h ≤ 18 -7 ≤ k ≤ 9 -22 ≤ l ≤ 22	-18 ≤ h ≤ 18 -9 ≤ k ≤ 9 -19 ≤ l ≤ 22
Reflections collected / unique	47882 / 8462 [R(int) = 0.0458	28102 / 5253 [R(int) = 0.0346]	19988 / 4198 [R(int) = 0.0650]	21431 / 4268 [R(int) = 0.0782]
Data / restraints / parameters	8462 / 196 / 549	5253 / 0 / 275	4198 / 0 / 240	4268 / 0 / 240
Goodness-of-fit on F^2)	1.181	1.111	1.089	1.055
Final R indices [I>2σ(I)]	R_1 = 0.0547, wR_2 = 0.1308	R_1 = 0.0261, wR_2 = 0.0571	R_1 = 0.0287, wR_2 = 0.0730	R_1 = 0.0492, wR_2 = 0.1107
R indices (all data)	R_1 = 0.0696, wR_2 = 0.1387	R_1 = 0.0329, wR_2 = 0.0599	R_1 = 0.0315, wR_2 = 0.0745	R_1 = 0.0638, wR_2 = 0.1178
Largest diff. peak and hole ($eÅ^{-3}$)	1.347 and -1.656	1.967 and -0.707	1.146 and -1.719	1.738 and -1.134

Table S3. Comparison of bond lengths (Å) as observed in the molecular structures of **1**, **2**, **4** and **5**.

bond	Compounds, bond lengths (Å)			
	1 (M = Ru)	**2** (M = Os)	**4** (M = Ir)	**5** (M = Rh)
M–Cl1	2.408(2)	2.4085(9)	2.382(1)	2.389(1)
M–O1	2.096(4)	2.100(2)	2.146(3)	2.151(3)
M–N	2.102(5)	2.103(3)	2.104(3)	2.113(3)
C8–O1	1.283(7)	1.282(4)	1.266(5)	1.274(5)
C8–C7	1.387(8)	1.385(5)	1.387(6)	1.394(6)
C7–Cl2	1.733(6)	1.733(3)	1.730(4)	1.734(5)
C7–C6	1.437 (9)	1.423(5)	1.430(6)	1.418(6)
C6–O3	1.222(7)	1.230(4)	1.227(5)	1.234(5)
C6–C5	1.542(9)	1.552(5)	1.541(6)	1.541(6)
C5–O2	1.224(8)	1.205(4)	1.204(5)	1.206(5)
C5–C4	1.485(9)	1.496(5)	1.490(6)	1.486(6)

Sulforhodamine B Cytotoxicity Assay

HCT116 and NCI-H460 cells were supplied by ATCC, while SiHa cells were from Dr. David Cowan, Ontario Cancer Institute, Canada. The cells were grown in αMEM (Life Technologies) supplemented with 5% fetal calf serum (Moregate Biotech) at 37 °C in a humidified incubator with 5% CO_2. The cells were seeded at 750 (HCT116, NCI-H460) or 4000 (SiHa) cells/well in 96-well plates and left to settle for 24 h. The compounds were added to the plates in a series of 3-fold dilutions, containing a maximum of 0.5% DMSO at the highest concentration. The assay was terminated after 72 h by addition of 10% trichloroacetic acid (Merck Millipore) at 4 °C for 1 h. The cells were stained with 0.4% sulforhodamine B (Sigma-Aldrich) in 1% acetic acid for 30 min in the dark at room temperature, then washed with 1% acetic acid to remove unbound dye. The stain was dissolved in unbuffered Tris base (10 mM; Serva) for 30 min on a plate shaker in the dark and quantified on a BioTek EL808 microplate reader at an absorbance wavelength of 490 nm with 450 nm as the reference wavelength to determine the percentage of cell-growth inhibition by determining the absorbance of each sample relative to a negative (no inhibitor) and a no-growth control (day 0). The IC50 values were calculated with SigmaPlot 12.5 using a three-parameter logistic sigmoidal dose-response curve between the calculated growth inhibition and the compound concentration. The presented IC_{50} values are the mean of at least 3 independent experiments, where 10 concentrations were tested in duplicate for each compound.

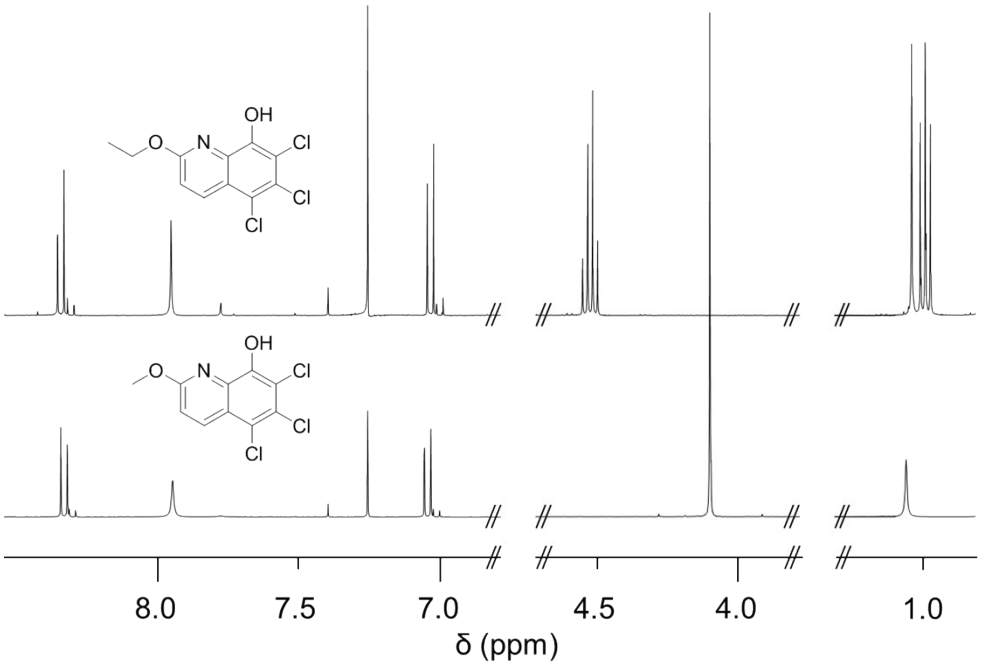


Figure S3. ^{1}H NMR spectra of a methoxy-and ethoxy-substituted hydroxyquinoline derivatives $^{Me}\mathbf{HQ_{Cl}}$ and $^{Et}\mathbf{HQ_{Cl}}$.

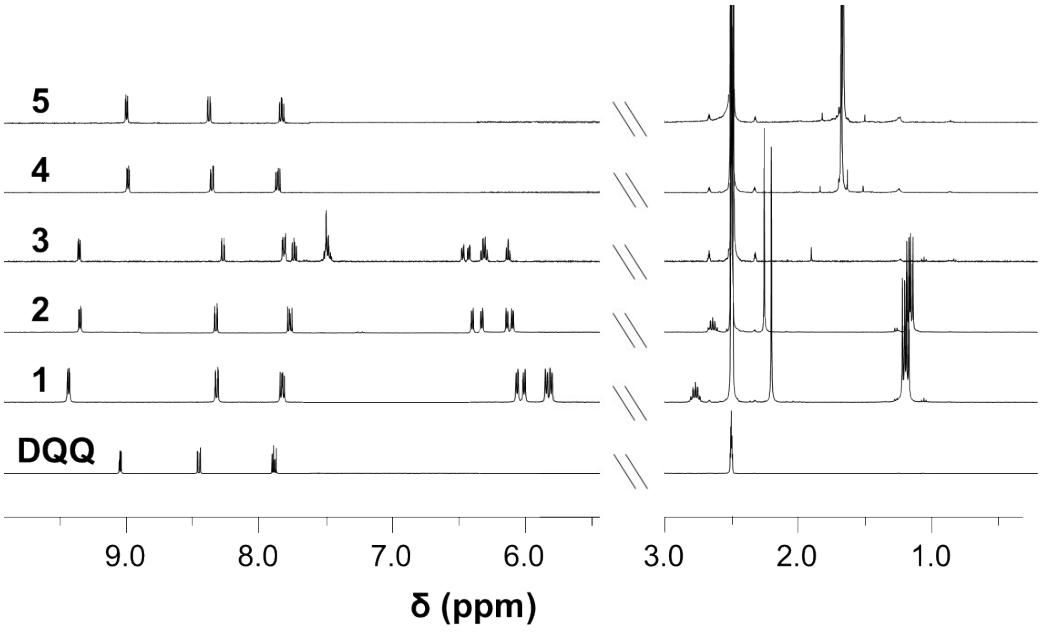


Figure S4. Comparison of the ^{1}H NMR spectra of compounds **1**–**5** and **DQQ**.

Pulse radiolysis studies of DQQ, 1–5

To ensure sufficient aqueous solubility for pulse radiolysis experiments, the compounds were either dissolved in 10 M 2-propanol (ISP) as stock solutions at a concentration of 1 mM and then diluted 1:10 to give 100 μM in 1 M ISP as a working solution, or made up directly in 1 M ISP. All solutions were sonicated and slightly warmed to ensure dissolution. The pH of all working solutions was controlled at pH 7.0 by adding 2.5 mM phosphate buffer and purged free of oxygen with N_2O gas. Such a system produces the 2-propanyl radical as the reductant upon irradiation. Pulse radiolysis using 4 MeV electrons instantaneously breaks down water into oxidising and reducing radicals and molecular products of known yields (yield given as $\mu M \cdot Gy^{-1}$).[9]

$H_2O \text{ ^^^}\rightarrow e^-_{aq}\ (0.28) + HO^\cdot\ (0.28) + H^\cdot\ (0.06) + H_2O_2\ (0.07) + H_2\ (0.045) + H_3O^+\ (0.28)$

In N_2O-saturated solution the e^-_{aq} are rapidly converted into the $HO^\cdot$ radical and under high radical scavenging condition of added formate (0.1 M) or 2-propanol (1 M), into reducing $CO_2^{\cdot-}$ radicals and 2-propanyl radicals (and minor non-reducing radicals).

$e^-_{aq} + N_2O \rightarrow HO^\cdot + HO^- + N_2$

$HO^\cdot/H^\cdot + HCOO^- \rightarrow H_2O + CO_2^{\cdot-}$

$HO^\cdot/H^\cdot + (CH_3)_2CHOH \rightarrow H_2O + (CH_3)_2C^\cdot OH + \{^\cdot CH_2(CH_3)CHOH + \ldots\}$

Under the above high radical scavenging conditions, the radical yield of the $CO_2^{\cdot-}$ radical is slightly increased to 0.68 μM Gy^{-1}.[10] Comparing the absorption per gray of one-electron reduced methylviologen at 600 nm by the $CO_2^{\cdot-}$ radical with that of the 2-propanyl radical, under the above condition, gave the yield of 2-propanyl radical as 0.56 μM Gy^{-1} (data not shown). Hence for a typical radiation dose of 3 Gy in 200 ns, 1.68 μM reducing 2-propanyl radicals are produced and used to reduce added substrates.

The formation and decay of radical spectra were measured by time-resolved spectrophotometry as previously described.[11] The 2-propanyl radical reacted with the compounds, k = 1.8 ± 0.2 x 10^9 M^{-1} s^{-1}, to produce radical spectra, which are presented as the change in absorption relative to those of the unreduced compounds. One-electron reduction potentials, $E(1)$, were determined by establishing redox equilibria between ≥4 mixtures of the compounds (S^+) and quinone redox indicators (Q) of known $E(1)$ (methyl-benzoquinone, MeQ, +23 ± 10 mV, and 2,6-dimethyl-benzoquinone, diMeQ, -80 ± 10 mV),[12] using the Nernst equation to calculate ΔE, allowing for ionic strength effects, E_{cor}, using Debye-Hückel theory.

$Q^{\cdot-} + S^+ \overset{K}{\rightleftharpoons} Q + S^{+\cdot-}$

(Note: $\mathbf{S}^{+}$ denotes a positively charged metal complex, and $\mathbf{S}^{+\cdot -}$ denotes a one-electron reduced ligand on the complex.)

Pulse radiolysis data

One-electron reduction of **DQQ** by the 2-propanyl radical, k = 3.2 x 10^9 M^{-1} s^{-1}, produced a spectrum exhibiting an absorption band centred at 400 nm (Figure S5). The redox equilibrium was established between one-electron reduced **DQQ** ($S^{\cdot -}$) and MeQ within 50 μs and observed at 400 nm giving K = 17.2 ± 2.3, ΔE = 73 ± 4, yielding E(**DQQ**/$^{\cdot -}$) = +96 ± 11 mV.

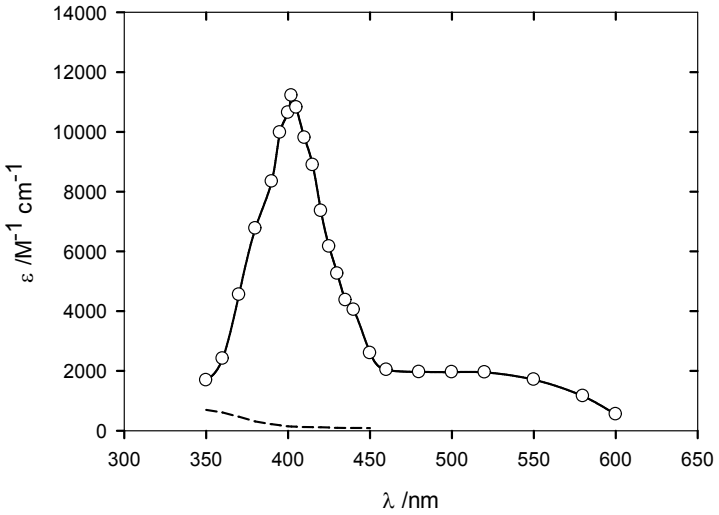


Figure S5. Absorption spectrum recorded for **DQQ** following one-electron reduction, ○. Spectrum corrected for ground-state absorption (dashed line).

Table S4. One-electron reduction potentials E(1) of **DQQ** and **1**–**5**.

compound	E(1) / mV
DQQ	+96 ± 11
1	-84 ± 12
2	-63 ± 8
3	-127 ± 16
4	-98 ± 12
5	-87 ± 10

One-electron reduction of **1**–**5** by the 2-propanyl radical produced complex spectra exhibiting a naphthoquinone-like absorption band centred near 400 nm and bleaching of the ground-state absorption in the 500 nm region (Figures 5, S6–S9 for **1**–**5**, respectively). A redox equilibrium was established between one-electron reduced **1** ($S^{+\cdot -}$) and reference 2,6-dimethylbenzoquinone (diMeQ) within 50 µs and observed both at 425 nm (semiquinone absorption band) and at 510 nm. K = 1.06 ± 0.23, Δ*E* = 2 ± 7, -6 mV ionic strength correction, yielding *E*(**1**/$^{\cdot -}$) = -84 ± 12 mV.

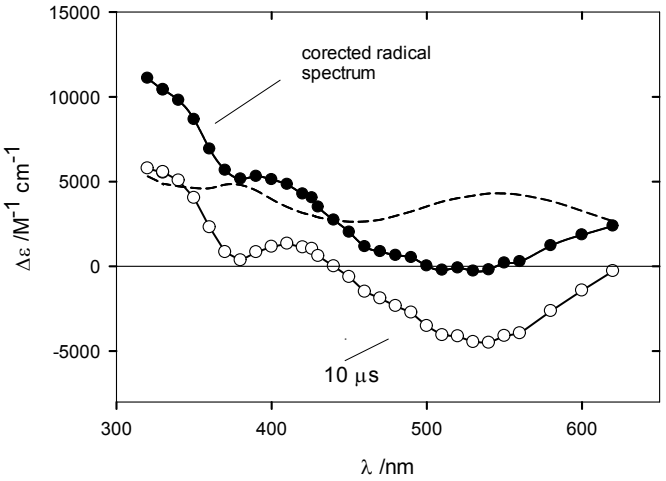


Figure S6. Changes in absorption spectrum recorded for **2** following one-electron reduction, ○. Spectrum corrected for ground-state absorption (dashed line), ●

The redox equilibria between one-electron reduced **2**–**5** ($S^{+\cdot -}$) and reference methylbenzoquinone (MeQ; **3** and **4**) or quinones (Q; **2** and **5**) were established within 50 µs and observed at 425 nm (semiquinone absorption band for all compounds) and at 510 (**2**), 520 (**3**), 350 (**4**) and 510 (**5**) nm.

Compound **2**: For MeQ, K = 0.034 ± 0.004, Δ*E* = -87 ± 4, +7 mV ionic strength correction, giving *E*(S/S$^{\cdot -}$) = -57 ± 11 mV, and for diMeQ, K = 1.25 ± 0.21, Δ*E* = 6 ± 4, +6 mV ionic strength correction, giving *E*(S/S$^{\cdot -}$) = -68 ± 12 mV, yielding *E*(**2**/$^{\cdot -}$) = -63 ± 8 mV.

Compound **3**: K = 0.203 ± 0.081, Δ*E* = -41 ± 12, -6 mV ionic strength correction, giving *E*(**3**/$^{\cdot -}$) = -127 ± 16 mV.

Compound **4**: K = 0.627 ± 0.128, Δ*E* = -12 ± 6, -6 mV ionic strength correction, giving *E*(**4**/$^{\cdot -}$) = -98 ± 12 mV.

Compound **5**: For MeQ, K = 0.018 ± 0.006, Δ*E* = -103 ± 11, +7 mV ionic strength correction, giving *E*($S^+/S^{+\cdot -}$) = -73 ± 15 mV, and for diMeQ, K = 0.345 ± 0.112, Δ*E* = -27 ± 13, +6 mV ionic strength correction, giving *E*($S^+/S^{+\cdot -}$) = -101 ± 16 mV, yielding *E*(**5**/$^{\cdot -}$) = -87 ± 10 mV.

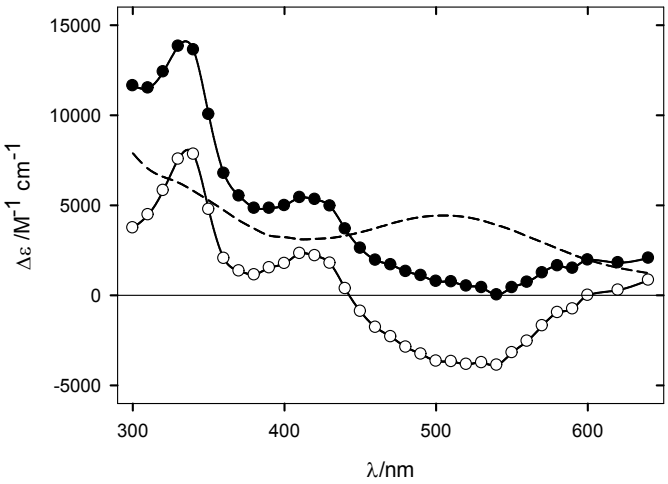


Figure S7. Changes in absorption spectrum recorded for **3** following one-electron reduction, ○. Spectrum corrected for ground-state absorption (dashed line), ●

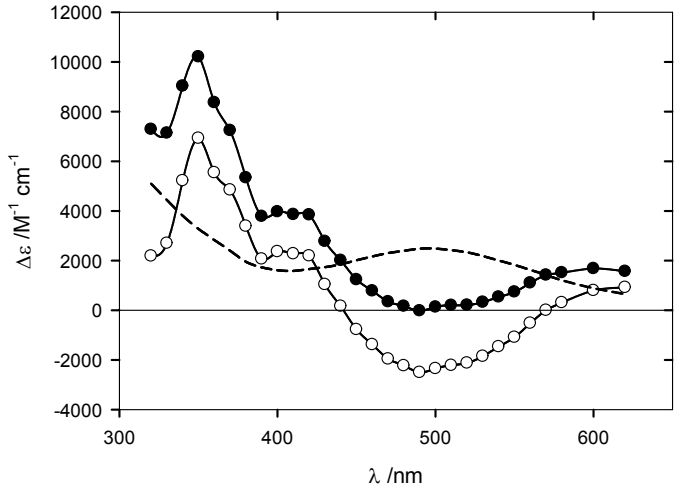


Figure S8. Changes in absorption spectrum recorded for **4** following one-electron reduction, ○. Spectrum corrected for ground-state absorption (dashed line), ●

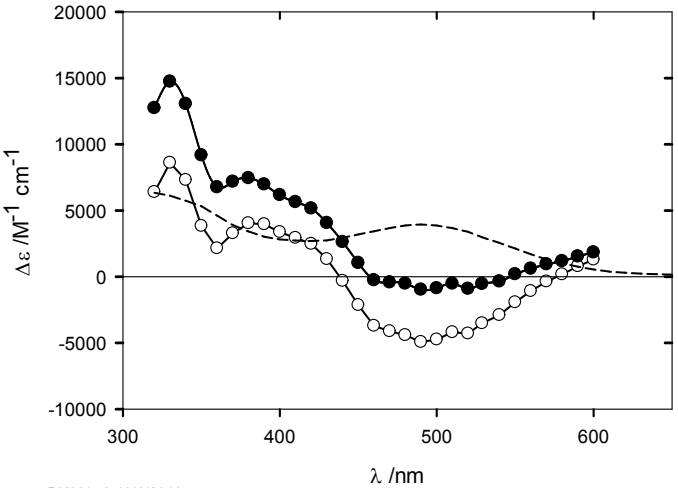


Figure S9. Changes in absorption spectrum recorded for **5** following one-electron reduction, ○. Spectrum corrected for ground-state absorption (dashed line), ●.

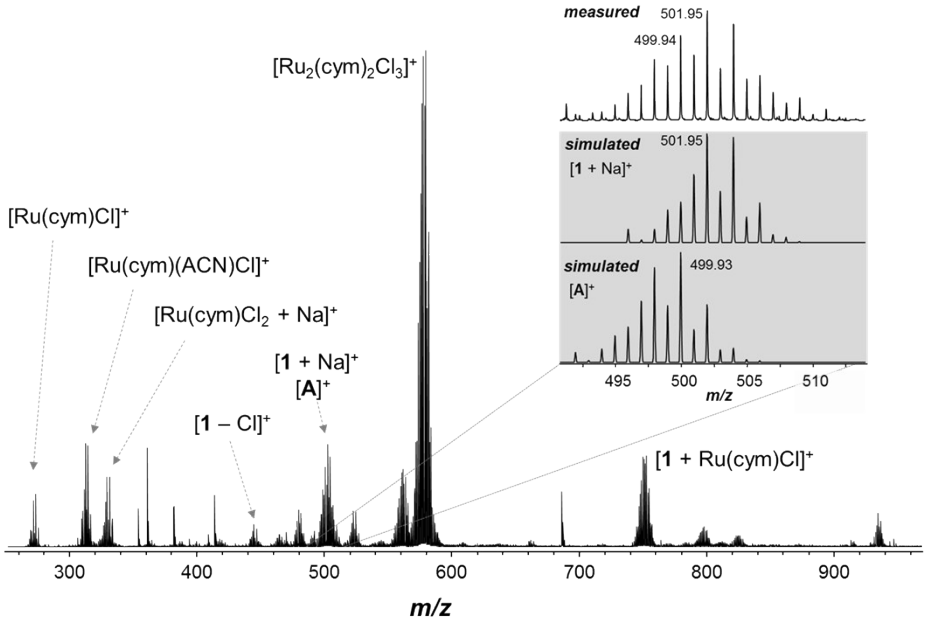


Figure S10. Mass spectrum of the reaction mixture to prepare **1**. Note the peak at around *m/z* 500 which we assigned to being a mixture of [**1** + Na]$^+$ + [**A**]$^+$. The inset shows a comparison of the isotope distribution measured and simulated for the latter ions.

References

[1] D. B. G. Williams, M. Lawton, *J. Org. Chem.* **2010**, *75*, 8351-8354.

[2] M. A. Bennett, A. K. Smith, *J. Chem. Soc., Dalton Trans.* **1974**, 233-241.

[3] W. A. Kiel, R. G. Ball, W. A. G. Graham, *J. Organomet. Chem.* **1990**, *383*, 481-496.

[4] B. L. Booth, R. N. Haszeldine, M. Hill, *J. Chem. Soc. A* **1969**, 1299-1303.

[5] a) R. G. Ball, W. A. G. Graham, D. M. Heinekey, J. K. Hoyano, A. D. McMaster, B. M. Mattson, S. T. Michel, *Inorg. Chem.* **1990**, *29*, 2023-2025; b) C. White, A. Yates, P. M. Maitlis, D. M. Heinekey, in *Inorganic Syntheses*, John Wiley & Sons, Inc., **2007**, pp. 228-234.

[6] M. R. Pressprich, J. Chambers, Bruker Analytical X-ray systems, Madison, **2004**.

[7] B. J. Mulchin, C. G. Newton, J. W. Baty, C. H. Grasso, W. J. Martin, M. C. Walton, E. M. Dangerfield, C. H. Plunkett, M. V. Berridge, J. L. Harper, M. S. M. Timmer, B. L. Stocker, *Bioorg. Med. Chem.* **2010**, *18*, 3238-3251.

[8] Q.-M. Chen, G.-B. Yi, L.-K. An, X.-L. Feng, *Acta Crystallogr., Sect. E* **2011**, *67*, o1108.

[9] G. V. Buxton, C. L. Greenstock, W. P. Helman, A. B. Ross, *J. Phys. Chem. Ref. Data* **1988**, *17*, 513-886.

[10] Q. G. Mulazzani, M. Dangelantonio, M. Venturi, M. Z. Hoffman, M. A. J. Rodgers, *J. Phys. Chem.* **1986**, *90*, 5347-5352.

[11] R. F. Anderson, W. A. Denny, W. J. Li, J. E. Packer, M. Tercel, W. R. Wilson, *J. Phys. Chem. A* **1997**, *101*, 9704-9709.

[12] P. Wardman, *J. Phys. Chem. Ref. Data* **1989**, *18*, 1637-1755.