Electronic Supplementary Information

Accompanying the manuscript

Straightforward approach to efficient oxidative DNA cleaving agents based on Cu(II) complexes of heterosubstituted cyclens

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S-1: Experimental Section

Synthesis of [12]aneN$_4$ (L1)

N,N',N''-Tris(*p*-tolylsulfonyl)diethylentriamine[1], disodium *N,N',N''*-tris(*p*-tolylsulfonyl)diethylentriamine[1], *N,O,O'*-tris(*p*-tolylsulfonyl)diethanolamine[2] and 1,4,7,10-tetrakis(*p*-tolylsulfonyl)-1,4,7,10-tetraazacyclododecane[3] were prepared as previously described. The deprotection was accomplished according to a procedure published by Brosse *et al.*[4] Alternatively, [12]aneN$_4$ was obtained as a donation from mivenion GmbH.

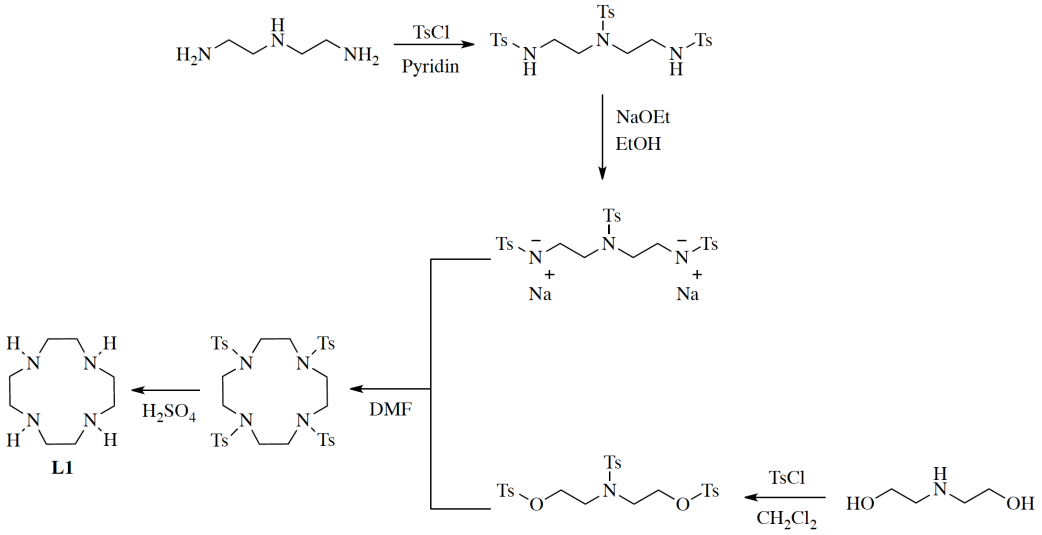


Fig. S-1,1. Synthesis of [12]aneN$_4$ (**L1**).

Synthesis of [12]aneN$_3$O (L2)

O,O'-Bis(*p*-tolylsulfonyl)-oxapentane[5], 4,7,10-tris(*p*-tolylsulfonyl)-1-oxa-4,7,10-triaza-cyclododecane[6] and 1-oxa-4,7,10-triazacyclododecane[7] were prepared as previously described.

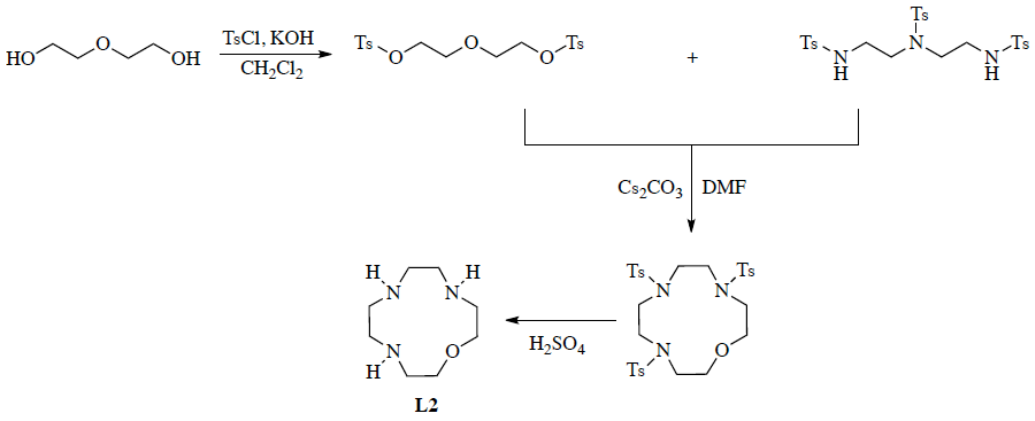


Fig. S-1,2. Synthesis of [12]aneN$_3$O (**L2**).

Synthesis of [12]aneN$_3$S (L3)

Bis[(*p*-tolylsulfonylamino)ethyl]sulfide[8], disodium bis[(*p*-tolylsulfonylamino)ethyl]sulfide[8] and 4,7,10-tris(*p*-tolylsulfonyl)-1-thia-4,7,10-triazacyclododecane[9] were synthesised as previously described. The deprotection of 4,7,10-tris(*p*-tolylsulfonyl)-1-thia-4,7,10-triazacyclododecane to 1-thia-4,7,10-triazacyclododecane was performed in analogy to the procedure published by Brosse *et al.*[4] originally developed for the deprotection of 1,4,7,10-tetrakis(*p*-tolylsulfonyl)-1,4,7,10-tetraazacyclododecane.

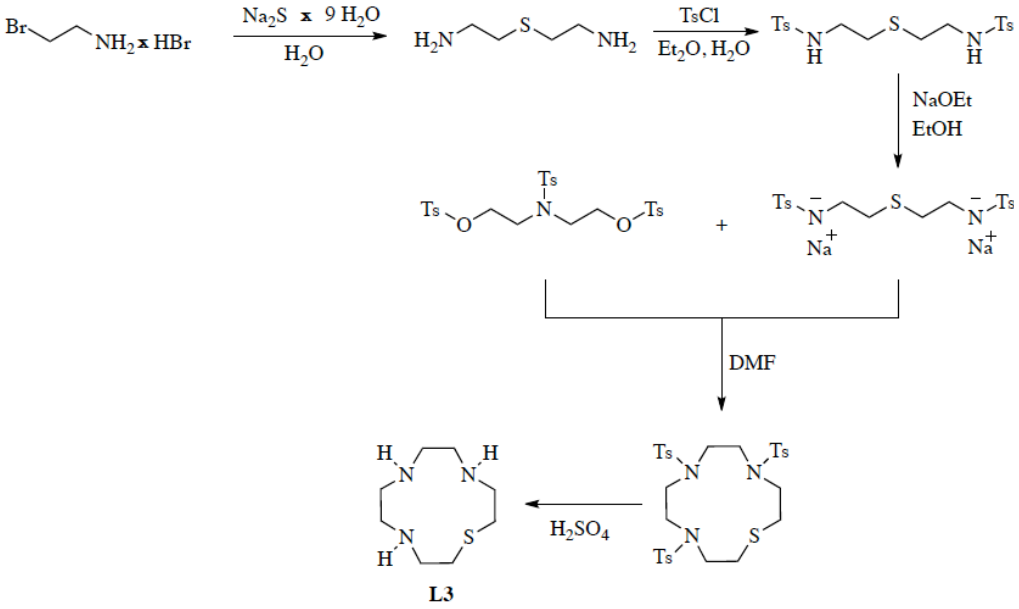


Fig. S-1,3. Synthesis of [12]aneN$_3$S (**L3**).

General procedure for the synthesis of the metal complexes 1, 2 and 3

To a solution of the corresponding ligand **L1** - **L3** (0.6 mmol) in 1 mL methanol a solution of copper nitrate trihydrate (0.6 mmol) in 2 mL methanol was added via a syringe. The solution was stirred for 10 minutes under reflux and the product was crystallised upon cooling at -19 °C. Crystals were filtered off, washed with ethanol and dried in vacuum. Crystals suitable for X-ray analysis of complexes **2** and **3** were obtained by slow diffusion of diethyl ether into a methanolic solution of the complex.

[Cu([12]aneN$_4$)(NO$_3$)]NO$_3$ (**1**): Yield: 0.1310 g (60%). Elemental analysis ($C_8H_{20}CuN_6O_6$): calcd. C 26.78, H 5.65 and N 23.31%; found C 26.70, H 5.60 and N 23.36%. IR $\tilde{\nu}$ = 3232 (m, ν NH), 2928 and 2881 (w, ν CH$_2$), 1425 (m, δ CH$_2$), 1300 (s, ν NO$_3^-$), 1078 (m), 981 (m), 812 (m) cm^{-1}. UV/VIS λ_{max} (fig. S-1,4): 600 nm (ε = 275.0 L mol^{-1} cm^{-1}). MS (ESI$^+$) (m/z): calcd. for [**1**-H-2NO$_3$]$^+$ 234.0900; found 234.0908.

[Cu([12]aneN$_3$O)(NO$_3$)]NO$_3$ (**2**): Yield: 0.1440 g (63%). Elemental analysis (C$_8$H$_{19}$CuN$_5$O$_7$): calcd. C 26.63, H 5.31 and N 19.41%; found C 26.64, H 5.34 and N 19.42%. IR $\tilde{\nu}$ = 3209 and 3156 (w, ν NH), 2940 and 2892 (w, ν CH$_2$), 1746 (vw, δ NH), 1483 (m, δ CH$_2$), 1316 and 1278 (s, ν NO$_3^-$), 1002 (s), 865 (m), 824 (m) cm^{-1}. UV/VIS λ_{max} (fig. S-1,4): 711 nm (ε = 179.5 L mol^{-1} cm^{-1}). MS (ESI$^+$) (m/z): calcd. for [**2**-H-2NO$_3$]$^+$ 235.0745; found 235.0748.

[Cu([12]aneN$_3$S)(NO$_3$)]NO$_3$ (**3**): Yield: 0.0905 g (40%). Elemental analysis (C$_8$H$_{19}$CuN$_5$O$_6$S): calcd. for C 25.50, H 5.08, N 18.58 and S 8.51%; found C 25.60, H 5.14, N 18.53 and S 8.51%. IR $\tilde{\nu}$ = 3216 and 3137 (w, ν NH), 2978, 2923 and 2871 (w, ν CH$_2$), 1740 (vw, δ NH), 1427 and 1388 (m, δ CH$_2$), 1297 (s, ν NO$_3^-$), 1099 (s) cm^{-1}. UV/VIS λ_{max} (fig. S-1,4): 621 nm (ε = 396.6 L mol^{-1} cm^{-1}). MS (ESI$^+$) (m/z): calcd. for [**3**-H-2NO$_3$]$^+$ 251.0512; found 251.0513.

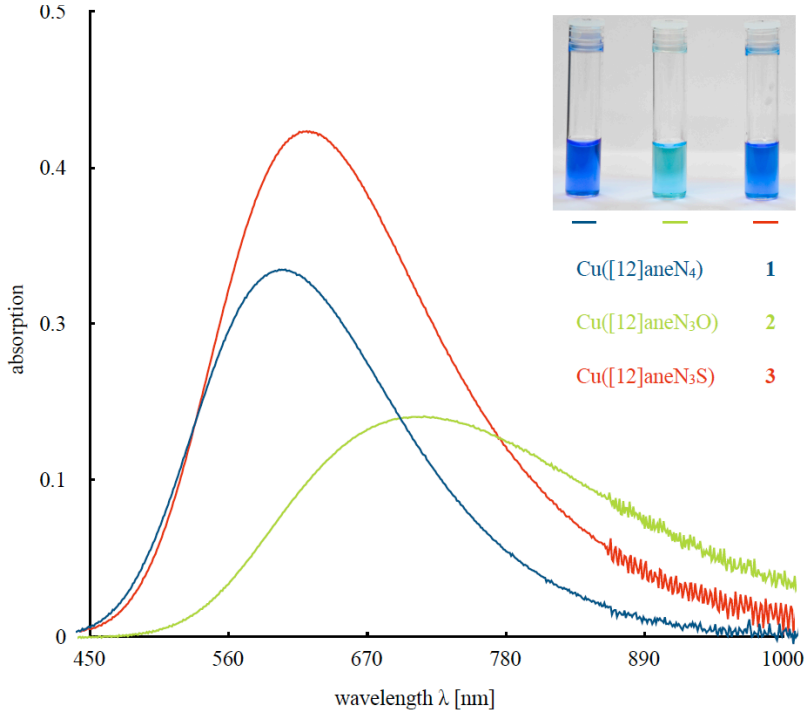


Fig. S-1,4. UV/Vis spectra of complexes **1**, **2** and **3** (5 mM) in 100 mM Tris-HCl buffer (pH 7.4).

S-2: Crystallographic data

Crystallographic details: X-ray diffraction data were collected using a Bruker-AXS SMART CCD system. The structures were solved by direct methods and refined by full matrix least square methods, SHELX-97.[10]

Table S-2,1. Crystallographic and experimental details of complex **2**

Empirical formula	$C_8H_{19}CuN_5O_7$
Formula weight	360.82
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	133(2)
a, b, c (Å)	7.9211(19), 11.979(3), 14.757(3)
β (°)	92.587(5)
Volume (Å^3)	1398.9(6)
Z	4
D_x (Mg m^{-3})	1.713
Radiation type	Mo-K_α
μ (mm^{-1})	1.604
F(000)	748
Crystal size (mm)	0.40 x 0.15 x 0.07
Theta range for data collection (°)	2.19 to 30.56
Index ranges	$-11 \le h \le 11$, $-16 \le k \le 13$, $-21 \le l \le 19$
Reflections collected	17378
Independent reflections	4238 [R(int) = 0.0253]
Completeness to Θ = 30.56° (%)	98.8
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.75 and 0.54
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4238 / 0 / 202
Goodness-of-fit on F^2	1.089

Final *R* indices [$I > 2\ \sigma\ (I)$]	$R_1 = 0.0290$, $wR_2 = 0.0683$
R indices (all data)	$R_1 = 0.0399$, $wR_2 = 0.0731$
Largest diff. peak and hole (e $Å^{-3}$)	0.597 and -0.399

Table S-2,2. Selected bond lengths [Å] of complex **2**

Cu(1)-N(2)	1.9837(15)	C(5)-C(7)	1.515(2)
Cu(1)-N(3)	2.0224(15)	C(7)-N(3)	1.493(2)
Cu(1)-N(1)	2.0267(14)	C(8)-N(3)	1.488(2)
Cu(1)-O(2)	2.0312(13)	C(8)-C(9)	1.518(2)
Cu(1)-O(1)	2.2310(12)	C(9)-O(1)	1.4348(19)
C(1)-O(1)	1.4347(19)	N(4)-O(4)	1.2227(19)
C(1)-C(2)	1.518(2)	N(4)-O(3)	1.2457(19)
C(2)-N(1)	1.491(2)	N(4)-O(2)	1.2955(17)
C(3)-N(1)	1.487(2)	N(5)-O(7)	1.2390(19)
C(3)-C(4)	1.516(2)	N(5)-O(6)	1.245(2)
C(4)-N(2)	1.478(2)	N(5)-O(5)	1.261(2)
C(5)-N(2)	1.478(2)		

Table S-2,3. Angles [°] of complex **2**

N(2)-Cu(1)-N(3)	86.73(6)	C(3)-N(1)-Cu(1)	106.34(10)
N(2)-Cu(1)-N(1)	86.54(6)	C(2)-N(1)-Cu(1)	110.47(10)
N(3)-Cu(1)-N(1)	159.40(6)	C(5)-N(2)-C(4)	116.26(13)
N(2)-Cu(1)-O(2)	152.88(5)	C(5)-N(2)-Cu(1)	108.56(10)
N(3)-Cu(1)-O(2)	95.04(5)	C(4)-N(2)-Cu(1)	109.51(10)
N(1)-Cu(1)-O(2)	99.78(5)	C(8)-N(3)-C(7)	116.14(14)
N(2)-Cu(1)-O(1)	110.88(5)	C(8)-N(3)-Cu(1)	109.56(10)
N(3)-Cu(1)-O(1)	82.29(5)	C(7)-N(3)-Cu(1)	107.12(10)
N(1)-Cu(1)-O(1)	81.97(5)	O(4)-N(4)-O(3)	122.78(13)
O(2)-Cu(1)-O(1)	96.15(4)	O(4)-N(4)-O(2)	119.69(14)
O(1)-C(1)-C(2)	107.37(13)	O(3)-N(4)-O(2)	117.52(13)

N(1)-C(2)-C(1)	113.26(13)	O(7)-N(5)-O(6)	120.67(16)
N(1)-C(3)-C(4)	110.72(13)	O(7)-N(5)-O(5)	120.30(15)
N(2)-C(4)-C(3)	107.68(13)	O(6)-N(5)-O(5)	119.03(14)
N(2)-C(5)-C(7)	107.96(14)	C(1)-O(1)-C(9)	114.87(13)
N(3)-C(7)-C(5)	111.10(13)	C(1)-O(1)-Cu(1)	105.20(8)
N(3)-C(8)-C(9)	112.92(13)	C(9)-O(1)-Cu(1)	106.23(9)
O(1)-C(9)-C(8)	107.24(13)	N(4)-O(2)-Cu(1)	102.11(9)
C(3)-N(1)-C(2)	115.28(13)		

Table S-2,4. Crystallographic and experimental details of complex **3**

Empirical formula	$C_8H_{19}CuN_5O_6S$
Formula weight	376.88
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	133(2)
a, b, c (Å)	8.5321(16), 11.903(2), 14.168(3)
β (°)	94.368(4)°
Volume (Å^3)	1434.7(5)
Z	4
D_x (Mg m^{-3})	1.745
Radiation type	Mo-K_α
μ (mm^{-1})	1.703
F(000)	780
Crystal size (mm)	0.40 x 0.15 x 0.07
Theta range for data collection (°)	2.24 to 30.56
Index ranges	$-11 \le h \le 12$, $-15 \le k \le 16$, $-19 \le l \le 20$
Reflections collected	17105
Independent reflections	4381 [*R*(int) = 0.0143]
Completeness to Θ = 30.56° (%)	99.7

Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4381 / 0 / 202
Goodness-of-fit on F^2	1.129
Final R indices [$I > 2\ \sigma$ (I)]	$R_1 = 0.0241$, $wR_2 = 0.0639$
R indices (all data)	$R_1 = 0.0264$, $wR_2 = 0.0649$
Largest diff. peak and hole (e Å^{-3})	0.619 and -0.288

Table S-2,5. Selected bond lengths [Å] of complex **3**

Cu(1)-N(2)	2.0027(13)	C(5)-N(2)	1.481(2)
Cu(1)-N(3)	2.0176(13)	C(5)-C(6)	1.516(2)
Cu(1)-N(1)	2.0423(13)	C(6)-N(3)	1.485(2)
Cu(1)-O(1)	2.1596(11)	C(7)-N(3)	1.478(2)
Cu(1)-S(2)	2.3283(5)	C(7)-C(8)	1.524(2)
S(2)-C(1)	1.8184(16)	N(4)-O(3)	1.2406(17)
S(2)-C(8)	1.8211(17)	N(4)-O(2)	1.2408(18)
C(1)-C(2)	1.523(2)	N(4)-O(1)	1.2848(16)
C(2)-N(1)	1.485(2)	N(5)-O(6)	1.2383(18)
C(3)-N(1)	1.492(2)	N(5)-O(5)	1.2442(18)
C(3)-C(4)	1.515(2)	N(5)-O(4)	1.2640(17)
C(4)-N(2)	1.4782(19)		

Table S-2,6. Angles [°] of complex **3**

N(2)-Cu(1)-N(3)	86.19(5)	N(3)-C(7)-C(8)	108.85(13)
N(2)-Cu(1)-N(1)	85.81(5)	C(7)-C(8)-S(2)	112.58(11)
N(3)-Cu(1)-N(1)	146.42(5)	C(2)-N(1)-C(3)	113.02(12)
N(2)-Cu(1)-O(1)	101.94(5)	C(2)-N(1)-Cu(1)	112.70(9)
N(3)-Cu(1)-O(1)	104.32(5)	C(3)-N(1)-Cu(1)	102.27(9)
N(1)-Cu(1)-O(1)	109.24(5)	C(4)-N(2)-C(5)	113.93(12)

N(2)-Cu(1)-S(2)	156.44(4)	C(4)-N(2)-Cu(1)	109.05(10)
N(3)-Cu(1)-S(2)	87.07(4)	C(5)-N(2)-Cu(1)	106.30(9)
N(1)-Cu(1)-S(2)	87.42(4)	C(7)-N(3)-C(6)	114.75(12)
O(1)-Cu(1)-S(2)	101.60(3)	C(7)-N(3)-Cu(1)	106.71(9)
C(1)-S(2)-C(8)	103.98(8)	C(6)-N(3)-Cu(1)	107.80(9)
C(1)-S(2)-Cu(1)	90.53(5)	O(3)-N(4)-O(2)	121.54(13)
C(8)-S(2)-Cu(1)	95.44(5)	O(3)-N(4)-O(1)	118.42(13)
C(2)-C(1)-S(2)	107.06(10)	O(2)-N(4)-O(1)	120.04(13)
N(1)-C(2)-C(1)	110.99(12)	N(4)-O(1)-Cu(1)	117.63(9)
N(1)-C(3)-C(4)	107.38(12)	O(6)-N(5)-O(5)	121.96(15)
N(2)-C(4)-C(3)	109.26(12)	O(6)-N(5)-O(4)	119.11(14)
N(2)-C(5)-C(6)	107.51(12)	O(5)-N(5)-O(4)	118.93(14)
N(3)-C(6)-C(5)	109.06(12)		

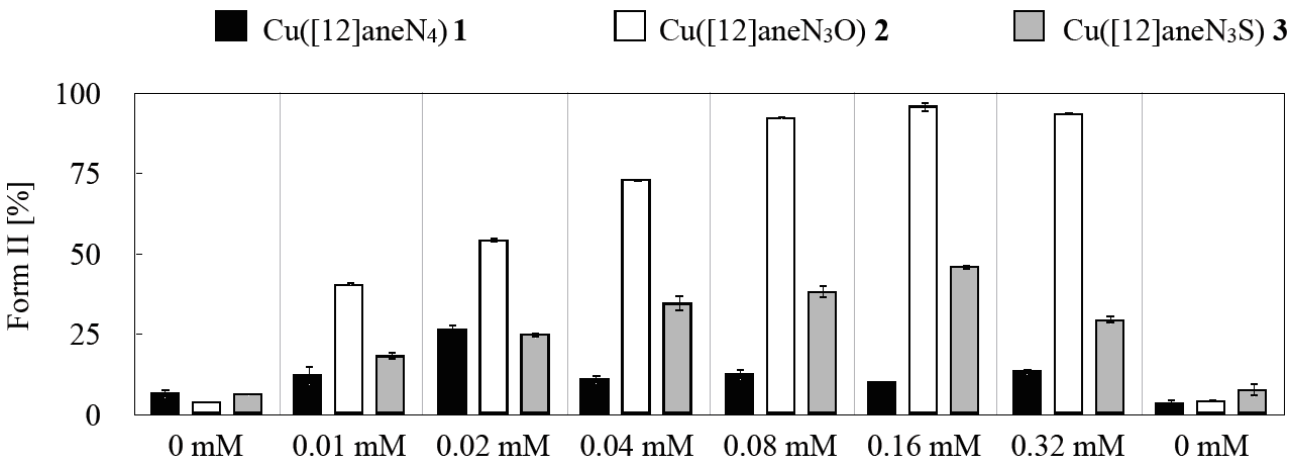
S-3: DNA cleavage experiments

The cleavage activity of complexes **1**, **2** and **3** towards pBR322 plasmid DNA (Carl Roth) was studied using gel electrophoresis. In a typical experiment plasmid DNA (0.025 µg mL^{-1}) in Tris-HCl buffer (100 mM, pH 7.4, Fisher Scientific) and ascorbic acid (0.32 mM, Acros) was mixed with different concentrations of complexes **1**, **2** and **3**. Deionized water (Millipore system) was added up to a total volume of 16 µL before the sample was incubated for given time and temperature. After incubation samples were analysed directly or kept at -20 °C for not more than 24 h. For analysis 3 µL of loading buffer (25 mg bromophenol blue and 4 g saccharose added up to a total volume of 10 mL with deionized water) was added and the sample was divided into two portions of 8 µL each. These were loaded onto an agarose (Lonza, SeaKem LE) gel (1% in 0.5X TBE buffer, Fisher Scientific) containing ethidium bromide (1.0 µg mL^{-1}, Fisher Scientific). Electrophoresis was carried out at 40 V for 2 h using an electrophoresis unit (Carl Roth, power supply: consort EV243) in 0.5X TBE buffer. Bands were visualised by UV light and photographed using a gel documentation system (GelDoc, Bio-Rad). The intensity of the bands was measured using the reference DNA as standard. Taking into account that the supercoiled form I of plasmid DNA has a smaller affinity to bind ethidium bromide, its intensity was multiplied with a correction factor of 1.4.[11]

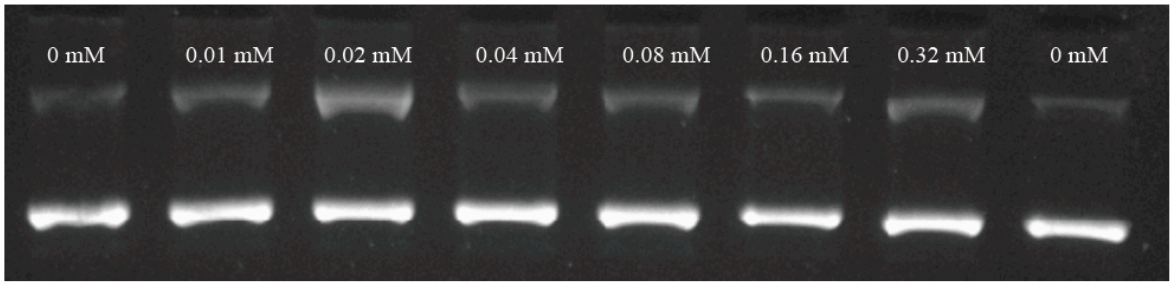
Experiments with radical scavengers were conducted as described above using either 200 mM *tert*-butanol or 200 mM DMSO as hydroxyl radical scavenger, 10 mM NaN_3 as singlet oxygen scavenger, 5 mg mL^{-1} catalase (bovine liver, 2000-5000 units mL^{-1}, Sigma Aldrich) in 0.25X phosphate buffered saline (PBS) as hydrogen peroxide scavenger or 313 units mL^{-1} superoxide dismutase (bovine liver, 2000-6000 units mg^{-1}, suspension in 3.8 M $(NH_4)_2SO_4$, Sigma Aldrich) as superoxide anion scavenger. For the sake of comparison, 214 mM $(NH_4)_2SO_4$ and 0.25X PBS was added to all samples, since superoxide dismutase was purchased as a suspension in an ammonium sulfate solution and catalase had to be pre-incubated at 37 °C in PBS.

However, experiments under argon atmosphere were conducted similar to aerobic experiments. Solutions were prepared using a glove bag (Sigma Aldrich) and degassed water (three freeze-pump-thaw cycles).

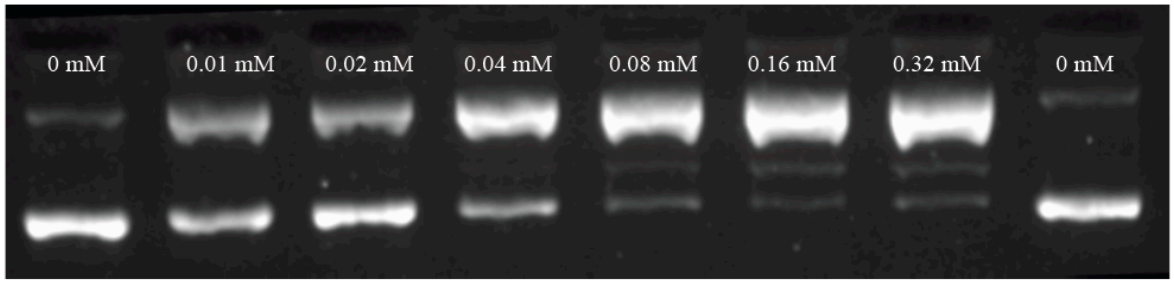
S-3,1. Concentration dependent:



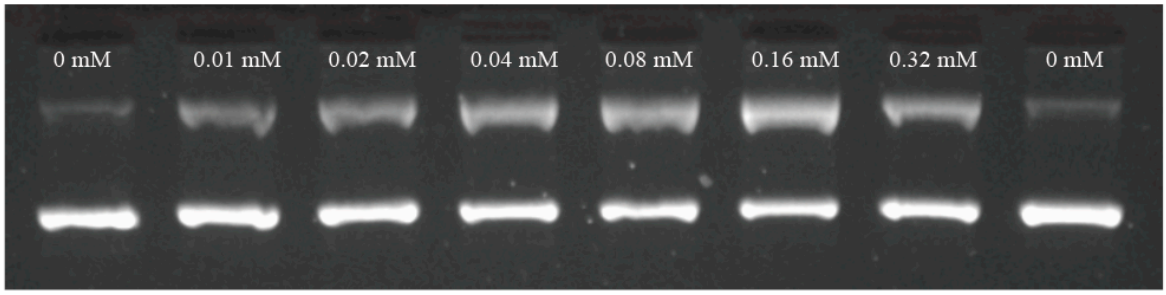
[Cu([12]aneN$_4$)(NO$_3$)]NO$_3$ **1**:



[Cu([12]aneN$_3$O)(NO$_3$)]NO$_3$ **2**:

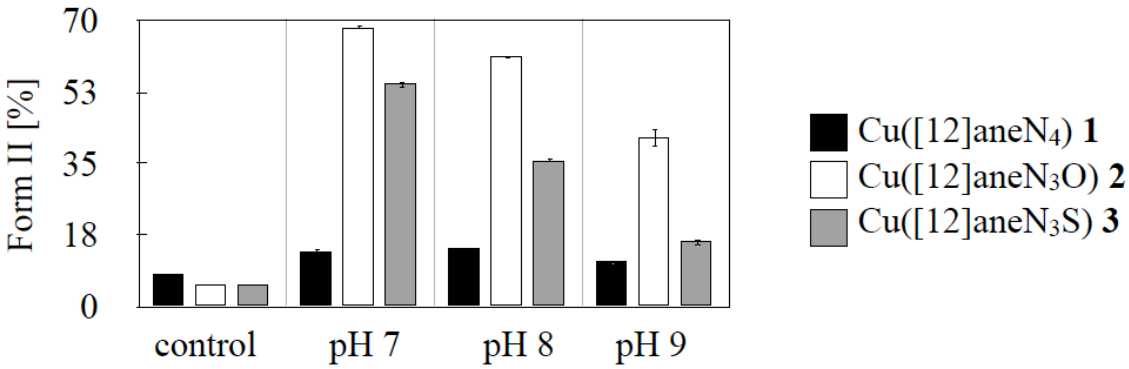


[Cu([12]aneN$_3$S)(NO$_3$)]NO$_3$ **3**:

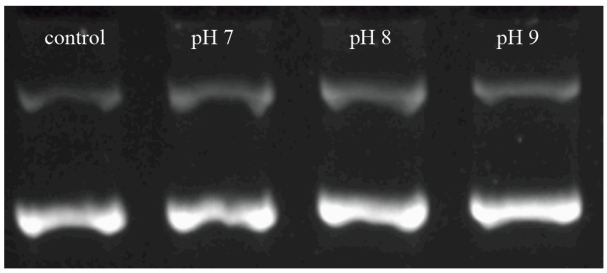


Effect of different concentrations of complexes **1**, **2** and **3** on pBR322 (0.025 µg µL^{-1}) cleavage activity in Tris-HCl buffer (100 mM, pH 7.4) and ascorbic acid (0.32 mM) at 37 °C for 2 h. Illustrated is the average of two measurements, the standard deviation is shown as error bars.

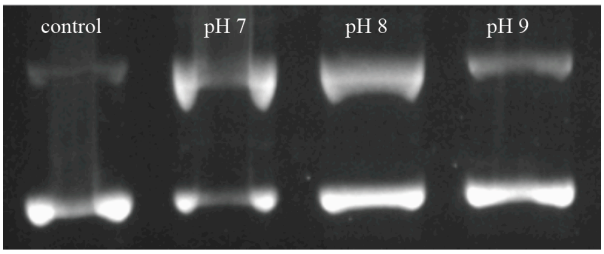
S-3,2. pH dependent:



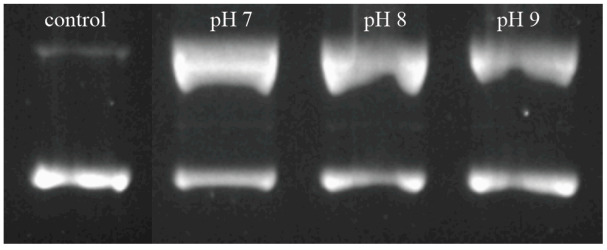
[Cu([12]aneN$_4$)(NO$_3$)]NO$_3$ 1:



[Cu([12]aneN$_3$O)(NO$_3$)]NO$_3$ **2**:

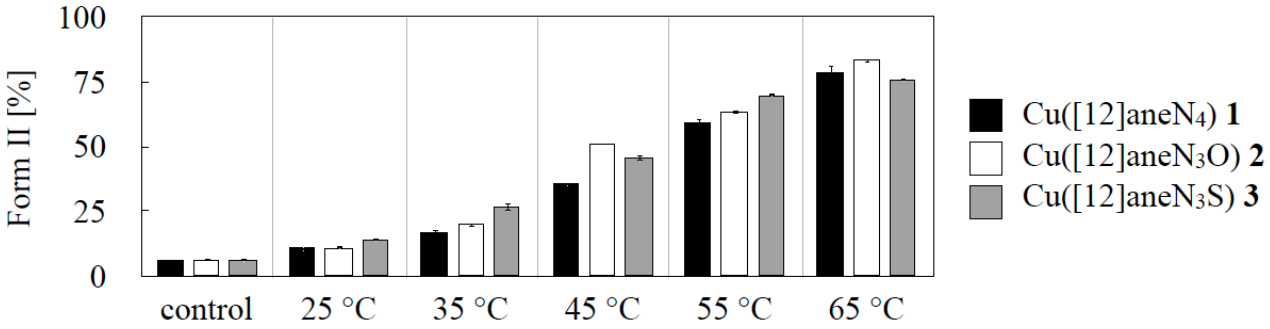


[Cu([12]aneN$_3$S)(NO$_3$)]NO$_3$ **3**:

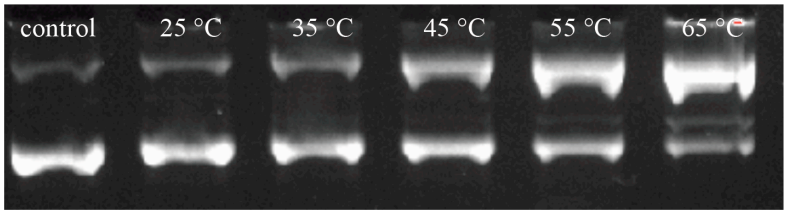


Effect of different pH values on pBR322 (0.025 µg µL^{-1}) cleavage activity of complexes **1**, **2** and **3** (0.04 mM) in Tris-HCl buffer (100 mM, pH 7, pH 8 and pH 9) and ascorbic acid (0.32 mM) at 37 °C for 2 h. A control pBR322 plasmid DNA was incubated without ascorbic acid and complexes **1**, **2** and **3** in Tris-HCl buffer (100 mM, pH 7). Illustrated is the average of two measurements, the standard deviation is shown as error bars.

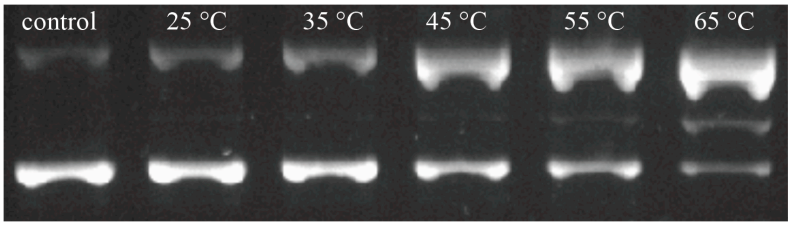
S-3,3. Temperature dependent:



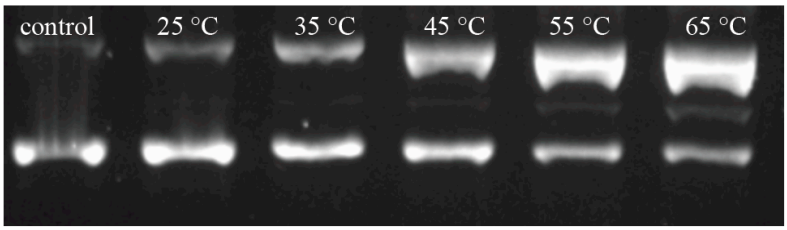
[Cu([12]aneN$_4$)(NO$_3$)]NO$_3$ **1**:



[Cu([12]aneN$_3$O)(NO$_3$)]NO$_3$ **2**:

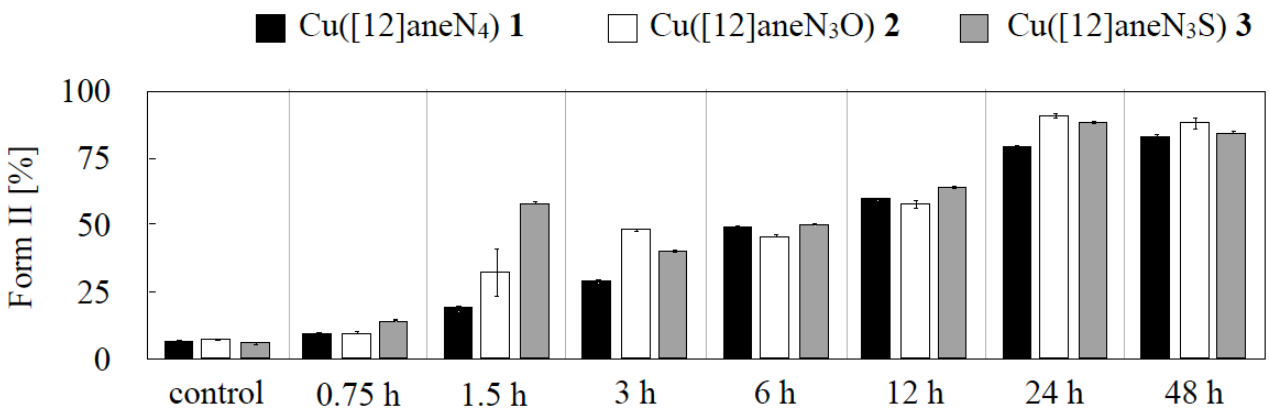


[Cu([12]aneN$_3$S)(NO$_3$)]NO$_3$ **3**:

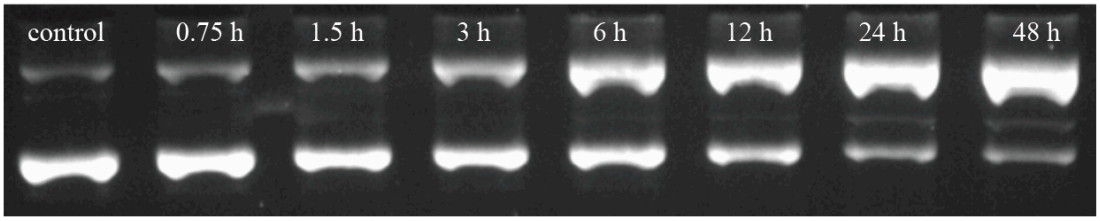


Effect of the incubation temperature on pBR322 (0.025 μg μL^{-1}) cleavage activity of complexes **1**, **2** and **3** (0.01 mM) in Tris-HCl buffer (100 mM, pH 7.4) and ascorbic acid (0.32 mM) for 2 h. A control pBR322 plasmid DNA was incubated without ascorbic acid and complexes **1**, **2** and **3** in Tris-HCl buffer at 25 °C. Illustrated is the average of two measurements, the standard deviation is shown as error bars.

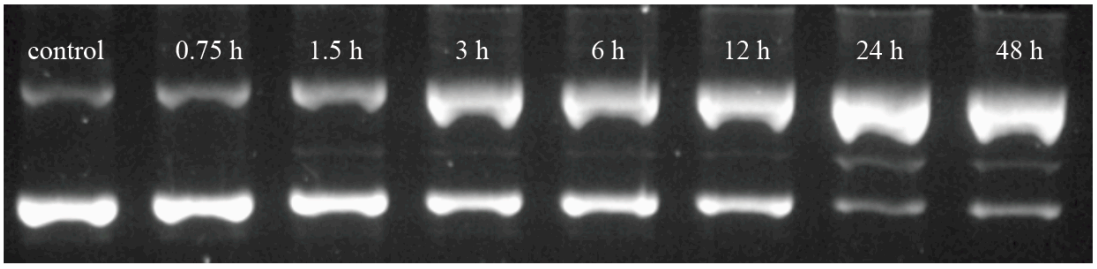
S-3,4. Reaction time dependent:



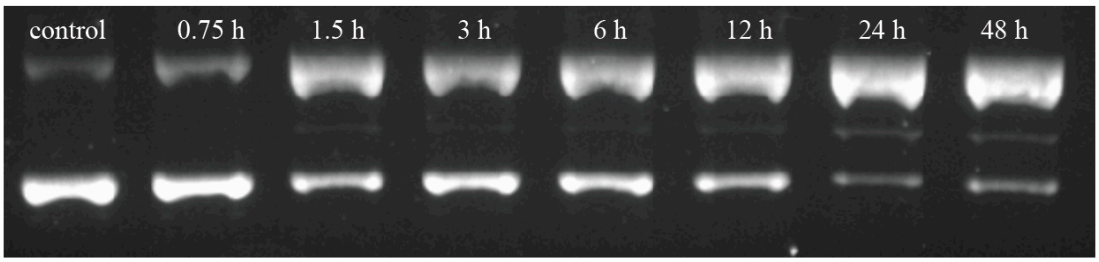
[Cu([12]aneN$_4$)(NO$_3$)]NO$_3$ **1**:



[Cu([12]aneN$_3$O)(NO$_3$)]NO$_3$ **2**:



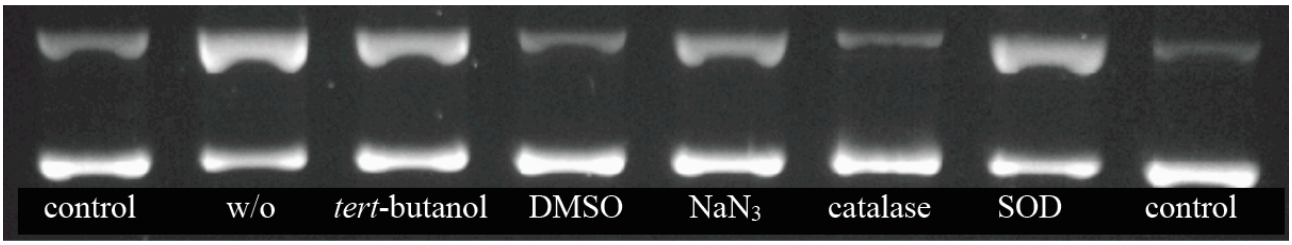
[Cu([12]aneN$_3$S)(NO$_3$)]NO$_3$ **3**:



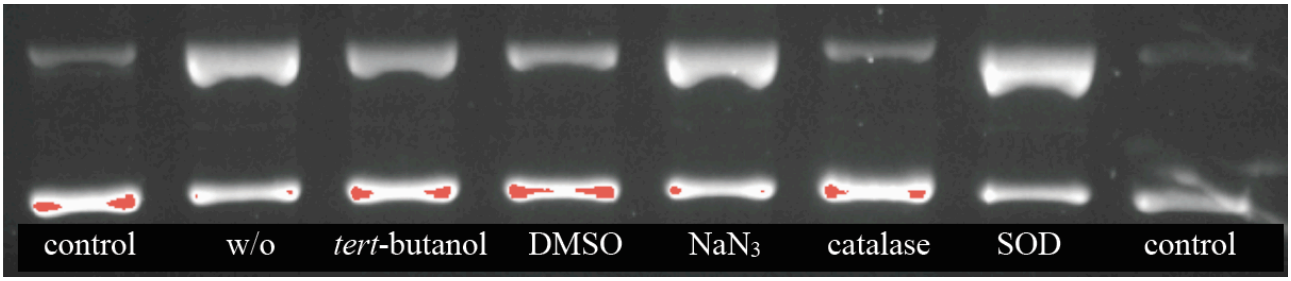
Effect of the reaction time on pBR322 (0.025 μg μL^{-1}) cleavage activity of complexes **1**, **2** and **3** (0.01 mM) in Tris-HCl buffer (100 mM, pH 7.4) and ascorbic acid (0.32 mM) at 37 °C. A control pBR322 plasmid DNA was incubated without ascorbic acid and complexes **1**, **2** and **3** in Tris-HCl buffer for 0.75 h. Illustrated is the average of two measurements, the standard deviation is shown as error bars.

S-3,5. Presence of reactive oxygen species (ROS) scavengers:

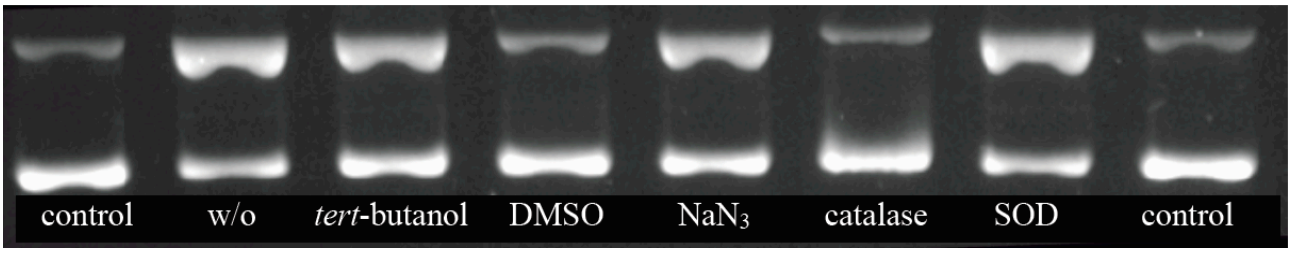
[Cu([12]aneN$_4$)(NO$_3$)]NO$_3$ **1**:



[Cu([12]aneN$_3$O)(NO$_3$)]NO$_3$ **2**:

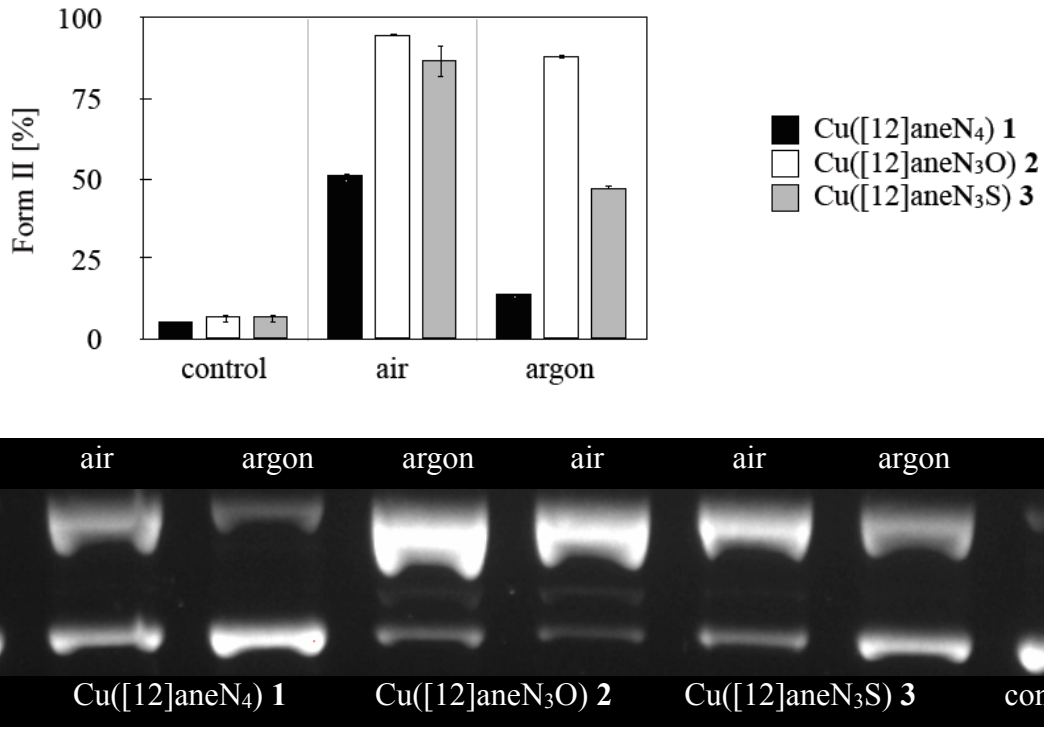


[Cu([12]aneN$_3$S)(NO$_3$)]NO$_3$ **3**:



Effect of ROS scavengers on pBR322 (0.025 μg μL^{-1}) cleavage activity of complexes **1**, **2** and **3** (0.04 mM) in Tris-HCl buffer (100 mM, pH 7.4) containing 214 mM $(NH_4)_2SO_4$, 0.25X PBS and ascorbic acid (0.32 mM) at 37 °C for 2 h. A control pBR322 plasmid DNA was incubated without ascorbic acid and complexes **1**, **2** and **3** in Tris-HCl buffer (control), additionally DNA was incubated with complexes **1**, **2** and **3**, but without ROS scavengers (w/o).

S-3,6. Aerobic and anaerobic:



Effect of aerobic and anaerobic conditions on pBR322 (0.025 µg µL^{-1}) cleavage activity of complexes **1**, **2** and **3** (0.04 mM) in Tris-HCl buffer (100 mM, pH 7.4) and ascorbic acid (0.32 mM) at 37 °C for 2 h. A control pBR322 plasmid DNA was incubated without ascorbic acid and complexes **1**, **2** and **3** in Tris-HCl buffer under aerobic and anaerobic conditions. Illustrated is the average of two measurements, the standard deviation is shown as error bars.

S-4: Electrochemical experiments

Cyclic voltammetry was carried out in 0.1 M KCl solutions (Millipore water) using a three-electrode configuration (glassy carbon working electrode, Pt counter electrode, Ag wire as pseudoreference) and PAR VersaSTAT 4 potentiostat. The ferrocene/ferrocenium (Fc/Fc^{+}) couple served as internal reference. Experimental conditions were adapted from reference 12.

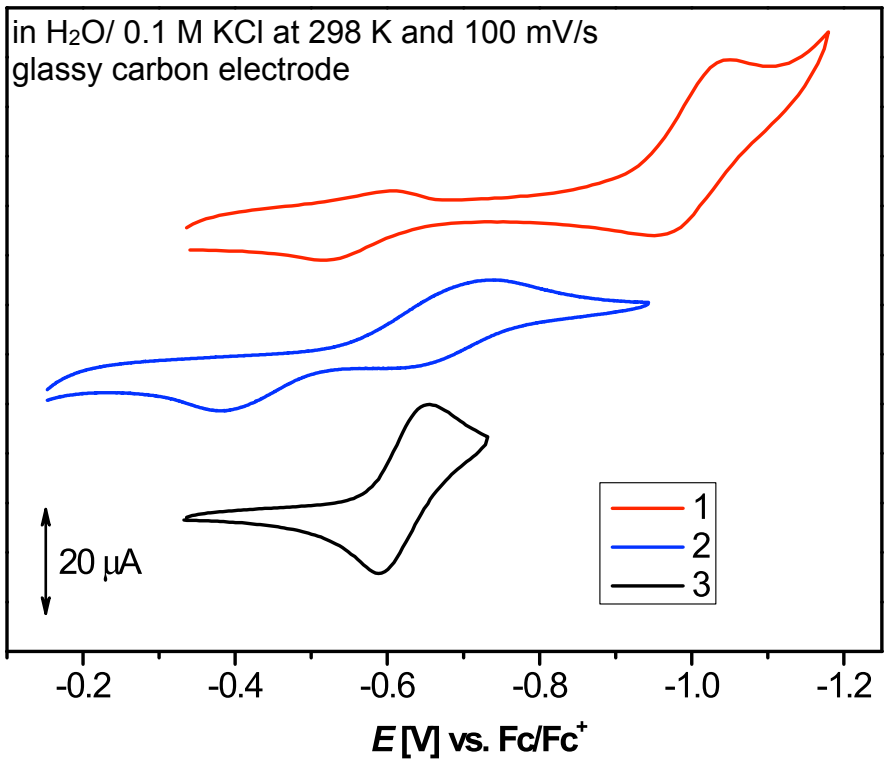
Redox potentials:

1: E_a = -1.0 V (copper set free upon reduction, $E_{1/2}$ = -0.57 V)

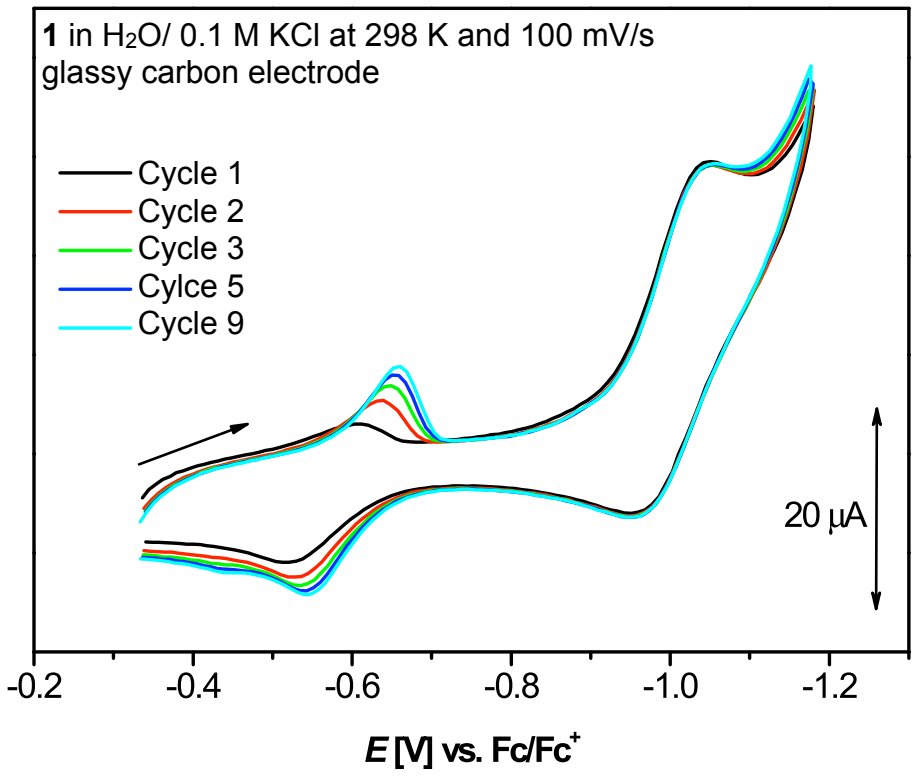
2: E_a = -0.74 V

3: $E_{1/2}$ = -0.62 V

S-4,1. Cyclic voltammogram of complexes **1**, **2** and **3**:



S-4,2. Dependence of copper release on number of cycles in the cyclic voltammogram of **1**:



1 T. J. Atkins, J. E. Richman, W. F. Oettle, *Org. Synth.,* 1988, **Coll. Vol. 6**, 652.

2 J. Huang, Z. Zhou, T. H. Chan, *Synthesis*, 2009, **14**, 2341.

3 J. E. Richman, T. J. Atkins, *J. Am. Chem. Soc.*, 1974, **96**, 2268.

4 V. Montembault, H. Mouaziz, V. Blondeau, R. Touchard, J.-C. Soutif, J.-C. Brosse, *Synth. Commun.*, 1999, **29**, 4279.

5 E. M. D. Keegstra, J. W. Zwikker, M. R. Roest , L. W. Jenneskens, *J. Org.Chem.*, 1992, **57**, 6678.

6 C. S. Rossiter, R. A. Mathews, J. R. Morrow, *Inorg. Chem.*, 2005, **44**, 9397.

7 C. S. Rossiter, R. A. Mathews, I. M. A. del Mundo, J. R. Morrow, *J. Inorg. Biochem.*, 2009, **103**, 64.

8 P. Hoffmann, A. Steinhoff, R. Mattes, *Z. Naturforsch.*, 1987, **42b**, 867.

9 S. T. Marcus, P. V. Bernhardt, L. Grøndahl, L. R. Gahan, *Polyhedron*, 1999, **18**, 3451.

10 G. M. Sheldrick, SHELX97 - Programs for Crystal Structure Analysis (Release 97-2), Institut für Anorganische Chemie der Universität, Tammannstrasse 4, D-37077 Göttingen, Germany, 1998.

11 C. W. Haidle, R. S. Lloyd, D. L. Robberson, In Bleomycin: Chemical, Biochemical, and Biological Aspects; Springer-Verlag: New York 1979, 222-243.

12 L. M. P. Lima, D. Esteban-Gómez, R. Delgado, C. Platas-Iglesias, R. Tripier, *Inorg. Chem.*, 2012, **51**, 6916.