[3] a) M. Nowakowska, V. P. Foyle, J. E. Guillet, *J. Am. Chem. Soc.* **1993**, *115*, 5975 – 5981; b) D. M. Watkins, M. A. Fox, *J. Am. Chem. Soc.* **1994**, *116*, 6441 – 6442; c) X. Schultze, J. Serin, A. Adronov, J. M. J. Fréchet, *Chem. Commun.* **2001**, 1160 – 1161.
[4] P. J. Dutton, L. Conte, *Langmuir* **1999**, *15*, 613 – 617.
[5] L. A. J. Christoffels, A. Adronov, J. M. J. Fréchet, *Angew. Chem. Int. Ed.* **2000**, *112*, 2247 – 2251; *Angew. Chem. Int. Ed.* **2000**, *39*, 2163 – 2167.
[6] a) E. Peeters, P. A. van Hal, J. Knol, C. J. Brabec, N. S. Sacriciftci, J. C. Hummelen, R. A. J. Janssen, *J. Phys. Chem. B* **2000**, *122*, 10174 – 10190; b) N. Armaroli, F. Barigelletti, P. Ceroni, J.-F. Eckert, J.-F. Nicoud, J.-F. Nierengarten, *Chem. Commun.* **2000**, 599 – 600; c) J.-F. Eckert, J.-F. Nicoud, J.-F. Nierengarten, S.-G. Liu, L. Echegoyen, F. Barigelletti, N. Armaroli, L. Ouali, V. Krasnikov, G. Hadziioannou, *J. Am. Chem. Soc.* **2000**, *122*, 7467 – 7479.
[7] N. Armaroli, J.-F. Eckert, J.-F. Nierengarten, *Chem. Commun.* **2000**, 2105 – 2106.
[8] a) P. H. Bolivar, G. Wegmann, R. Kersting, M. Deussen, U. Lemmer, R. F. Mahrt, H. Bässler, E. O. Göbel, H. Kurz, *Chem. Phys. Lett.* **1995**, *245*, 534 – 538; b) J. Morgado, F. Cacialli, R. Iqbal, S. C. Moratti, A. B. Holmes, G. Yahioglu, L. R. Milgrom, R. H. Friend, *J. Mater. Chem.* **2001**, *11*, 278 – 283; c) K. Brunner, J. A. E. H. van Haare, B. M. W. Langeveld-Voss, H. F. M. Schoo, J. W. Hofstraat, A. van Dijken, *J. Phys. Chem. B* **2002**, *106*, 6834 – 6841.
[9] a) A. P. H. J. Schenning, E. Peeters, E. W. Meijer, *J. Am. Chem. Soc.* **2000**, *122*, 4489 – 4495; b) A. El-ghayoury, A. P. H. J. Schenning, P. A. van Hal, J. K. J. van Duren, R. A. J. Janssen, E. W. Meijer, *Angew. Chem.* **2001**, *113*, 3772 – 3775; *Angew. Chem. Int. Ed.* **2001**, *40*, 3660 – 3663; c) A. P. H. J. Schenning, J. v. Herrikhuyzen, P. Jonkheijm, Z. Chen, F. Würthner, E. W. Meijer, *J. Am. Chem. Soc.* **2002**, *124*, 10252 – 10253.
[10] One of the reviewers pointed out a very recent publication on light-harvesting hydrogels: T. Nakashima, N. Kimizuka, *Adv. Mater.* **2002**, *14*, 1113 – 1116.
[11] a) P. Terech, R. G. Weiss, *Chem. Rev.* **1997**, *97*, 3133 – 3159; b) J. H. van Esch, B. L. Feringa, *Angew. Chem. Int. Ed.* **2000**, *112*, 2351 – 2354; *Angew. Chem. Int. Ed.* **2000**, *39*, 2263 – 2266; c) R. Wang, C. Geiger, L. Chen, B. Swanson, D. G. Whitten, *J. Am. Chem. Soc.* **2000**, *122*, 2399 – 2400; d) F. S. Schoonbeek, J. H. van Esch, R. Hulst, R. M. Kellogg, B. L. Feringa, *Chem. Eur. J.* **2000**, *6*, 2633 – 2643; e) L. A. Estroff, A. D. Hamilton, *Angew. Chem.* **2000**, *112*, 3589 – 3592; *Angew. Chem. Int. Ed.* **2000**, *39*, 3447 – 3450; f) J. H. Jung, Y. Ono, S. Shinkai, *Angew. Chem.* **2000**, *112*, 1931 – 1933; *Angew. Chem. Int. Ed.* **2000**, *39*, 1862 – 1865; g) U. Maitra, S. Mukhopadhyay, A. Sarkar, P. Rao, S. S. Indi, *Angew. Chem.* **2001**, *113*, 2341 – 2343; *Angew. Chem. Int. Ed.* **2001**, *40*, 2281 – 2283; h) G. Mieden-Gundert, L. Klein, M. Fischer, F. Vögtle, K. Heuzé, J.-L. Pozzo, M. Vallier, F. Fages, *Angew. Chem.* **2001**, *113*, 3266 – 3267; *Angew. Chem. Int. Ed.* **2001**, *40*, 3164 – 3166; i) S. Tamaru, M. Takeuchi, M. Sano, S. Shinkai, *Angew. Chem.* **2002**, *114*, 881 – 884; *Angew. Chem. Int. Ed.* **2002**, *41*, 853 – 856.
[12] a) T. M. Swager, C. J. Gil, M. S. Wrighton, *J. Phys. Chem.* **1995**, *99*, 4886 – 4893; b) T. Brotin, R. Utermohlen, F. Fages, H. Boucas-Laurent, J.-P. Desvergne, *J. Chem. Soc. Chem. Commun.* **1991**, 416 – 417; c) F. S. Schoonbeek, J. H. van Esch, B. Wegewijs, D. B. A. Rep, M. P. de Haas, T. M. Klapwijk, R. M. Kellogg, B. L. Feringa, *Angew. Chem.* **1999**, *111*, 1486 – 1490; *Angew. Chem. Int. Ed.* **1999**, *38*, 1393 – 1397; d) M. Grell, D. D. C. Bradley, X. Long, T. Chamberlain, M. Inbasekaran, E. P. Woo, M. Soliman, *Acta Polym.* **1998**, *49*, 439 – 444; e) C. Geiger, M. Stanescu, L. Chen, D. G. Whitten, *Langmuir* **1999**, *15*, 2241 – 2245; f) W. Y. Huang, S. Matsuoka, T. K. Kwei, Y. Okamoto, *Macromolecules* **2001**, *34*, 7166 – 7171.
[13] A. Ajayaghosh, S. J. George, *J. Am. Chem. Soc.* **2001**, *123*, 5148 – 5149.
[14] Energy transfer from PPVs to organic dyes has been shown to occur by the Förster type mechanism. See ref. [8] for details.
[15] Similar observations have been made by Fréchet and co-workers in chromophore-labeled self-assembled monolayers. See ref. [5]. Also: D. T. McQuade, A. H. Hegedus, T. M. Swager, *J. Am. Chem. Soc.* **2000**, *122*, 12389 – 12390.

Photochemotherapeutical Drugs

Nucleotide Cross-Linking Induced by Photoreactions of Platinum(IV)–Azide Complexes**

*Philippe Müller, Björn Schröder, John A. Parkinson, Nicole A. Kratochwil, Robert A. Coxall, Andrew Parkin, Simon Parsons, and Peter J. Sadler**

State-of-the-art lasers and fibre optics now have the ability to reach any tissue in the body. A site-specific activation of photochemotherapeutic agents is therefore possible, which minimizes the severe side-effects of chemotherapy. Photosensitizers which catalyze the production of singlet oxygen are used in clinics for photodynamic therapy.[1] This technique relies on the presence of oxygen in the target tissue. A new approach towards the development of oxygen-independent photochemotherapeutic agents has recently been developed.[2–4] Photoactive Pt^{IV} analogues of the anticancer drug cisplatin (*cis*-$[Pt^{II}Cl_2(NH_3)_2]$) are of special interest: it has been shown that nucleotide platination by Pt^{IV}–diiododiamine compounds can be induced by visible light.[4] However, slow photoreactions and low stability against biological reducing agents such as glutathione can be a problem with this class of complexes. We have therefore sought alternative Pt^{IV} compounds that are better suited to this purpose, especially those more stable towards reducing agents.[5]

[*] Prof. Dr. P. J. Sadler, P. Müller, B. Schröder, J. A. Parkinson, N. A. Kratochwil, R. A. Coxall, A. Parkin, S. Parsons
Department of Chemistry
The University of Edinburgh, King's Buildings
West Mains Road, Edinburgh EH9 3JJ (UK)
Fax: (+44) 131-650-6452
E-mail: p.j.sadler@ed.ac.uk

[**] We thank the Swiss National Science Foundation (TMR award to P.M.), EPSRC, EC (Marie Curie Fellowship to N.A.K.), and Wellcome Trust (Edinburgh Protein Interaction Centre) for support, and Dr. Anita Jones and Dr. Trevor Ridley for their help and advice with laser technology, and colleagues in EC COST D8/D20 for stimulating discussions.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

Pt^{IV}–azide coordination compounds are well known to be photoactive. Photoreactions, using UV light ($\lambda < 400$ nm), have been reported for Pt^{IV}–hexa- and –diazide compounds in water that lead to a reductive elimination of the azide ligands and the production of N_2.[6,7] We report here the first crystal structures of Pt^{IV}–diazidodiamine compounds and show that the Pt^{IV}–diazidodiam(m)ine cisplatin analogue *cis*,*trans*-[Pt^{IV}(en)$(N_3)_2(OH)_2$] (**4**; en = ethylenediamine) can be activated with visible light to give highly reactive Pt^{II} species which bind rapidly and stereospecifically to nucleotides, thereby forming known cisplatin–nucleotide cross-links. These complexes represent, therefore, a new class of potential photoactivatable platinum prodrugs.

First we determined the X-ray structures of the precursor Pt^{II} complexes *cis*-[$Pt^{II}(N_3)_2(NH_3)_2$] (**1**) and [Pt^{II}(en)$(N_3)_2$] (**3**; see Supporting Information) which were then oxidized to the corresponding Pt^{IV}–dihydroxy complexes, namely *cis*,*trans*-*cis*-[$Pt^{IV}(N_3)_2(OH)_2(NH_3)_2$] (**2**) and *cis*,*trans*-[Pt^{IV}(en)$(N_3)_2(OH)_2$] (**4**, Figure 1).[8] In the latter complexes the Pt^{IV} ion has close to octahedral geometry and the azide ligands are almost linear ($\sphericalangle N_\alpha$-N_β-N_γ: ca. 173°), with Pt-N_α-N_β angles between 115.5–119.6°. The N_β–N_γ bonds are approximately 0.07 Å shorter than N_α–N_β, which is typical for azide ligands.[12] The bond lengths and angles are in the expected range, and are in good agreement with reported Pt^{IV}–azido structures.[13–16]

The success of photochemotherapeutic agents is highly dependent on their stability under physiological conditions. NMR studies showed that complexes **2** and **4** reacted only slowly with the intracellular reducing agent glutathione (GSH) over a period of several weeks (see Supporting Information), and no reactions at all were observed in human blood plasma. 5′-GMP and d(GpG) did not react with these complexes over a period of one week at 298 K in the dark. The Pt^{IV} complexes **2** and **4** therefore possess the low chemical reactivity essential for potential photochemotherapeutic agents.

Photoreactions of the ^{15}N-labeled Pt^{IV} complexes **2** and **4** were carried out in water and in the presence of 5′-GMP and d(GpG), and followed by 1D ^{1}H, 2D [^{1}H,^{15}N] HSQC, and 2D [^{1}H,^{15}N] HSQC-TOCSY NMR spectroscopy. Photo-irradiation was carried out using an Ar-Kr ion laser equipped with a fibre optic link designed to deliver light directly into the sample within the magnet of the NMR spectrometer. The time-courses of the photoreactions of the chelated diamine-Pt^{IV}-diazide complex **4** in the presence of two molar equivalents of 5′-GMP or one molar equivalent of d(GpG) are shown in Figures 2 and 3 (for the structures and numbering of the complexes see the Supporting Information). The signals arising from **4** and 5′-GMP (en(CH_2): $\delta = 2.83$, H8: $\delta = 8.00$, Figure 2) decreased during irradiation with low-power visible light ($\lambda_{irr} = 457.9$ nm, 15 mW) and two new signals appeared in both the en(CH_2) and 5′-GMP H8 regions of the spectrum at $\delta = 2.71$ (***7b***), 2.58 (***8b***), 8.43 (***7a***), and 8.48 ppm (***8a***).

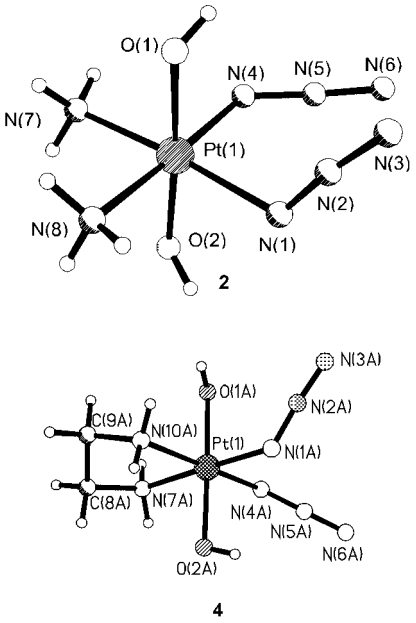

Figure 1. Molecular structures of complex **2** (top) and one of the two molecules of complex **4** which form the asymmetric unit. Selected bond lengths [Å] and angles [°]: **2**: Pt(1)-N(1) 2.036(9), Pt(1)-N(4) 2.038(9), Pt(1)-N(7) 2.043(8), Pt(1)-N(8) 2.022(9), Pt(1)-O(1) 2.005(7), Pt(1)-O(2) 2.007(7), N(1)-N(2) 1.201(13), N(2)-N(3) 1.167(13), N(4)-N(5) 1.224(13), N(5)-N(6) 1.158(13); N(1)-Pt(1)-N(4) 93.0(3); N(1)-N(2)-N(3) 172.9(10), N(2)-N(1)-Pt(1) 117.3(7), N(5)-N(4)-Pt(1) 115.2(6); **4** (molecule 1): Pt(1)-O(1A) 1.994(3), Pt(1)-O(2A) 2.001(3), Pt(1)-N(1A) 2.033(4), Pt(1)-N(4A) 2.040(5), Pt(1)-N(7A) 2.040(4), Pt(1)-N(10A) 2.045(4), N(7A)-C(8A) 1.477(7), C(8A)-C(9A) 1.506(7), N(1A)-N(2A) 1.207(6), N(2A)-N(3A) 1.147(6), N(4A)-N(5A) 1.211(6), N(5A)-N(6A) 1.139(6); N(7A)-Pt(1)-N(10A) 83.71(17), N(1A)-Pt(1)-N(4A) 93.7(2), C(8A)-N(7A)-Pt(1) 109.0(3), Pt(1)-N(1A)-N(2A) 117.4(4), Pt(1)-N(4A)-N(5A) 119.6(4), N(1A)-N(2A)-N(3A) 173.8(5).

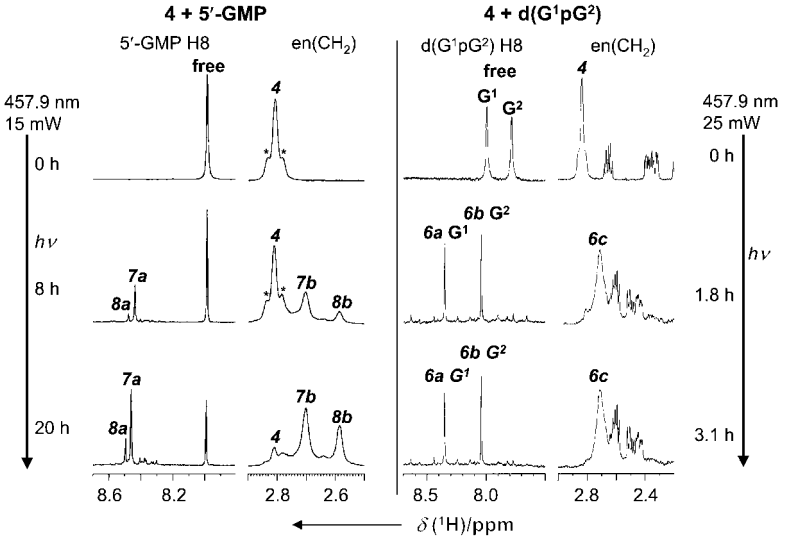

Figure 2. Selected regions of 500 MHz 1D ^{1}H NMR spectra acquired during the photoreactions of *cis*,*trans*-[Pt^{IV}(en)$(N_3)_2(OH)_2$] (**4**) in the presence of two molar equivalents of 5′-GMP, or one molar equivalent of d(G^1pG^2) ($\lambda_{irr} = 457.9$ nm, 15/25 mW, 1 mM, pH 5, at 298 K). ^{195}Pt satellites are indicated by *. Assignments in italics correspond to signals associated with a particular compound.

  0044-8249/03/11503-0350 $ 20.00+.50/0

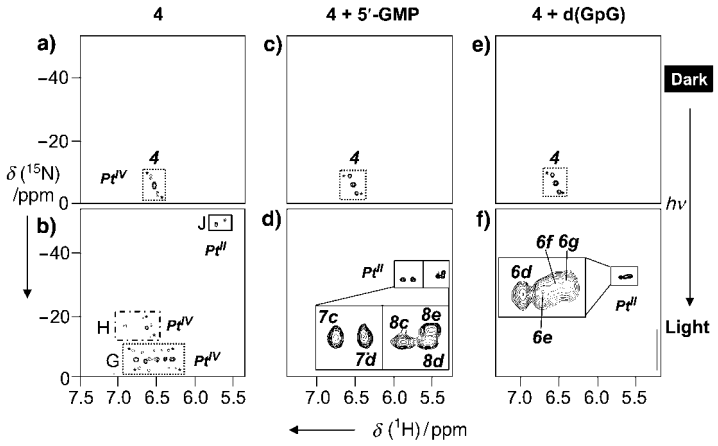

Figure 3. 2D [^{1}H,^{15}N] HSQC NMR spectra acquired during photoreactions (λ_{irr} = 457.9 nm) of *cis*,*trans*-[Pt^{IV}(en)(N$_3$)$_2$(OH)$_2$] (**4**) in water, in the presence of 5′-GMP (molar ratio 1:2, 2 mM) and d(GpG) (molar ratio 1:1, 1 mM) at irradiation times of a) 0 h, b) 4 h, c) 0 h, d) 20 h, e) 0 h, and f) 1.78 h, pH 5, 295 K. Asterisks indicate ^{195}Pt satellites.

Such a high frequency shift for the H8 resonance of 5′-GMP is typical of metal coordination to N7 of 5′-GMP.[17,18] Peaks ***7a*** (major) and ***8a*** (minor) accounted for 60% of the initial H8 signal intensity of 5′-GMP after 20 h irradiation. The 2D [^{1}H,^{15}N] HSQC NMR spectrum after 20 h irradiation (Figure 3d) exhibited two sets of ^{1}H/^{15}N cross-peaks, ***7c/d*** and ***8c/d/e*** (Table 1), which relate to the peaks ***7a/b*** and ***8a/b*** in the corresponding 1D ^{1}H NMR spectrum, as shown in the 2D HSQC-TOCSY NMR spectrum (see Supporting Information). Such ^{1}H/^{15}N chemical shifts are characteristic of {Pt^{II}N-H$_2$(en)} *trans* to an N atom rather than a Pt^{IV} complex, and the δ values of cross-peaks ***7c/d*** are the same as those reported previously for [Pt^{II}(^{15}N-en)(5′-GMP-*N7*)$_2$]$^{2+}$ (**7**; the charges on the nucleotides are ignored in the formulas).[17,18] No protonation at the 5′-GMP-*N7* site (pK_a = 2.48[19]) was observed for compounds **7** and **8** (no change in the chemical shift for H8 between pH 1–4) confirming platinum coordination to *N7* (Figure 4a).[20] No intermediate compounds were detected during the irradiation. The presence of **7** was confirmed by ESI-MS (see Supporting Information). Complex **8**, which may contain a modified 5′-GMP, was not further characterized.

In contrast to the above reaction, irradiation of **4** (λ_{irr} = 457.9 nm, 25 mW) in the presence of one molar equivalent of d(G^{1}pG^2) led to only one major product **6** (Figures 2 and 3e/f). A high frequency shift of 0.4 ppm was observed in the ^{1}H NMR spectrum for the d(G^{1}pG^2) H8 resonances (peaks ***6a/b***) after 1.8 h irradiation indicating platinum binding to d(G^{1}pG^2)-*N7^1*,*N7^2*. Four ^{1}H/^{15}N cross-peaks with equal intensity separated into two pairs associated with distinct ^{15}N shifts (δ(^{1}H/^{15}N) = 5.68 (***6d***), 5.63 (***6e***)/−30.9, 5.58 (***6f***), 5.55 (***6g***)/−31.22 ppm) appeared simultaneously. These values are in agreement with those reported for [Pt^{II}(^{15}N-en){d(G^{1}pG^2)-*N7^1*,*N7^2*}]$^{2+}$ (**6**).[17,21] The presence of complex **6** was further confirmed by a pH titration for ^{1}H peaks ***6a/b*** (Figure 4b). The pH

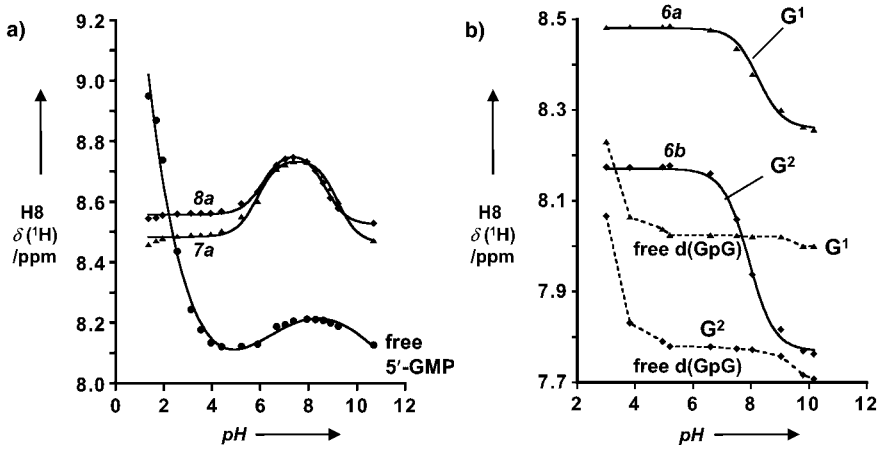

Figure 4. Variation of the chemical shift of H8 with pH value of a) 5′-GMP, and b) d(G^{1}pG^2) before and after the photoreactions with *cis*,*trans*-[Pt^{IV}(en)(N$_3$)$_2$(OH)$_2$] (**4**; λ_{irr} = 457.9 nm) at 298 K.

Table 1: ^{1}H and ^{15}N chemical shifts and coupling constants ^1J(^{195}Pt,^{15}N) [Hz].

Pt complex	NH_3/NH_2		CH_2	^2J(^{1}H,^{195}Pt)	^1J(^{15}N,^{195}Pt)
	δ(^{1}H) [ppm]	δ(^{15}N) [ppm]	δ(^{1}H) [ppm]		
cis-[Pt^{II}(N$_3$)$_2$(NH$_3$)$_2$] (**1**)	3.86	−69.5		57	305
cis,*trans*-[Pt^{IV}(N$_3$)$_2$(OH)$_2$(NH$_3$)$_2$] (**2**)	5.20	−39.8		46	258
[Pt^{II}(en)(N$_3$)$_2$] **3**	5.10	−33.8	2.61	53	337
cis,*trans*-[Pt^{IV}(en)(N$_3$)$_2$(OH)$_2$] (**4**)	6.50	−5.9	2.83	43	275
cis-[Pt^{II}(NH$_3$)$_2$\{d(GpG)-*N7^1*,*N7^2*\}]$^{2+}$ (**5**)	4.45/4.38	−68.3/−68.5			
[Pt^{II}(en)\{d(GpG)-*N7^1*,*N7^2*\}]$^{2+}$ (**6**)	5.65/5.56	−30.9/−31.2	2.84		
[Pt^{II}(en)(GMP-*N7*)$_2$]$^{2+}$ (**7**)	5.75/5.88	−30.7	2.71		
8	5.38/5.33	−31.7	2.58		
	5.35	−32.9			
G[a]	6.2 to 6.8	−6.0		43	277
H[a]	6.67/6.95	−16.21/−16.72		44	306
J[a]	5.70/5.59	−48.4/−49.9			

[a] See Figure 3.

  0044-8249/03/11503-0351 $ 20.00+.50/0

titration curves are in agreement with those reported for [Pt(en){d(GpG)-*N7(1),N7(2)*}]$^{2+}$ (**6**).[21,22] The lack of a high frequency shift in the pH range 3–4 indicates platinum binding at *N7* of G^1 and G^2. The only major species present after 1.8 h irradiation was [Pt^{II}(^{15}N-en){d(G^1pG^2)-*N7^1,N7^2*}]$^{2+}$ (**6**), which is indicative of a rapid stereospecific reaction.

The photoreaction pathway was elucidated by following the photoreaction of **4** alone in water (Figure 3 a/b). After 4 h irradiation (λ_{irr} = 457.9 nm, 20 mW), ^{1}H/^{15}N cross-peaks were present at δ(^{15}N) −6 (**G**), −16 (**H**), and −48 ppm (**J**). The δ(^{15}N) value for **G** is characteristic of {$Pt^{IV}NH_2$(en)} *trans* to N, that for **H** of {$Pt^{IV}NH_2$(en)} *trans* to O, and that for **J** of {$Pt^{II}NH_2$(en)} *trans* to O.[23] The cross-peaks of **G** and **H** can be assigned to stereoisomers of complex **4** on the basis of their chemical shifts and coupling constants (Table 1), and cross-peaks **J** must arise from {$Pt^{II}NH_2$(en)} *trans* to OH/OH_2 because of the absence of any other oxygen donors except OH_2/OH in solution. Pt^{II}–aqua complexes are known to be very reactive towards strong donor atoms such as 5′-GMP-*N7* or d(G^1pG^2)-*N7^1,N7^2* which are the reactive sites toward cisplatin.[24] Under physiological conditions, this photoreaction therefore transforms a stable Pt^{IV} complex into a highly reactive Pt^{II} species which can bind to nucleotides and hence has the potential to kill cancer cells. The site of the drug release could be chosen using site-specific irradiation, and the rate of the drug release could be adjusted by varying the light power.

Red light (λ_{irr} = 647.1 nm, 75 mW), which penetrates better through tissue than blue light, and is preferred for use in photochemotherapy, was also employed for irradiation of **4**. Such low-energy light also induced d(G^1pG^2)-*N7^1,N7^2* binding, which illustrates the potential of this type of Pt^{IV} complex as a photochemotherapeutic agent.[25]

Similar photoreactions were also carried out with the [Pt^{IV}(diammine)(diazide)] complex **2** in the presence of d(GpG). The nucleotide adduct *cis*-[Pt(NH_3)$_2${d(GpG)-*N7^1,N7^2*}]$^{2+}$ (**5**) was identified as a photoproduct by 1D ^{1}H and 2D [^{1}H,^{15}N] HSQC NMR, and the pH-dependence of the H8 chemical shifts confirmed *N7* platination (see Table 1 for δ(^{1}H,^{15}N) values of **5**; 1D/2D NMR spectra are shown in the Supporting Information). Hence, this photoactivation strategy should be generally applicable to Pt^{IV}–diazido complexes containing a variety of monodentate and chelated diamine ligands and may allow the site-specific delivery of a wide range of Pt^{II}–diamine drugs. This approach could therefore be used to target many commonly used Pt^{II}-containing anticancer drugs and has the potential to strongly reduce unwanted side-effects often associated with platinum chemotherapy.

Experimental Section

K_2[$PtCl_4$] was purchased from Alfa-Johnson Matthey plc., NaN_3 from BDH, $^{15}NH_4Cl$ and ^{15}N-potassium phthalimide from Aldrich, dibromoethane from Fisons, H_2O_2 (30 %) from Prolabo, GSH and 5′-GMP from Acros and 2′-deoxyguanylyl (3′→5′)-2′-deoxyguanosine sodium salt (d(GpG)) from Sigma. Human blood plasma (leucocyte depleted, blood group 0 Rh D positive) was provided by the Western General Hospital, Edinburgh.

1: KI (0.4 g, 24 mmol) was added to an aqueous solution (50 mL) of K_2[$PtCl_4$] (1 g, 2.41 mmol). After stirring for 30 min at ambient temperature, $^{15}NH_4Cl$ (0.26 g, 4.88 mmol) was added and the pH adjusted to 11 with 1M NaOH. The yellow precipitate (*cis*-[PtI_2($^{15}NH_3$)$_2$]) was filtered off, washed with water, ethanol, and diethyl ether, and dried under vacuum. $AgNO_3$ (2 mol equiv, 0.146 g, 0.86 mmol) was added to a suspension of *cis*-[PtI_2($^{15}NH_3$)$_2$] (0.2 g, 0.43 mmol) in water (20 mL) and then stirred in the dark for 24 h. The AgI precipitate was filtered off using an inorganic membrane filter (Whatman, Anotop 10, 0.02 μm). NaN_3 (20 mol equiv, 0.57 g, 8.77 mmol) was added and the solution stirred for 30 min in the dark at ambient temperature. The volume was reduced to 10 mL and the flask was stored at 277 K overnight. The yellow precipitate was washed with diethyl ether and dried in air. Yield: 97 mg (72 %). Crystals suitable for X-ray crystal-structure determination were obtained from an aqueous solution at 277 K.

2: H_2O_2 (40 mol equiv, 1.2 mL of 30 % H_2O_2, 11.75 mmol) was added to a suspension of *cis*-[Pt^{II}(N_3)$_2$(NH_3)$_2$] (0.086 g, 0.27 mmol) in water (10 mL) which was stirred in the dark at ambient temperature for 24 h. The volume of the solution was reduced, and on cooling to 277 K, complex **2** formed as a yellow precipitate which was filtered and washed with water and diethyl ether, yield: 32.8 mg (35 %). Crystals suitable for X-ray crystal-structure determination were grown from a water/ethanol (1/1 v/v) mixture at 277 K. Elemental analysis calcd for $H_8N_8O_2Pt$: H 2.30, N 32.28; found: H 2.64, N 31.85.

3: ^{15}N-labeled ethylenediamine was synthesized as previously described.[26] K_2[$PtCl_4$] (0.162 g, 0.39 mmol) was added to an aqueous solution of ^{15}N-en·2 HCl (0.052 g, 0.39 mmol, pH 8) and the solution stirred at ambient temperature. The yellow precipitate ([$Pt^{II}Cl_2$(^{15}N-en)]) was washed with water and diethyl ether and dried under vacuum. [$Pt^{II}Cl_2$(^{15}N-en)] (0.04 g, 0.12 mmol) and $AgNO_3$ (0.041 g, 0.24 mmol, 2 mol equiv) were stirred in water in the dark at room temperature for 24 h. The AgCl precipitate was filtered off and NaN_3 (25 mol equiv, 0.208 g, 3.2 mmol) was added to the solution. The volume was reduced and a yellow precipitate was obtained on cooling the solution to 277 K. This was washed with water and diethyl ether. Yield: 23.5 mg (57 %). Crystals suitable for X-ray crystal-structure determination were obtained from an aqueous solution at 277 K.

4: H_2O_2 (50 mol equiv, 0.3 mL of 30 % H_2O_2, 2.9 mmol) was added to a solution of [Pt(en)(N_3)$_2$] (0.021 g, 0.06 mmol) in water (5 mL). This was then stirred in the dark at ambient temperature for 24 h. The yellow precipitate was filtered off and washed with water and diethyl ether, yield 10 mg (40 %). Crystals suitable for X-ray crystal-structure determination were obtained from an aqueous solution at 277 K. Elemental analysis calcd for $C_2H_{10}N_8O_2Pt$: C 6.43, H 2.68, N 30.03; found: C 6.54, H 2.37, N 30.18.

Uv/Vis spectra of complexes **2** and **4** as well as the Raman spectra of complexes **1**–**4** are shown in the Supporting Information.

Irradiation was carried out using an argon-krypton ion laser (Coherent Innova 70C Spectrum) equipped with a fibre optic (FT-600-UMT, ∅ 600 μm; Elliot Scientific Ltd.) to deliver light (λ = 457.9 nm, 488 nm, 647.1 nm) directly into the sample within the magnet of the NMR spectrometer. The laser output, after the fiber, was in the range of 10 to 75 mW, as measured by a Coherent 210 power meter. 1D ^{1}H, 2D [^{1}H,^{15}N] HSQC and 2D [^{1}H,^{15}N] HSQC-TOCSY NMR spectra were recorded on a Bruker DMX 500 NMR spectrometer (^{1}H: 500.13 MHz, ^{15}N: 50.7 MHz) at pH 5 using sodium 3-(trimethylsilyl)-[2,2,3,3-D_4]-propionate (TSP, 0 ppm) as the internal δ(^{1}H) standard. All δ(^{15}N) values were referenced externally to $^{15}NH_4^+$ at δ = 0. pH values were measured with a pH meter (Orion 710A) equipped with a microcombination electrode (Aldrich) calibrated with Aldrich standard buffers (pH 4, 7, and 10) and were adjusted with dilute solutions of $HClO_4$ and NaOH. No correction was made for ^{2}H isotope effects on the glass electrode.

Received: July 30, 2002 [Z19849]

  0044-8249/03/11503-0352 $ 20.00+.50/0

[1] L. Milgrom, S. MacRobert, *Chem. Br.* **1998**, *34*, 45.

[2] N. A. Kratochwil, J. A. Parkinson, P. J. Bednarski, P. J. Sadler, *Angew. Chem.* **1999**, *111*, 1566; *Angew. Chem. Int. Ed.* **1999**, *38*, 1460.

[3] N. A. Kratochwil, P. J. Bednarski, H. Mrozek, A. Vogler, J. K. Nagle, *Anti-Cancer Drug Des.* **1996**, *11*, 155.

[4] N. A. Kratochwil, M. Zabel, K.-J. Range, P. J. Bednarski, *J. Med. Chem.* **1996**, *39*, 2499.

[5] N. A. Kratochwil, Z. J. Guo, P. D. Murdoch, J. A. Parkinson, P. J. Bednarski, P. J. Sadler, *J. Am. Chem. Soc.* **1998**, *120*, 8253.

[6] A. Vogler, A. Kern, B. Fusseder, *Z. Naturforsch. B* **1978**, *33*, 1352.

[7] A. Vogler, J. Hlavatsch, *Angew. Chem.* **1983**, *95*, 153; *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 154.

[8] Diffraction data were collected with $Mo_{K\alpha}$ X-rays ($\lambda = 0.71073$ Å) on a Bruker Smart APEX diffractometer equipped with an Oxford Cryosystems low-temperature device operating at 150 K, with the exception of **2**, for which data were collected at 100 K. Absorption corrections were applied using the program SADABS; the structures were solved either using Patterson methods (DIRDIF)[9] or direct methods (Shelxtl)[10] and refined by full-matrix least-squares against F^2 (Shelxtl) using all unique data. H atoms were treated either as part of a rotating rigid group (NH_3 and OH ligands), or with a riding model. Other analyses were carried out using Platon.[11] Crystal data for **1** (H_6N_8Pt), $M_r = 313.22$, yellow rod, $0.13 \times 0.06 \times 0.03$ mm^3, monoclinic, space group $P2_1/n$, $a = 8.6327(10)$, $b = 7.1432(8)$, $c = 10.5689(12)$ Å, $\beta = 104.323(2)°$, $V = 631.47(12)$ Å^{-3}, $\rho_{calcd} = 3.295$ Mg m^{-3}, 3431 reflections measured, of which 1270 were independent, $\theta_{max} = 26.38°$, $R_{int} = 0.024$, $\mu = 22.145$ mm^{-1} (range of transmission = 0.161–0.556), 84 parameters, $R = 0.0229$ (based on F and 1219 data with $F > 4\sigma(F)$), $R_w = 0.0532$ (based on F^2 and all data), the final difference map extremes were $+1.40$ and -1.79 e Å^{-3}. Crystal data for **2** ($H_8N_8O_2Pt$), $M_r = 347.23$, colorless plate, $0.13 \times 0.07 \times 0.04$ mm^3, triclinic, space group $P\bar{1}$, $a = 6.3232(11)$, $b = 7.9816(14)$, $c = 8.1663(14)$ Å, $\alpha = 82.247(3)$, $\beta = 67.294(2)$, $\gamma = 68.885(2)°$, $V = 354.67(11)$ Å^{-3}, $\rho_{calcd} = 3.251$ Mg m^{-3}, 2624 reflections measured, of which 1251 were independent, $\theta_{max} = 24.99°$, $R_{int} = 0.036$, $\mu = 19.752$ mm^{-1} (range of transmission = 0.18–0.51), 105 parameters, $R = 0.0339$ (based on F and 1144 data with $F > 4\sigma(F)$), $R_w = 0.0786$ (based on F^2 and all data), the final difference map extremes were $+2.69$ and -2.32 e Å^{-3} (all intense peaks were in the region of the Pt atom). Crystal data for **3** ($C_2H_8N_8Pt$), $M_r = 339.25$, yellow needle, $0.12 \times 0.06 \times 0.02$ mm^3, monoclinic, space group $P2/n$, $a = 7.778(8)$, $b = 3.405(3)$, $c = 14.139(14)$ Å, $\beta = 100.848(15)°$, $V = 367.8(6)$ Å^{-3}, $\rho_{calcd} = 3.063$ Mg m^{-3}, 2377 reflections measured, of which 726 were independent, $\theta_{max} = 26.50°$, $R_{int} = 0.066$, $\mu = 19.025$ mm^{-1} (range of transmission = 0.22–1.00), 77 parameters, $R = 0.0426$ (based on F and 718 data with $F > 4\sigma(F)$), $R_w = 0.0982$ (based on F^2 and all data), the final difference map extremes were $+3.57$ and -2.42 e Å^{-3} (all intense peaks were in the region of the Pt atom). The molecule is disordered about a crystallographic twofold axis, with common positions for the ligating nitrogen atoms; there appeared to be no weak diffraction spots that might have indicated a larger unit cell. This determination can reasonably be said to determine connectivity, but it should not be used for detailed analysis. Crystal data for **4**, $C_2H_{10}N_8O_2Pt$, $M_r = 373.27$, pale yellow chip, $0.20 \times 0.09 \times 0.06$ mm^3, monoclinic, space group $P2_1/c$, $a = 15.8580(12)$, $b = 6.2374(5)$, $c = 17.5220(13)$ Å, $\beta = 102.0720(10)°$, $V = 1694.8(2)$ Å^{-3}, $\rho_{calc} = 2.926$ Mg m^{-3}, 10251 reflections measured, of which 4093 were independent, $\theta_{max} = 29.11°$, $R_{int} = 0.021$, $\mu = 16.545$ mm^{-1} (range of transmission = 0.454–1.00), 240 parameters, $R = 0.0263$ (based on F and 3881 data with $F > 4\sigma(F)$), $R_w = 0.0601$ (based on F^2 and all data), the final difference map extremes were $+1.04$ and -1.44 e Å^{-3}. Further details of the crystal-structure investigations may be obtained from the Fachinformationszentrum Karlsruhe, 76344 Eggenstein-Leopoldshafen, Germany (fax: (+49) 7247-808-666; e-mail: crysdata@fiz-karlsruhe.de), on quoting the depository numbers CSD-412675 (**1**) and CSD-412674 (**2**). CCDC-190266 (**3**) and CCDC-190265 (**4**) contain supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

[9] P. T. Beurskens, G. Beurskens, W. P. Bosman, R. de Gelder, S. Garcia-Granda, R. O. Gould, R. Israel, J. M. M. Smits, Crystallography Laboratory, University of Nijmegen, The Netherlands, **1996**.

[10] G. M. Sheldrick, SHELXTL, version 5, Bruker AXS, Madison WI, **1995**.

[11] A. L. Spek, *Acta Crystallogr. Sect. A* **1990**, *46*, C34. PLATON, A Multipurpose Crystallographic Tool, Utrecht University, Utrecht, The Netherlands. Incorporated into the WinGX suite: L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837.

[12] A. F. Holleman, E. Wiberg, *Lehrbuch der anorganischen Chemie*, Walter de Gruyter, Berlin, **1985**.

[13] S. Schröder, W. Preetz, *Z. Anorg. Allg. Chem.* **2000**, *626*, 1757.

[14] S. Schröder, W. Preetz, *Z. Anorg. Allg. Chem.* **2000**, *626*, 1915.

[15] S. Schröder, W. Preetz, *Z. Anorg. Allg. Chem.* **2001**, *627*, 390.

[16] B. Neumueller, F. Schmock, S. Schlecht, K. Dehnicke, *Z. Anorg. Allg. Chem.* **2000**, *626*, 1792.

[17] S. J. Berners-Price, J. D. Ranford, P. J. Sadler, *Inorg. Chem.* **1994**, *33*, 5842.

[18] S. J. Berners-Price, U. Frey, J. D. Ranford, P. J. Sadler, *J. Am. Chem. Soc.* **1993**, *115*, 8649.

[19] H. Sigel, S. S. Massoud, N. A. Corfu, *J. Am. Chem. Soc.* **1994**, *116*, 2958.

[20] K. H. Scheller, V. Scheller-Krattiger, R. B. Martin, *J. Am. Chem. Soc.* **1981**, *103*, 6833.

[21] J.-P. Girault, G. Chottard, J.-Y. Lallemand, J.-C. Chottard, *Biochemistry* **1982**, *21*, 1352.

[22] E. L. M. Lempers, M. J. Bloemink, J. Reedijk, *Inorg. Chem.* **1991**, *30*, 201.

[23] S. J. Berners-Price, P. J. Sadler, *Coord. Chem. Rev.* **1996**, *151*, 1.

[24] J. Reedijk, *Chem. Commun.* **1996**, 801.

[25] A. M. Rouhi, *Chem. Eng. News* **1998**, *76*(31), 22.

[26] E. Zang, P. J. Sadler, *Synthesis* **1997**, 410.