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ARTICLE

Novel *cis*-[(NHC)^1(NHC)^2(L)Cl]platinum(II) complexes – synthesis, structures, and anticancer activities†

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Tobias Rehm,[a] Matthias Rothemund,[a] Julienne K. Muenzner,[a] Awal Noor,[b] Rhett Kempe,[b] and Rainer Schobert[a]*

A general synthesis of novel platinum(II) complexes bearing two different, *cis*-oriented, *N*-heterocyclic carbene (NHC) ligands is presented. Easily accessible *cis*-[Pt^{II}(NHC)(DMSO)] precursor complexes were converted to either *cis*-[Pt^{II}(NHC)$_2$Cl$_2$] complexes such as **5a** and **5b**, or to novel mixed *cis*-[Pt^{II}(NHC)^1(NHC)^{2}Cl$_2$] complexes such as **5c–h** by successive introduction of the individual carbene ligands. The 'symmetric' complexes **5a** and **5b** were also converted to cationic *cis*-[Pt^{II}(NHC)$_2$(PPh$_3$)Cl]$^+$Cl$^-$ complexes **8a** and **8b**. The structures of the ten new complexes, comprising benzylated and alkylated imidazol-2-ylidene ligands, were analysed by ^{1}H and ^{13}C NMR spectroscopy and also by X-ray diffraction for **5a**, **5d**, **5h**, and **8a**. The neutral complexes **5** were cytotoxic against a panel of seven human cancer cell lines with IC$_{50}$ values in the low micromolar range, while the cationic complexes **8** reached even nanomolar IC$_{50}$ values. Complex **5h** carrying the substitution pattern of the natural antitumoral agent Combretastatin A-4 showed a conspicuous specificity for cancer cell lines sensitive to this drug. In electrophoretic mobility shift assays, the *cis*-biscarbene complexes **5b** and **8b** led to an unwinding or aggregation of plasmid DNA, while the *trans*-biscarbene complex **1b** showed no such effect.

Introduction

Metal complexes of *N*-heterocyclic carbenes (NHCs) were reported as early as 1968 by Wanzlick *et al*. and others.[1,2] But it was not until the isolation of a crystalline carbene by Arduengo *et al*.[3] in 1991 that NHCs turned from mere curiosities into applicable chemical reagents. Nowadays, they are routinely used as organocatalysts for a wide range of established reactions.[4] NHC metal complexes are among the most efficient catalysts for reactions such as olefin metathesis[5] and Pd-catalysed coupling reactions.[6,7] More recently, their medicinal aspects came to the fore.[8,9] With the successful history of anticancer active platinum compounds[10] in mind, bioactive NHC complexes were devised of metals such as Pd,[11] Ag,[12] Cu,[13] Ru,[14] Au,[15] and Pt.[16] Meanwhile, a general picture of structure-activity correlations for such complexes is unfolding, allowing a prediction of the influence of the central metal, the NHC substituents, the charge, the lipophilicity, and the sterical encumbrance around the metal centre on their biological properties. We recently studied the influence of the latter factor, sterical congestion, in a series of platinum complexes.[17]

Unlike complexes *trans*-[Pt^{II}(NHC)$_2$Cl$_2$] **1**, featuring a poor NHC leaving group, the complexes *cis*-[Pt^{II}(DMSO)(NHC)Cl$_2$] **2** which bear a well accessible chlorido leaving ligand, had bound to DNA as expected. Substitution of DMSO for PPh$_3$ gave complexe **3** which still, though to a lesser extent, bound coordinatively to DNA but also initiated some DNA aggregation. The cationic complex *trans*-[Pt^{II}(PPh$_3$)$_2$(NHC)Cl]$^+$Cl$^-$ **4**, featuring a sterically shielded chlorido ligand, exclusively induced DNA aggregation (Figure 1).

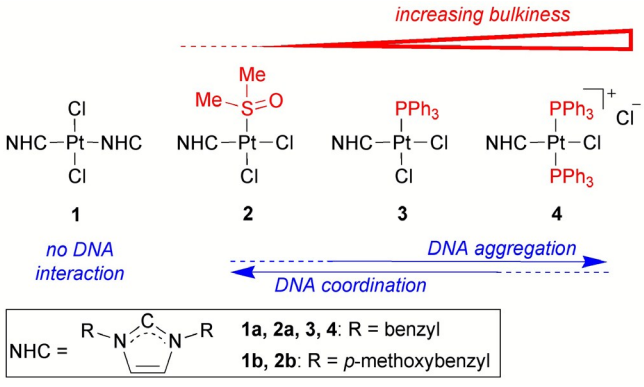

Fig. 1 NHC-platinum(II) complexes with spectator ligands of increasing bulkiness and their modes of DNA interaction.[17]

a. *Organic Chemistry Laboratory, University Bayreuth, Universitaetsstrasse 30, 95440 Bayreuth. E-mail: Rainer.Schobert@uni-bayreuth.de*
b. *Lehrstuhl fuer Anorganische Chemie II (Catalyst Design), University Bayreuth, Universitaetsstrasse 30, 95440 Bayreuth.*

†Electronic Supplementary Information (ESI) available: NMR spectra of **5a-h** and **5a**,**b**; synthesis of **1b**; ligand synthesis. See DOI: 10.1039/x0xx00000x

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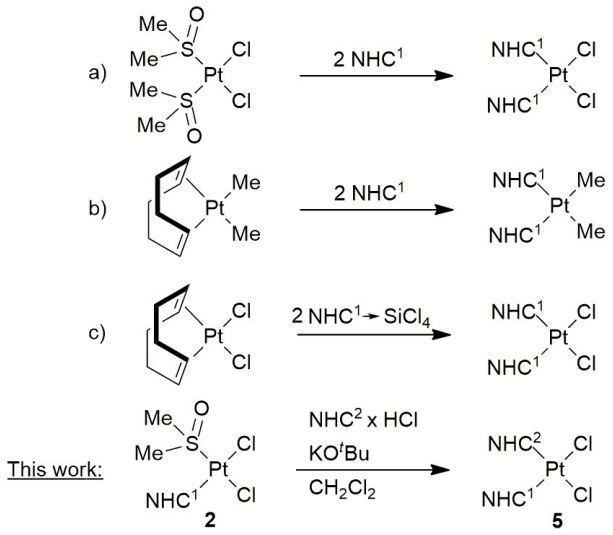


Scheme 1 Syntheses of *cis*-bis(NHC) complexes of platinum(II) by a) Nolan *et al.,*[19] b) Nolan *et al.,*[20] c) Röschenthaler *et al.,*[18] and a new access to complexes *cis*-[Pt^{II}(NHC)^1(NHC)^{2}Cl$_2$] **5**.

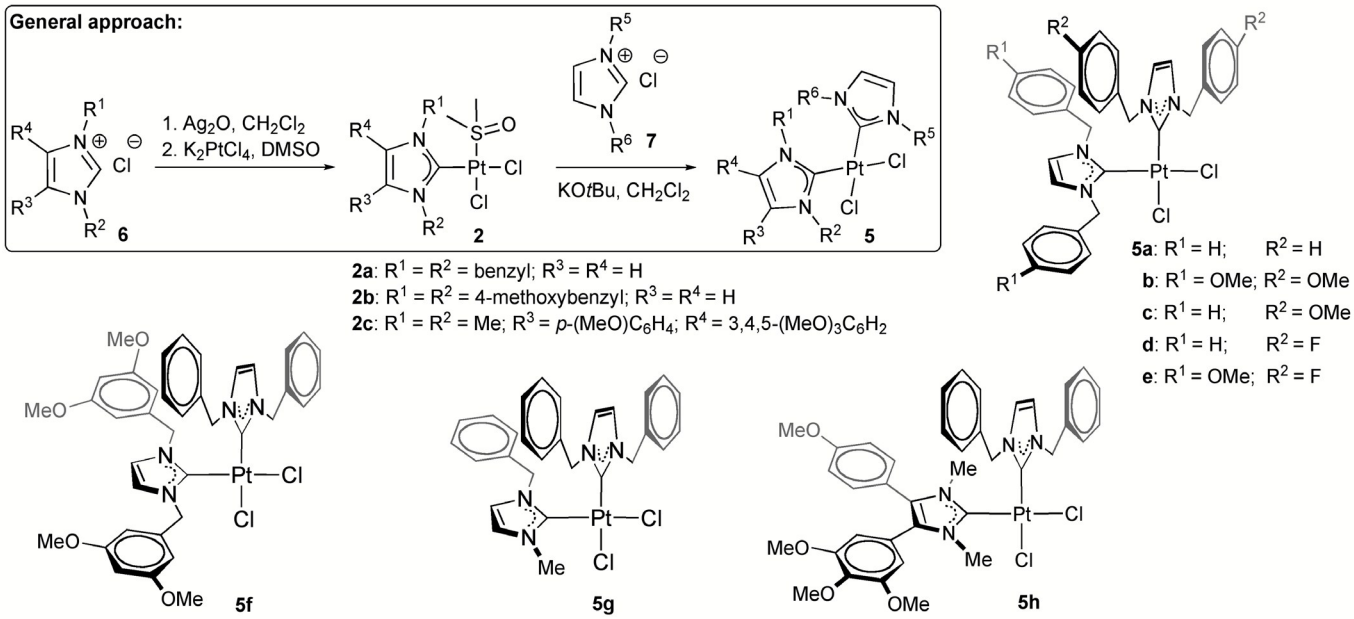
For a more nuanced assessment of such steric effects we now developed an access to platinum(II) complexes with two different, *cis*-positioned NHC ligands (Scheme 1). Complexes *cis*-[Pt^{II}(NHC)$_2$L$_2$] with two identical NHC ligands had been synthesised before by Röschenthaler *et al.,*[18] and Nolan *et al.*[19,20] using *cis*-[Pt(DMSO)$_2$Cl$_2$], [Pt(cod)Cl$_2$], or [Pt(cod)Me$_2$] as precursors. Displacement of the leaving ligands DMSO or cod, respectively, by two equivalents of the free or masked NHC led to the desired *cis*-biscarbene complexes. However, these protocols do not allow the synthesis of mixed *cis*-[Pt^{II}(NHC)^1(NHC)^{2}L$_2$] complexes.

Results and discussion

Synthesis and characterisation

The key intermediates for our new synthesis are *cis*-[Pt^{II}(NHC)(DMSO)L$_2$] complexes such as **2**, first synthesised by Rourke *et al.* in 2007.[21] This group found that using DMSO instead of CH_2Cl_2 as the solvent for the carbene transfer from silver NHC complexes to suitable sources of the desired metal, e.g. K_2PtCl_4, led to the formation of monocarbene complexes of type **2** rather than to the formation of *trans*-biscarbene complexes of type **1**. The DMSO ligand can then be substituted by a more electron-rich ligand such as a phosphane,[17,21] or, as detailed in this work, a second NHC ligand.

We prepared eight new *cis*-[Pt^{II}(NHC)^1(NHC)^{2}Cl$_2$] complexes **5** with six different NHCs as ligands via DMSO precursor complexes **2**. Since the two NHC ligands are introduced one at a time, complexes with two different NHCs can be synthesised starting from two different imidazolium salts **6** (ImH^1) and **7** (ImH^2)[22-26] (Scheme 2). We employed imidazolium chlorides that were 1,3-benzylated, or -alkylated. For the synthesis of *cis*-[Pt^{II}(NHC)^1(NHC)^{2}Cl$_2$] complexes **5** the respective complex *cis*-[Pt^{II}(DMSO)(NHC)^{1}Cl$_2$] **2** was treated with ImH^{2}Cl **7** and KO^{t}Bu to generate NHC^2. The resulting mixture was stirred in dry CH_2Cl_2 for 16 hours by which time the DMSO had been completely substituted by NHC^2 and the pure product complexes **5** were obtained by precipitation in yields of up to 93%. Replacing the base KO^{t}Bu by K_2CO_3, NaOMe or CaH_2 had little influence on the yields as had the use of acetonitrile as a solvent.



Scheme 2 General synthesis and structures of complexes **5a-h**.

The *cis* configuration of complexes **5** was confirmed by ^{1}H and ^{13}C NMR spectroscopy. In line with a previous study[17] of the complexes **2a** and **3**, the ^{1}H NMR spectra of complexes **5** showed an inequivalency of the two geminal protons of each benzylic CH_2 group (one facing the neighbouring chlorine, the other the second NHC) and their splitting up into two doublets. These corresponding signals are 0.44 to 1.13 ppm apart and couple with $^{2}J_{AB}$ = 14.34 to 14.95 Hz. This corroborates the *cis* configuration of the NHC ligands as well as the perpendicular orientation of the imidazole ring relative to the plane spanned by the $PtCl_2$ fragment (Figure 2).

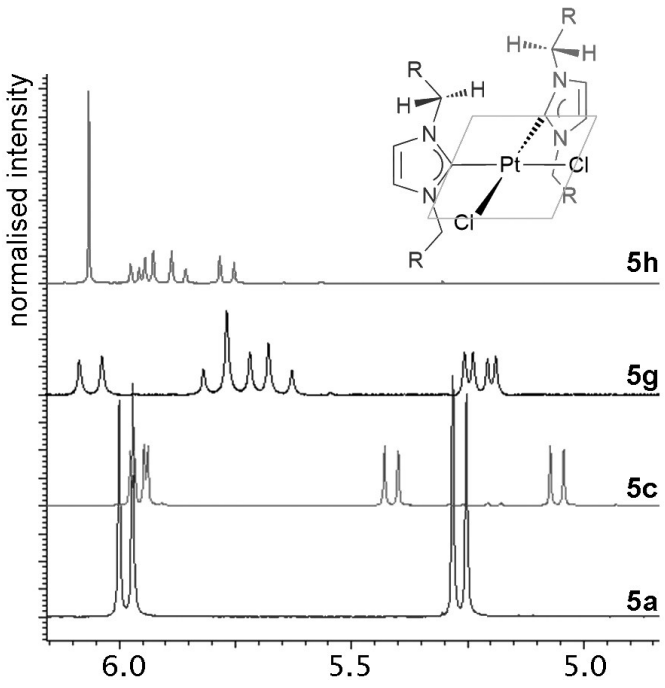
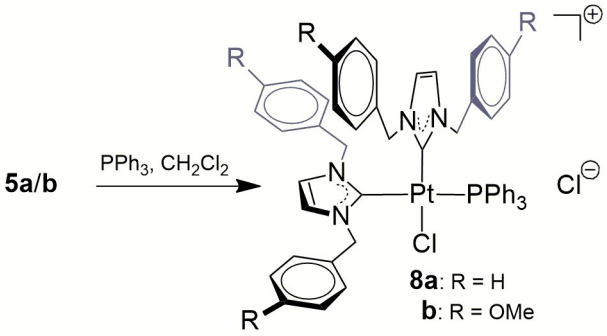


Fig. 2 Relevant ^{1}H NMR signals of inequivalent benzylic CH_2 protons of complexes **5** proving the *cis* configuration.

Further evidence is provided by the ^{13}C NMR shifts of the carbene carbon signals ranging from 147.8 to 149.9 ppm, typical of carbon atoms in a *cis*-NHC-L-$PtCl_2$ environment.[17,21,27] While the symmetric complexes **5a** and **5b** showed only one carbene carbon signal, the mixed complexes gave rise to two inequivalent signals for the different NHC ligands.

Complexes **5g** and **5h** showed distinct ^{1}H NMR spectra with coupling constants $^{2}J_{AB}$ = 15.11 to 15.26 Hz and overall more complex spectra as each CH_2 proton has a different surrounding and thus a distinctive shift. In the ^{13}C NMR spectrum of **5g** the carbene carbon of the N-methylated NHC ligand peaks at 146.6 ppm.

We also prepared cationic complexes **8** from the symmetric complexes **5a** and **5b** by substitution of a chlorido for a triphenylphosphane ligand (Scheme 3).



Scheme 3 Synthesis of cationic phosphane complexes **8** from *cis*-[Pt^{II}(NHC)$_2$Cl$_2$] complexes **5a** and **5b**.

Their ^{1}H NMR spectra showed more complex CH_2 signals due to the additional asymmetry. Their carbene carbon signals in the ^{13}C NMR spectra appeared as doublets with $^{2}J_{CP}$ = 10 Hz (*cis* to PPh_3) and 151 Hz (*trans* to PPh_3), respectively. The ^{31}P–^{195}Pt coupling of $^{1}J_{PPt}$ = 2366 Hz (**8a**) and 2361 Hz (**8b**) was visible as were the phosphane signals at 13.09 (**8a**) and 13.34 ppm (**8b**) in the ^{31}P NMR spectra.

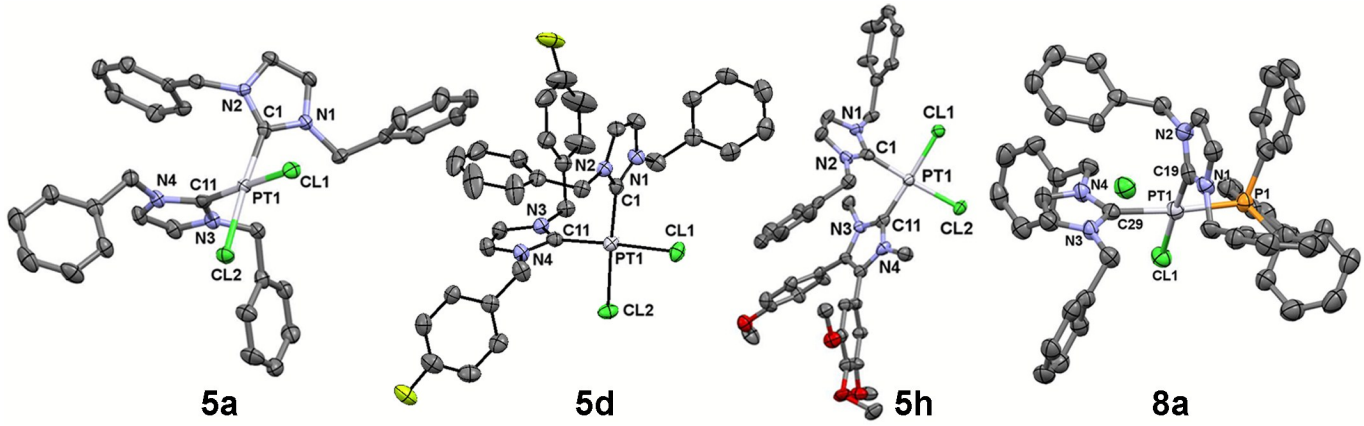


Fig. 3 Molecular structures of complexes **5a, 5d, 5h,** and **8a** as thermal ellipsoid representations at 50% probability level (H atoms omitted)**.** Selected bond lengths [Å] and angles [°]: **5a**: Pt1-Cl1 2.362(3), Pt1-Cl2 2.350(2), Pt1-C1 1.969(8), Pt1-C11 1.967(3), Cl1-Pt1-Cl2 90.5(7), Cl1-Pt1-C1 88.5(6), Cl1-Pt1-C11 176.5(1), Cl2-Pt1-C1 175.8(6), Cl2-Pt1-C11 86.2(9), C1-Pt1-C11 94.6(8); **5d**: Pt1-Cl1 2.355(6), Pt1-Cl2 2.355(6), Pt1-C1 1.971(4), Pt1-C11 1.971(4), Cl1-Pt1-Cl2 92.1(7), Cl1-Pt1-C1 85.7(6), Cl1-Pt1-C11 176.9(4), Cl2-Pt1-C1 176.9(4), Cl2-Pt1-C11 85.7(6), C1-Pt1-C11 96.4(0); **5h**: Pt1-Cl1 2.359(2), Pt1-Cl2 2.361(8), Pt1-C1 1.984(4), Pt1-C11 1.991(2), Cl2-Pt1-Cl1 89.5(3), Cl2-Pt1-C11 92.6(2), Cl2-Pt1-C1 176.9(2), Cl1-Pt1-C11 176.2(8), Cl1-Pt1-C1 87.4(0), C1-Pt1-C11 90.4(6); **8a**: Pt1-Cl1 1.348(7), Pt1-P1 2.312(7), Pt1-C29 2.072(7), Pt1-C29 2.016(4), Cl1-Pt1-P1 92.0(5), Cl1-Pt1-C29 87.0(9), Cl1-Pt1-C19 176.2(7), P1-Pt1-C29 172.6(1), P1-Pt1-C19 87.5(7), C19-Pt1-C29 93.7(5).

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Table 1 Means ± SD of IC_{50} (72 h) values [μM] of complexes **5**, **8**, and cisplatin (CDDP) in MTT assays against human cancer cell lines and an endothelial hybrid cell line as calculated from four independent measurements.

	IC_{50} (72h) [μM]										
Cell line	**5a**	**5b**	**5c**	**5d**	**5e**	**5f**	**5g**	**5h**	**8a**	**8b**	**CDDP**
518A2	6.2 ± 0.4	7.9 ± 0.4	5.6 ± 0.2	6.1 ± 0.5	5.2 ± 0.3	7.1 ± 0.5	39.0 ± 1.0	6.5 ± 0.2	0.86 ± 0.05	0.60 ± 0.15	5.3 ± 0.4
HT-29	14.6 ± 1.4	11.1 ± 2.0	13.9 ± 1.4	21.6 ± 1.5	4.1 ± 0.4	6.6 ± 0.5	39.7 ± 2.0	11.1 ± 0.7	0.82 ± 0.06	0.45 ± 0.03	> 100
DLD-1	4.7 ± 1.4	3.2 ± 0.1	5.1 ± 0.6	4.0 ± 0.2	5.7 ± 1.4	11.1 ± 0.9	30.2 ± 5.2	**0.39** ± 0.07	0.77 ± 0.04	0.66 ± 0.02	32.6 ± 2.4
U87	7.2 ± 0.2	7.7 ± 0.5	9.0 ± 1.1	5.0 ± 0.3	4.5 ± 0.4	7.3 ± 0.3	> 50	6.1 ± 2.1	0.89 ± 0.19	0.95 ± 0.21	4.0 ± 0.3
Panc-1	3.5 ± 0.7	2.9 ± 0.0	3.0 ± 0.1	4.2 ± 0.4	6.7 ± 1.3	6.0 ± 0.1	38.8 ± 3.7	**0.24** ± 0.05	0.36 ± 0.00	0.39 ± 0.03	4.8 ± 0.7
MCF7/Topo	8.6 ± 2.0	4.0 ± 0.2	11.1 ± 5.6	7.6 ± 0.9	3.2 ± 0.5	13.7 ± 0.9	42.1 ± 2.7	37.1 ± 5.6	0.43 ± 0.01	0.52 ± 0.03	10.6 ± 0.7
Kb-V1/Vbl	11.7 ± 0.8	13.9 ± 1.1	16.1 ± 0.8	18.1 ± 2.6	43.5 ± 2.1	21.0 ± 1.0	> 50	35.5 ± 1.3	7.3 ± 1.2	6.0 ± 0.3	> 100
Ea.Hy926	6.8 ± 1.6	4.2 ± 0.4	5.6 ± 1.9	7.6 ± 0.2	3.2 ± 0.5	13.4 ± 0.5	45.3 ± 1.2	**0.4** ± 0.08	0.48 ± 0.01	0.72 ± 0.03	17.3 ± 1.9

518A2 – human melanoma, HT-29 – human colon adenocarcinoma, DLD-1 – Dukes type C colorectal adenocarcinoma, U87 – human glioblastoma, Panc-1 – human pancreatic carcinoma, MCF7/Topo – human breast cancer, Kb-V1/Vbl – human cervix carcinoma, Ea.Hy926 – endothelial hybrid cells.

X-ray crystallography

Crystals suitable for X-ray diffraction analyses were grown by slow infusion of hexane into saturated solutions of **5a**, **5d**, **5h**, or **8a** in CH_2Cl_2 kept at 4 °C. Figure 3 shows their molecular structures. The characteristic bond lengths and angles were similar for all four complexes. The distances between the platinum and the carbene carbon atoms were in the range of 1.97−1.99 Å, only in the phosphane complex **8a** the distances were slightly longer with 2.02 Å and 2.07 Å. The Pt–Cl distances lay between 2.35 and 2.36 Å, while the Pt–P bond of **8a** was 2.31 Å long. The C–Pt–C angles ranged from 93.7° (**8a**) to 96.4° (**5d**) for those complexes that bore 1,3-dibenzylimidazol-2-ylidene ligands. In the case of **5h** the C–Pt–C angle was reduced to 90.4°.

Anticancer activity

Complexes **5** and **8** were investigated for their cytotoxicity against a panel of seven human cancer cell lines of six entities and an endothelial cell line using the MTT-based viability assay.[28,29] Table 1 summarises the resulting IC_{50} (72 h) values. All complexes **5a**-**h** showed remarkable efficacies with low micromolar IC_{50} values against all cell lines, save for the cisplatin resistant HT-29 colon[30] and the multidrug-resistant (mdr) KB-V1/Vbl cervix[31] carcinoma cell line. The latter, which overexpresses the detoxifying efflux transporter protein p-gp1, was surprisingly unresponsive to all complexes, especially to **5h** that bears the structural motif of the natural anticancer drug combretastatin A-4 (CA-4). Complex **5h** was also less active than most other test compounds against the mdr MCF7/Topo[32] mamma carcinoma cell line which overexpresses the efflux transporter BCRP34 (breast cancer resistance protein). This is an indication for **5h** being a substrate of these drug efflux pumps.

Against CA-4 sensitive cancer cell lines such as DLD-1 colon carcinoma and Panc-1 pancreatic cancer, and also against the hybrid endothelial Ea.Hy926 cells, complex **5h** retained the activity of the natural lead compound CA-4, showing IC_{50} concentrations in the low nanomolar range.

As we have already shown in previous work, exchange of one chlorido for a phosphane ligand can enhance the cytotoxicity significantly, probably due to an increase in lipophilicity, solubility and thus of cellular uptake.[17] This was observed here as well when going from the neutral dichlorido complexes **5a**-**b** to the phosphane complexes **8a**-**b** which are typical 'delocalised lipophilic cations' (DLCs). They were efficacious with submicromolar IC_{50} values against most of the cell lines. Again, the KbV1/Vbl cells were least responsive requiring single-digit micromolar IC_{50} concentrations (**8a**: 7 μM; **8b**: 6 μM).

In vitro DNA interaction

We investigated the DNA interaction of *trans*-$[Pt^{II}(NHC)_2Cl_2]$ complex **1b**, the isomeric *cis*-complex **5b**, and its cationic analogue *cis*-$[Pt^{II}(NHC)_2(PPh_3)Cl]^+Cl^-$ **8b** by means of an electrophoretic mobility shift assay (EMSA) with circular pBR322 plasmid DNA (Fig. 4). The *trans* configured complex **1b** did not alter the DNA morphology, i.e. the ratio of open circular (oc) and covalently closed circular (ccc) forms. In contrast, its *cis* isomer **5b** led to a distinct unwinding of the plasmid DNA in a concentration-dependent manner, as is also typical of cisplatin, apparent from a pronounced band shift with a maximum at a concentration of 10 μM of **5b**. At this concentration the DNA also seems to aggregate to adducts that remain in the gel pocket during electrophoresis, not able to permeate the pores of the gel. The same phenomenon was observed for **8b**, yet to a greater extent. It initiated immediate aggregation of the plasmid DNA without any conversion of its topological oc and ccc isomers. Such effects had previously been observed[17] and corroborated by light scattering experiments and studies of the DNA binding kinetics for complexes **3** and **4**. They suggest that the mode of DNA interaction is mainly governed by the sterical shielding of the chlorido leaving ligand or the metal centre.

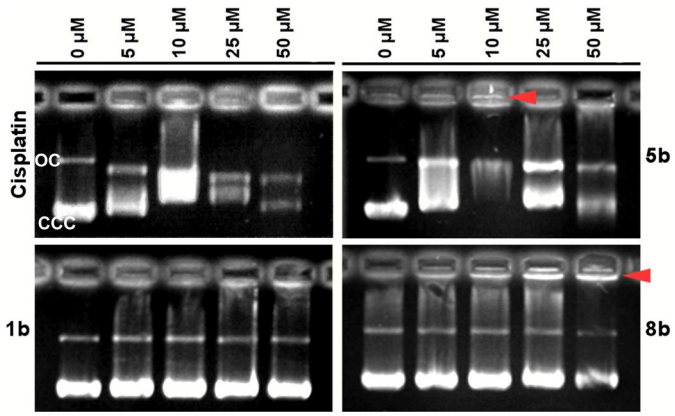

Fig. 4 Modification of gel electrophoretic mobility of pBR322 plasmid DNA when incubated for 24 h with different concentrations of DMF solutions of cisplatin, **1b**, **5b**, and **8b** (oc = open circular, ccc = covalently closed circular DNA form; the red arrows mark DNA aggregates).

Conclusions

We have developed a new synthetic protocol that gives access to *cis*-[Pt^{II}(NHC)^1(NHC)^2L^1L^2] complexes with two different NHC ligands. Ten complexes were prepared, structurally elucidated, and screened for antiproliferative activity against human tumour cells. Their activity was surprisingly high on average, with a considerable degree of structure-dependent cell line specificity. For some complexes we observed a breach of the cisplatin and multidrug resistance of certain cancer cell lines. Mechanistically, DNA seems to be a major target of these new platinum complexes, albeit in a more differentiated way when compared to cisplatin. In EMSA experiments with circular plasmid DNA, the neutral *cis*-biscarbene complex **5b** bound coordinatively to it leading to its unwinding. Apparently, complex **5b** also initiated the aggregation of this form of DNA to some extent. This needs to be confirmed by further experiments. The cationic *cis*-biscarbene complex **8b** seems to have led exclusively to DNA aggregation. The *trans*-biscarbene complex **1b** showed no such effects. Obviously, the mode of DNA interaction is correlated to the replaceability and sterical accessibility of the leaving ligand, and the overall charge of the complex.

Another interesting aspect is the retention of intrinsic ligand bioactivity in the complexes, e.g. for the CA-4 derived complex **5h**. This should allow a high degree of liberty in devising new pleiotropic anticancer complexes with various combinations of NHC ligands, spectator ligands, and leaving groups that contribute their inherent activity and so influence the overall pharmacological properties. Likewise, our new access to *cis*-biscarbene complexes, which is very likely not restricted to platinum, will be of interest to catalysis chemists as it offers a way to fine-tune the stereoelectronic properties of NHC complex catalysts more minutely than before.

Experimental

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Materials and methods

All chemicals and reagents were purchased from Sigma Aldrich, Alfa Aesar, or ABCR and were used without further purification. Melting points are uncorrected; NMR spectra were run on a 500 MHz spectrometer; chemical shifts are given in ppm (δ) and referenced relative to the internal solvent signal; ^{195}Pt NMR shifts are quoted relative to Ξ(^{195}Pt) = 21.496784 MHz, K_2PtCl_4 was used as external standard (δ = –1612.81); mass spectra: direct inlet, EI, 70 eV; elemental analyses: Vario EL III and HEKAtech EA 3000 elemental analysers; X-ray diffractometers: STOE-IPDS II and STOE-STADIVARI. All biotested compounds were >95% pure by elemental analysis. *N*-methyl- and *N*-benzylimidazolium salts were prepared according to literature procedures (*cf.* Supporting Information),[22-25] as were 1,3-dimethyl-4-(3‘,4‘,5‘-trimethoxyphenyl)-5-(4‘’-methoxyphenyl)imidazolium iodide[26] and complex **2a**.[17] Complex **1b** was prepared analogously to **1a**[17] and is described in the Supporting Information.

Syntheses and characterisation

***cis*-[Dichlorido-(1,3-di(4-methoxybenzyl)imidazol-2-ylidene)(dimethylsufoxide)]platinum(II) (2b)**. A mixture of 1,3-di(4-methoxybenzyl)imidazolium chloride (177 mg, 513 µmol) and CH_2Cl_2 (10 mL) was treated with silver(I) oxide (59 mg, 257 µmol) and stirred for 24 h at room temperature. Solids were filtered off and the silver NHC complex was precipitated by addition of hexane. After decanting and drying in vacuo this intermediate complex (200 mg, 443 µmol) was dissolved in DMSO (7.5 mL), treated with K_2PtCl_4 (184 mg, 443 µmol), and the mixture was stirred at 60 °C for 24 h. CH_2Cl_2 was added, the reaction mixture was filtered, and the filtrate was washed with water and dried over Na_2SO_4. The volatiles were removed in vacuo and the remainder was recrystallised from CH_2Cl_2/hexane to yield 225 mg (78 %) of white crystals of m.p. 206 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.26 (s, 6H, CH_3, DMSO), 3.81 (s, 6H, OCH_3), 5.60 (virt. t, *J*=15.3 Hz, 4H, CH_2), 6.78 (s, 2H, CH, imidazole), 6.92 (d, *J*=8.5 Hz, 4H, Ar), 7.33 (d, *J*=8.5 Hz, 4H, Ar); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 45.6 (DMSO), 53.9 (CH_2), 55.3 (OCH_3), 114.3 (Ar), 121.0 (CH, imidazole), 126.9 (Ar), 129.7 (Ar), 143.8 (NCN), 159.7 (Ar); EI-MS: *m/z* 502 (5%, –Cl_2, –DMSO), 416 (9), 401 (7), 308 (10), 241 (8), 188 (10), 121 (100), 78 (12).

***cis*-[Dichlorido-(1,3-dimethyl-4-(3’,4’,5’-trimethoxyphenyl)-5-(4’’-methoxyphenyl)imidazol-2-ylidene)(dimethylsufoxide)]platinum(II) (2c).** Analogously to **2b**, complex **2c** (155 mg, 78%) was obtained from 1,3-dimethyl-4-(3’,4’,5’-trimethoxyphenyl)-5-(4’’-methoxyphenyl)-imidazolium iodide (143 mg, 287 µmol), silver(I) oxide (33 mg, 144 µmol), K_2PtCl_4 (119 mg, 287 µmol), and DMSO (6 mL) as white crystals of m.p. 143 °C. ^{1}H NMR

($CDCl_3$, 500 MHz): δ 3.59 (s, 6H, CH_3, DMSO), 3.71 (s, 6H, 3'-, 5'-OCH_3), 3.79 (s, 3H, 4''-OCH_3), 3.83 (s, 3H, 4'-OCH_3), 3.90 (s, 3H, NCH_3), 3.94 (s, 3H, NCH_3), 6.33 (s, 2H, Ar), 6.86 (d, *J*=8.4 Hz, 2H, Ar), 7.10 (d, *J*=8.8 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 36.2 (N-CH_3), 46.3 (DMSO), 55.3 (4''-OCH_3), 56.2 (3'-, 5'-OCH_3), 60.9 (4'-OCH_3), 107.8 (Ar, C-2', -6'), 114.3 (Ar, C-2'', -6''), 119.5 (Ar, C-1''), 122.7 (Ar, C-1'), 131.5 (C-4, -5, imidazole), 131.8 (Ar, C-3'', -5''), 138.6 (Ar, C-4'), 142.5 (NCN), 153.3 (Ar, C-3', -5'), 160.2 (Ar, C-4''); EI-MS: *m/z* 712 (M^+, 1%), 635 (2, –DMSO), 562 (2, $–Cl_2$, –DMSO), 415 (6), 369 (11), 355 (67), 340 (34), 78 (56), 63 (56), 50 (100), 36 (98).

General procedure for the preparation of *cis*-[$Pt^{II}(NHC)^1(NHC)^2Cl_2$] complexes 5. Complex **2** (1 equiv) and the respective imidazolium chloride **7** (1 equiv) were dissolved in dry CH_2Cl_2 (60 mL/mmol) and treated with KO^{t}Bu (1.2 equiv) under an atmosphere of dry argon. After stirring at room temperature for 16 h solids were filtered off and the pure product **5** was precipitated by adding diethyl ether at 4 °C.

***cis*-[Dichlorido-bis(1,3-dibenzylimidazol-2-ylidene)] platinum(II) (5a).** Complex **5a** (60 mg, 93%) was obtained from **2a** (50 mg, 84.4 µmol), 1,3-dibenzylimidazolium chloride (24 mg, 84.4 µmol), and KO^{t}Bu (11 mg, 101 µmol) yield 60 mg (93 %) as white crystals of m.p. 287 °C. Elemental analysis (%): calc. for $C_{34}H_{32}N_4PtCl_2$ (762.63): C, 53.55; H, 4.23; N, 7.35. Found: C, 53.04; H, 4.48; N, 7.39. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.27 (d, *J*=14.6 Hz, 4H, CH_2), 5.99 (d, *J*=14.6 Hz, 4H, CH_2), 6.52 (s, 4H, imidazole CH), 7.12–7.19 (m, 8H, Ar), 7.27–7.33 (m, 12H, Ar); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 54.1 (CH_2), 120.5 (imidazole CH), 128.2 (Ar), 128.9 (Ar), 134.9 (Ar), 149.0 (NCN); ^{195}Pt NMR ($CDCl_3$): δ –3605.3; EI-MS: *m/z* 762 (M^+, 7%), 726 (11, –Cl), 689 (24, $–Cl_2$), 441 (18), 247 (51), 157 (29), 91 (100).

Crystal data: $C_{34}H_{32}N_4PtCl_2$, *M*=762.62, monoclinic, space group P2(1)/c, *a*=7.5380(3), *b*=33.6480(12), *c*=12.1810(5) Å, α=γ=90°, β=95.951(3)°, *V*=3072.9(2) Å^3, *Z*=4, λ=0.71069 Å, *µ*=4.77 mm^{-1}, *T*=133 K; 12924 reflections measured, 6540 unique; final refinement to convergence on F^2 gave *R*=0.0276 and *Rw*=0.0601, GOF=0.766. CCDC 1481381.

***cis*-[Dichlorido-bis(1,3-di(4-methoxybenzyl)imidazol-2-ylidene)]platinum(II) (5b).** Complex **2b** (88 mg, 135 µmol), 1,3-di(4-methoxybenzyl)imidazolium chloride (47 mg, 135 µmol), and KO^{t}Bu (18 mg, 162 µmol) yielded 74 mg (62%) of **5b** as white crystals of m.p. 211 °C. Elemental analysis (%): calc. for $C_{38}H_{40}O_4N_4PtCl_2$ (882.74): C, 51.70; H, 4.57; N, 6.35. Found: C, 51.75; H, 4.46; N, 6.39. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.77 (s, 12H, OCH_3), 5.19 (d, *J*=14.3 Hz, 4H, CH_2), 5.93 (d, *J*=14.3 Hz, 4H, CH_2), 6.53 (s, 4H, imidazole CH), 6.77–6.83 (d, *J*=8.5 Hz, 8H, Ar), 7.08–7.16 (d, *J*=8.5 Hz, 8H, Ar); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 53.7 (CH_2), 55.3 (OCH_3), 114.3 (Ar), 120.3 (imidazole CH), 126.9 (Ar), 129.9 (Ar), 148.2 (NCN), 159.6 (Ar); ^{195}Pt NMR ($CDCl_3$): δ –3601.0; EI-MS: *m/z* 882 (M^+, 2%), 845 (4, –Cl), 809 (18, $–Cl_2$), 502 (16), 379 (9), 307 (11), 187 (11), 121 (100).

***cis*-[Dichlorido-(1,3-dibenzylimidazol-2-ylidene)(1,3-di(4-methoxybenzyl)imidazol-2-ylidene)]platinum(II) (5c).** Complex **2a** (104 mg, 176 µmol), 1,3-di(4-methoxybenzyl)imidazolium chloride (61 mg, 176 µmol), and KO^{t}Bu (24 mg, 211 µmol) gave 78 mg (54%) of **5c** as white crystals of m.p. 243 °C. Elemental analysis (%): calc. for $C_{36}H_{36}O_2N_4PtCl_2$ (822.69): C, 52.56; H, 4.41; N, 6.81. Found: C, 52.18; H, 4.81; N, 6.98; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.77 (s, 6H, OCH_3), 5.06 (d, *J*=14.3 Hz, 2H, CH_2), 5.41 (d, *J*=14.3 Hz, 2H, CH_2), 5.96 (2 × d, *J*=14.3 Hz, 4H, CH_2), 6.45 (s, 2H, imidazole CH), 6.59 (s, 2H, imidazole CH), 6.80 (d, *J*=8.5 Hz, 4H, Ar), 7.12 (d, *J*=8.5 Hz, 4H, Ar), 7.16 (m, 4H, Ar), 7.29 (m, 6H, Ar); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 53.6 (CH_2), 54.1 (CH_2), 55.3 (OCH_3), 114.3 (Ar), 120.2 (imidazole CH), 120.6 (imidazole CH), 126.8 (Ar), 128.2 (Ar), 128.4 (Ar), 128.9 (Ar), 129.9 (Ar), 134.9 (Ar), 147.9 (NCN), 149.3 (NCN), 159.6 (Ar); ^{195}Pt NMR ($CDCl_3$): δ –3603.0; EI-MS: *m/z* 822 (M^+, 6%), 786 (8, –Cl), 749 (27, $–Cl_2$), 502 (9), 441 (22), 307 (11), 247 (38), 157 (30), 121 (100), 91 (79).

***cis*-[Dichlorido-(1,3-dibenzylimidazol-2-ylidene)(1,3-di(4-fluorobenzyl)imidazol-2-ylidene)]platinum(II) (5d).** Complex **2a** (80 mg, 135 µmol), 1,3-di(4-fluorobenzyl)imidazolium chloride (43 mg, 135 µmol), and KO^{t}Bu (18 mg, 162 µmol) afforded 57 mg (53%) of **5d** as white crystals of m.p. 241 °C. Elemental analysis (%): calc. for $C_{34}H_{30}N_4F_2PtCl_2$ (798.62): C, 51.13; H, 3.79; N, 7.02. Found: C, 50.61; H, 3.66; N, 7.04; ^{1}H NMR ($CDCl_3$, 126 MHz): δ 4.96 (d, *J*=14.3 Hz, 2H, CH_2), 5.48 (d, *J*=15.0 Hz, 2H, CH_2), 5.92 (d, J=15.0 Hz, 2H, CH_2), 6.08 (d, J=14.3 Hz, 2H, CH_2), 6.45 (s, 2H, imidazole CH), 6.63 (s, 2H, imidazole CH), 6.98 (t, *J*=8.7 Hz, 4H, Ar), 7.13–7.18 (m, 4H, Ar), 7.21 (dd, *J*=8.7, 5.2 Hz, 4H, Ar), 7.28–7.34 (m, 6H, Ar); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 53.4 (CH_2), 54.1 (CH_2), 115.9 (d, $^2J_{CF}$=21.8 Hz, Ar), 120.4 (imidazole CH), 120.8 (imidazole CH), 127.9 (Ar), 128.4 (Ar), 129.0 (Ar), 130.3 (d, $^3J_{CF}$=8.2 Hz, Ar), 130.6 (Ar), 134.8 (Ar), 149.0 (NCN), 149.1 (NCN), 162.7 (d, $^1J_{CF}$=248 Hz, Ar); ^{195}Pt NMR ($CDCl_3$): δ –3605.2; EI-MS: *m/z* 798 (M^+, 8%), 761 (28, –Cl), 725 (100, $–Cl_2$), 477 (24), 441 (33), 283 (45), 247 (81), 109 (60), 91 (44).

Crystal data: $C_{34}H_{28}N_4F_2PtCl_2$, *M*=796.59, monoclinic, space group C2/c, *a*=15.6790(6), *b*=14.1220(6), *c*=15.1390(8) Å, α=γ=90°, β=113.895(5)°, *V*=3064.8(3) Å^3, *Z*=4, λ=0.71069 Å, *µ*=4.80 mm^{-1}, *T*=133 K; 19249 reflections measured, 3070 unique; final refinement to convergence on F^2 gave *R*=0.0267 and *Rw*=0.0639, GOF=0.984. CCDC 1481378.

***cis*-[Dichlorido-(1,3-di(4-fluorobenzyl)imidazol-2-ylidene)(1,3-di(4-methoxybenzyl)imidazol-2-ylidene)]platinum(II) (5e).** Complex **5e** (13 mg, 11%) was obtained from **2b** (88 mg, 135 µmol), 1,3-di(4-fluorobenzyl)imidazolium chloride (43 mg, 135 µmol), and KO^{t}Bu (18 mg, 162 µmol) as white crystals of m.p. 223 °C. Elemental analysis (%): calc. for $C_{36}H_{34}N_4O_2F_2PtCl_2$ (858.67): C, 50.36; H, 3.99; N, 6.52. Found: C, 49.91; H, 4.13; N, 6.32; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.77 (s, 6H, OCH_3), 5.13 (d, *J*=14.6 Hz, 2H, CH_2), 5.22 (d, *J*=14.3 Hz, 2H, CH_2), 5.88 (d, *J*=14.3 Hz, 2H, CH_2), 6.04 (d, *J*=14.6 Hz, 2H, CH_2), 6.54 (s, 2H, imidazole CH), 6.56 (s, 2H, imidazole CH), 6.80 (d, *J*=8.5

Hz, 4H, Ar), 6.97 (t, *J*=8.7 Hz, 4H, Ar), 7.12 (d, *J*=8.5 Hz, 4H, Ar), 7.21 (dd, *J*=8.7, 5.2 Hz, 4H, Ar); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 53.4 (CH_2), 53.6 (CH_2), 55.3 (OCH_3), 114.3 (Ar), 115.9 (d, $^2J_{CF}$=21.8 Hz, Ar), 120.5 (imidazole CH), 120.5 (imidazole CH), 126.7 (Ar), 129.7 (Ar), 130.3 (d, $^3J_{CF}$=8.2 Hz, Ar), 130.6 (d, $^4J_{CF}$=2.7 Hz, Ar), 147.8 (NCN), 149.0 (NCN), 159.7 (Ar), 162.7 (d, $^1J_{CF}$=249 Hz, Ar); ^{195}Pt NMR ($CDCl_3$): δ –3601.7; EI-MS: *m/z* 858 (M^+, 6%), 822 (10, –Cl), 786 (39, –Cl_2), 663 (8), 502 (12), 477 (27), 283 (31), 175 (25), 121 (100), 109 (98).

***cis*-[Dichlorido-(1,3-dibenzylimidazol-2-ylidene)(1,3-bis(3,5-dimethoxybenzyl)imidazol-2-ylidene)]platinum(II) (5f).** Complex **5f** (35 mg, 26%) was obtained from **2a** (90 mg, 153 µmol), 1,3-bis(3,5-dimethoxybenzyl)imidazolium chloride (62 mg, 153 µmol), and KO^{t}Bu (21 mg, 184 µmol) as white crystals of m.p. 237 °C. Elemental analysis (%): calc. for $C_{38}H_{40}O_4N_4PtCl_2$ (882.74): C, 51.70; H, 4.57; N, 6.35. Found: C, 51.41; H, 5.18; N, 6.43; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.73 (s, 12H, OCH_3), 5.05 (d, *J*=14.3 Hz, 2H, CH_2), 5.32 (d, *J*=15.0 Hz, 2H, CH_2), 5.97 (dd, *J*=14.6, 1.8 Hz, 4H, CH_2), 6.35 (t, J=2.4 Hz, 2H, Ar), 6.42 (d, J=2.4 Hz, 4H, Ar), 6.52 (s, 2H, imidazole CH), 6.60 (s, 2H, imidazole CH), 7.17 (m, 4H, Ar), 7.28–7.33 (m, 6H, Ar); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 54.1 (CH_2), 54.1 (CH_2), 55.6 (OCH_3), 100.3 (Ar), 106.3 (Ar), 120.6 (imidazole CH), 120.8 (imidazole CH), 128.2 (Ar), 128.4 (Ar), 129.0 (Ar), 135.0 (Ar), 137.3 (Ar), 148.9 (NCN), 148.9 (NCN), 161.2 (Ar); ^{195}Pt NMR ($CDCl_3$): δ –3604.0; EI-MS: *m/z* 882 (M^+, 4%), 846 (14, –Cl), 809 (17, –Cl_2), 689 (17), 561 (13), 442 (16), 367 (37), 247 (100), 157 (22), 91 (74).

***cis*-[Dichlorido-(1,3-dibenzylimidazol-2-ylidene)(1-benzyl-3-methylimidazol-2-ylidene)]platinum(II) (5g).** Complex **5g** (29 mg, 50%) was obtained from **2a** (50 mg, 84,4 µmol), 1-benzyl-3-methylimidazolium chloride (18 mg, 84,4 µmol), and KO^{t}Bu (15 mg, 127 µmol) as white crystals of m.p. 243 °C. Elemental analysis (%): calc. for $C_{28}H_{28}N_4PtCl_2$ (686.54): C, 48.98; H, 4.11; N, 8.16. Found: C, 48.55; H, 3.80; N, 7.83; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.92 (s, 3H, CH_3), 5.23 (m, 2H, CH_2), 5.61–5.71 (d, *J*=15.1 Hz, 1H, CH_2), 5.71–5.83 (2 × d, *J*=15.1 Hz, 2H, CH_2), 6.08 (d, *J*=14.5 Hz, 1H, CH_2), 6.50 (d, *J*=1.4 Hz, 1H, imidazole CH), 6.52 (d, *J*=1.4 Hz, 1H, imidazole CH), 6.64 (d, *J*=1.4 Hz, 1H, imidazole CH), 6.67 (d, *J*=1.4 Hz, 1H, imidazole CH), 7.02–7.09 (m, 2H), 7.11–7.19 (m, 4H), 7.25–7.34 (m, 9H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 37.9 (CH_3), 53.8 (CH_2), 54.0 (CH_2), 54.1 (CH_2), 120.0 (imidazole CH), 120.4 (imidazole CH), 120.9 (imidazole CH), 122.4 (imidazole CH), 127.7 (Ar), 127.8 (Ar), 128.3 (Ar), 128.9 (Ar), 128.9 (Ar), 129.0 (Ar), 134.8 (Ar), 135.0 (Ar), 148.1 (NCN), 149.0 (NCN); ^{195}Pt NMR ($CDCl_3$): δ –3610.7; EI-MS: *m/z* 686 (M^+, 3%), 650 (9, –Cl), 613 (21, –Cl_2), 441 (8), 365 (18), 284 (7), 247 (43), 171 (80), 158 (16), 91 (100).

***cis*-[Dichlorido-(1,3-dibenzylimidazol-2-ylidene)(1,3-dimethyl-4-(3',4',5'-trimethoxyphenyl)-5-(4''-methoxyphenyl)imidazol-2-ylidene)]platinum(II) (5h).** Complex **5h** (19 mg, 73%) was obtained from **2c** (21 mg, 30 µmol), 1,3-dibenzylimidazolium chloride (9 mg, 30 µmol), and KO^{t}Bu (4 mg, 35 µmol) as white crystals of m.p. 266 °C. Elemental analysis (%): calc. for $C_{38}H_{40}N_4O_4PtCl_2$ (882.74): C, 51.70; H, 4.57; N, 6.35. Found: C, 51.51; H, 4.69; N, 6.26; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.66 (s, 6H, OCH_3), 3.73 (s, 3H, NCH_3), 3.79 (s, 3H, OCH_3), 3.81 (s, 3H, NCH_3), 3.82 (s, 3H, OCH_3), 5.77 (d, *J*=15.3 Hz, 1H CH_2), 5.87 (d, *J*=15.3 Hz, 1H, CH_2), 5.95 (2 × d, *J*=15.6 Hz, 2H, CH_2), 6.07 (s, 2H, Ar), 6.71 (d, *J*=2.1 Hz, 1H, imidazole CH), 6.73 (d, *J*=2.1 Hz, 1H, imidazole CH), 6.82 (m, 4H, Ar), 7.11 (dd, *J*=8.0, 1.8 Hz, 2H, Ar), 7.21 (dd, J=8.0, 1.8 Hz, 2H, Ar), 7.29–7.37 (m, 6H, Ar); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 36.2 (NCH_3), 36.3 (NCH_3), 54.2 (CH_2), 54.3 (CH_2), 55.3 (OCH_3), 56.2 (OCH_3), 60.9 (OCH_3), 107.7 (Ar), 114.1 (Ar), 119.8 (Ar), 120.7 (imidazole CH), 120.9 (imidazole CH), 123.0 (Ar), 127.6 (Ar), 127.9 (Ar), 128.3 (Ar), 129.0 (Ar), 131.1 (Ar), 131.5 (Ar), 135.2 (Ar), 138.5 (Ar), 146.6 (NCN), 149.3 (NCN), 153.1 (Ar), 160.0 (Ar); ^{195}Pt NMR ($CDCl_3$): δ –3616.9; EI-MS: *m/z* 882 (M^+, 1%), 847 (8, –Cl), 819 (39, –Cl_2), 690 (5), 561 (4), 369 (12), 247 (100), 157 (7), 91 (47).

Crystal data: $C_{38}H_{40}N_4O_4PtCl_2 \times CH_2Cl_2$, *M*=967.65, monoclinic, space group P2(1)/c, *a*=11.1330(4), *b*=29.7780(14), *c*=12.1160(4) Å, α=γ=90°, β=101.539(3)°, *V*=3935.5(3) Å^3, *Z*=4, λ=0.71069 Å, *µ*=3.88 mm^{-1}, *T*=133 K; 23066 reflections measured, 7701 unique; final refinement to convergence on F^2 gave *R*=0.058 and *Rw*=0.1494, GOF=0.934. CCDC 1481379.

General procedure for the preparation of *cis*-[Pt^{II}(NHC)$_2$(PPh$_3$)Cl]$^+$Cl$^-$ complexes 8. A solution of triphenylphosphane (5 equiv) and complex **5** (1 equiv) in CH_2Cl_2 (100 mL/mmol) was stirred at room temperature for 16 h. The solvent was removed in vacuo, and the residue was recrystallised from CH_2Cl_2/hexane.

***cis*-[Chlorido-bis(1,3-dibenzylimidazol-2-ylidene)(triphenylphosphane)]platinum(II) chloride (8a).** Complex **8a** (32 mg, 95%) was obtained from **5a** (25 mg, 32.8 µmol) and triphenylphosphane (43 mg, 164 µmol) as colourless crystals of m.p. 173 °C. Elemental analysis (%): calc. for $C_{52}H_{47}N_4PPtCl_2$ (1024.92): C, 60.94; H, 4.62; N, 5.47. Found: C, 60.74; H, 4.58; N, 5.37; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.68 (d, *J*=14.6 Hz, 2H, CH_2), 4.96 (d, *J*=14.0 Hz, 2H, CH_2), 5.69 (d, JJ=14.6 Hz, 2H, CH_2), 5.92 (d, *J*=14.0 Hz, 2H, CH_2), 6.68 (s, 2H, imidazole CH), 7.02 (d, *J*=7.6 Hz, 4H, Ar), 7.12 (t, J=7.6 Hz, 4H, Ar), 7.19–7.25 (m, 4H, imidazole CH, Ar), 7.25–7.29 (m, 5H, Ar), 7.31–7.42 (m, 17H, Ar, PPh_3), 7.47–7.53 (m, 3H, PPh_3); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 54.0 (CH_2), 54.3 (CH_2), 121.8 (imidazole CH), 123.2 (imidazole CH), 128.1 (Ar), 128.7 (Ar), 128.8 (Ar), 129.0 (d, $^1J_{CP}$=55 Hz, PPh_3), 129.0 (d, $^3J_{CP}$=11 Hz, PPh_3), 129.1 (Ar), 131.4 (d, $^4J_{CP}$=2.7 Hz, PPh_3), 133.7 (Ar), 134.2 (d, $^2J_{CP}$=11 Hz, PPh_3), 134.3 (Ar), 144.9 (d, $^2J_{CP\text{-}cis}$=10 Hz, NCN), 162.8 (d, $^2J_{CP\text{-}trans}$=151 Hz, NCN); ^{31}P NMR ($CDCl_3$, 202 MHz): δ 13.1 ($^1J_{PPt}$=2366 Hz); ^{195}Pt NMR ($CDCl_3$): δ –4098.7 / –4120.8 (d, J_{PtP} = 2377 Hz); EI-MS: *m/z* 762 (11%, –PPh_3), 726 (14, –Cl, –PPh_3), 689 (42, –Cl_2, –PPh_3), 597 (9), 441 (33), 350 (11), 262 (99), 247 (100), 183 (52), 157 (34), 91 (95).

Crystal data: $C_{52}H_{47}N_4PPtCl_2$, CH_2Cl_2, $2H_2O$, *M*=1145.84, triclinic, space group P-1, *a*=11.4460(4), *b*=11.7520(4), *c*=19.7120(8) Å, α=75.959(3)°, β=74.604(3)°, γ=73.708(3)°, *V*=2412.88(16) Å^3, *Z*=2, λ=0.71069 Å, *µ*=3.21 mm^{-1}, T = 133

K; 34049 reflections measured, 9655 unique; final refinement to convergence on F^2 gave R=0.0582 and Rw=0.1538, GOF=0.994. CCDC 1481380.

***cis*-[Chlorido-bis(1,3-di(4-methoxybenzyl)imidazol-2-ylidene)(triphenylphosphane)]platinum(II) chloride (8b).** Complex **8b** (23 mg, 88%) was obtained from **5b** (20 mg, 22.7 µmol) and triphenylphosphane (30 mg, 114 µmol) as colourless crystals of m.p. 138 °C. Elemental analysis (%): calc. for $C_{56}H_{55}N_4O_4PPtCl_2$ (1145.02): C, 58.74; H, 4.84; N, 4.89. Found: C, 58.39; H, 4.98; N, 4.93; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.71 (s, 6H, OCH_3), 3.79 (s, 6H, OCH_3), 4.55 (d, J=14.3 Hz, 2H, CH_2), 5.00 (d, J=14.3 Hz, 2H, CH_2), 5.52 (d, J=14.3 Hz, 2H, CH_2), 5.84 (d, J=14.3 Hz, 2H, CH_2), 6.56–6.64 (d, J=8.5 Hz, 4H, Ar), 6.71 (s, 2H, imidazole CH), 6.84–6.90 (d, J=8.5 Hz, 4H, Ar), 6.90–6.96 (d, J=8.5 Hz, 4H, Ar), 7.12 (s, 2H, imidazole CH), 7.22–7.26 (d, J=8.5 Hz, 4H, Ar), 7.29–7.41 (m, 12H, PPh_3), 7.47–7.52 (m, 3H, PPh_3); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 53.6 (CH_2), 53.9 (CH_2), 55.3 (OCH_3), 55.3 (OCH_3), 114.4 (Ar), 114.5 (Ar), 121.6 (imidazole CH), 122.7 (imidazole CH), 125.4 (Ar), 126.3 (Ar), 129.0 (d, $^3J_{CP}$=10 Hz, PPh_3), 129.1 (d, $^1J_{CP}$=55 Hz, PPh_3), 129.9 (Ar), 130.1 (Ar), 131.3 (d, $^4J_{CP}$=2.7 Hz, PPh_3), 134.2 (d, $^2J_{CP}$=10 Hz, PPh_3), 144.0 (d, $^2J_{CP\text{-}cis}$=10 Hz, NCN), 162.6 (d, $^2J_{CP\text{-}trans}$=151 Hz, NCN); ^{31}P NMR ($CDCl_3$, 202 MHz): δ 13.3 ($^1J_{PPt}$=2360 Hz); ^{195}Pt NMR ($CDCl_3$): δ –4097.4 / –4119.3 (d, J_{PtP} = 2361 Hz); EI-MS: *m/z* 848 (6%, –Cl, –PPh_3), 809 (21, –Cl_2, –PPh_3), 687 (6), 501 (19), 379 (10), 307 (14), 262 (86), 183 (97), 121 (100).

X-ray data collection and structural determination

Data collection and cell refinement by X-AREA-STOE. The single crystal samples were irradiated with Mo-Kα at 133 K. The structures were solved by direct methods using SIR 97 and refined by full matrix least-squares on F^2 for all data using SHELXL 2014. All hydrogen atoms were added at calculated positions and refined using a riding model. Anisotropic thermal displacement parameters were used for all non-hydrogen atoms. For **5d**, the two fluorine atoms on the phenyl rings were disordered and the corresponding hydrogens could not be located, yet detected in the 1H NMR spectrum. For further details *cf.* Supporting Information. The crystallographic data were deposited with The Cambridge Crystallographic Data Centre CCDC under no. 1481381 (**5a**), 1481378 (**5d**), 1481379 (**5h**), 1481380 (**8a**) and can be obtained free of charge at www.ccdc.cam.ac.uk/data_request/cif.

Growth inhibition assay (MTT assay)

The antiproliferative effect of the complexes **5a**-**h**, **8a**, and **8b** on cells of 518A2 melanoma, different human colon carcinomas (HT-29, DLD-1), U87 glioblastoma, Panc-1 pancreatic cancer, mdr MCF-7/Topo breast cancer, and KbV1/Vbl cervix carcinoma, and on endothelial hybrid cells Ea.Hy926 was assessed. Cells were seeded in flat-bottom 96-well microtiter plates at a density of 0.05 × 10^6/mL (0.1 × 10^6/mL for U87 and Ea.Hy926) in culture medium and incubated until the cells nearly reached confluency at 37 °C. Test compound solutions were diluted from freshly made 10 mM stock solutions in DMF (5 mM in DMSO for **5g**, 10 mM in DMSO for CDDP) with water, and added to each well of the microtiter plates with working concentrations ranging from 100 µM to 25 nM. DMF or DMSO was used as a negative control. Treatment of the cells with **5a**-**h** and **8a**-**b** lasted for 72 h at 37 °C. The culture medium was replaced with a solution of MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium-bromide] (0.05 % in PBS) and the cells were incubated for another 2 h. The MTT solution was discarded and the water-insoluble formazan crystals, formed by metabolically viable cells, were dissolved in SDS/DMSO. The absorbance of the formazan solution was measured at 630 nm, the background absorbance at 570 nm. Means ± SDs were calculated from four independent values.

Electrophoretic mobility shift assay (EMSA assay)

The complexes **1b**, **5b**, and **8b** were tested for their interaction with circular pBR322 plasmid DNA in electrophoretic mobility shift assays according to a general method by Huq *et al.*.[33] Briefly, 1.5 µg pBR322 plasmid DNA in freshly sterile-filtrated TE buffer (10 mM Tris/HCl, 1 mM EDTA, pH 8.0) were incubated with 0 µM (TE buffer with plasmid DNA), 5 µM, 10 µM, 25 µM and 50 µM of the complexes or cisplatin as a positive control for 24 h at 37 °C. Agarose gel electrophoresis (1%) was conducted at 66 V for 4 h. DNA bands were visualised via staining with 10 µg/mL ethidium bromide in 0.5x TBE buffer (900 mM Tris/HCl, 900 mM boric acid, 25 mM EDTA, pH 8.3) for 30 min at room temperature. The stained DNA was documented by UV excitation. EMSA assays were performed at least twice for each of the tested complexes.

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Platinum(II) complexes bearing two different, *cis*-oriented, *N*-heterocyclic carbene ligands are readily accessible for catalysis or as selective, pleiotropic anticancer agents