Electronic Supplementary Information for Dalton Transactions

Electronic supplementary information

One-end nucleophilic addition of di- and triamines to Pt^{IV} coordinated nitriles as an entry to (amidine)Pt^{IV} complexes bearing pendant NH_2-groups†

Nadezhda A. Bokach,* Nina P. Konovalova, Yu Wang, Yulia E. Moskalenko, Alexander V. Gribanov, and Vadim Yu. Kukushkin*

Department of Chemistry, St.Petersburg State University, Univeritetsky Pr. 26, 198504 Stary Petergof, Russian Federation. Fax: 007 812 4284582; Tel: 007 812 4284582; E-mail: kukushkin@vk2100.spb.edu

Antimetastatic and Chemosensibilizing Activity of Complex 1

Materials and methods

Cyclophosphamide (CPA) was obtained from "Deco" (Russian Federation), while *Doxorubicine* (DOX) was acquired from "Pharmacia" (Milano, Italy). The cytostatic were used in subtherapeutic doses. All drugs were administered intraperitonealey.

Animals

Ten-week-old male BDF_1 mice, weighting 22–23 g were employed.

Experimental tumor

LL – carcinoma (10^6 cells) was used in the experiment. LL-carcinoma was transplanted intramuscularly. The tumor transplantation was carried out by the standard method.[1] Mice bearing LL-carcinoma were preanesthetized with ether narcosis and sacrificed on day 24 after tumor transplantation.

Evaluation of therapeutic effect

Index inhibition of metastasis (IIM%) was used as criteria of therapy efficiency

$$IIM\% = \frac{(A_C \times B_C) - (A \times B)}{A_C \times B_C} \times 100$$

where A – frequency of metastasis in experimental group;

A_C – frequency of metastasis in control;

B – average number of metastases in the experimental group;

B_C – average number of metastases in control.

Results

Results of combined administration of drugs in mice bearing LL-carcinoma are given below in **Table S1**.

Table S1

Increase of CPA and DOX Therapeutic Efficiency upon Addition of Complex **1** (LL-carcinoma)

Drug	**Single dose, mg/kg**	**Schedule of injection, days**	**IIM%**
CPA	20	2; 7	9
DOX	1.5	2; 5; 8	17
Complex **1**	20	2–9	8
CPA+ Complex **1**	20 + 20	2; 7 2–9	46
DOX+ Complex **1**	1.5+ 20	2; 5; 8 2–9	65

The date given in **Table S1** demonstrates the augmentation of chemotherapeutic sensitivity of animals bearing LL-carcinoma. The combined administration resulted in increase of index inhibition of metastasis.

Reference

1. Z. Sophina and A. Goldin (Eds.), Experimental evaluation of anticancer drugs in USSR and USA. *Medicina Publishers*, Moscow, 1980.

Table S2. Crystal data and structure refinement for [**1**•H_2](Pic)$_2$•EtOH

Identification code	ic12569	
Empirical formula	C26 H44 Cl4 N12 O16 Pt	
Formula weight	1117.62	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.9708(6) Å	α = 61.723 (1)°.
	b = 11.5590(7) Å	β = 80.464 (1)°.
	c = 11.5958(7) Å	γ = 78.180 (1)°.
Volume	1033.18(11) Å^3	
Z	1	
Density (calculated)	1.796 Mg/m^3	
Absorption coefficient	3.735 mm^{-1}	
F(000)	558	
Crystal size	0.15 x 0.10 x 0.08 mm^3	
Theta range for data collection	2.00 to 27.50°.	
Index ranges	-11<=h<=11, -15<=k<=15, -15<=l<=15	
Reflections collected	13422	
Independent reflections	4739 [R(int) = 0.0328]	
Completeness to theta = 27.50°	99.8 %	
Absorption correction	multi-scan	
Max. and min. transmission	0.7543 and 0.6042	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4733 / 0 / 272	
Goodness-of-fit on F^2	1.055	
Final R indices [I>2sigma(I)]	R1 = 0.0266, wR2 = 0.0640	
R indices (all data)	R1 = 0.0266, wR2 = 0.0640	
Largest diff. peak and hole	1.289 and -1.082 e.Å^{-3}	

Table S3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for ic12569. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pt	0	0	0	16(1)
Cl(1)	-403(1)	1260(1)	1120(1)	28(1)
Cl(2)	-2212(1)	-905(1)	1052(1)	30(1)
N(1)	1120(3)	-1607(3)	1451(2)	21(1)
N(2)	2774(3)	-753(3)	2057(3)	26(1)
N(3)	2042(3)	-553(3)	4564(3)	27(1)
C(1)	2186(4)	-1771(3)	2182(3)	22(1)
C(2)	2760(4)	-3162(3)	3164(3)	28(1)
C(3)	4351(5)	-3655(4)	2714(5)	44(1)
C(4)	3915(4)	-787(3)	2842(3)	25(1)
C(5)	3297(4)	21(3)	3569(3)	26(1)
O(1)	2747(3)	-3136(2)	6204(2)	34(1)
O(2)	3738(3)	-1409(2)	6750(3)	36(1)
O(3)	4765(3)	-2256(3)	8583(3)	35(1)
O(4)	2964(3)	-5881(3)	12283(3)	39(1)
O(5)	1362(3)	-6961(2)	12113(3)	38(1)
O(6)	17(3)	-5809(2)	7768(3)	38(1)
O(7)	1957(3)	-5346(3)	6321(3)	43(1)
N(4)	3958(3)	-2312(3)	7851(3)	26(1)
N(6)	1263(3)	-5396(3)	7336(3)	29(1)
N(5)	2221(3)	-6108(3)	11628(3)	30(1)
C(6)	2660(4)	-3781(3)	7422(3)	25(1)
C(7)	3228(4)	-3491(3)	8327(3)	24(1)
C(8)	3121(4)	-4247(3)	9668(3)	26(1)
C(9)	2372(4)	-5337(3)	10216(3)	25(1)
C(10)	1737(4)	-5698(3)	9447(3)	25(1)
C(11)	1918(4)	-4969(3)	8115(3)	25(1)
O(8)	-783(3)	-998(3)	4080(2)	32(1)
C(12)	-1169(5)	-2405(5)	4666(5)	58(1)
C(13)	-2796(6)	-2432(6)	4719(5)	63(1)

Table S4. Bond lengths [Å] and angles [°] for [**1**•H_2](Pic)$_2$•EtOH

Pt-N(1)	2.031(2)
Pt-N(1)#1	2.031(2)
Pt-Cl(1)#1	2.3148(8)
Pt-Cl(1)	2.3148(8)
Pt-Cl(2)	2.3153(8)
Pt-Cl(2)#1	2.3153(8)
N(1)-C(1)	1.308(4)
N(2)-C(1)	1.324(4)
N(2)-C(4)	1.462(4)
N(3)-C(5)	1.480(4)
C(1)-C(2)	1.506(4)
C(2)-C(3)	1.528(5)
C(4)-C(5)	1.506(5)
O(1)-C(6)	1.244(4)
O(2)-N(4)	1.223(4)
O(3)-N(4)	1.234(4)
O(4)-N(5)	1.233(4)
O(5)-N(5)	1.235(4)
O(6)-N(6)	1.239(4)
O(7)-N(6)	1.217(4)
N(4)-C(7)	1.457(4)
N(6)-C(11)	1.457(4)
N(5)-C(9)	1.444(4)
C(6)-C(7)	1.433(5)
C(6)-C(11)	1.458(4)
C(7)-C(8)	1.375(5)
C(8)-C(9)	1.374(5)
C(9)-C(10)	1.384(5)
C(10)-C(11)	1.364(5)
O(8)-C(12)	1.527(6)
C(12)-C(13)	1.457(7)
N(1)-Pt-N(1)#1	180.0(3)
N(1)-Pt-Cl(1)#1	86.21(7)
N(1)#1-Pt-Cl(1)#1	93.79(7)
N(1)-Pt-Cl(1)	93.79(7)
N(1)#1-Pt-Cl(1)	86.21(7)
Cl(1)#1-Pt-Cl(1)	180.00(5)

N(1)-Pt-Cl(2)	86.55(7)
N(1)#1-Pt-Cl(2)	93.45(7)
Cl(1)#1-Pt-Cl(2)	89.59(3)
Cl(1)-Pt-Cl(2)	90.41(3)
N(1)-Pt-Cl(2)#1	93.45(7)
N(1)#1-Pt-Cl(2)#1	86.55(7)
Cl(1)#1-Pt-Cl(2)#1	90.41(3)
Cl(1)-Pt-Cl(2)#1	89.59(3)
Cl(2)-Pt-Cl(2)#1	180.00(7)
C(1)-N(1)-Pt	134.1(2)
C(1)-N(2)-C(4)	127.2(3)
N(1)-C(1)-N(2)	121.5(3)
N(1)-C(1)-C(2)	118.3(3)
N(2)-C(1)-C(2)	120.2(3)
C(1)-C(2)-C(3)	111.4(3)
N(2)-C(4)-C(5)	111.6(3)
N(3)-C(5)-C(4)	111.5(3)
O(2)-N(4)-O(3)	122.3(3)
O(2)-N(4)-C(7)	119.0(3)
O(3)-N(4)-C(7)	118.6(3)
O(7)-N(6)-O(6)	123.7(3)
O(7)-N(6)-C(11)	119.4(3)
O(6)-N(6)-C(11)	116.8(3)
O(4)-N(5)-O(5)	123.5(3)
O(4)-N(5)-C(9)	118.0(3)
O(5)-N(5)-C(9)	118.4(3)
O(1)-C(6)-C(7)	126.8(3)
O(1)-C(6)-C(11)	122.2(3)
C(7)-C(6)-C(11)	111.0(3)
C(8)-C(7)-C(6)	124.6(3)
C(8)-C(7)-N(4)	115.0(3)
C(6)-C(7)-N(4)	120.4(3)
C(9)-C(8)-C(7)	119.3(3)
C(8)-C(9)-C(10)	121.5(3)
C(8)-C(9)-N(5)	119.2(3)
C(10)-C(9)-N(5)	119.3(3)
C(11)-C(10)-C(9)	118.2(3)
C(10)-C(11)-N(6)	116.7(3)
C(10)-C(11)-C(6)	125.4(3)
N(6)-C(11)-C(6)	117.9(3)

C(13)-C(12)-O(8)	112.8(4)

Symmetry transformations used to generate equivalent atoms:

#1 -x,-y,-z

Table S5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for [**1**•H_2](Pic)$_2$•EtOH The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Pt	16(1)	17(1)	15(1)	-7(1)	0(1)	-3(1)
Cl(1)	37(1)	25(1)	25(1)	-14(1)	-3(1)	-1(1)
Cl(2)	22(1)	33(1)	26(1)	-6(1)	2(1)	-9(1)
N(1)	22(1)	19(1)	21(1)	-7(1)	-3(1)	-4(1)
N(2)	31(2)	20(1)	24(1)	-6(1)	-8(1)	-5(1)
N(3)	25(1)	28(1)	30(2)	-14(1)	-1(1)	-7(1)
C(1)	21(2)	22(2)	22(2)	-9(1)	2(1)	-2(1)
C(2)	29(2)	21(2)	32(2)	-8(1)	-10(1)	-3(1)
C(3)	39(2)	37(2)	65(3)	-31(2)	-20(2)	10(2)
C(4)	21(2)	30(2)	29(2)	-15(1)	-2(1)	-6(1)
C(5)	24(2)	23(2)	29(2)	-10(1)	-2(1)	-7(1)
O(1)	51(2)	27(1)	24(1)	-10(1)	1(1)	-13(1)
O(2)	41(2)	27(1)	36(1)	-4(1)	-9(1)	-16(1)
O(3)	36(1)	36(1)	37(1)	-16(1)	-6(1)	-14(1)
O(4)	43(2)	41(2)	31(1)	-12(1)	-8(1)	-7(1)
O(5)	44(2)	27(1)	32(1)	-5(1)	0(1)	-9(1)
O(6)	37(2)	29(1)	52(2)	-17(1)	-9(1)	-10(1)
O(7)	57(2)	45(2)	38(2)	-28(1)	0(1)	-15(1)
N(4)	22(1)	23(1)	33(2)	-13(1)	-1(1)	-6(1)
N(6)	34(2)	19(1)	36(2)	-11(1)	-10(1)	-2(1)
N(5)	30(2)	24(1)	29(2)	-8(1)	-2(1)	0(1)
C(6)	24(2)	21(2)	28(2)	-11(1)	-1(1)	-1(1)
C(7)	20(2)	20(2)	31(2)	-11(1)	0(1)	-5(1)
C(8)	22(2)	27(2)	30(2)	-15(1)	-5(1)	0(1)
C(9)	23(2)	21(2)	24(2)	-7(1)	-1(1)	0(1)
C(10)	22(2)	18(1)	34(2)	-10(1)	-1(1)	-3(1)
C(11)	23(2)	22(2)	31(2)	-13(1)	-2(1)	-4(1)
O(8)	31(1)	39(1)	25(1)	-13(1)	0(1)	-10(1)
C(12)	47(3)	83(4)	47(3)	-36(3)	-5(2)	1(2)
C(13)	64(3)	102(4)	34(2)	-33(3)	10(2)	-44(3)

Table S6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3).

	x	y	z	U(eq)
H(1)	823	-2357	1627	26
H(2)	2442	31	1431	31
H(3A)	1283	-607	4166	40
H(3B)	1668	-26	4962	40
H(3C)	2403	-1380	5176	40
H(2A)	2042	-3764	3285	34
H(2B)	2796	-3182	4022	34
H(3D)	4324	-3612	1853	66
H(3E)	4671	-4575	3352	66
H(3F)	5077	-3095	2649	66
H(4A)	4824	-436	2260	30
H(4B)	4238	-1718	3482	30
H(5A)	4131	60	4007	31
H(5B)	2916	940	2934	31
H(8)	3560	-4019	10211	31
H(10)	1189	-6434	9835	30
H(8A)	-1049	-561	3308	47
H(12A)	-599	-2840	4133	69
H(12B)	-827	-2921	5566	69
H(13A)	-3141	-1927	3830	94
H(13B)	-3363	-2035	5274	94
H(13C)	-2979	-3354	5088	94

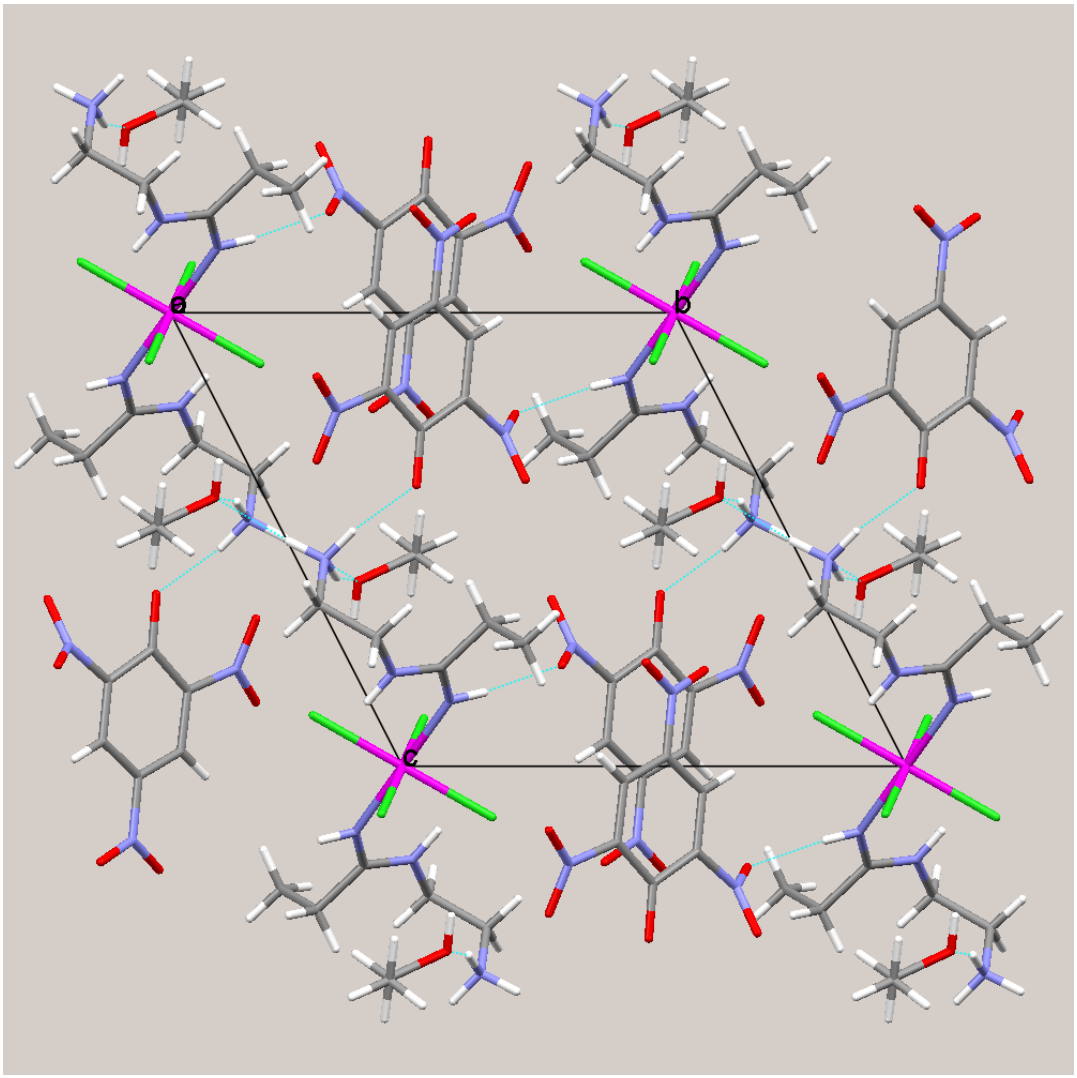

Figure S1. A packing diagram of [**1**•H_2](Pic)$_2$•EtOH within the unit cell