Potential multifunctional anti-cancer metal complexes II. Synthesis of some rhodium(II) and platinum(II) complexes of diamine-substituted acridine-4-carboxamides, and the X-ray structure of $[Rh(CH_3CO_2)_2L]_2$ (L = *N*-[2-(dimethylamino)hexyl]acridine-4-carboxamide)

David M. L. Goodgame, Caroline A. O'Mahoney, Christopher J. Page and **David J. Williams**
Chemistry Department, Imperial College of Science, Technology and Medicine, London SW7 2AY (U.K.)

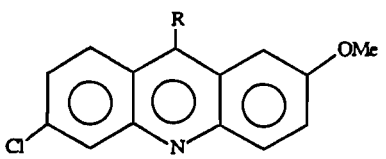
(Received February 6, 1990)

Abstract

The preparations are reported of $[Rh(RCO_2)_2L]_2$ (where $R = CH_3$, C_2H_5, and CH_3OCH_2; L is one of a series of *N*-[2-(dimethylamino)alkyl]acridine-4-carboxamide ligands in which the alkyl group is ethyl, n-butyl, or n-hexyl) and also the compounds $(LH)_2PtCl_4$. X-ray structural studies have been carried out on $\{Rh(CH_3CO_2)_2[N$-(2-dimethylamino)hexyl]acridine-4-carboxamide$\}_2$ (**1**). Compound **1** is triclinic, space group $P\bar{1}$, with $a = 8.149(1)$, $b = 8.494(2)$, $c = 37.647(10)$ Å, $\alpha = 92.49(2)$, $\beta = 95.45(2)$, $\gamma = 91.26(2)°$, $V = 2591$ Å^3, $Z = 4$ (two crystallographically independent molecules). The acridine-4-carboxamide binds to the dinuclear rhodium(II) acetate unit via the $N(CH_3)_2$ nitrogen atom with Rh–N bond distances of 2.339(6) and 2.349(5) Å, respectively for the two crystallographically independent molecules. In common with the analogous complex formed by 6-chloro-9-(2-dimethylaminoethyl)amino-2-methoxyacridine (D M. L. Goodgame, C. J. Page and D. J. Williams, *Inorg. Chim. Acta*, 153 (1988) 219), the acridine units form a continuous stack in the crystal, though with different overlapping orientations. In **1** the significantly longer diamine side chain distances the acridine nitrogen atom N(10) *c.* 11 Å from the nearest rhodium atom.

Introduction

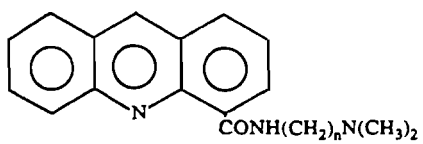
In a previous paper [1] we summarised the background to our interest in the development of multifunctional, metal-containing anti-cancer drugs, and described some rhodium(II) compounds with ligands of general formula **I**, incorporating an acridine ring



I

R = $NHCH_2CH_2NH_2$
$NHCH_2CH_2NMe_2$

with a diamine chain in the 9-position. Denny and his co-workers have recently reported [2] the synthesis of some acridine-4-carboxamide derivatives, represented by the general formula **II**, which they found to have high anti-leukemic activity and excellent *in vivo* activity against Lewis lung carcinoma. This is particularly true for compound **II** with $n = 2$.



n = 2, 4, 6

II

We report here the results of some studies of the interaction of some of those compounds with rhodium(II) carboxylates and with K_2PtCl_4, using samples very kindly made available to us by Professor Denny. The ligands concerned and their abbreviations are: **II**, $n = 2$, L2; $n = 4$, L4; $n = 6$, L6.

Experimental

Preparations

Ligands L2, L4, and L6 were obtained from Professor W. A. Denny of the Cancer Research Laboratory, University of Auckland School of Medicine, either as the dihydrochloride (L2) or the hydrochloride (L4 and L6) salts. They were converted to the free base by neutralisation with an excess of

0020-1693/90/$3.50 © Elsevier Sequoia/Printed in Switzerland

2 M sodium hydrogen carbonate in the minimum volume of water and isolated by dichloromethane extraction. After drying and solvent removal, the resulting yellow solids were dissolved in methanol to form a stock solution of free base.

The rhodium(II) carboxylate complexes were obtained by the very slow addition of the acridine ligand (0.5 mmol) in methanol (20 cm^3), without stirring, to a methanolic solution (20–30 cm^3) of the anhydrous rhodium(II) carboxylate (0.25 mmol). The red to pink crystalline or microcrystalline solids were formed in virtually quantitative yields, after solution concentration by allowing solvent evaporation for several days.

The platinum(II) compounds precipitated as yellow solids in virtually quantitative yields on mixing the stoichiometric amounts of the ligand hydrochlorides (or dihydrochloride in the case of L2) and K_2PtCl_4 in the minimum amount of water. After stirring for 30 min, the solids were collected by filtration, washed with small amounts of water, methanol and diethyl ether, and dried *in vacuo*.

Analytical data are given in Table 1.

X-ray studies

A summary of the crystal data and of the data collection and refinement parameters for compound **1** is given in Table 2. Refined unit cell parameters were obtained by centering 18 reflections on a Nicolet R3m diffractometer. Intensity data were measured with graphite monochromated Cu Kα radiation using ω-scans. The data were corrected for Lorentz and polarisation factors. A numerical absorption correction (face indexed crystal) was applied.

The structure was solved by the heavy atom method and the non-hydrogen atoms refined anisotropically. The protons on the amide nitrogen atoms, N(16) and N(66), were located from a ΔF map and refined isotropically. The remaining hydrogen atoms were placed at idealised positions d(C–H) = 0.96 Å, assigned isotropic thermal parameters U(H) = $1.2U_{eq}$(C) and allowed to ride on their parent atoms.

Refinement was by block-cascade full-matrix least-squares and computations carried out on an Eclipse S140 computer using the SHELXTL program system [3]. Atomic scattering factors were from ref. 4. Fractional coordinates for the non-hydrogen atoms are given in Table 3. Table 4 gives the bond lengths and angles.

Results and discussion

In view of the limited amounts of the acridine-4-carboxamide ligands at our disposal we concentrated on the synthesis and characterisation of the rhodium(II) carboxylate complexes analogous to those [1] formed by the 9-substituted acridine ligands of type I. As well as conferring the potential advantage of combining two intercalating ring systems per molecule, this approach would afford the opportunity to compare any influence arising from the change in the substitution position (9 to 4) on the acridine ring.

After conversion from the hydrochloride salts to the free bases, all three ligands L readily formed good yields of pink or red solids of stoichiometry $Rh(RCO_2)_2L$ (R – CH_3, C_2H_5, CH_3OCH_2) when reac-

TABLE 1. Analytical data for the complexes

Complex	Analytical results					
	Found (%)			Calculated (%)		
	C	H	N	C	H	N
$Rh(CH_3CO_2)_2$(L2)	50.8	4.8	8.0	51.4	4.9	8.2
$Rh(CH_3CH_2CO_2)_2$(L2)	53.1	5.4	7.7	53.1	5.4	7.8
$Rh(CH_3OCH_2CO_2)_2$(L2)	50.1	4.0	6.7	50.2	5.1	7.3
$Rh(CH_3CO_2)_2$(L4)	52.7	5.3	7.7	53.1	5.3	7.7
$Rh(CH_3CH_2CO_2)_2$(L4)	54.4	5.8	7.4	54.7	5.8	7.4
$Rh(CH_3OCH_2CO_2)_2$(L4)	51.9	5.5	7.0	52.7	5.6	7.1
$Rh(CH_3CO_2)_2$(L6)	54.5	5.7	7.3	54.7	5.8	7.4
$Rh(CH_3CH_2CO_2)_2$(L6)	56.3	6.2	7.0	56.2	6.2	7.0
$Rh(CH_3OCH_2CO_2)_2$(L6)	53.5	6.0	6.6	53.3	5.9	6.7
$(L2H_2)[PtCl_4]$	34.0	3.1	6.4	34.2	3.4	6.7
$(L4H)_2[PtCl_4]$	48.0	4.9	8.3	48.9	4.9	8.6
$(L6H)_2[PtCl_4]$	50.7	5.1	7.9	50.9	5.4	8.1

TABLE 2. Summary of crystal data and intensity collection

Formula	$C_{52}H_{66}N_6O_{10}Rh_2$
M_r	1140.91
Crystal system	triclinic
Space group	$P\bar{1}$
a (Å)	8.149(1)
b (Å)	8.494(2)
c (Å)	37.647(10)
α (°)	92.49(2)
β (°)	95.45(2)
γ (°)	91.26(2)
Cell volume (Å^3)	2591(1)
Z	4 (2 crystallographically independent half molecules)
Crystal dimensions (mm)	$0.04\times0.05\times0.10$
Max. and min. transmission factors	0.690, 0.518
ρ (calc.) (g cm^{-3})	1.46
μ (calc.) (cm^{-1})	58
Radiation	Cu Kα
Unique reflections measured	6504
Reflections considered observed $[F_o]>3\sigma([F_o])$	5435
Weight $(G)^a$	0.00037
No. parameters varied	664
R	0.052
R_w	0.053

[a] $w^{-1}=\sigma^2(F)+GF^2$

TABLE 3. Atom coordinates ($\times10^4$) and temperature factors (Å$^2\times10^3$) for **1**

Atom	x	y	z	U_{eq}[a]
Rh(1)	4060(1)	4679(1)	215(1)	48(1)*
C(1)	6337(11)	−6834(10)	2906(2)	87(2)*
C(2)	5584(11)	−5723(11)	3088(2)	92(2)*
C(3)	5038(10)	−4358(10)	2923(2)	79(2)*
C(4)	5156(9)	−4099(9)	2579(2)	63(1)*
C(5)	6828(10)	−6013(9)	1458(2)	72(1)*
C(6)	7511(10)	−7110(10)	1253(2)	85(2)*
C(7)	8157(11)	−8468(10)	1396(2)	88(2)*
C(8)	8112(11)	−8741(9)	1749(2)	83(2)*
C(9)	7254(10)	−7801(9)	2335(2)	75(1)*
N(10)	6041(7)	−5112(7)	2019(2)	59(1)*
C(11)	7395(9)	−7626(9)	1972(2)	69(1)*
C(12)	6739(9)	−6214(8)	1826(2)	59(1)*
C(13)	6510(9)	−6669(9)	2537(2)	64(1)*
C(14)	5895(8)	−5290(8)	2372(2)	59(1)*
C(15)	4476(9)	−2572(9)	2442(2)	66(1)*
O(15)	3945(8)	−1602(7)	2648(2)	97(1)*
N(16)	4490(8)	−2369(7)	2098(2)	69(1)*
C(17)	3819(10)	−983(9)	1932(2)	77(2)*
C(18)	4016(11)	−1115(10)	1541(2)	87(2)*
C(19)	3166(12)	239(10)	1331(2)	93(2)*
C(20)	3526(11)	203(10)	941(2)	87(2)*
C(21)	2469(11)	1400(9)	721(2)	84(2)*
C(22)	2657(10)	2980(9)	876(2)	70(1)*
N(23)	2196(7)	4229(7)	638(1)	54(1)*
C(24)	2213(10)	5703(10)	860(2)	83(2)*
C(25)	562(9)	3981(10)	456(2)	76(1)*
O(26)	2658(6)	3485(5)	−188(1)	53(1)*
O(27)	2901(6)	6727(5)	100(1)	57(1)*
O(28)	5589(6)	5868(6)	592(1)	60(1)*
C(29)	6881(9)	6549(7)	497(2)	53(1)*
C(30)	7913(9)	7459(8)	787(2)	68(1)*
O(31)	5366(6)	2700(5)	306(1)	59(1)*
C(32)	6539(8)	2396(7)	127(2)	54(1)*
C(33)	7374(9)	866(8)	183(2)	69(1)*
Rh(2)	8885(1)	4592(1)	4780(1)	46(1)*
C(51)	11745(10)	−6598(10)	2093(2)	80(1)*
C(52)	11235(11)	−5345(10)	1908(2)	87(2)*
C(53)	10520(10)	−4052(10)	2072(2)	78(2)*
C(54)	10265(9)	−4019(8)	2425(2)	64(1)*
C(55)	10940(9)	−6453(9)	3546(2)	70(1)*
C(56)	11471(10)	−7674(10)	3746(2)	80(2)*
C(57)	12233(10)	−8980(10)	3601(2)	84(2)*
C(58)	12387(10)	−9101(10)	3250(2)	83(2)*
C(59)	12034(10)	−7888(9)	2658(2)	73(1)*
N(60)	10615(7)	−5311(7)	2983(2)	58(1)*
C(61)	11854(9)	−7864(8)	3027(2)	65(1)*
C(62)	11123(9)	6520(8)	3177(2)	60(1)*
C(63)	11542(9)	6631(9)	2463(2)	64(1)*
C(64)	10809(8)	5321(8)	2633(2)	56(1)*
C(65)	9457(10)	−2561(9)	2566(2)	71(1)*
O(65)	9114(8)	−1497(7)	2367(2)	103(1)*
N(66)	9124(8)	−2527(7)	2902(2)	69(1)*
C(67)	8295(10)	−1247(9)	3062(2)	77(1)*
C(68)	8255(11)	−1493(9)	3458(2)	86(2)*
C(69)	7291(12)	−226(10)	3655(2)	101(2)*
C(70)	7798(13)	−127(10)	4064(2)	99(2)*

(*continued*)

TABLE 3. (*continued*)

(*continued*)

TABLE 3 (*continued*)

Atom	*x*	*y*	*z*	U_{eq}[a]
C(71)	6851(11)	1145(10)	4263(2)	86(2)*
C(72)	6956(11)	2654(10)	4115(2)	85(2)*
N(73)	6668(7)	3977(7)	4347(1)	57(1)*
C(74)	5183(8)	3816(9)	4538(2)	64(1)*
C(75)	6514(11)	5355(11)	4126(2)	94(2)*
O(76)	10125(6)	5643(5)	4409(1)	57(1)*
O(77)	7792(5)	6663(5)	4891(1)	54(1)*
O(78)	7803(6)	3543(5)	5177(1)	56(1)*
C(79)	8524(8)	3645(7)	5489(2)	51(1)*
C(80)	7699(10)	2845(9)	5778(2)	73(1)*
O(81)	10128(6)	2586(5)	4693(1)	57(1)*
C(82)	11489(8)	2374(7)	4882(2)	48(1)*
C(83)	12307(9)	822(8)	4822(2)	67(1)*

[a]Starred items: equivalent isotropic U defined as one third of the trace of the orthogonalised U_{ij} tensor.

ted with the corresponding rhodium(II) carboxylate in methanol. From their stoichiometry, colours, and carboxylate (CO) stretching frequencies ($\nu_{as}(CO_2)$ 1611–1592, $\nu_s(CO_2)$ 1432–1412 cm^{-1}) these compounds clearly have the standard dinuclear rhodium(II) carboxylate structure with the acridine-4-carboxamide ligands coordinated to rhodium in the axial positions. Furthermore we have determined the structure of one member of the series, $[Rh(CH_3CO_2)_2(L6)]_2$ (**1**), by X-ray methods, (i) to permit a study of the spatial relationships of the acridine and rhodium moieties, (ii) to investigate the structural parameters of the ligand as a representative member of a new group of important anticancer drugs [2], and (iii) to determine the preferred stacking arrangements of the acridine units for comparison with those of the 9-substituted acridines described earlier [1].

TABLE 4. Bond lengths and angles for **1**[a]

Bond lengths (Å)

Molecule **A**

Rh(1)–N(23)	2.339(6)	Rh(1)–O(26)	2.031(4)
Rh(1)–O(27)	2.041(4)	Rh(1)–O(28)	2.018(4)
Rh(1)–O(31)	2.034(4)	Rh(1)–Rh(1′)	2.403(1)
C(1)–C(2)	1.337(12)	C(1)–C(13)	1.424(11)
C(2)–C(3)	1.401(12)	C(3)–C(4)	1.332(11)
C(4)–C(14)	1.429(10)	C(4)–C(15)	1.514(11)
C(5)–C(6)	1.347(12)	C(5)–C(12)	1.413(11)
C(6)–C(7)	1.389(12)	C(7)–C(8)	1.361(12)
C(8)–C(11)	1.412(11)	C(9)–C(11)	1.394(11)
C(9)–C(13)	1.386(11)	N(10)–C(12)	1.330(9)
N(10)–C(14)	1.363(9)	C(11)–C(12)	1.434(10)
C(13)–C(14)	1.426(10)	C(15)–O(15)	1.221(10)
C(15)–N(16)	1.318(10)	N(16)–C(17)	1.450(10)
C(17)–C(18)	1.496(12)	C(18)–C(19)	1.561(12)
C(19)–C(20)	1.524(13)	C(20)–C(21)	1.560(12)
C(21)–C(22)	1.438(11)	C(22)–N(23)	1.452(9)
N(23)–C(24)	1.475(10)	N(23)–C(25)	1.445(9)
O(26)–C(29′)	1.254(8)	O(27)–C(32′)	1.268(8)
O(28)–C(29)	1.279(9)	C(29)–C(30)	1.491(9)
C(29)–O(26′)	1.254(8)	O(31)–C(32)	1.247(8)
C(32)–C(33)	1.494(10)	C(32)–O(27′)	1.268(8)

Molecule **B**

Rh(2)–N(73)	2.349(5)	Rh(2)–O(76)	2.025(5)
Rh(2)–O(77)	2.035(4)	Rh(2)–O(78)	2.034(5)
Rh(2)–O(81)	2.031(4)	Rh(2)–Rh(2′)	2.407(1)
C(51)–C(52)	1.350(12)	C(51)–C(63)	1.419(11)
C(52)–C(53)	1.401(12)	C(53)–C(54)	1.365(11)
C(54)–C(64)	1.437(10)	C(54)–C(65)	1.515(11)
C(55)–C(56)	1.362(11)	C(55)–C(62)	1.410(11)
C(56)–C(57)	1.397(12)	C(57)–C(58)	1.340(13)
C(58)–C(61)	1.423(11)	C(59)–C(61)	1.410(11)
C(59)–C(63)	1.368(11)	N(60)–C(62)	1.337(9)
N(60)–C(64)	1.341(9)	C(61)–C(62)	1.419(10)

(*continued*)

TABLE 4 (*continued*)

Bond lengths (Å)			
C(63)–C(64)	1.430(10)	C(65)–O(65)	1.221(10)
C(65)–N(66)	1.316(11)	N(66)–C(67)	1.433(10)
C(67)–C(68)	1.519(12)	C(68)–C(69)	1.550(13)
C(69)–C(70)	1.557(12)	C(70)–C(71)	1.547(13)
C(71)–C(72)	1.423(12)	C(72)–N(73)	1.431(10)
N(73)–C(74)	1.471(9)	N(73)–C(75)	1.467(11)
O(76)–C(79′)	1.262(8)	O(77)–C(82′)	1.250(7)
O(78)–C(79)	1.263(8)	C(79)–C(80)	1.509(11)
C(79)–O(76′)	1.262(8)	O(81)–C(82)	1.279(8)
C(82)–C(83)	1.508(9)	C(82)–O(77′)	1.250(7)
Bond angles (°)			
Molecule A			
N(23)–Rh(1)–O(26)	94.1(2)	N(23)–Rh(1)–O(27)	89.0(2)
O(26)–Rh(1)–O(27)	91.3(2)	N(23)–Rh(1)–O(28)	90.1(2)
O(26)–Rh(1)–O(28)	175.8(2)	O(27)–Rh(1)–O(28)	89.6(2)
N(23)–Rh(1)–O(31)	95.6(2)	O(26)–Rh(1)–O(31)	89.4(2)
O(27)–Rh(1)–O(31)	175.3(2)	O(28)–Rh(1)–O(31)	89.4(2)
N(23)–Rh(1)–Rh(1′)	176.3(1)	O(26)–Rh(1)–Rh(1′)	87.5(1)
O(27)–Rh(1)–Rh(1′)	87.6(1)	O(28)–Rh(1)–Rh(1′)	88.4(1)
O(31)–Rh(1)–Rh(1′)	87.8(1)	C(2)–C(1)–C(13)	119.8(8)
C(1)–C(2)–C(3)	120.4(8)	C(2)–C(3)–C(4)	123.8(8)
C(3)–C(4)–C(14)	117.3(7)	C(3)–C(4)–C(15)	116.9(7)
C(14)–C(4)–C(15)	125.7(7)	C(6)–C(5)–C(12)	120.9(7)
C(5)–C(6)–C(7)	121.2(8)	C(6)–C(7)–C(8)	121.1(8)
C(7)–C(8)–C(11)	119.5(8)	C(11)–C(9)–C(13)	121.1(7)
C(12)–N(10)–C(14)	120.6(6)	C(8)–C(11)–C(9)	124.2(7)
C(8)–C(11)–C(12)	119.8(7)	C(9)–C(11)–C(12)	116.0(7)
C(5)–C(12)–N(10)	119.1(6)	C(5)–C(12)–C(11)	117.6(7)
N(10)–C(12)–C(11)	123.3(7)	C(1)–C(13)–C(9)	122.0(7)
C(1)–C(13)–C(14)	118.5(7)	C(9)–C(13)–C(14)	119.5(7)
C(4)–C(14)–N(10)	120.5(6)	C(4)–C(14)–C(13)	120.0(6)
N(10)–C(14)–C(13)	119.4(6)	C(4)–C(15)–O(15)	120.1(7)
C(4)–C(15)–N(16)	116.8(7)	O(15)–C(15)–N(16)	123.2(7)
C(15)–N(16)–C(17)	122.0(6)	N(16)–C(17)–C(18)	108.8(6)
C(17)–C(18)–C(19)	112.7(7)	C(18)–C(19)–C(20)	112.6(7)
C(19)–C(20)–C(21)	112.0(7)	C(20)–C(21)–C(22)	112.4(7)
C(21)–C(22)–N(23)	115.8(6)	Rh(1)–N(23)–C(22)	114.2(4)
Rh(1)–N(23)–C(24)	105.5(4)	C(22)–N(23)–C(24)	106.9(5)
Rh(1)–N(23)–C(25)	109.1(4)	C(22)–N(23)–C(25)	112.6(6)
C(24)–N(23)–C(25)	108.2(6)	Rh(1)–O(26)–C(29′)	119.3(4)
Rh(1)–O(27)–C(32′)	118.9(4)	Rh(1)–O(28)–C(29)	118.4(4)
O(28)–C(29)–C(30)	115.3(6)	O(28)–C(29)–O(26′)	126.3(6)
C(30)–C(29)–O(26′)	118.3(6)	Rh(1)–O(31)–C(32)	119.6(4)
O(31)–C(32)–C(33)	117.5(6)	O(31)–C(32)–O(27′)	125.9(6)
C(33)–C(32)–O(27′)	116.6(6)		
Molecule B			
		N(73)–Rh(2)–O(76)	90.3(2)
N(73)–Rh(2)–O(77)	88.4(2)	O(76)–Rh(2)–O(77)	90.0(2)
N(73)–Rh(2)–O(78)	94.0(2)	O(76)–Rh(2)–O(78)	175.7(2)
O(77)–Rh(2)–O(78)	91.0(2)	N(73)–Rh(2)–O(81)	95.9(2)
O(76)–Rh(2)–O(81)	89.3(2)	O(77)–Rh(2)–O(81)	175.7(2)
O(78)–Rh(2)–O(81)	89.3(2)	N(73)–Rh(2)–Rh(2′)	176.1(1)
O(76)–Rh(2)–Rh(2′)	88.2(1)	O(77)–Rh(2)–Rh(2′)	88.1(1)
O(78)–Rh(2)–Rh(2′)	87.6(1)	O(81)–Rh(2)–Rh(2′)	87.6(1)
C(52)–C(51)–C(63)	119.7(8)	C(51)–C(52)–C(53)	121.7(8)

(*continued*)

TABLE 4 (*continued*)

Bond lengths (Å)			
C(52)–C(53)–C(54)	121.5(8)	C(53)–C(54)–C(64)	118.5(7)
C(53)–C(54)–C(65)	116.0(7)	C(64)–C(54)–C(65)	125.5(7)
C(56)–C(55)–C(62)	119.0(7)	C(55)–C(56)–C(57)	122.6(8)
C(56)–C(57)–C(58)	119.9(8)	C(57)–C(58)–C(61)	120.1(8)
C(61)–C(59)–C(63)	119.8(7)	C(62)–N(60)–C(64)	120.2(6)
C(58)–C(61)–C(59)	123.1(7)	C(58)–C(61)–C(62)	119.7(7)
C(59)–C(61)–C(62)	117.3(7)	C(55)–C(62)–N(60)	118.7(6)
C(55)–C(62)–C(61)	118.7(7)	N(60)–C(62)–C(61)	122.6(7)
C(51)–C(63)–C(59)	121.3(7)	C(51)–C(63)–C(64)	119.1(7)
C(59)–C(63)–C(64)	119.6(7)	C(54)–C(64)–N(60)	120.1(6)
C(54)–C(64)–C(63)	119.4(7)	N(60)–C(64)–C(63)	120.5(6)
C(54)–C(65)–O(65)	119.6(7)	C(54)–C(65)–N(66)	117.4(7)
O(65)–C(65)–N(66)	123.0(7)	C(65)–N(66)–C(67)	122.7(7)
N(66)–C(67)–C(68)	109.4(6)	C(67)–C(68)–C(69)	113.9(7)
C(68)–C(69)–C(70)	112.2(7)	C(69)–C(70)–C(71)	112.5(7)
C(70)–C(71)–C(72)	113.0(8)	C(71)–C(72)–N(73)	116.1(7)
Rh(2)–N(73)–C(72)	113.4(4)	Rh(2)–N(73)–C(74)	107.0(4)
C(72)–N(73)–C(74)	114.5(6)	Rh(2)–N(73)–C(75)	105.5(4)
C(72)–N(73)–C(75)	107.0(6)	C(74)–N(73)–C(75)	109.0(6)
Rh(2)–O(76)–C(79′)	118.5(4)	Rh(2)–O(77)–C(82′)	119.0(4)
Rh(2)–O(78)–C(79)	118.6(4)	O(78)–C(79)–C(80)	117.5(6)
O(78)–C(79)–O(76′)	127.0(6)	C(80)–C(79)–O(76′)	115.5(6)
Rh(2)–O(81)–C(82)	119.0(4)	O(81)–C(82)–C(83)	116.8(5)
O(81)–C(82)–O(77′)	126.2(6)	C(83)–C(82)–O(77′)	117.0(6)

[a]In molecule **B** equivalent C, N, and O atoms have numbers 50+ those in molecule **A**.

The X-ray studies show that there are two crystallographically independent centrosymmetric molecules in the unit cell (molecules **A** and **B**) that do not differ significantly in their molecular geometries. Their bond lengths and angles are given in Table 4. The molecular structure of **A** is shown in Fig. 1.

The acridine ligand L6 binds to the rhodium via the terminal NMe_2 groups. The geometry of the $Rh_2(CH_3CO_2)_4$ cage in **1** is very similar to that of the analogous complex with 6-chloro-9-(2-dimethylaminoethyl)amino-2-methoxyacridine (**2**) [1]. The Rh–Rh bonds are 2.403(1) and 2.407(1) Å in **A** and **B**, respectively (cf. 2.409 Å in **2**). The Rh–O bond lengths in molecules **A** and **B** are in the range 2.018(4)–2.041(4) Å, cf. 2.038(3)–2.047(3) Å in **2**. The Rh–N bonds are 2.339(6) (**A**) and 2.349(5) (**B**) Å, cf. 2.344(3) Å in **2**. The axial N–Rh–Rh′–N′ chain is again very nearly linear, with NRhRh′ angles of 176.3(1)° (**A**) and 176.1(1)° (**B**).

The conformation of the diamine side chain immediately adjacent to the rhodium centre is very similar to that displayed by **2**, with a retention of an *anti* geometry about the C(21)–C(22) bond. The remainder of the side chain from C(21) to the acridine carbon atom C(4) is essentially planar and *anti*, and is rotated by *c.* 54° about the C(20)–C(21) bond, relative to the C(20)–N(23) chain. Furthermore, as

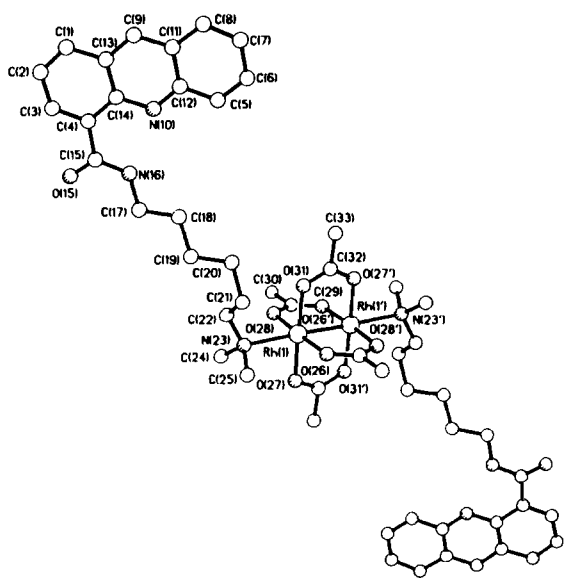


Fig. 1. Molecular structure of $\{Rh(CH_3CO_2)_2[N\text{-}(2\text{-dimethylamino})hexyl]acridine\text{-}4\text{-}carboxamide\}_2$ (molecule **A**), showing the crystallographic numbering scheme.

a consequence of the formation of an intramolecular N–H···N hydrogen bond (2.69 Å) between the amide nitrogen atom N(16) and the acridine nitrogen atom N(10), the ring is held essentially co-

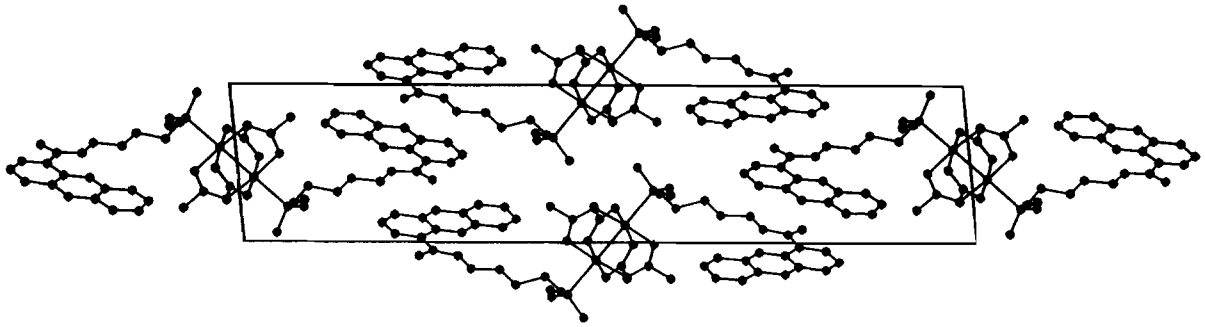
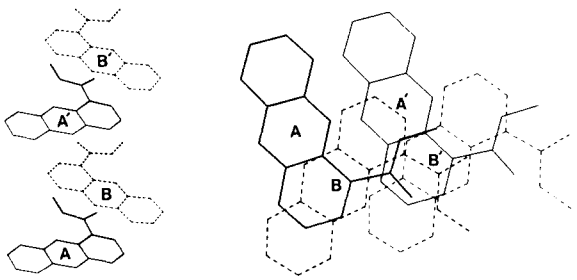


Fig. 2. The packing of molecules **A** and **B** in the crystal, viewed down the *b* direction.



(a) (b)

Fig. 3. Elevation (a) and plan (b) views of part of the continuous, alternately rotated, stacked acridine rings. The stacking sequence is shown, where **A** and **B** refer to molecules **A** and **B**, and **A'** and **B'** their lattice-translated counterparts in the *a* direction.

planar with the C(4)–C(21) side chain [C(14)–C(4)–C(15)–N(16) torsion angle 3.9(11)°].

The effect of this combination of an essentially all *anti* geometry for the side chain and its co-planarity with the acridine unit is to distance the ring from the rhodium acetate cage [Rh(1)····N(10) 11.0 Å; Rh(2)····N(60) 10.8 Å]. Retention of this arrangement in solution should permit intercalation of the acridine unit without undue hindrance from the rhodium carboxylate moiety. (Acridine····acridine distances are: N(10)····N(10') 23.4 Å in **A**, and N(60)····N(60') 22.8 Å in **B**.)

Figure 2 shows the packing of the molecules in the crystal viewed down the *b* direction. As can be seen, the distancing of the acridine units from the rhodium centres permits stacking of the acridine rings. The nature of the stacking differs from that observed [1] in **2**, where there is a co-alignment of the three-ring axis within the stack. In **1** a continuous stacked arrangement also exists, though with adjacent rings within each stack rotated by *c*. 60° in an alternating fashion (Fig. 3a, b). The interplanar spacing within each stack is *c*. 3.6 Å.

Until quite recently, compounds containing the $PtCl_4^{2-}$ ion or other anionic platinum species were generally regarded as not possessing significant anti-cancer activity. However Teicher and co-workers have reported [5, 6] that the compound [Rhodamine 123]$_2$[$PtCl_4$]·$4H_2O$ possesses *in vivo* anti-cancer and radiosensitizer activity in mice, showing that such activity for anionic platinum complexes may depend crucially on the nature of the cation. As the active, intercalating forms of the anti-tumour acridine-4-carboxamide ligands, **II**, are cations [2] under physiological conditions, we have prepared their $PtCl_4^{2-}$ derivatives. These were readily isolated from aqueous solution as yellow solids of stoichiometries (L2H$_2$)[$PtCl_4$], (L4H)$_2$[$PtCl_4$] and (L6H)$_2$[$PtCl_4$], respectively. Unfortunately, their very low solubility in water militates against their value as anti-cancer agents, so the incorporation of functional groups to improve aqueous solubility merits attention.

Acknowledgements

We thank the S.E.R.C. for Research Studentships to C.A.O'M and C.J.P., Johnson Matthey plc for loans of rhodium trichloride and K_2PtCl_4, and Professor W. A. Denny for the generous gift of the acridine-4-carboxamides.

References

1 D. M. L. Goodgame, C. J. Page and D. J. Williams, *Inorg. Chim. Acta, 153* (1988) 219.
2 G. J. Atwell, G. W. Rewcastle, B. C. Baguley, and W. A. Denny, *J. Med. Chem., 30* (1987) 664.
3 G. M. Sheldrick, *SHELXTL (revision 4.1)*, an integrated system for solving, refining, and displaying crystal structures from diffraction data, university of Gottingen, F.R.G., 1983.
4 *International Tables for X-ray Crystallography*, Vol. IV, Kynoch Press, Birmingham, 1974.
5 M. J. Abrams, D. H. Picker, P. H. Fackler, C. J. L. Lock, H. E. Howard-Lock, R. Faggiani, B. A. Teicher, and R. C. Richmond, *Inorg. Chem., 25* (1986) 3980.
6 B. A. Teicher and S. A. Holden, *Radiat. Res., 109* (1987) 58.