Interactions between Phenothiazine Drugs and Metal Ions. Part 1. Palladium(II) and Platinum(II) Complexes. Crystal and Molecular Structure of Protonated Trichloro[10-(2'-dimethylaminopropyl)phenothiazine-*S*]palladium(II)

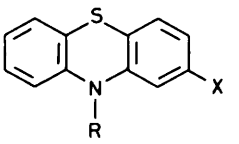
By **William J. Geary, Nigel J. Mason, Ian W. Nowell,** and **Leslie A. Nixon,** Chemistry Department, Sheffield City Polytechnic, Pond Street, Sheffield S1 1WB

Phenothiazine drugs form complexes with Pd^{II} and Pt^{II} of unusual stoicheiometry, *i.e.* $[MLX_3]$ (L = protonated drug; X = Cl or Br; M = Pd or Pt). The structure of the promethazine complex with Pd^{II} has been elucidated by single-crystal *X*-ray crystallography. Crystals are monoclinic, space group $P2_1$, $Z = 2$, in a unit cell with lattice parameters $a = 11.381(5)$, $b = 9.791(4)$, $c = 9.098(4)$ Å, $\beta = 100.85(5)°$. The structure has been solved using heavy-atom methods and refined by least squares to R 0.036 (R' 0.039) for 1 524 independent reflections collected by counter methods. The drug is sulphur-bonded to a $PdCl_3^-$ unit, the counter ion being a protonated nitrogen on the drug substituent. The side chain adopts an unusual conformation bending back over the heterocycle in order to facilitate intramolecular hydrogen bonding between the protonated nitrogen and one of the chlorine atoms on the palladium. Proton n.m.r. and solution i.r. data support the existence of this hydrogen bonding in solution. Electronic spectral data both from this work and the literature show that the interaction observed for the above complex is seen for all phenothiazine drugs so far examined. Far-i.r. data confirm the similarity of the equivalent platinum(II) compounds.

PHENOTHIAZINE drugs are versatile anticholinergic [1] and antihistamine compounds. Metal-ion interactions with the drugs and with the parent heterocycle have been extensively studied both *in vivo* [2] and *in vitro*.[3] However, few genuine co-ordination complexes have been isolated. Those reported have been poorly characterised [4] or assigned erroneous structures.[5]

The interactions usually observed between metal ions and drugs of this type involve oxidation of the drug molecule *via* a free-radical mechanism,[6] or salt formation involving protonation of the phenothiazine drug.[7]

As part [8] of a study of phenothiazine–metal ion interactions we present here the results of an investigation with bivalent palladium and platinum and a variety of typical phenothiazine drugs. The structures of these complexes are useful in rationalizing the solution chemistry and spectra of these interactions, both those reported here and in the literature.



Ligand and abbreviation		R	X
Phenothiazine	ptz	H	H
N-Ethylphenothiazine	eptz	CH_2CH_3	H
N-Dimethylcarbamoylphenothiazine	dptz	$CONMe_2$	H
Promethazine hydrochloride	pmzH·Cl	$CH_2CH(Me)NHMe_2^+$ Cl^-	H
Chlorpromazine hydrochloride	cpzH·Cl	$CH_2CH_2CH_2NHMe_2^+$ Cl^-	Cl
Thioridazine hydrochloride	tdzH·Cl	$CH_2CH_2CH(CH_3)CH_2CH_2NHMe^+$ Cl^-	SCH_3

RESULTS AND DISCUSSION

On the basis of the data presented here the complexes fall into two categories, the parent heterocycle and related ligands leading to complexes $[ML_2X_2]$ whereas those ligands showing drug activity [and having a quaternary nitrogen on the N(10) side chain] lead to complexes $[MLX_3]$. The latter complexes have a novel structure in which the side chain plays an important part. Details of the complexes are given in Table 1.

Complexes of 2 : 1 *Stoicheiometry*.—The reaction scheme for these complexes is as in equation (1) where

$$K_2[MX_4] + 2L \longrightarrow [ML_2X_2] + 2KX \quad (1)$$

M = Pd, L = ptz, eptz, or dptz, X = Cl; M = Pt, L = ptz, X = Cl or Br.

From previous work [9] it seemed likely that the heterocyclic sulphur was solely involved in co-ordination and to maximise the overlap of metal *d* orbitals with those on the sulphur a *cis* configuration would be expected, giving rise to two M–S stretching modes and two M–X stretching modes in the far-i.r. spectra of these complexes. In the spectrum of $[Pt(ptz)_2Br_2]$ there are two strong bands (Pt–Br str.) at 220 and 250 cm^{-1}, and two slightly weaker bands (Pt–S str.) at 305 and 315 cm^{-1}, thus confirming the complex is of *cis* configuration with the heterocycle *S*-bonded to the platinum. The far-i.r. spectra of $[Pt(ptz)_2Cl_2]$ and $[Pd(ptz)_2Cl_2]$ are complicated by the overlap of the metal–halogen and metal–sulphur bands, showing bands at 303 and 327 cm^{-1} in the case of the platinum complex and at 288 and 322 cm^{-1} in the case of the palladium complex.

The proton n.m.r. spectrum of phenothiazine shows only two bands, a multiplet around δ 7—8 attributed to

TABLE 1

Physical data for the complexes

Complex	M.p. (θ_c/°C) [a]	$\lambda_{max.}$/nm	Elemental analysis (%) [b] Formula	C	H	N
$[Pd(ptz)_2Cl_2]$	280—290	515	$C_{24}H_{18}Cl_2N_2PdS_2$	49.8 (50.05)	3.25 (3.15)	4.90 (4.85)
$[Pd(eptz)_2Cl_2]$	260—270	500	$C_{28}H_{26}Cl_2N_2PdS_2$	52.6 (53.2)	4.05 (4.15)	4.30 (4.45)
$[Pd(dptz)_2Cl_2]$	265—270	510	$C_{30}H_{28}Cl_2N_4O_2PdS_2$	50.2 (50.2)	4.05 (3.95)	7.75 (7.80)
$[Pd(cpzH)Cl_3]$	250—260	432	$C_{17}H_{20}Cl_4N_2PdS$	38.25 (38.35)	3.75 (3.80)	5.20 (5.25)
$[Pd(pmzH)Cl_3]$	260—270	434	$C_{17}H_{21}Cl_3N_2PdS$	40.7 (41.0)	4.10 (4.25)	5.55 (5.60)
$[Pd(tdzH)Cl_3]$	250—260	435	$C_{21}H_{27}Cl_3N_2PdS_2$	43.2 (43.15)	4.80 (4.65)	4.70 (4.80)
$[Pt(ptz)_2Cl_2]$	280—290	430	$C_{24}H_{18}Cl_2N_2PtS_2$	42.45 (43.4)	2.80 (2.75)	3.80 (4.20)
$[Pt(cpzH)Cl_3]$	300—310	*c*	$C_{17}H_{20}Cl_4N_2PtS$	32.8 (32.85)	3.45 (3.25)	4.40 (4.50)
$[Pt(pmzH)Cl_3]$	290—300	*c*	$C_{17}H_{21}Cl_3N_2PtS$	34.75 (34.8)	3.80 (3.60)	4.55 (4.75)
$[Pt(tdzH)Cl_3]$	300—310	*c*	$C_{21}H_{27}Cl_3N_2PtS_2$	37.25 (37.5)	3.75 (4.05)	4.15 (4.15)

[a] All compounds decomposed before melting. [b] Calculated values are given in parentheses. [c] It was not possible to measure the visible spectra accurately due to overlap of the u.v. band for the heterocycle.

the aromatic protons and a singlet at δ 8.5 attributed to the secondary amine proton. The chemical shift of these signals in $[^2H_6]$dmso (dmso = dimethyl sulphoxide) is not significantly altered upon co-ordination: this aspect is receiving more detailed study but preliminary evidence suggests decomposition of the complexes in $[^2H_6]$dmso. The N–H stretching band in the i.r. is shifted from 3 350 to 3 310 cm^{-1} upon complexation. This small shift is presumably due to the change in available intermolecular N–H · · · S hydrogen bonding upon complex formation. The other ligands (dptz and eptz) form complexes of the same colour and stoicheiometry as those found for phenothiazine itself and from the similarity of the visible spectra it seems reasonable to assign a *cis* square-planar structure to these also.

Complexes of 1 : 1 *Stoicheiometry*.—The reaction scheme for these complexes is as in equation (2) where M = Pd,

$$K_2[MX_4] + LH{\cdot}Cl \longrightarrow [M(LH)X_3] + KCl + KX \quad (2)$$

L = pmz, cpz, or tdz, X = Cl or Br; M = Pt, L = pmz, cpz, or tdz, X = Cl.

The drugs were used as their hydrochloride salts, the site of protonation being the exocyclic nitrogen. Upon complexation the drug remains protonated, the counter ion being the MX_3^- system. The far-i.r. spectra of the complexes are summarised in Table 2. The system

TABLE 2

Infrared absorption bands * (250—400 cm^{-1}) of solid dispersions in polyethylene

MX_3 M	MX_3 X	Metal–ligand stretch	MX_2 asym. str. B_1	MX_2 sym. str. A_1	MX (*trans* to L) str. *A*
Pd	Cl	324(3)	348(10)	297 (sh)	308(9)
Pd	Br	324(4)	263 (sh)	253(8)	230(10)
Pt	Cl		327(10)	258 (sh)	317(10)
Pt	Br		263 (sh)	256(7)	230(10)

* Relative intensities are given in parentheses.

MX_3^- has been investigated before [10] and the assignments used in Table 2 are based on this previous work. In the case of the MCl_3^- systems (M = Pd or Pt) it was not possible to assign the metal–ligand stretch because of the overlap of the M–Cl and M–S bands. The spectra are not significantly affected by the different N(10) and 2-position substituents.

The complexes were found to be soluble in dimethyl formamide (dmf) and dmso. The ^1H n.m.r. spectra of the complexes (recorded in $[^2H_6]$dmso at 220 MHz) were identical to those of the parent drug except that the methyl groups of the quaternary nitrogen were shifted downfield by *ca.* 0.1 p.p.m. The magnitude of this shift can be attributed to decomposition of the complex in dmso, and indeed preliminary studies in $[^2H_7]$dmf indicate significant shifts upon complexation of the type expected if the quaternary nitrogen was interacting with the MX_3^- system.

The interaction most likely to take place between the quaternary nitrogen and the metal halide anion is one of hydrogen bonding. This can be observed in the i.r. spectra of both the complexes and the drugs. In the drugs the $\overset{+}{N}$–H · · · Cl interaction is observed as a broad strong band at 2 500—2 800 cm^{-1} [11] when measured both as a solid dispersion in KBr discs and as a solution in dmf or dmso. Upon complexation the intensity of this band diminishes and moves to 2 800—3 200 cm^{-1} indicating a slight weakening in the hydrogen bonding. No other changes of significance in the i.r. region are seen upon complexation.

The visible spectra of the complexes consist of a single strong band (ε <3 000 $dm^3\ mol^{-1}\ cm^{-1}$) the positions of

TABLE 3

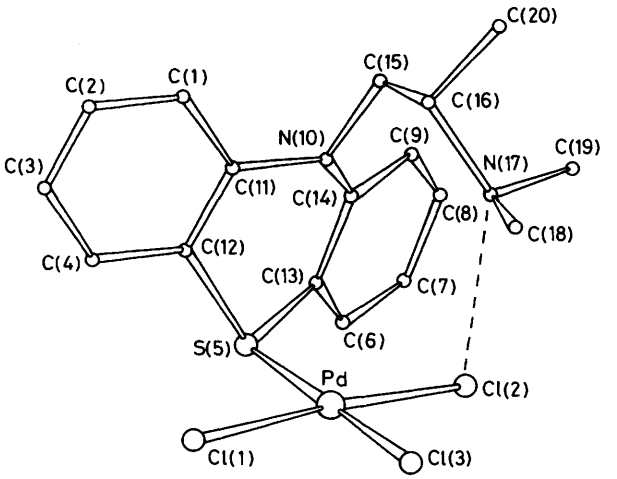
Visible spectral data for phenothiazine derivatives with M = Pd^{II} in aqueous solution from the literature

Ligand	L : M ratio	$\lambda_{max.}$/nm	Ref.
ptz	2 : 1	600	*a*
ptz	2 : 1	550	*b*
pmzH·Cl	1 : 1	495	9, *c*, *d*
cpzH·Cl	1 : 1	495	*c*, *e*
tdzH·Cl	1 : 1	490	*f*

[a] H. S. Gowda and B. Keshavan, *Mikrochim. Acta*, 1975, 437. [b] L. G. Overholser and J. H. Yoe, *Ind. Eng. Chem. Anal. Ed.*, 1942, **14**, 647. [c] L. Cavatorta, *J. Pharmacol.*, 1959, **11**, 49. [d] H. S. Gowda and B. Keshavan, *Indian J. Chem., Sect. A*, 1976, **14**, 293. [e] A. Farago, *Arch. Kriminol.*, 1967, **139**, 161; H. S. Gowda and B. Keshavan, *Fresenius' Z. Anal. Chem.*, 1975, **273**, 31; Kum-Tatt Lee and Ai-Mee Seet, *Mikrochim. Acta*, 1974, 955; J. A. Munoz Leyva and D. P. Bendito, *Quim. Anal.*, 1976, **30**, 76; M. Tarasiewicz, *Zesz. Nauk. Politech. Bialostochiej. (Ser) Nat. Fiz. Chem.*, 1976, **2**, 111. [f] H. S. Gowda, P. G. Ramappa, and B. N. Achar, *Fresenius' Z. Anal. Chem.*, 1975, **275**, 127.

which are listed in Table 1. These spectra fall into two distinct classes, the 2 : 1 non-drug complexes absorbing at 550 nm and the 1 : 1 drug complexes absorbing at 480 nm. This distinction is also noted in Table 3 which lists the relevant data from the literature. The values given in Table 3 differ from the values in Table 1, presumably because the latter were obtained as dmf solutions whilst the former were obtained in aqueous or aqueous ethanolic solutions. However, the distinction between the two classes is observed in both Tables. Thus the drugs, including types not investigated in this work,[5] all absorb, upon complexation, at the same wavelength and are all complexed with Pd^{II} in the same way.

Crystal Structure of [Pd(pmzH)Cl_3].—The protonated promethazine ligand is found to be sulphur-co-ordinated to $PdCl_3$ (Figure), such that the resulting $PdCl_3S$ unit is



Molecular structure of [Pd(pmzH)Cl_3]. For clarity all hydrogen atoms have been omitted and only one set of the disordered carbon atoms attached to N(17) is included

effectively planar and angles around Pd range from 86.4 to 92.2°. The promethazine ring system is both ' tilted ' and ' twisted ' with respect to the $PdCl_3S$ plane, with the Pd–S(5)–N(10) bond angle and the N(10)–S(5)–Pd–Cl(2) torsion angle being 90.1 and 68.5° respectively. The geometry within the fused ring system is similar to that in promethazine itself,[12] with the C_6 rings being planar and inclined at an angle of 41.3° to each other. However, in contrast to the uncomplexed ligand, the side chain in the present complex is bent back over the heterocycle in an unusual '*scorpion*' conformation. Such an arrangement appears to facilitate intramolecular hydrogen bonding and the Cl(2) · · · N(17) distance of 3.17 Å indicates the interaction to be strong. Although not included in the least-squares refinement, a peak was located near N(17) consistent with a proton attached to a quaternary nitrogen and directed towards the $PdCl_3$ unit [Cl(2) · · · H 2.34 Å]. Although the scorpion configuration does facilitate this strong intramolecular hydrogen bonding, the latter interaction does not appear to be the driving force for the orientation adopted by the promethazine ring system. Certainly the tilt of the latter with respect to the $PdCl_3S$ plane can be better attributed to the apparent use of the sp^3 orbitals by the sulphur in its σ interaction with the palladium. The deviation of the Cl(2)–Pd–S(5)–N(10) torsion angle from the expected value of 90° is more difficult to rationalise but may reflect an attempt to maximise overlap between *d* orbitals on the sulphur and palladium. In addition, in the related [Pd(cpzH)Cl_3] complex, we find the ring system adopts a similar orientation, yet the hydrogen bonding involves both intra- and inter-molecular N^+–H · · · Cl interactions.[13]

Conclusion.—The *X*-ray crystal structure confirms conclusively the different structural characteristics of the complexes of phenothiazine-based drugs compared to those of the parent heterocycle, and in particular shows the importance and novel influence of the side chain.

Whereas the parent heterocycle and related ligands lead to complexes with a 1 : 2 : 2 metal–ligand–halogen ratio, the ligand being bonded only through the heterocyclic sulphur, the drugs yield complexes with a 1 : 1 : 3 metal–ligand–halogen ratio. In addition to metal–sulphur bonding, the structure involves a type of zwitterion with the negative charge located on the MCl_3 unit and the positive charge on the quaternary nitrogen of the N(10) side chain, the two centres interacting by intramolecular hydrogen bonding.

These structural data lend strong support to the distinctions drawn earlier between the solution properties of the two sets of complexes, and in particular the difference in the visible spectra.

We also note that although in thioridazine the substituent at the 2-position is a sulphur atom, we find no evidence that this is implicated in any way in co-ordination.

This work has been limited to three types of phenothiazine drugs; evidence from the literature [5] indicates that those with a piperazine N(10) side chain (*e.g.* fluphenazine) also react in the same way, indeed all palladium(II) phenothiazine drug interactions published (>20) show the same reactions as those seen here. The far-i.r. evidence confirms the structural similarity of the platinum complexes to the palladium complex.

EXPERIMENTAL

Ligands.—The drugs were supplied by May and Baker Ltd. and by Sandoz Ltd. as the hydrochloride salts. Two of the ligands were synthesised as follows, the remainder being commercially available.

N-Ethylphenothiazine (eptz).—Potassium hydroxide (0.4 mol, 22.4 g) was added to dimethyl sulphoxide (200 cm^3) with stirring (5 min). Phenothiazine (Aldrich) (0.1 mol, 20 g) was then added to the mixture with stirring (45 min) followed by the addition of iodoethane (0.2 mol, 31.18 g) over 45 min with cooling and stirring. Water (200 cm^3) was added and the mixture extracted with diethyl ether (3 × 100 cm^3). Each extract was washed with water (3 × 50 cm^3). The ether solution was dried over solid $CaCl_2$ and the solvent removed under reduced pressure. Yield 13.5 g (58.9%). M.p. 101—103 °C (lit.,[14] 103—104 °C) (Found: C, 73.8; H, 5.65; N, 6.25. Calc. for $C_{14}H_{13}NS$: C, 73.95; H, 5.75; N, 6.15%).

N-Dimethylcarbamoylphenothiazine (*dptz*). *N*-Chloroformylphenothiazine (Aldrich) (0.1 mol, 26 g) was weighed into a 250-cm³ round-bottom flask. A liquid-nitrogen condenser was fitted to the top of the flask and dimethylamine (0.4 mol, 18 g) added. The mixture was allowed to reflux at room temperature for 4 h and the unreacted dimethylamine was then boiled off. The product was recrystallised from ethyl acetate–hexane (50 : 50 v/v). Yield 17.6 g (65%). M.p. 95—96 °C (Found: C, 66.5; H, 5.30; N, 10.3. Calc. for $C_{15}H_{15}N_2OS$: C, 66.4; H, 5.55; N, 10.35%).

Complexes with a 2 : 1 *Stoicheiometry*.—All complexes of 2 : 1 stoicheiometry involve ligands insoluble in water. They were prepared by mixing aqueous solutions of $K_2[MCl_4]$ with ethanolic solutions of the ligand (L) in a 1 : 2 mol ratio. This gave a green (L = ptz) or pink (L = dptz or eptz) precipitate which turned blue (M = Pd) or red (M = Pt) over a period of 5 min, the original precipitate being the water-insoluble ligand which subsequently reacts forming the complex. The precipitate was filtered off, washed with acetone, and dried *in vacuo* at 100 °C.

TABLE 4

Final atomic parameters ($\times 10^5$ for Pd; $\times 10^4$ for other atoms) with estimated standard deviations in parentheses for non-hydrogen atoms

Atom	*x*	*y*	*z*
Pd	24 447(5)	25 000	42 418(6)
Cl(1)	2 890(2)	4 338(3)	2 885(3)
Cl(2)	2 175(3)	555(3)	5 522(3)
Cl(3)	821(2)	1 940(4)	2 374(2)
S(5)	4 001(2)	3 200(3)	6 072(2)
C(1)	3 126(9)	1 795(13)	9 863(10)
H(1)	2 502	2 026	10 588
C(2)	3 911(11)	711(15)	10 221(13)
H(2)	3 864	79	11 181
C(3)	4 762(11)	439(15)	9 330(13)
H(3)	5 380	−401	9 603
C(4)	4 806(9)	1 247(15)	8 117(13)
H(4)	5 471	1 050	7 439
C(6)	4 095(9)	5 989(13)	6 221(11)
H(6)	4 753	5 911	5 512
C(7)	3 764(10)	7 244(14)	6 663(13)
H(7)	4 145	8 163	6 292
C(8)	2 929(10)	7 316(15)	7 589(13)
H(8)	2 680	8 305	7 960
C(9)	2 411(9)	6 167(12)	8 048(11)
H(9)	1 735	6 263	8 732
C(11)	3 117(6)	2 594(16)	8 602(8)
C(12)	4 008(7)	2 302(14)	7 747(9)
C(13)	3 579(7)	4 810(12)	6 689(10)
C(14)	2 751(7)	4 879(10)	7 643(9)
N(10)	2 306(6)	3 653(9)	8 164(8)
C(15)	1 182(8)	3 736(12)	8 821(11)
C(16A)	121(16)	3 480(24)	7 829(21)
C(16B)	329(12)	2 487(32)	8 394(15)
N(17)	181(6)	2 086(10)	6 909(11)
C(18A)	−735(20)	2 081(27)	5 654(25)
C(18B)	−323(30)	3 287(44)	5 686(36)
C(19A)	131(23)	872(34)	8 038(29)
C(19B)	−488(36)	858(52)	6 264(44)
C(20)	−948(11)	3 251(26)	8 674(17)

Complexes with a 1 : 1 *Stoicheiometry*.—These all involved ligands that are drug hydrochlorides and soluble in water. The reaction was carried out by mixing aqueous solutions of ligand (0.1 mol dm^{-3}) and $K_2[MCl_4]$. This gave a yellow (M = Pt) or a purple precipitate (M = Pd) which was filtered off, washed with water, and dried *in vacuo* at 100 °C. The complexes $[Pd(LH)Cl_3]$ (L = pmz or cpz) were recrystallised from dmf.

Instrumental Techniques.—Infrared spectra were obtained from KBr discs at 2% concentration using a Pye Unicam SP 1200 spectrophotometer calibrated with polystyrene at 1 600 cm^{-1}. Proton magnetic resonance spectra were obtained from solutions in $[^2H_7]$dmf or $[^2H_6]$dmso using a Hitachi–Perkin-Elmer FT 30 instrument. Visible spectra were obtained from dmf solutions using a Pye Unicam SP 800 spectrophotometer, far-i.r. spectra from pressed Polythene discs at 30% concentration using a Beckman FS 720 instrument.

Crystal Data.—$C_{17}H_{21}Cl_3N_2PdS$, $M = 498.21$, Monoclinic, space group $P2_1$, $a = 11.381(5)$, $b = 9.791(4)$, $c = 9.098(4)$ Å, $\beta = 100.85(5)°$, $U = 995.76$ Å³, $\lambda = 0.710\,69$ Å, $D_m = 1.67$, $Z = 2$, $D_c = 1.69$ Mg m^{-3}, μ(Mo-K_α) = 1.32 mm^{-1}, $F(000) = 500$.

X-*Ray Intensity Measurements*.—A crystal of approximate dimensions 0.47 × 0.32 × 0.08 mm was mounted with the *b* axis coincident with the ω axis of a Stöe Stadi 2 two-circle diffractometer. Data were collected using monochromated Mo-K_α radiation and the background–ω scan–background technique. Corrections for Lorentz and polarisation effects were applied but not for absorption. Of the 1 790 unique reflections collected, 1 524 had $I > 3.0\sigma(I)$ and were used in the subsequent structure analysis.

Structure Determination and Refinement.—While systematic absences do not distinguish between space groups $P2_1$ and $P2_1/m$, in the centrosymmetric space group $Z = 2$ requires the molecules to possess mirror symmetry. Subsequent analysis confirmed $P2_1$ to be the correct space group,

TABLE 5

Bond distances (Å) and angles (°) with estimated standard deviations in parentheses

(*a*) Bond distances

Pd–Cl(1)	2.292(3)	C(7)–C(8)	1.386(18)
Pd–Cl(2)	2.283(3)	C(8)–C(9)	1.372(25)
Pd–Cl(3)	2.328(2)	C(9)–C(14)	1.389(15)
Pd–S(5)	2.296(2)	C(13)–C(14)	1.397(13)
C(12)–S(5)	1.758(10)	C(6)–C(13)	1.397(16)
C(13)–S(5)	1.771(11)	C(11)–N(10)	1.396(15)
C(1)–C(11)	1.387(15)	C(14)–N(10)	1.418(13)
C(1)–C(2)	1.386(18)	N(10)–C(15)	1.515(12)
C(2)–C(3)	1.400(19)	C(15)–C(16)	1.35 *
C(3)–C(4)	1.367(18)	C(16)–C(20)	1.63 *
C(4)–C(12)	1.375(17)	C(16)–N(17)	1.50 *
C(11)–C(12)	1.418(12)	N(17)–C(18)	1.52 *
C(6)–C(7)	1.367(18)	N(17)–C(19)	1.53 *

(*b*) Bond angles

Cl(1)–Pd–Cl(2)	173.8(1)	C(11)–N(10)–C(14)	117.7(7)
Cl(1)–Pd–Cl(3)	91.0(1)	C(11)–N(10)–C(15)	119.3(8)
Cl(1)–Pd–S(5)	86.4(1)	C(14)–N(10)–C(15)	117.9(8)
Cl(2)–Pd–Cl(3)	90.6(1)	N(10)–C(14)–C(9)	123.0(8)
Cl(2)–Pd–S(5)	92.2(1)	N(10)–C(14)–C(13)	119.5(9)
Cl(3)–Pd–S(5)	176.2(1)	C(9)–C(14)–C(13)	117.6(9)
Pd–S(5)–C(12)	110.9(3)	C(8)–C(9)–C(14)	120.4(10)
Pd–S(5)–C(13)	106.1(3)	C(7)–C(8)–C(9)	121.8(13)
C(12)–S(5)–C(13)	97.3(5)	C(6)–C(7)–C(8)	118.8(12)
S(5)–C(12)–C(4)	118.9(8)	C(7)–C(6)–C(13)	119.9(10)
S(5)–C(12)–C(11)	119.8(8)	C(6)–C(13)–S(5)	119.0(8)
C(4)–C(12)–C(11)	121.6(10)	C(6)–C(13)–C(14)	121.4(10)
C(3)–C(4)–C(12)	120.7(11)	S(5)–C(13)–C(14)	119.6(8)
C(2)–C(3)–C(4)	119.5(12)	N(10)–C(15)–C(16)	114.3 *
C(1)–C(2)–C(3)	119.7(11)	C(15)–C(16)–N(17)	113.4 *
C(2)–C(1)–C(11)	120.0(10)	C(15)–C(16)–C(20)	104.4 *
C(1)–C(11)–N(10)	123.8(9)	N(17)–C(16)–C(20)	106.5 *
C(1)–C(11)–C(12)	116.4(11)	C(16)–N(17)–C(18)	112.1 *
N(10)–C(11)–C(12)	119.7(9)	C(16)–N(17)–C(19)	116.0 *
		C(18)–N(17)–C(19)	108.9 *

* C(16), C(18), and C(19) are disordered and average values are given for the bond distances and angles associated with these atoms.

with the two molecules occupying general positions. Interpretation of a three-dimensional Patterson map readily afforded the x and z co-ordinates of the palladium atom. Successive difference electron-density maps revealed the remaining atoms and showed the N(10) side chain to be partially disordered. Alternative positions were found for each of the carbon atoms C(16), C(18), C(19) and satisfactory refinement was achieved by the inclusion of carbon atoms having an occupancy factor of 0.50 at each position. Only the hydrogen atoms of the C_6 rings could be satisfactorily located and were included in positions calculated from the geometry of the molecule (C–H 1.08 Å). A common isotropic thermal parameter was applied to the located hydrogen atoms and refined to a final value of $U = 0.085(85)$ Å^2. Scattering factors were calculated [15] using an analytical approximation and the weighting scheme adopted was $w = 0.2622/[\sigma^2(F_o) + 0.0044(F_o)^2]$. Full-matrix refinement with isotropic thermal parameters for the disordered carbon atoms and with anisotropic thermal parameters for all other non-hydrogen atoms gave the final $R = 0.036$ and $R' = 0.039$. Final atomic parameters are given in Table 4, bond distances and angles in Table 5. Lists of structure factors and thermal parameters are given in Supplementary Publication No. SUP 23253 (11 pp.).*

* For details see Notices to Authors No. 7, *J. Chem. Soc., Dalton Trans.*, 1981, Index issue.

We thank the S.R.C. for computing facilities and an equipment grant (to I. W. N.), Dr. B. Peart for helpful discussions, and May and Baker and Sandoz Ltd. for gifts of the drugs.

[1/1309 *Received*, 14*th August*, 1981]

REFERENCES

[1] S. H. Snyder, *Am. J. Psychiatry*, 1976, **133**, 197.
[2] J. R. Holbrook, *J. Neurochem.*, 1961, **7**, 60.
[3] J. Byczkowski and R. Borysewicz, *Gen. Pharmacol.*, 1976, **7**, 365.
[4] V. Cimpu and D. Camboli, *Rev. Roum. Chim.*, 1976, **21**, 1327.
[5] H. S. Gowda and Jayarama, *J. Less-Common Met.*, 1980, **72**, P37.
[6] E. Pellizzetti, *J. Chem. Soc., Dalton Trans.*, 1980, 484.
[7] J. Barbe and J. Hurwic, *Ann. Pharm. Fr.*, 1973, **31**, 227.
[8] W. J. Geary, N. J. Mason, I. W. Nowell, and L. A. Nixon, *J. Chem. Soc., Chem. Commun.*, 1980, 1064.
[9] J. A. Ryan, *J. Am. Pharm. Assoc.*, 1959, **48**, 240.
[10] D. A. Duddell, P. L. Goggin, R. J. Goodfellow, M. G. Norton, and J. G. Smith, *J. Chem. Soc. A*, 1970, 546.
[11] R. J. Warren, *J. Pharm. Sci.*, 1966, **55**, 144.
[12] P. Marsau and A. Griffiths, *Acta Crystallogr., Sect. B*, 1973, **29**, 986.
[13] W. J. Geary, N. J. Mason, I. W. Nowell, and L. A. Nixon, unpublished work.
[14] H. Gilman, *J. Org. Chem.*, 1954, **19**, 560.
[15] ' International Tables for *X*-Ray Crystallography,' Kynoch Press, Birmingham, 1974, vol. 4.