Co-ordination of Promethazine {10-[2-(Dimethyl(amino)propyl]phenothiazine} Hydrochloride with Palladium(II): *X*-Ray Crystal Structure of a Trichloro-palladium(II) product

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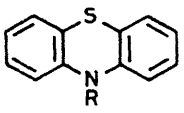
Summary Potassium tetrachloropalladate reacts with promethazine hydrochloride to give a unique complex in which the protonated promethazine is sulphur-bonded to palladium and takes up a 'scorpion' conformation, thereby facilitating electrostatic interaction between the quaternary nitrogen on the side chain and the $PdCl_3$ unit

DRUGS based on the phenothiazine heterocycle (**1**) are well established as anti-histamines and anti-psychotics. Their interactions with metal systems both *in vivo* and *in vitro* have been extensively studied.[1] While far-i.r. spectral evidence confirms that phenothiazine (**1**) co-ordinates *via* the



(**1**) R = H
(**2**) R = $CH_2CH(Me)N^+HMe_2\ Cl^-$
(**3**) R = $CH_2[CH_2]_2N^+HMe_2\ Cl^-$

ring sulphur[2] to divalent platinum and palladium, crystallographic studies to date are limited to structures in which phenothiazine and related drugs are unco-ordinated.[3] We now report the structure of a unique palladium complex: the first crystallographic evidence for a co-ordinated phenothiazine drug.

Potassium tetrachloropalladate and promethazine {10-[2-(dimethylamino)propyl]phenothiazine} hydrochloride (**2**) (1:1 molar ratio in aqueous solution) form a palladium

$$K_2PdCl_4 + PMZ.HCl \rightarrow Pd(PMZ\ H)Cl_3 + 2\ KCl \qquad (1)$$

complex [equation (1)] which has a low conductivity in nitromethane ($2{\cdot}12 \times 10^{-3}$ S m^{-2} mol^{-1}) and the band attributed to N^+–H s,[4] at 2550 cm^{-1} in the i.r. spectrum of PMZ.HCl, is shifted to a higher frequency upon complexation.

Crystal data: The complex $C_{17}H_{21}Cl_3N_2PdS$ crystallises from dimethylformamide as dark red crystals which are monoclinic with $a = 11{\cdot}381(5)$, $b = 9{\cdot}791(4)$, $c = 9{\cdot}098(4)$ Å, $\beta = 100{\cdot}84(5)°$, space group $P2_1$, $Z = 2$, $R = 0{\cdot}036$ for 1524 independent reflections having $I/\sigma(I) > 3{\cdot}0$.†

The complex is best considered as a zwitterion with the nitrogen in the side chain being protonated and the ring sulphur co-ordinated to $PdCl_3^-$. The $PdCl_3S$ unit is almost planar and the promethazine ring-system is orientated such that the outer C_6 rings are at dihedral angles of 78 and 94° to the $PdCl_3S$ mean-plane. In contrast to the uncomplexed ligand,[3b] the side chain in the present complex is bent back over the heterocycle in a unique 'scorpion' conformation,

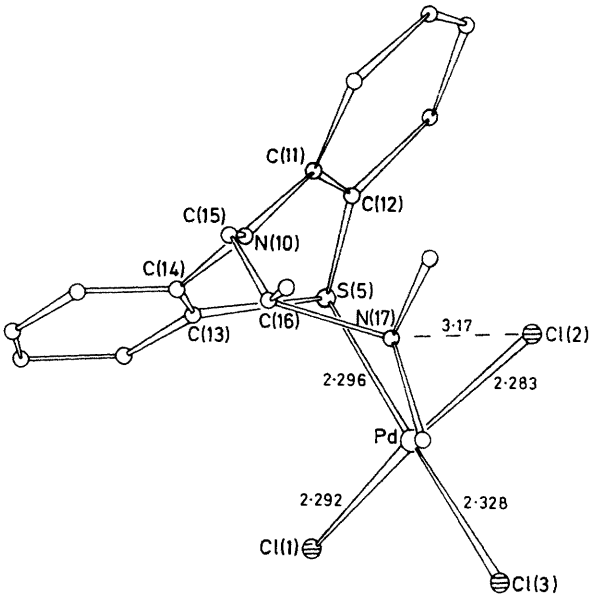


FIGURE. Molecular structure of $Pd(PMZ\ H)Cl_3$. Angles around the palladium range from 86·4 to 92·2°. The three carbon atoms attached to the quaternary nitrogen are disordered and, for clarity, only one set is shown. Bond lengths are in Å.

thereby facilitating electrostatic interaction between the quaternary nitrogen and one of the chlorine atoms. While the resulting N–Cl bond distance of 3·17 Å is very long and can only represent a weak interaction, the arrangement of carbon atoms about the nitrogen indicates that the N–H proton is directed toward Cl(2), hence facilitating hydrogen bonding.

Preliminary studies indicate that the analogous platinum complex has a similar structure and that other phenothiazine drugs, *e.g.* promazine (**3**), adopt the same 'scorpion' conformation with divalent palladium and platinum.

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† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

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