Novel Coordination in the First Tellurium Porphyrin Complex: Synthesis and Crystal Structure of [Te(ttp)Cl_2]**

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Despite the wealth of fundamental and applied research on porphyrin complexes of the metallic elements, non-metal porphyrin complexes have been much less extensively studied.[1] Porphyrin complexes of the groups 13–15 elements are well-established, but as yet no porphyrin complex of any group 16 element is known. Gouterman and co-workers reported UV/Vis spectral changes on reaction of free-base porphyrins with $TeCl_4$ and $SeCl_4$, but no well-characterized species were isolated.[2] As part of our continuing studies of main group porphyrin complexes,[3] we have investigated the synthesis, characterization, and molecular structure analysis of the first tellurium porphyrin complex.

The reaction between tellurium(IV) chloride and one equivalent of the dilithium *meso*-tetra-*p*-tolylporphyrin salt, Li_2(ttp), in refluxing hexane yielded a dark green solid of [Te(ttp)Cl_2] (72 % yield). [Te(ttp)Cl_2] is moisture sensitive in solution and decomposes on exposure to air within seconds. However, it is stable in the solid state for weeks at ambient temperature in the dark in an inert atmosphere.

The molecular structure of [Te(ttp)Cl_2][4] is presented in Figure 1. The two molecules are related by a crystallographic inversion center. The tellurium coordination sphere is best described as a square pyramid in which the atoms Cl(1), Cl(2), N(1), and N(3) form the square base of the pyramid and are coplanar to within 0.024 Å. The angles at the Te center from the apical atom to the basal atoms range from 78.27(10) to 89.73(8)°. Three of the porphyrin nitrogen atoms occupy one triangular face of the square pyramid, with the apical Te–N(2) bond length significantly shorter than those of the basal Te–N(1) and Te–N(3) bonds. Five-coordinate Te^{IV} complexes are typically square pyramidal with a short bond to the apical atom. Comparable examples with a $TeCl_2N_3$ coordination sphere are difficult to find, but several closely related $TeCl_3N_2$ complexes show basal Te–Cl bond lengths in the range 2.370–2.563 Å, basal Te–N bond lengths in the range 2.185–2.352 Å, and apical Te–N bond lengths in the range 1.996–2.096 Å.[5] The basal Te–Cl, basal Te–N, and apical Te–N bond lengths observed for [Te(ttp)Cl_2] are consistent with these.

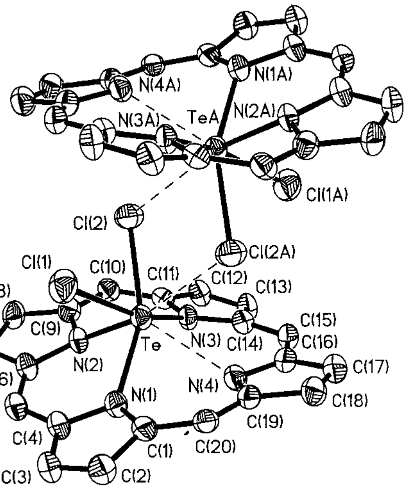

Figure 1. ORTEP plot of [Te(ttp)Cl_2]. The *meso*-tolyl groups and hydrogen atoms are omitted for clarity. Thermal ellipsoids are at the 30 % probability level. Selected bond lengths [Å] and angles [°]: Te-N(1) 2.274(3), Te-N(2) 2.094(3), Te-N(3) 2.361(3), Te-N(4) 2.598(3), Te-Cl(1) 2.5108(10), Te-Cl(2) 2.5530(10), Te-Cl(2A) 3.2206(10); N(2)-Te-N(1) 80.53(11), N(2)-Te-N(3) 78.27(10), N(1)-Te-N(3) 118.38(10), N(2)-Te-Cl(1) 89.47(8), N(1)-Te-Cl(1) 78.45(8), N(3)-Te-Cl(1) 156.51(8), N(2)-Te-Cl(2) 89.73(8), N(1)-Te-Cl(2) 157.35(8), N(3)-Te-Cl(2) 78.93(8), Cl(1)-Te-Cl(2) 81.08(4), N(2)-Te-N(4) 122.1(4).

The fourth porphyrin nitrogen atom (N(4)), and a chlorine atom from the symmetry-related molecule (Cl(2A)), are found on the open square face of [Te(ttp)Cl_2] at much longer Te–N and Te–Cl distances. The Te–N(4) separation (2.598(3) Å) considerably exceeds the sum (2.11 Å) of the covalent radii of tellurium and nitrogen atoms but is within the sum of the van der Waals radii (3.61 Å). Similarly, the long Te–Cl(2A) distance is within the sum of the van der Waals radii of Te and Cl atoms (3.81 Å).[6]

The remarkable aspect of the structure of [Te(ttp)Cl_2] is the fact that it adopts five-coordinate geometry with only three coordinated porphyrin nitrogen atoms when the normal situation for [M(Por)X_2] (Por = porphyrin) complexes is six coordination with either *trans* or, less commonly, *cis* geometry.[1] Octahedral, six-coordinate Te^{IV} complexes are well-known, so this geometry is not necessarily precluded. One rationale for the five-coordinate geometry is the VSEPR model for an AX_5E species, in which the Te^{IV} center bears a stereochemically active lone pair of electrons *trans* to the N(2) atom.

Density functional calculations[7] on the [Te(porphyrin)Cl_2] moiety confirm the unusual geometry, with qualitative agreement between the molecular structure observed by X-ray crystallography and the computed structure of the model complex (approximate C_s symmetry). This computed structure also shows square pyramidal geometry with a short apical Te–N bond, tridentate porphyrin coordination, and a long Te–N interaction involving the fourth porphyrin nitrogen atom. A view of the computed structure is given in Figure 2. The principal differences between the molecular structure of [Te(ttp)Cl_2] and the calculated model, [Te(porphyrin)Cl_2], are associated with the porphyrin ring conformation (saddle versus dome) and the effect of the additional weak Te–Cl(2A) interaction from the neighboring complex. A natural bond

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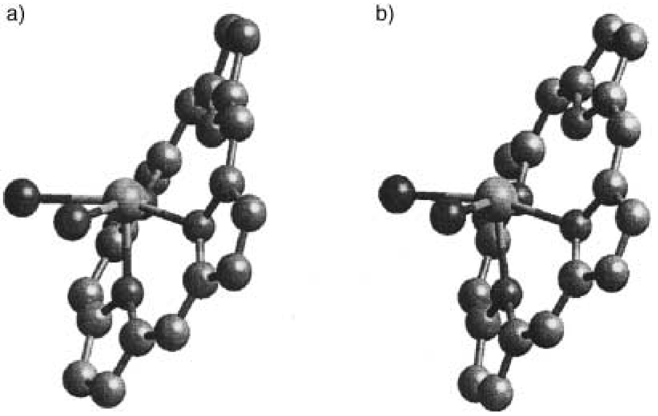

Figure 2. Experimental (a) and calculated (b) [Te(porphyrin)Cl_2] structures. Orientations are arranged to give maximum overlap of the TeN_4Cl_2 atoms in the two structures. The labeling scheme is as for Figure 1. Hydrogen atoms are omitted. Selected bond lengths [Å] and angles [°] in structure (b): Te-N(1) 2.395, Te-N(2) 2.170, Te-N(3) 2.399, Te-N(4) 2.595, Te-Cl(1) 2.515, Te-Cl(2) 2.517; N(2)-Te-N(4) 121.6.

orbital analysis shows the presence of a lone pair of electrons with predominantly *s* character on the tellurium atom.[8]

The ^1H NMR spectrum of [Te(ttp)Cl_2] in $CDCl_3$ shows two broad doublets ($\delta = 8.28$ and 8.03) and a doublet of doublets ($\delta = 7.59$) arising from the tolyl protons. These observations indicate that the two faces of the porphyrin macrocycle are chemically different, as expected from the molecular structure. However, the resonances for the β-pyrrole protons ($\delta = 9.20$) and for the tolyl methyl groups ($\delta = 2.72$) both appear as sharp singlets. As a result, the complex has apparent overall C_{4v} symmetry in solution at 25 °C which indicates that the $TeCl_2$ unit must be rapidly migrating around the N_4 porphyrin core. It was not possible to freeze out a static solution structure down to −50 °C.

In summary, the first tellurium porphyrin complex has been prepared. The five-coordinate, square-pyramidal geometry involving only three porphyrin nitrogen atoms represents an unusual bonding mode for the porphyrin ligand.[9] The structure is interesting in light of the relatively poor understanding that exists of the electronic structure and stereochemical effect of the lone pair of electrons in Te^{IV} complexes. Further reactivity studies of [Te(ttp)Cl_2] and a similar complex, [Te(oep)Cl_2] (oep = octaethylporphyrin), are underway.

Experimental Section

A solution of $TeCl_4$ (168 mg, 0.62 mmol) and [Li_2(ttp)(thf)$_2$] (451 mg, 0.52 mmol) in hexane was refluxed for 6 h after which time the dark green suspension was filtered. The residue was recrystallized at −20 °C from a solution of toluene layered with hexane. Filtration yielded microcrystalline green-black [Te(ttp)Cl_2] (325 mg, 72.2 % yield). Elemental analysis calcd for $C_{48}H_{36}Cl_2N_4Te$: C 66.47, H 4.18, N 6.46; found: C 66.68, H 4.72, N 6.36; ^1H NMR ($CDCl_3$): $\delta = 9.20$ (s, 8H, β-H), 8.28 (d, 4H, $^3J_{H,H} = 6$ Hz, *meso*-$C_6H_4CH_3$), 8.03 (d, 4H, $^3J_{H,H} = 6$ Hz, *meso*-$C_6H_4CH_3$), 7.59 (dd, 8H, $^3J_{HH} = 6$ Hz, *meso*-$C_6H_4CH_3$), 2.72 (s, 12H, *meso*-$C_6H_4CH_3$); UV/Vis: 458 (Soret), 550, 591, 640 nm.

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[4] Structure determination of **1**: Crystals were obtained from toluene/hexane, $C_{48}H_{36}Cl_2N_4Te$, $M_r = 867.31$, monoclinic, space group $P2_1/n$ (14), $a = 15.1181(9)$, $b = 16.2592(9)$, $c = 19.4662(11)$ Å, $\beta = 109.442(1)^\circ$; $V = 4512.1(4)$ Å^3; $Z = 4$; $\rho_{calcd} = 1.277$ g cm^{-3}; $\mu = 0.813$ mm^{-1}; $F(000) = 1752$. Data collected on a Siemens SMART system at 173(2) K, dark green crystal (0.42 × 0.26 × 0.23 mm), graphite-monochromated $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$). A total of 28020 reflections ($1.49 < \theta < -26.37^\circ$) were collected; 9180 were considered observed for 500 parameters (final agreement factors: $R = 0.0426$, $R_w = 0.0853$, GOF = 1.007; max/min residual electron density 1.095/−0.529 e Å^{-3}). The crystal structure was solved and refined using the SHELXTL (version 5.1) program library (G. Sheldrick, Bruker Analytical X-ray Systems, Madison, WI). Direct methods provided most non-hydrogen atoms from the *E* map, while the remaining non-hydrogen atoms were located in an alternating series of full-matrix least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were included in the structure factor calculation at idealized positions and refined as riding atoms with relative isotropic displacement parameters. Several peaks in the electron difference map, attributed to severely disordered solvent molecules, were present in the asymmetric unit. The SQUEEZE filter of the program PLATON (P. van der Sluis, A. L. Spek, *Acta Crystallogr. Sect. A* **1990**, *46*, 194) was used to correct the diffraction data for diffuse scattering effects and to identify the solvate molecules. Approximately 4.6 solvate molecules of toluene and/or hexane were present in the unit. All derived results are based on known contents. No data are given for the diffusely scattering species. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-168149. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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An Efficient Total Synthesis of (±)-Galanthamine**

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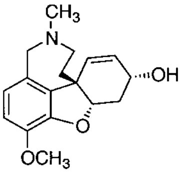
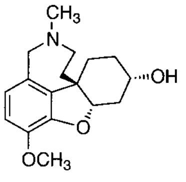
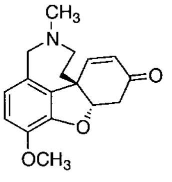
(–)-Galanthamine (**1**),[1] a tertiary alkaloid isolated from *Amaryllidaceae*, is a centrally acting, competitive, and reversible inhibitor of acetylcholinesterase which enhances cognitive functions in Alzheimer's patients.[2] This drug is available in Austria, and is the most recently approved acetylcholinesterase inhibitor for use in the United States and Europe. However, the botanical supplies of **1** are insufficient for its clinical uses.[3] Galanthamine (**1**) has a spiro quaternary carbon atom. Establishment of this quaternary center is the critical element in the total synthesis of galanthamine-type alkaloids. Most of the reported syntheses of **1** are based on a biomimetic intramolecular phenolic oxidative coupling.[4]



1 (–)-galanthamine



2 (–)-lycoramine

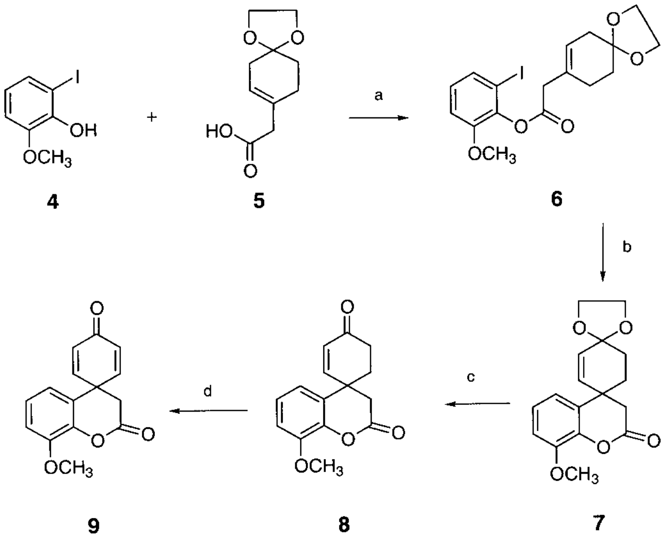


3 (–)-narwedine

We previously reported the use of an intramolecular Heck reaction as an alternative for creating the spiro quaternary carbon atom of galanthamine-type alkaloids. A formal synthesis of lycoramine (1,2-dihydrogalanthamine; **2**) was thus achieved.[5] Since then, the Heck reaction has been used to access 3-deoxygalanthamine.[6] However, many chemical transformations were required to introduce the allylic alcohol group,[6b] which is essential for anticholinesterase activity. The best total synthesis of galanthamine was achieved in 15 steps with an overall yield of only 1%.[6b]

An efficient synthesis of (–)-galanthamine (**1**) could be facilitated by a short and efficient synthesis of (±)-narwedine (**3**) or derivatives thereof (e.g., (±)-oxonarwedine (**11**), Scheme 2), since the transformation of (±)-narwedine into its (–) enantiomer has been shown to proceed in high yield.[7] Moreover, (±)-narwedine may be resolved by means of dynamic diastereoisomeric salt formation with di-*p*-toluoyl-D-tartaric acid.[8]

Here we report on an efficient route to (±)-galanthamine (**1**) based on the synthesis of (±)-oxonarwedine (**11**). Our strategy was to form the C12a–C12b bond by an intramolecular Heck reaction to access the spiro tricyclic dienone **9**, which could then be used as a valuable synthetic precursor of **1** and eventually narwedine (**3**). A short synthesis of **9** is summarized in Scheme 1. Esterification of acid **5** with 2-iodo-6-methoxyphenol (**4**)[9] furnished the ester **6** in 80% yield. Heck cyclization of **6** was accomplished in 65% yield in the presence of 10% [Pd$_2$(dba)$_3$], 20% dppe, and thallium acetate (1.2 equiv) in acetonitrile. The dioxolane group of **7** was deprotected with triphenylcarbenium tetrafluoroborate to give **8** in quantitative yield. The oxidation of the α,β-unsaturated ketone **8** to the corresponding dienone **9** proved difficult. Previous attempts to achieve this transformation



Scheme 1. a) EDCI, DMAP, CH$_2$Cl$_2$, 0→20 °C, 5 h, 80%; b) [Pd$_2$(dba)$_3$], dppe, TlOAC, CH$_3$CN, reflux, 3 d, 67%; c) Ph$_3$CBF$_4$, CH$_2$Cl$_2$, 20 °C, 1 h, 100%; d) 4 Å molecular sieves, (PhSeO)$_2$O, CH$_2$Cl$_2$, reflux, 20 h, 50%. dba = *trans,trans*-dibenzylideneacetone, DMAP = 4-dimethylaminopyridine, dppe = 1,2-bis(diphenylphosphanyl)ethane, EDCI = *N'*-(3-dimethylaminopropyl)-*N*-ethylcarbodiimide.

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