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Fused hexacyclic tin compounds derived from 3-(3,5-di-*t*-butyl-2-hydroxy-phenylimino)-3H-phenoxazin-2-ol

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ABSTRACT

The template synthesis of two tin compounds [N→Sn] 3-(2-oxo-phenylimino)-3H-phenoxazin-2-oxo-dimethyltin (**1**) and [N→Sn] 3-(2-oxo-phenylimino)-3H-phenoxazin-2-oxo-diphenyltin (**2**) is reported. The compounds are fused delocalized planar hexacyclic systems bearing a pentacoordinated diorganyl tin. They were identified by NMR, IR, TOF mass spectra and, for compound **1**, by X-ray diffraction analysis.

1. Introduction

We are currently working on the heterocyclic chemistry of main-group elements using phenolamines derivatives as ligands. Interest in these molecules is based on their polyfunctional nature, high reactivity and unusual electronic and structural properties. Phenolate substituents make the metal atom more Lewis-acidic and allow strong coordination of Lewis-basic nitrogen atom [1–8]. Their planar and rigid structures allow the stabilization of uncommon species [9–11].

The combination of planar aromatic polycyclic ligands and tin atoms produces models which are suitable for biological studies as biocides, due to the potential anticancer activity of tin [12–17] and the planar organic ligands which are biocides [18] and may act as DNA intercalators.

An interesting feature of the diphenolamine coordination compounds is that they can be found in different oxidation states depending on the coordination number and nature of the metallic substituents, which can modify the magnetic character of their derivatives. For example pentacoordinated diphenolamine tin compounds are paramagnetic, whereas the hexacoordinated compounds are diamagnetic [3], Scheme 1.

Phenolamines are excellent starting materials for the synthesis of planar compounds formed by five or more fused rings. For example the diphenoloxamides can afford planar penta- or hexacyclic compounds, Scheme 2 [5–8].

2. Results and discussion

Herein, we report the preparation and characterization of two new pentacoordinated tin hexacyclic compounds (**1** and **2**) derived from 3-(3,5-di-*tert*-butyl-2-hydroxy-phenylimino)-3H-phenoxazin-2-ol. Heterocycles **1** and **2** were synthesized by template reactions of di-*tert*-butylbenzoquinone, *ortho*-phenolamine, NH_4OH, and dimethyl or diphenyl tin chlorides respectively, Scheme 3. The reaction of the quinone, the phenolamine and the R_2SnCl_2 should give a diphenolimine linked to a tin atom and the elimination of two HCl molecules. The condensation of a second phenolamine could be simultaneous.

The new heterocycles **1** and **2** are diamagnetic which contrast with the paramagnetic nature of the diphenolamine pentacoordinated tin compounds, Scheme 1. The ^{119}Sn NMR spectra corresponded to pentacoordinated tin compounds. [δ ^{119}Sn ($CDCl_3$, ppm) **1**: −68.9; $^1J(^{119/117}Sn–^{13}C)$ 624/594 Hz; **2**: −243.6]. The ^{13}C NMR data were assigned by HETCOR and COSY experiments and by comparison with the reported data for 3-H-phenoxazin-3-ones [19]. Compounds **1** and **2** have very similar NMR spectra. The unequivocal assignment of the ^{13}C NMR data is given in Table 1.

2.1. X-ray diffraction analysis

Compound **1** gave dark violet crystals which were analyzed by X-ray diffraction, Tables S1 and S2. Unfortunately the dark green

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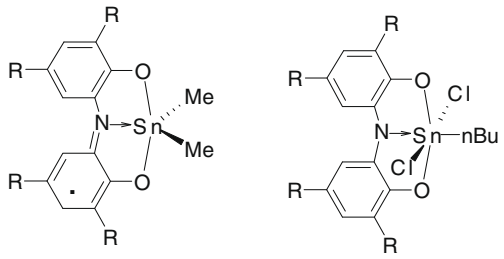
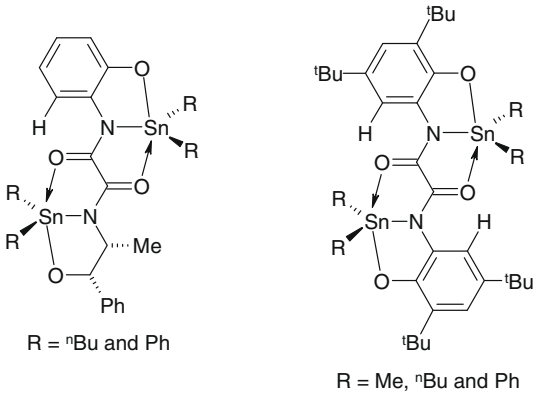
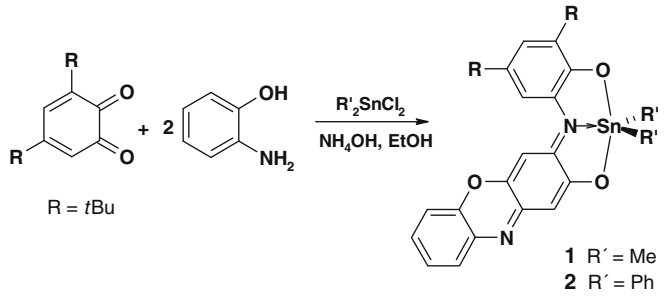


Scheme 1. Paramagnetic pentacoordinated and diamagnetic hexacoordinated tin heterocycles derived from diphenolamines [3].



Scheme 2. Pentacyclic [7] and hexacyclic fused tin compounds derived from diphenol-oxamides [5,6].

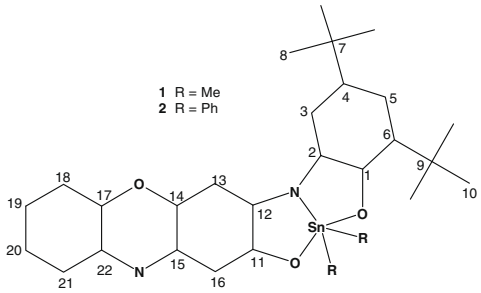


Scheme 3. Synthesis of compounds **1** and **2**.

crystals of compound **2** were not suitable for X-ray diffraction analysis. The structure of compound **1** showed the planar hexacyclic system, Fig. 1.

The ligand acts as tridentate. The tin substitutes the two OH protons and is coordinated by the imine nitrogen atom. The angles around the tin atom indicate square pyramid geometry, Sn–C34 being the axial bond [C33–Sn–C34 121.1(2), O8–Sn1–O2 144.4(1), C34–Sn–O8 102.8(1), C34–Sn–O2 102.2(1), C34–Sn–N5 103.1(2), N5–Sn–O8 74.5(1), N5–Sn–O2 75.4(1)]. The bond lengths around the tin atom are very similar for the five substituents, indicating a zwitterionic structure and the anionic nature of the tin where coordinative and covalent bonds are mixed (Sn–O2 2.092(2), Sn–O8 2.116(3), Sn–C33 2.121(4), Sn–C34 2.120(2), Sn–N5 2.183(4) Å. The Sn–N bond length is slightly longer than that of a Sn–N covalent bond ≈2.05 Å, [20,21], which indicates that it is a very strong coordination bond. The positive charge should be

Table 1
^{13}C NMR data of compounds **1** and **2**.



	1[a]	2[f]		1	2
C1	149.7	149.5	C12	161.1	161.0
C2	157.8[b]	157.3	C13	98.1[d]	97.9[h]
C3	113.6[c]	113.9[g]	C14	129.8[e]	130.4
C4	138.7	138.9	C15	147.5	147.6
C5	125.4	125.6	C16	105.1	106.0
C6	138.2	138.7	C17	143.1	143.1
C7	35.5	35.6	C18	116.2	116.0
C8	31.7	31.7	C19	129.2	129.5
C9	34.6	34.6	C20	125.8	125.9
C10	29.3	29.7	C21	128.7	128.9
C11	151.2	151.2	C22	135.6	135.7

[a] δ (Me) = −0.27 ppm [$^1J(^{119/117}Sn–^{13}C)$ = 619.6 and 592.7 Hz].
[b] $^2J(^{119}Sn–^{13}C)$ = 20.8 Hz.
[c] $^3J(^{119}Sn–^{13}C)$ = 26.1 Hz.
[d] $^3J(^{119}Sn–^{13}C)$ = 35.4 Hz.
[e] $^4J(^{119}Sn–^{13}C)$ = 44.6 Hz.
[f] δ (Ph) = 139.5 [C_i], 136.5 [C_o, $^2J(^{119}Sn–^{13}C)$ = 54 Hz], 128.9 [C_m, $^3J(^{119}Sn–^{13}C)$ = 83 Hz], 130.4 [C_p, $^4J(^{119}Sn–^{13}C)$ = 16.6 Hz].
[g] $^3J(^{119}Sn–^{13}C)$ = 29.1 Hz.
[h] $^3J(^{119}Sn–^{13}C)$ = 37.4 Hz.

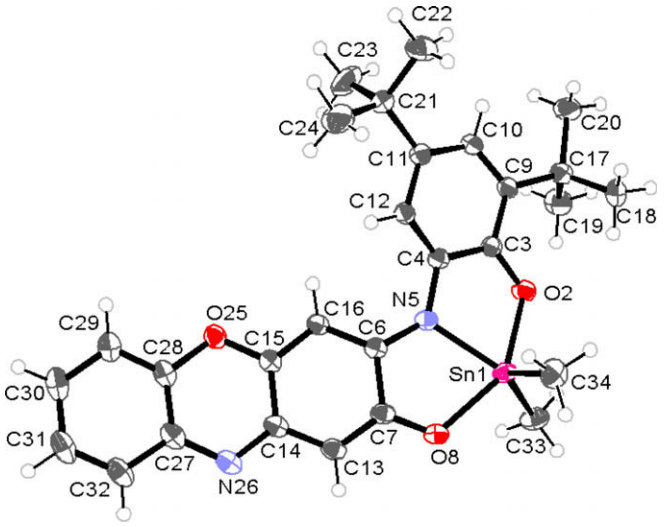
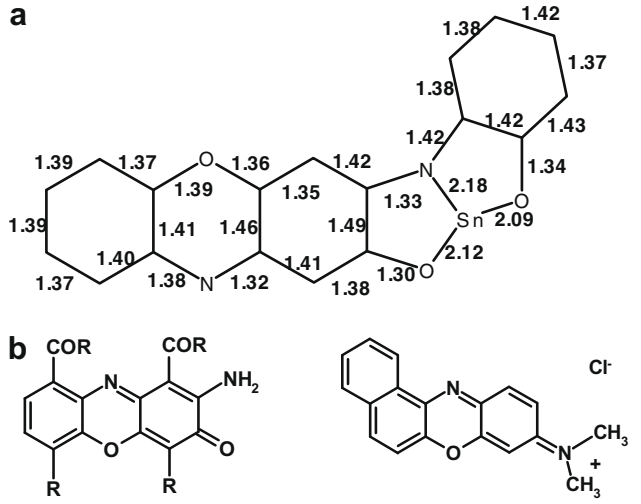


Fig. 1. ORTEP representation of the structure of compound **1**.

partially delocalized through the hexacyclic system. The analysis of the ligand bond lengths shows that **1** is not completely delocalized, there are single, double and delocalized bonds, Scheme 4.

The molecule is not completely planar. The dihedral angle between the phenoxazine rings and the tin phenolamine ring (17.5°) is probably due to a steric interaction between the aromatic hydrogen atoms (distance between H16 and H12 is 2.03 Å). Intramolecular hydrogen bonds are also shown, Fig. 2.



Scheme 4. (a) Bond lengths (Å) for the hexacyclic fragment of compound **1** obtained from the X-ray diffraction analysis, showing the electronic distribution in the fused rings. (b) Actinomycin basic framework (left) and Medola's blue (right).

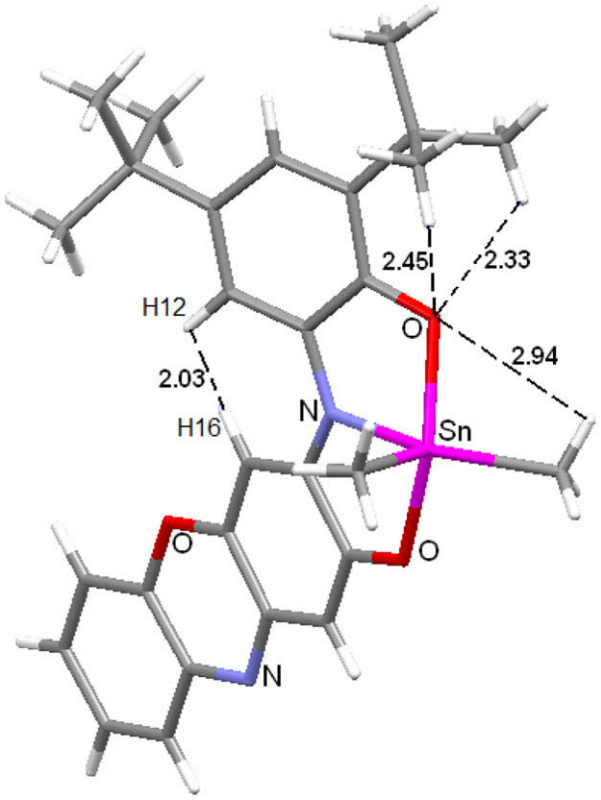


Fig. 2. View of the solid state structure of compound **1**. The distance between H12 and H16 is shown.

The molecules are π stacked in the crystal. The distances between the planes of two molecules correspond to strong π-interactions [22], Fig. 3.

Compounds **1** and **2** are rare examples of a six hexacyclic fused planar heterocycles. To our knowledge there are no a similar rings systems reported in the Cambridge Crystallographic Data Centre. The structure is quite interesting due to the fact that 3-iminophenoxazin-2-ol groups are chromophores in synthetic dyestuffs and redox indicators such as Nile blue and Nile red and Medola's blue [23] and that phenoxazine dyes show antitumoral activity Scheme 4, [24]. They present biocidal activity by intercalation of the phenoxazin-3-one ring in DNA, and form part of framework of actinomycins, antibiotics produced by some species of Streptomyces bacteria [25,26]. Actinomycin analogues to a fragment of compounds **1** and **2** present anti-leukemia activity [27]. They are cytostatic drugs [28] and anticancer antibiotics [29].

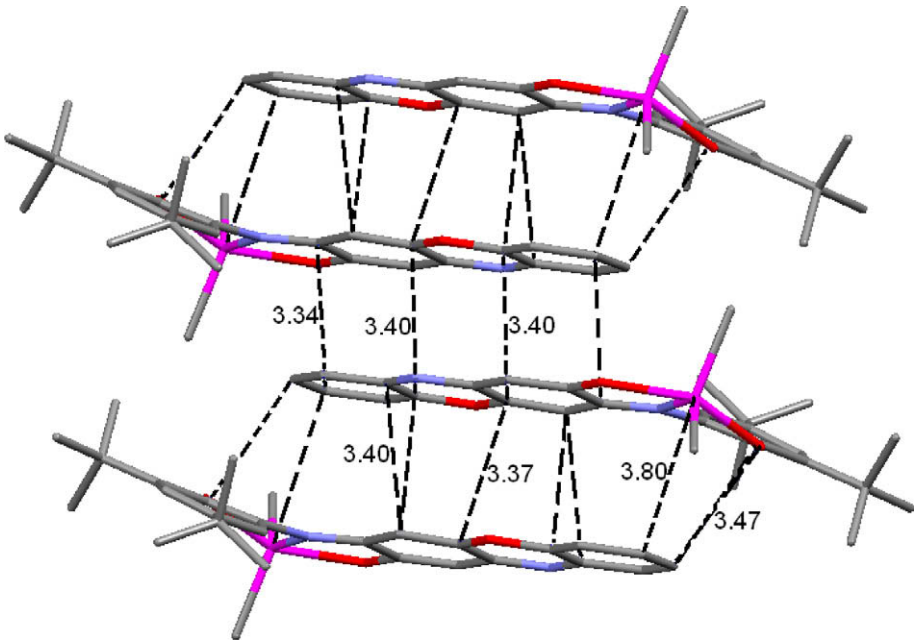


Fig. 3. View of the intermolecular π–π stacking in the solid state of compound **1**. The distances in Å. The dihedral angle between the benzoxazine fragment and the ditert-butyl-phenolamine is 17.5°.

3. Conclusions

We report herein simple template reactions which affords fused hexacyclic systems, which are very interesting from the point of view of their uncommon planar structure reminiscent of the actinomycin framework, and of interest as potential biocides. Biological investigation is under way.

4. Experimental

4.1. General

All solvents were freshly distilled before use according to established procedures. The tin reagents were commercials. The melting points were obtained on a Mel-Temp II apparatus and are uncorrected. Mass spectra in the EI mode were recorded at 20 eV on a Hewlett-Packard HP 5989 spectrometer. High resolution mass spectra were obtained by LC/MSD TOF on an Agilent Technologies instrument with APCI as ionization source. Elemental analyses were performed on Eager 300 equipment. ^{1}H, ^{13}C [Ξ = 25.145020, $Si(CH_3)_4$] and ^{119}Sn [Ξ = 37.290 $Sn(CH_3)_4$] and spectra were obtained by single pulse with broad decoupling experiments. NMR spectra were obtained on a Jeol GSX-270, Jeol Eclipse 400 MHz and Bruker Advance 300 MHz. IR spectra were taken in KBr disc using a FT Spectrum GX Perkin–Elmer spectrometer. X-ray diffraction studies of single crystals were determined on a Siemens P4 instrument equipped with CCD area detector and at low temperature device LTP2.

4.2. [N→Sn] 3-(2-oxo-phenylimino)-3H-phenoxazin-2-oxo-dimethyltin (**1**)

4.2.1. General procedure

To a solution of 3,5-di-*tert*-butyl-1,2-benzoquinone (1.1 g, 5 mmol) in 40 ml of 95% ethanol at 0 °C was added a solution of *o*-aminophenol (1.08 g, 10 mmol) in 15 ml of 95% ethanol. To this mixture NEt_3 (1.5 ml) and $SnCl_2Me_2$ (1.1 g, 5 mmol) were added. After stirring 2 h at 0 °C, the reaction was continued at rt. After 24 h, the dark violet solid product was filtered and washed with water and ethanol and vacuum dried. The main product was extracted with CH_2Cl_2. The solvent was vacuum evaporated and the dark violet crystalline product was recrystallized from CH_2Cl_2-ethanol 3.1; (350 mg, 12.5%). M.p. 178–180 °C. IR (KBr), ν cm^{-1} 1560 (C=C), 1268 (C=N), 1200 (C–O), 759 (N–Sn). NMR (ppm) ^{119}Sn −68.92 [$^{1}J(^{119/117}Sn–^{13}C)$ 624.5/593.7 Hz]. ^{1}H (see Table 1 for atoms numbering): 0.75 [Sn–CH_3, $^{2}J(^{119/117}Sn–^{1}H)$ 76.2/72.9], 1.40 [s, *t*Bu–C4], 1.44 [s, *t*Bu–C6], 6.62 [s, H16], 7.31 [s, H5], 7.34 [m, H20], 7.38–7.40 [m, H13, H18, H19], 7.59 [s, H3], 7.73 [d, ^{3}J 7.7 Hz, H21]. TOF-MS: $[M+H]^+$ Calc. $C_{28}H_{33}N_2O_3Sn$ 565.1507 a.m.u. Exp.: 565.1505 a.m.u. (Error = −0.47 ppm). Anal. Calc. for $C_{28}H_{32}N_2O_3Sn$: C, 59.71; H, 5.73; N, 4.97. Found: C, 59.41; H, 5.86; N, 4.98%.

4.3. [N→Sn] 3-(2-oxo-phenylimino)-3H-phenoxazin-2-oxo-diphenyltin (**2**)

Following the procedure for compound **1**, to a mixture of 3,5-di-*tert*-butyl-1,2-benzoquinone (550 mg, 2.5 mmol) in 20 ml of 95% ethanol, *o*-aminophenol (0.50 g, 5 mmol) in 15 ml of 95% ethanol, NEt_3(0.75 ml) and $SnCl_2Ph_2$ (860 mg, 2.5 mmol) in 10 ml of 95% ethanol were added. Compound **2** is a dark green crystalline powder (410 mg, 24%). M.p. 300–302 °C. IR (KBr) ν cm^{-1}: 1553 (C=C), 1265 (C=N), 1198 (C–O), 731 (N–Sn). NMR (ppm) ^{119}Sn −243.6 ppm. ^{1}H (see Table 1 for atoms numbering): 1.34 [s, H8], 1,60 [s, H10], 6.88 [s, H16], 7.2–7,4 [m, H_m, H_p, H5, H13, H18, H19, H20], 7.58 [s, H3], 7.76–7.78 [m, H21], 7.88–7.91 [m, Ho]. TOF-MS: $[M+H]^+$ Calc. $C_{38}H_{37}N_2O_3Sn$ 689.1826 a.m.u. Exp.: 689.1820 a.m.u. (Error = 1.5 ppm). Anal. Calc. for $C_{38}H_{36}N_2O_3Sn \cdot 1/2CH_2Cl_2$: C, 63.36; H, 5.11; N, 3.84. Found: C, 63.57; H, 5.07; N, 3.98%.

4.4. Crystallographic study

Data were measured on a Siemens SMART area-detector using graphite-monochromated Mo Kα radiation at 293 K, and hemisphere scan type and a crystal mounted in perfluorpolyetheroil. Intensities were measured using ϕ +ω scans. Compound **1** crystallized from CH_2Cl_2. Structure was solved using direct methods (SHELX-97) [30] and the refinement (based on F^2 of all data) was performed by full-matrix least-squares techniques with Crystals 12.84 [31]. All non-hydrogen atoms were refined anisotropically and all hydrogen atoms were placed on ideal positions and allowed to ride on their respective atoms.

Acknowledgments

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2008.11.070.

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