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Synthesis of novel benzodioxan and biphenyl based dien sulfonamide ligands and their platinum(II) complexes

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Eventhough thousands of platinum drugs have been synthesized and screened for anticancer activity, treatment has become limited due to toxicity and drug resistance. Understanding specific targets in cellular pathways and designing novel Pt drug candidates offer a powerful approach to cancer therapy. An amphipathic ligand system would be the best approach for synthesizing novel platinum complexes to target cells. This could be achieved by incorporating a lipophilic aromatic ring system to the hydrophilic diethylenetriamine backbone via a sulfonamide group simultaneously giving enhanced fluorescence activity. In this study, two novel bidentate ligands (L1 = $N(SO_2)$(bzd)dienH, L2 = $N(SO_2)$(4-Mebip)dienH) and their corresponding novel platinum complexes (C1 = $[Pt(N(SO_2)(bzd)dienH)Cl_2]$, C2 = $[Pt(N(SO_2)(4\text{-}Mebip)dienH)Cl_2]$) were synthesized and characterized by ^{1}H NMR, FT-IR, UV-Vis and fluorescence spectroscopies. The high energy bands observed between 200-300 nm due to π→π* transitions and n→π* transitions in absorption spectra of the free ligands and platinum complexes. The S-N stretching observed in FT-IR spectra at 932 cm^{-1} for L1, and 913 cm^{-1} for L2, are consistent with related compounds. ^{1}H NMR spectra obtained in DMSO-d_6 were utilized for structure elucidation. Signals observed at 3.00-2.30 ppm region in ^{1}H NMR were assigned to aliphatic protons in ligands. In the complexes, signals at 6.02 ppm, 6.84 ppm and 7.64 ppm in C1 and 6.05 ppm, 6.90 ppm and 7.77 ppm in C2 were assigned to NH peaks and confirmed the formation of complexes in which the new ligands display bidentate denticity (central N2 and terminal N1) vs tridentate. Emission spectra were recorded in methanol, and the $N(SO_2)$(bzd)dienH ligand showed enhanced fluorescence intensity at 331 nm, whereas its bidentate complex showed quenched fluorescence with a blue shift. Similarly, $N(SO_2)$(4-Mebip)dienH ligand showed high fluorescence intensity, while its bidentate complex showed lower intensity. The sulfonamides linked to diethylenetriamine can conjugate with small biomolecules. The ligands presented by us possess high fluorescence activity, allowing them to be used as diagnostic tools. In the near future, the synthesized novel bidentate platinum complexes will be investigated for their potential as anticancer drug leads.

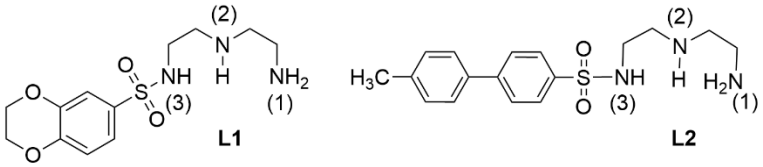

Figure: Line diagram of newly synthesized dien ligands; L1 = $N(SO_2)$(bzd)dienH, L2 = $N(SO_2)$(4-Mebip)dienH

Keywords: Diethylenetriamine, benzodioxan, biphenyl, platinum

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