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New Potent 5-Substituted Benzofuroxans as Inhibitors of Trypanosoma Cruzi Growth. Quantitative Structure-Activity Relationship Studies

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Benzofuroxan derivatives have been shown to inhibit growth of Trypanosoma Cruzi, the etiologic agent of Chagas' disease. In order to develop a pharmacophoric model for this activity, quantitative structure-activity relationships for selected benzofuroxans have been studied. In this study some derivatives were synthesized and in vitro evaluated to complete the set of compounds. Conventional multiple regression analysis of the substituents' physicochemical properties provided acceptable QSAR. Moreover, exigencies of three-dimensional activity were clearly observed from a 3D-QSAR study in terms of comparative molecular field analysis. In both approaches, 2D- and 3D-QSAR, it was necessary to include an indicator variable that takes into account the N-oxide position in the benzofuroxan system. For the new analogues, these positions were clearly established using low temperature-NMR experiments. The QSAR-results allow us to insight into the spatial and electronic exigencies to increase the anti-trypanosomal activity of the studied compounds.

A Preliminary Observation of Additive Thermodynamic Contribution of Pendant Arms to the Complexation of Calixarene Derivatives with Mercury (II)

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An additive thermodynamic contribution of pendant arms to the complexation of calixarene derivatives with mercury(II) in acetonitrile is for the first time demonstrated.

Solvent Control on the Selective, Non-selective and Absent Response of a Partially Substituted Lower Rim Calix(4)arene Derivative for Soft Metal Cations (Hg(II) and Ag(I)). Structural and Thermodynamic Studies

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The solvent control on the ability of a partially substituted lower rim calix(4)arene derivative, 5,11,17,23,tetra-tert-butyl[25,27-bis(hydroxy)-26,28-bis(ethylthio ethoxy)]-calix(4)arene, 1, to host soft metal cations (Hg(II) and Ag(I)) is demonstrated through 1H NMR, electrochemical (conductance measurements) and thermodynamic characterisation of the complexation process in a wide variety of solvents. Solvent-ligand interactions were assessed from 1H NMR measurements involving 1 and various solvents in CDCl3. Thus the formation of a 1:1, 1CH3CN, adduct is reported. As far as metal cations are concerned, depending on the medium their complexation of 1 was only observed with Hg(II) and Ag(I). Thus in acetonitrile 1 is more selective for Hg(II) relative to Ag(I) by a factor of 2.2 × 103. In methanol the selectivity is reversed to an extent that the affinity of 1 for Ag(I) is 1.4 × 103 higher than that for Hg(II). However, 1 is unable to recognise selectively these cations in N,N-dimethylformamide while in propylene carbonate the ability of 1 to interact with these cations is lost. An outstanding feature of thermodynamics emerges when an assessment is made on the solvent effect on the complexation of these cations and analogous calix(4)arene derivatives. Thus in acetonitrile the energetics of cation complexation by the hydrophilic cavity of a calix(4)arene containing mixed pendant groups is built up from thermodynamic data for the same process involving derivatives with common functional groups at the narrow rim. This unique example of additive contribution of pendant arms is for the first time demonstrated in the field of calixarene thermochemistry. The medium effect on the thermodynamics of complexation of 1 and soft metal cations is used for the isolation of Hg1(ClO4)2.2MeCN and Ag21(ClO4)2 complexes. The x-ray structured of theses complexes are reported. Final conclusions are given.

Chemoselective hydrolysis of the iminic moiety in salicylaldehyde semicarbazone promoted by ruthenium

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Ortho-Hydroxybenzaldehyde semicarbazone (salicylaldehyde semicarbazone) undergoes chemo-selective hydrolysis of the iminic carbon nitrogen double bond through its reaction with [RuCl2(dmso)4] in ethanol in the presence of water, yielding free salicylaldehyde and semicarbazide that remains coordinated to the ruthenium ion as a bidentate N,O-donor to afford [RuCl2(dmso)2(semicarbazide)]·2H2O complex. The ruthenium-semicarbazide complex has been characterized by 1H-NMR and FTIR spectroscopies and X-ray diffraction methods. Related semicarbazones, derived from p-hydroxybenzaldehyde and benzaldehyde, were not hydrolyzed under the same conditions, suggesting a significant role of the structural o-hydroxy motive in the reaction. Theoretical studies were performed in order to gain further insight on the mechanism of reaction. Results support the hypothesis that the ortho hydroxy moiety, in the keto tautomeric form, participates in the chemo-selective hydrolysis promoted by [RuCl2(dmso)4].

Step Wise Formation of s-Alkynyl, Vinylidene, and Vinylphosphonium Complexes of Manganese(I)

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Reaction of methyl propiolate with the diphosphino methanide complex [Mn(CO) 4(PPh2)2CH] (1) produces simultaneously the insertion of the alkyne into the C-H bond, giving [Mn(CO)4(PPh2)2C-C(H)=C(CO2-Me)H] (2), and the deprotonation of the alkyne mediated by the diphosphino methanide ligand, affording the ?-alkynyl derivative fac-[Mn(C?C-CO2Me)(CO)3(dppm)] (3). Protonation of 3 with HBF4 at 200K affords the corresponding vinylidene compound fac-[Mn(C=C(H)-CO2Me)(CO)3(dppm)]BF4 (5), which, on raising the temperature to 243K, undergoes the spontaneous insertion of the vinylidene ligand into a Mn-P bond.

Synthesis and Biological Properties of New 5-Nitroindazole Derivatives

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A series of new 3-alkoxy- or 3-hydroxy-1-[?-(dialkylamino)alkyl]-5-nitroindazoles has been synthesized and their trichomonacidal, antichagasic and antineoplastic properties studied. Five derivatives (5, 6, 8, 9 and 17) showed remarkable trichomonacidal activity against Trichomonas vaginalis, at 10 ?g/mL concentration. Three compounds (8, 10, 11) exhibited interesting antichagasic activity and these same compounds moderate antineoplastic activity against TK-10 and HT-29 cell lines. Unspecific cytotoxicity against macrophages has also been evaluated and only compounds 9, 10 and 11 resulted cytotoxic at the higher dose evaluated (100 ?g/mL), loosing cytotoxicity at lower doses. QSAR studies have been carried out.

Solid state 111Cd NMR studies on cadmium(II)-2,x-pyridindicarboxylates. Crystal structure of triaqua (pyridine-2,4-dicarboxylato)cadmium(II) hemihydrate: [Cd(II)(2,4-pydc)(H2O)3].1/2H2O

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The synthesis and characterization by solid-state 111Cd- NMR of Cd(2,3-), Cd(2,4-), Cd(2,5-) and Cd(2,6-pyridinedicarboxylato).xH2O is reported. Results indicate that the 111Cd-NMR signal is very sensitive to the to the relative position of both carboxylates. Similar shifts (at 54.0 and 55.4 ppm) are found for the 2,4- and the 2,6- isomers where carboxylates groups are meta to each other. For the 2,3- and 2,5- derivatives (carboxylates in orto and meta), the signals are detected at 119.6 and 84.2 ppm. The crystal and molecular structure of the seven-coordinated cadmium complex, [Cd(2,4-pyridinedicarboxylato)(H2O)3]·1/2H2O is also reported. This data allows a correlation between Cd-O and Cd-N coordination and geometry with 111Cd chemical shift. The ?iso value encountered for the 2,6-pydc derivative may indicate an heptacoordinated sphere for the compound. Additional coupling between 111Cd and 14N in 2,3- (also found in 2,4-pydc) suggests only one N coordinated to Cd. The anisotropy magnitude, and the asymmetry parametry, is also analysed.

Palladium(II) complexes of 2-benzoylpyridine-derived thiosemicarbazones: spectral characterization, structural studies and cytotoxic activity

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Palladium(II) complexes of 2-benzoylpyridine thiosemicarbazone (H2Bz4DH) and its N(4)-methyl (H2Bz4M) and N(4)-phenyl (H2Bz4Ph) derivatives were obtained and fully characterized. [Pd(2Bz4DH)Cl] (1) crystallizes in the monoclinic space group P21/c with a=11.671(1), b=10.405(1), c=13.124(1) Å, ?=115.60(1) , and Z=4; [Pd(2Bz4M)Cl] (2) in the monoclinic space group P21/c with a=9.695(1), b=15.044(1), c=10.718(1) Å, ?=105.38(1) , and Z=4 and [Pd(2Bz4Ph)Cl] (3) in the triclinic space group P-1 with a=9.389(1), b=13.629(1), c=15.518(1) Å, ?=70.25(1), ?=73.46(1), ?=83.57(1) , and two independent molecules per asymmetric unit (Z=4). All complexes show a quite similar planar four fold environment around palladium(II). A negatively charged organic molecule acts as a tridentate ligand and binds to the metal through the pyridine nitrogen, the imine nitrogen and the sulfur atom. A chloride ion occupies the fourth coordination site. The planar complexes stack nearly parallel to one another in the lattice conforming a layered crystal structure. The cytotoxic activity of the thiosemicarbazones and their metal complexes was tested against the MCF-7, TK-10 and UACC-62 human tumor cell lines. The ligands exhibit lower values of IC50 and LD50 than the complexes, H2Bz4Ph being the most active with IC50 < 0.003 M; LD50=13.4 M; IC50=9.3 M, LD50=12.9 M; IC50<0.003, LD50=13.8 M in the MCF-7, TK-10 and UACC-62 cell lines respectively. Among the complexes, [Pd(2Bz4Ph)Cl] (3) exhibited the lowest values of IC50 in the three studied cell lines.

Synthesis, crystal structure and spectroscopic characterization of a novel bis(oxo-bridged) dinuclear vanadium(V)-dipicolinic acid complex

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The reaction of [VO(dipic)(H2O)2].H2O with creatinine in H2O-CH3OH mixture yields yellow crystals of bis (oxo bridged) binuclear vanadium(V) compound of stoichiometry [CH3NHC(NH2)2]2 [V2O4(dipic)2], (dipic2-=pyridine 2,6 dicarboxylate; CH3NHC(NH2)2+=methyl guanidinum). The molecular structure of the compound was determined by X-ray diffraction methods. The binuclear complex crystallized in the monoclinic space group P21/c with a=9.557(1), b=12.363(1), c=10.466(1) Å,=101.56 (2)º, and Z=2. It sits at a crystallographic inversion center with the pair of V(V) atoms in an edge-sharing distorted octahedral environment. In the [VO2(dipic)]- halves of the dimer, the VO2+ cation is coordinated to a dipicolinate group acting as a tridentate planar ligand through one oxygen of each carboxylic group and the hetereocyclic nitrogen atom. The oxo ligand laying near the coordination plane bridges the dimer through a weak axial bond with the other half. This gives rise to a V=O2 bond length slightly longer than the other, terminal, V=O1 bond. The infrared and Raman spectra of the compound were recorded and discussed on the basis of its structural data and by comparison with those of the free acid. The results are also compared with the corresponding ones of related structures.

Vanadium(V) Complexes with Salicylaldehyde Semicarbazone Derivatives bearing in vitro Anti-tumor Activity toward Kidney Tumor Cells (TK-10). Crystal Structure of [VVO2(5-bromosalicylaldehyde semicarbazone)]

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As a contribution to the development of novel vanadium complexes with pharmacologically interesting moieties, new dioxovanadium(V) semicarbazone complexes with the formula cis-VO2L, where L=5-bromosalicylaldehyde semicarbazone and 2-hydroxynaphtalen-1-carboxaldehyde semicarbazone, have been synthesized. and characterized by 1H- and 13C-NMR, Raman and FTIR spectroscopies. Results were compared with those previously reported for other three analogous complexes of this series. The five complexes were tested in three different human tumor cell lines for bioactivity as potential anti-tumor agents, showing selective cytotoxicity on TK-10 cell line. Results showed that structural modifications on the semicarbazone moiety could have a significant effect on the anti-tumor activity of the vanadium complexes. In addition, the electrochemical behavior of all the complexes was studied. No apparent correlation could be demonstrated between reduction potentials of the complexes and their anti-tumor activities. The molecular structure of the novel [VVO2(5-bromosalicylaldehyde semicarbazone)] complex was solved by X ray diffraction methods. The vanadium atom shows a distorted square pyramidal coordination sphere. The (VO2)+ cation is coordinated to a nearly planar (L)- anion acting as a tridentate ligand through both oxygen and one nitrogen atoms.