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Tautomerism and reactivity in heterocycles N-oxides: a spectroscopic and theoretical strudy of benzimidazoles N-oxide derivatives (N-hydroxybenzimidazoles)

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The tautomeric forms of benzimidazole N-oxide derivatives in solution were studied using nuclear magnetic resonance (NMR) techniques and density functional theory (DFT) calculations. In the gas-phase the N-hydroxy tautomer is more stable than the N-oxide, whereas in solution the stabilization of one form or the other depends on hydrogen bond formation with the N-hydroxy/N-oxide moiety. Derivative 4, having a 2-carboxamide moiety, was the only one present as a mixture of tautomers, being N-oxide the predominant one. This was assigned to the formation of an internal hydrogen bond between the N-oxide group and the amide hydrogen atom. The tautomeric form present in the solid state was conclusively assigned by X-ray diffraction techniques to the N-hydroxy tautomer. In the crystal a strong O-H...N intermolecular bond gives rise to supramolecular polymeric chains in the lattice. This strong interaction was also seen in the infrared spectrum and was assigned to two broad bands at 2367 and 2526 cm-1. The vibrational spectrum was satisfactorily described by DFT calculations and an example of this is the prediction of the band corresponding to the N-O stretching (N-oxide) just 1% lower than the experimental value. Uncorrelated calculations (HF) were not able to give an unambiguous assignation of this band. The reaction of derivative 1 (Ethyl 5-nitrobenzimidazol-3-oxide 2-carboxylate) against different kinds of electrophiles, hard and soft, led only to O-substituted products. This result was explained in terms of the HSAB theory using a local-global approach.

The addition reaction of diamides to 1,2,5-thiadiazole 1,1-dioxide derivatives

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The reactions of several derivatives of 1,2,5-thiadiazole 1,1-dioxide (3,4-diphenyl (1a), 3,4-di(p-methoxiphenyl) (1b), phenanthro [9,10-c] (1c) and acenaphtho [1,2-c]- 1,2,5-thiadiazole 1,1-

dioxide (1d), 3,4-diphenyl-1,2,5-thiadiazoline 1,1-dioxide (2a) and 4-ethoxy-5-methyl-3,4-diphenyl-1,2,5-thiadiazoline 1,1-dioxide (2b)), with reagents possessing two nucleophilic nitrogen atoms (urea, N,N'-dimethylurea, thiourea, N-methylthiourea, N-ethylthiourea, N-allylthiourea, N, N'- diethylthiourea, N, N'-diphenylthiourea, dithioxamide and sulfamide), were followed by cyclic voltammetry (CV) and UV-VIS spectroscopy in aprotic solvents solution. The products were isolated, characterized by IR, 1H-NMR, 13C-NMR, and their structure was confirmed by single crystal X-ray diffraction. Several substrate-nucleophile combinations (1a-d and 2a with some ureas and thioureas) reacted to give good yields of new compounds formed by the addition reaction of the two nitrogen atoms of the nucleophile to the two >C=N double bonds of the 1,2,5-thiadiazole 1,1-dioxide ring. Some systems (1a-dithioxamide and 2b-thiourea) did not react, while in others (e.g. 1a-sulfamide) a monoaddition equilibrium reaction was observed.

Ethyl p-tert-butyl calix(4)arene ethanoate: the Role of Acetonitrile in the Extraction of Alkali-Metal Picrates and on the X-ray Structures of the Sodium Complexes

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Distribution data for alkali metal picrates in the water-chloroform solvent system in the absence and in the presence of acetonitrile were used to determine the partition constants of the dissociated electrolytes in the mutually saturated solvents and the ion-pair formation constants in the water saturated organic phase. These data were compared with those previously reported in water-benzonitrile and water-dichloromethane solvent systems. The same experiments carried out in the presence of ethyl p-tert-butylcalix(4)arene tetraethanoate, EtCalix(4), led to the calculation of distribution and extraction constants in these solvents systems. The presence of acetonitrile in the organic phase enhances significantly the extraction constant to an extent that these are the highest values so far obtained in the solvent systems investigated. This enhancement in extraction is attributed to metal complex stabilization promoted by the presence of acetonitrile in the hydrophobic cavity of the ligand. The X-ray structures of two sodium complexes (picrate as the counter-ion), isolated from water saturated chloroform with and without acetonitrile are reported for the first time. In the first complex, the macro-cycle is sited on a crystallographic four-fold axis and hosts an acetonitrile solvent molecule in its calix and a sodium ion in its hydrophilic cavity. The metal is in a eight fold Archimedean square anti-prism environment, coordinated to the phenol oxygen atom and to the carbonyl oxygen atom of the four rotationally symmetry related pendant arms. The macro-cycle of the other complex adopts a slightly distorted cone conformation and its hydrophilic cavity also hosts a sodium ion. But now the metal is in a seven-fold environment, coordinated to the four phenol oxygen atoms and to the carbonyl oxygen atoms of three pendant arms acting as bidentate ligands. The fourth, mono-dentate, pendant arm points away from the hydrophilic cavity and its terminal -CH2-CH3 group interacts hydrophobically with the calix of a neighboring complex giving rise to a supra-molecular polymeric structure in the lattice.

Thermodynamics of Host-Guest Interactions in Lower Rim Functionalized Calix[4]arenes and Metal Cations: The Medium Effect

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A new calix[4]arene derivative containing mixed pendant arms in its lower rim, 5,11,17,23-tetra-tert-butyl[25,27-bis(ethylethanoate)oxy-26,28-bis(ethylthioethoxy)]-calix[4]arene, 1, has been synthesised and characterised by 1H and 13C NMR. 1H NMR data carried out in CDCl3, CD3CN, CD3OD and C3D7NO suggest that as far as acetonitrile is concerned, the hydrophobic cavity is likely to embrace a solvent molecule. It is shown that the hosting capacity of 1 towards metal cations is greater in acetonitrile than in N,N-dimethylformamide and in methanol. Thus, in the former solvent, complexation with various cations (Li+, Na+, Ag+, Ca2+, Cu2+, Hg2+ and Pb2+) occurs while in the latter media, 1 interacts only with Ag+ and Hg2+. This statement is corroborated by 1H NMR, conductance, calorimetric and potentiometric measurements. It is concluded that through molecular inclusion of acetonitrile in the hydrophobic cavity of 1, the hydrophilic cavity of the adduct becomes more receptive to host metal cations than that of the free ligand. In propylene carbonate, the results show that the ligand loses its ability to interact with metal cations. Thus in acetonitrile, selective recognition of 1 for Hg2+ is demonstrated to an extent that the selectivity for this cation is greater by factors of 1.8 × 103, 1.9 × 103, 6.9 × 103, 1.8 × 104, 4.1 × 104 and 4.5 × 104, relative to Pb2+, Na+, Li+, Cu2+, Ag+ and Ca2+, respectively. This statement is supported by the thermodynamic characterization of the complexation process involving these systems in acetonitrile, N,N-dimethylformamide and in methanol. Thus, the medium effect on the binding process is carefully assessed. The results show that replacement of two ester groups in two alternate pendant arms of the tetraester calix[4]arene derivative by thiomethyl moieties has altered significantly the binding capacity and the selective behavior of the latter relative to the former. Final conclusions are given.

Metal-assisted Regio- and Stereospecific Insertion of Alkynes into a C-H Bond Leading to Functionalized Diphosphane Ligands

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Reaction of the complex fac-[Mn(CNtBu)-CO)3(PPh2)2C-H] (1) with dimethyl acetylene dicarboxylate and methylpropiolate affords the compounds fac-[Mn(CNtBu)(CO)3(PPh2)2CC(R)=C(R)-H] (2a, R=R'=CO2Me; 2b, R=H, R'=CO2Me),as a result of regio- and stereo specific insertion of the alkynesintothe C-H bond of the diphosphanyl methanide ligand, allowing highly selective metal-assisted synthesis of new functionalized diphosphane derivatives.

New Vanadium(V) Complexes with Salicylaldehyde Semicarbazone Derivatives: Synthesis, Characterization and In Vitro Insulin Mimetic Activity. Crystal Structure of [VVO2(salicylaldehyde semicarbazone)]

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A series of new dioxovanadate(V) semicarbazone complexes with the formula cis-VO2L, where L=salicylaldehyde semicarbazone (L1), N4-n-butyl salicylaldehyde semicarbazone (L2) or N4-(2-naphtyl) salicylaldehyde semicarbazone (L3), have been synthesized, characterized by 1H and 13C NMR and FTIR spectroscopies and tested for bioactivity as potential insulin mimetic agents. All dioxovanadate(V) complexes exhibited essentially non in vitro insulin mimetic activity, but VO2L2 complex developed weak activity in the presence of ascorbic acid. The molecular structure of the novel vanadium salicylaldehyde semicarbazone complex VO2L1 was solved by X ray diffraction methods. It crystallizes in the tetragonal space group P42/n with a=b=12.7674(7), c=11.5308(5)Å, and Z=8. The vanadium atom is in a distorted square pyramidal coordination, with L1 acting as tridentate ligand through its azomethynic nitrogen, its carbonyl oxygen and its deprotonated phenolic oxygen. The coordination sphere is completed with two oxo ligands at cis positions.