Ph. D. THESIS

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Preparation and characterization of unstable nitrile oxides and furoxans

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**Introduction**

Nitrile oxides (X-CNO) are well-known unstable molecules. They are very reactive and dimerize into their stable furan type derivatives, thus are prepared in situ in various chemical reactions. They usually behave as 1,3-dipolarophiles, and are important starting materials in cycloaddition reactions to synthesize various heterocycles, including biologically active compounds. Fulminates (their salts) are used as explosives for a long time. Covalent nitrile oxides are unstable compounds and usually dimerize rapidly to furoxans.

Nitrile oxides have interesting structures, especially the question of quasi-linearity of the XCNO skeleton was in focus of research in the last decades. For spectroscopical and theoretical point of view simple nitrile oxides with small substituents are of important relevance. Consisting solely of C, N, O and H of relatively high abundance in the interstellar medium, small nitrile oxides are also of potential astrophysical interest.

Furoxans (1,2,5-oxadiazole-2-oxides) are well-known stable compounds since the second part of XIX. century. As far as the connecting X ligands are concerned they can be divided into symmetric and asymmetric furoxans. The five-membered ring includes two nitrogen atoms and an oxygen atom, therefore furoxans are concerned as high-energy materials. Depending on the substituents the ring opening reaction can be very vigorous (for example NO$_2$-compounds).

Furoxans have also interesting and special structures. Because of N and O atoms the ring has negative charge, they are usually described as „electron-rich” compounds in the literature. The ring is planar and has a delocalised electronic structure. Depending on the substituents and the interaction between the ring and substituents, the geometry and stability of furoxans are varied. Furoxans are stable compounds, which can be easily thermolyzed into nitrile oxides depending on substituent X. (Figure 1)
Furoxans became important industrial starting materials in the XX. century, including important pesticides and biologically active compounds. It is important to note the biological effect of furoxans, which can be explained with \textit{in vitro} NO liberation from the five-membered ring.

\begin{center}
\begin{tikzpicture}
\node at (0,0) {\includegraphics[width=0.5\textwidth]{furoxan.png}};
\end{tikzpicture}
\end{center}

\textbf{Figure 1}

Connection between nitrile oxides and furoxans

The purpose of this work was to prepare and characterize unstable nitrile oxides and furoxans, especially those that are unknown or hardly investigated. Simple substituted derivatives are important spectroscopically, so this work was focused on H-, F-, Cl-, Br-, I-, CH\textsubscript{3}-, CF\textsubscript{3}-, NC- and HCC-substituted derivatives. IR and Raman-spectroscopy as well as quantum-chemical calculations were used to characterize molecules and to investigate their electronic and geometric structures.

\textbf{Experimental/Computational methods}

DFT methods are prooved to be powerful tools in describing the structure and energetics of nitrile oxides and furoxans. Quantum chemical calculations were performed with B3LYP method with different basis sets ranging from 6-311G(d) to cc-pVTZ depending on the type of problem. The electronic structure of nitrile oxides requires a good description of dynamic electron correlation, thus the CCSD(T)/cc-pVTZ method is used to calculate their
structures concerning the question of quasilinearity. Calculations were done with Gaussian 98 (Revision A9).

Infrared spectroscopical characterization of molecules in the gas phase was performed in the 4000-400 cm\(^{-1}\) region using Nicolet Nexus 870 FT-IR spectrometer, which was equipped with a single-pass cell suitable for gas phase measurements. For liquid phase IR measurements Perkin-Elmer System 2000 FT-IR spectrometer was used. Measurements were done at room temperature using liquid film between two KBr windows. Solid and liquid phase Raman spectroscopical measurements were performed in the 4000-150 cm\(^{-1}\) region using a Bruker RFS 100 FT-Raman spectrometer equipped with Nd-YAG (1064 nm) laser.

Results

I. Dimerization of simple nitrile oxides

1. Quantum-chemical calculations indicated that the dimerization of nitrile oxides into furoxans is a multi-step process which goes through dinitrosoethylene-like intermediates. The lowest energy pathway can be seen in Figure 2. The rate determining step is the first one (TS1). In case of halide derivatives (F\(-\), Cl\(-\), Br\(-\)) the activation barrier is low (no barrier for FCNO dimerization), in case of alkyl derivatives (CH\(_3\)-, CF\(_3\)-) and NC-derivatives the barriers are higher. In these latter cases the furoxans are thermodynamically less stable than in case of halide derivatives compared to the two corresponding monomers. In case of alkyl derivatives the energies of dinitrosoethylene-type transition states are much more closer to the energy of TS1.

2. The one-step dimerization of nitrile oxides yields 1,2,4-oxadiazole-4-oxides and 1,4,2,5-dioxadiazines. These derivatives are thermodynamically more stable than furoxans, but the activation barrier of the process is 1.5-2 times higher.
The dimerization of nitrile oxides into furoxans on the lowest energy pathway

3. In case of NCCNO, not only the CNO-group, but the NC-group is also capable to take part in cycloaddition reactions. The number of possible reactions is therefore higher. NCCNO may dimerize to yield besides furoxan other dimers, having a free CNO-group. This CNO-group can react further with another NCCNO, and oligomerization or polymerization can also be anticipated. The activation barriers and thermodynamic stability for all dimers are comparable, thus all reaction routes are feasible.
II. The oligomerization of HCNO

1. From the quantum-chemical investigation of oligomerization of HCNO, it can be stated that besides the dimerization that produces furoxan and proceeds through open-shell biradical intermediates, there is another reaction route leading to the nitrile oxide dimer 2-hydroximino-acetonitrile oxide (HO-N=CH-CNO). In this process a hydrogen atom „jumps” from a carbon atom to the other. The relative stability of this product is about the same as the relative stability of furoxan and this nitrile oxide is vital in the formation of trimers and tetramers.

2. HO-N=CH-CNO can react further with HCNO or HO-N=CH-CNO to produce trimers and tetramers. Trimerization yields either furoxan derivatives or trimer nitrile oxide (2,3-bis(hydroximino)propionitrile oxide, HO-N=C(CH=NOH)-CNO). The mechanism of the formation of the trimers is analogous with that of the dimers, although the trimerization processes require higher activation barriers.

3. During trimerization, metafulminuric acid forms by the ring cyclisation of the trimer nitrile oxide above. The activation energy of ring closure is high, but decreases by the assistance of a water molecule.

4. In case of tetramerization, the dimer HO-N=CH-CNO reacts with another dimer to produce the furoxan derivative, isocyanilic acid. The formation of isocyanilic acid requires higher activation energy than the formation of trimers, but it is still exothermic compared to the two dimers (HO-N=CH-CNO).

5. The reaction between monomer HCNO and trimer 2,3-bis(hydroximino)propionitrile oxide (HO-N=C(CH=NOH)-CNO) yields asymmetric tetrameric structures including furoxans and a nitrile oxide. The reaction energies are comparable with the reactions above, so the formation of these compounds is also feasible.
6. HCNO was prepared by a literature method, and dimerization of the pure compound was investigated experimentally. The trapped solid HCNO reacted vigorously at -20 °C, and exploded.

III. The structure and stability of HCCCNO

1. According to calculations, the structure of 2-propinonitrile N-oxide (HCC-CNO) is linear, similarly to the isoelectronic NCCNO derivative. The deformational potential curves of the molecule show linear equilibrium structure with small anharmonicity.

2. According to the calculations of the possible monomolecular and bond dissociation processes of the molecule it can be concluded that the preparation of the molecule is feasible, but it is likely that it isomerizes at higher temperatures into the thermodynamically more stable HCCNCO derivative, and it dimerizes in the condensed phase like other nitrile oxide derivatives or polimerizes like NCCNO.

IV. The structure and stability of CF₃CNO

1. The structure of trifluoroacetonitrile oxide (CF₃CNO) was determined by quantum-chemical calculations. B3LYP method gave linear CCNO structure, while CCSD(T) method showed bent frame. The deformational potential curves of the molecule were similar to those of other typical quasilinear nitrile oxides, like BrCNO and ClCNO.

2. Besides dimerization processes of CF₃CNO (I/1.) the unimolecular isomerization routes and bond dissociation processes were also investigated. According to the calculations CF₃CNO is expected to isomerize at higher temperature to the stable CF₃NCO derivative or decompose in the CF₃CNO → CF₃CN + O process. Like other nitrile oxides, CF₃CNO also dimerizes in the condensed phase.
V. Preparation and infrared spectroscopical study of CF₃CNO

1. CF₃CNO was prepared from trifluoro-acetohidroximoyl bromide (CF₃C(Br)NOH) by HBr elimination. HBr elimination was obtained with three methods: gas phase reaction with triethyl amine, gas phase thermolysis and solid-gas reaction with HgO. Pure nitrile oxide with the best yield could be obtained with the solid-gas reaction with HgO. Raw CF₃CNO was lead through a U-trap cooled to -126 °C. Only CF₃CNO had enough vapour pressure to get into the spectrometer.

2. The structure of the IR bands of CF₃CNO in the spectrum shows linear or quasilinear CCNO frame. Because of the complicated combination bands, the small resolution of the bands and the hot bands it can not be clearly decided that the molecule is linear or quasilinear.

VI. Experimental attempts to obtain diiodofuroxan

1. Diiodofuroxan was tried to be prepared by means of literature methods analogously to other furoxans. The reaction of monoiodo acetic acid with fuming nitric acid, as well as the ring closure reactions of diiodoglyoxime were unsuccessful.

2. According to a published procedure mercury fulminate was reacted with iodine. The reaction was repeated several times, and the solvent was also changed as well as the ratio of starting materials, but diiodofuroxan couldn’t be obtained.

3. Experimental work on diiodofuroxan was extended with the preparation of dichloro-, dibromo- and diiodoglyoxime. A new method to prepare dibromoglyoxime was suggested. According to the procedure glyoxime was reacted with N-bromosuccinimide in the presence of a base (DMF).
VII. Preparation and characterization of the parent furoxan

1. Furoxan was prepared by modification of a published method. Glyoxime was reacted with NO₂ gas. With this method almost pure (>95%) raw material could be obtained. The product was purified by distillation, thus the obtained pure material was suitable for spectroscopical studies.

2. Similarly to halide derivatives the gas phase thermolysis of furoxan did not result monomer nitrile oxide. The pyrolysis begins already at 200 °C, and it is already complete at 400 °C. The most intensive pyrolysis-products are: HNCO, HCN, CO₂ and H₂O.

3. According to the calculated NPA-charges the ring is „electron-rich”. According to Gordy bond orders the strongest bond in the molecule is the exocyclic NO bond. The most sensitive point for a cleavage is the endocyclic NO bond, which is the weakest bond.

4. The furoxan is an asymmetric prolate with C₅ symmetry. The rotational fine structure of the infrared spectrum shows this statement. According to the normal coordinate analysis the most intensive peak of the spectrum could be assigned to the exocyclic NO bond.

VIII. Preparation and characterization of bis(trifluoromethyl)furoxan

1. Bis(trifluoromethyl)furoxan was attempted to prepare with oxidation (MnO₂) of CF₃CH=NOH, as well as with the reaction of CF₃CH₂COOH with fuming nitric acid, but they both were unsuccessful.

2. Bis(trifluoromethyl)furoxan was prepared with the dimerization of the nitrile oxide. Pure CF₃CNO was trapped in liquid N₂ (-196 °C), and left to warm up to room temperature to dimerize. The obtained product was purified at -77 °C under vacuum.

3. Similarly to alkyl furoxans and dicyanofuroxan the thermolysis of bis(trifluoromethyl)furoxan yields monomer nitrile oxide. Pyrolysis started at 400 °C,
clean CF$_3$CNO could be obtained at 500 °C, and above 600 °C no signs of the dimer were observed.

4. According to calculated NPA-charges the ring is also „electron-rich“. Gordy bond orders show that the strongest bond in the molecule is the exocyclic NO bond. The most sensitive point for a cleavage is the endocyclic NO bond, which is the weakest bond.

5. The infrared and Raman-spectra showed typical „fingerprints“ of furoxan molecules as far as bands, assignment and vibrational analysis are concerned. According to normal coordinate analysis the most intensive peak of the furoxan ring in the spectrum can be assigned to the exocyclic NO bond.
List of Publications:

1. Tibor Pasinszki, Balázs Havasi, Nicholas P. C. Westwood: accepted for publication (J. Phys. Chem. A);
   Dimerization of nitrile oxides: a quantum-chemical study

   Gas-phase infrared and \textit{ab initio} study of the unstable CF\textsubscript{3}CNO molecule and its stable
   furoxan ring dimer

   Quantum-chemical study of the structure and stability of ethynyl pseudohalides:
   HC≡C–NCO and its isomers

Publications not included in the thesis:

   Midinfrared and quantum-chemical study of the structure, conformation, and
   isomerization of the unstable CH\textsubscript{3}CH\textsubscript{2}OCN molecule

   Synthesis, spectroscopy and structure of CF\textsubscript{3}CH\textsubscript{2}OCN, CF\textsubscript{3}CH\textsubscript{2}NCO, and
   (CF\textsubscript{3}CH\textsubscript{2}O)\textsubscript{2}CNH