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Deuterium disturbs – influence of deuterium on the aggregation of pyridine-N-oxides

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Hydrogen/Deuterium (H/D)-exchange, the smallest possible modification of a molecule, is generally seen as a non-dominating parameter as far as the crystal structures or physical properties of the molecule are concerned.

Only some rare examples of observable isotope effect of deuterated compounds are known. For example, H/D-exchange can be purposefully used to improve such physical properties as ferroelectricity or dielectric constant of some inorganic materials [1]. Recent investigations of pyridine showed the existence of a further low-temperature crystallographic phase for perdeuteropyridine in contrast to the non-deuterated pyridine [2].

This background encourage us to investigate how the partial deuteration of pyridine-N-oxides influence the aggregation of the molecules in solid state?

In previous studies, we have shown that the substitution pattern on the benzene backbone of iodo-substituted benzonitriles and nitrobenzenes have an influence on the formation of the packing motifs in corresponding crystal structures [3]. Furthermore, our X-ray crystallographic studies of low melting fluorinated pyridines indicate the replacement of hydrogen by fluorine leads to significant changes in the molecular aggregation in solid-state [4].

Continuing our investigations on aggregation of substituted aromatic molecules in the solid state, herein, we report the crystallization behaviour of several deuterated pyridine-N-oxides. The crystal packing of pyridine-N-oxides were found to be very sensitive to H/D-exchange [5]. Using a carefully controlled *in situ* crystallization technique, we were able to characterize crystallographically two isotopomorphic low-temperature and high-temperature phases. The results are verified by DSC measurements.

[1] Koval S., Kohanoff J., Lasave J., Collizi G., Magoli R.L., *Phys. Rev. B*, 2005, 71, 184102. [2] Crowford S., Kirchner M.T., Bläser D., Boese R., David W.I.F., Dawson A., Gehrke A., Ibberson R.M., Marshall W.G., Parsons S., Yamamuro O., *Angew. Chem. Int. Ed.*, 2009, 121, 769. [3] Merz K., *Cryst. Growth Des.*, 2006, 6(7), 1615. [4] Vasylyeva V., Merz K., *J. Fluor. Chem.*, 2010, 131(3), 446. [5] Vasylyeva V., Kedzioriski T., Schauerer C., Merz K., *Angew. Chem.*, 2010, submitted.

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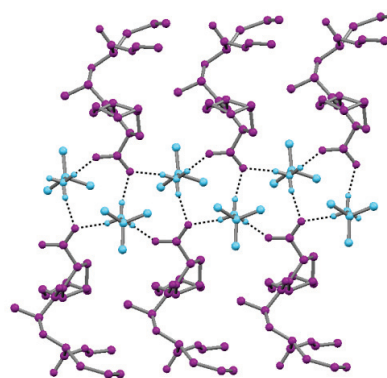
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Alternative crystal forms of the antihypertensive

Perindopril Erbumine. Vânia André^a, M. Teresa Duarte^a, Luís Cunha-Silva^b, Pedro Paulo Santos^a
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Besides the antihypertensive effect, perindopril also possess other properties, such as vasculoprotective and antithrombotic effects that can play a favorable role in terms of cardiovascular morbidity [1]. Perindopril erbumine is known to exist in different polymorphic forms. Perindopril is orally administered in the form of tablets containing its salts (1:1) with erbumine (tert-butylamine) or L-arginine. These pharmaceutical salts involve the transfer of a proton between the API and the coformer. New forms of these salts can have improved pharmaceutical properties and they often rely on different intermolecular hydrogen bonds between the active pharmaceutical ingredient and other components (coformers) with well-defined stoichiometries [2]. Forms alpha, beta and gamma were reproduced using different synthetic methods and some of them were for the first time characterized by single crystal X-Ray diffraction. Furthermore, a new hydrated form as also been disclosed and fully characterized. Tests have shown that this form is quite stable and its dissolution profile is very similar to the commercially available form.



[1] M. Remko, *European Journal of Medicinal Chemistry*. 2009, 44, 101-108. [2] V. André, D. Braga, F. Grepioni, M. T. Duarte, *Crystal Growth and Design*, 2009, 9, 5108-5116.

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Hydrogen bond interaction energies of selected n-alkyldiammonium halide salts.

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Studies of the halide salts of short-chain n-alkyldiamines form the basis of our research of these materials since they have important applications [1 – 2]. The compounds investigated in this work consist of materials that have the general chemical formula $C_nH_{2n} \cdot 2(NH_3^+) \cdot 2X^-$, with $X = Cl^-; Br^-; \text{and } I^-$ where we focus specifically on salts of compounds where $n = 2, 3, 4$ and 6 . They form interesting packing motifs and have extensive, complex three-dimensional hydrogen bonding networks [3].

As a result of our previous work carried out on these materials [3,4], we have established that the packing of these materials in the crystal structure is stabilized by the hydrogen bonding networks. Since these networks are so extensive and complex, the intermolecular interaction energies have become an added point of interest to our research. This current work focuses on DFT theoretical calculations of the hydrogen bond interaction