SJEZD CHEMICKÝCH SPOLEČNOSTÍ – DODATKY

PREPARATION OF COBALT OXIDES NANOPARTICLES AND METAL COBALT NANOPARTICLES BY TEMPERATURE DECOMPOSITION OF COBALT GLYCEROLATE

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Metal cobalt nanoparticles and cobalt oxide nanoparticles CoO and Co_3O_4 can be used in various scientific, medicinal and industrial applications. In this work we describe preparation of metal cobalt nanoparticles with average diameter about 30 nm and CoO and Co_3O_4 nanoparticles with various sizes. Co, CoO and Co3O4 nanoparticles were prepared by thermal decomposition of cobalt glycerolate under 50 % H_2 – 50 % N_2, 100 % N_2 and 50 % O_2 – 50 % N_2 atmospheres respectively. Cobalt glycerolate was prepared by reaction of cobalt nitrate with glycerol under reflux for 4 hours. Obtained nanoparticles were analyzed by X-Ray diffraction and in the case of metallic Co nanoparticles by SEM and magnetic measurements. It has been discovered sizes of oxidic nanoparticles are dependent on temperature of decomposition. By this method simple preparation of Co, CoO or Co_3O_4 is possible with possibility to preparation of various sizes of nanoparticles only by changing reaction conditions in furnace. This could be very useful for future research and for application in practice.

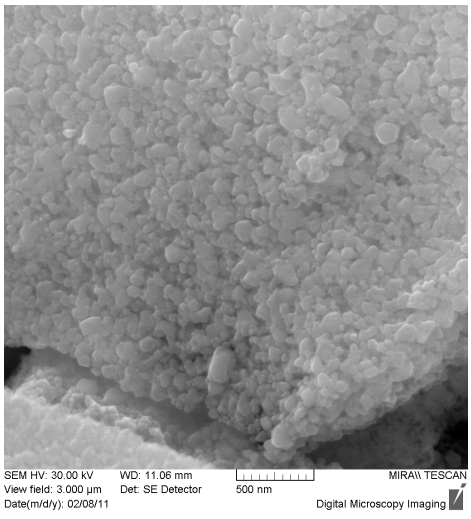

Fig. 1. **SEM image of prepared Co metal nanoparticles**

PENTAMETHINE SALTS FOR SUPERIOR FLUORESCENCE IMAGING OF MITOCHONDRIA BASED ON CARDIOLIPIN BINDING

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Labeling of mitochondria for fluorescence microscopy is generally achieved using transiently expressed mitochondrial protein markers or dyes specifically accumulating in this organelle. Here we demonstrate a series of novel fluorescent dyes from γ-aryl substituted pentamethine family possessing excellent photostability, fluorescence properties and low phototoxicity. They localize in mitochondria of various cell lines with unique selectivity and are detectable in nanomolar concentrations. Our results indicate that these novel mitochondrial dyes effectively cross the cell plasma membrane and then accumulate in inner mitochondrial membrane due to binding to cardiolipin. Pentamethine salts label mitochondria with high specificity and their low toxicity enables to study morphological changes and structural complexity of these dynamic organelles in different cell lines in real time by live cell fluorescence microscopy. Moreover, they are suitable also for mitochondria staining in fixed cells as they are retained during washing and fixation procedures.

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PARALLEL TRIS-TRÖGER'S BASES

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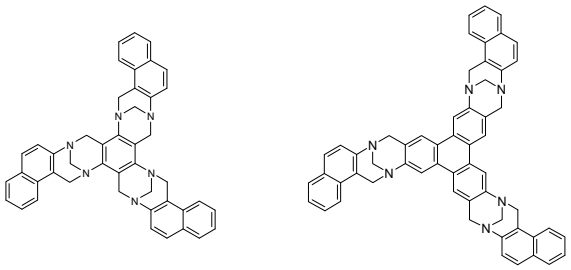
Tröger's bases (TB) are compounds containing two aromatic systems connected by 1,5-diazabicyclo[3.3.1] nonane (TB unit). Thanks to their geometry (C2 symmetry, concave V-shape and chirality), TB derivatives can be used as useful building blocks in molecular engineering. Parallel Tröger's bases (trisTB) include three TB units annelated to a single arene (e.g. benzene). These compounds have two diastereoisomers: non-cavity *throne*-trisTB and *calix*-trisTB having a cavity. TrisTB diastereoisomers can be interconverted to each other in acid medium; thus, the cavity can be created or disposed by a change in pH. This unique property differs of *calix*-trisTBs from other known cavitands. Preparation, structure and diastereoisomerisation study of trisTB will be presented.



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REFERENCES

1. Dolenský B., Elguero J., Král V., Pardo C., Valík M.: Adv. Heterocycl. Chem. *93*, 1 (2007).
2. Dolenský B., Havlík M., Král V.: Chem. Soc. Rev. *41*, 3839 (2012).
3. Havlík M., Dolenský B., Kessler J., Císařová I., Král V.: Supramol. Chem. *24*, 127 (2012).

THE FIRST BINDING STUDIES OF BIS-TRÖGER'S BASE

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The youngest family of rigid molecular tweezers, bis-Tröger's base (bisTB) derivatives[1,2], is based on a motive of Tröger's base (TB)[3]. BisTB can be figuratively described as two aromates connected through two TB units (1,5-diazabicyclo[3.3.1]nonane) to central aromate. The TB unit provides about perpendicular orientation of connected aromates, thus the side aromates are about parallel. The side aromates can be on the same side of the plane of central aromate (syn diastereoisomers) or on its opposite sides (anti diastereoisomers). To date, only bisTB derivatives having benzene as the central aromate are known. There are five possibilities how to connect side aromates to central benzene[3] wherein only three could fulfill requirements on molecular tweezers. Each that possibility is presented in this work by one naphthalene bisTB derivative **1**, **2**, **3** and **4**. For a preliminary test of a complexation ability of syn- and anti-bisTB **1-4** we chosen widely used TCNB (1,2,4,5-tetracyanobenzene) as guest molecules. Titration experiments monitored by ^{1}H NMR spectra showed that the *syn*-bisTB form stable complexes than *anti*-bisTB, and that the stability of complexes with 1,2,4,5-tetracyanobenzene increases in the following order: *syn*-**1** (K_a = 18 M^{-1}), *syn*-**2** (K_a = 105 M^{-1}), *syn*-**3** (K_a = 665 M^{-1}), the *syn*-**4** (K_a = 2724 M^{-1}). Significantly higher value of the new K_a bisTB derivatives **3** and **4** gives hope for their use as molecular tweezers for applications in analytical chemistry.

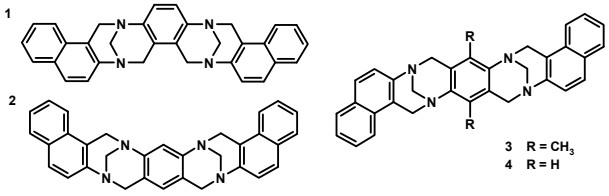

Schéma 1. **Structure of studied naphtalene bis-Tröger's base**

This work was supported by the Grant Agency of the Czech Republic (203/08/1445).

REFERENCES

1. Klärner F. G., Kahlert B.: Acc. Chem. Res. *36*, 919 (2003).
2. Pardo C., Sesmilo E. and all: J. Org. Chem. *66*, 1607 (2001).
3. Valík M., Dolenský B., Petříčková H., Král V.: Collect. Czech Chem. Comm. *67*, 609 (2002).

CYKLODEXTRIN-PORFYRINOVÉ KONJUGÁTY JAKO SUPRAMOLELÁRNÍ SYSTÉM PRO KOMBINOVANOU TERAPII A CÍLENÝ TRANSPORT LÉČIV

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Zvýšení účinnosti protinádorové léčby je jeden významných cílů farmaceutického výzkumu. Toho se dá dosáhnout novými léčivy, nebo efektivnějším použitím již známých léčiv. Redukce toxicity léčiv a zvýšení jejich selektivity pro cílovou tkáň/buňku může být dosažena pomocí cíleného transportu. Zvýšení jejich účinku se dá dosáhnout pomocí synergického efektu kombinované terapie. V ideálním případě použitím kombinací obou metod[1]. Proto jsme připravily a testovaly nový vysoce účinný a variabilní systém zahrnující tři různé terapeutické módy (photodynamická terapie, chemoterapie a imunoterapie) umožňující cílený transport s vysokou selektivitou pro nádorové tkáně[2–5]. Tento systém je založený na kombinaci léčiva, Zn-porphyrin-cyklodextrin konjugátu, a terapeutického proteinu. Naše analytické, biochemické, *in vitro* a *in vivo* studie zaměřené na jeho použití pro cílený transport a terapii, jasně demonstrovaly vysokou efektivitu, selektivitu a variabilitu našeho systému.

Tato práce byla podpořena Grantovou agenturou AV ČR (KAN200100801), Grantovou agenturou ČR (P303/11/1291, 203/09/1311), BIOMEDREG (CZ.01.05/2.1.00/01.00.30) a Univerzitou Karlovou (UNCE 204011/2012 and P24/LF1/3)

LITERATURA

1. Kejík Z., Kaplánek R., Bříza T., Králová J., Martásek P., Král V.: Supramol. Chem. 24, *106* (2012).
2. Kejík Z., Bříza T., Králová J., Poučková. P., Král. A., Martásek, P., Král V. Bioorg. Med. Chem. Lett. *21*, 5514 (2011).
3. Králová J., Kejík Z., Bříza T., Poučková P., Král A., Martásek P., Král V.: J. Med. Chem. *53*, 128 (2010).
4. Král V., Bříza T., Kejík Z., Králová J., Poučková P.: CZ 300197 B6 20090311 (2009).
5. Kejik Z., Bříza T., Poučková P., Králová J., Král V., Martásek P.: J. Controlled Release *132*, e27 (2008).

NOVEL PHTHALAZINYL HYDRAZONES - SYNTHESIS AND ANTICANCER ACTIVITY

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Heteroaryl hydrazones are class of compounds with significant biological activity and many of these compounds display anticancer activity. Therefore we designed and synthesized set of phthalazinyl hydrazones for testing their activity against tumour cells. Anticancer activity evaluation on the human promyelocytic leukemia cells (HL60) and mouse mammary carcinoma cells (4T1) showed that some phthalazinyl hydrazones have significant inhibitory effect against both cancer cell lines. Complexation studies toward biologically important metal ions at biologically relevant conditions show general ability to bind Cu^{2+}, Co^{2+}, Ni^{2+} and Fe^{3+} (with some exceptions) and rarely Zn^{2+} and Fe^{2+}. There is not any clear correlation of binding ability with anticancer activity; however all derivatives able to bind Zn^{2+} display very high activity (IC_{50} < 1 μM) and opposite way all derivatives without binding ability towards Co^{2+} do not display any significant activity (IC_{50} > 10 μM). Hydrazones are known to display tautomerism; QD/MD calculations in aqueous media show preference of hydralazine form. Calculations also show that metallo-complexes of derivatives are relatively planar and thus potentially allow intercalation into DNA in contrast to derivatives themselves. This is in good agreement with experimental observation that metallo-complexes of many derivatives display ability to interact with DNA but derivatives themselves do not.

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REFERENCES

1. Richardson D. R.: Curr. Med. Chem. *12*, 2711 (2005).
2. Buss J. L., Greene B. T., Turner, J., Torti, F. M., Torti S. V.: Curr. Top. Med. Chem. *4*, 1623 (2004).
3. Kogan V. A., Levchenkov S. I., Popov L. D., Shcherbakov I. A.: Russ. J. Gen. Chem. *79*, 2767 (2009).