SOLID-STATE NMR STUDY OF ADSORPTION OF INDOMETHACIN MOLECULES IN THE MIL-53 FRAMEWORK

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ABSTRACT

In this contribution, we report about the solid-state NMR study of indomethacin molecules adsorbed in the MIL-53(Al) framework. MIL-53 framework functionalized with two OH groups was loaded with indomethacin molecules and the behavior of adsorbed indomethacin molecules was studied.

Keywords: MOF, MIL-53(Al), indomethacin, NMR

INTRODUCTION

In the last decade Metal-Organic Frameworks (MOFs) surfaced as a promising new group of materials [1]. Due to their high surface area, tunable pore size and accessible metal sites MOFs can be used for variety of applications [2,3] ranging from gas and heat adsorption to separation of mixtures of gases, catalysis, chemical sensing and diverse medical applications. Biomedical applications include MOFs as the contrast agents for magnetic resonance imaging [4] and computed tomography [5] and delivery matrices for bioactive gasses [6] and miscellaneous drugs [7,8]. MOFs are especially promising as a new class of drug carriers because of their high and regular porosity combined with the presence of organic and functional groups which allows for encapsulation of various drugs and controlled release of adsorbed molecules. Not all types of MOFs are biocompatible and some present a health risk due to possible leaching of toxic metal ions and other hazardous components. Such problems can be eluded with selection of suitable nontoxic MOFs (iron III carboxylate MOFs for example) or so called bio-MOFs built from rigid biomolecules and biocompatible metal cations [9]. Adsorption of drugs can be further improved by incorporation of functional groups into the framework. Here we report about the solid-state NMR study of MIL-53(Al) framework loaded with indomethacin molecules. The NMR spectroscopy proved to be a powerful tool for this type of research as it offers an insight into intermolecular and intramolecular interactions between the adsorbed drug molecules as well as between these molecules and the MIL-53 framework.

EXPERIMENTAL

MIL-53(Al)-$(OH)_2$ framework used for the NMR studies was crystallized from reaction mixture with molar ratios of reactants $AlCl_3 \cdot 6H_2O$: H_2BDC-$(OH)_2$: 153 DMF after solvothermal treatment at 398 K for 16 hours in a Teflon-lined autoclave. As-synthesized framework was then activated in boiling solution of methanol and water (volume ratio 60:40) at 353K under reflux for 3 days.

Indomethacin is non-steroidal anti-inflammatory drug commonly used to reduce fever, pain and swelling. Solution of 100 mg/ml indomethacin in THF was prepared and activated MIL-53(Al)-$(OH)_2$ was added. After 3 hours the material was filtrated and dried.

^{1}H echoMAS, ^{13}C opMAS and ^{1}H-^{13}C CPMAS NMR spectra of the activated and loaded MIL53 framework have been recorded on the 600MHz Varian NMR system equipped with the Varian 1.6 mm MAS probe.

The adsorption of Indomethacin molecules in MIL53 framework was also confirmed with XRD and nitrogen sorption analysis.

RESULTS AND DISCUSSION

Effectiveness of loading procedure was tested with nitrogen sorption. Loaded framework showed approximately 80% smaller BET surface than activated one which indicates that pores of framework are filled with indomethacin molecules.

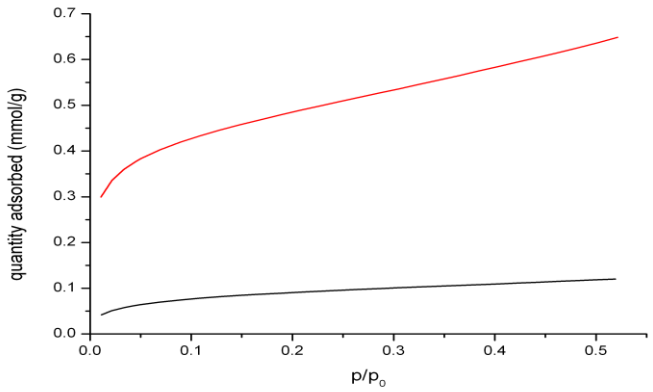

Figure 1. Nitrogen sorption in activated (red) and loaded (black) MIL-53(Al)-$(OH)_2$.

Comparison of NMR spectra also indicates that indomethacin molecules were successfully adsorbed into the pores of MIL53 framework.

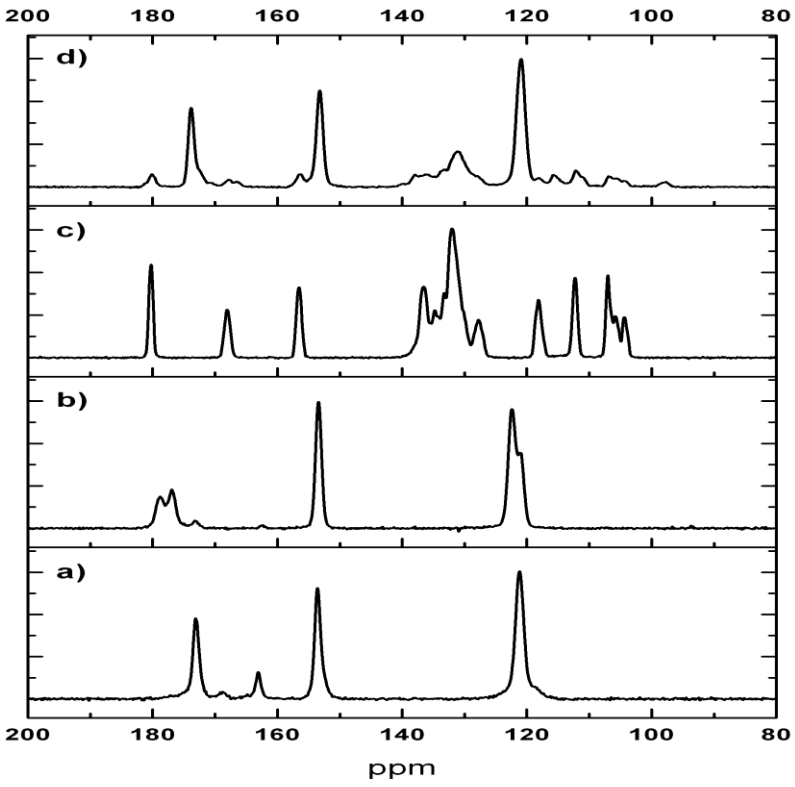

Figure 2. ^{1}H-^{13}C CPMAS spectra of as-synthesized (a) and activated (b) MIL-53(Al)-$(OH)_2$, indomethacin crystalized from THF solution (c) and MIL-53(Al)-$(OH)_2$ loaded with indomethacin molecules (d).

On the ^{1}H-^{13}C CPMAS spectrum of the loaded framework (Figure 2d) peaks corresponding to the indomethacin molecules are clearly visible (from 100 to 120 ppm, from 125 to 140 ppm and from 165 to 170 ppm) and they perfectly match the peaks on the spectrum of crystalized indomethacin. Peaks at 121, 154 and 173 ppm correspond to framework carbons and their shapes and positions match the shapes and positions of framework carbons on the spectrum of as-synthesized framework (Figure 2a) which suggests that the indomethacin molecules are located in the pores of the framework and not on the surface.

Interactions between indomethacin molecules were not observed on the ^{1}H-^{13}C CPMAS spectra. Comparison of ^{1}H echoMAS spectra however give some inside into the behavior of adsorbed molecules. Proton spectrum of indomethacin crystalized from the THF solution (Figure 3a) shows strong contribution from protons forming hydrogen bonds between indomethacin molecules (peak at 12ppm indicated by black arrow). Similar peak is also shown on a spectrum of MIL-53(Al)-$(OH)_2$ framework loaded with indomethacin molecules (Figure 3b) which suggests that indomethacin molecules in pores are close to each other and that they form hydrogen bonds.

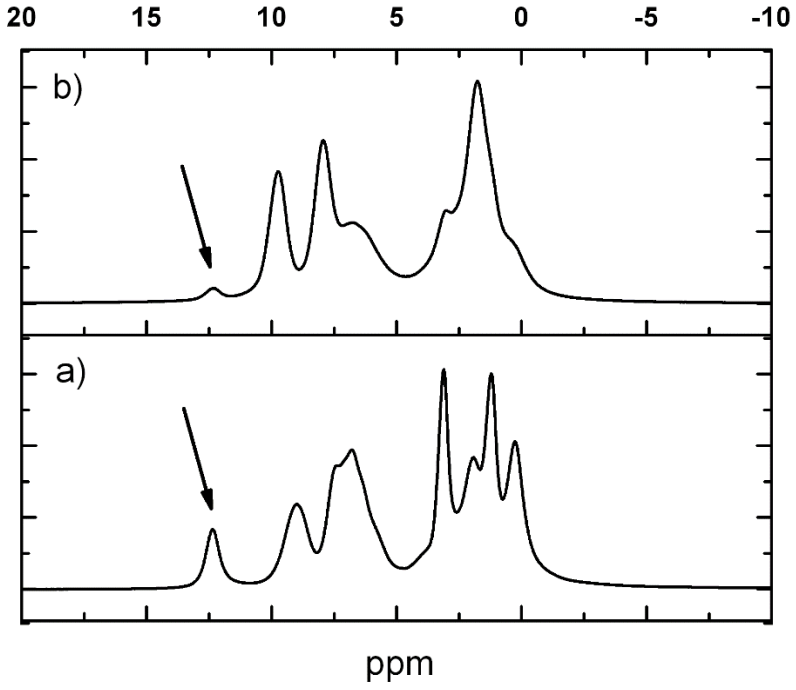

Figure 3. ^{1}H echoMAS spectra of indomethacin crystalized from THF solution (a) and MIL-53(Al)-$(OH)_2$ loaded with indomethacin molecules (b). Arrows indicate peaks corresponding to protons included in hydrogen bonds between indomethacin molecules.

CONCLUSION

We successfully loaded the MIL-53(Al)-$(OH)_2$ framework with indomethacin molecules and examined the behavior of adsorbed molecules with solid-state NMR spectroscopy. ^{1}H and ^{1}H-^{13}C CPMAS measurements indicate that indomethacin molecules are located inside the pores of the framework and that they are close enough to form hydrogen bonds.

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