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Diastereoselective Heterogeneous Bromination of Stilbene in a Porous Metal−Organic Framework

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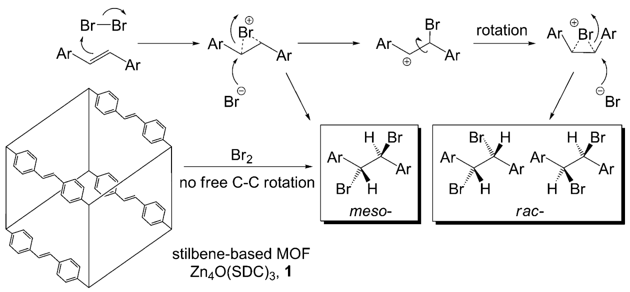
Metal−organic frameworks (MOFs) are a relatively new class of crystalline coordination polymers that have potential in a myriad of applications, including gas storage, catalysis, separations, drug delivery, and sensing.[1] A topic of considerable contemporary investigation is postsynthetic modification (PSM) of MOFs, whereby the framework species undergo heterogeneous chemical transformations while the overall crystalline structure is retained.[2] These reactions typically occur for porous frameworks in which the reagents gain access via open channels in the structure, and they can afford materials that may not be possible to generate using traditional MOF synthetic methods. Both the metal unit and the ligand can be modified, and a variety of PSM reaction types have been described.[3] MOF ligands are typically based on π-conjugated organic species, although only a few PSM reactions of the ligand π-system itself have been reported, including reduction[4] and organometallic matrix isolation-type chemistry.[5] We recently described the synthesis and application of luminescent MOFs based on *trans*-4,4′-stilbene dicarboxylate (SDC),[6] including a porous, cubic material having the formula $Zn_4O(SDC)_3$ (**1**), which should be amenable to PSM via typical reactions of alkenes, in particular the electrophilic addition of Br_2. Postsynthetic bromination of a side-chain alkene functionality has recently been demonstrated as part of a multistep, tandem PSM methodology.[7]

The reactivity of organic compounds in the solid state is of significant current interest, as solid-state reactions can offer potential advantages over their analogues in solution, including greater stereoselectivity (arising from crystal packing influences on the sterics of reaction), lack of side-products, and no solvent requirement.[8] Addition of halogens to stilbene represents a classic reaction for the study of stereochemistry and mechanism in this context, as two sets of diastereomers may result, a racemic (rac) pair of enantiomers and the corresponding meso isomer. From the polar mechanism for bromination in solution (see Scheme 1), the relative diastereomer composition can be seen to be determined by the stability of the carbocation intermediate that arises after initial formation of the cyclic bromonium ion. Stereochemical scrambling can occur via free rotation of the C−C bond in this intermediate, which enables formation of the isomerized bromonium ion. The product composition can therefore be affected by changes in solvent polarity and substituent electronics.[9] In the solid state, if the bromide ion cannot migrate within the crystal lattice to give back-side attack on the cyclic bromonium species, cis addition to give the *rac*-dibromide (from *trans*-stilbene) is expected. Experimentally, a mixture with a meso/rac ratio of ~4:1 is generated from *trans*-stilbene and Br_2 in CH_2Cl_2 solution (we observed similar results in $CDCl_3$), whereas the heterogeneous gas/solid reaction is less stereoselective, resulting in a relative isomer distribution of ~2:1.[10] Such heterogeneous reactions are also often low-yielding (~20%) and can be influenced by crystal size effects, as surface layers may be generated that block access of reagents for further reaction. PSM of MOFs represents an interesting extension of "solution-like" reactivity of organic species to heterogeneous chemistry (due to the open, porous nature of the framework) while retaining some of the advantages of solid-state processes.[11] We reasoned that heterogeneous bromination of **1** should give *meso*-4,4′-(1,2-dibromoethane-1,2-diyl)dibenzoate (*meso*-**2**) species exclusively by overall trans addition, as the bromonium intermediate should be accessible to back-side attack by Br^- while C−C rotation in this intermediate should be inhibited by the strong ligand coordination within the framework.[12]

Scheme 1. Polar Mechanism for Electrophilic Addition of Br_2 to Stilbenes



Reaction of crystals of **1** with Br_2 in $CHCl_3$ in the dark afforded a colorless crystalline material, which was extensively washed and then digested using DCl in DMSO-d_6 for analysis. ^{1}H NMR studies (Figure 1b) suggested the presence of both **2** and unreacted SDC. Their relative concentrations were found to be a function of reaction time, with the concentration of **2** reaching a maximum value of

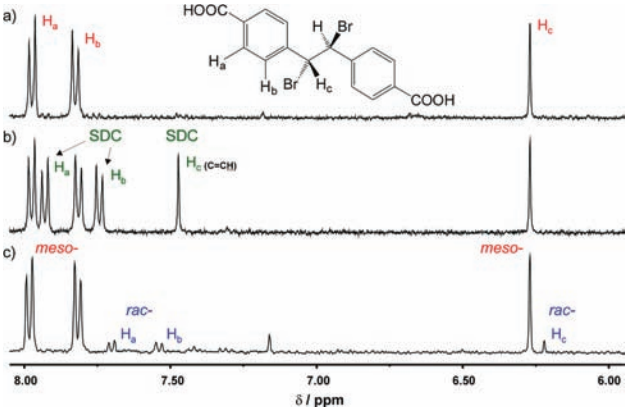


Figure 1. ^{1}H NMR spectra of digested reaction products of **1** at (a) 100 °C and (b) RT for 24 h. A single diastereomer, *meso*-**2**, is evident, in contrast to (c) reaction of **3** at RT, which forms both diastereomers of **2**.

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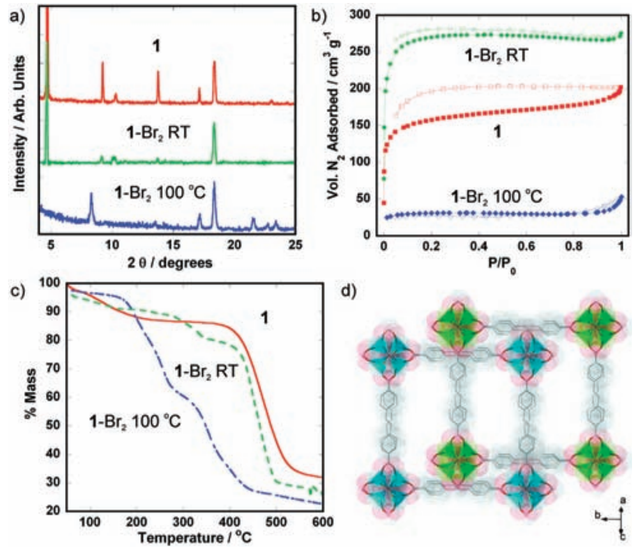

Figure 2. (a) Powder XRD data indicate that **1** retains its framework architecture upon bromination at RT, although exhaustive reaction at 100 °C results in transformation to a different structure. (b) N_2 sorption profiles at 77 K (adsorption, solid markers; desorption, open markers) show an *increase* in measured porosity after bromination at RT. (c) TGA data reveal that the thermal stability of **1** is unchanged by bromination at RT, although the fully brominated product is less stable. (d) Representation of the interpenetrated nature of **1** (blue and green cubic units).

~60% after 48 h of reaction time at room temperature (RT). A similar reaction of solid Na_2SDC (**3**) as a control gave two isomers of **2** distinguishable by ^1H NMR analysis (Figure 1c), with a relative concentration of ~4:1 as determined by integration. We assign these as *meso*-**2** and *rac*-**2** accordingly, thus indicating that only *meso*-**2** was obtained from **1**, as proposed. These conclusions are supported by LC−MS experiments, in which only one diastereomer of **2** was observed in the LC trace from reaction of **1** but two were observed after reaction of **3** [see the Supporting Information (SI)].

Use of CH_2Cl_2 as the reaction solvent at RT produced identical results. However, reaction of **1** at 100 °C in $CHCl_2CH_2Cl$ resulted in essentially complete conversion after 24 h (Figure 1a). The crystal structure of **1** consists of two identical, nearly cubic frameworks that are anisotropically interpenetrated, with the catenated units closest along the *b* axis (Figure 2d).[6a] Therefore, steric access of Br_2 to framework stilbene units may not be the same in all directions in the crystal, and thermal activation to open the closely interpenetrated channels is necessary for full bromination to occur.

In situ NMR experiments at RT confirmed that reaction of **1** with Br_2 is heterogeneous, with no **2** or SDC detected in solution after 24 h of reaction time (see the SI); for comparison, reaction of **3** revealed both diastereomers of **2** in solution after 4 h, alongside unreacted SDC. Powder X-ray diffraction (XRD) (Figure 2a) showed that the constitution of **1** is substantially unchanged by reaction with Br_2 at RT. The product is somewhat less crystalline than the starting material and, unfortunately, was not suitable for single-crystal XRD. However, the framework structure is retained, as indicated by the low-angle reflections evident after reaction. N_2 sorption studies at 77 K (Figure 2b) revealed the materials to be microporous, with Langmuir surface areas of 700 ± 6 and 1194 ± 5 $m^2\ g^{-1}$ for **1** before and after reaction with Br_2 at RT, respectively. Interpenetrated frameworks such as **1** are susceptible to structural collapse under certain conditions (such as extended evacuation), which is likely a result of misalignment of the catenated units. This often leads to lower-than-anticipated internal surface areas as measured by gas sorption methods. Interestingly, after bromination, the *increase* in measured porosity, lack of significant hysteresis in the desorption profile,[6a] and observed crystallinity after sorption studies (see the SI for PXRD) suggest that the framework structure becomes stabilized upon reaction with Br_2. Hence, partial bromination of the linker may increase the robustness of **1** by reducing attractive interactions between the catenated units. The thermogravimetric analysis (TGA) profiles for **1** before and after reaction at RT (Figure 2c) were very similar, further supporting preservation of the porous framework assembly in the product. Full conversion of the stilbene units in **1** to *meso*-**2** by heating resulted in a transformation to a different structure with significantly reduced porosity (Langmuir surface area 139 ± 1 $m^2\ g^{-1}$) and thermal stability. Extensive reaction with Br_2 at high temperature therefore results in an irreversible structural change and loss of framework integrity, potentially due to increased thermal motion of the linker units, which causes channel collapse. Nevertheless, the SDC building blocks of **1** can be converted in full to *meso*-**2** under these conditions without resultant loss in stereochemical integrity, and comparison of PXRD patterns with those of H_2SDC and the product from **3** (see the SI) suggest that long-range metal−organic coordinative interactions are retained to some degree in this product.

In conclusion, we have demonstrated a high degree of diastereoselectivity in the PSM of a stilbene-based MOF. The stereocontrol arises from the rigidity of the coordinated ligand and the porous nature of the MOF. Such an approach may have potential application to organic solid-state reactions and suggests that PSM of suitable MOFs could be employed as a method for stereoselective synthesis. In addition, partial modification appears to stabilize the framework of this MOF toward evacuation.

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Supporting Information Available: Experimental details and supporting and control data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) PSM of a homochiral MOF has recently been used to generate a highly active heterogeneous asymmetric catalyst system with enantioselectivity comparable to that of its homogeneous analogue in solution and superior to that of an alternative heterogeneous (non-MOF) system. See: Wu, C.-D.; Hu, A.; Zhang, L.; Lin, W. *J. Am. Chem. Soc.* **2005**, *127*, 8940.
(12) The electronic effect of the carboxylate group is approximately similar to that of −H ($\sigma_p^+ = -0.02$ for $-COO^-$; see: Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165). Therefore, we anticipate that the reactivity of *trans*-stilbene in solution will be a good electronic model for electrophilic addition reactions of **1** and **3**.

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