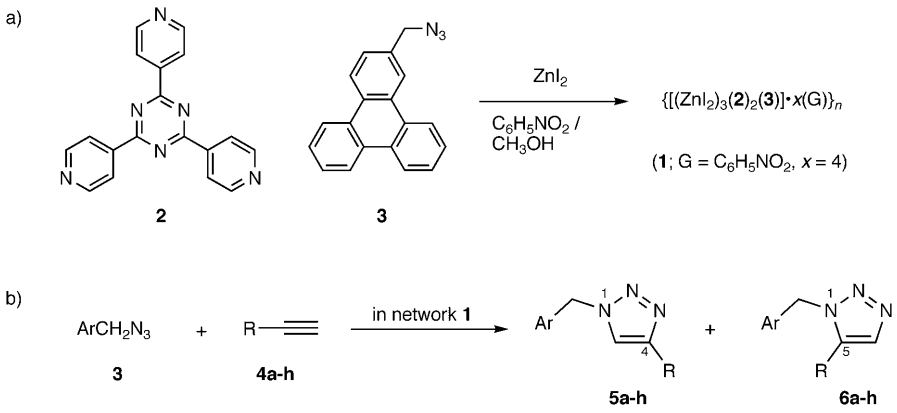
Porous Networks

DOI: 10.1002/anie.201000018

Regioselecitive Huisgen Cycloaddition within Porous Coordination Networks**

*Takehide Kawamichi, Yasuhide Inokuma, Masaki Kawano, and Makoto Fujita**

Chemical reactivity within porous coordination networks is a current topic of significant interest.[1] Recently, we and others have shown that the pores of coordination networks can be used as "crystalline molecular flasks" wherein pseudo solution state organic reactions, even those involving surprisingly bulky reagents, can smoothly occur while crystallinity is maintained throughout.[2,3] Reaction centers are held at fixed geometries in the crystalline state, and with this close proximity, restricted motion can be exploited to obtain high regio- and stereoselectivity. Herein we report that regioselective 1,3-dipolar cycloadditions between azides and alkynes (Huisgen reaction) proceed within the pores of the coordination network **1** (Scheme 1). Typically, the Huisgen reaction gives two regioisomers (i.e. 1,4- and 1,5-substituted-1,2,3-triazoles) in solution, with a slight excess of the 1,5-isomer. Within the pores of network **1**, however, the 1,4-regioisomers are obtained with high selectivity. The robust structure of the coordination network facilitates reaction monitoring by using in situ single crystal X-ray analysis, which not only provides structural information about the product but can also elucidate the structural basis of reaction selectivity. There exist a few reports on Huisgen reactions within porous coordination networks, but none have discussed the regioselectivity and, hence, achieved an understanding of the structural aspects of network pores and how they relate to the reaction selectivity.[4]



Scheme 1. a) Preparation of network **1**. b) Huisgen cycloaddition reactions.

Coordination network **1** was obtained when ZnI_2 and tri(4-pyridyl)triazine (**2**) were mixed in the presence of azide **3** in nitrobenzene/methanol (4:1).[5] From elemental analysis, the molecular formula of the as-synthesized network **1** was shown to be $[\{(ZnI_2)_3(\mathbf{2})_2(\mathbf{3})\}\cdot x(C_6H_5NO_2)]_n$ (x = ca. 4.0). After replacing the nitrobenzene in the pores with ethyl acetate the crystal structure of **1** was unambiguously determined by X-ray crystallographic analysis (Figure 1, and see the Supporting Information). As in similar previous networks, guest **3** was embedded within a columnar stack of ligand **2**. The structure of **1** exhibited two distinct pores and the azido groups point into the larger of the two cylindrical pores (Figure 1).

Crystals of network **1** (20 mg) were immersed in a small amount of methyl propiolate (**4a**; 0.1 mL) at 10 °C. The reaction proceeded and was monitored by using single-crystal microscopic IR methods. The strong N_3 stretching band of **3** at $\nu = 2099\ cm^{-1}$ gradually disappeared, and **3** was completely consumed after three days. The crystals of robust network **1** retained crystallinity and the product of the single-crystal-to-single-crystal transformation was determined by X-ray diffraction. By X-ray analysis, 1,4-substituted-1,2,3-triazole **5a** selectively formed in the pores of network **1**. The network complex was decomposed with $[D_6]$DMSO, and ^{1}H NMR analysis revealed a small amount of the 1,5-adduct (11%), which was not detected by X-ray analysis.

High 1,4-regioselectivity was also observed for phenylacetylene derivatives **4b–4h** (Figure 2). The observed 1,4-selectivity warrants additional discussion because the Huis-

[*] T. Kawamichi, Dr. Y. Inokuma, Prof. Dr. M. Fujita
Department of Applied Chemistry, School of Engineering
The University of Tokyo
Hongo, Bunkyo-ku, Tokyo 113-8656 (Japan)
Fax: (+81) 3-5841-7257
E-mail: mfujita@appchem.t.u-tokyo.ac.jp
Prof. Dr. M. Kawano
Department of Chemistry, POSTECH
San 31 Hyojadong, Pohang 790-784 (South Korea)

[**] This research was supported by the CREST project of the Japan Science and Technology Agency (JST), for which M.F. is the principal investigator, and also in part by KAKENHI (20044006), JSPS, and the Global COE Program (Chemistry Innovation through Cooperation of Science and Engineering), MEXT (Japan). This work has been approved by Photon Factory Program Advisory Committee (Proposal No. 2008G052).

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201000018.

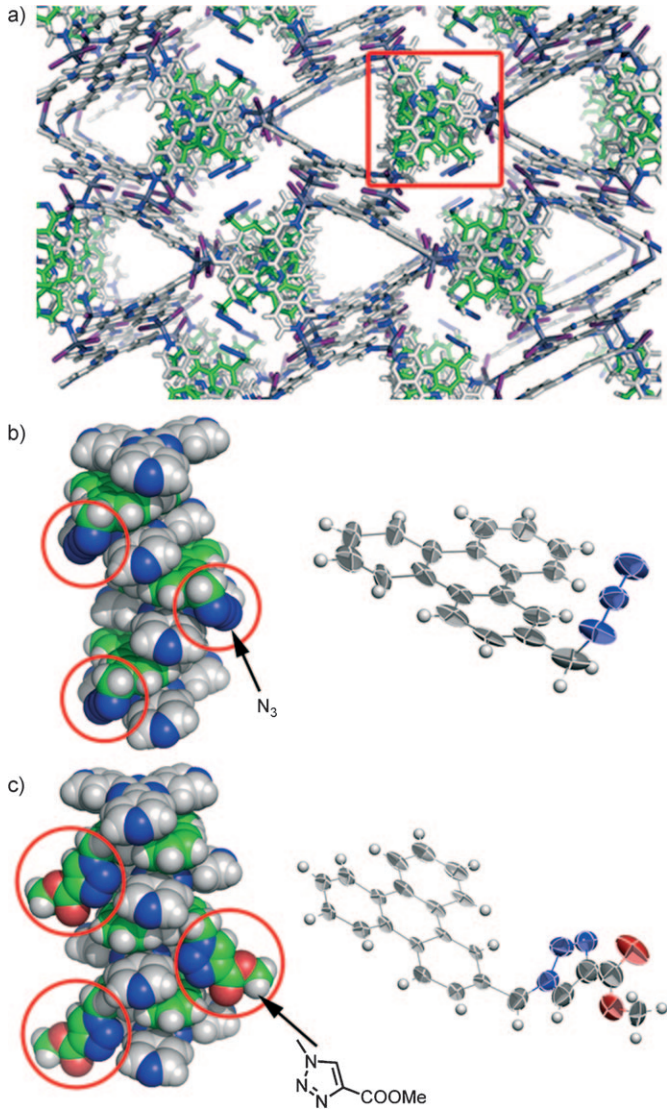


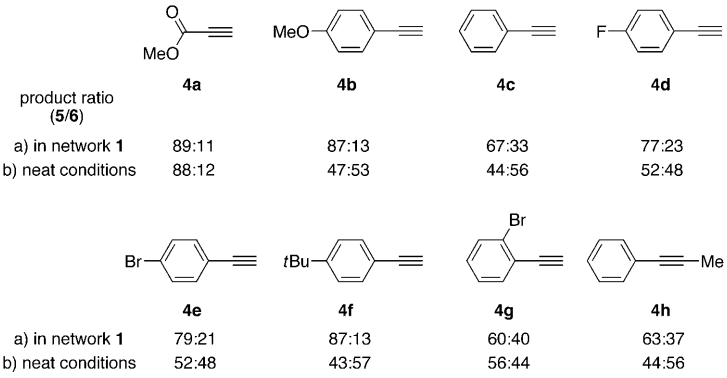
Figure 1. a) Crystal structure of network complex **1**. In the highlighted region, azide **3** stacks alternatively with triazine ligand **2**. ORTEP drawings (30% probability) of a triphenylene unit before (b) and after (c) the reaction between **3** and **4a** (solvent molecules were omitted for clarity).

gen reaction of these substrates under standard solution conditions displays no selectivity or a slight selectivity for the 1,5-regioisomer. For example, when *p*-methoxyphenylacetylene (**4b**) was treated with crystals of **1**, the 1,4-regioisomer was selectively formed (1,4-isomer/1,5-isomer = 87:13) in the network pores. In solution, however, there is only a minor preference (45:55) for the 1,5-isomer. The Huisgen cycloadditions of alkynes **4c**–**4h** in the porous network **1** showed similar selectivities (good to high) for the 1,4-regioisomer. Again, the solution state regioselectivities were trivial (Figure 2). Only **4a** shows latent high 1,4-selectivity in solution most likely due to the electronic effect of COOMe.[6]

Though far away from the reaction center, the size of the *para* substituents of the phenylacetylene substrates influenced the selectivity. When the steric bulk of the *para* substituents increased (H < F < Br < OMe) the 1,4-selectivity increased (67% < 77% < 79% < 87%, respectively). Phenylacetylene **4g** having the Br groups in the *ortho* position to the alkyne, and **4h** having a terminal methyl group, both showed only moderate 1,4-selectivity (60:40 and 63:37, respectively) despite the closer proximity of the bulky substituents to the reaction center. Thus, in the confining pores of **1**, the steric effects of the *para* position play a greater role in controlling the regioselectivity. In addition, the result with internal alkyne **4h** can exclude a possibility of copper contamination, which can catalyze regioselective cycloadditions.[7] There is, however, a size limit and no additional increase in the regioselectivity was obtained with 4-*tert*-butylphenylacetylene (**4f**). The steric demand of **4f** actually inhibited the reaction (most likely because of product inhibition; see the Supporting Information) and only approximately 65% conversion was obtained, even under forced conditions.

X-ray crystal analyses of **1** both before and after the reaction, provided a better understanding for the 1,4-selectivity and the steric effects of the *para* substituent. The azide group in **3** is pointed towards the center of the pore, and to furnish the 1,5-substituted triazole **6**, phenylacetylenes **4b**–**h** would need to direct their pendant aryl groups towards the column or side wall of **2** (see Figure S7 in the Supporting Information). In this case, bulky *para* substituents will prevent the ethynyl group from adopting favorable orientations for the 1,5-cycloaddition. In contrast, the orientations leading to the 1,4-substituted triazoles **5b**–**h** align well within the space provided by the network pores.

In summary, we have demonstrated that the typically disfavored 1,4-regioselective Huisgen cycloaddition between 2-(azidomethyl)triphenylene (**3**) and alkynes **4a**–**h** does occur within the pores of coordination network **1**. Whereas regioselective Huisgen reactions without transition metal catalysts have been achieved in cavitand molecules, polymers, and supramolecular assemblies,[8] porous coordination networks have not yet been successfully used as regioselective reaction media. Unlike other molecular hosts, coordination network **1** possesses a robust crystallinity and a porous pseudo solution state which enables monitoring of reactions by using



product ratio (**5**/**6**)	**4a**	**4b**	**4c**	**4d**
a) in network **1**	89:11	87:13	67:33	77:23
b) neat conditions	88:12	47:53	44:56	52:48

	4e	**4f**	**4g**	**4h**
a) in network **1**	79:21	87:13	60:40	63:37
b) neat conditions	52:48	43:57	56:44	44:56

Figure 2. Alkynes **4a**–**h** employed for Huisgen cycloaddition. Results given for products obtained using a) the network complex **1** and b) neat conditions. See the Experimental section for details.

in situ X-ray analysis. Reactions within the crystalline state or "crystalline molecular flasks" effectively couple with in situ X-ray analyses for an in depth structural study of regio- and stereoselective reactions under controlled and predicable way.

Experimental Section

General procedure for Huisgen reaction in the pore of **1**: Crystals of **1** were dipped in liquid alkynes at 10 °C (for **4a**), 50 °C (for **4b–d**, **f–h**) and 70 °C (for **4e**) for 7 d. Elemental analyses of the resulting crystals were carried out after filtration. The NMR spectra were obtained after decomposing crystals by the addition of $[D_6]$DMSO.

General procedure for Huisgen reaction under neat conditions: Azide **3** (30 mg, 0.11 mmol) was dissolved in 1 g of an alkyne. The solution was stirred at 100 °C for 2 d (see the Supporting Information for more detail).

Received: January 4, 2010 [Z18]
Published online: February 23, 2010

Keywords: azides · cycloaddition · solid-state structures · huisgen reactions

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