# Responsive Backbones Based on Alternating Triazole-Pyridine/Benzene Copolymers: From Helically Folding Polymers to Metallosupramolecularly Crosslinked Gels

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Step-growth polymerization using Cu-catalyzed 1,3-dipolar cycloaddition reactions, commonly referred to as "click chemistry," has been used to prepare poly[(1,2,3-triazol-4-yl-1,3-pyridine)-*alt*-(1,2,3-triazol-1-yl-1,3-phenylene)]s. The recently discovered strong preference of the 2,6-bis(1,2,3-triazol-4-yl)pyridine (BTP) subunits to adopt an *anti–anti* conformation enables the extended heteroaromatic polymer strands to adopt a helical conformation, as shown by circular dichroism (CD) spectroscopy. Addition of various transition metal ions leads to coordinative crosslinking and therefore efficient gelation of the polymer solutions. The integration of the BTP scaffold in the main chain of the described polymers illustrates a synthetically inspired approach to readily access new functional macromolecules with potential applications as sensing and magnetic/emissive materials.
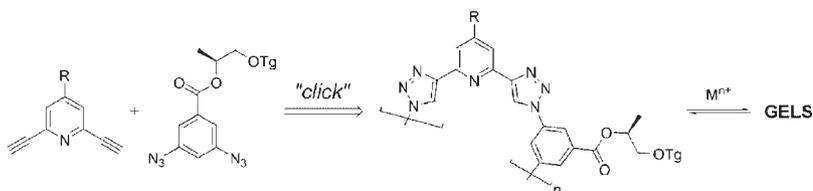
## Introduction

Improvements in synthetic methodology have sparked polymer synthesis, enabling the custom design of a large variety of macromolecular architectures under incorporation of desired functional units.[1] Assembly of such nanoscale building blocks into larger structures is governed by their size, shape, and topology as well as (local) polarity/amphiphilicity. Several approaches have proven valuable including for example dendrimers[2] and dendronized polymers,[3] other 2D/3D shape-persistent objects,[4] and foldamers.[5] However, when control over chain conformation is targeted, i.e., in the case of foldamers, a judicious choice of the backbone structure is required, rendering unsuitable advanced polymerization techniques, such as controlled free radical as well as anionic polymerizations based on vinylic monomers, since in most cases saturated backbones with ill-defined conformational preferences in solution are formed. Therefore, there is a need for new synthetic methods to access polymers with well-defined main chain conformation, while still maintaining control over functionalization.

Recently, we have utilized the Cu-catalyzed[6] 1,3-dipolar cycloaddition reaction,[7] frequently referred to as "click reaction,"[8,9] of 2,6-diethynylpyridines with various aromatic azides to prepare a variety of 2,6-bis(1,2,3-triazol-4-yl)pyridines (BTPs).[10] Due to its strong conformational preference for the kinked *anti–anti* conformation and coordinating ability of the *syn–syn* conformation,[10,11] the BTP building blocks appear to be ideally suited for the integration into larger macromolecular architectures, which should display strong response to external stimuli, e.g., pH and metal ions. Here, we disclose

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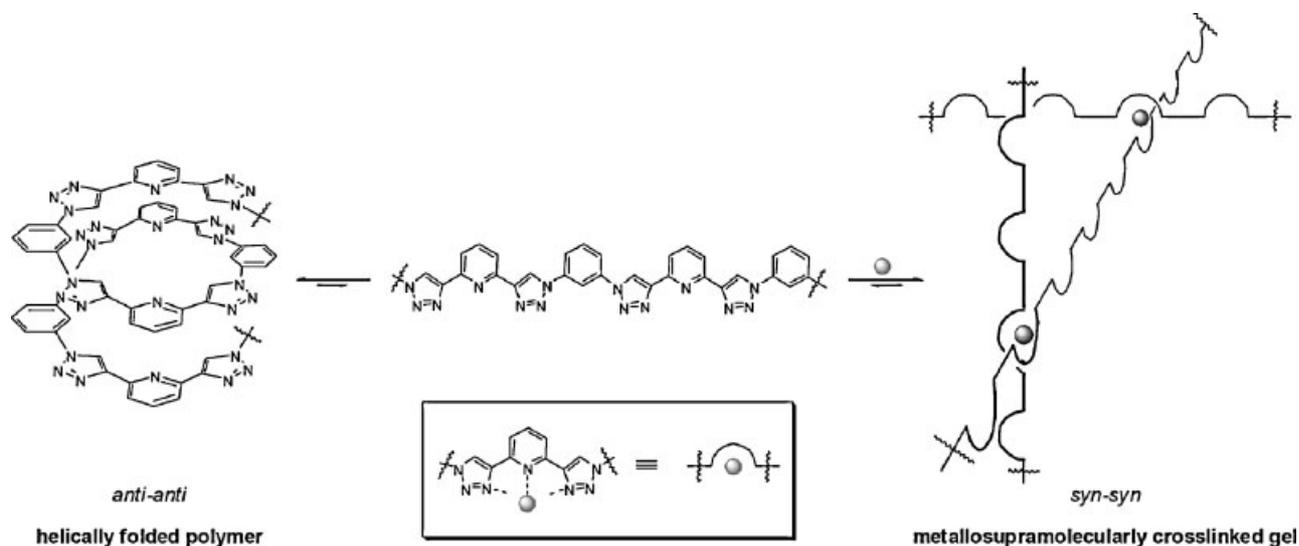Fax: (+49) 30 2093-6940; E-mail: sh@chemie.hu-berlin.de

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**Figure 1.** Responsive extended heteroaromatic polymers having BTP units in the main chain: The BTP scaffold induces helical folding of the backbone due to its favorable *anti–anti* conformation (left) and metal coordination in its chelating *syn–syn* conformation leading to crosslinked gels (right), respectively.

our first results on BTP-containing linear main chain polymers, their solution conformation, and formation of metallosupramolecular gels[12] upon metal induced crosslinking (Figure 1).

## Experimental Part

### General Methods

All reagents were purchased from commercial suppliers and used without purification. Solvents were distilled prior to use. The chiral side chain (2S)-4,7,10,13-tetraoxatetradecan-2-ol,[13] 1-azido-4-toluene,[10] and Fe[(OTf)$_2$(CH$_3$CN)$_2$][14] were prepared using previously published procedures. The Cu-catalyzed cycloaddition reactions were performed in the dark under argon atmosphere. Either solid Cu(CN)$_4$PF$_6$ or concentrated aqueous CuSO$_4$ stock solutions (10 mg CuSO$_4$/0.1 mL H$_2$O) were used as Cu-sources. An aqueous EDTA-disodiumsalt solution (16 g Na$_2$-EDTA/L), adjusted to a pH $\approx$ 8–9, was used to remove Cu-ions in aqueous extraction steps. Column chromatography was carried out with 130–400 mesh silica gel using the eluents specified. NMR spectra were recorded on a 300 MHz Bruker Avance II spectrometer at 23 °C using residual protonated solvent signals as internal standard ($^1$H: $\delta$(CHCl$_3$) = 7.26 ppm). Assignments are based on chemical shifts (Ar is used as abbreviation for assigning both aromatic and triazole moieties). UV-vis absorption and circular dichroism (CD) spectra were recorded in quartz cuvettes of 1 cm path length on a Cary 50 Spectrophotometer and a JASCO J-710 spectropolarimeter, respectively, each equipped with a Peltier thermostated cell holder at 25 ± 0.05 °C using spectrophotometric grade solvents. GPC measurements were performed on a WGE Dr. Bures system equipped with three 300 × 8 mm$^2$ SDV columns (50, 500, and 1 000 Å 5 μ PSS) and one 50 × 8 mm$^2$ SDV column using both UV (300 nm) and RI detection. The measurements were performed in THF at 30 °C using a flow rate of 1 mL · min$^{-1}$. PSS

Win GPC 7.2.1 was used as software. The columns were calibrated with several narrow polydispersity polystyrene samples. For the gelation experiments employing Fe[(OTf)$_2$(CH$_3$CN)$_2$] degassed acetonitrile solutions have been used.

### General Polymerization Procedure

In a two-necked flask equipped with an argon inlet the 2,6-diethynylpyridine monomer (1 equiv.) and the 3,5-diazidobenzoate monomer (1 equiv.) were dissolved in CH$_3$CN (0.6 mol · L$^{-1}$) and the solution was degassed for 10 min by bubbling argon through the solution. Cu-turnings (0.5 equiv.) and Cu(CH$_3$CN)$_4$PF$_6$ (0.2 equiv.) were added, the mixture cooled down to 0 °C in an ice-water bath, and N,N'-dimethylethylenediamine (0.4 equiv.) was added to the stirred solution in the counterflow of argon, whereupon the solution turned dark. The mixture was allowed to warm to r.t. and stirred under argon in the dark by wrapping the flask into aluminum foil. To assure for constant stirring, additional CH$_3$CN was added to the mixture in cases where too viscous polymerization solutions were formed. After stirring for 4 d the solution was diluted with CH$_3$CN and remaining alkyne termini on the polymer chain were capped by addition of 1-azido-4-toluene (2 equiv.), Cu(CH$_3$CN)$_4$PF$_6$ (0.1 equiv.) and N,N'-dimethylethylenediamine (0.2 equiv.) and the mixture was stirred overnight. The reaction was diluted with CH$_2$Cl$_2$, transferred into a separation funnel, and washed with aqueous Na$_2$-EDTA solution (3×), brine (1×), and dried over MgSO$_4$. The solvent was removed in vacuum and after drying the residue (oil pump vacuum) for 3 h, the residue was dissolved in a small amount of CH$_2$Cl$_2$ and the resulting concentrated polymer solution slowly added to a stirred solution of diethyl ether, whereupon a beige precipitate formed. The precipitate was filtered off, washed with diethyl ether, and after drying dissolved in a mixture of CH$_3$CN/H$_2$O = 7/3 and degassed. An aqueous stock solution of CuSO$_4$ (0.2 equiv.) and solid sodium ascorbate (0.5 equiv.) were added. 4-Ethynyltoluene (4 equiv.) was added and the mixture was stirred at r.t. for 12 h in the
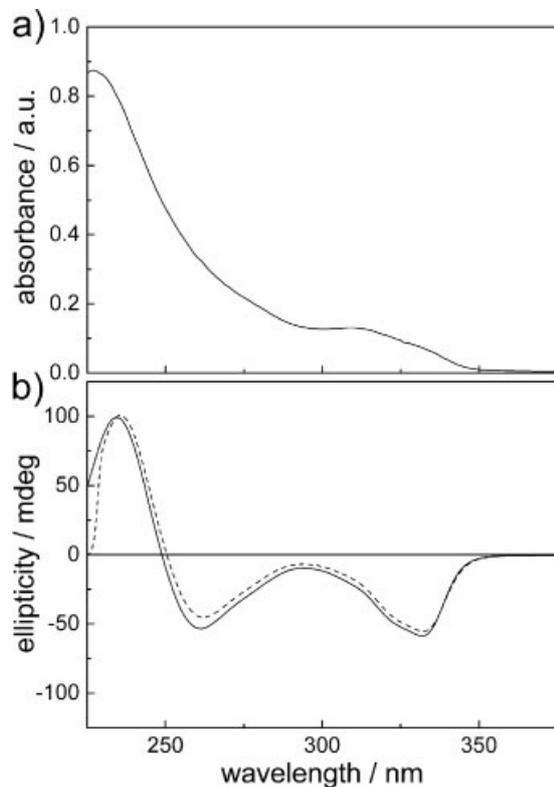
*Figure 2.* (a) UV-vis absorption spectra of polymer **P-1** in aceto-nitrile solution. (b) CD spectra of polymer **P-1** in acetonitrile (solid) and methylene chloride (dashed) solutions. In all cases, samples had concentrations of 15 mg · L$^{-1}$ and were measured at 25 °C.

dark. Again, the crude polymer was washed with aqueous Na$_2$-EDTA solution aqueous Na$_2$-EDTA solution (3×), brine (1×), and dried over MgSO$_4$. The solvent was removed in vacuum and after drying the residue (oil pump vacuum) for 3 h, the crude polymer was purified by precipitation in diethyl ether. Filtration through a short silica gel plug using CH$_2$Cl$_2$ (or gradients of CH$_2$Cl$_2$ → CH$_2$Cl$_2$ + 25% MeOH) as the eluent gave the polymers as viscous brown oils.

## Polymer Characterization

$^1$H NMR (CDCl$_3$): $\delta = 10.0-9.0$ (br s, Ar-*H*), 8.6–7.9 (br s, Ar-*H*), 7.2–6.8 (br s, Ar-*H*), 5.7–5.3 (br s, C*H*CH$_3$), 5.3–4.9 (m, OC*H$_2$*), 4.6–3.0 (m, OC*H$_2$*, OC*H$_3$*), 2.5–2.2 (m, ArC*H$_3$*), 1.8–1.0 (m, CHC*H$_3$*). GPC (THF): $\overline{M}_w = 1.6 \times 10^3 - 5.3 \times 10^3$ g · mol$^{-1}$, PDI ($\overline{M}_w/\overline{M}_n$) = 1.5–2.3. UV-vis (CH$_3$CN): $\lambda_{max} = 227$ nm and shoulder at 310 nm (see Figure 3).

## Results and Discussion

Our polymer synthesis is based on an A$_2$ + B$_2$ step-growth polymerization process using multiple efficient Cu-catalyzed 1,3-dipolar cycloaddition reactions of 2,6-diethy-nylpyridine A$_2$ monomers and 3,5-diazidobenzoate B$_2$ monomers (Scheme 1).[15] The thus prepared polymers

were terminated by successive reaction with mono-functional tolyl azide and acetylene end-cappers, respec-tively, to afford final polymers **P-1** and **P-2**. While the electronics of the pyridine moiety and hence the resulting BTP unit can be conveniently tuned by introducing either electron-donating ether or electron-withdrawing ester substituents in the 4-position,[10] the other monomer carries a chiral lactate derived side chain[13] to facilitate conformational analysis by means of CD spectroscopy. The
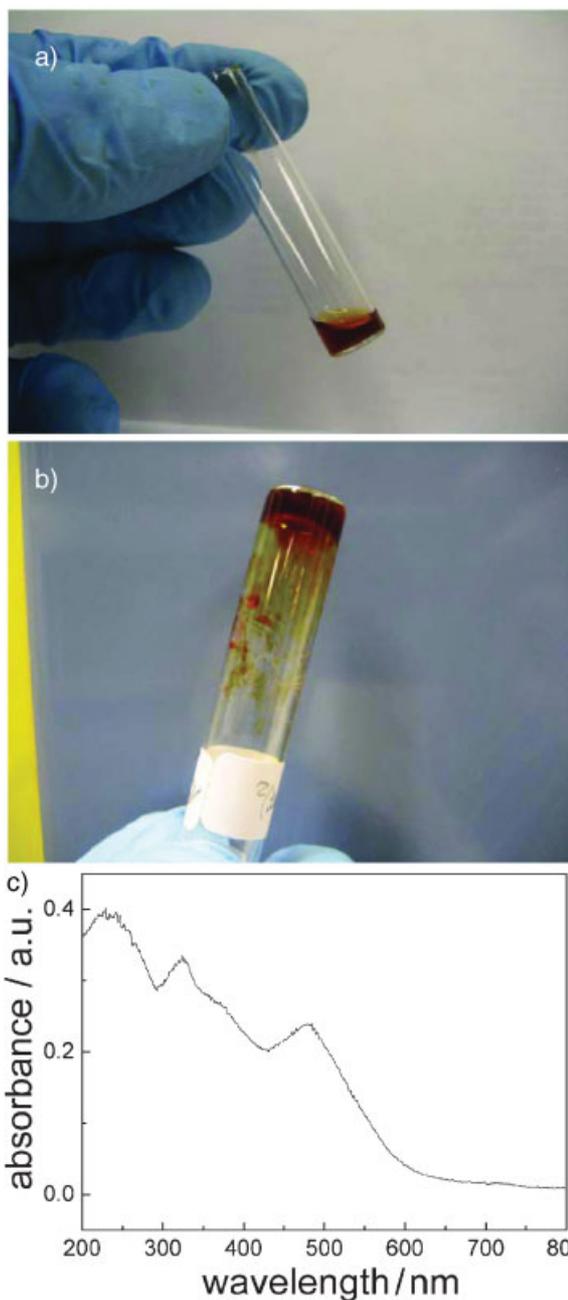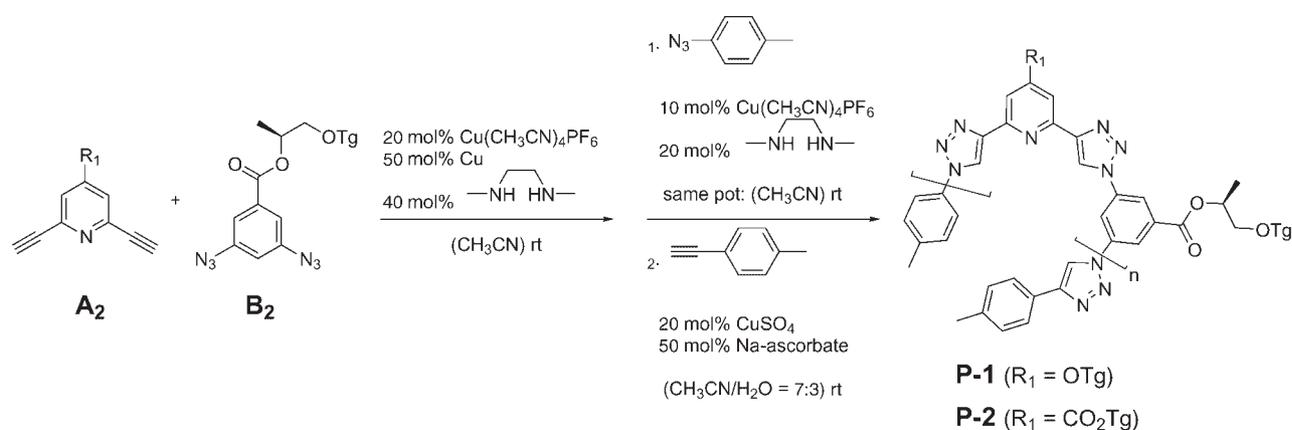


*Figure 3.* Solution of polymer **P-1** in acetonitrile: (a) before and (b) after the addition of Fe[(OTf)$_2$(CH$_3$CN)$_2$]. (c) Optical absorption spectrum of a film of Fe-gel (b) on a quartz slide.

**Scheme 1.** Synthesis of target polymers via $A_2 + B_2$ step-growth polymerization, followed by termination of the remaining chain end functionalities ($T_g = (CH_2CH_2O)_3CH_3$).

side chains in both monomers are composed of short oligo(ethylene glycol) tails to provide solubility in both non-polar and polar solvents and enforce folding driven by solvophobic forces acting upon the hydrophobic backbone in polar solvents.[16] In order to obtain polymers with moderate degrees of polymerization conditions had to be optimized to account for solubility of monomers, forming polymer, and reagents. Acetonitrile as the solvent and copper turnings as solid reductant provided the best results producing polymers with weight average molecular weights ($\overline{M}_w$) in the range of 1 600–5 300 $g \cdot mol^{-1}$ and polydispersity indices (PDIs) around 1.5–2.3, as expected for a polyaddition process. Comparison of these values for the polymers with long discrete oligomers (details will be published elsewhere) shows that $\overline{M}_n$ is underestimated by a factor of approximately 1.6, suggesting a more compact shape and hence smaller hydrodynamic radius of the polymers as compared to the random coil polystyrene standards used for GPC calibration. In most cases, GPC traces also show a sharp peak at lower molecular weight ($\overline{M}_n = 2\,000\ g \cdot mol^{-1}$) presumably associated with macrocycle formation (details will be published elsewhere). The polymers reveal diagnostic signals in their $^1H$ NMR spectra and in higher molecular weight polymers vanishing peak integrals, associated with the aromatic protons, indicate folding and/or aggregation.

Polymers **P-1** and **P-2** were investigated with regard to their conformational behavior in solution. UV-vis absorption spectra in various solvents show a typical intense band around 230 nm with a shoulder at 310 nm, associated with $\pi \rightarrow \pi^*$ transitions of the heteroaromatic backbone (Figure 2a). The respective CD spectra reveal an intense bisignate signal exhibiting a negative exciton chirality[17] and zero-crossing at 250 nm, associated with the more intense short wavelength absorption maximum, as well as another bathochromically shifted, negative signal at 330 nm (Figure 2b). The observed CD activity as well as the

bisignate shape and position of the CD signal indicate the presence of a helical backbone conformation, in which chirality transfer from the chiral side chains on each benzoate unit to the heteroaromatic backbone takes place.[18] Interestingly, the polymer adopts a helical conformation in both polar and non-polar solvents, a finding that illustrates the large degree of pre-organization in the polymer due to the presence of the BTP units.

Solutions of the polymers **P-1** and **P-2** were mixed with various transition metal ions such as $Zn^{2+}$, $Fe^{2+}$, and $Eu^{3+}$, known to form complexes with the BTP ligand framework.[10] Instantaneously, gels were formed as illustrated for the case of addition of iron(II)triflate in Figure 3. As control experiments in the absence of metal ions did not lead to gelation, gel formation must result from coordinative crosslinking of the polymer chains. Metal complex formation could be verified by recording UV-vis spectra of the Fe-gel showing a typical broad band at 480 nm, most likely associated with the MLCT/LMCT transition in the iron complex. As previously shown by us, the BTP scaffold forms stable 1:2 complexes in the case of $Fe^{2+}$ and 1:3 complexes in the case of $Eu^{3+}$,[10] with binding constants in the order of $10^7\ M^{-1}$ as measured by isothermal calorimetry (ITC) (details will be published elsewhere). Therefore, the metal ions added presumably connect the polymer chains at various points leading to a rather efficient supramolecular crosslinking process, primarily based on coordinative bonds.

## Conclusion

Poly[(1,2,3-triazol-4-yl-1,3-pyridine)-*alt*-(1,2,3-triazol-1-yl-1,3-phenylene)]s have been prepared via click chemistry from readily available bisacetylene and bisazide monomers. The polymers adopt helical conformations in various solvents illustrating the predictive power of foldamer

design in the synthesis of helical polymers. Importantly, the built-in binding sites in the polymer main chain can also serve as ligands for various transition metal ions. Hence, metal-containing gels can be prepared simply by the addition of, for example, $Zn^{2+}$, $Fe^{2+}$, or $Eu^{3+}$ ions to the polymer solution. Efficient gelation is based on the formation of the bridging metal complexes, which not only serve as crosslinking points but also impart various functions, potentially useful for the design of new magnetic (Fe) or emissive (Eu) materials.

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