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# Synthesis of a Kinetically Stabilized Homoditopic Nitrile *N*-Oxide Directed toward Catalyst-free Click Polymerization

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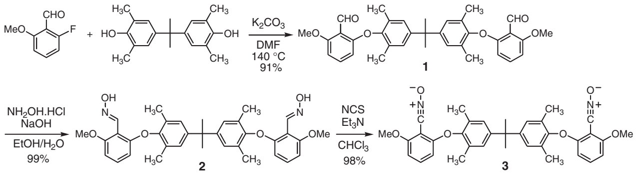
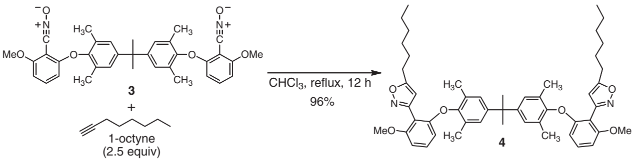
A kinetically stabilized homoditopic nitrile *N*-oxide was prepared for a catalyst-free click polymerization that efficiently proceeded via 1,3-dipolar cycloaddition with several bifunctional alkyne, alkene, and nitrile monomers. The polymerization afforded the corresponding polymers with high molecular weights and yields.

Click chemistry[1] based on the Cu(I)-catalyzed Huisgen cycloaddition of azides with alkynes has generated particular interests as a powerful synthetic tool for molecular integration.[2] The reaction has been successfully used in polymer chemistry for selective modification of versatile polymers to afford unique architectures such as cyclic, block, dendritic, and network polymers.[3,4] However, the toxicity and explosiveness of azides, in addition to the requirement of a Cu(I) catalyst, has led to limitations in the use of this method.[5] A promising substitute 1,3-dipole of azide would be nitrile *N*-oxide that has potential utility to overcome these problems.[6] [2 + 3]Cycloaddition of nitrile *N*-oxide efficiently proceeds with not only alkynes but also alkenes and nitriles to selectively produce the corresponding nitrogen-containing heterocycles.[7] Iwakura's original work[6a] prompted us to recently report a new click polymerization exploiting homoditopic nitrile *N*-oxide generated in situ with ditopic olefinic and acetylenic monomers through molecular sieves-promoted polycycloaddition.[8a,8c] The polymerization features mild reaction conditions, simple procedure, and broad applicability based on the main chain heterocycles formed.[8b] To avoid some limitations based on the use of precursor for unstable ditopic nitrile *N*-oxide such as the requirement of molecular sieves (4 Å) and restricted temperature allowance, we have undertaken the polycycloaddition using stable ditopic nitrile *N*-oxide, considering Kanbara's work.[6d] Herein, we disclose the catalyst-free click polymerization exploiting a new kinetically stabilized ditopic nitrile *N*-oxide[9] as a 1,3-dipole with various bifunctional dipolarophiles to emphasize the versatility and productivity of the click reaction in polymer chemistry.

Scheme 1 shows the synthetic route of kinetically stabilized homoditopic nitrile *N*-oxide **3**. We found that **3** could be easily obtained in a high yield from a bisphenol A derivative as a bulky spacer moiety, suggesting that various nitrile *N*-oxides can be prepared by changing the diol spacer. Prior to the click polymerization, the model click reaction of **3** with 1-octyne was carried out as shown in Scheme 2. The product **4** obtained in a high yield as a single diastereomer certainly proved the successful efficient polymerization. The regiochemistry of the isoxazole moiety of **4** was confirmed by the NOESY correlations observed between the isoxazole methyne proton and the methyl protons of the spacer.[10]

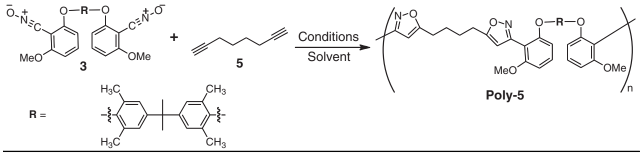


**Scheme 1.** Synthetic route of stable ditopic nitrile *N*-oxide **3**.



**Scheme 2.** Reaction of stable nitrile *N*-oxide **3** with 1-octyne.

**Table 1.** Effects of solvent and reaction time on click polymerization



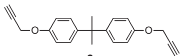
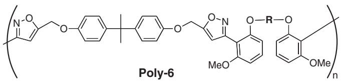
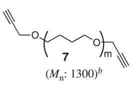
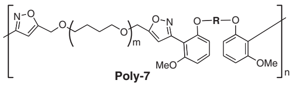
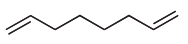
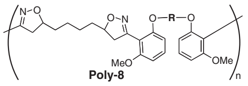
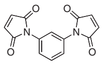
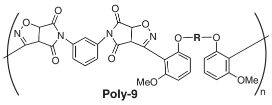
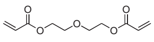
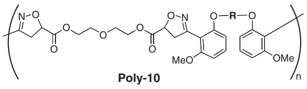
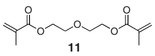
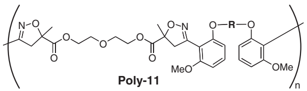
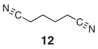
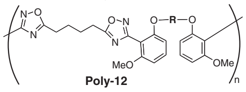
| Entry | Solvent | Temp /°C | Time /h | $M_w$[a] | $M_n$[a] | $M_w/M_n$[a] | Yield /% |
|---|---|---|---|---|---|---|---|
| 1 | DMF | 80 | 12 | 3600 | 1600 | 2.2 | 94 |
| 2 | $CH_2Cl_2$ | reflux | 2 | 19000 | 10300 | 1.9 | 80 |
| 3 | $CH_2Cl_2$ | reflux | 12 | 20000 | 11000 | 1.9 | 93 |
| 4 | $CHCl_3$ | reflux | 1 | 18000 | 7000 | 2.6 | 60 |
| 5 | $CHCl_3$ | reflux | 2 | 24000 | 10000 | 2.4 | 84 |
| 6 | $CHCl_3$ | reflux | 12 | 35000 | 16000 | 2.2 | 95 |

[a] $M_n$: number-average molecular weight and $M_w$: weight-average molecular weight were estimated by size exclusion chromatography (SEC, $CHCl_3$, polystyrene standards).

Table 1 summarizes the results of the click polymerization using 1,7-octadiyne (**5**), mainly to clarify the effects of solvent and reaction time. The polymerization of **3** and **5** in DMF was first investigated to result in the formation of polyisoxazole **Poly-5** with a relatively low molecular weight ($M_w = 3600$), probably due to the hydrolysis of **3** to afford the corresponding hydroxamic acid (Entry 1). Various experimental results of Table 1 revealed that the click polymerization efficiently proceeds in less-polar solvents such as $CH_2Cl_2$ and $CHCl_3$.

In $CH_2Cl_2$, polymer molecular weight did not significantly depend on reaction time (Table 1, Entries 2 and 3). On the other hand, in $CHCl_3$, the molecular weight of **Poly-5** continuously increased with the reaction time, to eventually give **Poly-5** with $M_w = 35000$ in 95% yield (Entries 4–6). In both solvent systems, only one regioisomer was preferentially formed as confirmed by $^1H$ NMR.[10]

**Table 2.** Synthesis of polyisoxazoles, polyisoxazolines, and polyoxadiazole via polycycloaddition[a]

| Entry | Dipolarophile | Products | Yield/% |
|---|---|---|---|
| 1 |  **6** |  **Poly-6** | 93 |
| 2 |  **7** ($M_n$: 1300)[b] |  **Poly-7** | 92 |
| 3 |  **8** |  **Poly-8** | 98 |
| 4 |  **9** |  **Poly-9** | 91 |
| 5 |  **10** |  **Poly-10** | 99 |
| 6[c] |  **11** |  **Poly-11** | 99 |
| 7[c] |  **12** |  **Poly-12** | 91 |

[a]Reaction condition: $CHCl_3$, reflux, 12 h. [b]Determined by integral ratio of $^1H$ NMR spectrum. [c]Reaction condition: chlorobenzene, reflux, 12 h.

Various bifunctional acetylenes, olefins, and nitrile monomers could be employed as monomers (Tables 2 and 3). The polymerization of diyne monomers such as **6** and acetylene-terminated polytetrahydrofuran **7** proceeded well to afford the corresponding polyisoxazoles with high molecular weights (Table 3, Entries 2 and 3). We found that diene monomers such as 1,7-octadiene (**8**), *N*,*N*′-1,3-phenylenedimaleimide (**9**), and bisacrylate **10** were also reactive enough to afford polyisoxazolines with high molecular weights in high yields. Synthesis of polyisoxazoline **Poly-11** with a similar molecular weight to **Poly-10** required high temperature due to the lower reactivity resulting from the steric hindrance of the methacrylate moiety of **11** (Table 3, Entries 6 and 7).

It was noticed that nitrile groups were also active to this click reaction and the polymerization of adiponitrile (**12**) actually proceeded well to give polyoxadiazole **Poly-12**, although it showed low molecular weight, probably owing to the low reactivity.[10]

The thermal properties of the obtained polymers were studied using DSC and TGA (Table 3). The glass transition temperature ($T_g$) appeared in the range from −41 to 259 °C, depending on the structure of dipolarophile monomers. The thermal weight loss temperature ($T_{d5}$) was in the range from 312 to 365 °C, indicating the thermal stability of the isoxazoles, isoxazolines, and oxadiazole skeletons.

In summary, this paper has demonstrated a new click polymerization utilizing a kinetically stabilized nitrile *N*-oxide **3** in the absence of additive. The advantageous features of the present click polymerization include good monomer versatility (bifunctional alkene, alkyne, and nitrile), stable C–C bond formation, catalyst-free reaction, and a non-explosive 1,3-dipole. Thus, the present click polymerization will provide a new entry to the syntheses of various polymers including functionalized polymers.

**Table 3.** Molecular weights and thermal properties of polyisoxazoles, polyisoxazolines, and polyoxadiazole

| Entry | Products | $M_w$[a] | $M_n$[a] | $M_w/M_n$[a] | $T_g$/°C[c] | $T_{d5}$/°C[d] |
|---|---|---|---|---|---|---|
| 1 | **Poly-5** | 35000 | 16000 | 2.2 | 170 | 365 |
| 2 | **Poly-6** | 33000 | 20000 | 1.6 | 165 | 341 |
| 3 | **Poly-7** | 23000 | 7000 | 3.3 | −41 | 324 |
| 4 | **Poly-8** | 54000 | 31000 | 1.7 | 152 | 338 |
| 5 | **Poly-9** | 21000[b] | 9400[b] | 2.2[b] | 259 | 357 |
| 6 | **Poly-10** | 21000 | 11000 | 1.9 | 151 | 312 |
| 7[e] | **Poly-11** | 19000 | 11000 | 1.7 | 114 | 335 |
| 8[e] | **Poly-12** | 7000 | 5100 | 1.4 | 146 | 336 |

[a]Estimated by SEC ($CHCl_3$, [b]DMF, polystyrene standards). [c]Glass transition temperature ($T_g$) was obtained at a heating rate of 10 °C min$^{-1}$ under $N_2$ (flow rate 50 mL min$^{-1}$). [d]5% Thermal weight loss temperatures ($T_{d5}$) were obtained at a heating rate of 10 °C min$^{-1}$ under $N_2$ (flow rate 50 mL min$^{-1}$). [e]Reaction condition: chlorobenzene, reflux, 12 h.

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