

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

Young-Gi Lee, Morio Yonekawa, Yasuhito Koyama, and Toshikazu Takata*

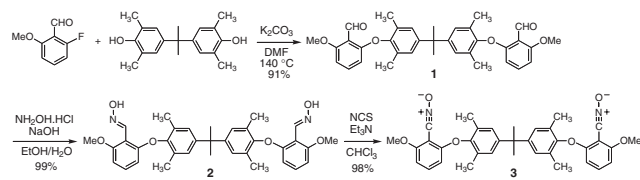
Department of Organic and Polymeric Materials, Tokyo Institute of Technology, 2-12-1 O-okayama, Meguro-ku, Tokyo 152-8552

(Received January 8, 2010; CL-100026; E-mail: ttakata@polymer.titech.ac.jp)

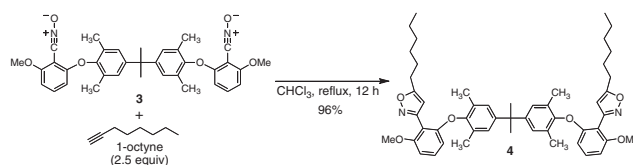
A kinetically stabilized homoditopic nitrile *N*-oxide was prepared for a catalyst-free click polymerization that efficiently proceeded via 1,3-dipolar cycloaddition with several bifunctional alkyne, alkene, and nitrile monomers. The polymerization afforded the corresponding polymers with high molecular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

Click chemistry¹ 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*-oxide⁹ 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



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 ₂ Cl ₂	reflux	2	19000	10300	1.9	80
3	CH ₂ Cl 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, CHCl₃, polystyrene standards).

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

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 CH₂Cl₂ and CHCl₃.

In CH₂Cl₂, polymer molecular weight did not significantly depend on reaction time (Table 1, Entries 2 and 3). On the other hand, in CHCl₃, 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			93
2			92
3			98
4			91
5			99
6 ^c			99
7 ^c			91

^aReaction condition: CHCl₃, reflux, 12 h. ^bDetermined by integral ratio of ¹H NMR spectrum. ^cReaction 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,

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

Entry	Products	<i>M_w</i> ^a	<i>M_n</i> ^a	<i>M_w</i> / <i>M_n</i> ^a	<i>T_g</i> /°C ^c	<i>T_{d5}</i> /°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 ^c	Poly-11	19000	11000	1.7	114	335
8 ^e	Poly-12	7000	5100	1.4	146	336

^aEstimated by SEC (CHCl₃, ^bDMF, polystyrene standards).

^cGlass transition temperature (*T_g*) was obtained at a heating rate of 10 °C min^{−1} under N₂ (flow rate 50 mL min^{−1}). ^d5% Thermal weight loss temperatures (*T_{d5}*) were obtained at a heating rate of 10 °C min^{−1} under N₂ (flow rate 50 mL min^{−1}). ^eReaction condition: chlorobenzene, reflux, 12 h.

the present click polymerization will provide a new entry to the syntheses of various polymers including functionalized polymers.

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