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New Synthetic Entry to OH-Functionalized Nitrile N-Oxide and Polyfunctional Nitrile N-Oxides For Click Crosslinking and Decrosslinking of Natural Rubber

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New Synthetic Entry to OH-Functionalized Nitrile *N*-Oxide and Polyfunctional Nitrile *N*-Oxides For Click Crosslinking and Decrosslinking of Natural Rubber

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A new synthetic route for obtaining polyfunctional nitrile *N*-oxides from OH-tethering nitrile *N*-oxide is reported. OH-tethering nitrile *N*-oxide is synthesized using the proposed route by using an intermediary nitroalkane and derived to polyfunctional ones via OH-involving condensations. The polyfunctional nitrile *N*-oxides undergo the catalyst-free crosslinking reaction to form crosslinked natural rubber (NR). The physical properties of the crosslinked NR indicate the occurrence of effective crosslinking. A crosslinker with ester-connected two nitrile *N*-oxide functions is demonstrated to have favorable decrosslinking ability.

Click chemistry is a very powerful molecular integration tool, and it is applied in various fields, including biochemistry, supramolecular chemistry, material sciences, and polymer synthesis.[1] Nitrile *N*-oxide is 1,3-dipole, which undergoes [3+2] cycloaddition with several unsaturated bonds, such as alkynes, alkenes, and nitriles, in the absence of any catalyst.[2] Considering the benefits of the functions of nitrile *N*-oxide, we developed kinetically stable nitrile *N*-oxides[3] as useful click reagents that are expected to serve as substitutes for azide derivatives, which are used in the Cu(I)-catalyzed Huisgen cycloaddition reaction. Especially, so far, efficient polymer synthesis and crosslinking reactions have been achieved using homoditopic nitrile *N*-oxides[4] and nitrile *N*-oxide-based orthogonal reagents.[5] Generally, the nitrile *N*-oxide function is generated in the last step of the synthesis to avoid undesirable side reactions.[2–7] However, it would be more beneficial if the nitrile *N*-oxide functionality were to be introduced into the structures directly via a simple reaction. Nucleophilic substitution using metal fulminates (M-CNO) seems to be the candidates for one of the most simple and direct methods, although there is only one literature to date.[8] Moreover, as both free fulminic acid and metal fulminates are highly explosiveness, other safe introduction method should be developed. Meanwhile, decrosslinking of the crosslinked polymer has attracted considerable interest over an extended period because of its applicability to polymer recycling, shape-memory polymers, and self-healing polymer.[9] Considering from these backgrounds, herein, we describe a novel synthetic strategy for OH-functionalized nitrile *N*-oxide and polyfunctional nitrile *N*-oxides for catalyst-free crosslinking and decrosslinking of natural rubber (NR) (Figure 1)
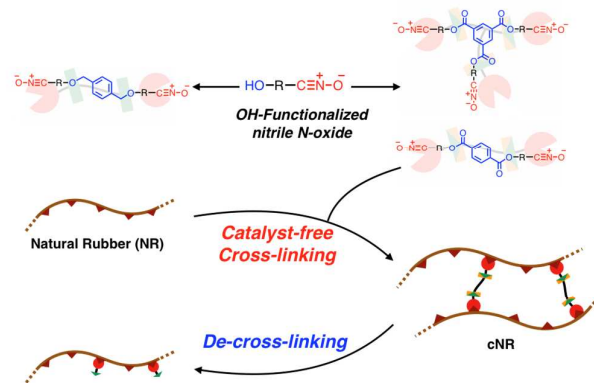

Figure 1. Schematic illustration of use of OH-functionalized nitrile *N*-oxide

The nitrile *N*-oxide precursor with a hydroxy functional group was prepared according to Scheme 1. Starting with commercially available 4-hydroxybenzophenone, **1** was obtained in moderate yield (44% overall yield over 6 steps). Notably, deprotection of the triisopropylsilyl (TIPS) moiety occurred without any adverse effect on the nitrile *N*-oxide functionality. The formation of **1** was confirmed by ^{1}H NMR, ^{13}C NMR, IR spectroscopy, and mass spectrometry (see ESI). The nitrile *N*-oxide bearing dihydroxy group **2** was also prepared in a manner similar as **1** by starting with 4,4'-dihydroxybenzophenone. Introduction of diphenyl groups close to the nitrile *N*-oxide function imparted adequate thermal

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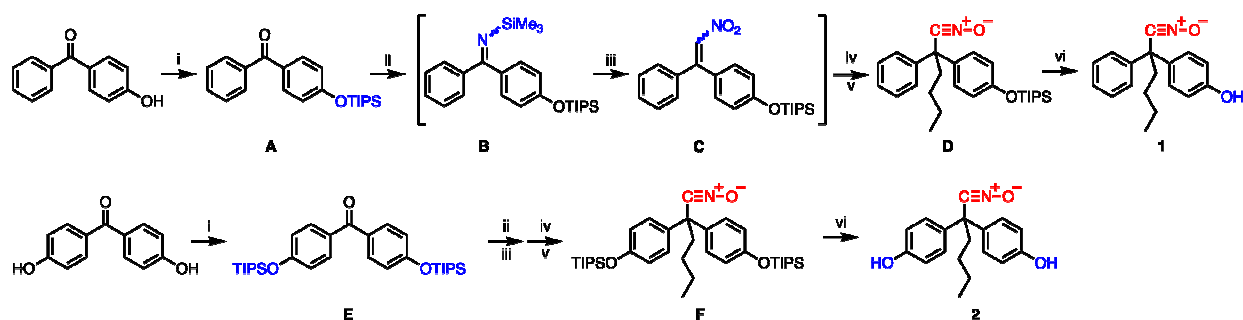
Scheme 1. Synthesis of nitrile *N*-oxide bearing hydroxy group **1** and **2**. Reaction condition: (i) Triisopropylsilylchloride (TIPS-Cl), imidazole, DMAP, THF, rt, 1 d, **A**: 95%, **E**: 73%; (ii) LiHMDS, THF, r.t., 1 d; (iii) CH$_3$NO$_2$, reflux, 1 d; (iv) *n*-BuLi, THF, −78 °C, 30 min; (v) H$_2$SO$_4$, −78 °C to 0 °C, 30 min; **D**: 52%, **F**: 31% for 4 steps (vi) TBAF, THF, r.t., 10 min, **1**: 96%, **2**: 94%

stability to **1** and **2** at 0 °C and room temperature, which is consistent with the results of our previous reports.[10] Moreover, time-dependent IR and ^{1}H NMR spectra of **1** revealed slight fluctuations for 8.5 h at 60 °C and 1.5 h at 100 °C, respectively (see ESI). Based on these results, simple etherification and esterification of **1** with *p*-xylene dibromide, terephthaloyl chloride, and trimesic acid trichloride were carried out at room temperature to obtain the corresponding polyfunctional nitrile *N*-oxides **3–5**, respectively (Scheme 2). Not only the deprotection of the TIPS moiety but also these reactions proceeded smoothly without any side reaction. The strong absorption peaks of **3–5** at around 2292 cm^{-1} directly indicate the existence of the nitrile *N*-oxide group. Moreover, to evaluate the reactivity and validity of nitrile *N*-oxide function, the catalyst-free click reaction was carried out with allyltrimethylsilane (see ESI) in CHCl$_3$ at 40 °C for 16 h to obtain the corresponding isoxazoline products in quantitative yield. Because the integral ratios of the aromatic and TMS protons in all ^{1}H NMR spectra coincided exactly with the theoretical calculation results, high reactivity and conversion between nitrile *N*-oxide and olefin were revealed. Although we have

previously reported the synthesis of tritopic aliphatic nitrile *N*-oxide by using alkoxy nucleophile,[7a] this synthetic protocol has a large potential to be applied to more convenient synthesis of nitrile *N*-oxide compounds with larger number of functional groups.

Next, crosslinking reactions of natural rubber (NR) containing internal olefins was carried out using the polyfunctional nitrile *N*-oxides **3** in toluene at 90 °C for 1 day under catalyst-free and mild conditions.[11] Moreover, the crosslinking reactions employing the nitrile *N*-oxides **4** and **5** were conducted under the same reaction condition. The experimental conditions and the physical properties of the crosslinked NR (cNR) films and their stress-strain curves are summarized and shown in Table 1 and in Figure 2, respectively. The results demonstrate that cNRs were formed successfully when the nitrile *N*-oxide crosslinker was added at concentrations higher than 0.20 mol%. The concentration of the nitrile *N*-oxide crosslinker was inversely proportional to the swelling ratio and positively related to the elastic modulus (*E*) of cNR. The welling ratios of the cNRs in CHCl$_3$ and *E* when using the ditopic nitrile *N*-oxides
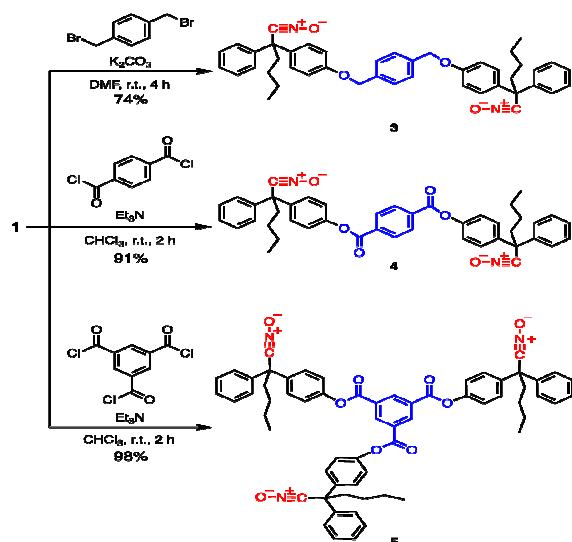
Scheme 2. Synthesis of di- and tritopic nitrile *N*-oxides **3–5**

Table 1. Cross-linking conditions of cNR using **3–5**

Entry	Cross-linker	Feed ratio (mol%)	Yield (%)[a]	Swelling ratio (%)[b]	*E* (MPa)[c]
1	**3**	0.10	0[d]	−[e]	−[e]
2		0.20	95	3300	0.13
3		0.50	96	1100	0.52
4		1.0	96	810	1.07
5	**4**	0.10	0[d]	−[e]	−[e]
6		0.20	79	3200	0.20
7		0.50	96	1100	0.66
8		1.0	95	840	1.09
9	**5**	0.10	0[d]	−[e]	−[e]
10		0.20	90	1700	0.44
11		0.50	94	1000	0.98
12		1.0	87	970	1.30

[a]CHCl$_3$-insoluble part. [b]In CHCl$_3$; calculated as $(W_s-W_d)/W_d$, where W_s is the weight of the swelling gel, and W_d is the weight of the dry gel. [c]Determined by the stress between 0 and 10% strain. *E* of virgin NR was estimated to be 0.06 MPa. [d]The obtained polymers were soluble in CHCl$_3$. [e]Not determined.

3 and **4** showed no significant difference, indicating that the chemical structures of ether and ester linkages in the crosslinkers have little influence on their crosslinking ability and physical properties. Tritopic nitrile *N*-oxide was considered more effective for the crosslinking reaction than ditopic nitrile *N*-oxide owing to its high density of reaction points. In fact, the cNRs with tritopic nitrile *N*-oxide showed lower swelling ratio and higher elastic modulus than the CNRs with the same mole of ditopic nitrile *N*-oxides.[12]

Finally, the cNRs obtained with **3** and **4** (entries 2 and 6) were immersed in a KOH suspension in THF/MeOH/H$_2$O mixture for 1 day to check the decrosslinking ability of NRs.[13] In spite of the similarity of the mechanical property of obtained cNRs, hydrolysis occurred only for cNRs with ester linkages at the crosslinking points to yield decrosslinked NR, which was soluble in CHCl$_3$ (Scheme 3a). The SEC result of the CHCl$_3$-soluble part revealed the complete cleavage of the ester linkage by the hydrolysis. ^{1}H NMR was also measured to identify the remaining of the partial structures of the cross-linker. Unfortunately, only the peaks corresponded to NR

were observed probably because of too low concentration of these structures (see ESI). Meanwhile, cNRs with ether linkages perfectly maintained their structures under the same reaction condition (Scheme 3b). No detectable product remained after the evaporation of the CHCl$_3$ layer. In addition, there was no weight loss of cNRs before and after the reaction. These results clearly indicate that the nitrile *N*-oxide crosslinker with some functionality such as decomposability could be achieved by tuning its linkage structure. It also should be noted that cNR formed by cross-linker **5** (tritopic cross-linker, entry 10) exhibited similar tendency to that of formed by ditopic cross-linker **4**, indicating the density of reaction points does not affect a lot for the degradation behaviour of cNR (see ESI). The degradation of cNRs in acidic condition was also attempted with 1 M HCl, but no decrosslinking occurred for any cNRs.

Conclusions

We demonstrated a novel synthetic route for obtaining OH-functionalized nitrile *N*-oxide and polyfunctional nitrile *N*-oxides for catalyst-free crosslinking of natural rubber. The ditopic and tritopic nitrile *N*-oxide cross-linkers could be prepared with high yields by using the phenolic OH group, which can coexist with the nitrile *N*-oxide function. Decrosslinking of the crosslinked
natural rubber was achieved using ester-connected ditopic nitrile *N*-oxide. The results of this study shine light on an unprecedented synthetic protocol and on the molecular design
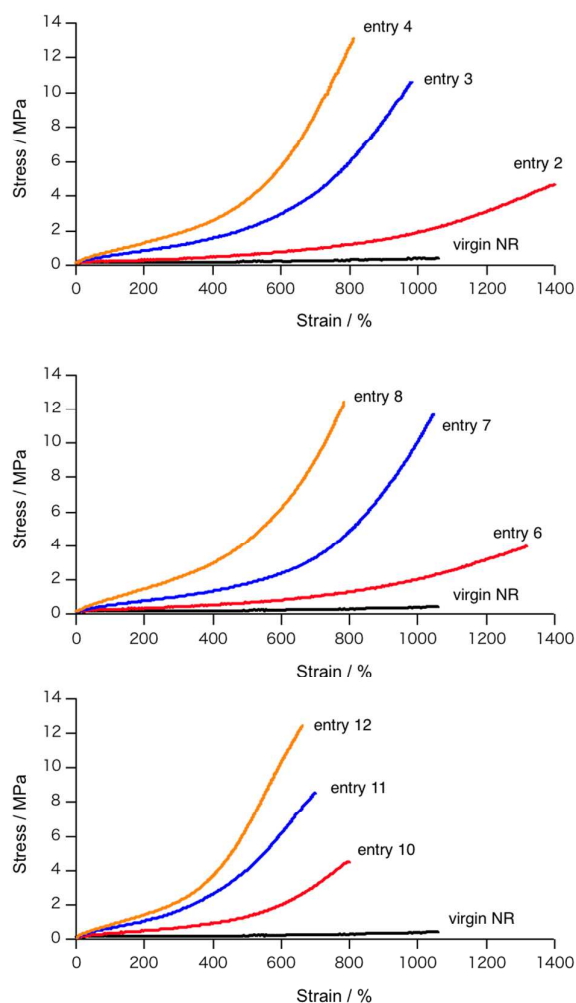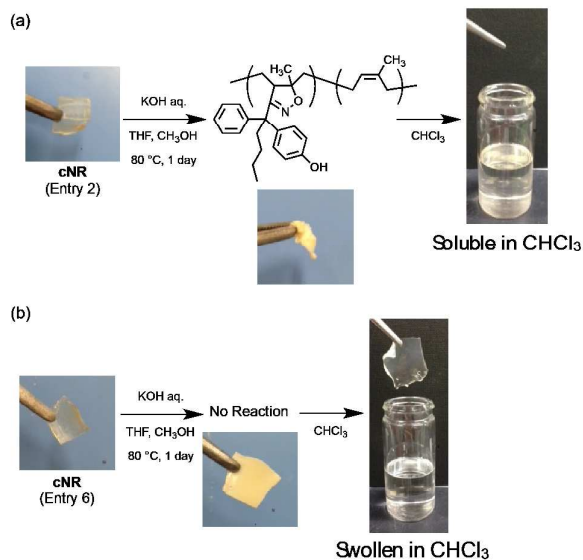

Figure 2. Stress-strain curves of cNR obtained using crosslinker **3** (top), **4** (middle),. and **5** (bottom). Elongation rate: 10 mm/min.

Scheme 3. Decrosslinking reaction of cNRs

of functionalized nitrile *N*-oxides.

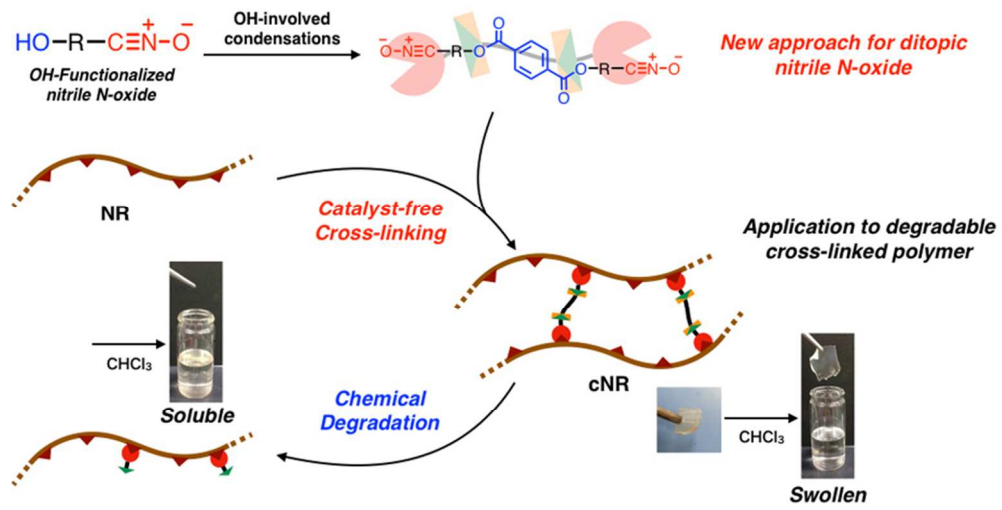## Conflicts of interest

There are no conflicts to declare.

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