Synthesis of Noria-like Macrocycles Containing Alkoxy Groups based on a Dynamic Covalent Chemistry (DCC) System by the $A_2 + B_4$ Condensation

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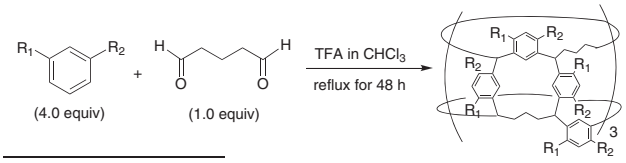
We succeeded in the synthesis of new noria-like macrocycles by condensation of 3-alkoxyphenol as A_2 type monomers, and pentanedial as B_4 type monomer. These condensation reactions were performed using several acids as catalysts in ethanol and $CHCl_3$. It was found that these reactions proceeded by DCC to afford soluble polymers, oligomers, and noria-like ladder macrocycles. As the result, the selective synthesis of the targeted noria-like macrocycles was achieved successfully in high yields.

Dynamic covalent chemistry (DCC) has attracted attention because the final products depending on thermodynamic stability under equilibrium control, and a one-pot method can be used.[1] That is, DCC is a powerful tool for the synthesis of nonlinear products selectively. Certain dynamic covalent bonds are well known such as acetal,[2] disulfide,[3] ester,[4] and imine.[5] Gutsche et al.[6] reported that calixarene was successfully synthesized in high yield through a DCC system. Very recently, Xu and Warmuth[7] examined DCC systems using imine bonds by the reaction of aldehydes and amines in the various reaction conditions, and it was found that large ladder macrocycles could be synthesized selectively. They also succeeded in the synthesis of chiral nanocube in this DCC system.[8] On the other hand, we[9] have succeeded in the synthesized ladder cyclic oligomer (noria) through a DCC system by the condensation of resorcinol with pentanedial, which is similar to the synthesis of calixarene. The resulting noria had 24 hydroxy groups, 6 cavities in the side, and a large hydrophobic central hole, i.e., a water wheel like structure with ladder cyclic rings. Furthermore, noria derivatives containing acid labile groups are good candidates for next-generation electron beam (EB)- and extreme ultraviolet (EUV)-resist materials,[10] because their photosensitivity and structural stability are excellent. However, the solubility of noria is insufficient for practical application. If hydroxy groups of noria are converted to alkoxy groups in part, the resulting noria derivatives show improved solubility, and are applicable as novel next generation resist materials. In this paper, we therefore explored the synthesis of new noria-like macrocycles by the condensation reaction of 3-methoxyphenol (MP), 3-ethoxyphenol (EP), 3-butoxyphenol (BP), or 1,3-dimethoxybenzene (DB) with pentanedial (Scheme 1).

First, we examined the condensation of MP (2.4 g, 20 mmol) with pentanedial solution (50% in water, 1 g, 5 mmol) in the presence of HCl as an acid catalyst in ethanol at 80 °C for 48 h, which are the same conditions as the synthesis of noria. The initially homogenous reaction mixture changed to heterogeneous within 1 h. Figure 1a shows an SEC profile of the resulting



	R_1	R_2
MP	OH	OMe
EP	OH	OEt
BP	OH	OBu
DB	OMe	OMe

	R_1	R_2
$noria_{MO}$	OH	OMe
$noria_{EO}$	OH	OEt
$noria_{BO}$	OH	OBu
$noria_{DMO}$	OMe	OMe

Scheme 1. Condensation reaction of alkoxyphenol with pentanedial.

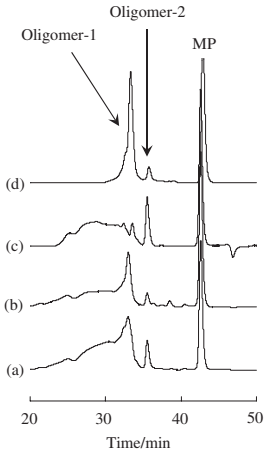


Figure 1. SEC profiles of solutions obtained by condensation of MP with pentanedial at reflux for 48 h. (a) HCl in ethanol, (b) HCl in $CHCl_3$, (c) TFA in ethanol, (d) TFA in $CHCl_3$.

mixture obtained after 48 h. The peaks corresponding to the polymer with $M_n = 9510$, $M_w/M_n = 17.46$ and two oligomers with $M_n = 2200$, $M_w/M_n = 1.04$ (oligomer-1) and $M_n = 1040$, $M_w/M_n = 1.01$ (oligomer-2) at the retention times of 30, 33, and 35 min are observed, respectively. These product ratios were calculated by SEC to be 58:38:4. Furthermore, this condensation reaction was carried out in $CHCl_3$, polymer with $M_n = 5340$, $M_w/M_n = 5.26$ and the same two oligomers were obtained, and their ratios were 72:21:7 (Figure 1b). This indicates that the ratios of polymers and oligomers were depended on the reaction conditions. We further examined this condensation reaction

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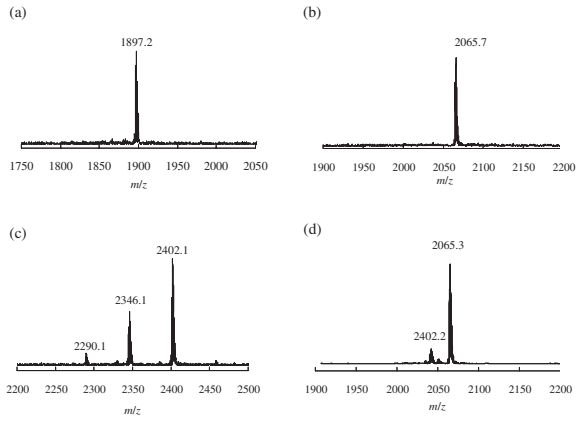

Figure 2. MALDI-TOF mass spectra of noria-like macrocycles. (a) noria$_{MO}$, (b) noria$_{EO}$, (c) noria$_{BO}$, and (d) noria$_{DMO}$.

using trifluoroacetic acid (TFA) as a catalyst. Although, the polymer with $M_n = 5450$, $M_w/M_n = 2.34$ and same two oligomers (oligomer-1 and oligomer-2) were obtained in ethanol (Figure 1c), only oligomer-1 and oligomer-2 were obtained (Figure 1d) in $CHCl_3$ in which the condensation reaction proceeded homogeneously. After 48 h, the reaction mixture was poured into methanol and the precipitated product was washed with diethyl ether several times, and then dried in vacuo at 60 °C for 24 h, yielding only an oligomer-1. The structure of oligomer-1 ($M_n = 2200$) was estimated by ^{1}H NMR, IR, and MALDI-TOF mass. The ^{1}H NMR spectrum showed the signals of aromatic, methyl, methine, and methylene protons which were produced by the condensation reaction of MP with pentanedial. The ratio of the units derived from MP and pentanedial was calculated to be 2:1 from the integration ratios of the signals of aromatic protons and methine protons.[11] The MALDI-TOF mass spectrum of this product after Na^+ doping shows a major peak at m/z 1897.2 (Figure 2a), which corresponds to the m/z value of a noria-like macrocycle including 12 methoxy groups obtained by condensation reaction of two equivalents of MP with one equivalent of pentanedial. These results show that oligomer-1 is a noria-like macrocycle containing twelve methoxy groups and twelve hydroxy groups, and it was named noria$_{MO}$. To examine the mechanism of the condensation leading to noria$_{MO}$, we examined SEC profiles of the obtained products with reaction time. As the result, polymer and oligomer were produced at the first period, and then these products converted to only noria$_{MO}$ after 48 h. This result indicated that noria$_{MO}$ was constructed by reversible reaction between polymer, oligomer, 3-methoxyphenol, and pentanedial under thermodynamic control., ie, DCC system. It was noteworthy that only noria$_{MO}$ could be synthesized in one pot in high yield (87%) under the new DCC reaction conditions.[11] Noria$_{EO}$, noria$_{BO}$, and noria$_{DMO}$ were also obtained by the reaction of EP, BP, and DB with pentanedial under the same conditions. The MALDI-TOF mass spectra of these macrocycles are shown in Figures 2b, 2c, and 2d. The major peaks of noria$_{EO}$, noria$_{BO}$, and noria$_{DMO}$ after Na^+ doping appear at m/z 2065.7, 2402.1, and 2065.3, respectively, which corresponds to m/z values of targeted macrocycles. Two fragment peaks in the mass spectrum displayed in Figure 2c are due to desorption of butoxy groups under strong laser power. A minor peak in Figure 2d corresponds to the m/z value of noria$_{DMO}$ after H^+ doping. Noria$_{EO}$, noria$_{BO}$, and noria$_{DMO}$ were obtained in 74, 51, and 82% yields, respectively. In addition, other acid catalysts were examined.[11] Selective synthesis of macrocycles could not be archived under these conditions. The new DCC conditions using TFA in $CHCl_3$ were suitable for synthesis of noria-like macrocycles from 3-methoxyphenol and pentanedial in high yield. These macrocycles obtained in this work have good solubility in common organic solvents compared the noria.[11] The order of solubility is noria$_{BO}$ > noria$_{EO}$ > noria$_{MO}$ > noria. This means that solubility of these macrocycles increased with the length of alkoxy groups. However noria$_{DMO}$ was insoluble in common organic solvents.

In summary, synthesis of noria-like macrocycles containing alkoxy groups could be achieved by condensation of MP, EP, BP, or DB with pentanedial using TFA as a catalyst in $CHCl_3$ at reflux for 48 h. This reaction proceeded through DCC, yielding noria-like macrocycles containing alkoxy groups such as noria$_{MO}$, noria$_{EO}$, noria$_{BO}$, and noria$_{DMO}$ in 51–87% yields. It was found that the solubilities of these macrocycles were influenced by the length of alkoxy groups in the molecule. The applications of noria$_{MO}$, noria$_{EO}$, and noria$_{BO}$ are under now investigation for EB- and EUV-resist materials.

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