doi:10.1246/cl.2011.464

Published on the web April 13, 2011

Condensation Reaction of Phenols with 1,5-Pentanedial for Synthesis of Noria-like Ladder-cyclic Oligomer by Dynamic Covalent Chemistry Mechanism

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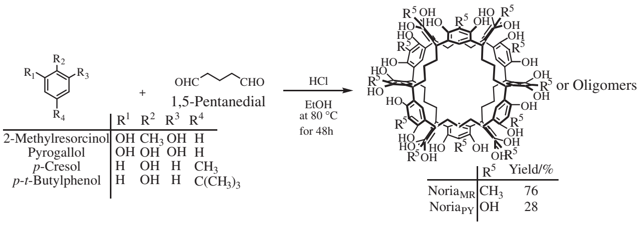
Condensation reaction of 2-methylresorcinol and pyrogallol with 1,5-pentanedial [$CH_2(CH_2CHO)_2$] in the presence of concentrated HCl in ethanol at 80 °C for 48 h proceeded according to a dynamic covalent chemistry (DCC) mechanism to afford the noria-like ladder-cyclic oligomers noria$_{MR}$ and noria$_{PY}$, respectively.

Dynamic covalent chemistry (DCC)[1] is a powerful tool for the synthesis of unique molecules that is applicable to imines,[2,3] esters,[4] acetals,[5] alkoxy amines,[6] boron esters,[7,8] and disulfides.[9] Reactions based on DCC proceed under equilibrium control, to afford thermodynamically stable product. Warmuth and his co-workers reported that a DCC strategy in the reaction of calixarene-based cavitand having formyl groups with 1,2-diaminoethane using trifluoroacetic acid (TFA) as a catalyst provided selectivity for an octahedral molecular cage.[10] Furthermore, the DCC approach could provide several molecular cages, depending on the reaction solvent.[3e] Recently, we have succeeded in the synthesis of ladder-type cyclic oligomer, noria (water wheel in Latin), through a DCC approach based on the condensation reaction of resorcinol and 1,5-pentanedial.[11] This reaction proceeded quantitatively with feed ratios of resorcinol and 1,5-pentanedial = 4:1 in the presence of HCl as a catalyst in ethanol at 80 °C for 48 h. Noria, which has 24 hydroxy groups, six outer cavities, and a large hydrophobic center hole in the molecule, i.e., a water wheel-like structure with ladder cyclic rings, was obtained in more than 80% yield. Very recently, this DCC approach has also been employed in the reactions of 3-methoxyphenol (MP), 3-ethoxyphenol (EP), 3-butoxyphenol (BP), and 1,3-dimethoxybenzene (DMB) with 1,5-pentanedial using trifluoroacetic acid as a catalyst in chloroform as a solvent.[12] Thus, we considered that DCC might be applicable to the reaction of phenol and α,ω-alkanedial, depending on the reaction conditions. The condensation reactions of various phenols with 1,5-pentanedial might provide the unique molecules. In this paper, we examined in detail the applicability of DCC to the condensation reactions of 2-methylresorcinol, pyrogallol, *p*-cresol, and *p*-*t*-butylphenol with 1,5-pentanedial.

The condensation of phenols, i.e., 2-methylresorcinol, pyrogallol, *p*-cresol, and *p*-*t*-butylphenol, with 1,5-pentanedial (50% aqueous solution) was carried out in ethanol at 80 °C in the presence of concd HCl (the same reaction conditions as used for the synthesis of noria) (Scheme 1). These phenols and 1,5-pentanedial have two and four condensation points, respectively, i.e., this reaction system is an $A_2 + B_4$ type condensation. Oligomers were obtained in all cases, and no gel product was formed. Figure 1 depicts the SEC profiles of these oligomers. These results are also summarized in Table 1.



Scheme 1. Condensation reaction of various phenols with 1,5-pentanedial.

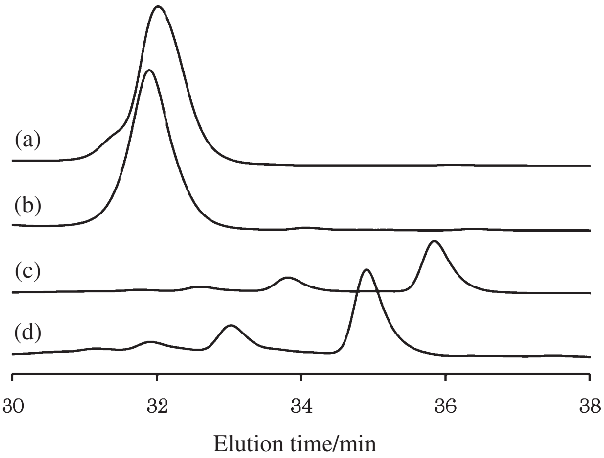


Figure 1. SEC profiles of the products by the condensation reaction of various phenols and 1,5-pentanedial. (a) 2-Methylresorcinol, (b) pyrogallol, (c) *p*-cresol, and (d) *p*-*t*-butylphenol.

Table 1. The reaction of phenols with 1,5-pentanedial[a]

Run	Phenols	M_n (M_w/M_n)[b]	
1	2-Methylresorcinol	2310 (1.02)[c]	[unimodal peak]
2	Pyrogallol	2470 (1.03)[d]	[unimodal peak]
3	*p*-Cresol	980 (1.19)[e]	[multimodal peak]
4	*p*-*t*-Butylphenol	1310 (1.18)[e]	[multimodal peak]

[a] The condensation reactions of various phenols with 1,5-pentanedial were carried out using concd HCl as a catalyst in ethanol at 80 °C for 48 h. [b] Estimated by SEC (DMF) based on polystyrene standard. [c] Insoluble part in diethyl ether. [d] Insoluble part in methanol. [e] Insoluble part in H_2O.

In the case of 2-methylresorcinol and pyrogallol, the SEC profiles showed unimodal peaks and the value of molecular dispersity ratios (M_w/M_n) were very narrow: 1.02 and 1.03 (Figures 1a and 1b, respectively). The condensation reaction of *p*-cresol and *p*-*t*-butylphenol with 1,5-pentanedial provided

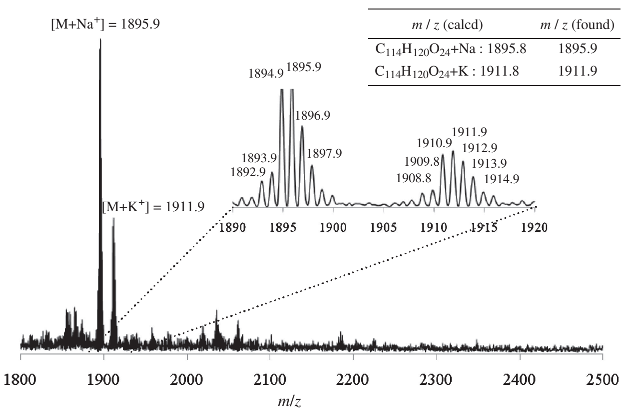


Figure 2. MALDI-TOF mass spectra of noria$_{MR}$.

soluble oligomers showing multimodal peaks with $M_n = 980$ and 1310 and $M_w/M_n = 1.19$ and 1.18, respectively (Figures 1c and 1d). It seems that these condensation reactions proceeded according to a DCC mechanism, affording soluble oligomers. Although, the soluble oligomers formed from *p*-cresol and *p*-*t*-butylphenol might have unique structures, it was difficult to separate the products and confirm their structures. In the case of 2-methylresorcinol, the reaction mixture in ethanol was poured into a large amount of ethyl ether, and a single oligomer was precipitated. The structure of this molecule was confirmed by ^{1}H NMR and MALDI-TOF mass spectrometry. In the ^{1}H NMR spectrum, the peaks assignable to hydroxy, aromatic, methine, methyl, and methylene protons were seen at 9.25–8.12, 7.37–6.15, 4.46–4.04, and 2.30–0.72 ppm, respectively.[13] The ratio of the units derived from 2-methylresorcinol and 1,5-pentanedial was calculated to be 2:1 from the ratios of the signal integrals of aromatic protons and methine protons. Furthermore, MALDI-TOF mass spectra of this product doping with Na$^+$ and K$^+$ showed molecular ion signals at m/z 1895.9 and 1911.9 (Figure 2), which correspond to the mass of a cyclic oligomer formed by the condensation reaction of twelve equivalents of 2-methylresorcinol with six equivalents of 1,5-pentanedial.[14] These results strongly indicate that the condensation reaction of 2-methylresorcinol with 1,5-pentanedial afforded a noria-like ladder-cyclic oligomer with 24 pendant hydroxy groups and 12 methyl groups, as shown Scheme 1. We named this product noria$_{MR}$ (yield: 76%). Furthermore, in the case of pyrogallol, similar noria-like ladder-cyclic oligomer, noria$_{PY}$, with 36 pendant hydroxy groups was obtained in 28% yield.[15]

Next, we examined the effect of reaction time on the condensation reaction leading to noria$_{MR}$ and noria$_{PY}$ by means of SEC. Figure 3 shows the time course of SEC profiles of the products formed by reaction of 2-methylresorcinol with 1,5-pentanedial. Initially, polymer and oligomer were produced, and then these products were converted to noria$_{MR}$ with increasing reaction time. This result shows that this reaction proceeded according to a DCC mechanism to give the most thermodynamically stable compound, noria$_{MR}$, selectively. A similar tendency was also observed in the synthesis of noria$_{PY}$.

Next, the thermal stability, solubility, and film-forming property of noria$_{MR}$ and noria$_{PY}$ were examined. The temperature of 5 wt % loss ($T_d{}^{5\%}$) of noria$_{MR}$ and noria$_{PY}$ was measured by thermogravimetric analysis; the values of $T_d{}^{5\%}$ of noria$_{MR}$ and noria$_{PY}$ were 281 and 260 °C, respectively. Noria$_{PY}$ had solubility similar to noria, showing good solubility in aprotic highly polar solvent such as dimethyl sulfoxide (DMSO), *N*,*N*-dimethylformamide (DMF), and *N*,*N*-dimethylacetamide (DMAc). However, noria$_{MR}$ had good solubility and was soluble in solvents such as methanol, acetone, and tetrahydrofuran. Noria$_{MR}$ also had good film-forming ability. As already mentioned, noria derivatives with pendant photochemical groups are useful as photofunctional materials such as UV-curing materials[16] and photoresist materials.[17–21] Thus, noria$_{MR}$ and noria$_{PY}$ may be superior to noria due to their good solubility, in addition to the film-forming properties of noria$_{MR}$ and the larger number of hydroxy groups of noria$_{PY}$. Derivatives of noria$_{MR}$ and noria$_{PY}$ with pendant photofunctional groups are therefore candidates for novel UV-curing materials or higher-resolution photoresist materials.

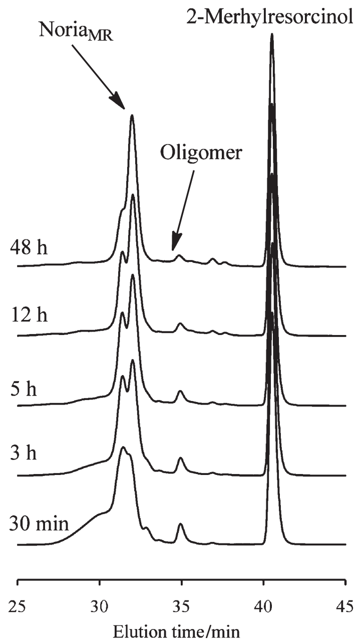


Figure 3. Time course of SEC profiles during the condensation reaction of 2-methylresorcinol with 1,5-pentanedial.

In summary, we investigated the reaction of phenols (2-methylresorcinol, pyrogallol, *p*-cresol, and *p*-*t*-butylphenol) as A$_2$-type monomers with 1,5-pentanedial as B$_4$-type monomer. 2-Methylresorcinol and pyrogallol afforded noria-like cyclic oligomers, noria$_{MR}$ and noria$_{PY}$, respectively, via a DCC mechanism. Introduction of pendant photofunctional groups into noria$_{MR}$ and noria$_{PY}$ should provide good candidates for novel UV-curing materials or high-resolution photoresist materials. Furthermore, the reaction of *p*-cresol and *p*-*t*-butylphenol with 1,5-pentanedial under DCC conditions also afforded novel molecules which are currently under investigation.

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14 Spectra data of noria$_{\mathrm{MR}}$; IR (film) ν: 3320 (νO–H), 2970, 2933, and 2863 (νC–H), 1605, 1475, and 1464 (νC=C aromatic). ^{1}H NMR (600 MHz, DMSO-d_6, tetramethylsilane): δ 0.72–2.30 (m, 36H, –CH$_2$CH$_2$CH$_2$–), 4.04–4.46 (m, 12H, >CH–), 6.15–7.37 (m, 12H, aromatic H), 8.12–9.25 (m, 36H, OH). MALDI-TOFMS m/z: $[\mathrm{M+Na}]^+$ calcd for ($\mathrm{C_{114}H_{120}O_{24}+Na}$), 1895.8; found, 1895.9, $[\mathrm{M+K}]^+$ calcd for ($\mathrm{C_{114}H_{120}O_{24}+K}$), 1911.8; found, 1911.9.

15 Spectra data of noria$_{\mathrm{PY}}$; IR (film) ν: 3320 (νO–H), 2981, 2935, and 2861 (νC–H), 1623, 1610, and 1477 (νC=C aromatic). ^{1}H NMR (600 MHz, DMSO-d_6, tetramethylsilane): δ 0.57–2.41 (m, 36H, –CH$_2$CH$_2$CH$_2$–), 3.92–2.41 (m, 12H, >CH–), 5.78–7.10 (m, 12H, aromatic H), 7.39–9.34 (m, 36H, OH). MALDI-TOFMS m/z: $[\mathrm{M+H}]^+$ calcd for ($\mathrm{C_{102}H_{96}O_{36}+H^+}$), 1897.56; found, 1897.55, $[\mathrm{M+Na}]^+$ calcd for ($\mathrm{C_{102}H_{95}O_{36}+Na}$), 1919.56; found, 1919.56.

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