A Supramolecular Polymer of Nitroxide Radicals via Hydrogen Bonding

Satoshi Nakajima,[1] *Eisuke Kato,*[1] *Masayuki Minatozaki,*[1] *Hiroyuki Nishide**[1,2]

Summary: 2,2,6,6-Tetramethylpiperidinyl-*N*-oxy (TEMPO) is a robust nitroxide radical molecule under ambient conditions. We found that the TEMPO derivatives act as a proton acceptor to form an intermolecular hydrogen-bonding complex with many kinds of phenol or urea derivatives. ORTEP analysis of the crystals of TEMPO with the phenol derivatives indicated that hydrogen bonding could be formed between the oxygen of the nitroxide and the phenolic proton and the N–O bond of the hydrogen-bonded TEMPO was lengthened in comparison to that of the free N–O bond. The formation constant of the hydrogen-bonding complex of TEMPO with the phenol or urea derivatives in a chloroform solution was spectroscopically determined by IR to be 10–100 M^{-1}. Hydrogen bonding of the thelechelic bis-TEMPO derivatives with thelechelic bis-phenol or bis-urea derivatives provided a supramolecular structure. The estimated molecular weights of the supramolecules in the chloroform solution, based on DOSY-NMR spectroscopy, were 3000–4000. The potential of the nitroxide radical's supramolecule as a new functional material is also described.

Keywords: hydrogen bonding; macromolecular complex; nitroxide radical; radical polymer; supramolecular structures

Introduction

Hydrogen bonding is one of the most important non-covalent interactions in both natural compounds and organic materials.[1] In nature, all biopolymers such as nucleic acids, proteins, and polysaccharides have hydrogen-bonding groups, which participate in the formation of supramolecular structures and the induction of their functions.[2–7] In synthetic polymers, for example, polyamides, the hydrogen bonding significantly contributes to their high performance properties. If a variety of hydrogen bonding moieties are strategically introduced into synthetic polymeric and organic materials, it could lead to new polymeric materials exhibiting a variety of functions.

The hydrogen bonds are characterized by their bonding energy of 10–50 kJ/mol and a directional interaction, represented by $-X...H-Y-$ (X, Y=N, O, etc). Dynamic, but relatively stable molecular complexes are formed by the less-energy consuming, simply mixing of two components or through spontaneous self-assembling based on the hydrogen bonding interaction. Many supramolecular polymers or macromolecular complexes formed by the hydrogen bonding have been extensively studied. Supramolecular main-chain polymers were introduced by Lehn and co-workers,[8,9] who used triple hydrogen bonds in bifunctional diaminopyridine and uracil residues of the repeating molecules. A variety of self-assembled, supramolecular liquid crystalline, columnar, and array polymers has been reported that describe the advantages of the non-covalent strategy using hydrogen bonding, in forming the characteristic polymers.[10–16]

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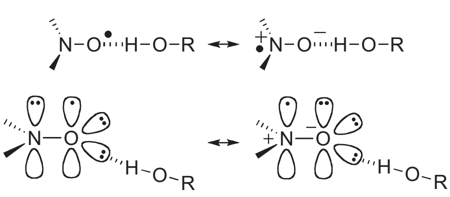
[1] Department of Applied Chemistry, Waseda University, Tokyo 169-8555, Japan
E-mail: nishide@waseda.jp
[2] Department of Nanobio Materials and Electronics, Gwangju Institute of Science and Technology, Gwangju 500-712, Korea

We are developing so-called "radical polymers" as a new class of electroactive materials.[15–17] An organic radical molecule bears one unpaired electron and is short-lived and highly reactive, and has been classified as an unstable and intractable material. However, some of them have been chemically converted into robust compounds. A typical example is nitroxide radicals, such as 2,2,6,6-tetramethylpiperidinyl-*N*-oxy (TEMPO), which exist for appreciable lengths of time under ambient conditions. We extended these robust radical species to their polymeric analogues, exemplified by poly (2,2,6,6-tetramethylpiperidinyloxy-4-ly) methacrylate (PTMA). They were widely studied as a spin-label for biomedical molecules, organic magnetic materials based on spin alignment,[18,19] a bistable electroconductive layer for organic memory devices,[20–22] and electrode-active materials for rechargeable batteries.[23–26] For example, the organic radical battery composed of a radical polymer electrode has been characterized by a high charging capacity ascribed to the one-electron redox reaction of the radical moieties, very high-power rate performance derived from the rapid electron-transfer process, and long cycle life ascribed to the chemical stability of the radical moieties and to the amorphous electrode structure.

It is known that the N–O bond in nitroxide radical molecules is represented by the resonance formula (the upper formula in Scheme 1; the dot symbolizes an unpaired electron) or that the unpaired electron on the oxygen is involved in the resonance to form an amminium oxy anion. In this study, we expected that the nitroxide radical molecules could form supramolecular complexes with hydrogen-bonding proton-donors such as the phenol (the middle and bottom formulas in Scheme 1). The formation of a macromolecular complex or supramolecular polymer based on the hydrogen-bonding of the nitroxide radical was examined by simply mixing the solution of a thelechelic nitroxide radical derivative with the solution of a proton-donating bisphenol derivative (Scheme 2). The effects of the hydrogen-bonding complex formation on the properties of the nitroxide radicals were also discussed from the viewpoints of the N–O bond nature, the chemical stability, and the redox potential.

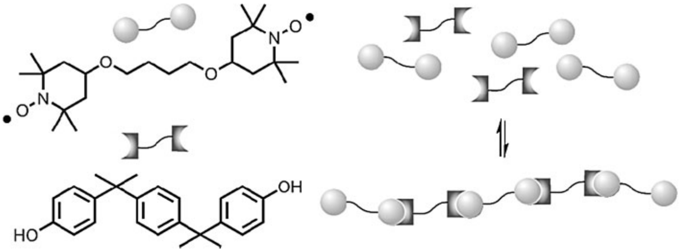


Scheme 1.
Resonance formulas of the nitroxide radical itself and of the nitroxide radical with a phenol derivative through a hydrogen bonding.

Experimental Part

1,3-Dihexylurea 1

A 500 mL pear-shaped flask was charged with a solution of *n*-hexylamine (2.31 g, 22.8 mmol) in 200 mL of dichloromethane, then cooled in an ice-bath. Hexyl isocyanate (2.90 g, 22.8 mmol) was dropwise added with vigorous stirring. After the addition, the reaction mixture was stirred for 3 hours at room temperature. The mixture with a white precipitate was washed with concentrated hydrochloric acid (50 mL × 3 times). The organic layer was collected and washed again with water (50 mL × 3 times). The organic layer was collected, dried over $MgSO_4$, and evaporated to give the pure product as a white powder (5.15 g. 99%). ^{1}H-NMR ($CDCl_3$, δ): 4.33 (s, 2H, NH), 3.15 (t, 4H, CH_2), 1.48 (m, 4H, CH_2), 1.29 (m, 12H, CH_2), 0.88 (t, 6H, CH_3); ^{13}C-NMR ($CDCl_3$, δ): 14.0 22.6 26.6 30.2 31.5 40.6 158.4; GC-MS: Found ($M + H^+ = 229.3\,m/z$) calcd ($M^+ = 228.4$ g/mol). Found: C, 68.4; H, 12.9; N, 12.1%, Calcd for $C_{13}H_{28}N_2O$: C, 68.3; H, 12.7; N, 12.3%;



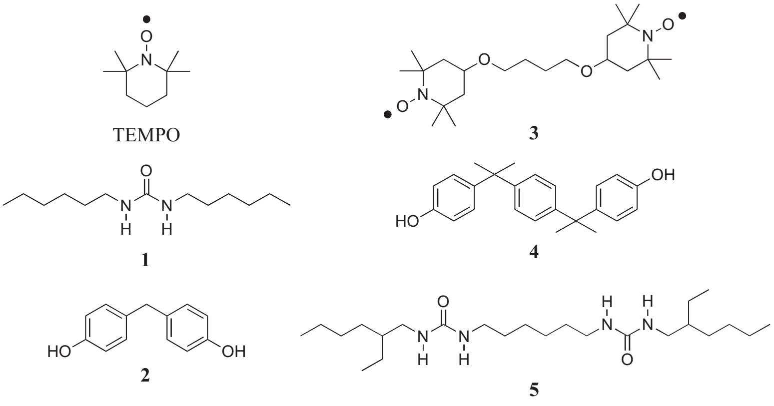
Scheme 2.
Supramolecular formation of a thelechelic bis-nitroxide radical molecule with a thelechelic bis-phenol molecule via hydrogen bonding.

1,1′-(Hexane-1,6-diyl)bis[3-(2-ethylhexyl)urea] 5

A 300 mL three-necked round bottom flask was charged with a solution of ethylhexylamine (0.96 g, 1.22 mmol) in 100 mL of dichloromethane, then cooled in an ice-bath. 1,6-Diisocyanatehexane (0.50 g, 0.48 mmol) was dropwise added with vigorous stirring. After the addition, the reaction mixture was stirred for 3 hours at room temperature. The mixture with a white precipitate was washed with concentrated hydrochloric acid (30 mL × 3 times). The organic layer was collected and washed again with water (30 mL × 3times). The organic layer was collected, dried over $MgSO_4$, and evaporated. Recrystallization in acetonitrile afforded the product as white crystals (1.19 g. 94%). ^{1}H-NMR ($CDCl_3$, δ): 5.10 (s, 4H, NH), 3.15 (t, 4H, CH_2), 3.07 (t, 4H, CH_2), 1.77 (m, 2H, CH), 1.46 (m, 4H, CH_2), 1.39 (m, 4H, CH_2), 1.32 (m, 8H, CH_2), 1.26 (m, 8H, CH_2), 0.88 (t, 12H, CH_3); ^{13}C-NMR ($CDCl_3$, δ): 10.9, 14.1, 23.0, 24.1, 25.7, 28.9, 29.9, 31.0, 39.6, 39.9, 43.2, 159.1; GC-MS: found ($M + H^+ =$ 427.5 *m/z*) calcd. ($M^+ = 426.7$ g/mol). Found: C, 67.4; H, 11.6; N, 7.5%, Calcd for $C_{24}H_{50}N_4O_2$: C, 67.6; H, 11.8; N, 7.5%;

Characterization of the Radical Derivatives

The radical or unpaired electron concentration per the TEMPO unit was determined by the slope of the Curie plots for the magnetic susceptibility from 10 to 300 K in a 1.0 T field and the saturated magnetization in the SQUID measurement using a Quantum Design MPMS-7S magnetometer. The radical concentration was also analyzed by integration of the ESR signal standardized with that of the solution of 2,2,6,6-tetramethylpiperidinyl-*N*-oxy (Spe-



Scheme 3.
Structures of **1–5**.

cial grade purchased from Aldrich Co.). The ESR spectra were measured by a JEOL JES-TE200 ESR spectrometer with a 100 kHz field modulation. These radical concentration values estimated by the two methods agreed with each other.

Other Spectroscopies

The ^{1}H-, ^{13}C-NMR, and mass spectra were recorded using a JEOL ECX 500 or a BRUKER AVANCE 600 spectrometer and a JEOL JMS-GC mate II spectrometer.

DFT Calculation

The theoretical calculation based on the density functional methods was performed with Gaussian 03. Becke's three-parameter gradient-corrected functional (B3LYP) with 6-31G* basis was used to optimize the geometry and to compute the electronic structure at the determined minimum.

Results and Discussion

Electrospray ionization mass spectrometry (ESI-MS) is known to have a very soft ionization process, and its mass spectra are regarded to reflect the state of molecules in the solution.[27,28] We first employed the ESI-MS technique to directly detect a dimer complex of TEMPO with the urea derivative **1**, 1,3-dihexylurea, in the chloroform solution. As the example shown in Figure 1, the ESI-MS spectra of a 1 mM solution of TEMPO with the urea **1** revealed the strong mass peaks of 386 *m/z* [TEMPO – the urea **1**]$^+$, 158 *m/z* [TEMPO]$^+$, and a weak mass peak of 458 *m/z* [the urea **1** dimer]$^+$, attributed to the heterodimer complex, TEMPO itself, and the homodimer of the urea derivative, respectively. This result indicated the complex formation of the nitroxide TEMPO radical with the urea even in solution.

A crystal of TEMPO with the bis-phenol **2**, 4,4’’-dihydroxydiphenylmethane was grown from their equimolar toluene solution (sublimation method for the crystallization). An X-ray single crystallographic analysis provided an ORTEP drawing of the crystal (Figure 2). The nitroxide radical of TEMPO appears to interact with the phenolic proton. The N–O bond of TEMPO was lengthened as compared to the free N–O bond of TEMPO itself, which suggests that the nitroxide radical could form hydrogen bonding with the phenolic proton of the phenol. Deviation of the nitrogen atom on the N–O bond of TEMPO from the C_2O plane was reduced by ca 0.3 Å, which suggested that the sp^2 character of the nitrogen is enhanced through the bonding interaction of the oxygen on the N–O bond. A density functional theory method was applied to estimate the spin and electron density distribution of the nitroxide's unpaired electron (Table 1). The data indicated an

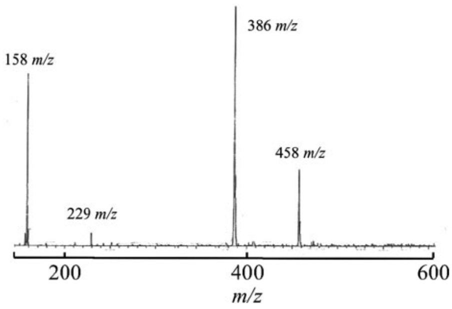


Figure 1.
ESI-MS spectrum of TEMPO with the urea **1** in $CHCl_3$/CH_3OH (4/1 v/v). Capillary temperature; 180 °C, flow rate; 5 μl min^{-1}, and the spray voltage; 4 kV.

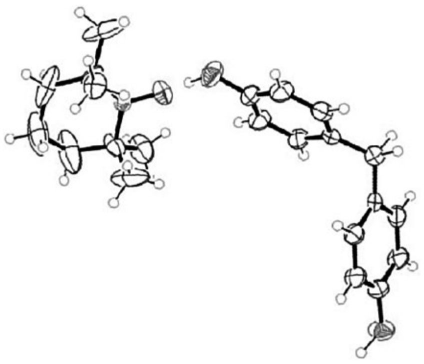


Figure 2.
ORTEP drawing for TEMPO and the bis-phenol **2**.

Table 1.
Crystallographic data for TEMPO and the calculated spin density and Mulliken charge by DFT.

	N–O bond length (Å)	Deviation of the N–O bond from the C_2O plane (Å)	Spin density	Mulliken charge
TEMPO	1.284	0.1765	N: 0.440 O: 0.520	N: −0.050 O: −0.405
hydrogen-bonded TEMPO	1.291	0.1404	N: 0.535 O: 0.404	N: −0.053 O: −0.445

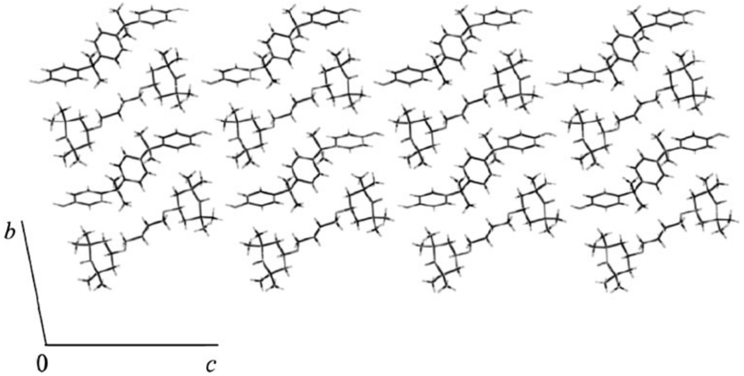


Figure 3.
Mercury diagram showing the crystal structure of the diradical **3** and the bisphenol **4** projected along *a* axis.

increased electron density on the nitrogen of the N–O bond probably through the hydrogen bonding. A single crystal of the thelechelic dinitroxide derivative **3**, 1,4-bis(2′,2′,6′,6′-tetramethyl-piperidine-*N*-oxyl-4′-ether)butane, and the bisphenol derivative **4**, α,α′-bis (4-hydroxy- phenyl)-1,4-diisopropylbenzene, was also grown from a toluene solution. The crystal structure analysis (Figure 3) showed that the molecules were stacked along the *a*-axis through a hydrogen-bonding interaction.

The infrared spectrum of the chloroform solution of TEMPO with the urea O or the phenol O was studied. Figure 2 shows an example of the IR spectra of the TEMPO with the urea solution recorded in the 1300 – 1700 cm^{-1} range. The absorption ascribed to the stretching vibration of the N–O bond shifted from 1311 to 1303 cm^{-1}, supporting the intermolecular hydrogen bonding of the nitroxide radical with the urea. The formation constant *K* was estimated by the following procedure.[29] The integrated absorbance of the peak at 3600 cm^{-1} ascribed to the free phenol plotted vs. the concentration of the free species as a function of the concentration of the nitroxide radical; the formation constant was obtained from the slope. *K* of the nitroxide radical with the phenol was estimated to be 8.8 M^{-1} in the chloroform solution; this

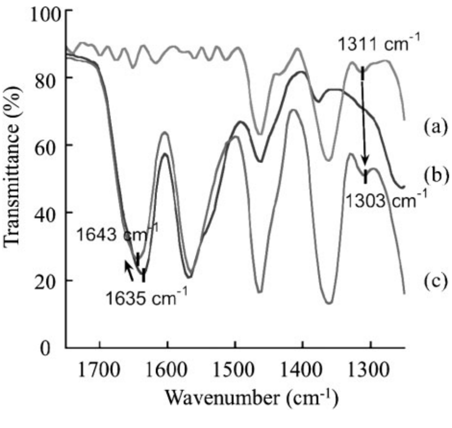


Figure 4.
IR spectrum of (a) TEMPO, (b) the urea **1** and (c) TEMPO with the urea **1** in $CHCl_3$ at room temperature.

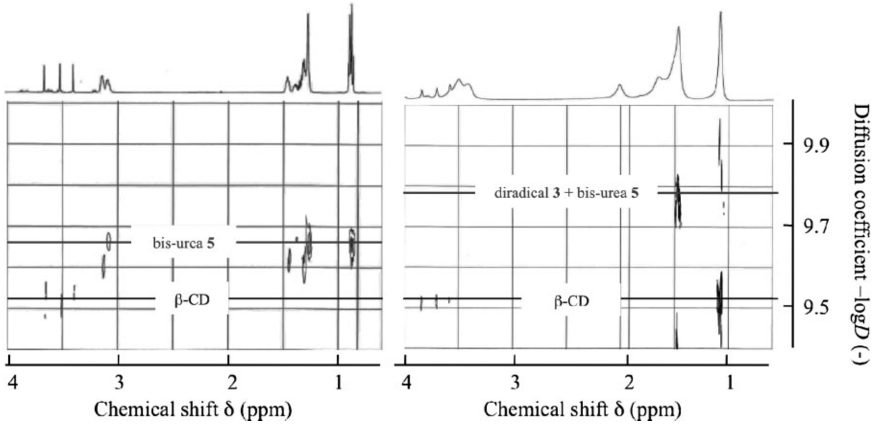


Figure 5.
DOSY spectra of (a) the bis-urea **5** and (b) the bis-urea **5** with the diradical **3** in $CDCl_3$ at room temperature.

value was almost similar to that for the hydrogen-bonding complex of the phenol with the pyridine derivative.[1,7] This result suggested that the hydrogen-bonding energy of the nitroxide radical with the phenol formed a supramolecular structure. (Aliaga and co-workers[30] reported that TEMPO abstracted the phenolic hydrogen to yield the phenoxyl radical. However, ESR measurement on the dichloromethane solution of TEMPO with the phenol derivatives gave no signal ascribed to the phenoxyl radical ($g = 2.004$)).

Chloroform solutions of the diradical **3** and the bis-phenol **2** or the bis-urea **5**, 1,1′-(hexane-1,6-diyl)bis[3-(2-ethylhexyl)urea], were simply mixed to form supramolecular complexes through hydrogen bonding. The molecular weight of the formed polymer was estimated by DOSY (diffusion ordered spectroscopy[12]). A calibration curve was made using the normalized diffusion coefficient D_{norm} for normalized with the diffusion coefficient of an internal standard, heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin (β-CD) standard polystyrenes. The molecular weights of the supramolecular polymers of the diradical **3** with the bis-phenol **2** or the bis-urea **5** were estimated to be 2800 and 4200 g/mol, respectively (Table 2). These results suggested the supramolecular complex formation of the nitroxide radical through hydrogen bonding.

Table 2.
Diffusion coefficient and molecular weight for the supramolecular polymers in $CDCl_3$ at room temperature by DOSY.

	D_{norm} (−)	Estimated M_w
diradical 3 + bis-urea 5	0.51	4200
diradical 3 + bis-phenol 4	0.75	2800
β-CD	1.00	1429

Conclusion

The intermolecular hydrogen-bonding complexes of nitroxide radicals with proton donors were studied for the first time. The conformation and bond character of the nitroxide moiety were influenced by the hydrogen bonding. It is expected that the redox potential of the nitroxide radical could be tuned by hydrogen-bonding donors. The bonding energy was high enough to form a supramolecular structure. Supramolecular nitroxide radical polymers involve unpaired electrons in the main chain and would be potential functional materials that respond to electric and/or magnetic stimulus.

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