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Quadruply Hydrogen-Bonded Building Block from Hydrazide–Quinolinone Motif and Gelation Ability of Its Analogous Oxalic Monoester–Monoamide Derivative

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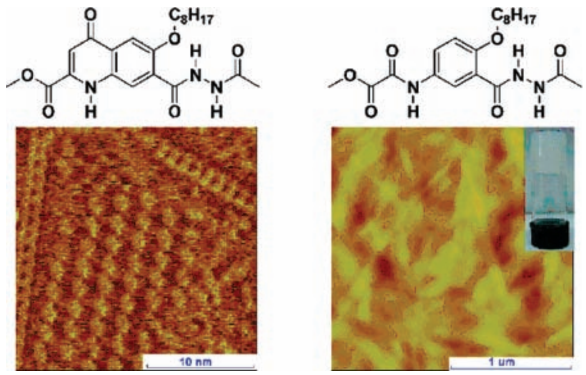
ABSTRACT



NMR and STM studies revealed that the hydrazide–quinolinone-based building block 5 exhibited a monomer–dimer–polymer equilibrium, while its acyclic analogue 6, due to conformational flexibility, exhibited a more complicated mode of aggregation and formed a gel in dichloromethane/hexane.

Due to its directionality, specificity, and strength, hydrogen bonding has been described as the “master key interaction in supramolecular chemistry”.[1] Multiple hydrogen-bonded systems, especially quadruple hydrogen-bonded systems, have gained great success in the construction of many superstructures and applications in the fields of material science, catalysis, and template synthesis.[2] Inspired by the hydrogen-bonding capability of nucleobases found in DNA duplexes, quadruple hydrogen-bonded systems are mainly based on functionalized nucleobases, especially urea derivatives. Heterocycle-based quadruple hydrogen-bonded systems developed by the groups of Meijer et al.[3] and Zimmerman et al.[4] are examples of great success. However, the number of quadruple hydrogen-bonded modules available for use in supramolecular assembly is limited.[5] There is a strong need for the development of new quadruple hydrogen-bonded systems to meet the demand of increasing applications.

Organogels are a new class of soft materials, composed of a self-assembled superstructure of low-molecular-mass organic gelators (LMOGs) through specific interactions and a large volume of organic liquid immobilized therein.[6]

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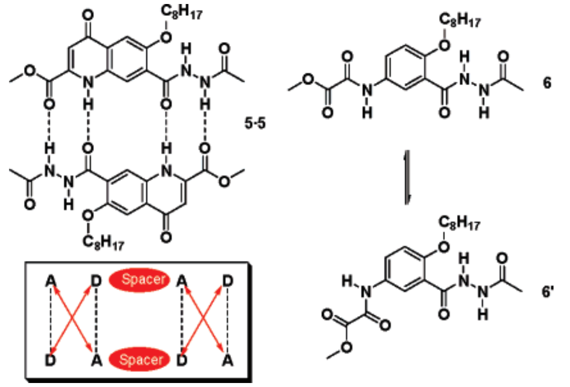
Stimulated by the potential applications in sensors, molecular electronics, and catalysts, great efforts have been paid to this kind of new material. In hydrogen bond-mediated self-assembly systems, little attention has been paid to the hydrazide derivatives,[7] considering their high density of hydrogen-bonding sites (two acceptor sites and two donor sites) and convenient fixation of conformation.

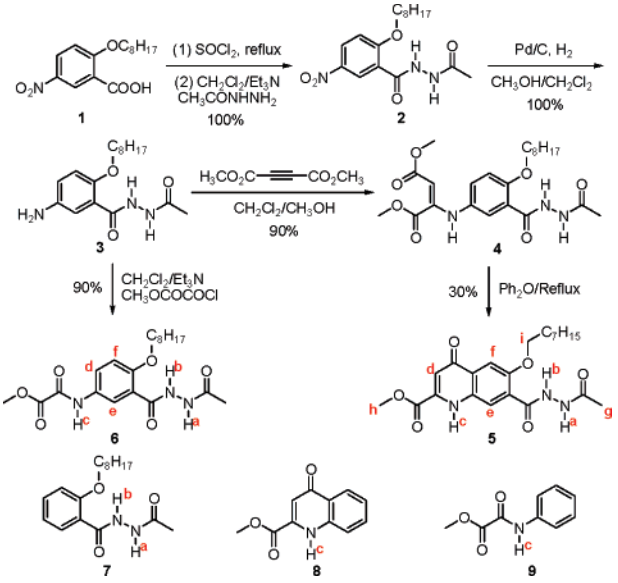
As stated above, most heterocycle-based quadruple hydrogen-bonded systems came from urea derivatives. Continuing our current interest in the hydrazide motif as an excellent building block in self-assembly,[8] we herein report a new quadruple hydrogen-bonded motif based on hydrazide−quinolinone derivative. Its acyclic analogue oxalic monoester−monoamide derivative gelates organic liquid to form organogel. To increase the strength, in the design of the target molecule **5** the following factors have been considered (Scheme 1): (i) the rigid quinolinone framework and introduction of an *S*(6)-type hydrogen-bonded ring[9] confine the molecule to be planar and preorganize hydrogen-bonding sites staying in register for the formation of a quadruple hydrogen-bonded homodimer; (ii) the aromatic ring as a spacer reduces 2-fold repulsive electrostatic interactions;[10] (iii) the reservation of α-carbonyl vinyl motif renders good proton donability of the NH group and consequent high stability of the resulting homodimer. In the case of its acyclic analogue **6**, the self-assembly process may be complicated by large conformational mobility.

Scheme 1. Secondary Electrostatic Interaction Analysis of Homodimer **5·5** and Conformational Analysis of Acyclic **6**



2-(Octyloxy)-5-nitrobenzoic acid (**1**)[11] was first converted into its acyl chloride in refluxing thionyl chloride and then coupled with acetylhydrazide to give compound **2** in quantitative yield. The nitro functional group was reduced under the catalytic hydrogenation conditions and then was reacted with dimethyl acetylenedicarboxylate to give compound **4** or was coupled with methyl oxalyl chloride to give compound **6**. Compound **4** further underwent thermal cycloaddition reaction in reflux diphenyl ether to give compound **5** in satisfying yield. As control, compounds **7**,[8a] **8**,[12] and **9**[13] were also synthesized (Scheme 2).

Scheme 2. Synthetic Route of **5** and **6**, Chemical Structures of Controls **7**, **8**, and **9**



^1H NMR studies (Figure 1, each 5 mM) in $CDCl_3$ revealed significant downfield shifts of NH signals of **5** (11.64 ppm for H^b, 10.45 ppm H^a, and 10.88 ppm for H^c) compared to those of control compounds **7** (10.91 ppm for H^b, 9.03 ppm H^a), and **8** (8.99 ppm for H^c), while minor downfield shifts were observed for compound **6** (11.03 ppm for H^b, 9.42 ppm for H^a, and 9.53 ppm for H^c) compared to controls **7** and **9**

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(5) Selected examples: (a) Ducharme, Y.; Wuest, J. D. *J. Org. Chem.* **1988**, *53*, 5787−5789. (b) Lafitte, V. G. H.; Aliev, A. E.; Horton, P. N.; Hursthouse, M. B.; Bala, K.; Golding, P.; Hailes, H. C. *J. Am. Chem. Soc.* **2006**, *128*, 6544−6545. (c) Martin, A. M.; Butler, R. S.; Ghiviriga, I.; Giessert, R. E.; Abboud, K. A.; Castellano, R. K. *Chem. Commun.* **2006**, 4413−4415. (d) Davis, A. P.; Draper, S. M.; Dunne, G.; Ashton, P. *Chem. Commun.* **1999**, 2265−2266. (e) Prabhakaran, P.; Puranik, V. G.; Sanjayan, G. J. *J. Org. Chem.* **2005**, *70*, 10067−10072. (f) Lüning, U.; Kühl, C. *Tetrahedron Lett.* **1998**, *39*, 5735−5738. (g) Gong, B. *Polym. Int.* **2007**, *56*, 436−443 and references therein.

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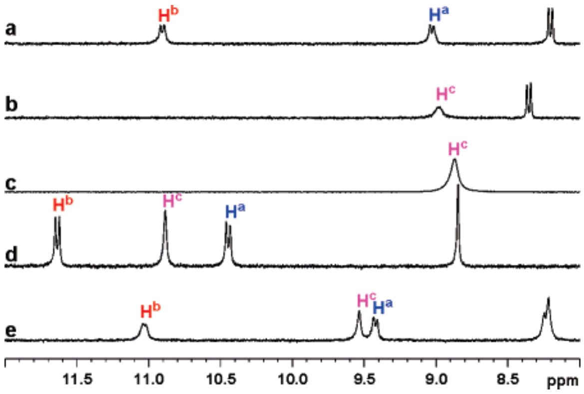

Figure 1. Stacked partial spectra of (a) **7**, (b) **8**, (c) **9**, (d) **5**, (e) **6**, each 5 mM in CDCl$_3$, 298 K, 300 MHz.

(8.87 ppm for H^c). In addition to the different electrostatic effects of the frameworks, different aggregation modes might mainly account for these great differences.

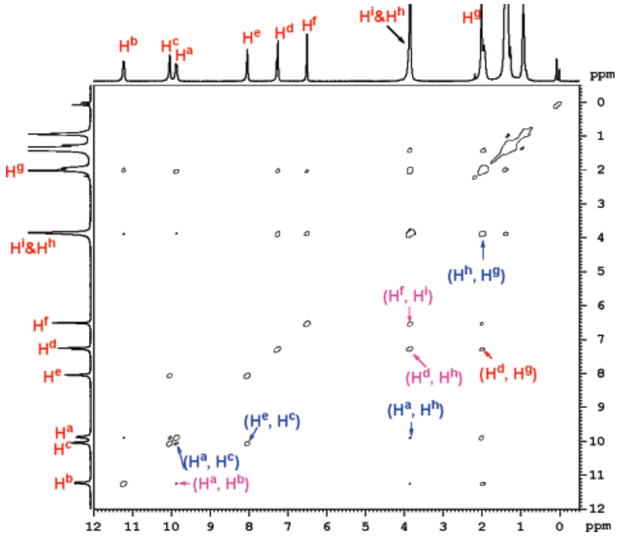

Figure 2. 2D NOESY spectrum of **5**, 100 mM, CDCl$_3$, 298 K, 300 MHz, with important NOE contacts highlighted.

Dilution ^{1}H NMR experiments[14] (298 K, 300 MHz, CDCl$_3$) on **5** revealed unique concentration dependency. Within the concentration range investigated (from 100 mM to 0.5 mM), almost all resonances of the protons of **5** shifted downfield with the lowering of the concentration, especially those for H^c ($\Delta = 1.03$ ppm) and H^e ($\Delta = 1.12$ ppm). This phenomenon might suggest the existence of different aggregation modes in CDCl$_3$ solution. A 2D NOESY experiment (Figure 2) further revealed important contacts between H^h and H^g, H^h and H^a, H^a and H^c, and H^c and H^e. In addition to H^c and H^e, distances between the above-mentioned protons are much too long for any cross-peaks to be observed within the same molecule of **5**; the signals must correspond to intermolecular contacts between the two constituent molecules of the homodimer. ESI-MS[14] provided more evidence for the formation of a homodimer; in additon to a signal corresponding to monomer (432.4, $[M + H]^+$, calcd: 432.2), signals corresponding to the homodimer structure (885.7, $[2M + Na]^+$, calcd: 885.4; 863.7, $[2M + H]^+$, calcd: 863.4) were observed. Another important NOE contact between H^d and H^g was also observed, which cannot be explained intramolecularly based on a monomer or intermolecularly based on a homodimer. There should exist an equilibrium of monomer−homodimer−polymer as depicted in Figure 3.[15]

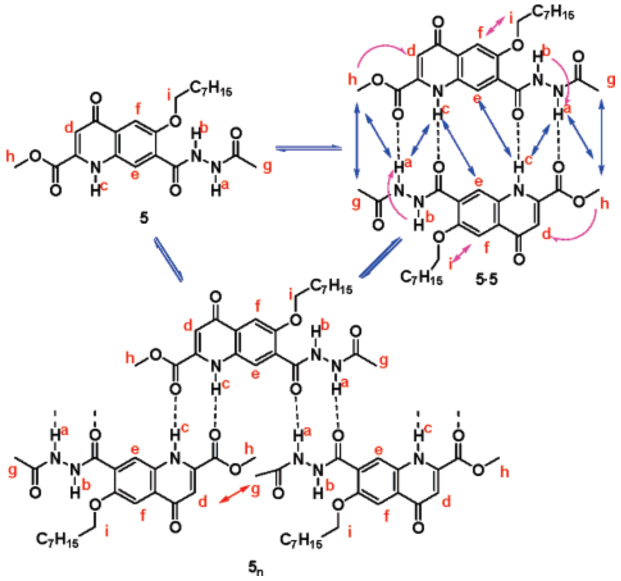

Figure 3. Representation of a monomer−homodimer−polymer equilibrium of **5**, with important NOE contacts indicated by arrows.

Variable-temperature ^{1}H NMR experiments[14] (10 mM, CDCl$_3$, 600 MHz) further confirmed the above hypothesis. With lowering the temperature, the spectra became unresolvable. This might come from slowing the above-mentioned equilibrium, which complicated the picture of NMR spectra. Scanning tunneling microscope (STM) technology provided other evidence. An STM image of **5** on high oriented pyrolytic graphite (HOPG) is shown in Figure 4. The image clearly shows the homodimer structure and the zipperlike polymeric structure.

In the case of its acyclic analogue **6**, because of flexible comformation, there were great differences. First, dilution ^{1}H NMR experiments (CDCl$_3$, 300 MHz, 298 K)[14] revealed that below a concentration of 5 mM, it displayed a well-

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[14] See Supporting Information for details.

[15] At higher concentrations, the two hydrogen bond-linked polymer might be favored, while the quadruple hydrogen-bonded homodimer might be favored at lower concentrations. As a result, formation of quadruple hydrogen bonds and the deshielding effects of the aromatic rings led to downfield shifts of the protons. This unique phenomenon would need further investigation. Because of the complicated picture of self-assembly, no apparent association constant was provided.

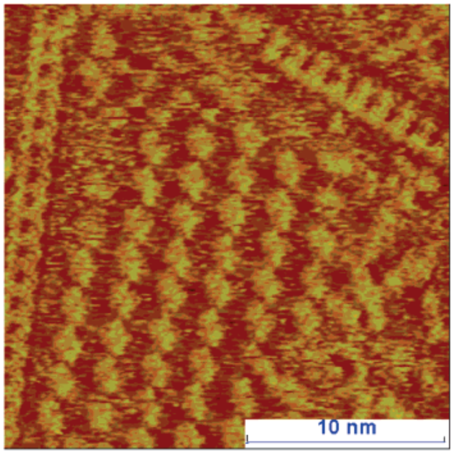

Figure 4. STM image of **5** on HOPG, showing homodimer structure and zipperlike polymeric structure.

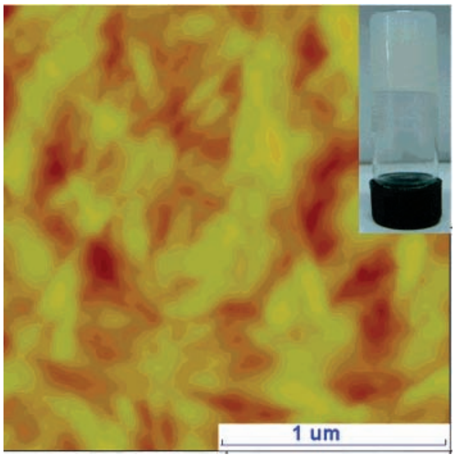

Figure 5. AFM image of a gel formed from **6** in CH_2Cl_2/hexane, ca. 2% (w/w), with digital photography of the gel inserted.

resolved spectrum, while with increase of the concentration, the spectrum became unresolvable. Lowering the temperature also led to unresolvable spectra.[14] These all suggested a more complicated aggregation mode of **6** compared to those of **5**. Slow evaporation of a solution of **6** in CH_2Cl_2/hexane led to an opaque gel at a concentration of ca. 2% (w/w). An AFM image (Figure 5) on xerogel revealed fibrous structure. We proposed that the single molecule of **6** first self-assembled into a polymeric structure via hydrogen bonding, and then the polymeric structures entangled with each other to form a network. The nonpolar solvent was then immobilized mainly through van der Waals interactions.

In summary, we have presented a new hydrazidequinolinone-based quadruple hydrogen-bonded building block. NMR and STM studies showed that there exists a monomer–dimer–polymer equilibrium. Contrary to many heterocycle-based systems, no isomerization in our system was observed. While its acyclic analogue displayed a more complicated aggregation mode due to its conformational flexibility. It formed gel in dichloromethane/hexane at a concentration of 2% (*w/w*). We believe that the new building block we presented here can find wide applications in the development of new self-assemblies, material science, and construction of various nanostructures.

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Supporting Information Available: Experimental procedure, characterization data, NMR spectra for new compounds; VT and dilution ^1H NMR spectra; ESI-MS of **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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