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Solid State Structures of Amide-Substituted 8-Hydroxyquinoline Derivatives

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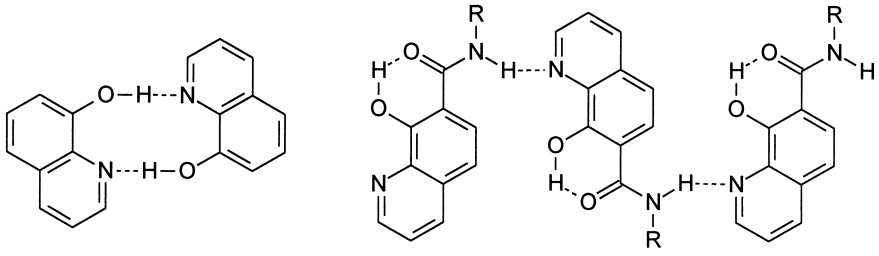
Abstract—The amide substituted 8-hydroxyquinoline derivatives **3** and **4** form, in the solid state, hydrogen bonded polymers. Polymeric **3** adopts a helical conformation while **4** forms a double-stranded ladder-type structure. © 2000 Elsevier Science Ltd. All rights reserved.

Introduction

Hydrogen bonding interactions play a crucial role in natural and non-natural molecular recognition processes. Therefore the study of the structures of simple hydrogen bonded systems or hydrogen bonded networks seems to be important for an understanding of the influence of this non-covalent interaction on the resulting structures of the supramolecular aggregates. Unfortunately, up to now, no predictions can be made on the solid state superstructures of non-covalently linked molecules. However, systematic investigation of different derivatives should lead to a better understanding of, for example, the influence of hydrogen bonding interactions on different processes.[1]

Just recently we described a number of alkyl-bridged bis(8-hydroxyquinoline) derivatives which in the solid state form polymeric chains using 8-hydroxyquinoline as a self-complementary moiety, which is able to dimerize and connect the monomeric units (as shown for **1**). With the alkyl-bridged derivatives two types of polymer structures were obtained. Hereby the structures depend on the chain length of the spacer leading in the case of an odd number of carbon atoms in the chain to a zigzag structure, while an even number results in a 'doubly wound' structure.[2,3]

Based on those results we started to investigate 8-hydroxyquinoline derivatives like **2** in which amide substituents are introduced to act as additional hydrogen bond donor/acceptor units (Scheme 1).[3]



1 **2**

Scheme 1.

In the amide-substituted derivative **2** a hydrogen bond donor/acceptor is attached as a substituent which leads to intramolecular hydrogen bonding and suppresses the formation of ten-membered rings as observed for **1**. A polymer is obtained which is connected by only one intermolecular hydrogen bond between the amide NH and the aromatic nitrogen atom of **2**.[3]

Keywords: hydrogen bonds; 8-hydroxyquinoline derivative; solid state structure.

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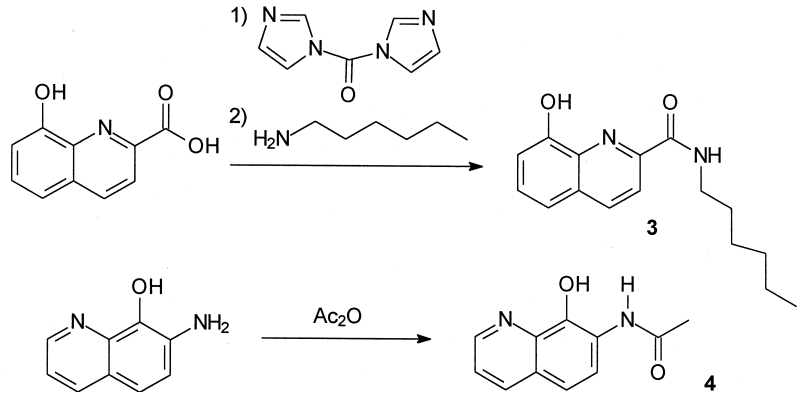

Scheme 2.

Results and Discussion

To do further investigations on the influence of amide substituents on the solid state superstructure of amide-substituted 8-hydroxyquinoline derivatives, we synthesized the compounds **3** and **4** and determined their solid state structures (Scheme 2).

In derivative **3** the carbon atom of the amide is connected to the 2-position of the quinoline. The compound is obtained in 63% yield by successive reaction of 8-hydroxyquinoline 2-carboxylic acid with carbonyl diimidazole and *n*-hexylamine.[4] X-Ray quality crystals of **3** were obtained from ether/hexane (Fig. 1).

Compound **4** with the amide N-atom attached to the 7-position of the quinoline is prepared in 93% yield from 7-amino-8-hydroxyquinoline as was described by

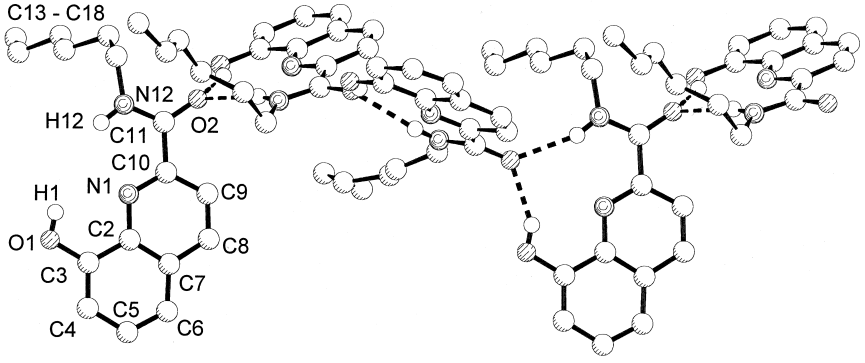

Figure 1. The polymeric structure of **3** formed in the solid state. Intermolecular hydrogen bonding distances: O2–O1A=2.747 Å, O2A–O1B=2.786 Å, O2B–O1′=2.803 Å; O2–N12A=2.928 Å, O2A–N12B=2.989 Å, O2B–N12′=3.068 Å.

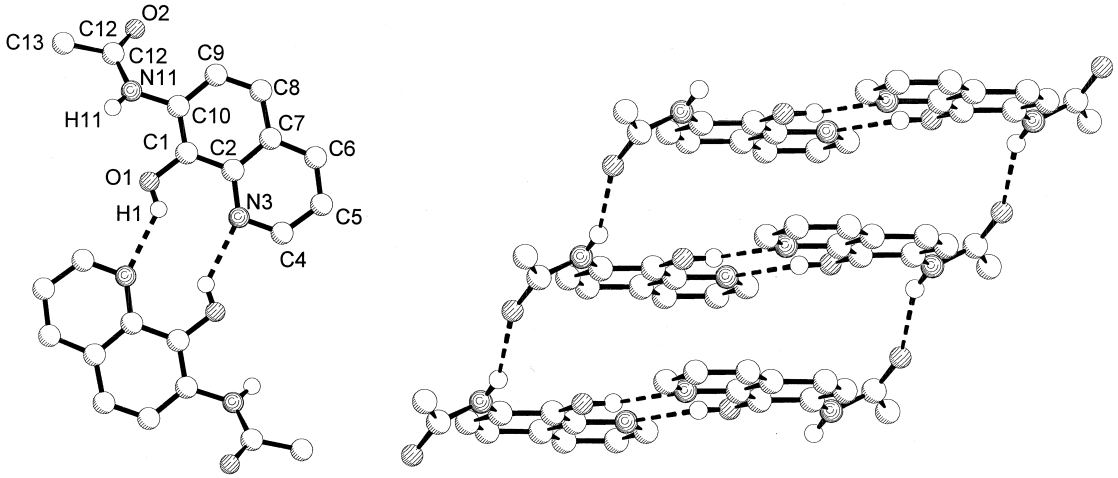

Figure 2. The structure of **4** in the solid state. Left: representation of the dimer which is formed from two molecules **4** by dimerization of the self-complementary 8-hydroxyquinoline units; right: the polymeric anti-parallel double strand. Intermolecular hydrogen bonding distances: O1–N3′=2.818 Å, O2–N11′=2.921 Å.

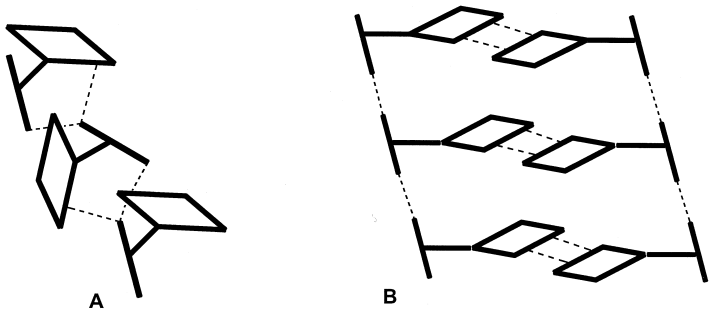

Figure 3.

Matsumura in 1927.[5] X-Ray quality crystals of **4** were obtained from methanol (Fig. 2).[6]

Compound **3** crystallizes in the triclinic space group *P*-1. In the solid state, **3** forms a polymeric chain by hydrogen bridging. In contrast to **1** or **2**, the OH and NH hydrogen donors of one monomer both bind to the carbonyl oxygen atom of the next one. The aromatic nitrogen atom does not participate in hydrogen bonding interactions. Neighboring 8-hydroxyquinoline units in the strand are twisted by approximately 120° leading to a repeating unit of three independent molecules of **3**, which form a helical polymer.

Compound **4** crystallizes in the space group $P2_1/n$. Two self-complementary hydroxyquinoline units dimerize by formation of a ten-membered hydrogen bonded ring. The corresponding dimer of **1** adopts a folded structure[2] while in the case of **4** a planar arrangement of the two hydroxyquinoline units is observed. This is due to hydrogen bonding between the amide substituents, leading to a double stranded ladder-type polymer in the solid state.

Therefore the polymeric structure is related to linear double-stranded PNA[7] or pyranosyl-RNA.[8] The 8-hydroxyquinoline units act as self-complementary bases which dimerize and which are attached to two linear hydrogen bond connected polymeric backbones. The orientation of the two strands is anti-parallel.

In this manuscript we described the two amide-substituted 8-hydroxyquinoline derivatives **3** and **4** which in the solid state form hydrogen bonded polymers. Hereby compound **3** adopts a single-stranded helical structure as is schematically depicted in Fig. 3 **A**. Compound **4** on the other hand forms a double-stranded ladder-type system **B**, which is similar to the structure of double-stranded PNA or *p*-RNA. The observation of two different structures for **3** or **4** in the solid state shows that there is still a long way to go to understand the factors which control the preferred formation of one hydrogen bonding interaction over another.

At the moment we are trying to crystallize further amide-substituted 8-hydroxyquinolines and bis(8-hydroxyquinoline)s to study their structure and to investigate the hydrogen bonded networks. Hopefully in the future those studies will allow us to use hydrogen bond donor/acceptor molecules like **2**–**4** as building blocks for rationally designed superstructures in the solid state.

Experimental

General remarks

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX 500, AM 400, or WM 250 NMR spectrometer using DEPT techniques for the assignment of the multiplicity of carbon atoms. FT-IR spectra were recorded by diffuse reflection (KBr) on a Bruker IFS spectrometer. Mass spectra (EI, 70 eV) were measured on a Finnigan MAT 90 mass spectrometer. Elemental analyses were obtained with a Heraeus CHNO-Rapid analyzer. Solvents were purified by standard methods. Melting points: Büchi 535 (uncorrected). 8-Hydroxyquinoline-2-carboxylic acid was purchased from Fluka.

2-(*N*-*n*-Hexylcarboxamide)-8-hydroxyquinoline (3). 8-Hydroxyquinoline-2-carboxylic acid (300 mg, 1.59 mmol) and carbonyl diimidazole (284 mg, 1.75 mmol) in chloroform were refluxed for 1.5 h under Ar. A solution of *n*-hexylamine (161 mg, 1.59 mmol) in 2 ml of chloroform was added and the mixture refluxed for additional 2 days. After cooling to room temperature the organic phase was washed with water, dried ($MgSO_4$) and the solvent removed in vacuum. After column chromatography (silica gel, CH_2Cl_2) **3** was obtained in 63% yield (270 mg) as a white solid. Mp 82°C. ^{1}H NMR ($CDCl_3$): δ=8.48 (t, J=7.2 Hz, 1H), 8.38 (s, 1H), 8.35 (d, J=8.5 Hz, 1H), 8.26 (d, J=8.5 Hz, 1H), 7.51 (pseudo-t, J=8.0 Hz, 1H), 7.36 (dd, J=8.8, 0.9 Hz, 1H), 7.21 (dd, J=8.0, 0.9 Hz, 1H), 3.48 (pseudo-q, J=7.2 Hz, 2H), 1.59 (m, 2H), 1.29 (m, 2H), 1.23–1.17 (m, 4H), 0.80 (m, 3H). ^{13}C NMR ($CDCl_3$): δ=164.4 (C), 152.4 (C), 148.1 (C), 137.8 (CH), 136.6 (C), 129.7 (CH), 129.3 (C), 119.8 (CH), 118.2 (CH), 111.3 (CH), 39.9 (CH_2), 31.5 (CH_2), 29.7 (CH_2), 26.7 (CH_2), 22.5 (CH_2), 14.0 (CH_3). IR: $\tilde{\nu}$=3285, 2954, 2928, 2857, 1651, 1587, 1545, 1504, 1468, 1392, 1359, 1331, 1304, 1231, 1192, 1163, 1089, 1048, 854, 757, 725, 645 cm^{-1}. MS: m/z=272 (79%) [M^+], 145 (100%). HRMS calcd for $C_{16}H_{20}N_2O_2$: 272.1525; found: 272.1515. Elemental analysis calcd for $C_{16}H_{20}N_2O_2$: C 70.56, H 7.40, N 10.29; found: C 70.66, H 7.40, N 10.27.

X-Ray structural analysis of **3**: $C_{16}H_{20}N_2O_2$, M=272.34, space group *P*-1, a=14.3574(2), b=15.1932(2), c=23.1587(4) Å, α=92.897(1), β=90.228(1), γ=115.590(1), V=4548.49(12) Å^3, μ(MoK_α)=0.079 mm^{-1}, Z=12, D_c=1.193 g cm^{-3}, F(000)=1752, T=173(2) K. 81 984 collected reflections, 21 004 unique reflections [12 525

$I>2\sigma(I)$] were used for refinement. R=0.0994, wR^2=0.2335 [$I>2\sigma(I)$], R=0.1622, wR^2=0.2749 (all data) for 1075 parameters. The full details have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-133179.

7-Amino-8-hydroxyquinoline. 7-Amino-8-hydroxyquinoline was prepared in a 3 step procedure starting from 8-hydroxyquinoline-5-sulfuric acid as described in the literature.[9]

7-Acetamido-8-hydroxyquinoline (4).[5] 7-Amino-8-hydroxyquinoline (102 mg, 0.638 mmol) was dissolved in 2 ml of dichloromethane and acetic anhydride (65 mg, 0.638 mmol) was added. After 1 h at room temperature, the mixture was washed with saturated aquous $NaHCO_3$, dried ($MgSO_4$) and the solvent removed in vacuum to obtain **4** in 93% yield (117 mg) as a yellow-brown solid. Mp 180°C (lit. 177°C)[5]. ^{1}H NMR ($CDCl_3$): δ=8.72 (dd, J=3.5, 1.1 Hz, 1H), 8.58 (d, J=9.0 Hz, 1H), 8.11 (dd, J=8.3, 1.1 Hz, 1H), 7.91 (br, 1H), 7.35 (d, J=9.0 Hz, 1H), 7.33 (m, 1H), 2.28 (s, 3H). ^{13}C NMR ($CDCl_3$): δ=168.7 (C), 148.3 (CH), 139.5 (C), 137.6 (C), 136.4 (CH), 125.1 (C), 123.6 (C), 121.4 (CH), 120.4 (CH), 118.0 (CH), 24.8 (CH_3). MS: m/z=202 (36%) [M^+], 160 (100%). HRMS calcd for $C_{11}H_{10}N_2O_2$: 202.0742, found: 202.0757. Elemental analysis calcd for $C_{11}H_{10}N_2O_2$: C 65.34, H 4.98, N 13.85; C 65.29, H 5.24, N 13.50.

X-Ray structural analysis of **4**: $C_{11}H_{10}N_2O_2$, M=202.21, space group $P2_1/n$, a=10.4299(5), b=4.8145(3), c =19.0451(9) Å, α=99.971(4), V=941.90(9) Å^3, $\mu(MoK_\alpha)$ =0.101 mm^{-1}, Z=4, D_c=1.426 g cm^{-3}, $F(000)$=424, T=173(2) K. 11 314 collected reflections, 2203 unique reflections [1746 $I>2\sigma(I)$] were used for refinement. R=0.0473, wR^2=0.1045 [$I>2\sigma(I)$], R=0.0649, wR^2=0.1140 (all data) for 138 parameters. The full details have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-133180.

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