

Control of Molecular Self-Assembly by Hydrogen-Bonding and Aromatic Interactions: Formation of Discrete Cyclic Tetrameric Aggregates

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Abstract: Four molecules of 3-phenyl-4-pyridin-4'-yl-3-buten-2-on-oxime **1** form discrete cyclic aggregates stabilized by a network of 8 hydrogen bonds and stacking interactions. © 1999 Elsevier Science Ltd. All rights reserved.

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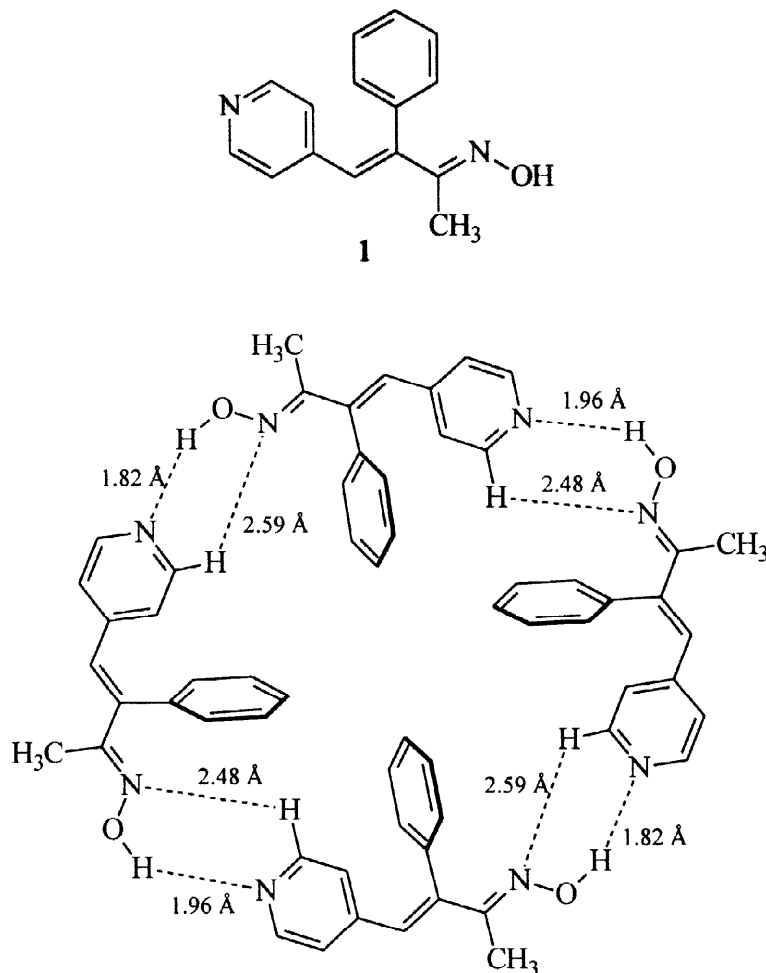
Development of strategies for controlling molecular aggregation is a contemporary challenge in organic chemistry. A current biomimetic strategy, which can be considered as an alternative to covalent synthesis and may provide well-defined aggregates including three or more components (structures with nanometer dimensions¹⁻³), relies on the programmed self-assembly of smaller subunits through hydrogen bonding and other non-covalent interactions.⁴ Within this context the formation of discrete supramolecular ring-shaped aggregates is of particular interest, among other things, owing to their potential host properties. Only a few examples of discrete hydrogen-bonded assemblies in the solid state and /or solution, including 3-6 subunits, can be found in the literature.⁵⁻¹⁰

Here, an interesting cyclic self-assembly of the molecules of 3-phenyl-4-pyridin-4'-yl-3-buten-2-on-oxime **1** is described (Scheme 1). 3-Phenyl-4-pyridin-4'-yl-3-buten-2-on-oxime **1** was obtained in 85 % overall yield by oximation of 3-phenyl-4-pyridin-4'-yl-3-buten-2-one, the latter being prepared by condensation of pyridine-4-carbaldehyde with 1-phenyl-2-propanone.

Four molecules of **1** form a discrete cyclic aggregate stabilized by a network of 8 hydrogen bonds and stacking interactions in the solid state, as shown by X-ray crystallography (Scheme 1).

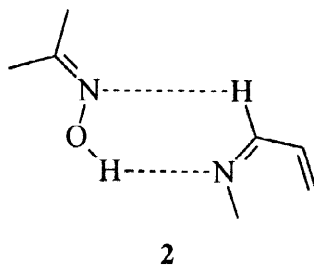
A single molecule of 3-phenyl-4-pyridin-4'-yl-3-buten-2-on-oxime has three potential proton acceptor atoms (pyridine-N, hydroxy-O and imine-N) and two proton donors (OH and aromatic CH groups, which can act as weak hydrogen bond donors) available for hydrogen bonding to neighbouring molecules. The CH groups that are adjacent to nitrogen atoms are particularly likely to participate in short C-H \cdots O or C-H \cdots N interactions.¹¹ The X-ray crystallographic analysis of a single crystal of **1**, obtained by slow evaporation of the solvent from ethanol solutions, established that all proton acceptors and donors, except

hydroxy-O, are used in the hydrogen bonding pattern. Compound **1** crystallizes in space group $P2_1/c$ with two independent molecules in the asymmetric unit.



Scheme 1. Structure of **1** and the schematic structure of the tetrameric aggregate of **1**.

The crystal structure of 3-phenyl-4-pyridin-4'-yl-3-buten-2-one oxime shows an arrangement in which each molecule forms four hydrogen bonds to two neighbouring residues (Figure 1). The resulting tetrameric structure leads to cavities with an inner diameter of about 11 Å, each established by four oxime molecules and filled by four phenyl groups. The backbone of the tetramer is constructed from four intermolecular O-H \cdots N and four weaker C-H \cdots N hydrogen bonds. Each of the four pairs of O-H \cdots N and C-H \cdots N contacts displays the structural motif **2** with bidentate hydrogen bonds.



The O-H \cdots N and C-H \cdots N distances in two pairs of hydrogen bonds on opposite sides of the tetramer are 1.82 Å (O-H \cdots N angle, 159°) and 2.59 Å (C-H \cdots N angle, 120°), respectively, and the O-H \cdots N and C-H \cdots N distances in the two remaining opposite pairs of hydrogen bonds are 1.96 Å (O-H \cdots N angle, 146°) and 2.48 Å (C-H \cdots N angle, 120°; Scheme 1). In both types of C-H \cdots N interactions the distance between the proton and the acceptor atom is shorter than the sum of their van der Waals radii (2.75 Å).¹²

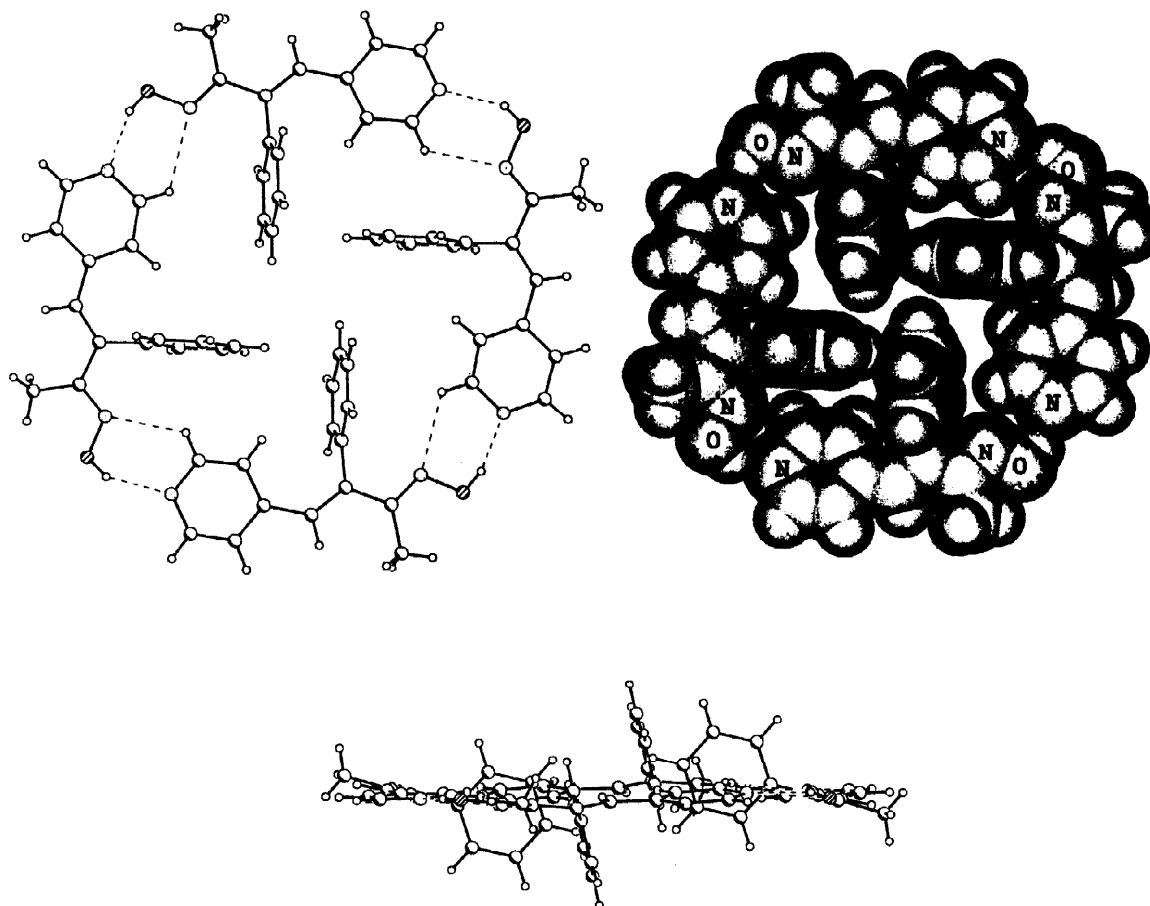


Figure 1. The tetragonal motif of **1** in the crystal (top and side view).

The pyridine and the phenyl rings of the neighbouring molecules show the edge-to-face orientations in which H atoms on the pyridine ring interact with negatively charged regions on the phenyl residue. The distances of pyridine H-6 atoms (atom numbering in Figure 2) to the center of the phenyl rings of the neighbouring molecules are alternating by 2.76 and 3.36 Å (the interplanar angles between pyridine and phenyl rings of the neighbouring molecules are alternating 76° and 79°).

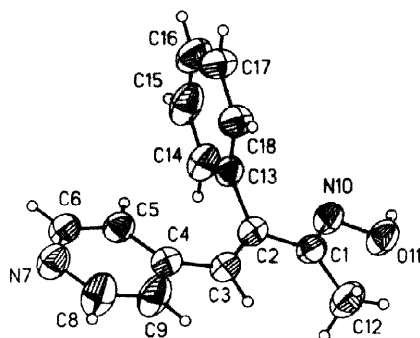


Figure 2. ORTEP drawing of **1** showing the monomeric unit.

The methyl groups are located on the outside of the cavities. Figure 3 shows the stacking of supramolecular discrete aggregates in the crystal.

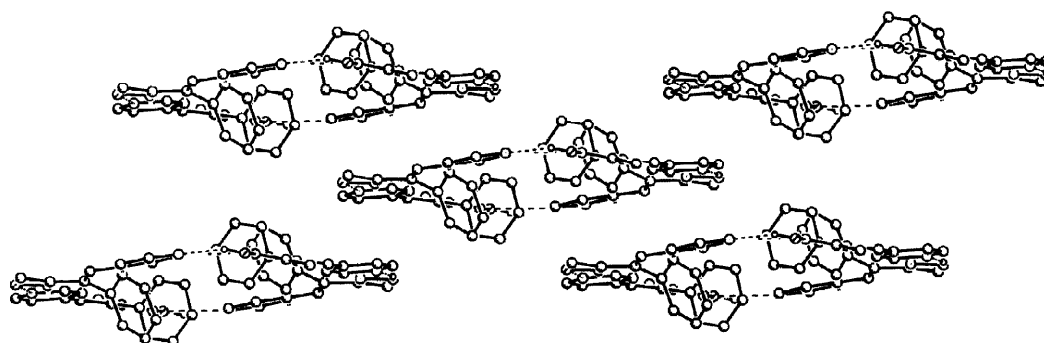


Figure 3. Packing of the supramolecular ring-shaped structures.

The formation of discrete cyclic aggregates of **1** is an example for control of molecular self-assembly by both hydrogen bonding and aromatic interaction. Presently the aggregation behaviour of a variety derivatives of **1** are under investigation.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were recorded on Bruker DRX 500 spectrometer; chemical shifts are reported in ppm downfield from TMS as internal standard (solvent CDCl_3). Mass spectra were measured with a Fisons VG Prospec 3000 and a Hewlett Packard HP 5971A MSD spectrometer. IR spectrum were obtained with a Perkin-Elmer FT-IR 1600 spectrometer. UV spectrum were measured using a SPECORD M-40 spectrophotometer. Analytical TLC were carried out on Merck Kieselgel 60 F_{254} plates employing a benzene-ethyl acetate mixture 3:1 (v/v) as the mobile phase.

Synthesis of 3-Phenyl-4-pyridin-4'-yl-3-buten-2-on-oxime (1): The mixture of pyridine-4-carbaldehyde (5.35 g, 0.05 mol) and 1-phenyl-2-propanone (13.4 g, 0.1 mol) in chloroform (200 ml) was saturated with gaseous hydrogen chloride (0.1 mol). The reaction mixture was kept at 25 °C for 48 hours. Chloroform was evaporated, and the residue was washed several times with diethyl ether and then dried under vacuum. The crude 3-phenyl-4-pyridin-4'-yl-3-buten-2-one hydrochloride was obtained as a yellowish powder and used for the oximation reaction without further purification. A mixture of 3-phenyl-4-pyridin-4'-yl-3-buten-2-one hydrochloride (0.05 mol), hydroxylamine hydrochloride (0.15 mol), and sodium hydroxide (0.1 mol) in ethanol (200 ml) was refluxed for 4h and then poured into water (250 ml). Ethanol was evaporated and the water solution was extracted several times with chloroform. After the chloroform separation the residual product was crystallized from ethanol. The product was obtained as white crystals. Yield 85%. M.p. 172-174°C. ¹H NMR (500 MHz): between 2.01 and 2.10 concentration dependent (s, 3H, CH₃), 6.67 (d, 2H_{Arom}, J = 6.30 Hz), 6.75 (s, 1H, CH), 7.02-7.04 (m, 2H_{Arom}), 7.27-7.29 (m, 3H_{Arom}), 8.22 (d, 2H_{Arom}, J = 6.30 Hz), between 7.30 and 10.01 concentration dependent (s, 1H, NOH). ¹³C NMR (125 MHz): 158.35 (C=N), 149.68, 144.36, 137.06, 129.79, 129.22, 128.46, 128.22, 124.39, 11.61 (CH₃). IR (KBr): 3258, 3147, 3026, 2826, 1597, 1543, 1488, 1442, 1419, 1360, 1278, 1224, 1205, 1172, 995, 886 cm⁻¹. MS m/z (rel.int.%): 238 (M⁺, 59), 237 (92), 221 (100), 206 (12), 195 (13), 180 (27), 167 (11), 160 (10), 152 (27), 144 (21), 127 (9), 91 (10), 77 (17), 51 (20), 43 (27). UV (methanol), λ_{max} (ε × 10⁻³): 227 (23.6), 294 (26.4). HRMS: calcd. for C₁₅H₁₄N₂O 238.1106, found 238.1108. Elemental analysis: C 75.49, H 5.91, N 11.78 calcd. C 75.63, H 5.88, N 11.76. R_f 0.13.

X-Ray crystallographic analysis

Formula C₁₅H₁₄N₂O, M = 238.28, monoclinic, space group *P*2₁/*c*, a = 10.04010(10), b = 9.76230(10), c = 26.4632(4) Å, β = 93.7980(10)°, V = 2588.08(5) Å³, Z = 8, D_c = 1.223 gcm⁻³, μ = 0.078 mm⁻¹, 18213 reflections collected (full sphere, θ-range 2.47-25.70°), 4235 independent reflections (R_{merge} = 0.0331, empirical absorption correction), 3340 observed [F_o ≥ 4σ(F_o)], 325 parameters, R1 = 0.0543, wR2 = 0.1419, residual electron density 0.234 eÅ⁻³. The structure was solved using Direct Methods and refined on F² using SHELXTL (Vers.5.03). The data were obtained with a Siemens SMART-CCD three circle diffractometer (MoK_α-radiation, graphite-monochromator) at 293 K. All non-H atoms were anisotropically refined and aromatic and methyl H atoms were treated as riding groups with the 1.2 fold U-value (1.5 for methyl hydrogens) of the corresponding C-atoms, hydroxy hydrogen atoms were located in a difference Fourier map and then treated as riding atoms. The mentioned distances to H-atoms are based on normalized C-H distances (d_{C-H} = 1.08 Å). Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-104999. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223 336-033; e-mail: deposit@ccdc.cam.ac.uk).

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REFERENCES AND NOTES

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