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Synthesis, crystal structure and infrared spectra of new 6- and 7-propylamine-5,8-quinolinediones

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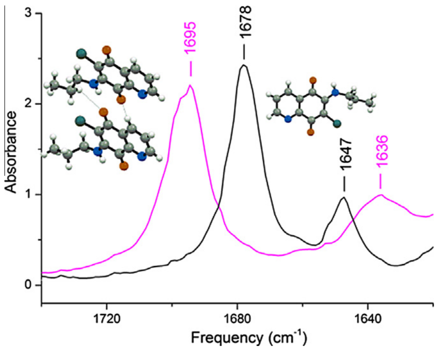
HIGHLIGHTS

- New propylamine-5,8-quinolinediones were synthesized and characterized by X-ray diffraction, IR and DFT methods.
- Crystal structures are stabilized mainly by N—H···O, C—H···O and C—H···N type hydrogen bonds.
- We report interesting correlation between frequency separation of carbonyl bands and position of substituents.

GRAPHICAL ABSTRACT



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ABSTRACT

We synthesized 6-chloro-7-propylamine-5,8-quinolinedione and 7-chloro-6-propylamine-5,8-quinolinedione and characterized these new compounds by X-ray diffraction and IR spectroscopy techniques supplemented by DFT calculations. Analyses were performed with the special attention to the structural changes caused by different positions of the propylamine chain in the studied 6- and 7-propylamine-5,8-quinolinediones. It was found that the title compounds differ significantly in crystal structures that strongly affects the formation of H-bonds. The detailed analysis of H-bonding in crystal structures of 6- and 7-substituents as well as in starting compound 6,7-dichloro-5,8-quinolinedione was performed. It was found that crystal structures were stabilized mainly by N—H···O, C—H···O and C—H···N type hydrogen bonds. For 7-substituted 5,8-quinolinedione a strong twist of the propylamine chain against rings' plane (near 90°) causing changes in formation of H-bonds was observed. The studied compounds were also analyzed due to their interesting carbonyl stretching bands in the infrared spectra. Considerable changes in the frequency separation of the carbonyl stretching bands for different positions of the propylamine chain were found. Correlation between frequency separation of the carbonyl bands and the nature and position of the 6- and 7-substituents may provide the opportunity to use the IR spectroscopy to study substitution reactions and regioisomerism in related compounds.

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Introduction

The 6,7-disubstituted-5,8-quinolinediones are an important class of compounds that have attracted increasing attention as a source of new compounds with wide spectrum of biological activities such as anticancer, antifungal, antimalarial [1–5]. The quinoline-5,8-dione is also the essential functional group in different quinone antitumor antibiotics, such as streptonigrin, streptonigron and lavendamycin. Unfortunately, their clinical use has been limited because of their toxicity and modest selectivity for cancer cell [1–7]. Over several decades the synthesis and biological activities of variously substituted quinolinediones have been reported. The majority of these reports deal with the chemistry and biological activities of the C-6 and/or C-7-substituted derivatives of 5,8-quinolinediones encompassing functionalities such as amino, hydroxyl or thiol groups and the regioselectivity in the reaction of 6,7-dichloro-5,8-quinolinedione with different nucleophiles [6–13]. However, the structure and function of many biologically active molecules are to a large degree determined by hydrogen bonding because it is sufficiently strong and directional [14].

The derivatives of 5,8-quinolinediones stimulated also great interest because of its carbonyl stretching bands in the infrared spectra. Among the different bands, the carbonyl stretching band is one of the most important and sensitive to morphology. Either one or two carbonyl absorption bands can be observed for para-quinones. The amount and frequency of carbonyl stretching bands can be influenced by plenty of intra- and intermolecular interactions and conformational changes. It can give a specific tool for some structural investigations. For example, analysis of carbonyl stretching bands and molecular simulations performed by Sun et al. for liquid crystalline polymer allowed them to determine the subtle chain conformational changes [15].

In the present study, we focus our work on structural properties of two new derivatives of 6,7-dichloro-5,8-quinolinedione (**1**), that is: 6-chloro-7-propylamine-5,8-quinolinedione (**2**) and 7-chloro-6-propylamine-5,8-quinolinedione (**3**) and report results of their structural studies performed using a monocrystal X-ray diffraction method and IR spectroscopy supplemented by the density functional theory (DFT) calculations.

The X-ray diffraction method provided comprehensive insights into crystal structure of investigated compounds. Therefore, it was not only possible to inspect the position of the quinoline ring substitution by propylamine chain, but also to investigate the formation of hydrogen bonds which are able to control and direct molecular structures.

Experimental

General techniques

Melting points were taken in open capillary tubes and are uncorrected. Mass spectra were recorded on a Finningan MAT 95 spectrometer at 70 eV. All ^{1}H and ^{13}C NMR spectra were measured with a Bruker 600 MLS spectrometer at 600 MHz for ^{1}H nuclei and 150 MHz for ^{13}C nuclei in deuterochloroform using trimethylsilane as an internal standard. All substances were purified on gravitational column chromatography using silica gel 60 (Merck, particles size mesh 40–63 μm).

Thin Layer Chromatography (TLC) analyses were performed employing Merck's aluminum plates using chloroform:ethanol (40:1) as an eluent. Others chemicals were purchased from Sigma–Aldrich, Acros Organics, POCH and Chempure.

Chemical synthesis

The starting compound, that is, 6,7-dichloro-5,8-quinolinedione (**1**) was synthesized following the procedure described by Urbanski and Krzyżanowski [16]. Mp. 220–221 °C, according to literature [16] mp. 220–222 °C.

Synthesis of (**2**) and (**3**) was performed using a mixture of (**1**) (100 mg, 0.441 mmol) and potassium carbonate (61 mg, 0.441 mmol) in dry tetrahydrofurane (THF) (1 ml). Next, the solution of propylamine (26 mg, 0.441 mmol) in dry THF (0.2 ml) was added and the reaction mixture was stirred for 4 h at room temperature. After that, the solvent was removed under reduced pressure.

The crude reaction mixture was separated by column chromatography using chloroform/ethanol (40:1) as an eluent. Finally, pure products 6-chloro-7-propylamine-5,8-quinolinedione (**2**) (78 mg, 71%) as a dark red solid and 7-chloro-6-propylamine-5,8-quinolinedione (**3**) (20 mg, 18%) as a red solid were obtained.

*6-Chloro-7-propylamine-5,8-quinolinedione (**2**)*

Mp. 135–136 °C. Mass spectrum (EI, 70 eV) m/z (rel. int.): = 250 [M]$^+$ (base peak), 221 (79), 215 (17), 208 (17), 194 (39), 173 (20), 158 (4), 137 (9), 116 (4), 102 (19), 77 (7). ^{1}H NMR ($CDCl_3$): $\delta = 1.03$ (t, $J = 7.8$ Hz, 3H, CH_3), 1.71–1.76 (m, 2H, CH_2), 3.85 (q, $J = 6.0$ Hz, $J = 8.4$ Hz, 2H, CH_2), 6.26 (s, 1H, NH), 7.66 (dd, $J = 4.8$ Hz, $J = 7.8$ Hz, 1H, H-3), 8.48 (dd, $J = 1.8$ Hz, $J = 7.8$ Hz, 1H, H-4), 8.92 (dd, $J = 1.8$ Hz, $J = 4.8$ Hz, 1H, H-2) ppm. ^{13}C {^{1}H}NMR ($CDCl_3$): $\delta = 11.05$ (CH_3), 24.31 (CH_2), 45.81 (CH_2), 128.39 (C-3, C-6), 129.99 (C-5a), 134.70 (C-4), 144.67 (C-7), 146.00 (C-8a), 153.35 (C-2), 175.62 (C-5), 178.91 (C-8) ppm. IR (KBr) $\nu = 3287$, 3078, 1695, 1636, 1515 cm^{-1}.

*7-Chloro-6-propylamine-5,8-quinolinedione (**3**)*

Mp. 134–135 °C. Mass spectrum (EI, 70 eV) *m/z* (rel. int.) = 250 [M]$^+$ (78), 221 (base peak), 215 (4), 209 (24), 194 (5), 173 (2), 157 (4), 137 (2), 116 (2), 102 (7), 77 (4). ^{1}H NMR ($CDCl_3$): $\delta = 1.03$ (t, $J = 7.2$ Hz, 3H, CH_3), 1.71–1.77 (m, 2H, CH_2), 3.85 (m, 2H, CH_2), 6.06 (s, 1H, NH), 7.58 (dd, $J = 4.2$ Hz, $J = 7.8$ Hz, 1H, H-3), 8.35 (dd, $J = 1.8$ Hz, $J = 7.8$ Hz, 1H, H-4), 9.01 (dd, $J = 1.8$ Hz, $J = 4.2$ Hz, 1H, H-2) ppm. ^{13}C {^{1}H}NMR ($CDCl_3$): $\delta = 11.06$ (CH_3), 24.26 (CH_2), 46.76 (CH_2), 126.43 (C-3, C-6), 126.73 (C-5a), 134.62 (C-4), 148.56 (C-7, C-8a), 155.28 (C-2), 180.16 (C-5, C-8) ppm. IR (KBr) $\nu = 3226$, 3190, 3025, 1678, 1647, 1515 cm^{-1}.

X-ray diffraction

The single crystal X-ray experiments were performed for all samples at 100.0(1) K. For each measurement a good quality single crystal was preselected under a polarization microscope. For the compound (**1**) a white single crystal of dimensions $0.08 \times 0.1 \times 0.6$ mm^3 was selected for analysis, while red crystals of dimensions $0.04 \times 0.2 \times 0.52$ mm^3 and $0.09 \times 0.27 \times 0.28$ mm^3 were selected for the compounds (**2**) and (**3**), respectively. The crystals were mounted on a glass capillary and cooled down by a cold, dry nitrogen gas stream using a Cryostream Cooler (Oxford Cryosystems Ltd., Oxford, UK). The data were collected using an Oxford Diffraction kappa diffractometer with a Sapphire3 CCD detector (Oxford Diffraction Ltd., Yarnton, UK). For the integration of the collected data the CrysAlis RED software (versions 1.171.32.29, Agilent Technologies) was used.

The solving and refining procedures were similar for all three compounds. The structures were solved using direct methods with the SHELXS97 software and then the solutions were refined using SHELXL97 program [17]. The aromatic hydrogen atoms were treated as "riding" on their parent carbon atoms with d(C—H) = 0.95 Å and assigned isotropic atomic displacement parameters equal to