

Spectroscopic and structural study of novel 8-aminoquinoline derivative embedded in nematic host

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Abstract We have reported a novel derivative of 8-aminoquinoline, which represents ester-amide of squaric acid ethyl ester (**1**). The novel derivative was characterized by both the conventional and linear polarized IR-spectroscopy of oriented colloid suspensions in nematic host, UV-spectroscopy, $^1\text{H-NMR}$ and mass spectrometry. The correlation between the structure and spectroscopic properties was estimated by using the known crystallographic data of the compound studied.

Keywords Ester amide of squaric acid ethyl ester of 8-aminoquinoline · Structure · IR-LD and UV-spectroscopy · $^1\text{H-NMR}$ · HPLC ESI MS/MS

Introduction

Aminopyridines and aminoquinolines are bioactive aromatic *N*-heterocyclic tertiary amines, which are known to increase the strength of nerve signals [1] by inhibition of the voltage-dependent K^+ -channels [2]. On the other hand, the biological activities of ester-amides of some squaric acid derivatives have also been studied [3–8]. Here, our work, associated with spectroscopic and structural elucidation of a novel ester-amide, derived from diethyl squarate and 8-aminoquinoline (**1**) is presented, suggesting that the combination of two fragments with inherent biological activity could “tune” the known biological action of such novel derivatives. The synthesized compound is studied in

both the solution and solid state, and is characterized by employing conventional and linear polarized IR-spectroscopy of solids, oriented as colloid suspensions in nematic host as well as by $^1\text{H-NMR}$, positive ESI mass spectrometry (MS) and UV-spectroscopy. The spectroscopic results obtained are compared with the available crystallographic data of the compound studied [9], which have been extracted from the CCDC database (CCDC 715957).

Experimental

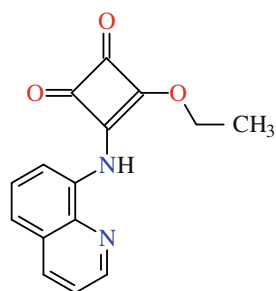
Materials and methods

Conventional and polarized IR-spectra were measured on a Thermo Nicolet 6700 FTIR-spectrometer (4,000–400 cm^{-1} , 2 cm^{-1} resolution, 200 scans), equipped with a Specac wire-grid polarizer. Non-polarized solid-state IR spectra were recorded, using the KBr disk technique. The oriented samples were obtained as colloid suspensions in a nematic liquid crystal ZLI 1695. The theoretical approach, the experimental technique for preparation of samples, the procedures for polarized IR-spectra interpretation, and the validation of the linear-dichroic infrared (IR-LD) solid-state orientation method with respect to its accuracy and precision have already been reported elsewhere [10–13]. For biologically active systems, the method has been applied for the study of some amino acid derivatives, small peptides, alkaloids, etc. [14–18].

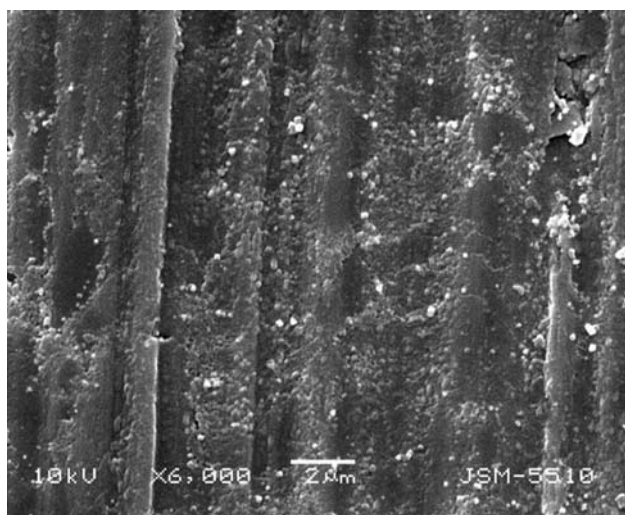
The application of colloid suspensions in nematic liquid crystal host contribute to the facile IR-spectroscopic and structural elucidation of embedded solid particles. Such an approach was demonstrated in a series of papers, dealing with the characterization of inorganic compounds and glasses and, also, organic and coordination compounds. It

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Scheme 1 Chemical diagram of the compound studied (**1**)



was found, that a partial orientation (15–20%) of suspended particles (Scheme 2), which was adequate for recording reasonable linearly polarized IR-spectra could be achieved. The procedure was conducted as 5 ± 1 wt% from a given solid compound of average particle size within 0.3–0.9 μm were mixed with nematic liquid crystal substance (ZLI 1695, ZLI 1538 or MLC 6815), which was appropriate for IR spectroscopy studies [14–18]. The resulting slightly viscous suspension was then phase-pressed between two KBr-plates. Their surface was processed by subsequent “rubbing” in one direction with fine sandpaper (C800, size 5 μm) before use. Both the KBr-plates and the pressed suspension were then processed by 100-times-repeated mutual “skidding”, with the average velocity of 3 $\mu\text{m}/\text{s}$. The optimum cell thickness was 100 μm . The validation of the orientation solid-state method for accuracy and precision, the influence of the liquid crystal medium on peaks positions and integral absorbencies of the bands of the guest molecule were given. Moreover, the rheological model, the nature, and the balance of forces, acting on the nematic liquid crystal suspension system as well as the mathematical model, and morphology of the suspended particles were also discussed.



Scheme 2 Electron microscopic data of the colloid suspension in nematic host [19], showing the orientation of particles towards the main director of the nematic host

The *positive ESI mass spectra* were recorded on *Fisons VG autospect instrument*, employing 3-nitrobenzylalcohol (*Sigma-Aldrich*) as a matrix.

Ultraviolet (UV-) spectra were recorded on *Tecan Safire Absorbance/Fluorescence XFluor 4 V 4.40 spectrophotometer*, operating between 190 and 900 nm with ethanol (*Uvasol, Merck*) as solvent 1 with concentration of 1.10^{-5} M by employing 0.0921 cm quartz cells.

The *thermal analyses* were performed within the 300–500 K temperature region on a *Differential Scanning Calorimeter Perkin-Elmer DSC-7*, and a *Differential Thermal Analyzer DTA/TG (Seiko Instrument, model TG/DTA 300)*. The experiments were conducted at the scanning rate of 10 K/min under argon atmosphere.

The *elemental analyses* were carried out, according to the standard procedure for determination of C and H (as CO_2 , and H_2O), and N (*Dumas method*).

Synthesis

The novel compound, 8-aminoquinoline ester-amide of squaric acid ethyl ester (**1**) was synthesized, according to the following general procedure: Equimolar amounts of 8-aminoquinoline (0.1442 g) and diethyl squarate (1 mmol), dissolved in 20 mL ethanol (95%) were mixed by continuous stirring at room temperature for 30 h. As a result, a yellow precipitate was formed. The latter was then filtered, washed with ethanol and dried with P_2O_5 at 25 $^\circ\text{C}$. (Found: C, 67.20; H, 4.51; N, 10.44; [$\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_3$]; Calcd.: C, 67.18; H, 4.51; N, 10.44%). The TG and DSC data of (**1**) within the temperature range of 300–500 K showed the absence of any solvent molecules, included in both compounds. This synthetic method was first published previously [20].

Results and discussion

The crystal structure of (**1**) belongs to the monoclinic space group P21/n (Fig. 1), and consists of four discrete molecules of 8-aminoquinoline ester-amide of squaric acid ethyl ester in a unit cell (Fig. 1). The squaric acid fragment is almost planar, with some small deviation of $0.1(2)^\circ$. The quinoline fragment is also almost co-planar with respect to the discussed squaric acid moiety (deviation of $0.1(1)^\circ$). This points to a co-linear orientation of the transition moments, corresponding to the out-of-plane (o.p.) bending vibrations of these structural fragments. Within the frame of the unit cell, the four molecules are mutually oriented by pairs, closing an angle of $75.1(7)^\circ$ (Fig. 1). The bond lengths and angles obtained for the squaric acid fragment for the compound studied are similar to those of other ester-amides, reported previously [16, 21–31].

Fig. 1 Structure of (**1**), according to CCDC and unit cell content

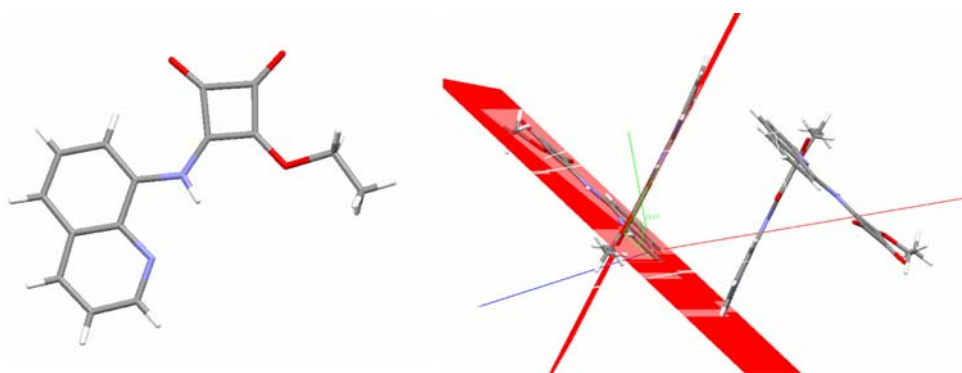
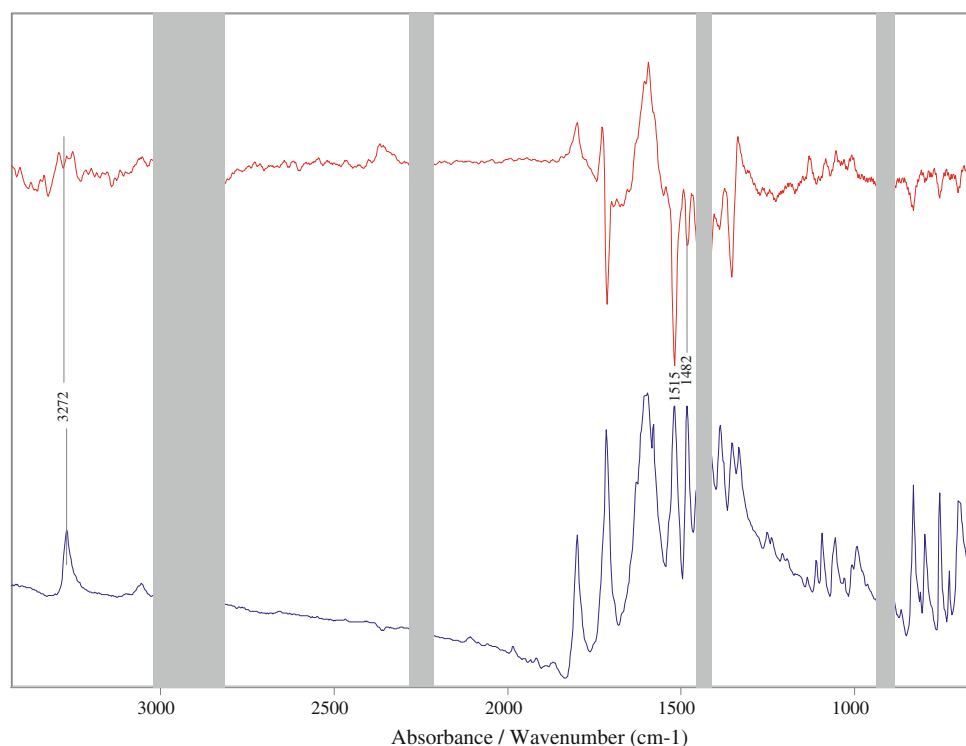


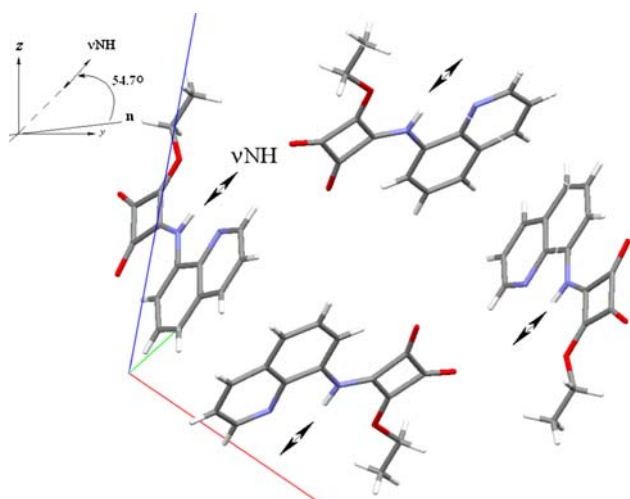
Fig. 2 Non-polarized IR-(1) and difference IR-LD (2) spectra of (**1**) oriented as suspension in nematic host. In grey boxes are given the area of self absorption of the nematic host



The non polarized IR- and differential IR-LD spectra of (**1**) are shown on Fig. 2. The strong band at $3,272\text{ cm}^{-1}$, corresponded to ν_{NH} -stretching vibration. Other strong bands within $1,800\text{--}1,600\text{ cm}^{-1}$ (more particularly, at $1,799$, $1,713$ and $1,600\text{ cm}^{-1}$) corresponded to $\nu_{\text{C}=\text{O}}^{\text{s}}$, $\nu_{\text{C}=\text{O}}^{\text{as}}$ and $\nu_{\text{C}=\text{C}}$ stretching vibrations of the squaric acid fragment. These bands overlapped the in-plane (i.p.) stretching vibrations of quinoline fragments, commonly observed at, approximately, $1,600\text{ cm}^{-1}$. The data were in accordance with those of other heterocyclic compounds, reported previously [32–37]. The differential IR-LD spectrum of (**1**) was characterized by elimination of the band, corresponding to ν_{NH} , which suggested an orientation of the suspended chemical, as shown in Scheme 3. Within the frame of the crystal structure, the transition moments, corresponding to ν_{NH} of all of the four molecules were

co-linearly oriented, and the resulting direction was also depicted in Scheme 3. The elimination of the discussed IR-band suggests that the angle between the orientation director (\mathbf{n}) and the transition moment of the resulting ν_{NH} -stretching vibration was close to 54.7° , which was in accordance with the theory [13]. The i.p. bands at $1,515$ and $1,482\text{ cm}^{-1}$ were found to be oriented negatively. This was valid for the o.p. modes at, approximately, 831 , 754 (quinoline fragment), and 694 cm^{-1} (squaric acid fragment), respectively. The latter bands were eliminated at equal dichroic ratio, which proved their origin as o.p. modes.

The UV-spectra of (**1**), depicted on Fig. 3 were characterized with a band at 255 , 275 nm ($\epsilon = 10,000\text{ L mol}^{-1}\text{ cm}^{-1}$), corresponding to the $\pi \rightarrow \pi^*$ transitions in aminoquinoline fragment. The bands at 317 and 341 nm



Scheme 3 Orientation of the resulting transition moment of ν_{NH} stretching vibration and the orientation director (\mathbf{n}) of the liquid crystal

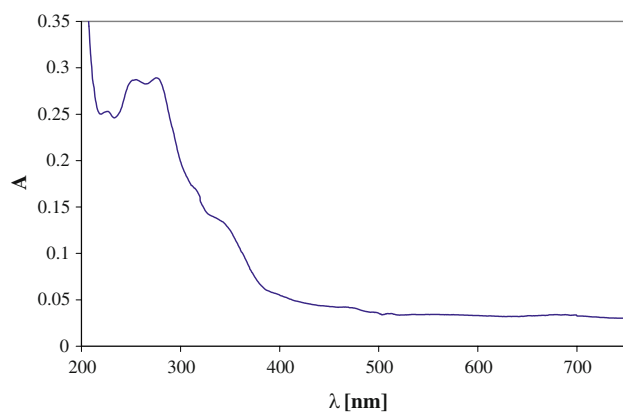


Fig. 3 UV-spectrum of (1) in ethanol at concentration $1 \cdot 10^{-5}$ M and 0.0921 cm quartz cells

Fig. 4 ESI-MS spectrum of compound (1)

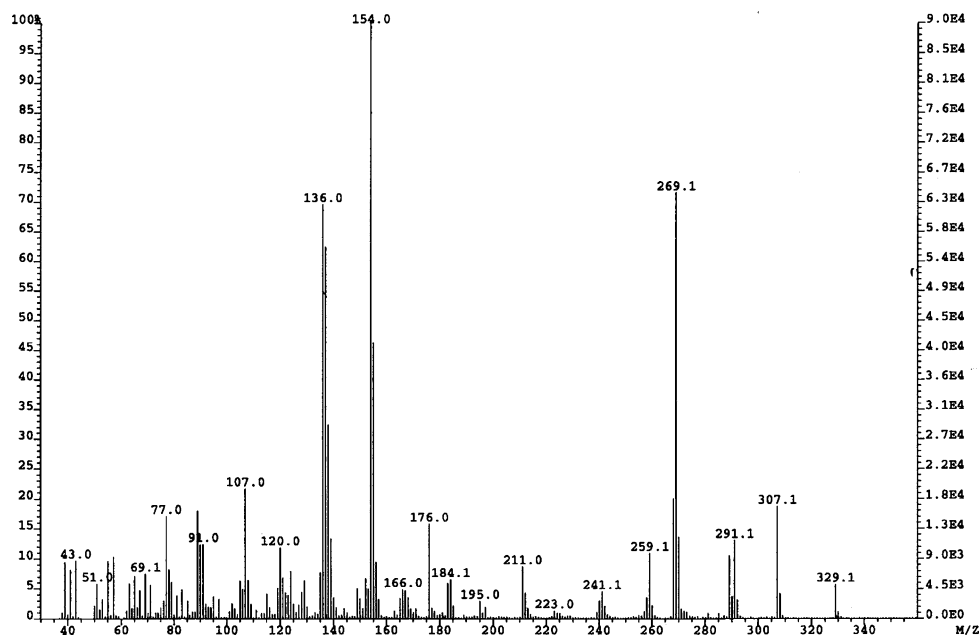


Fig. 5 ^1H , ^1H -COSY-NMR spectrum of (1)

($\epsilon = 1,000 \text{ L mol}^{-1} \text{ cm}^{-1}$) corresponded to the $\mathbf{n} \rightarrow \pi^*$ transition of the squaric acid fragment.

The positive ESI mass spectrum of (1) showed a peak at m/z 269.1, corresponding to single-charged $[\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_3]^+$ with molecular mass of 269.1 (Fig. 4).

The ^1H - and ^1H , ^1H -COSY-NMR spectra of (1) on Fig. 5 showed chemical shift signals within 7.5–9.0 ppm, belonging to the aromatic CH protons of the quinoline fragment. The signal at 4.9 ppm corresponded to CH_2 protons, whereas the signal at 1.5 ppm could be assigned to the protons of CH_3 group. These values were found to be in accordance with the corresponding data obtained for other ester amides of the squaric acid ethyl esters [28–31].

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