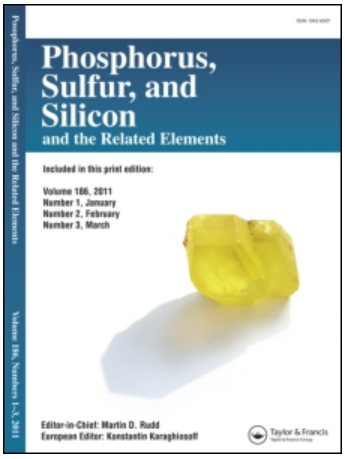

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Substituted Esters of Coumarin-3-phosphonic Acid—Linear-Polarized IR-Spectroscopic Elucidation

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*Correlation between the structure and IR-spectroscopic properties of two halogen and one amino substituted esters of coumarin-3-phosphonic acid has been studied by means of linear-polarized IR-spectroscopy of oriented colloid suspensions in nematic host. The influence of the ester group on the peak positions of the IR-characteristic bands of these derivatives and in particular, on phosphorus group is investigated by a comparison with the data for corresponding coumarin-3-phosphonic acids. Theoretical quantum chemical DFT calculations (B3LYP/6-311++G**) are carried out, thus supporting the experimental assignment of the IR-bands and predicting the electronic structure of all of the compounds studied.*

Keywords Coumarin; IR-LD analysis; phosphonates; solid-state DFT calculations

INTRODUCTION

Interest in the derivatives of 2-oxo-2H-1-benzopyran (coumarin) has been continuous for more then 50 years. It is based on the elucidated wide spectrum of biological activity of these organic molecules. A spasmolytic effect, antiarrhythmic, cardiothonic, antiviral, and anticancer properties have been reported.[1–3] Phosphorus-containing coumarins

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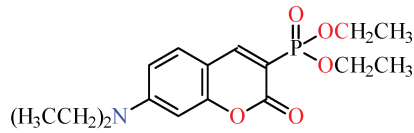
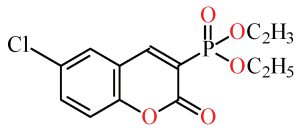
represent a novel group of compounds characterized by remarkable cytotoxicity, alkylating, and anticancer activity.[1–3] Derivatives containing a phosphorus atom at position 2 of a γ -pyrone ring have been known as efficient antibacterial agents.[4–7] A large number of our systematic synthetic investigations are focused on the different substituted phosphorus-containing coumarins, namely for the above stated reasons.[8–12]

IR-spectroscopy and nuclear magnetic resonance are powerful methods for elucidation of the correlation structure-spectroscopic properties. Numerous papers include ^{1}H-, ^{13}C-, and ^{31}P-NMR data for these derivatives. However, IR-spectroscopic investigations are rare.[13–15] For these reasons, this paper deals with a detailed IR-spectroscopic assignment and correlation study between the structure and optical properties of different substituted phosphorus-containing coumarins, depicted in Scheme 1.

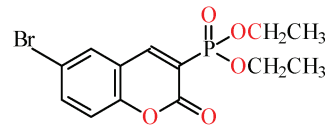
We utilized the possibilities of linear-polarized IR-LD spectroscopy of oriented colloid suspensions in nematic host[16–19] for the experimental assignment of the IR-characteristic bands as well as the structural elucidation of solids.[19] We cannot obtain good single crystals for single crystal X-ray diffraction experiments, and for this reason, the demonstrated IR- spectroscopic tool appears to be unique for obtaining of information to assist in the structural elucidation of solids. Quantum chemical calculations were performed with a view to obtain electronic structure of the compounds studied. Vibrational analysis supports the experimental IR-characteristic band assignment, as well.



(**1**)

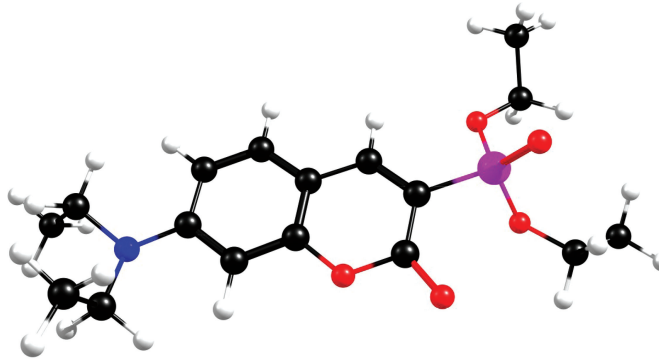


(**2**)

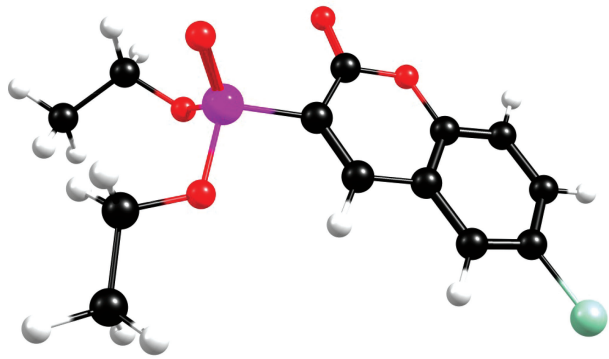


(**3**)

SCHEME 1 Chemical diagram of compounds studied.



(1)



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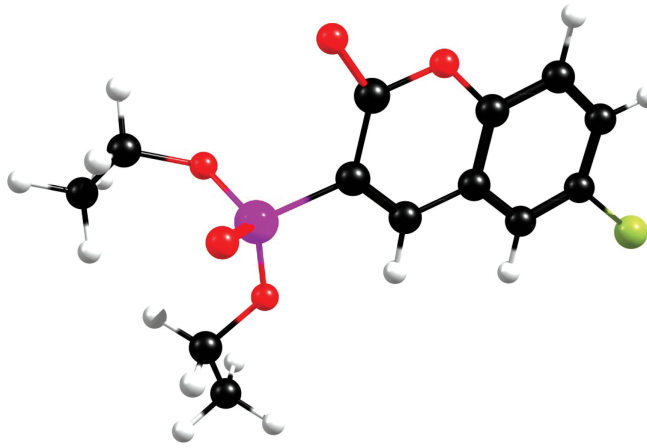


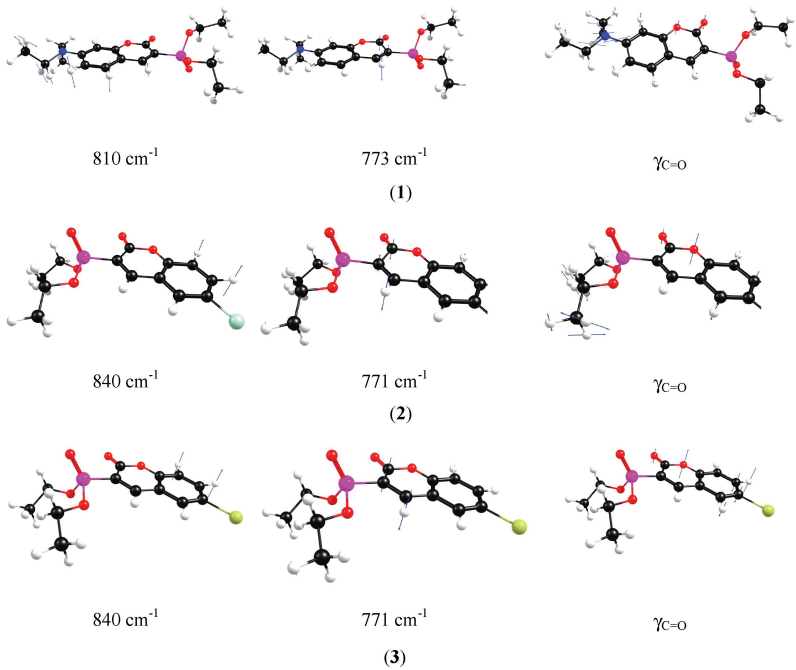
(3)

SCHEME 2 Most stable conformers of (**1**)-(**3**).

EXPERIMENTAL

Materials and Methods

Conventional and polarized IR-spectra were measured on a Bomem Michelson 100 FTIR-spectrometer (4000–400 cm^{-1}, 2 cm^{-1} resolution, 200 scans) equipped with a Perkin-Elmer wire-grad polarizer (polarized obtained by the KRS5 materials with gold surface and possibility to separate the IR-radiation into two mutual perpendicular planes). Non-polarized solid-state IR spectra were recorded using the nujol mull technique. The oriented samples were obtained as a colloid suspension in a nematic liquid crystal ZLI 1695. The theoretical approach, experimental technique for preparing the samples, procedures for polarized IR-spectra interpretation and the validation of this new linear-dichroic infrared orientation solid-state method for accuracy and precision has been presented. The influence of the liquid crystal medium on peak positions and integral absorbances of the guest molecule bands, the rheological model, the nature and balance of the forces in the nematic



SCHEME 3 Visualization of the selected transition moments in the molecules of (**1**)-(**3**).

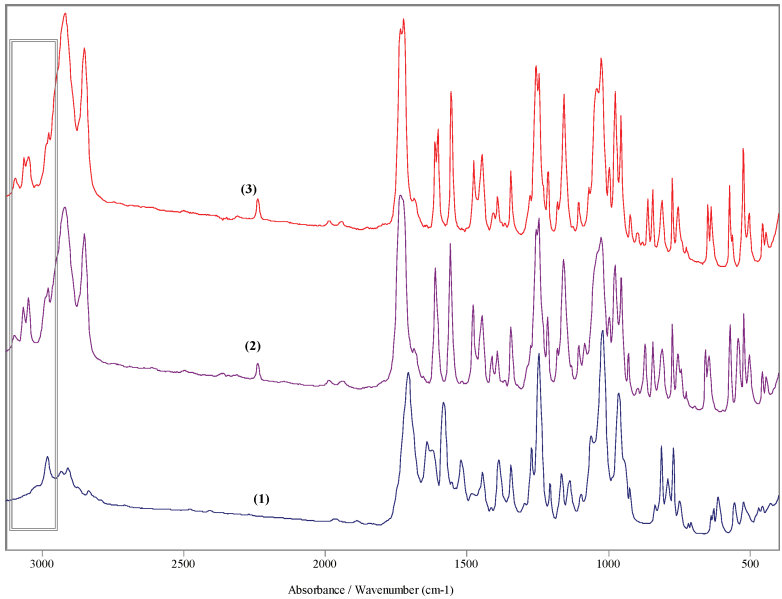


FIGURE 1 Non-polarized IR- spectra of compounds (**1**–**3**) in solid-state.

liquid crystal suspension system, and morphology of the suspended particles also been discussed.[16–19] IR-spectra in chloroform solution are recorded using 0.04_4 cm KBr cell.

Quantum chemical calculations were performed with the GAUSSIAN 98 and Dalton 2.0 program packages.[20,21] The output files were visualized by means of the ChemCraft program.[22] The geometries of (**1**–**3**) were optimized at density functional theory (DFT) using the 6-311++G** basis set. The DFT method employed was B3LYP, which combines Becke's[23] three-parameter non-local exchange function with the correlation function of Lee, Yang, and Parr.[24] Molecular geometries of the studied species were fully optimized by the force gradient method using Bernys' algorithm. For every structure, the stationary points found on the molecule potential energy hypersurfaces were characterized using standard analytical harmonic vibrational analysis. The absence of the imaginary frequencies, as well as of negative eigenvalues of the second-derivative matrix, confirmed that the stationary points correspond to minima of the potential energy hypersurfaces. The calculated vibrational frequencies and infrared intensities were checked to establish which kind of performed calculations agreed best with the experimental data. The DFT method provides accurate vibrational data, as far as the calculated standard deviations of less then 8 cm^{-1} are

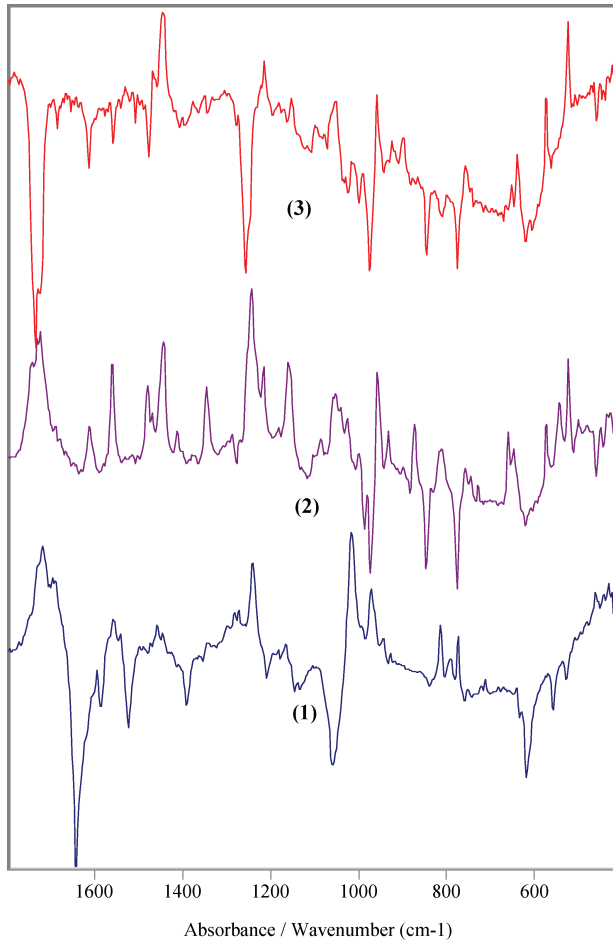


FIGURE 2 Difference IR-LD spectra of compounds (**1**–**3**).

concerned, which correspond to groups, not participating in significant intra- or intermolecular interactions. A modification of the results using the empirical scaling factor 0.9614 is done to achieve better correspondence between the experimental and theoretical values.

Compounds (**1**–**3**) were *synthesized* according.[8] To a solution of triethylphosphonoacetate (20 mmol) and corresponding salicylaldehyde (20 mmol) in dry toluene (60 ml) piperidine (0.5 ml) was added drop wise. The solution was refluxed for 4 h, and the reaction mixture was worked up as described.[8] The products were recrystallized from ether and melting points were in agreement with the proposed

TABLE I IR-characteristic Bands of (1)-(3) in Solid-State

	ν[cm^{-1}]		
Assignment	(1)	(2)	(3)
$\nu_{C=O}$	1706	1735	1737
$\nu_{C=C}$	1687	1716	1722
i.p. (a′)*	1617, 1590, 1515	1614, 1604, 1558	1616, 1562
i.p. (a′)	1475	1479	1475, 1275
$\nu_{P=O}$	1245	1255	1255
ν^{as}_{P-O}	1028	1151	1159
ν^{s}_{P-O}	964	1025	1020
i.p. (a′)	938	932	931
o.p. (a″)*	811, 773	844, 775	842,754
i.p. (a′)*	844,721	870,706	860,705
i.p. (a′)	613	618	613
$\gamma_{C=O}$	520	530	572
$\delta_{C=O}$	599	568	563

*The a′ and a″ modes are assigned according the C_s symmetry of the molecules.

values (109−110°C for bromo derivative, 109−111°C for chloro derivative and 92−93°C for 7-diethylamino-3-phosphonocoumarin).

RESULTS AND DISCUSSION

Molecular Geometry

Conformational analysis is generated by the variation of the dihedral angles. The most stable conformers of the (**1**−**3**) are depicted in Scheme 2. They correspond to energy values E_{rel} of 0.5 kJ/mol (**1**), 0.1 kJ.mol (**2**) and 0.0 kJ/mol (**3**), respectively. The coumarin fragment is flat in all of the obtained geometries with a maximal deviation of the total planarity less then 0.2° (**1**), 0.3° (**2**), and 1.1°(**3**), respectively. This result supposes that the transition moments of the out-of-plane modes of the different substituted aromatic benzene ring are co-linearly oriented (Scheme 3). The same is valid for the $\gamma_{C=O}$ [out-of-plane (o.p.)] modes and those of a", respectively (Scheme 3). The obtained geometry parameters, i.e., bond lengths and angles correlate reasonably well with the corresponding values of other coumarins, where the structures have been elucidated by means of single crystal X-ray diffraction.[25–29] The obtained differences between the theoretical and experimental values are less then 0.023 Å and 4.0(2)°, respectively. These data, indicate the successful application of the theoretical approximation method

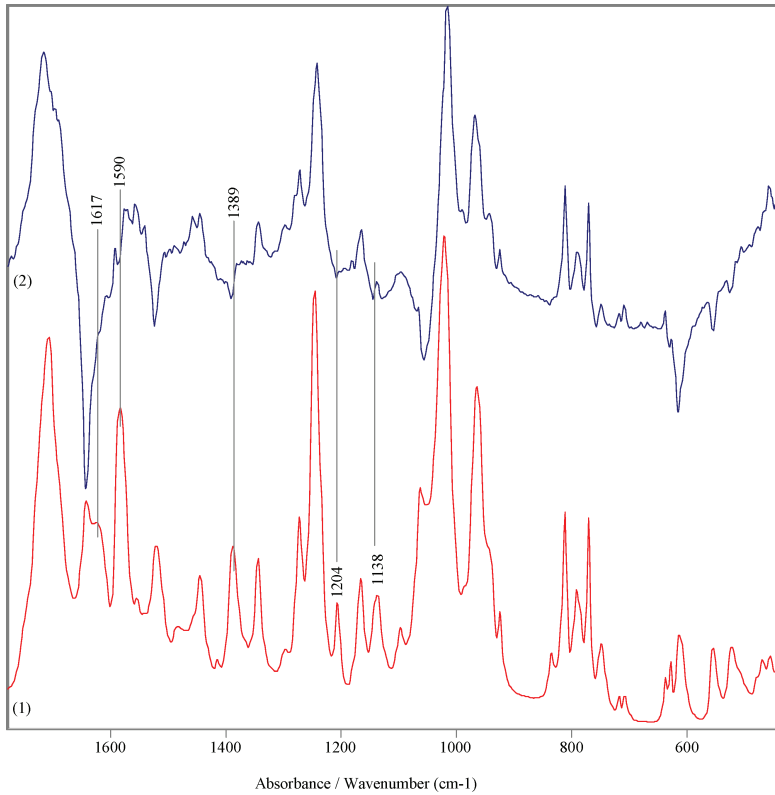


FIGURE 3 Non-polarized IR-(1) and reduced IR-LD (2) spectra of (**1**) after elimination of the band at 1617 cm^{-1}.

described here for geometry optimization and vibrational analysis of these organics.

Conventional and Linear-Polarized IR-Spectroscopy

Phosphorus-containing coumarins are characterized with a reasonable degree of orientation of suspended particles,[17–19] thus allowing the precise interpretation of the IR-characteristic bands (see difference IR-LD spectra of (**1**–**2**) in Figure 2. In contrast to coumarins with phosphonic acid fragment,[13–15] where the broad absorption bands within −2500 cm^{-1} belong to hydrogen bonded ν_{OH} stretching vibration of the OH-group, the compounds (**1**–**3**) are characterized with well define IR-bands corresponding to in-plane (i.p.) stretching vibrations of benzene fragment (Figure 1). Independently of the different type of the substituents in the benzene ring the IR-spectroscopic patterns within

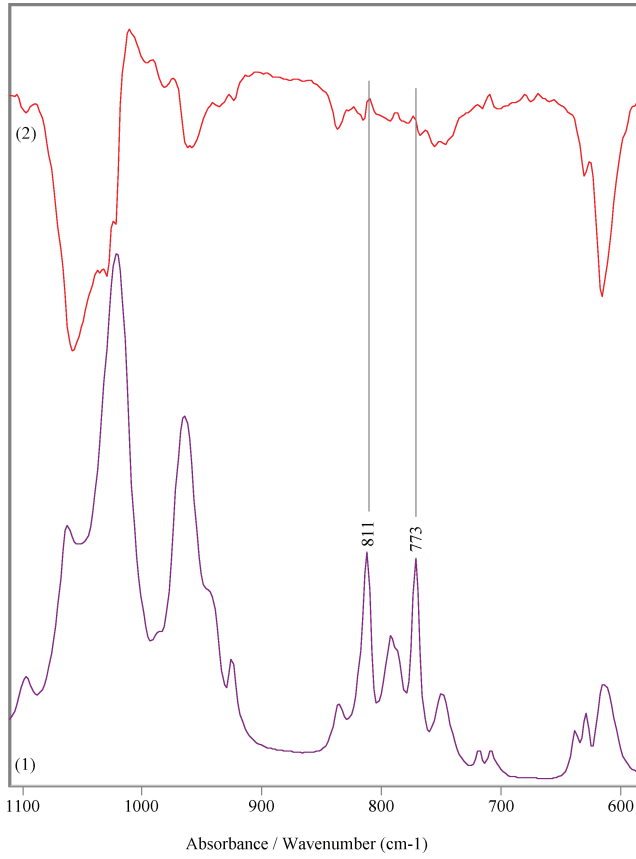


FIGURE 4 Non-polarized IR-(1) and reduced IR-LD (2) spectra of (**1**) after elimination of the band at 811 cm^{-1}.

the 1800–1300 cm^{-1} IR-regions are similar to those of corresponding coumarins with phosphonic acid fragment.[13–15] The IR-characteristic band assignment is listed in Table I. In the region 850–600 cm^{-1}, typical for in-plane and out-of plane stretching and bending vibrations of aromatic system the IR-spectroscopic patterns of (**1**) and those of (**2**) and (**3**) are differ. In the first case, the aromatic system is described as 1,2,5-trisubstituted benzene, while the other two compounds, as 1,2,4-trisubstituted derivatives (Table I). The presence of phosphonic esters in (**1**–**3**) weakly affect the peak position of the characteristic bands of benzene fragment, comparing with the data of corresponding phosphonic acid derivatives. A difference of 2 cm^{-1} is obtained. The listed values in Table I values are experimentally proven by the application

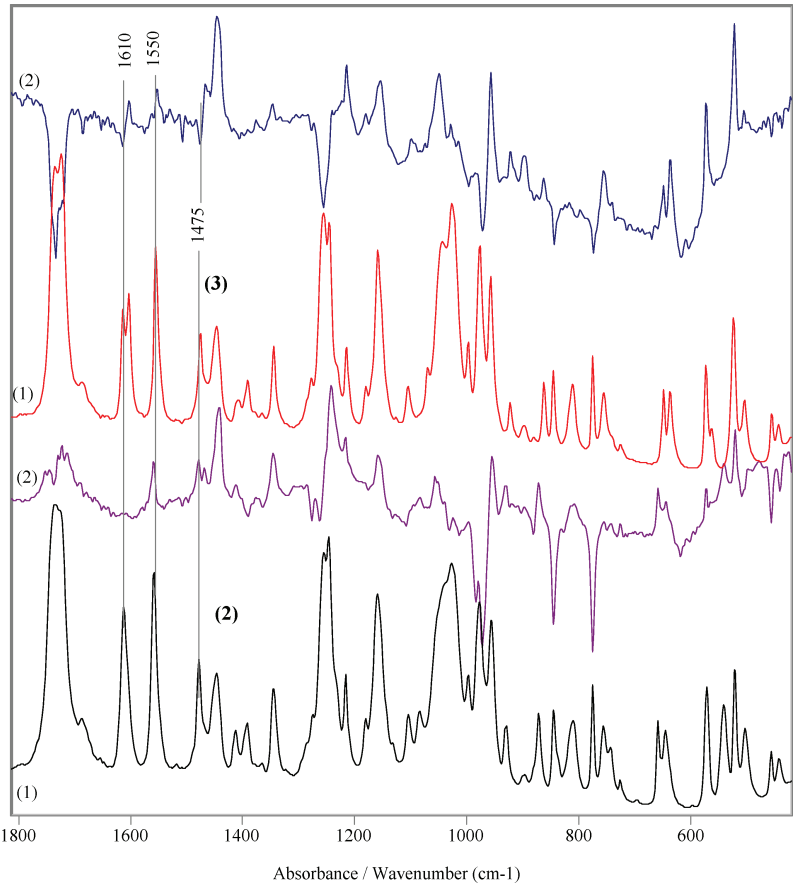


FIGURE 5 Non-polarized IR-(1) and reduced IR-LD (2) spectra of (**2**) and (**3**) after elimination of the bands about 1610 cm^{-1} (Table I).

of the reducing-difference procedure to the corresponding polarized IR-LD spectra.

The elimination of the *i.p.* band at 1617 cm^{-1} in (**1**) leads to the disappearance of the maxima belonging to same symmetry class (Figure 3.2, Table I). In contrast, the elimination of the bands at 811 cm^{-1} and 773 cm^{-1} at equal dichroic ratio (Figure 4.2) proved the origin of the corresponding IR-bands to o.p. (a" vibrations of the benzene ring. For compound (**1**) is characteristic a band at 1643 cm^{-1} in solid state, which is absent in the corresponding IR-spectrum in solution. Its elimination leads to disappearance of the bands at 1145 cm^{-1} and 500 cm^{-1}, thus proposing a combination character of the discussed IR-band. The

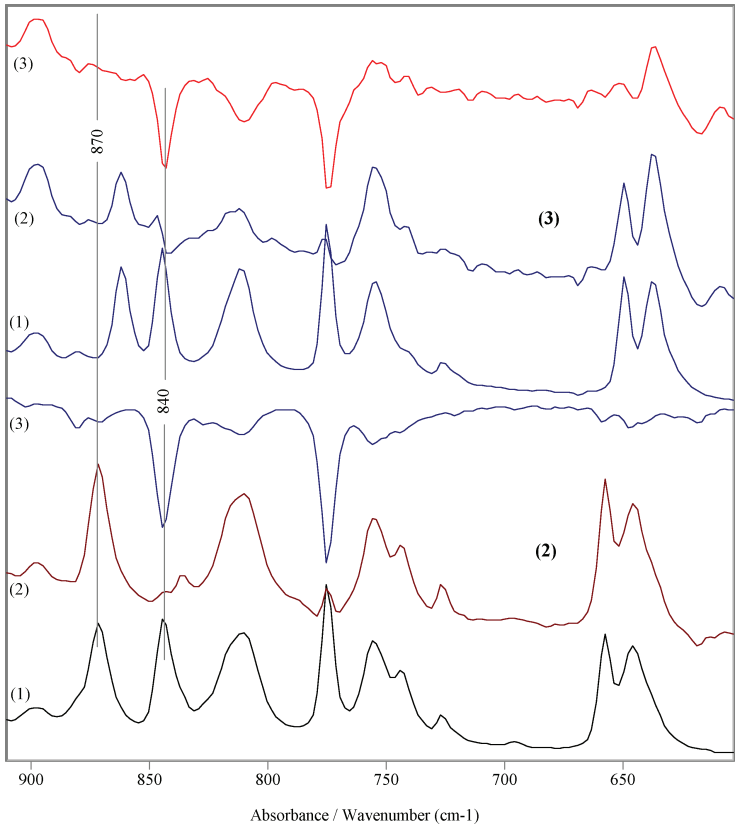


FIGURE 6 Non-polarized IR-(1) and reduced IR-LD spectra of (**2**) and (**3**) after elimination of the bands about 840 cm^{-1} (2) and 870 cm^{-1} (3) (Table I).

simultaneously vanishing of the bands at 844 cm^{-1} and 721 cm^{-1} at equal dichroic ratio proves their origin as *i.p.* bands (see Figure 6).

Similar to the results obtained for (**1**), the elimination of the *i.p.* bands about 1610 cm^{-1} of (**2**) and (**3**) (Table 1) lead to a disappearance of the maxima possessing to same symmetry class (Fig. 5). In both (**2**) and (**3**) the elimination of the band about 840 cm^{-1} leads to disappearance of corresponding maxima about 450 cm^{-1} and 443 cm^{-1} (Figure 6). The procedure applied to 870 cm^{-1} bands leads to disappearance of corresponding maxima at 805 cm^{-1}, 750 cm^{-1}, 705 cm^{-1}, 651 cm^{-1}, 520 cm^{-1} as well as about 1340 cm^{-1} (Fig. 6), thus proving the assignment listed in Table I.

The comparison of the data for corresponding phosphonic acid derivatives 13 (Table I) within the region of 1250–900 cm^{-1}, where are

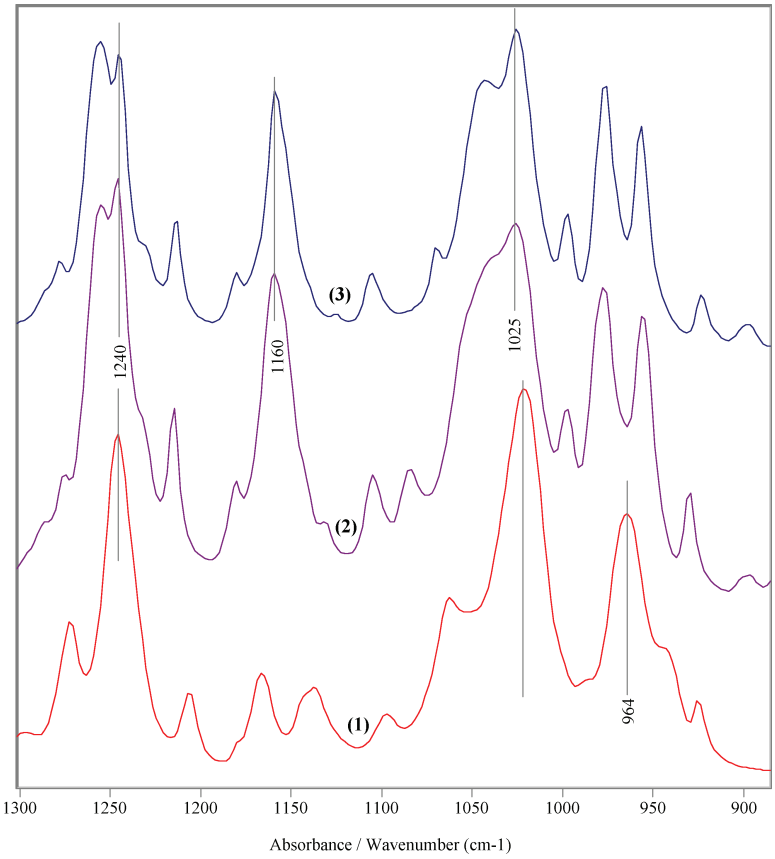


FIGURE 7 IR-spectroscopic patterns of (**1**) - (**3**) within 1250 – 900 cm^{-1} region.

observed the IR-bands of $\nu_{P=O}$, ν^{as}_{PO2} and ν^{s}_{PO2} with the IR-characteristics of (**1**–**3**) is carried out using the deconvolution and curve fitting procedures for determination of the peak positions. Series of maxima (Table I) are observed. The formation of the ester groups leads to a high frequency shifting of the last discussed bands within 15–23 cm^{-1} in (**2**) and (**3**), while the $\nu_{P=O}$ stretching vibration is observed about 1240 cm^{-1} (Figure 7). Last region typical is typical for other coumarins as well.[13] In (**1**), the IR-spectroscopic patter is similar to those of corresponding phosphonic acid derivatives (Fig. 7, Table I). The elimination of the *o.p.* bands in all of the compounds studied leads to strong reduction of the $\nu_{P=O}$ band about 1240 cm^{-1}, due to a near to perpendicular oriented P=O group towards the direction of the *o.p.* transition moments within 8.0(7) –11.2(1)°, respectively.

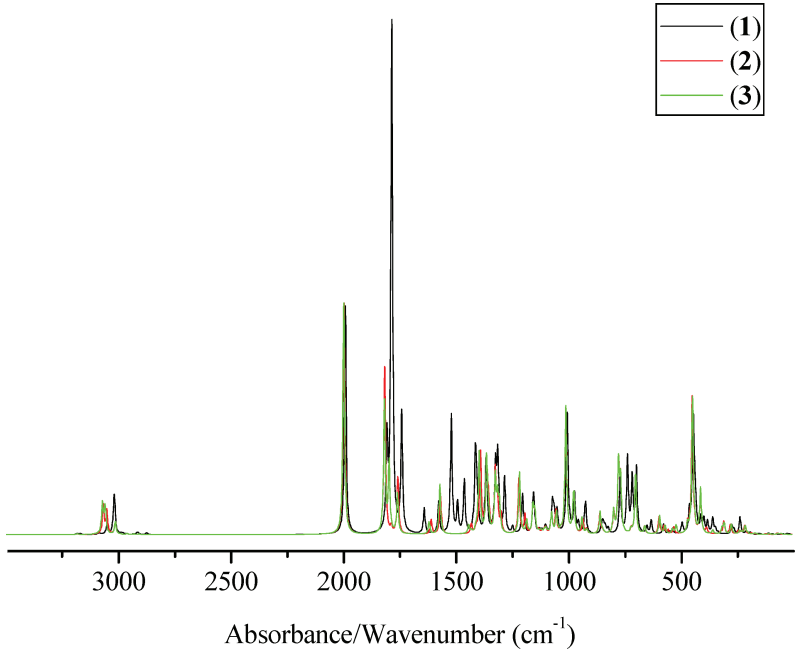


FIGURE 8 Non-scaled calculated IR-spectra of (**1**–**3**).

The experimental IR-band assignment is compared and supported with corresponding theoretical vibrational analysis (Figure 8). The obtained theoretical frequencies of *i.p.* and *o.p.* modes of the aromatic fragment in coumarin correlate well with those observed in Figure 1. The obtained differences between the values less then 8 cm^{-1} show a reasonable application of B3LYP/6-311++G** approximation. In contrast to phosphonic acid derivatives, where the predicted values of $\nu_{P=O}$, ν^{as}_{PO2} and ν^{s}_{PO2} stretching modes are differed with values within 15–45 cm^{-1},[13] as a result of the participation of phosphoric acid fragments in intramolecular interactions in solid-state, in esters (**1**–**3**) the calculated and experimental values are differ less then 8 cm^{-1}. This result indicates that the steric effects in esters difficult the participation of the P=O in strong hydrogen bonding in condense phase.

CONCLUSION

Correlation between the structure and IR-spectroscopic properties of different substituted esters of coumarin-3-phosphonic acid are

elucidated by means of the polarization IR-spectroscopy of oriented colloid suspensions in nematic host. The experimental IR-characteristic band assignment is performed by a comparison with the previous data of derivatives with phosphonic acid fragment. [13] The influence of the formation of the ester group on the IR-spectroscopic patterns is discussed. Theoretical quantum chemical DFT calculations B3LYP/6-311++G** are applied. Electronic structure and optical IR-properties of studied compounds are obtained.

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