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EXPERIMENTAL AND THEORETICAL INVESTIGATION OF THE ELECTRONIC ABSORPTION SPECTRA OF 2-H(METHYL, METHYLTHIO, PHENYL)-3,4-DIHYDRO-4-QUINAZOLINYLIDENECYANOACETIC ESTER

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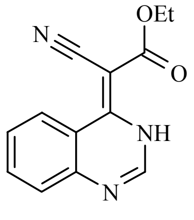
The effect of substituents (Me, SMe, Ph) in position 2 has been studied on the nature of the absorption bands of 2-H-3,4-dihydro-4-quinazolinylidenecyanoacetic esters and a very high sensitivity on the substituent has been detected for the short wave maxima. On the basis of data calculated by the ZINDO/S method the featureless long-wave absorption band was assigned to an electronic transition from HOMO to LUMO caused by charge transfer from fragments of the benzene ring and the N=C–N bond to the >C=C–C=O fragment.

Keywords: 2-substituted 4-quinazolinylidenecyanoacetic esters, quantum-chemical calculations, UV spectra.

Quinazoline derivatives are of considerable interest in connection with their photochemical and biological properties [1-3]. 2-H-3,4-Dihydro-4-quinazolinylidenecyanoacetic ester (**1**) and its 2-methyl, methylthio, and phenyl derivatives **2-4** may also prove to be promising substances in this direction due to their planar structure (except for the ethyl group of the ester fragment) and the presence of conjugation between the quinazoline ring and the fragments of the cyanoacetate residue, and also the phenyl substituent in the case of compound **4**. This leads to a significant change of electron density in molecules **1-4** in comparison with the separate fragments. In addition, from a theoretical point of view, these compounds are extremely interesting quinazoline derivatives due to the presence of several possible tautomeric forms [4].



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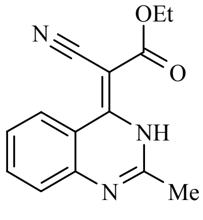

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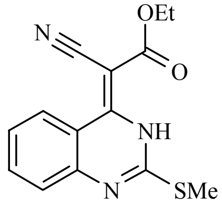

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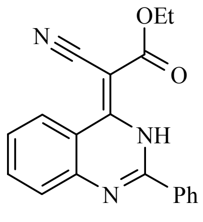

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* Dedicated to Professor L. I. Belen'kii on his 75th birthday.

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Since it seemed of interest to investigate the effect of the nature of a substituent in position 2 on the IR and UV spectral characteristics of derivatives of molecule **1**, we have carried out an experimental and theoretical investigation of the electronic absorption spectra of compounds **1**-**4**.

The theoretical calculation of the electronic spectra (singlet transitions) was carried out by the ZINDO/S semiempirical method [5, 6] using a completely optimized geometry of the molecules in a PM3 approach [7] and with an estimate of the configurational interaction of the six occupied and unoccupied MO (73 singly excited configurations). The calculations were carried out with the Hyperchem 6.0 (Hypercube Inc.) set of programs.

The synthesis and investigation of the tautomerism of derivatives of 2-H(methyl)-3,4-dihydro-4-quinazolinylidenecyanoacetic ester by X-ray structural analysis and ^{1}H NMR spectroscopy was reported previously [4]. The data of ^{1}H NMR spectra showed the presence of an intramolecular hydrogen bond (IMHB) between the hydrogen atoms at the $N_{(3)}$ atom and the carbonyl group of the ester residue. Results of an analysis of the IR spectral data for compounds **1**-**4**, carried out in the present work, also confirm the presence of an IMHB between these atoms, to which the very low values of the frequencies of the stretching vibrations of the NH and C=O bonds correspond (Table 1).

The electronic spectrum of compound **1** in ethanol is characterized by the presence of absorption bands at 220-250, 260-310, and 320-340 nm (Fig. 1, Table 2).

Of these the longest wave absorption band (320-410 nm) is markedly distinguished by higher intensity and resolved fine structure. In addition, from an analysis of the UV spectra of compounds **1**-**4**, the very high sensitivity of the absorption bands at 220-250 and 260-310 nm towards the substituents was discovered. Introduction of a methylthio group into position 2 of the **1** molecule leads in the UV spectrum of compound **3** to a significant bathochromic shift of all the maxima and a simultaneous increase in the intensity of the shortest wave maximum relative to the absorption band at 280-330 nm, compared with the spectrum of the methyl substituted compound **2**. Introduction of a phenyl residue into position 2 of compound **1**, i. e. compound **4**, extends the *p*-conjugation in the molecule and leads to a bathochromic shift of the more long wave and short wave maxima. At the same time a hypsochromic shift of the absorption band at 260-310 nm occurs and this absorption band appears as a shoulder on the background of an intense short wave absorption (Fig. 2).

The greatest bathochromic shift of the long wave maxima (Fig. 1, Table 2) and the reduction of the bands for the stretching vibrations of the N=C and C=O bonds (Table 1) in the UV and IR spectra of compounds **3** and **4**, relative to compounds **1** and **2**, indicates the more effective mesomeric interaction (+M effect) of the SMe and Ph groups with the π–electrons of the heterocyclic system of the molecule of **1**.

TABLE 1. IR Spectra of Compounds **1**-**4**, Cyanoacetic Acid Ethyl Ester (**5**), and 2-Methyl-4(3H)-quinazolinone (**6**)

Bond	Frequency of vibrations, ν, cm^{-1}					
	1	**2**	**3**	**4**	**5***	**6***^{2}
NH	3127	3127	3125	3125	—	—
C=O	1661	1661	1656	1648	1749	—
C=N	1615	1622	1590	1592	—	1625
C≡N	2206	2207	2208	2211	2265	—

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* Data from [8] are given for compound **5**.

*^{2} According to [3, 9] ν(NH) is a broad absorption band at 3000-3300 cm^{-1}.

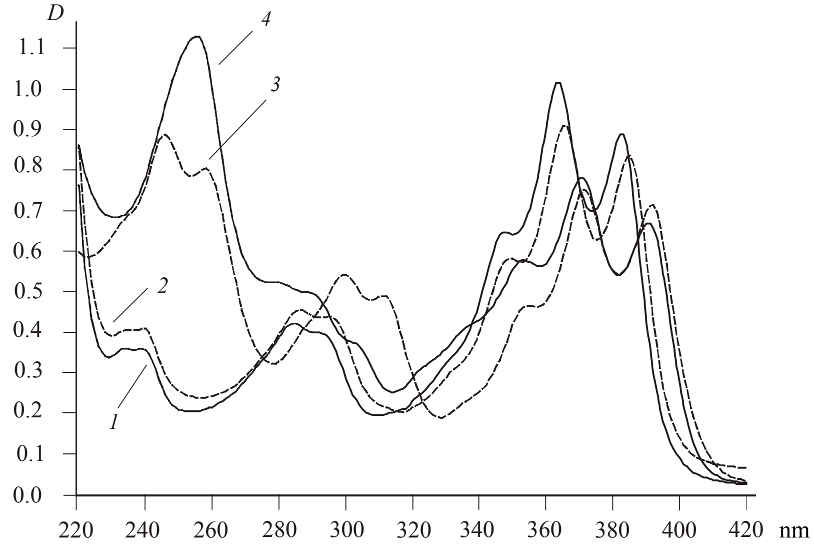

Fig. 1. UV spectrum (in ethanol) of compounds 1) **1**; 2) **2**, 3) **3**, and 4) **4**.

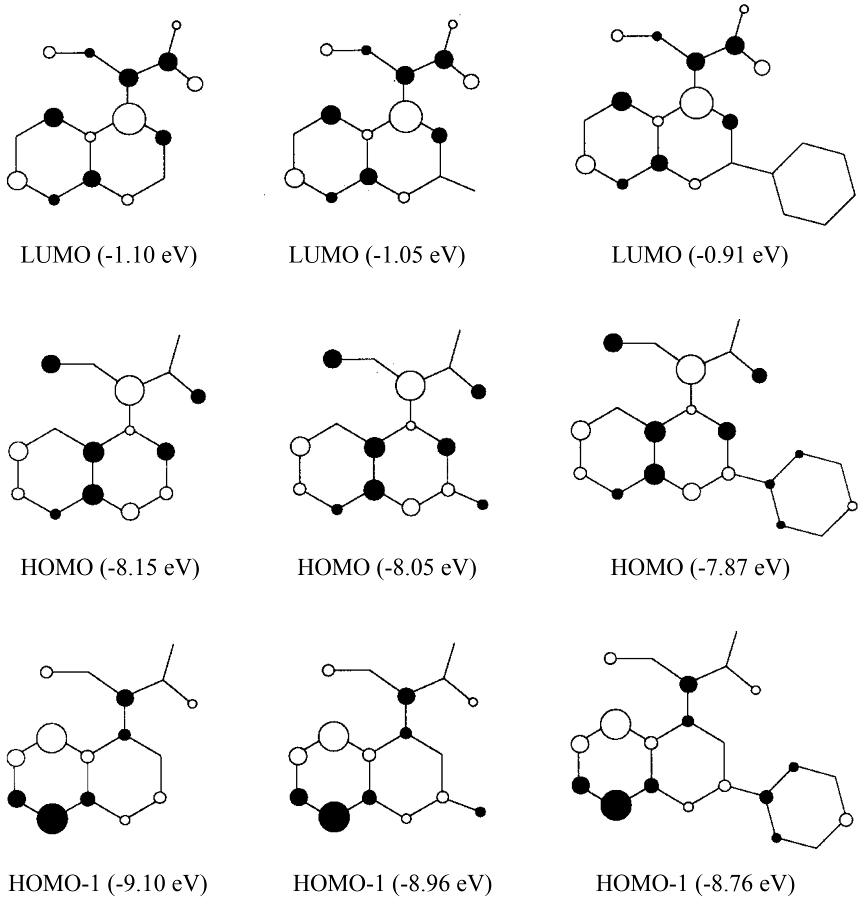
LUMO (-1.10 eV)
LUMO (-1.05 eV)
LUMO (-0.91 eV)
HOMO (-8.15 eV)
HOMO (-8.05 eV)
HOMO (-7.87 eV)
HOMO-1 (-9.10 eV)
HOMO-1 (-8.96 eV)
HOMO-1 (-8.76 eV)

Fig. 2. Distribution of electron density on atoms, and energies (in parentheses) of HOMO, HOMO-1, and LUMO of compounds **1**, **3**, and **4** (ZINDO/S).

TABLE 2. Experimental and Calculated Characteristics of the UV Spectra of Compounds **1-4**

Compound	λ_{max}, nm (log ε)	Calculation	Type of transition	Assignment*
		λ_{max}, nm (f)		
1	382 (4.30) 364 (4.35) 348 (4.16)	349.1 (0.592)	$\pi\to\pi^*$	H→L
	—	322.6 (0.001)	$n\to\pi^*$	H-2→L (L+2)
	284 (3.96)	282.7 (0.375)	$\pi\to\pi^*$	H→L+1
		268.9 (0.009)	$n\to\pi^*$	H-4(5)→L+1
	239 (3.88)	248.7 (0.016)	$\pi\to\pi^*$	H-1→L (L+1)
	234 (3.89)	234.5 (0.117)	$\pi\to\pi^*$	H→L+2(3)
2	385 (4.33) 365 (4.37) 349 (4.16)	353.5 (0.585)	$\pi\to\pi^*$	H→L
	—	321.3 (0.001)	$n\to\pi^*$	H-2→L
	295 (4.02)	289.9 (0.067)	$\pi\to\pi^*$	H-1→L
	286 (4.04)	282.1 (0.373)	$\pi\to\pi^*$	H→L+1
		266.0 (0.010)	$n\to\pi^*$	H-4→L+1
	239 (3.98)	248.7 (0.011)	$\pi\to\pi^*$	H→L+2 H-1→L (L+1)
	234 (3.97)	235.8 (0.112)	$\pi\to\pi^*$	H→L+3
3	392 (4.31) 371 (4.33) 354 (4.11)	355.1 (0.539)	$\pi\to\pi^*$	H→L
	—	315.3 (0.002)	$n\to\pi^*$	H-3→L (L+2)
	311 (4.13)	292.4 (0.046)	$\pi\to\pi^*$	H→L+1 H-1→L
	299 (4.18)	284.9 (0.446)	$\pi\to\pi^*$	H→L+1
		263.9 (0.010)	$n\to\pi^*$	H-4(5)→L+1
	258 (4.36)	251.4 (0.022)	$\pi\to\pi^*$	H→L+2 H-1→L (L+1)
	246 (4.41)	235.5 (0.060)	$\pi\to\pi^*$	H→L+3
4	390 (4.26) 371 (4.33) 353 (4.19)	356.1 (0.543)	$\pi\to\pi^*$	H→L
	303_{sh} (3.99)	311 (0.442)	$\pi\to\pi^*$	H→L+1
	279_{sh} (4.15)	288.3 (0.266)	$\pi\to\pi^*$	H-1→L
	—	280.0 (0.009)	$n\to\pi^*$	H-4→L
	—	273.5 (0.010)	$n\to\pi^*$	H-2→L+1
	255 (4.49)	246.5 (0.392)	$\pi\to\pi^*$	H→L+3

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* H is the highest occupied MO (in English HOMO); L is the lowest unoccupied MO (LUMO).

According to the calculated data (Table 2) the theoretical electronic transition from HOMO to LUMO at λ_{max}^{calc} 352 ± 3 nm corresponds to the long wave absorption maximum at 320-410 nm for compounds **1-4**. The fall in electron density on the atoms of the Ph and N=C–N fragments and the increase on the LUMO of the >C=C–C=O chain indicates the charge-transfer character of this transition.

The absorption bands at 220-260 and 260-310 nm in the spectra of compounds **1-4** are $\pi\to\pi^*$ transitions and correspond to a localized transition in the benzene fragment. The electronic transition caused by the π electrons of the ester oxygen of the >C=O group and the nitrogen atoms of compounds **1-3** is overlapped by the intense long wave absorption at 320-420 and by the absorption at 250-320 nm respectively. In the case of compound **4** both transitions are overlapped by the absorption band of the benzene ring at 250-310 nm.

The nature of the absorption bands of compounds **1-4** has therefore been established by the ZINDO/S semiempirical method. Study of the effect of substituents in position 2 on the nature of the absorption bands in the spectra of compounds **1-4** permitted discovery of the very high sensitivity of the short wave maxima to the nature of the substituent in position 2.

EXPERIMENTAL

The UV spectra of compounds **1-4** were measured on a Lambda 16 instrument (Perkin-Elmer) in quartz cuvettes with a 1 cm absorbing layer at a solution concentration of 3.3×10^{-5} to 4.3×10^{-5} M. The IR spectra were obtained on a FTIR System 2000 spectrometer (Perkin-Elmer) in KBr disks. The conditions for recording the ^{1}H NMR spectra were analogous to those described in [4].

The initial compounds 4-quinazolone, 2-thioxo-4-quinazolone, 2-methylthio-4-quinazolone, and 4-chloro-2-methylthioquinazoline were obtained by the procedures of [10-13] respectively. 4-Chloroquinazoline, 4-chloro-2-methylquinazoline, and 4-chloro-2-phenylquinazoline were synthesized by the procedures given in [14, 15].

The procedure for synthesizing compounds **1** and **2** is described in [4].

2-Methylthio-3,4-dihydro-4-quinazolinylidenecyanoacetic Ester (3). A mixture of DMF (12 ml, 5.6 mmol), cyanoacetic ester (0.6 ml, 5.6 mmol), and sodium hydride (0.14 g, 5.6 mmol) was stirred at room temperature for 30 min. 4-Chloro-2-methylthioquinazoline (1.18 g, 5.6 mmol) was then added and the reaction mixture heated at ~100°C for 8 h. After cooling, water was added to the reaction mixture, and the precipitated crystals were filtered off. The filtrate was extracted with benzene, the extract dried with anhydrous sodium sulfate, and the benzene distilled off. The residue was recrystallized from methanol. Compound **3** (1.15 g, 72%) was obtained; mp 197-198°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.1-7.7 (4H, m, Ar); 4.18 (2H, q, $J = 7.5$, $OC\underline{H_2}CH_3$); 2.50 (3H, s, SCH_3); 1.12 (3H, t, $J = 7.5$, $OCH_2C\underline{H_3}$). Found, %: C 58.83; H 4.61; N 14.47. $C_{14}H_{13}N_3O_2S$. Calculated, %: C 58.55; H 4.53; N 14.62.

2-Phenyl-3,4-dihydro-4-quinazolinylidenecyanoacetic Ester (4) was synthesized by a procedure analogous to the above. Compound **4** (2.2 g, 73%) was obtained; mp 192-193°C (acetone). ^{1}H NMR spectrum, δ, ppm (*J*, Hz) in $CDCl_3$: 14.82 (1H, br. s, NH); 9.25 (1H, dd, $J = 8.4$, $J = 1.3$, H-6 Ar); 8.15 (2H, m, H Ar); 7.39-7.80 (6H, m, $J = 8.4$, $J = 4.7$, $J = 2.3$, $J = 0.9$, H Ar); 4.34 (2H, q, $J = 7.0$, $OC\underline{H_2}CH_3$); 1.37 (3H, t, $J = 7.0$, $OCH_2C\underline{H_3}$); in DMSO-d$_6$: 8.89 (1H, d, $J = 7.5$, H Ar); 7.30-7.90 (8H, m, H Ar); 4.18 (2H, q, $J = 7.0$, $OC\underline{H_2}CH_3$); 1.10 (3H, t, $J = 7.0$, $CH_2C\underline{H_3}$). Found, %: C 71.82; H 4.97; N 13.31. $C_{19}H_{15}N_3O_2$. Calculated, %: C 71.95; H 4.73; N 13.24.

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