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Synthesis, spectroscopic and theoretical study of isoquinoline alkaloid dehydrosalsolinol base and its triacetylated derivative

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Abstract

Dehydrosalsolinol and its triacetylated derivative i.e. are synthesized, isolated, and the spectra and structure are elucidated. Solid-state linear-dichroic infrared spectroscopy, ¹H and ¹³C NMR, TGV and DTA methods are applied. The potential energy surface of both compounds are explored with DFT correlation functional B3LYP method and MP2, using the $6-311++G^{**}$ basis set. Single point calculations are performed at levels up to B3LYP/ $6-311++G^{**}//$ MP2/ $6-311++G^{**}$ and MP2/ $6-311++G^{**}$. Two isomers of dehydrosalsolinol are located and the relative energies are determined. The planar quinoidal structure with strong intramolecular OH...O hydrogen bond and dipole moment of 7.392 D is more stable than the diphenolic form. Calculated vibrational frequencies are used to determine the type of molecular motions associated with each of the experimental IR-bands observed. IR-spectroscopic data show that dehydrosalsolinol exists in solid-state as the quinoide form in contrast to solution, where ¹H NMR data indicate a keto-diphenolic equilibrium. Comparison between calculated and experimental IR-frequencies of triacetyl derivative shows the presence of two phenolic ester carbonyl and one-amide groups and an exocyclic double bond. The same conclusions are obtained by corresponding ¹H NMR data. © 2008 Published by Elsevier B.V.

Keywords: Dehydrosalsolinol; Solid-state IR-LD spectroscopy; Ab initio and DFT calculations; Vibrational analysis; ¹H NMR; TGA and DSC

1. Introduction

Dehydrosalsolinol (4) as a metabolite of the salsolinol-1-carboxylic acid [1], which is a central nervous system alkaloid, might be related to chronic alcohol consumption and Parkinson's disease [2,3], when it is present in the mammalian brain. This, along with the interesting structural features, prompted us to study a new approach for its synthesis and to carry out some computational structural investigations.

Dehydrosalsolinol has previously been synthesized by demethylation of 3,4-dihydro-6,7-dimethoxy-1-methyl isoquinoline, which yields the target compound as its hydrobromide salt [3]. The approach presented herein is experimentally simple and gives the free base **4** directly. It has been demonstrated earlier that 3,4-dimethoxyphenylethyl amine reacts readily with 1,3-dicarbonyl compounds to give enaminones which can later cyclize to 1,1-disubstituted tetrahydroisoquinolines in acidic media [4]. Extending these studies to different phenylethyl amines, it is not surprising that dopamine also gives enaminone **2** upon reaction with ethyl acetoacetate (Scheme 1).

The cyclization of **2**, however, does not require acidic catalysis and proceeds under solvent-free conditions at 80-100 °C. The tetrahydroisoquinoline **3** formed in this way is not isolated as it spontaneously eliminates ethyl acetate in a retro-Mannich manner and gives dehydrosalsolinol (**4**) in 60% overall yield (Scheme 2).

Present research is focused on the spectroscopic and theoretical characterization of **4** and **5** (Scheme 2) by means of solid-state linear-polarized IR-spectroscopy of oriented

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Scheme 2. Synthesis scheme.

samples as suspension in nematic liquid crystal, ¹H NMR, and quantum chemical calculations at *ab initio* (MP2) and DFT (B3LYP) levels of theory and the 6-311++ G^{**} basis set.

2. Experimental

Unless otherwise noted, all the reagents and solvents were purchased from Sigma–Aldrich and were used as commercially supplied.

2.1. Synthesis

2.1.1. Synthesis of the enaminone (2)

To a suspension of dopamine hydrochloride (0.5689 g, 3 mmol) in methanol (7 ml), triethylamine (0.3036 g, 3 mmol) was added, followed by ethylacetoacetate (0.3904 g, 3 mmol). The mixture was stirred at r.t. for 24 h. Then water (100 ml) was added and extraction with dichloromethane (2× 30 ml) was performed. The organic layer was dried with Na₂SO₄ and the solvent was distilled to yield **2** as a clean to slightly brown oil (0.5870 g, 73%).

2.1.2. Synthesis of dehydrosalsolinol (4)

The enaminone 2 (0.2653 g, 1 mmol) was heated at 100 °C for 4 h in a sealed vial. It was then allowed to cool

down to r.t. and the solidified mass was triturated with Et₂O:MeOH 2:1 (v:v) to give **4** as a yellow powder (0.106 g, 60%). Elemental analysis (Found: C, 68.15; H, 5.75; N, 7.96; [C₁₀H₁₁NO₂] calcd.: C, 68.13; H, 5.79; N, 7.93%). M.p. 232 (with decomposition). ¹H NMR (DMSO- d_6 , δ ppm): 6.81 (s, 1H), 6.25 (s, 1H), 3.41 (t, 2H, J = 7.7), 2.54 (t, 2H, J = 7.7), 2.23 (s, 3H).

2.1.3. Acetic acid 7-acetoxy-2-acetyl-1-methylene-1,2,3,4tetrahydro-isoquinolin-6-yl ester (5)

Acetic anhydride (0.6 ml) was added to dehydrosalsolinol (0.1000 g, 0.565 mmol) and the mixture was heated at 100 °C for 15 min. Then the mixture was allowed to cool down to r.t. and with vigorous magnetic stirring, water (6 ml) was added to hydrolyze the excess acetic anhydride. NaHCO₃ was then carefully added to adjust the pH to 7–8, and the mixture was extracted with DCM (2×50 ml). The organic layers were dried (Na₂SO₄) and dry-loaded onto silica. Column chromatography in Et₂O afforded the product (5) as colourless crystals (0.130 g, 76%). Elemental analysis (Found: C, 63.36; H, 5.66; N, 4.64; [C₁₆H₁₇NO₅] calcd.: C, 63.36; H, 5.65; N, 4.62%.). M.p. 123 (with decomposition). ¹H NMR (CDCl₃, δ ppm): 7.55 (s, 1H), 6.98 (s, 1H), 5.66 (s, 1H), 5.08 (s, 1H), 3.96 (t, 2H, J = 6.0) 2.87 (t, 2H, J = 6.0), 2.30 (s, 3H), 2.28 (s, 3H), 2.20 (s, 3H).

The most intensive signals in the mass spectra of the compounds studied are that of the peak at m/z 178.01 and 304.11, corresponding to the singly charged cations $[C_{10}H_{12}NO_2]^+$ and $[C_{16}H_{18}NO_5]^+$, with molecular weights of 178.24 and 304.16, respectively. These findings confirm the synthesis and isolation of **4** and **5**.

2.2. Materials and methods

IR-spectroscopic measurements within $4000-400 \text{ cm}^{-1}$ range were obtained on a Bruker 113v FT-IR spectrometer (resolution 2 cm^{-1} , 250 scans). A Specac wire-grid polarizer was used. Oriented solid samples were obtained as a suspension in a nematic liquid crystal of the 4'-cyano-4'alkylbicyclohexyl type (ZLI 1695, Merck), mesomorphic at r.t. Its weak IR-spectrum permits recording of the guest-compound IR-bands in the whole $4000-400 \text{ cm}^{-1}$ range. The isolated nitrile stretching IR-band at 2236 cm^{-1} serves additionally as an orientation indicator. The effective orientation of the samples was achieved through the following procedure: 5 mg of the compound to be studied was mixed with the liquid crystal substance until a slightly viscous suspension was obtained. The phase thus prepared was pressed between two KBr-plates for which, in advance, one direction had been rubbed out by means of fine sandpaper. The grinding of the mull in the rubbing direction promotes an additional orientation of the sample. The validation of this new orientation solidstate method [5] used in linear-dichroic infrared (IR-LD) spectroscopy for accuracy, precision and the influence of the liquid crystal medium on peak positions and integral absorbances of the guest molecule bands, as well as the optimization of experimental conditions and an experimental design for quantitative evaluation of the impact of four input factors, have been presented [6,7]. The number of scans, the rubbing-out of KBr-pellets, the amount of studied compounds included in the liquid crystal medium and the ratios of Lorentzian to Gaussian peak functions in the curve-fitting procedure on the spectroscopic signal at five different frequencies has been studied [6,7]. It has been found that the procedure for the position (v_i) and integral absorbancies (A_i) determination for each *i*-peak have been carried out by deconvolution and curve-fitting procedures at 50:50% ratio of Lorentzian to Gaussian peak functions, χ^2 factors within 0.00066–0.00019 and 2000 iterations [6,7]. The means of the two treatments were compared by Student t-test. The experimental IR-spectral patterns have been acquired and processed by GRAMS/AI 7.01 IR spectroscopy (Thermo Galactic, USA) and STATISTICA for Windows 5.0 (StatSoft, Inc., Tulsa, OK, USA) program packages. The nature and balance of the forces in the nematic liquid crystal suspension system, the mathematical model for their clearance, morphology of the suspended particles and the influence of the space system types on the degree of orientation i.e. ordering parameter have been shown [8] using five liquid crystal and 15 compounds. Applicability of the last approach for experimental



Scheme 3. Optimized geometry of (4).

Table 1

Selected geometrical parameters (bond lengths [Å] and angles [°]) of **4** and **5**, obtained at the MP2/6-311++G^{**} level of theoretical approximation, using atom numbering Schemes 3 and 4

| Name definition | Values | Name definition | Values |
|-----------------|--------|-------------------|----------|
| 4 | | | |
| R(1,2) | 1.482 | A(2, 1, 3) | 122.6(5) |
| R(1,3) | 1.250 | A(3, 1, 4) | 123.3(7) |
| R(1,4) | 1.460 | A(1,2,9) | 122.0(8) |
| R(2,5) | 1.384 | A(5,2,9) | 124.6(7) |
| R(6,7) | 1.522 | A(1,4,6) | 124.0(3) |
| R(7,10) | 1.537 | A(4, 6, 7) | 121.9(7) |
| R(8,12) | 1.387 | A(4, 6, 8) | 120.5(4) |
| R(10,11) | 1.476 | A(6, 7, 10) | 110.1(4) |
| R(11,12) | 1.364 | A(6, 8, 12) | 119.8(1) |
| | | A(9, 8, 12) | 122.9(3) |
| D(3, 1, 2, 5) | 0.0 | D(7, 6, 8, 12) | 5.7 |
| D(4, 1, 2, 9) | 0.7 | D(6,8,9,2) | 1.6 |
| D(2, 1, 4, 6) | 1.2 | D(6,8,12,11) | 9.2 |
| D(1,2,9,8) | 0.6 | D(9, 8, 12, 13) | 6.4 |
| D(1,4,6,8) | 0.3 | D(7, 10, 11, 12) | 41.8 |
| D(4, 6, 7, 10) | 148.5 | D(10, 11, 12, 8) | 10.6 |
| D(8, 6, 7, 10) | 36.8 | | |
| D(4, 6, 8, 9) | 1.1 | | |
| 5 | | | |
| R(1,2) | 1.391 | A(1, 2, 4) | 125.7(5) |
| R(1,9) | 1.396 | A(3, 2, 4) | 114.7(8) |
| R(3,6) | 1.388 | A(2, 3, 5) | 114.4(2) |
| R(4,8) | 1.396 | A(6,7,9) | 118.9(3) |
| R(5,15) | 1.396 | A(4, 8, 18) | 107.5(2) |
| R(8,18) | 1.510 | A(4, 8, 20) | 124.7(6) |
| R(8,20) | 1.222 | A(18, 8, 20) | 127.7(1) |
| | | A(1,9,10) | 122.0(8) |
| | | A(9, 10, 11) | 107.8(1) |
| | | A(5, 15, 21) | 107.5(0) |
| D(9, 1, 2, 3) | 0.9 | D(14,7,9,10) | 5.6 |
| D(2,1,9,7) | 0.0 | D(6,7,14,12) | 153.7 |
| D(1, 2, 3, 6) | 0.5 | D(9,7,14,12) | 28.2 |
| D(4, 2, 3, 5) | 0.5 | D(1,9,10,11) | 139.2 |
| D(1,2,4,8) | 0.7 | D(9, 10, 11, 12) | 61.2 |
| D(6, 3, 5, 15) | 1.0 | D(10, 11, 12, 13) | 141.3 |
| D(2, 3, 6, 7) | 0.7 | D(11, 12, 13, 19) | 2.4 |
| D(2,4,8,20) | 0.1 | D(14, 12, 13, 17) | 5.0 |
| D(3,6,7,9) | 1.6 | D(11, 12, 14, 7) | 2.5 |
| D(6,7,9,10) | 176.3 | D(13, 12, 14, 16) | 7.1 |

IR-spectroscopic band assignment and especially for obtaining structural information, has been demonstrated in a series of organic systems and metal complexes [9], Cu(II) complexes [10], polymorphs [11], codeine derivatives [12], peptides and their Au(III) complexes, and hydrochlorides and hydrogensquarates [13–15]. It has been found that enough (15–20%) for reasonable linear-polarized IR-spectra orientation is achieved when 5 ± 1 wt% of the compound with particle size within 0.3–0.9 µm are mixed with appropriate for IR-spectroscopy nematic liquid crystal substance. The KBr-plates, which are in advance in one direction, are rubbed out with size 5 µm. The KBr-plates are moved repeatedly with 3 µm/s for 100 times. The optimal cell thickness is 100 µm. The theoretical backgrounds of IR–LD spectroscopy are described in [16–19].

The elemental analysis was carried out according to the standard procedures for C and H (as CO_2 and H_2O) and N (by the Dumas method).

The *thermogravimetric* and *calorimetry* study were performed on a Stanton Redcroft 1500 under argon with heating at $10 \text{ }^{\circ}\text{C/min}$.

¹*H* measurements were made at 298 K with a Bruker DRX-250 spectrometer using CDCl₃ or DMSO- d_6 as the solvent.

The *FAB mass* spectra were recorded on a Fisons VG autospect instrument employing 3-nitrobenzylalcohol (Sigma–Aldrich) as the matrix.

Quantum chemical calculations were performed using GAUSSIAN 98 program package [20] and the output fails were visualized by means of ChemCraft program [21]. Geometries of **4** and **5** (Scheme 2) were optimized at two levels of theory: second-order Moller–Pleset perturbation theory (MP2) and density functional theory (DFT) using

 $6-311++G^{**}$ basis set. In the second case, the B3LYP method, which combines Becke's three-parameter nonlocal exchange functional with the correlation function of Lee et al. [22,23], is applied. Molecular geometries of the studied species were fully optimized by the force gradient method using Bernys' algorithm [24]. For every structure, the stationary points found on the molecule potential energy hypersurfaces were characterized using standard analytical harmonic vibrational analysis. Absence of the imaginary frequencies and negative eigenvalues of the second-derivative matrix confirmed that the stationary points correspond to minima of the potential energy hypersurfaces. The calculation of vibrational frequencies and infrared intensities were checked to see which kind of calculation performed agreed best with the experimental data. In cases of 4 and 5, the DFT method provided more accurate vibrational data, as the calculated standard deviations are 9 cm^{-1} (B3LYP) and 21 cm^{-1} (MP2), respectively. B3LYP/6-311++ G^{**} data are presented for the above discussed modes, where for better correspondence between the experimental and theoretical values, a modification of the results using the empirical scaling factor 0.9614 [25] was made. In the case of MP2 calculations, the scaling factor of 0.8929 was used.

3. Results and discussion

3.1. Theoretical data

3.1.1. Molecule structures

According to quantum chemical calculations at the MP2 and DFT levels of theory, two distinct stable conformers of 4 exist, differing by internal rotation around



Scheme 4. Optimized geometry of (5).

the C2–O5 bond (Scheme 3) with C1–C2–O5–H15 of 0.1° and 177.6° (MP2/6-311++G^{**}), respectively. When energies are corrected by zero point vibrational energy contribution, the first conformer is more stable with 4 kJ/mol. The geometry is characterized with an intramolecular OH...O hydrogen bond with length of 2.781 Å and OHO angle of $111.2(6)^{\circ}$, respectively. Predicted geometrical parameters are summarized in Table 1. The comparison between MP2 and DFT data shows that the *ab initio* approach gives better structural parameters [22,23] with a difference of 9% in some cases. For the purpose of the next IR/LD spectral analysis, where the geometrical prediction of compounds studied is a main

aim, we are focused on the values obtained by MP2/6- $311++G^{**}$. Molecule **4** is absolutely flat excepting both CH₂ groups, which are deviated from co-planarity at angles of 4.3° and 13.9° , respectively (Scheme 3).

The calculated geometrical parameters of **5** are shown in Table 1. Similar to **4**, the geometry of **5** is flat excepting both CH₂ groups disposed at angles of 2.6° and 5.6° towards the plane of the molecule (Scheme 4). Carboxylic groups are co-planar with the plane of the benzene ring with the maximum deviation of 0.6°. The amide C=O and C=C double bonds are co-linear, disposed (5.1°), and lie in a plane supposing the co-linearity of corresponding stretching $v_{C=O}$ (Amide I) and $v_{C=C}$ modes.



Fig. 1. Non-polarized IR-(1) and difference IR-LD (2) spectra of 4 (down) and 5 (up) in nematic liquid crystal suspension.

3.1.2. Vibrational analysis

A comparison between calculated gas-phase and experimental IR-frequencies in solid-state are made for 4 and 5. The calculated IR-spectrum of 4 is characterized with the highest absorption maximum at 3622 cm^{-1} assigned to stretching mode of OH group (v_{OH}) included in intramolecular hydrogen bonding. The band at 3100 cm⁻¹ corresponds to v_{NH} mode. The untypical low-frequency value could be explained with the conjugation of the unpaired electronic couple with quinoide structure in the molecule of 4. The IR-bands within $3500-2500 \text{ cm}^{-1}$ correspond to symmetric and asymmetric stretching modes of CH, CH₂ and CH₃ groups. The 1650–1500 cm⁻¹ IR-spectroscopic region shows a series of bands with mixed character starting with the 1630 cm⁻¹ peak with predominant $v_{C=0}$ character. The bands at 1609 and 1510 cm^{-1} correspond to $v_{C=C}$ stretch, while the band at 1457 cm⁻¹ to stretching $v_{\rm C=C}$ and bending $\delta_{\rm NH}$ modes. Low-frequency shifting of the $v_{C=O}$ shows a stabilization of the quinoide structure in solid-state, due to a conjugation with significant single charge redistribution and distortion of the aromatic character of the phenyl ring in enolic form (Scheme 2). Disappearance of characteristic maxima for 1,2,4,5tetrasubstituted benzene and the observation of typical peaks for conjugated double bonds is also obtained. The maxima at 955 and 944 cm⁻¹ correspond to out-of-plane (o.p.) frequencies of trisubstituted double bonds in the molecule of **4**.

The highest frequency peak in the predicted IR-spectrum of 5 at 3211 cm^{-1} is assigned to the $v_{CH_2}^{as}$ mode of the double bond. The corresponding $v_{CH_2}^{s}$ maximum is predicted at 3002 cm⁻¹. The maxima within $3500-2500 \text{ cm}^{-1}$ IR-spectroscopic region correspond to asymmetric and symmetric CH₂ and CH₃ stretching frequencies, as well as the in-plane (i.p.) vibrations of the aromatic fragment (pseudo 1,2,4,5-tetrasubstituted phenyl [26]). The peaks at 1772 and 1768 cm⁻¹ are assigned to symmetric and asymmetric stretching vibrations of the carboxylic C=O groups, while the peaks at 1662 and 1650 cm⁻¹ correspond to Amide I, and $v_{C=C}$ corresponds to a peak at 1650 cm⁻¹. The band at 980 cm⁻¹ corresponds to the o.p. mode of disubstituted C=C bond. Since the molecule structure excludes the strong intermolecular interactions due to the absence of protondonation groups, excellent correlation



Fig. 2. Non-polarized IR-(1) and reduced IR-LD (2) spectra of 4 after elimination of the peak at 1600 cm⁻¹.



Fig. 3. Non- and deconvoluted (γ factor of 3.8, increment of 1) IR-spectroscopic pattern of **4** in 1650–1550 cm⁻¹ region.

between the calculated and experimentally obtained data are established using the B3LYP/6-311++ G^{**} approach. The calculated standard deviation in the data of **5** is 9 cm^{-1} . It is important to note that the last value is obtained in the cases of the molecular motion connected with the fragments, where intramolecular or intermolecular hydrogen bonding is absent. When the MP2/6-311++ G^{**} approach is used, the obtained difference of 23% between both theoretical methods is connected namely with the last discussed modes.

3.2. Experimental conventional and linear-polarized IR-data

Experimental IR-spectroscopic patterns of **4** and **5** are preliminary deconvolution and curve fitting. The number of peaks and their positions are obtained. The experimental confirmation of IR-characteristic band assignment is achieved by means of linear-polarized IR-spectroscopic spectra and the application of reducing-difference procedure.

The difference IR–LD spectra (Fig. 1) of **4** and **5** show a good orientation of the crystalline samples in the liquid crystal medium, resulting to adequate conclusions of the data obtained by the IR–LD spectra interpretation, using the criteria of [6–8].

The application of the reducing-difference procedure to polarized IR-LD spectra of both compounds resulted in the following data:



Fig. 4. Non-polarized IR-(1) and reduced IR-LD (2) spectra of 4 after elimination of the peak at 1600 cm⁻¹.

4: It can be seen the co-linear disposition of transition moments of $v_{C=O}$ and $v_{C=C}$ of both the trisubstituted double bonds suppose an elimination of corresponding maxima at 1625, 1600, 1504 and 1459 cm^{-1} in equal dichroic ratio, which is obtained experimentally in Fig. 2. In parallel an elimination of 927, 933 and 466 cm^{-1} peaks belonging to o.p. γ_{CH} of disubstituted C=C and OH groups is also obtained. As far as in the frame of one molecule is impossible to be obtained the elimination of i.p. and o.p. maxima in the same dichroic ratio, this result assumes the presence of pairs of molecules in the unit cell of compound studied mutual near to perpendicular oriented. Similar data are observed in the monoclinic polymorphs of paracetamol [11] with space group $P2_I/n$ and Z = 4. The presence of two co-planar by pairs molecules in the unit cell, oriented at an angles about 90° leads to a simultaneous elimination of i.p. and o.p. modes of unsaturated structural fragments in molecules. The procedure gives rise to a second peak at 1631 cm^{-1} (deconvoluted IR-spectroscopic pattern is given in Fig. 3), which reduction does not affect the IR-bands in $1700-400 \text{ cm}^{-1}$. Only the disappearance of the peak at 1377 cm^{-1} is obtained (Fig. 4), supposing a combination character of the band at 1631 cm⁻¹ (1377 + 254). Moreover, vibrational



Fig. 5. Non-polarized IR-(1) and reduced IR–LD (2) spectra of 5 after elimination of the peak at 1644 cm^{-1} .



Fig. 6. TGV and DTA data of dehydrosalsolinol.

analysis shows the same i.p. symmetry class of both eliminated maxima.

5: The data of the obtained vibrational analysis suppose a co-linear disposition of transition moments of Amide I and $v_{C=C}$ in the molecule of **5**, which explains the obtained simultaneous elimination of the peaks at 1656 and 1644 cm⁻¹ (Fig. 5(2)). On the other hand, the obtained reduction of the peaks at 923, 840 and 677 cm⁻¹, are all predicted as o.p. bending modes of 1,2,4,5-tetrasubstituted benzene [26].

3.3. TGV and DTA

The TGV and DTA data of dehydrosalsolinol are presented in Fig. 6. As can be seen in the 100–400 °C temperature range, a weight loss of 8.25% is established which corresponds to an effect of $-19.2 \,\mu\text{V}$ at 272.1 °C. The next weight loss of 13.12% between 303 and 345 °C can be explained with decomposition of the compound studied. The high melting point of dehydrosalsolinol is in accordance with significant dipole moment of 7.392 D derived from quantum chemical calculations and the presence of strong intramolecular hydrogen bond in the molecule.

The complete acetylation of this compound leads to a product which has a higher molecular weight, but lack of hydrogen bond, which results in a significantly lower melting point of $122 \,^{\circ}$ C and dipole moment of 5.085 D.

4. Conclusion

Dehydrosalsolinol and its completely acetylated product were synthesized, and theoretically and experimentally elucidated. On the basis of optical and magnetic spectral and theoretical data, the following essential conclusions were made: (i) the molecule of dehydrosalsolinol exists in solid-state as quinoidal form; (ii) in the solution, a ketoenolic equilibrium is found; (iii) the predicted electronic structures of the keto form of dehydrosalsolinol and its completely acetylated product are planar in the frame of the conjugate systems; (iv) it is proven that during the process of the acetylation, an isomerization takes place, leading to the formation of exocyclic double bound. This was proven unambiguously by means of theoretical and experimental data; (v) the theoretical vibrational and polarized IR-spectroscopy of dehydrosalsolinol show a mixed character of vibrational modes of the quinoline part of the molecule; (vi) the existence of strong intramolecular hydrogen bonds between the OH and O=C groups in the keto form of dehydrosalsolinol, established by IR-spectroscopy, is confirmed by non-empirical quantum chemical calculations.

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