# ELECTRONIC STRUCTURE AND NMR SPECTRA OF SOME DERIVATIVES OF FURANOQUINOLINE, 5,6,7,8-TETRAHYDROFURANOQUINOLINE, AND DIHYDROQUINOLIN-2-ONE ALKALOIDS

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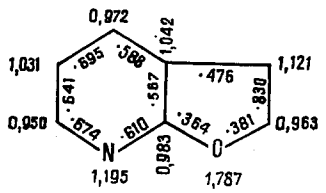
In determining the structure of natural furanoquinoline and dihydroquinolinone alkaloids and their derivatives the method of NMR spectroscopy is widely used [1-11]. Robertson [1], having studied the NMR spectra of many furanoquinoline alkaloids and their derivatives, made an assignment of the signals of the protons. In the assignment of the signals it must be borne in mind that the chemical shifts (CSs) of the protons in the NMR spectra of complex molecules are functions which depend, in the first place, on the electron density and its asymmetry and the magnetic anisotropy and electric field of the dipoles of polar groups and heteroatoms, and also on ring currents within the molecule. Consequently, to make an unambiguous assignment of the CSs of the protons in the NMR spectra it is necessary to take these factors into account quantitatively.

The present paper gives the results of an analysis of the NMR spectra* of some derivatives of the furanoquinoline and dihydroquinolin-2-one alkaloids taking into account factors governing CSs in heteroaromatic systems (Tables 1 and 2). Using the MO LCAO method in Hückel's approximation† we have calculated the $\pi$-electron densities (EDs) on the carbon atoms and the energy characteristics of a number of molecules, making use of B. and A. Pullman's parameters [12].

Below we give the molecular diagrams (MDs), MO energies, total energies of the $\pi$-electrons ($E_\pi$), and the delocalization energies ($DE_\pi$) of compounds (I-VI).

## MOLECULAR DIAGRAMS




I

| Levels | |
|---|---|
| −2,113 | +0,630 |
| −1,420 | 0,945 |
| −1,090 | 1,425 |
| −0,755 | 1,938 |
| | 2,842 |

$E_\pi = 15,560_\beta$; $DE_\pi = 3,120_\beta$

* The spectra were obtained on a JNM-4H-100/100 MHz instrument in $CDCl_3$; 0 − TMS.

† The program for calculation was drawn up and kindly provided by A. V. Tutkevich (Institute of Heteroorganic Compounds, Academy of Sciences of the USSR).

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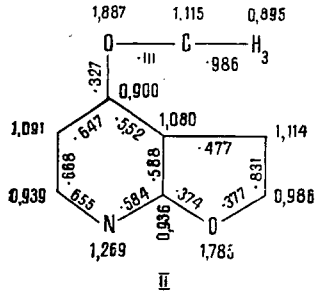
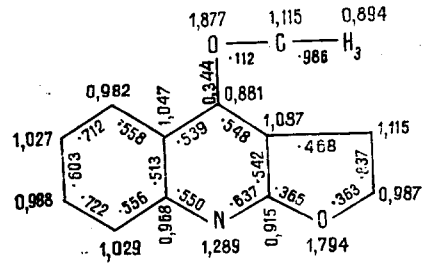



II

Levels

| | |
|---|---|
| −2,300 | +0,538 |
| −2,113 | 0,848 |
| −1,393 | 1,301 |
| −1,096 | 1,527 |
| −0,788 | 1,835 |
| | 2,497 |
| | 2,844 |

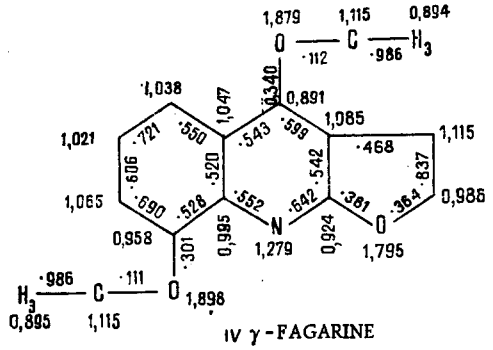
$E_\pi = 22{,}780_\beta$ ; $DE_\pi = 3{,}249$




III DICTAMNINE

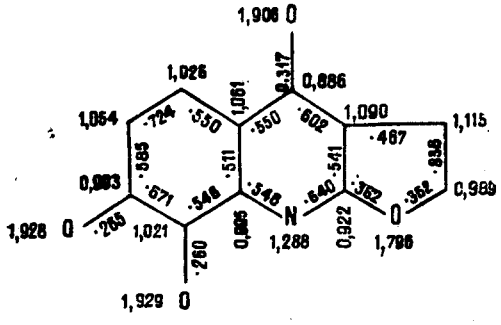
| | |
|---|---|
| −2,356 | +0,850 |
| 2,283 | 1,074 |
| 1,830 | 1,314 |
| 1,360 | 1,503 |
| 1,233 | 1,696 |
| 1,013 | 2,156 |
| 0,584 | 2,529 |
| 0,400 | 2,875 |

$E_\pi = 28{,}994_3$ : $DE_\pi = 4{,}823_\beta$



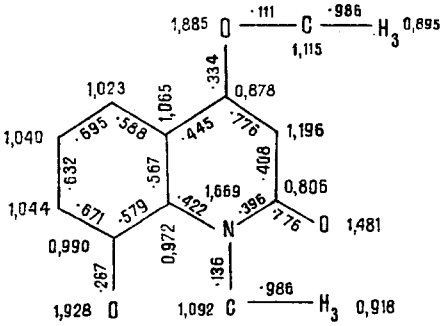

IV γ-FAGARINE

| | |
|---|---|
| −2,373 | +0,348 |
| 2,297 | 0,726 |
| 2,280 | 0,968 |
| 1,851 | 1,305 |
| 1,368 | 1,499 |
| 1,271 | 1,532 |
| 1,024 | 1,712 |
| 0,622 | 2,042 |
| $E_\pi = 36{,}170_3$ | 2,483 |
| $DE_\pi = 5{,}468_\beta$ | 2,589 |
| | 2,881 |




V SKIMMIANINE

| | |
|---|---|
| −2,366 | +0,330 |
| −1,879 | 0,743 |
| −1,371 | 0,836 |
| −1,310 | 1,362 |
| −1,039 | 1,442 |
| −0,633 | 1,910 |
| $E_\pi = 33{,}998_\beta$ | 2,298 |
| $DE_\pi = 5{,}558_\beta$ | 2,497 |
| | 2,691 |
| | 2,890 |




VI FOLIOSIDINE

| | |
|---|---|
| −2,426 | +0,472 |
| 2,306 | 0,616 |
| 2,266 | 1,044 |
| 1,412 | 1,326 |
| 1,962 | 1,605 |
| 1,127 | 1,826 |
| 0,705 | 1,993 |
| $E_\pi = 34{,}008_\beta$ | 2,476 |
| $DE_\pi = 4{,}326_\beta$ | 2,581 |
| | 3,065 |

**TABLE 1. Chemical Shifts and Spin–Spin Coupling Constants of the Protons of the Furan and Aromatic Rings in Some Derivatives of Furanoquinoline and Dihydroquinolin-2-one Alkaloids**

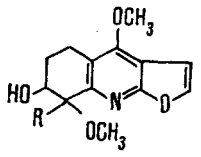
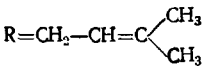
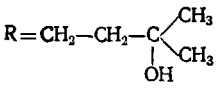
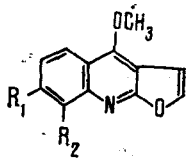
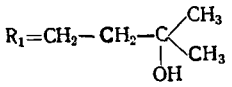
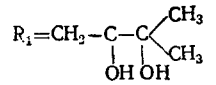
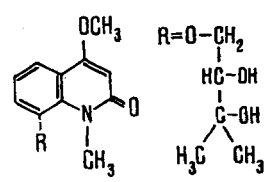
| Substance | Solvent | Chemical shift, ppm | | | | | J, Hz | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | $H_2$ | $H_3$ | $H_5$ | $H_6$ | $H_7$ | $H_{23}$ | $H_{56}$ | $H_{67}$ | $H_{58}$ |
|  | $CDCl_3$ | 7,56 | 6,94 | — | — | — | 2,3 | — | — | — |
|  | | | | | | | | | | |
| Haplophyllidine(I) [6] | | | | | | | | | | |
|  | | | | | | | | | | |
| Perforine (II) [6] | | 7,52 | 6,91 | — | — | — | 2,4 | — | — | — |
|  | | | | | | | | | | |
| $R_1=R_2=H$ | | | | | | | | | | |
| Dictamine (III) [1] | $CDCl_3$ | 7,53 | 6,95 | 7,25 | | 8,30 | — | — | — | — |
| $R_1=H$; $R_2=OCH_3$ | | | | | | | | | | |
| γ-Fagarine (IV) | | 7,60 | 7,00 | 7,80 | 7,35 | 7,03 | 2,3 | 8,0 | 1,5 | 8,0 |
| $R_1=H$; $R_2=OH$ | | | | | | | | | | |
| Robustine (V) | | 7,52 | 6,96 | 7,64 | 7,25 | 7,12 | 2,3 | 8,0 | 2,0 | 8,0 |
|  | | | | | | | | | | |
| $R_2=OCH_3$ | | | | | | | | | | |
| O-Me-folifinine (VI) [7] | $CCl_4$ | 7,47 | 6,92 | 7,95 | 7,07 | — | 2,3 | 9,0 | — | — |
| Diacetylfolifinine (VII) [7] | $CDCl_3$ | 7,55 | 6,97 | 8,10 | 7,12 | — | 2,5 | 9,0 | — | — |
| $R_1=R_2=OCH_3$ | | | | | | | | | | |
| Skimmianine (VIII) | $CDCl_3$ | 7,57 | 7,02 | 8,0 | 7,22 | — | 2,5 | 9,0 | — | — |
|  | | | | | | | | | | |
| $R_2=OCH_3$ Evoxine (IX) [1] | | 7,55 | 6,96 | 7,95 | 7,15 | — | 2,5 | 9,0 | — | — |
| Diacetylevoxine (X) | $CCl_4$ | 7,43 | 6,85 | 7,70 | 6,97 | — | 2,5 | 9,0 | — | — |
| $R_1=OAc$; $R_2=OCH_3$ | | | | | | | | | | |
| Haplopine acetate (XI) | | 7,53 | 6,99 | 7,95 | 7,13 | — | 2,3 | 9,0 | — | — |
|  | $CDCl_3$ | | | | | | | | | |

TABLE 1, (continued)

| Substance | Solvent | Chemical shift, ppm | | | | | J, Hz, ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | $H_2$ | $H_3$ | $H_5$ | $H_6$ | $H_7$ | $H_{23}$ | $H_{56}$ | $H_{57}$ | $H_{58}$ |
| Foliosidine (XII) [4] | $CDCl_3$ | — | — | 7,48 | 7,07 | — | — | — | — | — |
| R=$OCH_3$ | | | | | | | | | | |
| Folimine (XIII) [9] | | — | — | 7,55 | 7,05 | — | — | — | — | — |

The results of a comparison of the values of the $\pi$-electron densities on the $C_2$ and $C_3$ carbon atoms of the furan nucleus in the molecules of (I) with (II-V) (MDs) show that the introduction of the electron-donating substituent $OCH_3$ into position 4 of the pyridine ring affects not only the redistribution of the ED over the corresponding $C_2$ and $C_3$ atoms but also leads to an appreciable decrease in the magnitude of their differences ($\Delta_{2,3}$) from 0.158 in (I) to 0.128 in (II) (MD). At the same time, the condensation of a furano-pyridine with a benzene ring has little effect on the value of the ED at $C_2$ and $C_3$ of the furan nucleus ($\Delta_{2,3}$ = 0.171). The introduction of a methoxy group into various positions of the benzene ring also has practically no effect on these magnitudes.

In a comparison of the CSs of the $H_2$ and $H_3$ protons of the furan nuclei of compounds (I-VI) (see Table 1) with the EDs on the corresponding carbon atoms only a qualitative correspondence is observed, i.e., in all cases a weak-field signal of the $\alpha$-furan protons corresponds to a low value of the ED, and a strong-field signal of the $\beta$ protons to a high value of the ED. The values of the ED on the $C_5$ and $C_6$ carbon atoms of the aromatic nucleus of O-Me-folifinine (VI), skimmianine (VIII), and evoxine (IX) (Table 1) also correlate qualitatively with the CSs of the protons of the corresponding atoms, but not quantitatively. The values of the ED of the aromatic carbon atoms $C_5$, $C_6$, and $C_7$ in $\gamma$-fagarine (IV, MD) and robustine do not correlate with the values of the CSs of the corresponding protons (see Table 1, IV and V). The signals of the $H_5$, $H_6$, and $H_7$ protons in the NMR spectrum of $\gamma$-fagarine give a typical pattern corresponding to a ABC three-spin system, a first-order analysis of which leads to the following values: $\delta^5_C = 7.80$, $\delta^7_A = 7.03$; $\delta^6_B = 7.35$ ppm, $J^{5,6}_{BC} = 8.0$ Hz, $J^{5,7}_{AC} = 1.5$ Hz, $J^{6,7}_{AB} = 8.0$ Hz, i.e., the signal of the $C_5$ proton is found in the weakest field although the ED on it is greater than on the $C_6$ atom. A similar pattern is observed in robustine (V). Consequently, in an analysis of the CSs of the aromatic protons $H_5$, $H_6$, and $H_7$ in $\gamma$-fagarine, robustine, and the other analogous alkaloids, in addition to the EDs of the corresponding carbon atoms, other factors affecting the CSs must be taken into account.

In condensed heteroaromatic compounds, neglecting contributions from intermolecular and dispersion interactions, the CSs of the protons can be represented approximately in the form of the sum of the contributions

$$\sigma=\sigma_A+\sigma_\chi+\sigma_E+\sigma',$$

where: $\sigma_A$ is the atomic contribution to the magnetic screening due to the electronic currents of the given atom;

$\sigma_\chi$ and $\sigma_E$ are the contributions including the magnetic anisotropy and electric field of the intramolecular atoms and groups; and

$\sigma'$ is the sum of the contributions due to the ring currents, magnetic anisotropies ($\sigma^N_\chi$), and electric fields ($\sigma^N_E$) of the heteroatoms.

In calculating the contribution of $\sigma_A$ to the CSs of the aromatic protons $H_5$, $H_6$, and $H_7$ in $\gamma$-fagarine and related compounds, we started from the fact that in aromatic and heteroaromatic compounds the value of $\sigma$ depends linearly on the electron density ($q_\pi$) of the corresponding carbon atoms [13-19], i.e., $\sigma = Kq_\pi$, where the proportionality coefficient K = 7-13.6 ppm per electron. In the calculations we used an average value of K = 10 ppm per electron.

Considering the contributions $\sigma_\chi$ and $\sigma_E$ from $CH_3$ in the CSs of the protons under consideration of $\gamma$-fagarine to be small, we took into account the contributions $\sigma_\chi$ and $\sigma_E$ from the $C_4-O$ and $C_8-O$ bonds on the CSs of the $H_5$, $H_6$, and $H_7$ protons in accordance with the McConnell [20] and Buckingham-Musher relations [21, 22]. The contributions of the ring current of the pyridine ring and the contributions of the magnetic anisotropy and electric field of the heteroatom on the CSs of the $H_5$, $H_6$, and $H_7$ protons were borrowed from the results of a calculation for quinoline [17]. For a comparison between the calculated and experimental values of the CSs of the $H_5$, $H_6$, and $H_7$ protons, see Table 2.

It can be seen from Table 2 that although there is no strict correlation between the calculated and observed CSs of the aromatic protons $H_5$, $H_6$, and $H_7$ in $\gamma$-fagarine and robustine, nevertheless, this approach

TABLE 2. Changes in the CSs of the Aromatic Protons $H_5$, $H_6$, and $H_7$ Due to the Effects of Magnetic Anisotropy ($\Delta\delta$), the Electric Field ($\Delta\delta_E$) of the $C_4-O$ and $C_8-O$ Bonds and of the Heteroatom N, of the Ring Current, and of $\Delta\delta_A$ in $\gamma$-Fagarine and Robustine, ppm*

| Proton | $\Delta\delta_\chi^{C_4-O}$ | $\Delta\delta_\chi^{C_8-O}$ | $\Delta\delta_E^{C_4-O}$ | $\Delta\delta_E^{C_8-O}$ | $\Delta\delta_\chi^{N}$ | $\Delta\delta_E^{N}$ | $\Delta\delta$ ring current | $\Delta\delta_A$ rel. $C_6H_6$ | $\Sigma\Delta\delta$ | calc. CS $\Delta\nu=7{,}24+\Sigma\Delta\delta$ | Experiment, CS: $\gamma$-fagarine | Experiment, CS: robustine |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $H_5$ | 0,12† | 0,0 | —0,33 | 0,0 | 0,0 | —0,06 | —0,38 | 0,38 | —0,27 | 7,51 | 7,80 | 7,64 |
| $H_6$ | 0,01 | 0,0 | —0,05 | 0,0 | 0,0 | —0,03 | —0,17 | 0,27 | 0,03 | 7,21 | 7,35 | 7,25 |
| $H_7$ | 0,0 | 0,08 | 0,0 | —0.49 | 0,0 | —0,03 | —0,17 | 0,65 | 0,04 | 7,20 | 7,03 | 7,12 |

* The calculations were performed by using the following parameters of the molecule [23, 24]: 1C—O = 1.43 A°; C—H = 1.09 A°; C = C = 1.34 A°; ∠C = C—O = 120°; ∠C = C—H = 120°, $\mu_{C-O}$ = 0.86 D; $\Delta\chi_{C-O}$ = 5.3. $10^{-6}$ cm$^3$/mole.

† The absence of sign denotes an upfield shift and the sign — a downfield shift.

permits a correct assignment of the signals in the NMR spectrum to be made. Furthermore, a substantial influence on the CS of the proton at $C_5$ in (IV) and (V) is made by contributions due to the ring currents of the pyridine nucleus and the electric field of the $C_4-O$ bond. So far as concerns the cause of the difference between the calculated values of the CSs of the $H_5$, $H_6$, and $H_7$ protons in (IV) and (V) and the experimental values, they are obviously the following: the approximate values of the EDs according to the simple Hückel method used in the present work; the use of the contributions $\Delta\delta_\chi^{C-O}$ and $\Delta\delta_E^{C-O}$ in the dipole approximation; the neglect of the anisotropic contribution from the lone pairs of electrons of the oxygen atom [24]; and the influence of the $\sigma$-electrons on the CSs of $H_5$, $H_6$, and $H_7$. In spite of these limitations, the evaluation of the other contributions permits an unambiguous identification of the signals of the aromatic protons in the NMR spectra of derivatives of the furanoquinoline and dihydroquinolinone alkaloids. The following is an illustration of what has been said: in a qualitative consideration of the signals of the aromatic protons of the alkaloid foliosidine (XII, Table 1) we [4] previously assigned the weak-field signal at $\delta$ 7.48 ppm to the $H_7$ proton. The facts given above (see Table 2) and the values of the EDs for the $C_5$, $C_6$, and $C_7$ atoms (MD of (VI)) show that the signal at $\delta$ 7.48 ppm in the NMR spectrum of foliosidine is due to the $H_5$ proton.

## CONCLUSIONS

1. The $\pi$ charges, the bond orders, and the energy characteristics of 12 derivatives of furanoquinoline and dihydroquinolin-2-one alkaloids have been calculated by the MO LCAO method in Hückel's approximation.

2. It has been established that the CSs of the $\alpha$- and $\beta$-protons of the furan ring are qualitatively comparable with the EDs on the corresponding carbon atoms $C_2$ and $C_3$, and the CSs of the aromatic protons of $\gamma$-fagarine and robustine do not correlate with the values of the EDs of the corresponding carbon atoms.

3. By performing quantitative calculations of the contributions due to the CSs, it has been shown that a substantial contribution is made to the CSs of $H_5$ in $\gamma$-fagarine, robustine, and other related compounds by $\Delta\delta_{r.c.}$ of the pyridine ring and $\Delta\delta_E^{C-O}$ of the C—O bond of the $OCH_3$ group at $C_4$; the assignment of the signals of the aromatic protons of foliosidine has been refined.

## LITERATURE CITED


1. A. V. Robertson, Austr. J. Chem., 16, 451 (1963).
2. R. H. Prager, E. Ritchie, A. V. Robertson, and W. C. Taylor, Austr. J. Chem., 15, 301 (1962).
3. S. R. Johns, J. A. Lamberton, and A. A. Simons, Austr. J. Chem., 20, 1975 (1967).
4. M. R. Yagudaev and S. Yu. Yunusov, Khim. Prirodn. Soedin., 201 (1968).
5. Z. Sh. Faizutdinova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 360 (1968).
6. I. A. Bessonova, Z. Sh. Faizutdinova, Ya. V. Rashkes, M. R. Yagudaev, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 273 (1969).

7. D. Kurbanov, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 58, 373 (1968).
8. V. A. Tel'nov, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 724 (1970).
9. D. M. Razzakova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 133 (1972).
10. S. M. Sharafutdinova and S. Yu. Yunusov, Khim. Prirodn. Soedin., 394 (1969).
11. Z. Sh. Faizutdinova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 455 (1969).
12. B. Pullman and A. Pullman, Quantum Biochemistry, Wiley (1963).
13. G. Fraenkel, R. E. Garter, N. McLachlan, and J. H. Richards, J. Amer. Chem. Soc., 82, 5846 (1960).
14. H. Spiesecke and W. G. Shneider, Tetrahedron Lett., 468 (1961).
15. G. G. Dvoryantseva, V. P. Lezina, V. F. Bystrov, T. N. Ul'yanova, G. P. Syrova, and Yu. N. Sheinker, Izv. Akad. Nauk SSR, Ser. Khim., No. 5, 994 (1968).
16. A. H. Gawer and B. P. Dailey, J. Chem. Phys., 42, 2658 (1965).
17. P. J. Black, R. A. Brown, and M. L. Heffernan, Austr. J. Chem., 20, 1305, 1325 (1967).
18. T. B. Cobb and J. D. Memory, J. Chem. Phys., 50, 4262 (1969).
19. G. G. Dvoryantseva, L. M. Alekseeva, T. N. Ul'yanova, Yu. N. Sheinker, P. M. Kochergin, and A. N. Krasovskii, Khim. Geterotsikl. Soedin., No. 7, 937 (1971).
20. H. M. McConnell, J. Chem. Phys., 27, 226 (1957).
21. A. D. Buckingham, Can. J. Chem., 38, 300 (1960).
22. R. F. Zürcher, Progr. Nuc. Mag. Res. Spectrosc. 2, Ch. 5 (1967).
23. Yu. Yu. Samitov, Dokl. Akad. Nauk SSSR, 164, 347 (1965).
24. A. V. Bogatskii, Yu. Yu. Samitov, N. L. Garkovik, and S. A. Andronati, Khim. Geterotsikl. Soedin., No. 2, 195 (1967).