2. V. K. Daukshas, R. S. Martinkus, V. L. Geneitite, and S. L. Urbonene, Khim. Geterotsikl. Soedin., No. 9, 1215 (1982).
3. C. Kisast and L. F. Teitre, Angew. Chem., 88, 261 (1976).

PORPHYRINS.

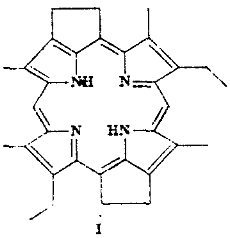
22.* SYNTHESIS OF PORPHYRINS WITH TWO CYCLOPENTANE RINGS

G. V. Ponomarev and A. M. Shul'ga

UDC 547.514.1'979.733.07:542.921.7:543.422

The Vilsmeier formylation of meso-methylporphyrins and a porphyrin with a cyclopentane ring was investigated. A meso substituent increases the ability of free meso positions to undergo electrophilic substitution reactions. Schiff bases of meso-formylporphyrins were subjected to thermolysis, and a porphyrin with two cyclopentane rings was synthesized for the first time.

Recent years have been marked by significant advances in the study of "geological" porphyrins isolated from petroleum oils, bitumens, shales, and sedimentary rocks [2, 3]. It has been accurately established that "geological" porphyrins are complex mixtures of compounds consisting primarily of two major and three "minor" homologous series of vanadyl and/or nickel complexes: a) the etioporphyrin series; b) the desoxophylloerythroetioporphyrin series; c) the didesoxophylloerythroetioporphyrin series; d) the rhodoetioporphyrin series; e) the rhododesoxophylloerythroetioporphyrin series (in other words, the M–, M–2, M–4, M–6, and M–8 series, respectively [3]). The structures of some porphyrins of the major series have been established [2, 4-6], but reliable information relative to the structures of porphyrins of the "minor" series, viz., M–4, M–6, and M–8, is not available in the literature. It has been suggested, for example, that compounds of the M–4 series are porphyrins with two saturated rings of the I or II type, while structures of the benzoporphyrin III and IV type correspond to porphyrins of the M–6 and M–8 series [3].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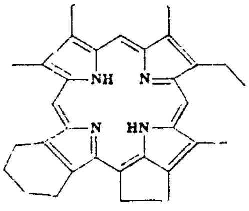
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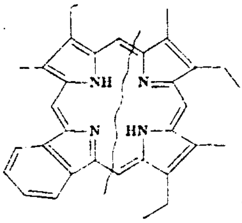
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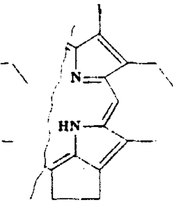
IV

To investigate the spectral and chromatographic characteristics of compounds of the M–4 series we attempted to synthesize model porphyrins containing two five-membered exocycles. We assumed that they might be synthesized by thermolysis of the corresponding Schiff bases of diformylporphyrins, for example, porphyrin V, to a mixture of porphyrins VI and VII by the method that we previously developed for the synthesis of monocyclopentanoporphyrins [7].

We found that pronounced destruction of the substance occurs in the thermoloysis of Schiff base V, and only porphyrins with one cyclopentane ring are formed in low yield. The absence in the products of thermolysis of porphyrins of the M–4 series is probably due to the formation of unstable intermediate porphyrins of the VIII type.

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*See [1] for communication 21.

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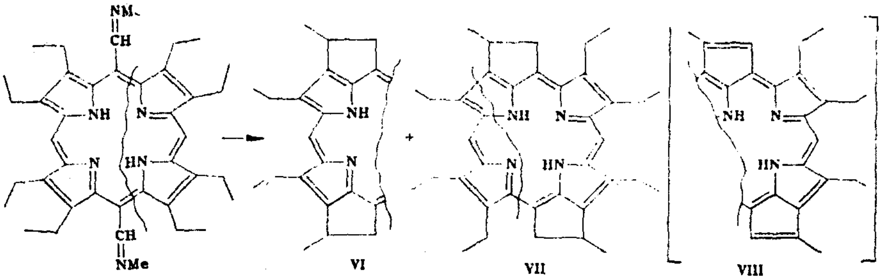
0009-3122/87/2307-0757$12.50

TABLE 1. PMR Spectra of Porphyrins IX-XIV*

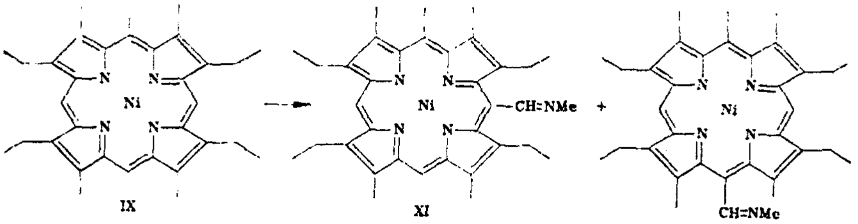
Compound	δ, ppm					
	meso-H	meso-CH_3	Ring CH_3	CH_2	CH_3	meso-CH = N − CH_3
IX	9,40 [10, 15, 20]	3,81	3,41; 3,7 3,36; 13,17	3,805 3,80	1,71; 2,8 1,68; 12,18	
X	9,38 [10, 20] 9,33 [15]	3,85	3,34; 2,8 3,33; 12,18	3,88 3,79	1,71; 3,7 1,69; 13,17	
XI	9,27 [15, 20]	3,63	3,305; 3,0 3,30; 7,0 3,26; 17,0 3,25; 13,0	3,71 3,71 3,54 3,54	1,68; 2.0 1,68; 18,0 1,49; 8,0 1,42; 12,0	10,65; 3,31
XII	9,21 [10, 20]	3,71	3,33; 3,7 3,10; 13,17	3,71	1,64	10,56; 3,82
XIII	9,15 [20] 9,11 [15]	3,69; 3,0	3,26; 2.18 3,06; 12,0 3,04; 8,0	3,78 3,68 3,70	1,65 1,63 1,62	10,46; 3,80
XIV	9,19 [10, 20]	3,74	3,25; 2,8; 12,18	3,80 3,56	1,66; 3,7 1,48; 12,18	10,59; 3,73

*The numbering of the substituent is indicated in brackets. The signals of the $-CH{=}N{-}CH_3$ group appear in the form of a quartet and a doublet (J = 1.8 Hz), the signals of the C_2H_5 group show up in the form of a quartet and a triplet (J = 7.5 Hz), and the remaining protons show up in the form of singlets.

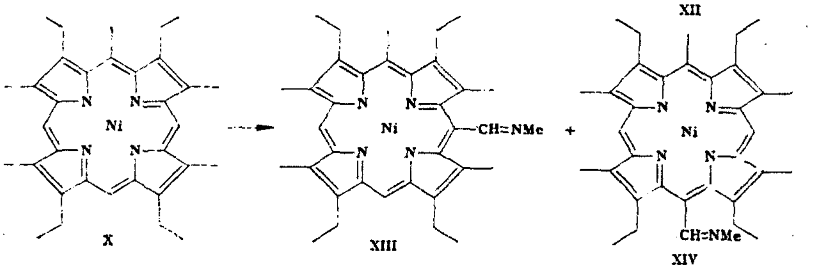


V VI VII VIII

Since the direct synthesis of dicyclopentanoporphyrins was unsuccessful, we decided to obtain a porphyrin with one cyclopentane ring and use it for the synthesis of a new Schiff base, the thermolysis of which may lead to the desired result. Since Vilsmeier formylation of porphyrins with a cyclopentane ring has not been described in the literature, we initially studied the formylation of two model compounds — derivatives of meso-methyletioporphyrin-II — IX and X.



IX XI XII



X XIII XIV

The presence of a meso-methyl group in porphyrins IX and X leads to an appreciable increase in the reactivity of the molecule in electrophilic substitution; this is manifested in decreasing the reaction time by a factor of 10 to 15 as compared with the formylation of meso-unsubstituted etioporphyrin-II [8].

TABLE 2. PMR Spectra of XV and XVII

Protons	δ, м. д.			
	XV	XVII	ONE XV	ONE XVII
20-H	9,49 s	9,96 s	3,84	3,66; 3,55
15-H	9,47 s	9,82 s	3,84	4,09; 3,94
10′-CH_2	5,03 m	5,34 m		
5-CH_3	4,03 s	4,59 s	3,93; 3,97	4,13; 4,08
8′-CH_2	3,99 m	4,05 m		
7-C_2H_5	3,97 q	4,08 q		
	1,85 t	1,91 t		
3-C_2H_5	3,93 q	4,13 q		
	1,70 t	1,82 t		
13,17-C_2H_5	3,84 q	4,09 q, 3,98 q		
	1,73 t	1,84 t, 1,84 t		
	1,74 t			
2-CH_3	3,39 s	3,66 s	9,49; 3,93	9,96; 4,13
18-CH_5	3,38 s	3,55 s	9,49; 3,84	9,96; 3,98
12-CH_3	3,34 s	3,57 s	5,03; 3,84	5,34; 4,09

A mixture of isomers XI and XII in a ratio of 1:1 is formed in the formylation of complex IX, while a mixture of isomers XIII and XIV in a ratio of 9:1 [according to data from the PMR spectra and the results of thin-layer chromatography (TLC) on Silufol] is formed in the formylation of complex X. This result constitutes evidence for an appreciable steric effect of the β-alkyl substituents on the reaction, as in the formylation of complexes of etioporphyrin-II [8].

Isomers XI, as well as XIII and XIV, can be separated by means of TLC on Silufol; the structures in which the azomethine groups are located between adjacent β-ethyl substituents correspond to the more mobile isomers.

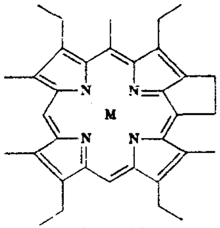
The structures of the isomers were established by means of the PMR spectra (Table 1). The introduction of a methyl group in the meso position of the porphyrin ring leads to a shift of the signals of the protons of the ring methyl substituents to weak field, while the introduction of an N-methylformaldimino group leads to a shift to strong field. These results also served as a basis for the interpretation of the PMR spectra.

In studying the thermal cyclization it is desirable to use individual isomers in order to avoid the formation of a mixture of porphyrins. Since the chromatographic separation of the isomers of the Schiff bases and their isolation in any significant amounts constitute an extremely laborious task, for the thermolysis we selected a mixture of isomers XIII and XIV containing primarily isomer XIII. Since the formation of two similarly constructed isomers, viz., XV and XVI, form complex XIII is possible in the cyclization process, the accurate establishment of the structure of the thermolysis product as XV was made on the basis of an analysis of its PMR spectrum with the use of the Overhauser nuclear effect (ONE) (Table 2).

In the case of irradiation of the CH_3 group (3.34 ppm) in the differential spectrum one observed intensification of the signal of the methyl group of the cyclopentane ring in the 10^1 position and of the signal of the CH_2 group (3.84 ppm) of the ethyl substituent. Irradiation of the methylidyne proton (9.47 ppm) leads to intensification of the quartet (3.84 ppm) belonging to the two ethyl groups in the 13 and 17 positions. Irradiation of the CH_3 group (3.39 ppm) leads to intensification of the signal of the methylidyne proton in the 20 position and of the quartet at 3.39 ppm, intensification of which is also observed in the case of irradiation of the CH_3 group in the 5 position. The interrelationship of the side substituents detected by the ONE method corresponds to the structure of complex XV. Demetallation of complex XV yielded porphyrin XVII with a typical phyllotype of electronic spectrum, which, with respect to the intensities of the bands, differed from the spectra of both meso-methylporphyrins and porphyrins with a cyclopentane ring (see scheme on following page).

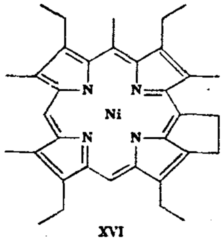
Thus, despite the low yield of porphyrin XVII (~5%), which is due to significant destruction of complex XIII in the thermolysis process, the results obtained provide evidence for the possibility of the construction of a cyclopentane ring in porphyrins with two meso substituents.

We then studied the formylation of porphyrins with a cyclopentane ring. To avoid the formation of a large number of isomeric dicyclopentanoporphyrins in the cyclization process we selected complex XVIII, the synthesis of which we accomplished in [8], as the subject of investigation.



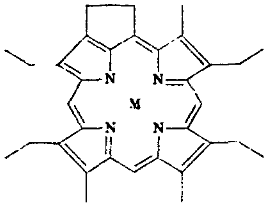
XV, XVII

XV M=Ni; XVII M=2H

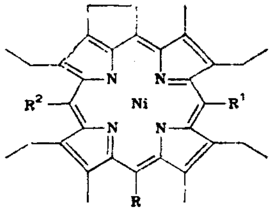


XVI

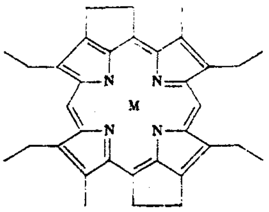
As a result of formylation, which proceeds just as readily as for meso-methylporphyrins, and subsequent treatment of the reaction mixture with methylamine, the formation of all three possible isomers — XIX, XX, and XXI — was detected by TLC on Silufol. It follows from the PMR spectral data that the principal products are complexes XIX and XX in a ratio of 4:1, while isomer XXI is present in trace amounts.



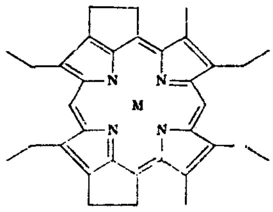
XVIII, XXVI



XIX–XXI



XXII, XXIV



XXIII, XXV

XVIII, XXII, XXIII M=Ni, XXIV–XXVI M=2H; XIX R=CH=NMe, $R^1=R^2=H$; XX $R=R^2=H$, $R^1=CH=NMe$; XXI $R=R^1=H$, $R^2=CH=NMe$

For the preparative synthesis of the dicyclopentanoporphyrin we carried out the thermolysis of the mixture of XIX and XX, since it is known [8] that the formation of an unsubstituted cyclopentane ring is the primary process in thermolysis, and the formation of dicyclopentanoporphyrins from isomer XX is unlikely. A substance corresponding, according to the mass-spectral data, to a porphyrin with two cyclopentane rings with a small amount of admixed starting complex XVIII was isolated by chromatography from the mixture of thermolysis products. It followed from the PMR spectral data that the dicyclopentanoporphyrin is a mixture of isomers XXII and XXIII in a ratio of 4:1. Three signals of meso protons at 9.83, 9.81, and 9.80 ppm with an intensity ratio of 1:2:1 are observed in the PMR spectrum of the dicyclopentanoporphyrin; this corresponds to symmetrical and unsymmetrical orientations of the two exocycles in the porphyrin molecule relative to the meso protons, i.e., to isomers XXII and XXIII. Correspondingly, the signals from the ring methyl protons appear in the form of two singlets, and consequently isomers XXII and XXIII are symmetrical relative to the methyl substituents.

A mixture of isomers XXIV and XXV with a phyllotype of electronic spectrum was isolated after demetallation. With respect to their chromatographic properties, porphyrins XXIV/XXV proved to be significantly more polar than the porphyrin with one cyclopentane ring (XXVI); this made it possible to isolate them in the individual state by means of chromatography on Silufol.

Thus we have demonstrated the possibility of the synthesis of porphyrins with two cyclopentane rings. Data on the chromatographic mobilities and from the electronic, PMR, and mass spectra of the porphyrins obtained can be used in the search for, isolation of, and establishment of the structures of "geological" porphyrins, since we are confident that porphyrins that are structurally similar to XXIV or XXV will be isolated from natural sources.

EXPERIMENTAL

The electronic spectra of solutions of the compounds in chloroform were recorded with a Hitachi-320 spectrophotometer. The PMR spectra of solutions in $CdCl_3$ were obtained with a Bruker WM-360 spectrometer with tetramethylsilane (TMS) as the internal standard. The electron-impact mass spectra were recorded with a Varian MAT-311 spectrometer; the mass spectra of the nickel complexes of the porphyrins are presented for the Ni^{58} isotope.

Nickel Complex (XI) of 10-(N-Methylformaldimino)-3,5,7,13,17-pentamethyl-2,8,12,18-tetraethylporphyrin and Nickel Complex (XII) of the 15-(N-Methylformaldimino) Isomer. A 100-mg sample of complex IX (obtained from the corresponding porphyrin [9] and nickel acetate by heating in DMF; quantitative yield) was added to the Vilsmeier complex obtained from 0.3 ml of $POCl_3$ and 1 ml of DMF, 10 ml of dichloroethane was added, and the mixture was heated at 60-70°C for 1 min. It was then cooled and treated with 5 ml of a 25% solution of methylamine. After 5 min, 50 ml of chloroform was added, and the solution was washed with 100 ml of water. The organic layer was separated and concentrated to 10 ml, and the concentrate was chromatographed with a column (3.5 × 10 cm) packed with silica get by elution with chloroform. The principal fraction was evaporated to give an uncrystallized mixture of Schiff bases in 90-95% yield. For the isolation of individual isomers XI and XII, part of the substance was chromatographed on Silufol plates in a chloroform–ether system (9:1). The more mobile XI isomer had R_f 0.6, and isomer XII had R_f 0.5. Mass spectrum of isomer XI:* 589 (M^+, 24), 574 (9), 560 (91), 558 (100), 543 (33. Mass spectrum of isomer XII: 589 (M^+, 40), 574 (15), 560 (56), 558 (100), 543 (33). According to the PMR spectral data, XI/XII = 1:1. The PMR spectra of individual isomers XI and XII are presented in Table 1.

Nickel Complex (XIII) of 10-(N-Methylformaldimino)-2,5,8,12,18-pentamethyl-3,7,13,17-tetraethylporphyrin and Nickel Complex (XIV) of the 15-(N-Methylformaldimino) Isomer. These complexes were obtained from complex X by a procedure similar to that used to prepare complexes XI and XII. The XIII/XIV ratio was 9:1. The more mobile XIV isomer had R_f 0.6, and isomer XIII had R_f 0.5. Mass spectrum of isomer XIV: 589 (M^+, 32), 574 (10), 560 (80), 558 (100), 543 (20). Mass spectrum of isomer XIII: 589 (M^+, 52), 574 (13), 560 (59), 558 (100), 543 (26). The PMR spectra of individual isomers XIII and XIV are presented in Table 1.

$8^1,10^1$-Cyclo-2,5,12,18-tetramethyl-3,7,13,17-tetraethylporphyrin (XVII). A mixture of isomers XIII/XIV obtained from 400 mg of complex X was heated for 10 min at 300-310°C in vacuo ($1 \cdot 10^{-2}$ mm), after which it was cooled and chromatographed with a column (3.5 × 30 cm) packed with silica gel by elution with CCl_4. The fraction with the principal mobile substance was evaporated in vacuo, the residue was refluxed for 5 min in 100 ml of hexane, and the mixture was filtered. According to the PMR spectral data, the filtrate contained primarily a mixture of isomers IX and X. The residue was dissolved in 10 ml of a mixture of chloroform with benzene (1:2) and chromatographed with a column (3.5 × 40 cm) packed with aluminum oxide (activity II) by successive elution with mixtures of chloroform with benzene (1:4, 1:3, and 1:2). After elution of the most mobile complexes IX and X, the most polar zone was removed from the column mechanically and subjected to additional purification with a column (3.5 × 20 cm) packed with silica gel by elution with CCl_4; crystallization from chloroform–methanol gave 22 mg (5% based on complex X) of complex XV. UV spectrum of complex XV, λ_{max} ($\varepsilon \cdot 10^{-3}$): 405 (196), 524 (10.6), 564 nm (9.4). Porphyrin XVII was obtained in 79% yield by demetallation of complex XV in concentrated H_2SO_4. Mass spectrum of porphyrin XVII: 504 (M^+, 100), 489 (18), 475 (6). UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 407 (134), 508 (15.5), 543 (3.4), 573 (6.1), 625 nm (2.1).

$3^1,5^1;13^1,15^1$-Dicyclo-7,17-dimethyl-2,8,12,18-tetraethylporphyrin (XXIV) and $3^1,5^1;15^1;17^1$-Dicyclo-7,13-dimethyl-2,8,12,18-tetraethylporphyrin (XXV). A solution of 150 mg of complex XVIII and the Vilsmeier complex from 2 ml of $POCl_3$ and 2.5 ml of DMF in 50 ml of dichloroethane was heated for 5 min at 70°C, after which it was cooled and treated with 30 ml of an aqueous solution of methylamine. The mixture was stirred for 10 min, after which the organic layer was washed with 200 ml of water and evaporated to dryness in vacuo. The residue was chromatographed with a column (3.5 by 10 cm) packed with silica gel by elution wich chloroform, and the product was crystallized from chloroform–methanol to give 115 mg (71%) of XIX/XX in a ratio of 4:1 (according to the PMR spectral data, from the intensities of the signals of the meso protons at 9.67 and 9.66 ppm for isomer XIX and at 9.61 and 9.59 ppm for ixomer XX). Mass spectrum of XIX/XX: 587 (M^+, 41), 572 (9), 558 (64), 556 (100), 546 (40). A 100-mg sample of the XIX/XX mixture was heated in vacuo (0.01 mm) for 6 min at 300-305°C, after which

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*Here and subsequently, the m/z values (and the relative intensities in percent) are presented.

it was cooled and chromatographed with a column (3.5 × 30 cm) packed with silica gel. The principal fraction was evaporated to dryness, the residue was refluxed in 50 ml of CCl_4 for 5 min, and the mixture was filtered. The solid material was dissolved in 10 ml of concentrated H_2SO_4; after 1 h, the mixture was poured over 100 g of ice, and the substance was extracted with three 50-ml portions of chloroform. The solvent was evaporated in vacuo to give 20 mg of a mixture of porphyrins XXIV and XXV containing, according to the mass-spectral data, 20-25% admixed porphyrin XXVI. To obtain a sample of XXIV/XXV that does not contain porphyrin XXVI a part of the product was chromatographed on plates with Silufol by elution with chloroform with ventilation of the plate with ammonia vapors. Porphyrin XXVI had R_f 0.7, and XXIV/XXV had R_f 0.5. Mass spectrum of XXIV/XXV: 502 (M^+, 100), 487 (37), 473 (10). UV spectrum, λ_{max} (intensity ratio): 404 (14.4), 504 (1.0), 540 (0.37), 569 (0.43), 620 nm (0.28). PMR spectrum of XXIV/XXV ($CDCl_3$ + 1% CF_3COOH): 10.60 and 10.44 (meso-H, XXV); 10.53 (s, meso-H, XXIV); 5.70 (m, $5^1,15^1$-CH_2); 4.44 (m, $3^1,13^1,17^1$-CH_2); 4.18 and 4.17 (q, CH_2CH_3); 3.70 (s, CH_3, XXV); 3.73 (s, CH_3, XXIV); 2.0 and 1.77 (two t, CH_2CH_3, XXV); 1.98 and 1.80 (t, CH_2CH_3, XXIV); −4.43 ppm (s, NH).

LITERATURE CITED

1. G. B. Maravin, G. V. Ponomarev, and A. M. Shul'ga, Khim. Geterotsikl. Soedin., No. 2, 214 (1987).
2. P. Sundararaman, Anal. Chem., 57, 2204 (1985).
3. G. Eglinton, R. P. Evershed, J. P. Gill, and C. S. Hein, Anal. Proc., 22, 263 (1985).
4. R. Okampo, H. J. Callott, and P. Albrecht, Chem. Commun., No. 4, 200 (1985).
5. R. Okampo, H. J. Callott, and P. Albrecht, Chem. Commun., No. 4, 198 (1985).
6. M. I. Chicarelli, G. A. Wolff, and J. R. Maxwell, Chem. Commun., No. 11, 723 (1985).
7. G. V. Ponomarev, A. M. Shul'ga, and V. P. Suboch, Dokl. Akad. Nauk SSSR, 259, 1121 (1981).
8. G. V. Ponomarev and A. M. Shul'ga, Khim. Geterotsikl. Soedin., No. 4, 479 (1984).
9. A. M. Shul'ga and G. P. Gurinovich, Dokl. Akad. Nauk Belorusk. SSR, 25, 55 (1981).

Z,E ISOMERISM OF 1-FORMYL- AND 1-ACETYL-2-PYRAZOLINES

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UDC 543.422.25:547.776

The conformational equilibrium in the 1-acyl-2-pyrazoline series caused by retarded rotation about the $N_{(1)}$—CO bond in the case of protonation of the $N_{(2)}$ atom was studied by NMR spectroscopy.

It was previously established by measurement of the dipole moments and PMR spectroscopy that 1-acyl-2-pyrazolines in low-polarity solvents exist in the s-trans form relative to the $N_{(1)}$—Co bond (E isomers) because of repulsion of the like-charged nitrogen and oxygen atoms [1, 2]. It might be assumed that in solvents with high dielectric permeabilities, which partially compensate this effect, the probability of the existence of the Z conformer increases, particularly in the case of favorable steric factors. Precisely this principle is followed in related series of hydrazides [3], acylhydrazones [4], and acylamidrazones [5]. In addition, it has been shown [4] that 1-formyl-3,5,5-trimethyl-2-pyrazoline, which is the E isomer in CCl_4, is a mixture of the Z and E forms in aqueous solution. Taking this into account, we examined the phenomenon of Z, E isomerism for a series of 1-formyl- and 1-acetyl-2-pyrazolines (I-XIV) by means of ^1H and ^{13}C NMR spectroscopy (see scheme on following page).

The data from the PMR spectra of I-XIV in inert and low-polarity solvents are in complete agreement with the data presented in [1, 2] and indicate the existence of a single isomer.

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