Chemistry of Heterocyclic Compounds, Vol. 31, No. 3, 1995

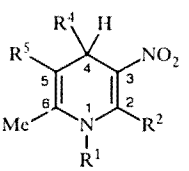
FREE RADICALS IN ELECTROCHEMICAL REDUCTION OF DERIVATIVES OF 3-NITRO-1,4-DIHYDROPYRIDINES

Ya. Stradyn', L. Baumane, R. Gavars, B. Vigante, and G. Dubur

By means of ESR, under conditions of electrochemical generation of particles, the formation of four types of secondary free radicals has been confirmed in the process of electrochemical reduction of molecules of N-unsubstituted derivatives of 3-nitro-1,4-dihydropyridine in dimethylformamide - specifically, a dianion radical of the molecule of the original compound; an anion radical of the corresponding isomeric 4,5-dihydropyridine; a radical of the nitroalkane type; and in addition, for the compound substituted with a nitrobenzene group, a free radical with the nitrobenzene structure. Methods for synthesis of the individual compounds are described, and a scheme is presented for the mechanism of their electrochemical conversion.

In searches for new medicinal substances, compounds of the 1,4-dihydropyridine series substituted with a nitrophenyl grouping continue to occupy an important place [1]. It was shown in [2-5] that during the course of electrochemical reduction of such compounds, the same as in the case of nitro-substituted furans [6, 7], not only the primary anion radicals but also certain radicals with a different structure may be formed; these are accessible for investigation by means of ESR under conditions of their electrochemical generation. In this area of research, however, less attention has been given to compounds having a nitro group located immediately on the dihydropyridine ring, even though in studies of similar compounds in the pyridine series it has been shown that during the course of their electrochemical reduction, both primary anion radicals [8] and secondary free radicals [9] may be formed.

In continuing our studies of free radicals formed in the electrochemical reduction of nitro derivatives of dihydropyridine compounds, we have used polarography and cyclic voltammetry to determine the electrochemical characteristics of the 3-nitro-1,4-dihydropyridines (I-XIII); we have also accomplished the electrochemical generation [10] of the corresponding free radicals and have registered the hyperfine structure of the ESR spectra of the resulting radicals.



I–XIII

I, II, IV-VI, VIII-XIII) R^1 = H; III, VII) R^1 = Me; I, III, IV, VI-XIII) R^2 = H; II, V) R^2 = Me; I-V) R^4 = C_6H_5; IX) R^4 = m-$O_2NC_6H_4$; VIII, XIII) R^4 = o-$CH_3OC_6H_4$; VI, VII, XII) R^4 = o-$CHF_2OC_6H_4$; X, XI) R^4 = p-$CH_3OC_6H_4$; IV-X) R^5 = COOMe; I-III) R^5 = COOEt; XI-XIII) R^5 = CN.

Latvian Institute of Organic Synthesis, Riga LV-1006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 355-364, March, 1995. Original article submitted February 21, 1995.

0009-3122/95/3103-0307$12.50

TABLE 1. Potential ($E_{1/2}$, V, Relative to Aqueous Saturated Calomel Electrode) and Standard Values of Limiting Current (i, μA) of Polarographic Waves, and Reversibility (+) of Electron Transfer in Individual Stages of Electrochemical Reduction with a Potential Sweep Rate of 50 mV/sec, for Compounds I-XIII in Dimethylformamide, with Background Electrolyte 0.1 M $(C_4H_9)_4NPF_6$

Compound	R^1	R^2	R^4	R^5	$-E_{1/2}$ (i, +)
I	H	H	C_6H_5	COOEt	1,26 (2,8; -); 1,97 (0,9; +); 2,4 (3; -)
II	H	CH_3	C_6H_5	COOEt	1,38 (2,4; -); 2,11 (1,5; +); 2,47 (2,6; +)
III	CH_3	H	C_6H_5	COOEt	1,28 (3,2; -); 2,30 (3,8; -)
IV	H	H	C_6H_5	COOMe	1,23 (2,0; -); 1,76 (1,7; +); 2,20 (3,8; +)
V	H	CH_3	C_6H_5	COOMe	1,38 (1,6; -); 2,08 (1,1; +); 2,42 (2,3; +)
VI	H	H	o-$CHF_2OC_6H_4$	COOMe	1,21 (2,7; -); 1,85 (1,2; +); 2,05 (0,8; -); 2,34 (6,9; -)
VII	CH_3	H	o-$CHF_2OC_6H_4$	COOMe	1,21 (2,1; -); 2,20 (4,0; -)
VIII	H	H	o-$CH_3OC_6H_4$	COOMe	1,28 (2,4; -); 1,93 (1,2; +); 2,38 (11,8; -)
IX	H	H	m-$O_2NC_6H_4$	COOMe	1,03 (1,6; -); 1,19 (1,9; +); 1,95 (10,1; +); >2,7 (...)
X	H	H	p-$CH_3OC_6H_4$	COOMe	1,24 (1,8; -); 1,84 (1,0; +); 2,4 (8,7; +)
XI	H	H	p-$CH_3OC_6H_4$	CN	1,16 (1,6; -); 1,81 (1,1; +); 2,26 (1,6; +); ~2,6 (...)
XII	H	H	o-$CHF_2OC_6H_4$	CN	1,15 (2,1; -); 1,73 (1,1; +); 2,18 (2,1; +)
XIII	H	H	o-$CH_3OC_6H_4$	CN	1,17 (3,1; -); 1,86 (1,0; +); 2,5 (3,7; +)

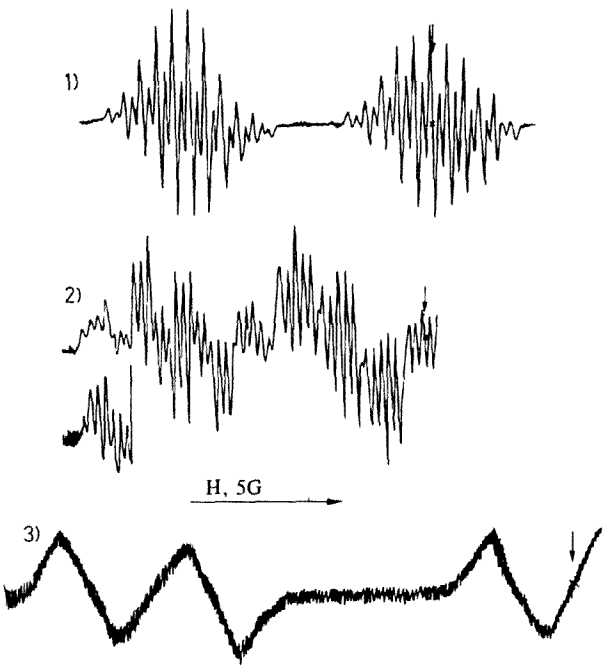


Fig. 1. Downfield part of ESR spectra of electrochemically generated free radicals: 1) type **A** for compound V; 2) type **B** for compound XIII; 3) type **C** for compound VIII.

The electroreduction of compounds I-XIII in dimethylformamide (DMF) on a mercury dropping electrode takes place in several stages (Table 1); however, we have not established a common scheme characterizing the reduction of all of these compounds. For example, compounds III and VII are reduced in two stages, whereas the other compounds are reduced in three or four stages. From the values of the limiting current of the polarographic waves, for which a current of 3.2 μA nominally

corresponds to transfer of one electron, we can conclude that the total number of electrons involved per molecule, under the condition that all of the molecules present are reduced on the electrode through exactly the same mechanism, may be anywhere from two to six electrons.

Apparently serving as the reaction center of the first stage of electron transfer is the nitro group, as the most electrophilic grouping in the molecules of these compounds. The values of the potential of the first polarographic wave of the mononitro compounds (I-VIII, X-XIII) are more negative than the potential of the compounds in the series of similar derivatives of 3-nitropyridine [9]. This difference is explained by the smaller possibility of delocalizing the added electron through the π-electron system in the molecules of the 3-nitro-1,4-dihydropyridines than in the molecules of 3-nitropyridines. The primary influence on changes in potential of the first wave of electroreduction is that of the substituent R^2, which is in the fragment of the molecule conjugated with the nitro group. Substitution by a methyl group at position 2 increases the reduction potential by about 0.1 V, whereas such substitution at the nitrogen atom of the heterocycle has practically no effect on the reduction potential.

The limiting current of the first polarographic wave reaches the one-electron level only in the case of compound III, whereas this level is lower for the other compounds. This may indicate that before transfer of an electron, some of the molecules are chemically transformed on the electrode into less electrophilic species that are not capable of electrochemical reduction at the potential of the first wave. N-unsubstituted dihydropyridines apparently may be subject to such chemical transformation. This process may be splitting out of a proton at the nitrogen atom of the heterocycle, so that the molecule is converted into the more difficultly reducible anion. It is also possible that the formation of such anions at the potential of the first polarographic wave takes place, as was found in the case of nitropyrazoles [11], by reduction of a proton at the nitrogen atom of the heterocycle; in this case, however, the first polarographic wave of reduction of molecules of N-unsubstituted 1,4-dihydropyridine compounds should reach the one-electron level, which does not actually occur.

We found by means of cyclic voltammetry that with a potential sweep rate up to 1 V/sec, for all of the compounds investigated, the first stage of reduction is irreversible: on the anodic branch of the voltammetric curve, there is no manifestation of oxidation of products from the first stage of reduction. Consequently, if in the first wave of electroreduction there is only one electron that is transferred (which, however, has not been confirmed unambiguously by data from the electrochemical study), then the resulting anion radicals will be rapidly subjected to further chemical conversion. In this stage of electrochemical reduction, therefore, we should not expect the formation of primary anion radicals that are stable on the time scale of registration of the hyperfine structure of their ESR spectra.

The second wave of polarographic reduction of N-unsubstituted dihydropyridines is also below the one-electron level. The total level of the first and second waves of these compounds is close to the one-electron transfer level, although it may be slightly higher, thus supporting the view that the electroreduction of these compounds on the cathode takes place in two stages, in each of which one particular form of the compound, differing in electrophilicity, is reduced. In turn, for N-substituted dihydropyridines (III, VII), the total level of the first two waves is considerably above the one-electron level. We can assume that in this case the original molecules are undergoing successive electrochemical reduction. The electroreduction of compounds III and VII in these stages is irreversible, and we should not expect the formation of radicals sufficiently stable for investigation of their structure by means of ESR.

In contrast to the N-substituted dihydropyridines, the reduction of N-unsubstituted dihydropyridines in the second stage is partly reversible; and here we can postulate the formation of sufficiently stable free radicals. For certain N-unsubstituted dihydropyridines, the following stage of electrochemical reduction is also partly reversible. This means that in the course of electrochemical generation of free radicals of the N-unsubstituted dihydropyridines that we have investigated, different types of free radicals may be formed, for which the structure can be investigated by means of ESR.

As expected from the results of electrochemical reduction of the 3-nitro-1,4-dihydropyridines I-XIII, in the course of electrochemical generation at the potentials of the first polarographic wave, we were not able to register any free radicals by means of ESR. This means that as a result of primary addition of one electron to the original molecule, the anion radicals that are formed may be subjected to rapid chemical or electrochemical conversion, losing their paramagnetic properties. The same as at higher potentials in the course of electrochemical generation of free radicals of N-substituted 3-nitro-1,4-dihydropyridines, in accordance with the results of the electrochemical study, no ESR signals were registered. For all of the other compounds, however, specifically the N-unsubstituted 3-nitro-1,4-dihydropyridines, ESR signals were registered at this high level of generation potential (Fig. 1). All of the free radicals that were obtained, other than the cyano derivatives (XI-XIII) and the m-nitrophenyl derivative (IX) of the 3-nitro-1,4-dihydropyridines, were found to be comparatively unstable. With the exception of the free radicals of compound I, for which we were not able to obtain a concentration of radicals sufficient for deciphering

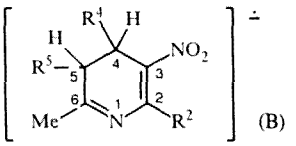
TABLE 2. Electrochemical Generation Potentials (E, V, Relative to Pt Electrode), Character and Constants of Hyperfine Coupling with Nuclei of Atoms in Corresponding Positions of Heterocycle (a_i, G), and Type of Free Radicals of Compounds II, IV-VI, and VIII-XIII

Compound	R^1	R^2	R^4	R^5	$-E$	Type	Character of HFC	a_i					
								a_1	a_2	a_3	$a^*_{5(4)}$	a_5	a_6
II	H	CH_3	C_6H_5	COOEt	2,7	B	$3_N \times 4_H \times 4_H \times 3_H \times 2_H$	1,43	8,35	9,81	0,77	–	3,58
IV	H	H	C_6H_5	COOMe	2,7	B	$3_N \times 2_H \times 4_H \times 3_N \times 2_H \times 4_H$	1,30	8,72	8,72	1,30	0,38	3,52
V	H	CH_3	C_6H_5	COOMe	2,0	A	$3_N \times 4_H \times 4_H \times 3_N$	0,47	1,99	14,74	–	–	1,05
					2,4	B	$3_N \times 4_H \times 4_H \times 3_N \times 2_H$	1,50	8,10	9,10	0,70	–	3,75
VI	H	H	o-$CHF_2OC_6H_4$	COOMe	2,3	B	$2_N \times 3_N \times 4_H \times 3_N \times 2_H$	1,20	9,00	8,70	1,26	–	3,65
VIII	H	H	o-$CH_3OC_6H_4$	COOMe	1,5	C	$3_N \times 2_H$	$a_N = 24,4$; $a_H = 7,6$					
IX	H	H	m-$O_2NC_6H_4$	COOMe	2,0	D	$3_N \times 2_H \times 2_H \times 2_H \times 2_H \times 2_H$	$a_N = 10,18$; $a_H = 3,63$; 3,28; 3,28; 1,05; 0,35					
X	H	H	p-$CH_3OC_6H_4$	COOMe	2,1	B	$3_N \times 2_H \times 4_H \times 3_N \times 2_H$	1,10	9,02	9,79	1,10	–	3,41
XI	H	H	p-$CH_3OC_6H_4$	CN	2,2	B	$3_N \times 2_H \times 4_H \times 3_N \times 3_N \times 2_H$	0,82	8,53	10,29	0,33	0,33	2,31
XII	H	H	o-$CHF_2OC_6H_4$	CN	2,2	B	$3_N \times 2_H \times 4_H \times 3_N \times 3_N \times 2_H$	0,82	8,52	10,01	0,33	0,33	2,48
XIII	H	H	o-$CH_3OC_6H_4$	CN	2,2	B	$3_N \times 2_H \times 4_H \times 3_N \times 3_N \times 2_H$	0,82	8,52	9,80	0,43	0,43	2,44

*Constant of coupling with single proton in position 4 or 5 of heterocycle.

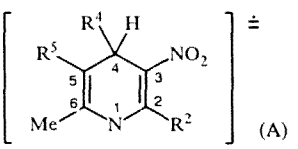
the hyperfine structure of their ESR spectrum, we obtained hyperfine coupling constants characterizing the structure of all of the other free radicals (Table 2).

On the basis of the hyperfine structure of the ESR spectra, we conclude that the free radicals that have been obtained can be classified into four types (**A**, **B**, **C**, **D**; see Table 2). Most of the free radicals are characterized by features of hyperfine structure of their ESR spectra that are characteristic for type B free radicals. In these radicals, the unpaired electron interacts with nuclei of atoms located in five (or six) positions. For example, in the cases of free radicals of compounds IV and X-XIII, for each of the radicals we have established five different values for the constant of hyperfine coupling with nuclei of the atoms in these radicals, specifically, with nuclei of atoms located at positions 1, 2, 3, 5, and 6 of the heterocycle. With respect to the character of the hyperfine structure and also the magnitude of the constant, these radicals are similar to the anion radicals of nitrodienes [8]. In our case, they can be represented in the form of anion radicals of 3-nitro-4,5-dihydropyridine (**B**).


(B)

The hyperfine coupling constants of the radicals that we have obtained are assigned to the corresponding positions of the heterocycle (Table 2), the same as in the cases of anion radicals of nitrodienes [8]. In the structure of **B**, however, the smaller constant due to the single proton ($a_{5(4)}$) can be assigned to the proton in either position 4 or position 5 of the heterocycle, since through a hyperconjugation mechanism, depending on the steric structure of the radical, interaction of the π-system of the unpaired electron is possible with a proton in either position of the heterocycle. We tend to assign the constant $a_{5(4)}$ to the proton in position 5 of the heterocycle. The following considerations support this view. As shown by quantum-chemical calculations, in anion radicals of nitro-substituted organic molecules, the unpaired electron density on the carbon atom in the α-position relative to the nitro group is usually quite low in comparison with the density on other carbon atoms of the conjugated system [12, 13]. In the second place, in the free radicals of compounds IV and XI-XIII, there is already such interaction with protons of IV and the nucleus of the nitrogen atom (XI-XIII) of the substitutents R^5. This interaction with protons of the substituent R^5 is also quite probably observed in the case of other compounds (II, V, VI, X); however, because of the broadened ESR signals, we were unable to establish the corresponding hyperfine coupling constants.

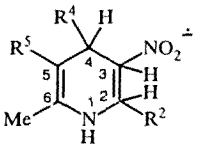
In the case of compound V with more positive potentials of electrochemical generation, in addition to the type **B** free radicals we were able to register another type (**A**). In these radicals, the value of the constant due to the nucleus of the nitrogen atom of the nitro group is considerably higher than for type **B** free radicals, indicating increased electron-donor properties of the remaining system of π-electrons conjugated with the nitro group. Such increased electron-donor properties apparently may be governed by the $1s^2 2p^2 \sigma^2 \pi^2$ electron state of the nitrogen atom of the heterocycle in a radical of the general type **A**, in comparison with the $1s^2 2p^2 \sigma^2 \pi^1$ electronic state of this atom in free radicals in the form of **B**.


(A)

The easier formation of type **A** free radicals in comparison with type **B** can possibly be explained by the more extensive π-electron conjugation system, in which π-electrons of the carbon atoms in positions 5 and 6 of the heterocycle participate by means of spin polarization of the π^2-state at the nitrogen atom of the heterocycle. For other similar N-unsubstituted dihydropyridines, type **A** free radicals evidently could not be registered, because of their instability.

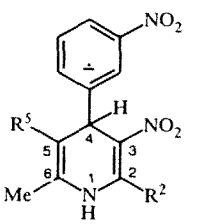
A different type of free radical was registered in the electrochemical generation of free radicals of compound VIII. These radicals are distinguished by a particularly high value of the constant for hyperfine coupling with the nitrogen atom nucleus, characteristic for anion radicals of nitroalkanes [8]. Also, the second constant of this radical, due to a single proton, is similar in magnitude to the constant due to the proton at C_α in the anion radicals of nitroalkanes. Consequently, if we do

not consider other transformations of the molecules that are undoubtedly possible but very difficult to judge unambiguously on the basis of the data obtained, the radical that was registered can be represented in general form by the structure **C**.



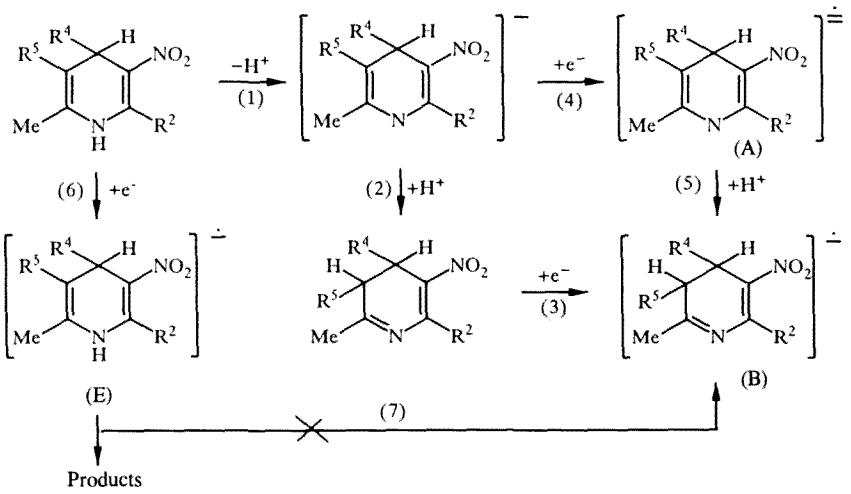
(C)

In the case of 4-(m-nitrophenyl)-3-nitro-1,4-dihydropyridine (IX), by means of electrochemical generation we obtained free radicals giving ESR spectra indicating interaction of the unpaired electron with the nucleus of the nitrogen atom and five protons differing in electronic environment. The hyperfine structure of these spectra provides evidence in favor of the view that this is an anion radical of nitrobenzene substituted with a 3-nitro-1,4-dihydropyridine group. Similar radicals for 1,4-dihydropyridines had been obtained previously [4]. Without considering electrochemical changes of the 3-nitro-1,4-dihydropyridine part of the molecule, this type of radical can be represented by the general structure **D**.



(D)

Consequently, electrochemical reduction of these compounds is a set of various associated parallel and consecutive reactions. The results of electrochemical generation of free radicals make it possible to single out certain possible stages in the conversion of these molecules. Ignoring any possible association with another type of reaction, we can represent the formation of types **A** and **B** radicals by the following scheme, which should be taken as a rough approximation:



The free radicals **B** are formed in the one-electron process (3) of reduction of the 4,5-dihydropyridine isomer of the molecules that had been investigated. In turn, the formation of this isomer proceeds by means of protonation (2) of the anion formed as a result of cathodic deprotonation (1) of part of the N-unsubstituted molecules of 1,4-dihydropyridines. The anions of the compounds, in the process (4) of adding one electron, may form dianion radicals **A** (for example, in the case of compound V). We can assume that free radicals **B** are also formed as a result of a competing process - transformation of the dianion radical **A** by means of (5), addition of one proton to the dianion radical. However, we have not obtained any experimental confirmation of such a path of isomerization of the heterocycle. Moreover, in the case of compound V, for the

formation of free radicals **A** and **B**, different reduction potentials of the predecessor are necessary; and at the generation potential of the dianion radical **A**, its conversion to the radical **B** is not observed. However, the results in electrochemical generation of free radicals of other N-unsubstituted compounds do not exclude the possibility of such transformation (5) of the dianion radicals **A**, even though the traces of reversibility for the two stages of electrochemical reduction (Table 1) may indicate that for these compounds as well, the free radicals **A** and **B** are formed at different reduction potentials.

Another possibility that cannot be ignored is the formation of primary anion radicals **E** from the original compounds, although no experimental confirmation of such anion radicals could be obtained, either by electrochemical methods or ESR: The first stage of electroreduction is irreversible; and in the course of electrochemical generation of free radicals from the original compounds, with the exception of VIII, we were unable to detect by ESR the formation of any such radicals at the potentials of the first polarographic wave of their electrochemical reduction. If primary anion radicals are formed in the course of such reduction, they are rapidly converted to particles of a different type. This process cannot be their isomerization to anion radicals **B** of the 4,5-dihydropyridine type. In the case of compound VIII, the intermediate species in transformation of the primary anion radicals proved to be a free radical of the nitroalkane type **C** (Tables 1 and 2). Consequently, if the formation of anion radicals of the nitro compounds does take place, in which the reaction center of electron addition to the molecule is undoubtedly the nitro group as the most electrophilic part of the molecule, then, with preservation of the nitro group, further chemical conversion of the molecules is accomplished spontaneously. The ability of nitro compounds in the anion-radical state to promote chemical transformation of other, less active reaction centers of these compounds had been observed previously in [5-7].

EXPERIMENTAL

The electrochemical reduction of compounds I-XIII ($C = 5 \cdot 10^{-4}$ M) was performed in anhydrous dimethylformamide [14] on a background of tetrabutylammonium hexafluorophosphate ($C = 10^{-1}$ M).

The free radicals were generated in the steady-state mode on the surface of a flat platinum electrode placed in a rectangular Type H_{102} resonator of an ER-9 ESR spectrometer (Carl Zeiss, Jena), following procedures described in [10].

The ESR spectra were registered with a magnetic field sweep rate of 0.04 G/sec with a depth of high-frequency (100 kHz) modulation of the magnetic field 0.05 G and a registration time constant of 0.45 sec. The sweep of the magnetic field was calibrated on the basis of the ESR spectrum of the nitrobenzene anion radical [15].

For electrochemical generation of free radicals, we used solutions of compounds I-XIII in anhydrous dimethylformamide at concentrations from $5 \cdot 10^{-5}$ to 10^{-3} M [8]; the solutions contained 10^{-1} M tetrabutylammonium hexafluorophosphate.

IR spectra were obtained in a UR-20 instrument (in white mineral oil), UV spectra in a Specord M 40 Carl Zeiss spectrophotometer (in ethanol), NMR spectra in Bruker WH-90 and WH-360 spectrometers (in DMSO-D_6). Mass spectra were taken in an AEI MS-50 instrument. The individuality of the synthesized substances was verified by TLC on Silufol UV-254 plates in a solvent system consisting of chloroform, hexane, acetone, and ethanol in a 9:7:2:1 ratio.

The elemental analyses for C, H, and N matched the calculated values.

The 2,6-dimethyl-3-nitro-1,4-dihydropyridines II and V were obtained in a Hantzsch reaction, following procedures given in [16, 17].

The procedures used in synthesizing the 4-aryl derivatives of 2-unsubstituted 3-nitro-1,4-dihydropyridines (VI-XIII) will be published separately [18].

6-Methyl-4-phenyl-3-nitro-5-ethoxycarbonyl-1,4-dihydropyridine (I) ($C_{15}H_{16}N_2O_4$). A 2.19-g quantity (10 mmoles) of benzylideneacetoacetic ester with 1.06 g (12 mmoles) of 2-amino-1-nitroethylene [19] in 50 ml of ethanol, with the addition of 5 ml of glacial acetic acid, was refluxed for 25 h. The solvents were removed under vacuum, and the residue was poured into 100 ml of water. This was extracted with ethyl acetate (3 × 50), washed with water (2 × 50), and dried with anhydrous sodium sulfate. The solvent was removed under vacuum; the residue was dissolved in 10 ml of acetone and chromatographed in two stages on a 220 × 260 mm preparative plate with a 2-3 mm thickness of the unbonded silica gel layer. The bright yellow band was collected. The substance was extracted from the silica gel by acetone, the solvent was removed under vacuum, and the residue was recrystallized from methanol. Obtained 1.3 g (46%) of compound (I) with mp 162°C (from ethanol). UV spectrum (in ethanol), λ_{max} in nm (and log ε): 221 Sh (4.23); 270 (3.92); 417 (4.02). IR spectrum, ν, cm^{-1}: 3260; 1700; 1670; 1630. ^1H NMR spectrum (in DMSO-D_6), δ, ppm: 1.11 (3H, t, CH_2CH_3); 2.24 (3H, s, 6-CH_3); 3.96 (2H,

q, CH_2CH_3); 5.18 (1H, s, 4-CH); 7.18 (5H, s, C_6H_5); 7.98 (1H, d, J = 5 Hz, 2-CH); 9.87 (1H, d, J = 5 Hz, N-H). ^{13}C NMR spectrum (DMSO-D_6): 166.14 (C=O); 144.79 ($C_{(3)}$); 143.27 ($C_{(i)}$); 134.47 ($C_{(2)}$); 128.85 ($C_{(6)}$); 128.08 ($C_{(o)}$); 127.83 ($C_{(m)}$); 126.75 ($CC_{(p)}$); 106.75 ($C_{(5)}$); 59.52 (OCH_2); 39.46 ($C_{(4)}$); 17.68 (3-CH_3); 13.76 (2-CH_3). Mass spectrum (m/z): 288 (M^+).

1.6-Dimethyl-4-phenyl-3-nitro-5-ethoxycarbonyl-1,4-dihydropyridine (III) ($C_{16}H_{18}N_2O_4$). Dissolved 4.38 g (20 mmoles) of benzylideneacetoacetic ester in 30 ml of glacial acetic acid, with heating up to 30°C. Added 2 g (20 mmoles) of 2-methylamino-1-nitroethylene and stirred for 3 days at room temperature. The solution was poured into water (100 ml); after cooling, oily crystals separated out. These were purified by passing through a column with Silpearl and eluting with chloroform–hexane–acetone–alcohol, 9:7:1:1. The bright yellow band was collected. After recrystallization from methanol, obtained 2.53 g (42%) of compound III with mp 157°C. UV spectrum, λ_{max} in nm (and log ε): 221 Sh (4.20); 278 (3.90); 425 (4.00). ^1H NMR spectrum (in DMSO-D_6), δ, ppm: 1.11 (3H, t, CH_3); 2.38 (3H, s, 6-CH_3); 3.44 (3H, s, N-CH_3); 4.00 (2H, q, OCH_2); 5.20 (1H, s, 4-CH); 7.20 (5H, s, arom. prot.); 8.27 (1H, s, 2-CH).

This research was performed through grants of the Latvian Council on Science, Nos. 93–467 and 93–468, and also ISF grants.

REFERENCES

1. J. R. Prous, The Year's News: Therapeutic Targets, Prous Science Publishers, Barcelona (1994).
2. L. Kh. Baumane, Ya. P. Stradyn', R. A. Gavar, A. P. Gaukhman, and G. Ya. Dubur, Khim. Geterotsikl. Soedin., No. 11, 1494 (1988).
3. L. Kh. Baumane, Ya. P. Stradyn', R. A. Gavar, B. S. Chekavichus, and G. Ya. Dubur, Khim. Geterotsikl. Soedin., No. 4, 481 (1991).
4. L. Baumane, J. Stradins, R. Gavars, and G. Duburs, Electrochim. Acta, **32**, 2599 (1992).
5. Ya. Stradyn', L. Baumane, R. Gavars, B. Chekavichus, and G. Duburs, Khim. Geterotsikl. Soedin., No. 11, 1498 (1992).
6. R. A. Gavar, Ya. P. Stradyn', L. Kh. Baumane, and K. Enish, Khim. Geterotsikl. Soedin., No. 12, 1631 (1991).
7. M. Trushule, É. Kupche, I. Augustane, V. M. Verovskii, É. Lukevits, L. Kh. Baumane, R. A. Gavar, and Ya. P. Stradyn', Khim. Geterotsikl. Soedin., No. 12, 1687 (1991).
8. Landolt-Börnstein, Zahlenwerte und Funktionen aus Naturwissenschaften und Technik. Neue Serie, Springer Verlag, Berlin (1980), Group II, Vol. 9, No. d1.
9. Ya. Stradyn', R. Gavars, L. Baumane, B. Vigante, and G. Duburs, Khim. Geterotsikl. Soedin., No. 8, 1079 (1993).
10. Ya. P. Stradyn', R. A. Gavar, and L. Kh. Baumane, Izv. Akad. Nauk Latv. SSR, No. 2, 73 (1986).
11. T. I. Bakul'skaya, L. I. Larina, O. B. Nefedova, and V. A. Lopyreva, Khim. Geterotsikl. Soedin., No. 4, 523 (1984).
12. P. H. Rieger and G. K. Fraenkel, J. Chem. Phys., **39**, No. 3, 609 (1963).
13. M. B. Fleisher, R. A. Gavar, Ya. P. Shvets, and Ya. P. Stradyn', Izv. Akad. Nauk Latv. SSR, Ser. Khim., No. 5, 604 (1977).
14. Yu. M. Kargin, V. V. Kondranina, and N. I. Semakhina, Izv. Akad. Nauk SSR, Ser. Khim., No. 2, 278 (1971).
15. L. H. Piette, P. Ludwig, and R. N. Adams, Anal. Chem., **34**, No. 11, 467 (1962).
16. G. Franckowiak, H. Böshagen, F. Bossert, S. Goldman, H. Meyer, E. Weninger, J. Stoltefus, M. Schram, G. Thomas, and R. Toward, FRG Offenleg. 3,206,671; Chem. Abstr., **98**, 215488 (1982).
17. G. Franckowiak, FRG Offenleg. 3,447,169; Chem. Abstr., **105**, 215488.
18. B. Vigante, Ya. Ozols, and G. Dubur, Khim. Geterotsikl. Soedin. (1995) (in press).
19. A. Krowczynsky and L. Kozerski, Synthesis, No. 6, 489 (1983).