UDC 547.024:66.095.22/.24:535.685.32:544.433.22

DOI: 10.15372/CSD2022426

EDN: SFGYOX

Acid-Catalyzed Pyridylimidazoline Rearrangement

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Abstract

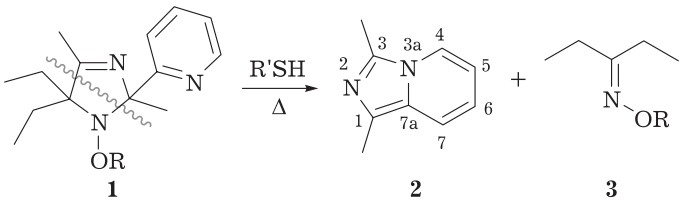
1-Alkoxy-3-imidazolines derived from stable nitroxide radicals, as well as nitroxide radicals themselves, bearing the 2-pyridyl substituent in position 2, under mild conditions undergo acid-catalyzed rearrangement with the fragmentation of the imidazoline ring and the formation of imidazo[1,5-*a*]pyridine. This rearrangement does not occur in superacid media due to the protective protonation of the nitrogen atom of the pyridyl substituent.

Keywords: 1-alkoxy-3-imidazolines, nitroxide radicals, imidazo[1,5-*a*]pyridin, rearrangement, superacids, NMR, DFT

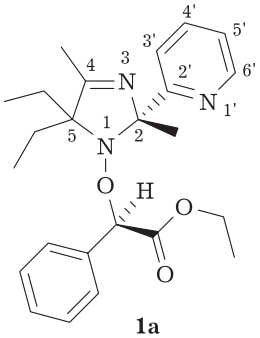
INTRODUCTION

Alkoxyamines of the imidazoline series are used as the source of radicals for the controlled olefin polymerization due to their ability to undergo reversible homolysis [1]. In a recent work [2], homolysis of alkoxyamines with pyridine group providing the possibility to form complexes with metal ions has been investigated. It was discovered that in the presence of β-mercaptoethanol, used as a trap for radicals, at increased temperature the alkoxyamines under investigation, as well as the initial nitroxide, degrade with the destruction of imidazoline cycle to form, among many components of a complicated mixture, the products presented in Scheme 1. We did not find any published similar examples of fragmentation-cyclization, so this unusual reaction (see Scheme 1) and its mechanism are of substantial interest.

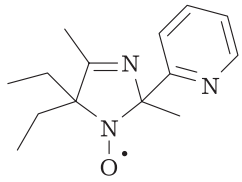
Alkoxyamines **1**, synthesized as described in [2] from nitroxide **1**•, differed from each other only in substituents R of the same kind, occupying the positions far from reaction centres of the molecule, so we chose only one of them, **1a**, in the form of a racemic mixture of diastereoisomer *RR*/*SS*, as the object of investigation. The choice of this object was due to the fact that its NMR spectrum contains the signals of only one invertomer with respect to nitrogen atom N1, which simplified data interpretation.



Scheme 1.



1a



1•

The goal of the present work was to establish the mechanism of rearrangement according to Scheme 1 by the example of compound **1a** and radical **1•**, and to reveal the factors promoting or hindering the progress of this reaction.

EXPERIMENTAL

Materials and reagents

Trifluoroacetic acid (TFA, pure reagent grade, distilled), trifluoromethanesulphonic acid (TfOH, ACROS, 99 %), fluorosulphonic acid (FSO_3H, technical grade, twice distilled), antimony pentafluoride (SbF_5, technical grade, freshly distilled), deuterated chloroform ($CDCl_3$, 99.8 at. % D), dichlorometahne-D2 (CD_2Cl_2, 99.5 at. % D), methanol-D4 (CD_3OD, 99.5 at. % D).

Investigation methods

The structures of the compounds under investigation were determined by means of NMR spectroscopy with the help of correlations: ^1H-^1H (COSY, NOESY, ROESY) and ^1H-^{13}C, ^1H-^{15}N (HSQC, HMQC, HMBC). NMR spectra were recorded with the help of AV-600 and DRX-500 spectrometers (Bruker, Germany). The internal standards in NMR ^1H spectra were residual signals from protons in the solvents CD_2Cl_2 (δ 5.33 ppm) and $CDCl_3$ (δ 7.24 ppm), in NMR ^{13}C spectra – the signals from carbon atoms of these solvents (δ 53.6 and 76.9 ppm, respectively). For solutions in FSO_3H-SbF_5, the internal standard was $Me_4N^+BF_4^-$ (δ_H 3.20 ppm, δ_C 55.0 ppm). The chemical shifts of ^{15}N with respect to the external standard NH_3 were extracted from two-dimensional correlation spectra. Temperature sensor of the spectrometer was calibrated using the standard methanol sample.

EPR spectra were recorded with the help of ELEXSYS–II E500/540 spectrometer (Bruker, Germany), using the following parameters: microwave frequency 9.83 GHz, microwave power 2 mW, modulation amplitude 1 G, number of points 1024, conversion time 20 ms, sweep width 80 G.

Synthesis procedures and spectral characteristics of the generated species are listed in the corresponding section at the end of the paper.

Quantum chemical methods

Investigation of reaction pathways (the search for transition states and their relationship with energy minima according to IRC procedure) was carried out by means of DFT with the help of PRIRODA software [3, 4] (PBE functional [5], Λ01 basis [6, 7]). Complete results of this investigation, including the coordinates of all the detected stationary points, are presented at http://limor1.nioch.nsc.ru/quant/heterocycle/. The energies of stationary points were additionally calculated by means of r^2SCAN-3c [8] taking the solvent (dichloromethane) into account with the help of SMD [9] using ORCA software [10]. Thermodynamic corrections to the Gibbs energy were taken from Hessian calculation by means of DFT/PBE/Λ01. Conformation analysis was carried out using the CREST software [11]. Atomic charges were determined by means of NBO [12] using the GAMESS software [13].

RESULTS AND DISCUSSION

It has been demonstrated in [2] that rearrangement according to Scheme 1 proceeds more readily in the presence of β-mercaptoethanol, and the mechanism of this process is in no way connected with alkoxyamine homolysis or with the ability of mercaptoethanol to interact with the intermediate radical species. Taking into account the known facts, we assumed an alternative reaction mechanism – electrophilic. This mechanism is quite possible: the structure of compound **1a** contains three nitrogen atoms as nucleophilic centres that are available for interaction at the first stage of reaction with acid protons, which are present also in mercaptoethanol. To test this hypothesis, it was necessary to study the behaviour of alkoxyamine **1a** under the action of stronger acids that would surely provide protonation of at least one nitrogen atom in this compound. We chose to use the following acids: TFA, TfOH and an equimolar mixture of FSO_3H and SbF_5, known under the name of the "magic acid". These acid systems are convenient because they form a series with substantial increase in Hammett acidity (H_0 −3, −14 [14] and −25 [15], respectively), are soluble in aprotic non-nucleophilic sol-

vents, are suitable for NMR studies, and sulphonic acids TfOH and FSO_3H in mixture with SbF_5 do not exhibit sulphurizing action.

*Protonation of compound **1a***

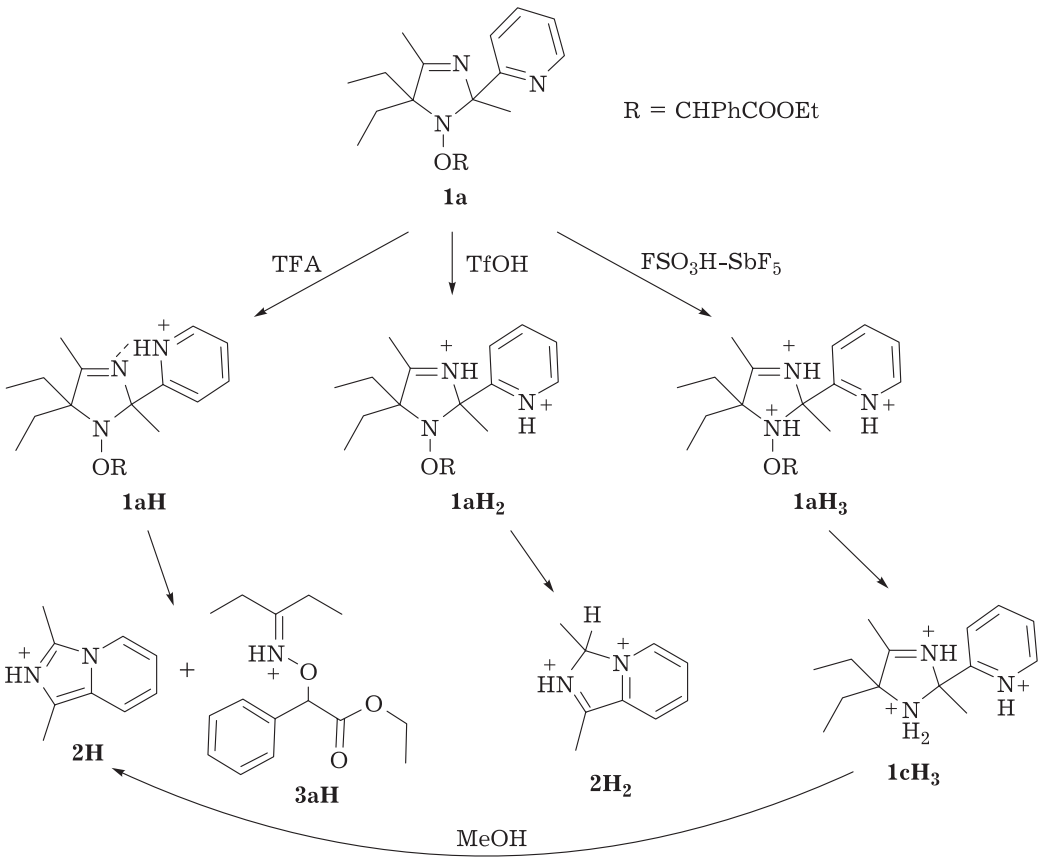
In the presence of TFA (0.5 M solution in CD_2Cl_2), compound **1a** is protonated at the nitrogen atom of pyridine fragment, see Procedure 1. This follows from the changes of chemical shifts in the NMR ^1H and ^{13}C spectra of this fragment, and from an increase in the spin-spin coupling constant $^3J_{H6'\text{-}H5'}$ (from 4.5 to 5.8 Hz). The changes of this kind are characteristic of azine protonation [16]. In addition, as suggested by a substantial downfield shift of the signal from C4 carbon atom (from 174.3 to 195.9 ppm) and the protons of methyl group 4-Me (from 1.97 to 2.60 ppm), nitrogen atom N3 can also be protonated, at least partially. On the other hand, quantum chemical calculations of chemical shifts allow us to assign descreening of C4 and 4-Me to the participation of nitrogen atom N3 in the formation of hydrogen bond with H–N1′ – a proton of the correctly oriented pyridine fragment of monoprotonated structure (**1aH**, Scheme 2).

Under the action of a stronger acid, TfOH, both nitrogen atoms N1′ and N3 are protonated (see Scheme 2), which follows from the direct observation of NMR ^1H signals from the protons attached to these atoms (procedure 2). Meanwhile, the third nitrogen atom N1 is not prone to protonation in TfOH: the rate of inversion of this nitrogen atom, observed in the NOESY/EXSY spectra, is almost the same as that in the neutral compound **1a**. Its inversion would be impossible in a particle completely protonated at the nitrogen atom N1.

In FSO_3H-SbF_5, which is even a stronger acid, all three nitrogen atoms of compound **1a** are completely protonated (see Scheme 2). This is confirmed by the fact that individual signals from the protons attached to each of these nitrogen atoms are observed in the NMR spectra (procedure 3).

*Reactions of compound **1a** in acids*

Under the action of TFA (procedure 4), compound **1a** is selectively, quantitatively and rapidly ($t_{1/2}$ = 25 min at 27 °C) transformed into an equimolar mixture of the protonated forms of com-



Scheme 2.

pounds **2** and **3a** (see Scheme 2). The conclusion concerning the formation of protonated forms (**2H** and **3aH**) was made relying on the presence of clearly pronounced cross-peaks in the NOESY spectrum, corresponding to the cross-relaxation between the protons of the acid and both methyl groups of **2H**, as well as between the protons of the acid and CH- and methylene protons N=C–Et_2 of **3aH**. The easy rearrangement of compound **1a** in the presence of TFA is in dramatic contrast with the reaction in the presence of mercaptoethanol, proceeding under substantially more severe conditions ($t_{1/2}$ = 4 h at 74 °C, selectivity with respect to product **2** is about 20 %). This provides evidence of the key role of the acid and of the electrophilic nature of the process.

In TfOH-CD_2Cl_2 (volume ratio 4 : 1) (procedure 5), the reaction proceeds slower than under the action of TFA: $k = (5.8\pm0.2)\cdot10^{-5}$ s^{-1}, $t_{1/2}$ = 33 h at 27 °C. In this process, compound **1a** is completely transformed into the diprotonated form of compound **2** (**$2H_2$**, see Scheme 2), as well as a mixture of the products of destruction of oxime **3a**.

In even more acidic medium FSO_3H-SbF_5 (procedure 7), compound **2** is not formed at all. Detachment of OR group occurs, leading to triple-protonated amine **1c** (**$1cH_3$**, see Scheme 2). Nevertheless, decomposition of the reaction mixture with methanol and related decrease in acidity also causes rearrangement of amine **1c** into heterocycle **2**.

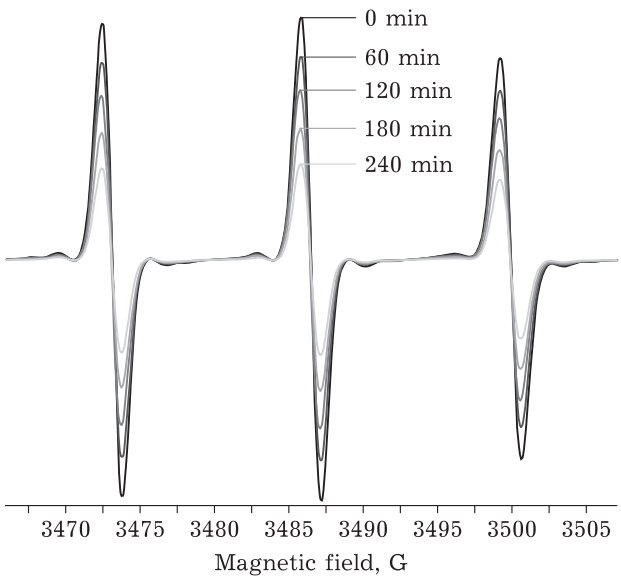


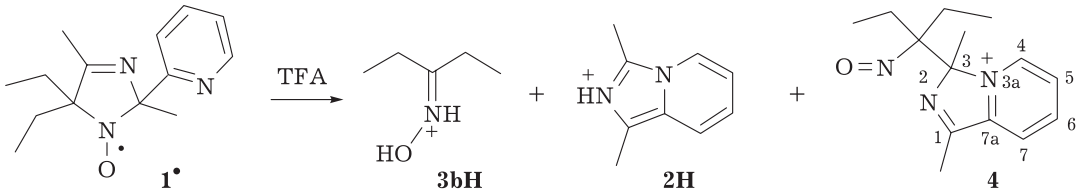
Fig. 1. Kinetics of the intensity of EPR spectrum of radical **1•** at 60 °C.

Reactions of radical 1• in acids

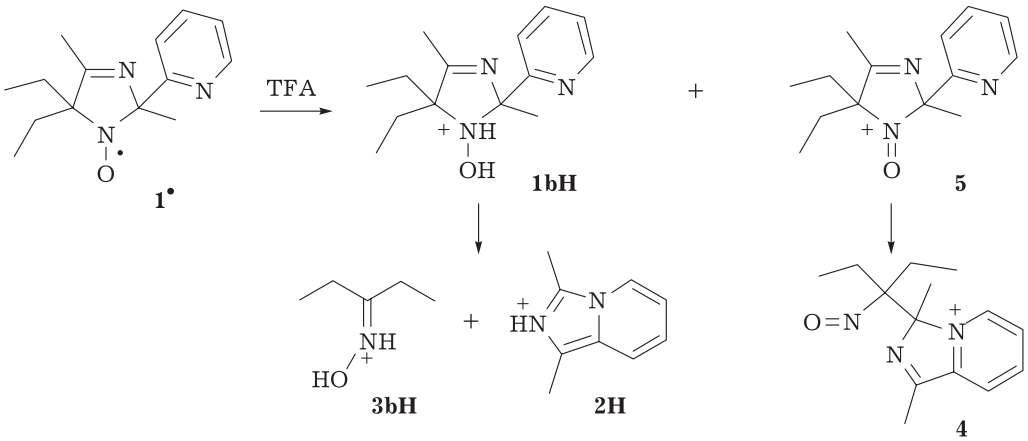
Reactions of radical **1•** in acidic medium were studied by means of EPR and NMR spectroscopy. According to EPR data, the addition of TFA (0.5 M) to the initial solution of the radical in chlorobenzene leads to a decrease in the value of hyperfine splitting constant at nitrogen atom N1 by 0.14 G, which is a sign of protonation of functional groups [17]. Further increase in TFA concentration does not affect EPR spectra. At 60 °C, gradual decrease in the intensity of the signal from the radical is observed (by 30 % within 2 h in 0.5 M TFA-PhCl, Fig. 1, procedure 11).

According to NMR data, radical **1•** is less reactive than alkoxyamine **1a**. Under the same conditions (0.5 M TFA in CD_2Cl_2, room temperature), the half-life of **1•** is about 20 h, in comparison with 25 min for **1a**. At 60 °C, the reaction is complete within 2 h. The higher rate of radical disappearance in comparison with the EPR experiment at the same temperature may be caused by an increase in the initial concentration of the radical (0.06 M for NMR and $2\cdot10^{-4}$ M for EPR). Acceleration of the reaction is also observed with an increase in TFA concentration to 10 M (4 : 1 by volume with CD_2Cl_2, procedure 8). With this concentration of the acid, the transformation is over within 2 h at 25 °C. In this process, an equimolar mixture of the protonated forms (**2H** and **3bH**) and nitroso compound **4** is quantitatively formed (Scheme 3, Fig. 2). The formation of nitroso compound is revealed by the typical blue-green colour of the solution, unusual for Alk_3CX downfield chemical shift of carbon atom (109.3 ppm) and, most important, chemical shift of nitrogen atom (956.2 ppm), which is characteristic only of nitroso compounds.

It is well known that nitroxides disproportionate under the action of strong acids, to form diamagnetic compounds: hydroxylamine (in the protonated form) and oxoammonium salt [18, 19] (Scheme 4). The acidity of TFA is quite sufficient for this [20], and we suppose that disproportionation is the first stage of the process presented in Scheme 3. The same stage is also a limiting one: the reaction order is higher than 1, which is an evidence that the reaction is participated by two particles corresponding to the initial radical (the medium reaction rate in EPR and NMR experiments). It should be noted that hydroxylamine **1b** is shown in Scheme 4 in the form protonated at N–OH only as an illustration. Actually, **1b** in



Scheme 3.



Scheme 4.

the presence of TFA should be protonated similarly to alkoxyamine **1a** (see above).

The reason for assuming that **3bH** + **2H** are formed from one of the products of nitroxide disproportionation, namely protonated hydroxylamine **1bH**, is a similar reaction of alkoxyamine: **1aH** → **3aH** + **2H**. To provide a direct confirmation, radical **1**• was reduced by zinc in the pres-

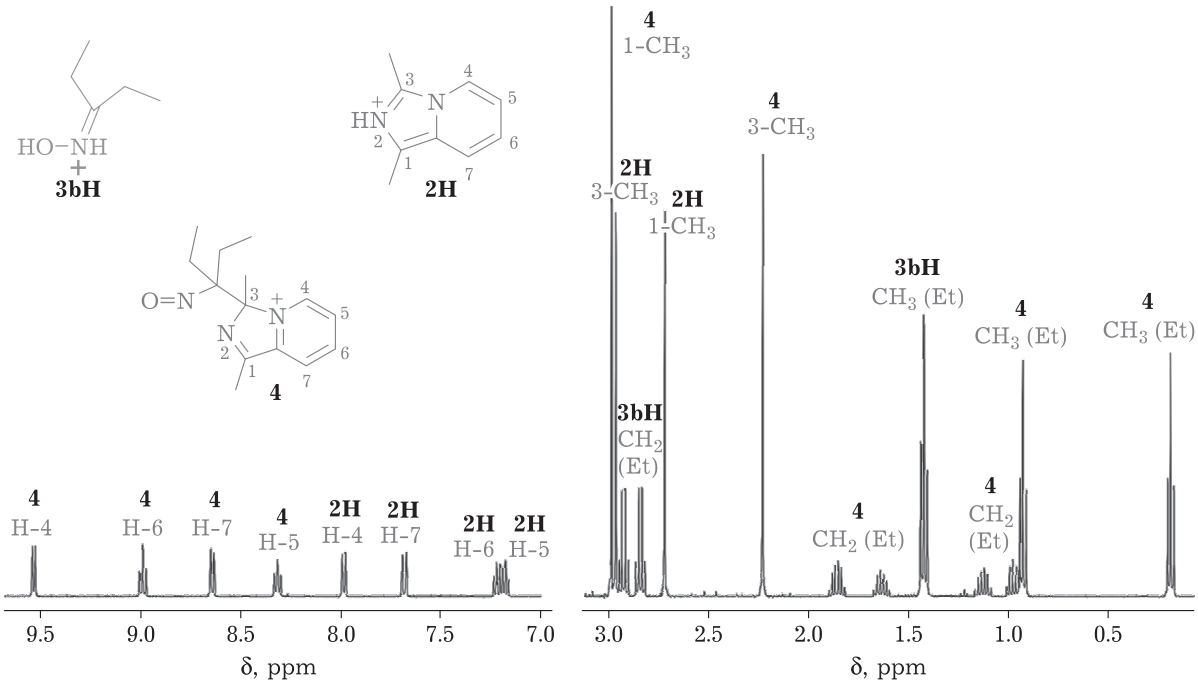
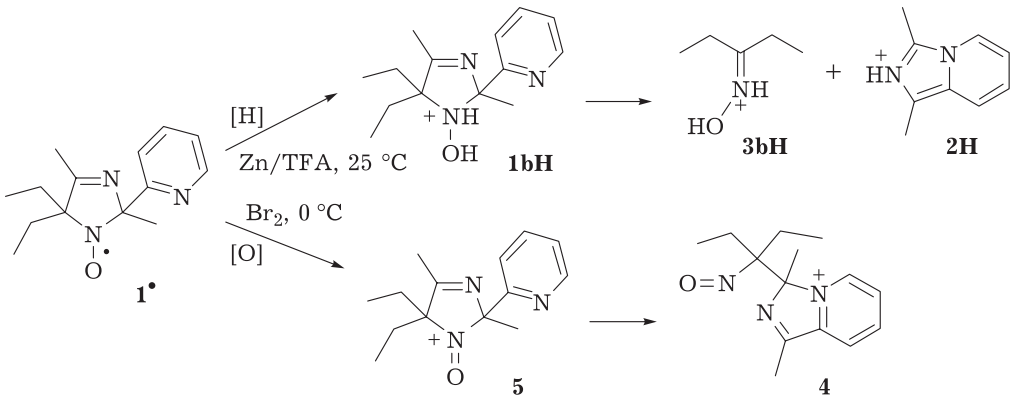


Fig. 2. NMR ^{1}H spectrum (500 MHz) and assignment of the signals in reaction mixture formed from radical **1**• in TFA-CD_2Cl_2 (4 : 1 by volume) within 2 h at 25 °C.



Scheme 5.

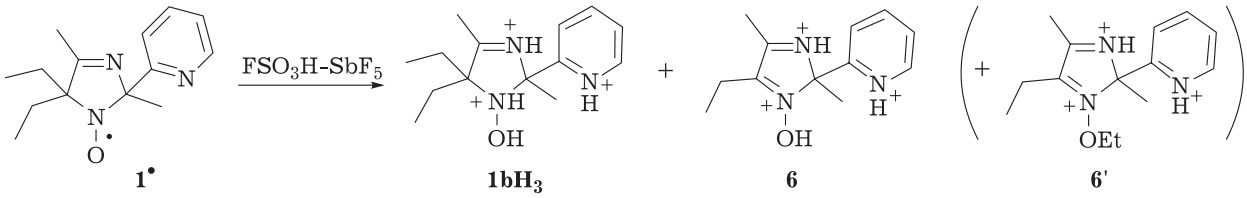
ence of TFA (procedure 9). Under these conditions, hydroxylamine formed through reduction of the radical [21] undergoes immediate rearrangement and gives an equimolar mixture of **3bH** and **2H**. In this process, nitroso compound **4** is not formed at all (Scheme 5).

To confirm the mechanism of the formation of nitroso compound from the second product of disproportionation in the presence of TFA, radical **1**• was preliminarily oxidized with bromine [20] (procedure 10). It has been demonstrated previously that oxoammonium salts formed through bromination of 3-imidazoline-1-oxides are unstable. The heterolytic breakage of N1–C2 bond leads to a carbocation, which tends to get stabilized, for example through recyclization with the neighbouring nucleophilic centres, but in the absence of this possibility it undergoes destruction [22]. In our case, a labile oxoammonium intermediate **5** is also not detected. It enters rearrangement immediately, similarly to hydroxylamine **1bH**, however, the fragment containing nitroso group is not detached from the heterocyclic scaffold. The formed nitroso compound **4** is gradually decomposed, perhaps due to the side reaction with excess bromine. So, two intercomplementary experiments in Scheme 5 serve as a direct confirmation that the rearrangement of nitroxide **1**• under the action of TFA proceeds according to Scheme 4.

No significant changes of process rate are observed in TfOH, in spite of its substantially higher acidity in comparison with TFA. Radical **1**• is transformed in this medium into diamagnetic compounds within 1.5 h at 25 °C. Similarly to the case of TFA, the major products identified in the mixture are protonated oxime **3b** (in the form of **3bH**, see Scheme 3) and heterocycle **2** (in the N,C-diprotonated form $\mathbf{2H_2}$, see Scheme 9 below). Evidently, these particles are formed as a result of radical disproportionation followed by rearrangement of the reduced form – protonated hydroxylamine (**1bH**). However, unlike for TFA, the signals of the oxidized form, nitroso compound **4**, are absent from the spectra, and other products are observed in the reaction mixture. We suppose that nitroso compound **4** in more acidic TfOH is prone to protonation at nitrogen atom N2. Additional ionization of **4** simplifies its decomposition with detachment of protonated oxime (**3bH**) and non-selective formation of various oxidized forms of heterocycle **2** from the residual fragment (the structure of two prevailing forms has been established: **14** and **15**, procedure 14).

In the super-acidic medium of FSO_3H-SbF_5, radical **1**• reacts at room temperature according to Scheme 6 (procedure 12) to form an equimolar mixture of triply protonated compounds: hydroxylamine **1b** ($\mathbf{1bH_3}$, as a mixture of diastereoisomers at nitrogen atom N1) and N-oxide **6**, so that one of the ethyl groups is absent from the latter. If this reaction is carried out at decreased temperature (procedure 13), additional species **6′** is observed in the mixture: it is protonated N-oxide, which is ethylated at the oxygen atom.

We suppose that here, similarly to previous cases, the first step is radical disproportionation, however, unlike of TFA and TfOH, pyridine nitrogen atom is fully protonated in the super-acidic medium and does not exhibit any nucleophilic properties. So, the formed hydroxylamine does not react further on, and the labile oxoammonium salt is stabilized through the formation of a system of conjugated bonds through a shift or complete detachment of ethyl cation. It should be noted that, similarly to the case of alkoxyamine **1a**, imidazoline cycle does not undergo opening in FSO_3H-SbF_5.

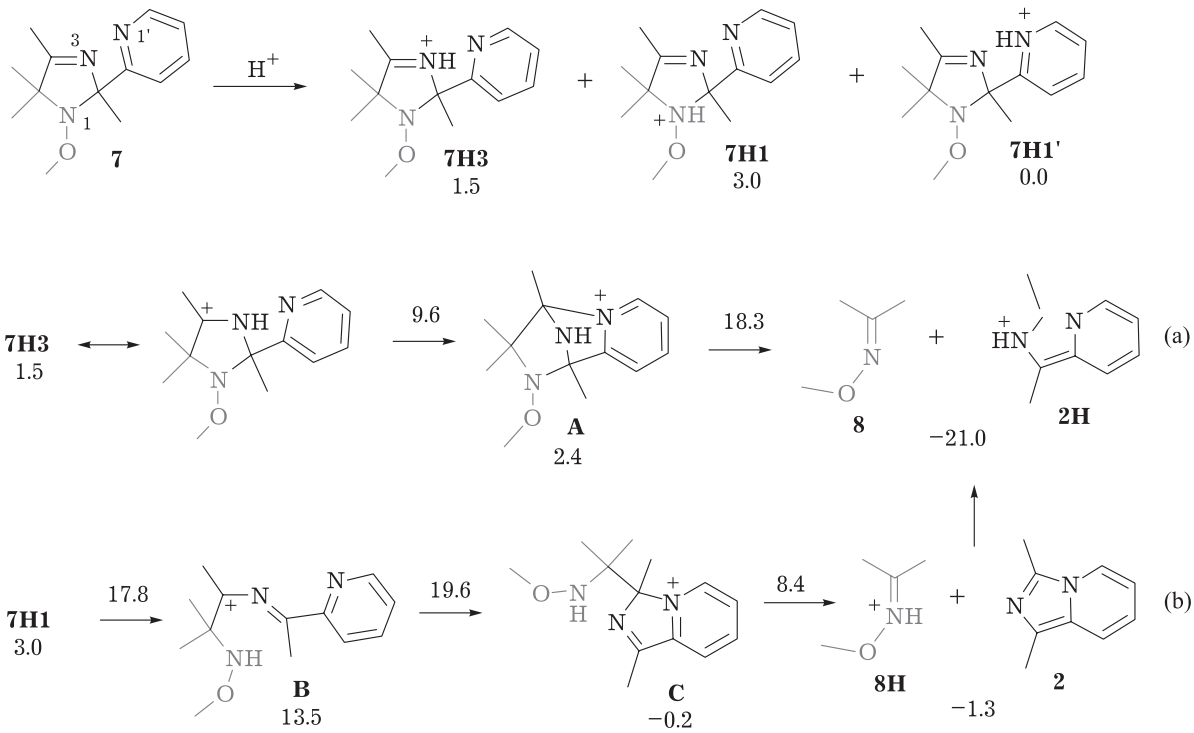


Scheme 6.

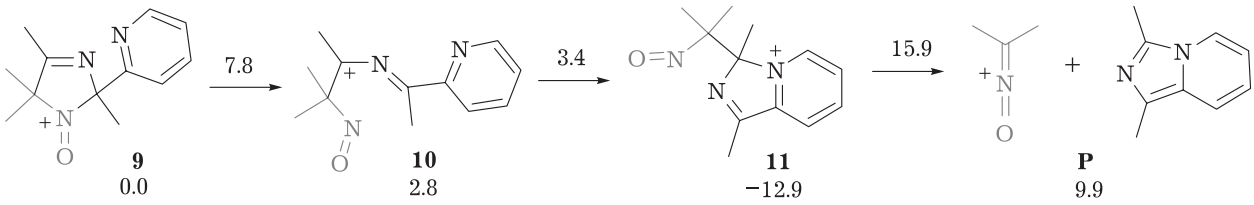
Quantum chemical calculations

The electrophilic nature of compound **1a** rearrangement into heterocycle **2** and oxime **3a** implies that one of the protonated forms of initial compound enters the reaction. To reveal the possible mechanism of this process, quantum chemical calculations were carried out. To decrease the number of conformers of initial protonated forms and reaction intermediates, compound **7** in which the fragments CEt_2 and OR that do not participate directly in the reaction were replaced by structurally more rigid CMe_2 and OMe, respectively, was chosen as the calculation model. The initial molecule **7** contains three evident nucleophilic centres (nitrogen atoms); we considered protonation at each of them. Calculations predict two alternative mechanisms of pyridylimidazoline rearrangement, leading to the experimentally observed products (Scheme 7). The numbers under the structures of this Scheme, as well as Scheme 8, are relative energies of the most stable conformers of the corresponding species, calculated by means of r^{2}SCAN-3c/SMD(CH_2Cl_2)//PBE/L1 (kcal/mol, taking into account ΔG from Hessian calculations for stationary points by means of PBE/L1), and the numbers above the arrows are the energies of transition states. More detailed data, including all the determined conformers with geometric parameters, are shown as an interactive diagram at the site http://limor1.nioch.nsc.ru/quant/heterocycle/.

One of the mechanisms – (a) (see Scheme 7) – starts from structure **7H3**, which is formed as a result of protonation at nitrogen atom N3. A similar reaction pathway (intramolecular cyclization followed by retro-Diels–Alder stage) was assumed in [23]. The alternative mechanism (b)



Scheme 7.



Scheme 8.

starts from the protonation of another nitrogen atom of the imidazoline fragment, N1. According to calculations, the energy barriers of the limiting stages in both mechanisms are close to each other, which does not allow making unambiguous choice. It should be noted that the most basic is nitrogen atom N1′ of the pyridine substituent (see Scheme 7). However, protonation at this nitrogen atom blocks the lone electron pair which is necessary to attack carbon atom C4, thus preventing the reaction.

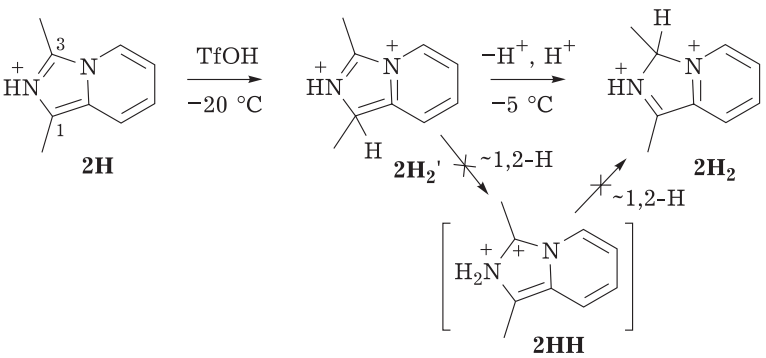
In the case of the reaction of the model oxoammonium salt **9**, we did not consider the mechanism according to (a) (see Scheme 7), which requires protonation at nitrogen atom N3. This kind of protonation would lead to a dication, while the acidity of TFA is clearly insufficient for this purpose. An alternative mechanism, starting from the rupture of N1–C2 bond, is presented in Scheme 8.

Calculations predict that the stages of this bond rupture and subsequent cyclization at the pyridine fragment should proceed readily. As a result, nitroso compound **11** is formed, but its further fragmentation should not take place due to the high energy barrier (28.8 kcal/mol with respect to **11**). This theoretical prediction is in complete agreement with the experimental observations and explains the differences in the behaviour of alkoxy/hydroxyl amine and oxoammonium salt in the acid medium.

Kinetic and thermodynamic control of the protonation of cation 2H

In the presence of TFA, compound **2** is in the form **2H** protonated at nitrogen atom N2. In the medium with higher acidity containing TfOH, additional protonation occurs at carbon atom (Scheme 9, procedure 6). At decreased temperature, exclusively dication $\mathbf{2H_2}'$ is formed; however, at increased temperature it is completely transformed into dication $\mathbf{2H_2}$, $k = (2.41\pm0.04)\cdot10^{-5}$ s^{-1} at −5 °C. Dication $\mathbf{2H_2}$ has been observed in the reaction mixture obtained from compound **1a** in TfOH at room temperature.

The mechanism of dication $\mathbf{2H_2}$' transformation into $\mathbf{2H_2}$ is evidently intermolecular, through deprotonation with the formation of cation **2H** and protonation of the latter at another position. This assumption is confirmed by the fact that the transformation of dication $\mathbf{2H_2}'$ into $\mathbf{2H_2}$ does not proceed in superacid medium FSO_3H-SbF_5, where deprotonation is almost impossible. Quantum chemical calculations by means of DFT/PBE/Λ01 (PRIRODA software) show that the intramolecular proton 1,3-shift does not occur, while sequential 1,2-shifts through intermediate **2HH** proceed with a very high barrier 60 kcal/mol. According to calculations, dication $\mathbf{2H_2}$ is more stable than $\mathbf{2H_2}'$ (by 3.7 kcal/mol), which is in agreement with the experimentally detected irreversibility of the transformation of $\mathbf{2H_2}'$ into $\mathbf{2H_2}$.



Scheme 9.

The sequential formation of dications $\mathbf{2H_2}'$ and $\mathbf{2H_2}$, differing from each other only by protonation position, is an interesting case of the kinetic ($\mathbf{2H_2}'$) and thermodynamic ($\mathbf{2H_2}$) control of reaction products. Various factors providing changes in protonation direction are considered in chemical literature, in particular a change of solvent [24, 25], conformation composition of the compound to be protonated [26], steric surroundings of reaction centres [27]. It is evident that all the listed factors are insignificant in the case under consideration: the solvent in the same, molecule **2H** exhibits no conformational diversity, the steric availability of C1 and C3 atoms is approximately the same. We suppose that the charge control of protonation direction occurs here [28]. Quantum chemical calculation by means of NBO (B3LYP/6-31G*, GAMESS software) shows that the charge at C3 atom is +0.44, while the charge at C1 atom is +0.17. So, the attack of a positively charged protonating particle at position C1 should proceed easier due to the smaller coulomb repulsion of the positive charges [29]. The case under consideration is interesting because it is a refined example of the kinetic charge control of protonation because all other factors of kinetic control can be rejected with high probability.

Synthesis procedures and spectral characteristics

Radical **1**$^{\bullet}$ was synthesized according to the procedure described in [2].

Compound **1a** was synthesized according to the procedure described in [2]. NMR ^{1}H spectrum ($CDCl_3$, 25 °C), δ, ppm: 1.71 (2-Me), 1.97 (4-Me), 1.66, 2.46 (5-Et-CH_2-a,b), 1.02 (5-Et-CH_3), 1.46, 1.80 (5′-Et-CH_2-a,b), 0.36 (5′-Et-CH_3), 7.39 (3′-H), 7.56 (4′-H), 7.12 (5′-H), 8.65 (6′-H), 6.03 (CH), 3.95, 4.09 (OEt-CH_2-a,b), 1.10 (OEt-CH_3), 7.51 (*o*-Ph), 7.33 (*m*-Ph), 7.31 (*p*-Ph). NMR ^{13}C spectrum ($CDCl_3$, 25 °C), δ, ppm: 96.9 (C2), 23.6 (2-Me), 174.3 (C4), 16.6 (4-Me), 82.0 (C5), 27.2 (5-Et-CH_2), 10.8 (5-Et-CH_3), 29.7 (5′-Et-CH_2), 8.7 (5′-Et-CH_3), 164.8 (C2′), 119.9 (C3′), 135.5 (C4′), 121.6 (C5’), 148.6 (C6′), 83.4 (CH), 172.5 (C=O), 60.3 (OEt-CH_2), 13.9 (OEt-CH_3), 135.6 (*i*-Ph), 127.5 (*o*-Ph), 128.2 (*m*-Ph), 128.3 (*p*-Ph).

1. Protonation of 1a in TFA. Compound **1a** (7 mg, 0.017 mmol) was dissolved in 0.5 mL of CD_2Cl_2, then 30 mg (0.26 mmol) of TFA was added at −40 °C, followed by mixing. NMR spectra of the resulting solution were recorded. NMR ^{1}H spectrum (−17 °C), δ, ppm: 2.15 (2-Me), 2.60 (4-Me), 1.86, 2.04 (5-Et-CH_2-a,b), 1.08 (5-Et-CH_3), 1.67, 1.71 (5′-Et-CH_2-a,b), 0.42 (5′-Et-CH_3), 16.44 (NH), 8.30 (3′-H), 8.74 (4′-H), 8.25 (5′-H), 9.08 (6’-H), 5.43 (CH), 4.41, 4.53 (OEt-CH_2-a,b), 1.34 (OEt-CH_3), 7.18 (*o*-Ph), 7.43 (*m*-Ph), 7.48 (*p*-Ph). NMR ^{13}C spectrum (−17 °C), δ, ppm: 88.8 (C2), 29.0 (2-Me), 195.9 (C4), 17.1 (4-Me), 83.9 (C5), 30.9 (5-Et-CH_2), 8.6 (5-Et-CH_3), 28.3 (5′-Et-CH_2), 9.7 (5′-Et-CH_3), 149.7 (C2′), 125.7 (C3′), 148.6 (C4′), 128.3 (C5′), 142.4 (C6′), 88.2 (CH), 176.9 (C=O), 65.6 (OEt-CH_2), 13.6 (OEt-CH_3), 131.3 (*i*-Ph), 126.9 (*o*-Ph), 129.6 (*m*-Ph), 130.6 (*p*-Ph).

2. Protonation of 1a in TfOH. Compound **1a** (16.8 mg, 0.041 mmol) was dissolved in 0.1 mL of CD_2Cl_2, then 0.4 mL (4.5 mmol) TfOH was added, followed by mixing. The NMR spectra of the resulting solution were recorded. Two forms **A** and **B** of $\mathbf{1aH_2}$ species were observed (**A**/**B** = 3 : 2) with insignificantly different diffusion coefficients in DOSY spectra, with a slow (in the NMR scale) chemical exchange between them (observed in NOESY/EXSY spectra). As suggested by NOESY spectra, the pyridine fragment and OR group in **A** are in *syn*-configuration, while in **B** − in *anti*-configuration.

$\mathbf{1aH_2}$**-A** species. NMR ^{1}H spectrum (26 °C), δ, ppm: 2.47 (2-Me), 11.17 (N2-H), 2.86 (4-Me), 2.55, 2.64 (5-Et-CH_2-a,b), 1.41 (5-Et-CH_3), 2.28, 2.41 (5′-Et-CH_2-a,b), 1.39 (5′-Et-CH_3), 11.66 (N1′-H), 8.15 (3′-H), 8.78 (4′-H), 8.23 (5′-H), 8.38 (6′-H), 5.90 (CH), 4.94 (OEt-CH_2), 1.60 (OEt-CH_3), 7.50 (*o*-Ph), 7.53 (*m*-Ph), 7.65 (*p*-Ph). NMR ^{13}C spectrum (26 °C), δ, ppm: 89.2 (C2), 21.1 (2-Me), 200.1 (C4), 18.2 (4-Me), 85.8 (C5), 26.7 (5-Et-CH_2), 8.9 (5-Et-CH_3), 30.1 (5′-Et-CH_2), 8.9 (5′-Et-CH_3), 147.2 (C2′), 126.5 (C3′), 150.6 (C4′), 129.8 (C5′), 142.5 (C6′), 84.7 (CH), 179.3 (C=O), 74.0 (OEt-CH_2), 12.3 (OEt-CH_3), 130.9 (*i*-Ph), 128.8 (*o*-Ph), 131.1 (*m*-Ph), 133.1 (*p*-Ph).

$\mathbf{1aH_2}$**-B**. species. NMR ^{1}H spectrum (26 °C), δ, ppm: 2.40 (2-Me), 2.95 (4-Me), 2.05, 2.44 (5-Et-CH_2-a,b), 1.25 (5-Et-CH_3), 1.83, 1.94 (5’-Et-CH_2-a,b), 0.66 (5′-Et-CH_3), 16.76 (N1′-H), 8.17 (3′-H), 8.86 (4′-H), 8.40 (5′-H), 9.21 (6′-H), 5.68 (CH), 4.62, 4.63 (OEt-CH_2-a,b), 1.42 (OEt-CH_3), 7.33 (*o*-Ph), 7.53 (*m*-Ph), 7.57 (*p*-Ph). NMR ^{13}C spectrum (26 °C), δ, ppm: 88.1 (C2), 28.2 (2-Me), 204.5 (C4), 18.1 (4-Me), 84.7 (C5), 30.0 (5-Et-CH_2), 7.9 (5-Et-CH_3), 28.2 (5′-Et-CH_2), 8.7 (5′-Et-CH_3), 147.8 (C2′), 124.5 (C3′), 148.7 (C4′), 129.1 (C5′), 143.6 (C6′), 89.2 (CH), 176.9 (C=O), 65.8 (OEt-CH_2), 12.6 (OEt-CH_3), 131.2 (*i*-Ph), 126.9 (*o*-Ph), 129.5 (*m*-Ph), 130.7 (*p*-Ph).

3. Protonation of 1a in FSO_3H-SbF_5. The solution of compound **1a** (15 mg, 0.40 mmol) in 0.1 mL of CD_2Cl_2 was added to the solution of FSO_3H-SbF_5 (molar ratio 1 : 1, 274 mg, 0.86 mmol) in 0.3 mL of SO_2ClF at −90 °C, and mixed. NMR

spectra of the resulting solution were recorded. NMR ^{1}H spectrum (−28 °C), δ, ppm: 12.89 (N1-H), 2.45 (2-Me), 10.40 (N3-H), 2.81 (4-Me), 2.32, 2.38 (5-Et-CH_2-a,b), 1.39 (5-Et-CH_3), 2.47, 2.66 (5′-Et-CH_2-a,b),1.39 (5′-Et-CH_3), 11.35 (N1′-H), 8.03 (3′-H), 8.66 (4′-H), 8.12 (5′-H), 8.33 (6′-H), 6.01 (CH), 5.24 (OEt-CH_2), 1.70 (OEt-CH_3), 7.43 (*o*-Ph), 7.49 (*m*-Ph), 7.63 (*p*-Ph). NMR ^{13}C spectrum (−28 °C), δ, ppm: 88.3 (C2), 20.0 (2-Me), 200.5 (C4), 18.3 (4-Me), 85.3 (C5), 29.4 (5-Et-CH_2), 9.0 (5-Et-CH_3), 26.6 (5′-Et-CH_2), 8.8 (5′-Et-CH_3), 146.0 (C2′), 126.7 (C3′), 150.8 (C4′), 130.0 (C5′), 142.8 (C6′), 83.6 (CH), 184.5 (C=O), 81.2 (OEt-CH_2), 12.5 (OEt-CH_3), 128.7 (*i*-Ph), 129.0 (*o*-Ph), 131.6 (*m*-Ph), 134.1 (*p*-Ph).

4. Reaction of 1a in TFA. The solution of **1a** in TFA-CD_2Cl_2, prepared according to procedure 1, was kept for 40 min at 64 °C. An equimolar mixture of **2H** and **3aH** was formed. The NMR ^{1}H spectrum of the mixture exhibited a signal at δ 13.54 ppm, with the intensity corresponding to 1H, broadened as a consequence of exchange with the acid and evidently related to one of the protonated forms. It is impossible to determine what species does this proton belong to, because this signal, due to its substantial width, did not appear in any correlation spectra (nevertheless, see procedure 8).

Cation **2H**. NMR ^{1}H spectrum (25 °C), δ, ppm: 2.64 (1-Me), 2.89 (3-Me), 7.86 (4-H), 7.08 (5-H), 7.12 (6-H), 7.59 (7-H). NMR ^{13}C spectrum (25 °C), δ, ppm: 119.7 (C1), 8.7 (1-Me), 131.3 (C3), 9.8 (3-Me), 120.5 (C4), 118.1 (C5), 122.0 (C6), 118.3 (C7), 126.6 (C7a). NMR ^{15}N spectrum (25 °C), δ, ppm: 180.2 (N2), 188.9 (N3a).

Cation **3aH**. NMR ^{1}H spectrum (25 °C), δ, ppm: 2.46 (N=C-Et-CH_2), 1.20 (N=C-Et-CH_3), 2.61, 2.69 (N=C-Et′-CH_2-a,b), 1.21 (N=C-Et′-CH_3), 5.83 (CH), 4.26, 4.30 (OEt-CH_2-a,b), 1.27 (OEt-CH_3), 7.50 (*o*-Ph), 7.47 (*m*-Ph), 7.47 (*p*-Ph). NMR ^{13}C spectrum (25 °C), δ, ppm: 174.4 (N=C), 26.5 (N=C-Et-CH_2), 10.7 (N=C-Et-CH_3), 22.5 (N=C-Et′-CH_2), 9.4 (N=C-Et′-CH_3), 83.0 (CH), 171.4 (C=O), 62.9 (OEt-CH_2), 13.5 (OEt-CH_3), 133.2 (*i*-Ph), 127.7 (*o*-Ph), 128.9 (*m*-Ph), 129.8 (*p*-Ph). NMR ^{15}N spectrum (25 °C), δ, ppm: 305.1 (N=C).

5. Reaction of 1a in TfOH. The solution of **1a** in TfOH-CD_2Cl_2, prepared according to procedure 2, was kept for 7 days at room temperature. Dication $\mathbf{2H_2}$ was formed. In addition, the signals of some non-identified products formed, judging from the presence of characteristic fragments $=CEt_2$, OEt and Ph, as a result of destruction of oxime **3a** were observed in the spectra.

Dication $\mathbf{2H_2}$. NMR ^{1}H spectrum (27 °C), δ, ppm: 3.45 (1-Me), 12.61 (N2-H), 7.20 (C3), 2.42 (3-Me), 9.51 (4-H), 8.87 (5-H), 9.29 (6-H), 9.15 (7-H). NMR ^{13}C spectrum (27 °C), δ, ppm: 178.8 (C1), 15.7 (1-Me), 86.6 (C3), 17.6 (3-Me), 142.1 (C4), 134.6 (C5), 150.6 (C6), 129.0 (C7), 142.1 (C7a). NMR ^{15}N spectrum (27 °C), δ, ppm: 205.9 (N2), 219.1 (N3a).

6. Rearrangement of dication $\mathbf{2H_2}'$ into dication $\mathbf{2H_2}$. TfOH in the amount of 0.4 mL (4.5 mmol) was added to the solution containing an equimolar mixture of cations **2H** and **3aH**, prepared according to procedure 4, at −40 °C, and mixed. Two-phase solution containing the layered nondissolved CD_2Cl_2 in the top phase was obtained. The NMR spectra of the bottom phase were recorded. An equimolar mixture of dication $\mathbf{2H_2}'$ and cation **3aH** was formed. At −5 °C, a rearrangement of $\mathbf{2H_2}'$ into $\mathbf{2H_2}$ was observed. Cation **3aH** was partially decomposed (see procedure 5).

Dication $\mathbf{2H_2}'$. NMR ^{1}H spectrum (−5 °C), δ, ppm: 6.35 (H1), 2.20 (1-Me), 12.60 (N2-H), 3.59 (3-Me), 9.54 (4-H), 8.74 (5-H), 9.41 (6-H), 8.84 (7-H). NMR ^{13}C spectrum (−5 °C), δ, ppm: 66.9 (C1), 14.4 (1-Me), 173.1 (C3), 14.1 (3-Me), 138.3 (C4), 130.0 (C5), 156.3 (C6), 124.9 (C7), 157.8 (C7a). NMR ^{15}N spectrum (−5 °C), δ, ppm: 195.3 (N2), 211.2 (N3a).

Dication $\mathbf{2H_2}$. NMR spectra are practically the same as those presented in procedure 5. NMR ^{1}H spectrum (−5 °C), δ, ppm: 3.44 (1-Me), 12.59 (N2-H), 7.20 (3-H), 2.40 (3-Me), 9.51 (4-H), 8.86 (5-H), 9.28 (6-H), 9.15 (7-H). NMR ^{13}C spectrum (−5 °C), δ, ppm: 178.7 (C1), 15.7 (1-Me), 86.6 (C3), 17.5 (3-Me), 142.1 (C4), 134.5 (C5), 150.6 (C6), 128.9 (C7), 142.1 (C7a). NMR ^{15}N spectrum (−5 °C), δ, ppm: 206.0 (N2), 219.1 (N3a).

Cation **3aH**. NMR ^{1}H spectrum (−5 °C), δ, ppm: 11.44 (N-H), 2.90 (N=C-Et-CH_2), 1.36 (N=C-Et-CH_3), 2.94 (N=C-Et′-CH_2), 1.31 (N=C-Et′-CH_3), 6.29 (CH), 4.92, 4.95 (OEt-CH_2-a,b), 1.61 (OEt-CH_3), 7.63 (*o*-Ph), 7.72 (*m*-Ph), 7.78 (*p*-Ph). In the NOESY spectrum, correlation of protons of N-H and N=C-Et-CH_2 is observed. NMR ^{13}C spectrum (−5 °C), δ, ppm: 194.2 (N=C), 27.9 (N=C-Et-CH_2), 8.3 (N=C-Et-CH_3), 25.2 (N=C-Et′-CH_2), 8.5 (N=C-Et′-CH_3), 85.4 (CH), 177.6 (C=O), 72.9 (OEt-CH_2), 12.4 (OEt-CH_3), 126.7 (*i*-Ph), 128.8 (*o*-Ph), 130.5 (*m*-Ph), 133.2 (*p*-Ph). NMR ^{15}N spectrum (−5 °C), δ, ppm: 221.1 (N=C).

7. Reaction of 1a in FSO_3H-SbF_5. The formation of a small amount of trication $\mathbf{1cH_3}$ was observed in reaction mixture obtained according to procedure 3 at decreased temperature. The same trication is formed as the major product in the acid system FSO_3H-SbF_5 without a solvent from compound **1a**′, which is diastereoisomer of compound **1a**, differing only by the configuration of

carbon atom in the substituent OCHPhCOOEt. The "magic acid" (an equimolar mixture FSO_3H-SbF_5, 1.37 g) cooled to the viscous state was added to compound **1a′** (16 mg). The mixture was stirred to achieve complete dissolution of solid **1a′**, under heating to the room temperature. NMR spectra exhibit only the signals of triply protonated amine **1c** (**1c**H_3). The signals that could be assigned to the derivatives of the detached substituent OCHPhCOOEt are absent (it is likely to participate in the reduction of the nitroxide fragment to form amine **1c**, transforming into a mixture of the products of oxidation and oligomerization).

Trication **1c**H_3. NMR ^{1}H spectrum (26 °C), δ, ppm: 7.90, 8.01 (N1-H_2-a,b), 2.97 (2-Me), 11.25 (N3-H), 3.32 (4-Me), 2.69, 2.77 (5-Et-CH_2-a,b), 1.50 (5-Et-CH_3), 2.55, 2.69 (5′-Et-CH_2-a,b), 1.38 (5′-Et-CH_3), 12.54 (N1′-H), 8.43 (3′-H), 9.24 (4′-H), 8.73 (5′-H), 9.25 (6′-H). NMR ^{13}C spectrum (26 °C), δ, ppm: 87.1 (C2), 22.6 (2-Me), 202.7 (C4), 18.2 (4-Me), 89.5 (C5), 28.1 (5-Et-CH_2), 6.5 (5-Et-CH_3), 29.2 (5′-Et-CH_2), 6.4 (5′-Et-CH_3), 138.8 (C2′), 126.6 (C3′), 152.7 (C4′), 133.5 (C5′), 147.2 (C6′). NMR ^{15}N spectrum (26 °C), δ, ppm: 82.1 (N1), 195.1 (N3), 187.2 (N1′).

Reaction mixture containing trication **1c**H_3 was added drop by drop at 0 °C under mixing to 5 mL of methanol, and filtered. In the NMR ^{1}H spectrum of the solution, we observed the signals from cation **2H** (procedure 9), as well as a quartet and triplet (δ 2.71 and 1.17 ppm, respectively) of ethyl groups, likely related to imine Et_2C=NH.

8. Reaction of 1$^\bullet$ in TFA. Trifluoroacetic acid in the amount of 0.4 mL (0.53 mmol) was added to the solution of radical **1$^\bullet$** (7.5 mg, 0.030 mmol) in CD_2Cl_2 (0.1 mL) and kept for 2 h at room temperature. The initial yellowish-orange colour of the solution, characteristic of the nitroxide, became weak blue-green, characteristic of nitroso compounds. Judging from NMR spectra, an equimolar mixture of **2H**, **3bH** and **4** was formed (see Fig. 1).

NMR spectra of cation **2H** are very similar to those presented in procedure 3. We succeeded in determining in this experiment that the downfield signal observed in the NMR ^{1}H spectrum belongs to the proton bound with N2 atom of cation **2H**.

Cation **2H**. NMR ^{1}H spectrum (5 °C), δ, ppm: 2.72 (1-Me), 12.35 (N2-H), 2.97 (3-Me), 7.99 (4-H), 7.18 (5-H), 7.22 (6-H), 7.69 (7-H). NMR ^{13}C spectrum (5 °C), δ, ppm: 120.9 (C1), 9.0 (1-Me), 132.7 (C3), 10.2 (3-Me), 121.7 (C4), 119.8 (C5), 123.8 (C6), 119.3 (C7), 128.4 (C7a). NMR ^{15}N spectrum (5 °C), δ, ppm: 175.9 (N2), 189.4 (N3a).

Cation **3bH**. NMR ^{1}H spectrum (5 °C), δ, ppm: 2.85 (Et-CH_2), 1.43 (Et-CH_3), 2.93 (Et′-CH_2), 1.43 (Et′-CH_3). NMR ^{13}C spectrum (5 °C), δ, ppm: 180.9 (N=C), 28.2 (Et-CH_2), 9.4 (Et-CH_3), 24.4 (Et′-CH_2), 9.0 (Et′-CH_3). NMR ^{15}N spectrum (5 °C), δ, ppm: 221.9 (N=C).

Cation **4**. NMR ^{1}H spectrum (5 °C), δ, ppm: 3.00 (1-Me), 2.23 (3-Me), 9.57 (4-H), 8.33 (5-H), 9.00 (6-H), 8.66 (7-H), 1.62, 1.87 (Et-CH_2-a,b), 0.93 (Et-CH_3), 0.97, 1.12 (Et′-CH_2-a,b), 0.18 (Et′-CH_3). NMR ^{13}C spectrum (5 °C), δ, ppm: 166.1 (C1), 15.9 (1-Me), 110.3 (C3), 22.8 (3-Me), 144.2 (C4), 129.4 (C5), 150.0 (C6), 124.2 (C7), 148.5 (C7a), 109.3 (C-N=O), 21.1 (Et-CH_2), 8.5 (Et-CH_3), 19.5 (Et′-CH_2), 6.5 (Et′-CH_3). NMR ^{15}N spectrum (5 °C), δ, ppm: 334.2 (N2), 244.9 (N3a), 956.2 (N=O).

9. Reduction of radical 1$^\bullet$ and reaction with TFA. TFA, 0.01 mL (1.32 mmol) was added to a mixture of **1$^\bullet$** (13 mg, 0.053 mmol), zinc powder (75 mg, 1.15 mmol) and CD_3OD (0.6 mL); mixing was carried out for 5 min at room temperature. The liquid phase of the mixture became colourless almost immediately. The mixture was separated by filtering from unreacted zinc, and 0.03 mL (3.95 mmol) of TFA was added. NMR spectra suggested that an equimolar mixture of cations **2H** and **3bH** was formed. It should be noted that under these conditions the exchange of protons of 3-CH_3 in **2H** for deuterium was observed (by 1/4 for 3 h).

Cation **2H**. NMR ^{1}H spectrum (25 °C), δ, ppm: 2.60 (1-Me), 2.84 (3-Me), 2.82 (3-CH_2D), 8.14 (4-H), 7.03 (5-H), 7.07 (6-H), 7.67 (7-H). NMR ^{13}C spectrum (25 °C), δ, ppm: 120.3 (C1), 8.9 (1-Me), 133.4 (C3), 10.0 (3-Me), 9.8 (3-CH_2D), 122.7 (C4), 118.4 (C5), 122.9 (C6), 119.2 (C7), 127.9 (C7a).

Cation **3bH**. NMR ^{1}H spectrum (25 °C), δ, ppm: 2.31 (Et-CH_2), 1.11 (Et-CH_3), 2.44 (Et′-CH_2), 1.10 (Et′-CH_3). NMR ^{13}C spectrum (25 °C), δ, ppm: 169.0 (N=C), 27.5 (Et-CH_2), 11.2 (Et-CH_3), 22.1 (Et′-CH_2), 10.0 (Et'-CH_3).

10. Oxidation of radical 1$^\bullet$ and reaction with TFA. Br_2, 0.045 mL of 1 M solution in CCl_4 (0.045 mmol), was added to the solution of **1$^\bullet$** (5.5 mg, 0.022 mmol) in CD_2Cl_2 at 0 °C, and mixed for 3 min. Then 0.4 mL (5.3 mmol) of TFA was added. NMR ^{1}H spectrum shows that compound **4** was formed, but it degraded rapidly at room temperature. Instability of compound **4** under these conditions may be due to the presence of excess bromine in the reaction mixture, which causes the side process of nitroso group substitution by bromine [22].

11. Recording EPR spectra of radical 1$^\bullet$. A portion of radical **1$^\bullet$**, 2 mg in mass, was dissolved

in 0.1 mL of chlorobenzene. The resulting solution (0.08 M) was diluted to the concentration of $2 \cdot 10^{-4}$ M, then 50 mL of this mixture was placed in a glass capillary, and EPR spectrum was recorded. Then TFA was added to the solution with radical concentration $2 \cdot 10^{-4}$ M to achieve the acid concentration 0.5 M, and EPR spectrum of the resulting solution was recorded. Then the sample containing TFA was degassed in vacuum, the capillary was sealed and kept at 60 °C in the oil thermostat. EPR spectra were recorded at room temperature every hour. A decrease in the intensity of EPR signal with time was observed (see Fig. 1).

12. Reaction of radical 1• in FSO_3H-SbF_5. The "magic acid" (an equimolar mixture FSO_3H-SbF_5, 0.45 mL) cooled to the viscous state was added to the portion of radical **1•** (13 mg) in the NMR tube. The radical was not soluble in the acid even under mixing at room temperature, but it readily formed a homogeneous solution when the NMR tube was placed in an ultrasonic bath. NMR spectra exhibited the signals of triply protonated compounds: hydroxylamine **1b** (**$1bH_3$**, in the form of a mixture of diastereomers at atom N1 **$1bH_3$-A** and **$1bH_3$-B** at a ratio of 3 : 1) and N-oxide **6**. The ratio **1bH3/6** is equal to 1 : 1. As suggested by the NOESY spectra, in **$1bH_3$-A**, OH group and the pyridine fragment are in *syn*-configuration, while in **$1bH_3$-B** – *anti*. The signal from the proton of OH group in trication 6 was not observed under these conditions; the conclusion concerning substantial degree of protonation of the oxygen atom in N-oxide was made relying on the presence of distinct cross peaks in the NOESY spectrum, corresponding to cross-relaxation between the protons of the acid and groups 2-Me and 5-Et. It should be noted the signal from the proton of OH-group (δ 11.94 ppm) was recorded at −50 °C, see procedure 13.

Trication **6**. NMR ^{1}H spectrum (27 °C), δ, ppm: 3.05 (2-Me), 12.87 (N3-H), 3.69 (4-Me), 3.70 (5-Et-CH_2), 1.86 (5-Et-CH_3), 12.59 (N1′-H), 8.36 (3′-H), 9.16 (4′-H), 8.70 (5′-H), 9.23 (6′-H). NMR 13C spectrum (27 °C), δ, ppm: 97.2 (C2), 20.7 (2-Me), 187.3 (C4), 19.5 (4-Me), 167.8 (C5), 21.8 (5-Et-CH_2), 8.0 (5-Et-CH_3), 133.7 (C2′), 127.3 (C3′), 152.7 (C4′), 133.4 (C5′), 147.3 (C6′). NMR 15N spectrum (27 °C), δ, ppm: 270.0 (N1), 209.8 (N3), 187.0 (N1′).

Trication **$1bH_3$-A**. NMR ^{1}H spectrum (27 °C), δ, ppm: 10.27 (N1-H), 8.89 (1-OH), 3.00 (2-Me), 11.51 (N3-H), 3.38(4-Me), 2.43, 2.64 (5-Et-CH_2-a,b), 1.36 (5-Et-CH_3), 2.73, 2.81 (5-Et′-CH2-a,b), 1.53 (5-Et′-CH_3), 12.50 (N1′-H), 8.42 (3′-H), 9.20 (4′-H), 8.70 (5′-H), 9.25 (6′-H). NMR 13C spectrum (27 °C), δ, ppm: 94.8 (C2), 22.3 (2-Me), 203.9 (C4), 19.9 (4-Me), 95.8 (C5), 25.1 (5-Et-CH2), 7.0 (5-Et-CH_3), 28.0 (5-Et′-CH_2), 6.0 (5-Et′-CH_3), 136.4 (C2′), 127.9 (C3′), 151.7 (C4′), 133.0 (C5′), 147.1 (C6′). NMR 15N spectrum (27 °C), δ, ppm: 140.5 (N1), 192.7 (N3), 189.6 (N1′).

Trication **$1bH_3$-B**. NMR ^{1}H spectrum (27 °C), δ, ppm: 10.03 (N1-H), 8.78 (1-OH), 2.90 (2-Me), 11.48 (N3-H), 3.35 (4-Me), 2.62, 2.77 (5-Et-CH_2-a,b), 1.42 (5-Et-CH_3), 2.72, 2.87 (5-Et′-CH_2-a,b), 1.53 (5-Et′-CH_3), 12.59 (N1′-H), 8.47 (3′-H), 9.26 (4′-H), 8.76 (5′-H), 9.28 (6′-H). NMR 13C spectrum (27 °C), δ, ppm: 94.8 (C2), 18.4 (2-Me), 202.9 (C4), 19.7 (4-Me), 95.9 (C5), 28.6 (5-Et-CH_2), 5.8 (5-Et-CH_3), 25.3 (5-Et′-CH_2), 7.2 (5-Et′-CH_3), 137.8 (C2′), 126.4 (C3′), 152.9 (C4′), 133.9 (C5′), 147.7 (C6′). NMR 15N spectrum (27 °C), δ, ppm: 139.8 (N1), 193.6 (N3), 187.0 (N1′).

According to NOESY spectra, groups Et and Et′ in **$1bH_3$-A** and **$1bH_3$-B** are in *syn*- and *anti*-positions with the pyridine fragment, respectively.

13. Reaction of radical 1• in FSO_3H-SbF_5/SO_2ClF/CD_2Cl_2. The solution of radical 1• (18 mg) in CD_2Cl_2 (0.1 mL) was added to the solution of the "magic acid" (368 mg) in SO_2ClF (0.3 mL) at −90 °C and mixed. NMR spectra exhibited the signals from **$1bH_3$-A**, **$1bH_3$-B**, **6** (procedure 12), as well as **6′**, **12** (CH_3CH_2X) and **13** (CH_3CH_2X'). Substituents X and X' in the species **12** and **13** contain no carbon atoms. These may be protonated forms of fluorosulphonates. At −40 °C 13 is rapidly and irreversibly transformed into 12. The ratios ((**$1bH_3$-A** + **$1bH_3$-B**)/(**6** + **6′**) and (**12** + **13**)/**6** are equal to 1 : 1.

Trication **6′**. NMR ^{1}H spectrum (−50 °C), δ, ppm: 2.89 (2-Me), 12.84 (N3-H), 3.53 (4-Me), 3.58, 3.65 (5-Et-CH_2-a,b), 1.77 (5-Et-CH_3), 12.55 (N1′-H), 8.29 (3′-H), 8.99 (4′-H), 8.54 (5′-H), 9.11 (6′-H), 5.05, 5.14 (OEt-CH_2-a,b), 1.78 (OEt-CH_3). NMR ^{13}C spectrum (−50 °C), δ, ppm: 98.0 (C2), 20.5 (2-Me), 188.1 (C4), 20.3 (4-Me), 173.9 (C5), 24.1 (5-Et-CH_2), 10.5 (5-Et-CH_3), 134.9 (C2′), 128.5 (C3′), 153.1 (C4′), 134.0 (C5′), 147.8 (C6′), 91.6 (OEt-CH_2), 13.9 (OEt-CH_3).

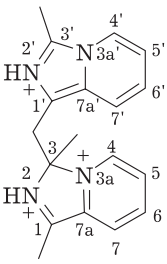
Species **12** (late). NMR ^{1}H spectrum (−50 °C), δ, ppm: 5.03 (CH_2), 1.94 (CH_3). NMR ^{13}C spectrum (−50 °C), δ, ppm: 72.2 (CH_2), 14.8 (CH_3).

Species **13** (early). NMR 1H spectrum (−50 °C), δ, ppm: 5.42 (CH_2), 2.05 (CH_3). NMR ^{13}C spectrum (−50 °C), δ, ppm: 77.5 (CH_2), 14.9 (CH_3).

14. Reaction of radical 1• in TfOH/CD_2Cl_2. A mixture of radical 1• (19 mg), CD_2Cl_2 (0.1 mL) and TfOH (0.5 mL) was kept for 1 h at 25 °C.

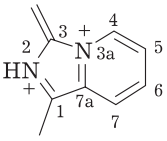
During this time, the radical had almost completely transformed into diamagnetic products. NMR spectra of the resulting solution revealed protonated oxide **3bH**, N,C-diprotonated heterocycle $\mathbf{2H_2}$, dimer **14** and olefin **15** at the molar ratio of 10 : 5.7 : 1.0 : 1.3, respectively. After long-term exposure (3 months) of the sample at room temperature, the content of oxime **3bH** decreases substantially, while the signals of the cations of dimer **14** and olefin **15** disappear completely. According to NMR data, reaction mixture containing N-ethylated propionitrile **16** and oxime **3bH**, dications $\mathbf{2H_2}$ and **17**, as well as dimeric trication **18** at a ratio of 9 : 5 : 5 : 1 : 3, respectively, is formed. The solution is gradually getting intensively blue-coloured, which is likely to be caused by the accumulation of the conjugated trication **18**.

NMR spectra of oxime **3bH** see in procedure 8, heterocycle $\mathbf{2H_2}$ – in procedure 6.



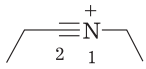
14

Dimer **14**. NMR ^{1}H spectrum (27 °C), δ, ppm: 3.46 (1-Me), 2.49 (3-Me), 9.49 (4-H), 8.90 (5-H), 9.34 (6-H), 9.41 (7-H), 4.08, 4.43 (CH_2-a,b; $^1J_{ab}$ = 16 Hz), 11.98 (N2′-H), 3.08 (3′-Me), 8.22 (4′-H), 7.41 (5′-H), 7.58 (6′-H), 7.71 (7′-H). NMR ^{13}C spectrum (27 °C), δ, ppm: 180.7 (C1), 17.5 (1-Me), 98.5 (C3), 23.7 (3-Me), 142.4 (C4), 136.8 (C5), 152.9 (C6), 131.6 (C7), 142.3 (C7a), 35.5 (CH_2), 109.1 (C1′), 138.4 (C3′), 11.1 (3′-Me), 123.7 (C4′), 120.3 (C5′), 129.7 (C6′), 116.7 (C7′), 132.7 (C7a′). NMR ^{15}N spectrum (27 °C), δ, ppm: 212.3 (N2), 224.0 (N3a), 174.4 (N2′), 192.5 (N3a′).



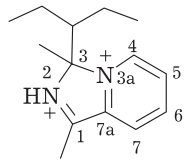
15

Olefin **15**. NMR ^{1}H spectrum (27 °C), δ, ppm: 3.46 (1-Me), 9.74 (4-H), 8.84 (5-H), 9.27 (6-H), 9.10 (7-H), 7.30, 7.61 (CH_2-a,b; $^1J_{ab}$ = 8 Hz). NMR ^{13}C spectrum (27 °C), δ, ppm: 174.9 (C1), 16.9 (1-Me), 135.2 (C3), 138.8 (C4), 136.5 (C5), 152.5 (C6), 129.2 (C7), 141.5 (C7a), 119.3 (CH_2; $^1J_{CH}$ = 179 Hz). NMR ^{15}N spectrum (27 °C), δ, ppm: 204.4 (N3a).



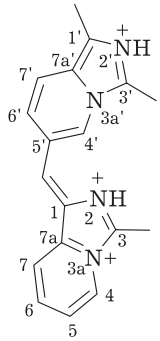
16

Propionitrile **16**. NMR ^{1}H spectrum (27 °C), δ, ppm: 1.60 (2-Et-CH_3), 1.67 (1-Et-CH_3), 3.21 (2-Et-CH_2), 4.20 (1-Et-CH_2). NMR ^{13}C spectrum (27 °C), δ, ppm: 8.4 (2-Et-CH_3), 12.9 (1-Et-CH_3), 112.1 (C2, $^1J_{C\text{-}14N}$ = 43 Hz), 12.9 (2-Et-CH_2), 43.7 (1-Et-CH_2, $^1J_{C\text{-}14N}$ = 4 Hz). NMR ^{15}N spectrum (27 °C), δ, ppm: 151.1 (N1).



17

Dication **17**. NMR ^{1}H spectrum (27 °C), δ, ppm: 3.42 (1-Me), 12.84 (2-H), 2.40 (3-Me), 2.55 (3-CH), 9.41 (4-H), 8.85 (5-H), 9.25 (6-H), 9.14 (7-H), 0.67, 1.19 (Et-CH_2-a,b), 0.91 (Et-CH_3), 1.81, 2.06 (Et′-CH_2-a,b), 1.30 (Et′-CH_3). NMR ^{13}C spectrum (27 °C), δ, ppm: 179.1 (C1), 16.9 (1-Me), 104.5 (C3), 142.2 (C4), 136.5 (C5), 151.7 (C6), 131.2 (C7), 142.4 (C7a), 17.1 (1-Me), 24.2 (3-Me), 52.9 (3-CH), 21.5 (Et-CH_2), 12.0 (Et-CH_3), 23.8 (Et'-CH_2), 13.1 (Et′-CH_3). NMR ^{15}N spectrum (27 °C), δ, ppm: 213.4 (N2), 228.2 (N3a).



18

Trication **18**. NMR ^{1}H spectrum (27 °C), δ, ppm: 8.93 (1-CH), 3.61 (3-Me), 9.20 (4-H), 8.42 (5-H), 9.02 (6-H), 8.97 (7-H), 3.01 (1′-Me), 12.13 (N2′-H), 3.13 (3′-Me), 8.31 (4′-H), 7.70 (5′-H), 8.94 (7′-H). NMR ^{13}C spectrum (27 °C), δ, ppm: 128.3 (C1), 145.6 (1-CH), 163.1 (C3), 14.0 (3-Me), 133.4 (C4), 128.7 (C5), 150.2 (C6), 122.7 (C7), 145.6 (C7a), 138.8 (C1′), 11.0 (1′-Me), 141.6 (C3′), 11.3 (3′-Me), 125.7 (C4′), 116.1 (C5′), 127.7 (C6′), 140.8 (C7′), 128.5 (C7a′). NMR ^{15}N spectrum (27 °C), δ, ppm: 177.5 (N2), 203.4 (N3a), 183.5 (N2′), 186.1 (N3a′).

CONCLUSION

An important goal of our work was to reveal the factors affecting the stability of alkoxyamines of the imidazoline series. One can readily conclude that substituted alkoxyamines may be subjected to electrophilic reactions in acid media, and the presence of a nucleophilic cenrtre in the substituent is the main factor of decreased stability. The effect of acidity is less evident. Thus, in the media with very low acidity, such as mercaptoethanol or dimethylsulphoxide, with insignificant admixture of water, rearrangement of alkoxyamine **1a** is observed only at increased temperature, proceeds non-selectively, and its rate is comparable with the rate of radical homolysis [2]. It is demonstrated that in rather strong trifluoroacetic acid alkoxyamine rearranges easily and quantitatively even at room temperature. However, passing from trifluoroacetic acid to much stronger trifluoromethanesulphonic acid (TfOH), the stability of alkoxyamine **1a** is not decreased; quite contrary, it increases substantially (almost by two orders of magnitude). The reason is that the above-considered acid-catalyzed rearrangement of alkoxyamine **1a** requires at least partial protonation of one (any) of nitrogen atoms of the imidazoline cycle, but the lone electron pair of nitrogen atom of the pyridine fragment should remain free. Trifluoromethanesulphonic acid protonates the pyridine nitrogen atom almost completely and efficiently blocks up its lone pair. This protective protonation may be considered as a factor promoting the stability of alkoxyamines. For instance, in FSO_3H-SbF_5, possessing even higher acidity, the factor of protective protonation becomes dominating, and rearrangement of pyridylimidazoline is ceased completely.

Acknowledgements

The work was carried out within the State Assignment for the NIOCh SB RAS No. AAAA-A21-121011490019-9 and with support from RFBR, Projects Nos. 20-03-00187 and 20-33-90133.

The authors are grateful to the Multi-Access Chemical Research Center SB RAS for the spectral and analytical measurements and thank the Novosibirsk University Scientific Computing Center (http://www.nusc.ru) for the computing resources.

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