1,3-Dipolar Cycloaddition Reaction of 4,5-Dihydro-1*H*-imidazole 3-oxides with Alkynes

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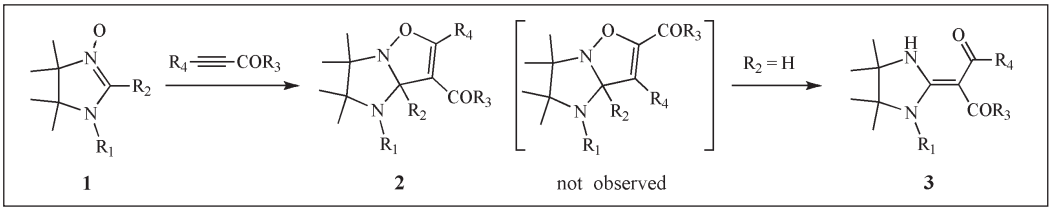

4,5-Dihydro-1*H*-imidazole 3-oxides bearing different substituents at positions 1 and 2 of the heterocycle were shown to react with a wide range of acceptor-substituted alkynes forming corrsponding cycloadducts – derivatives of 1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole. High regioselectivity of this process stipulated by conjugation of the nitrogen atom with the nitrone group was revealed.

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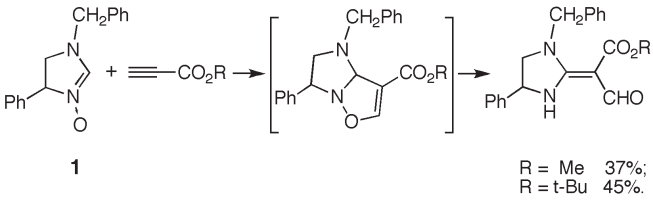
Introduction.

Over the past decades, reactions of 1,3-dipolar cycloaddition have been attracting attention due to the great possibilities of this synthetic approach. One of the advantages of this methodology is the vast variety of compounds of different classes taking part in this reaction as dipoles and dipolarophiles. This allows a wide spectrum of cycloadducts as well as products of their subsequent transformations to be obtained. Since the 60-s of the last century, scientists dealing with 1,3-dipolar cycloaddition reactions pay the highest attention to nitrones as 1,3-dipoles. The numerous approaches to obtaining compounds of different classes have been developed, which are based on cycloaddition of various dipolarophiles to nitrones. It should be mentioned that over the past few years, chemistry of isolated nitrones containing no functional substituents at the nitrogen or α-carbon atom as well as cycloaddition reactions of such nitrones have been thoroughly investigated [1-12].Unlike this, the nitrone group attached to the heteroatomic substituent at the α-carbon atom is a poorly studied, though interesting, target [13-18]. Derivatives of 4,5-dihydro-1*H*-imidazole 3-oxide, which can be considered as α-aminonitrones, are just such objects. The lone pair of the amino group is conjugated with the π-electron system of nitrone influencing the chemical properties of the latter.

The first attempts of using the derivative of the 4,5-dihydro-1*H*-imidazole 3-oxide in 1,3-dipolar cycloaddition reactions have been recently made (Scheme 1) [19-21].

Scheme 1

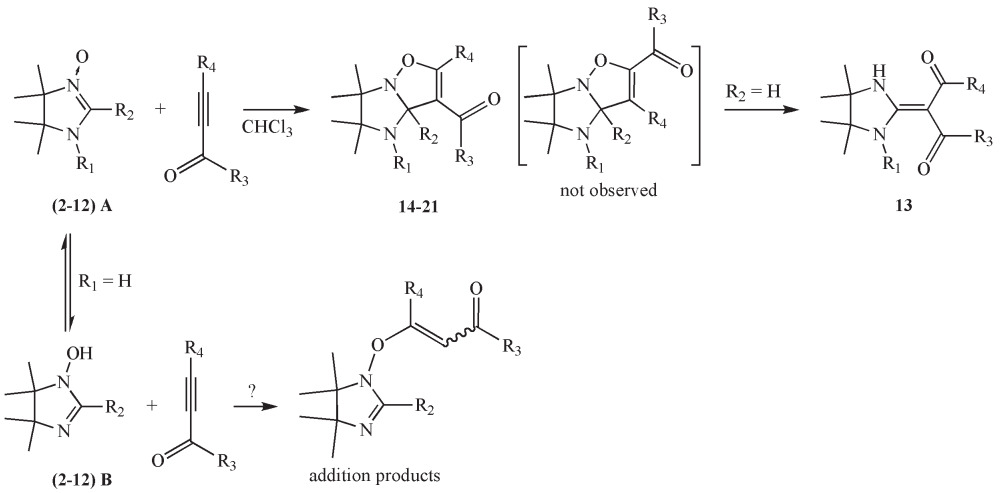


It should be pointed out that the authors have investigated only 4,5-dihydro-1*H*-imidazole 3-oxide **1**, containing the benzyl fragment at the nitrogen atom and hydrogen at position 2, *i.e*. compounds **1** can be related to cyclic aldonitrones, which are known to be more reactive than cyclic ketonitrones [22]. Besides, N-unsubstituted derivatives of 4,5-dihydro-1*H*-imidazole 3-oxide, as we showed previously [24], exist in solution as a mixture of two tautomeric forms - aminonitrone **A** and N-hydroxyaminoimine **B**. Only aminonitrone **A** is capable of taking part in the cycloaddition reaction, while N-hydroxyaminoimine **B** can act only as nucleophile (R_1 = H, Scheme 2).† It is not, therefore, obviously that N-non-substituted derivatives of 4,5-dihydro-1*H*-imidazole 3-oxide containing a substituent at position 2 of heterocycle can be involved in the reaction of 1,3-dipolar cycloaddition and this reaction is not described for related systems, apart from our previous paper [23].

Results and Discussion.

Methods for the preparation of a wide variety of 2-substituted derivatives of 4,5-dihydro-1*H*-imidazole 3-oxide **2-12** were reported earlier [24]. In the present paper these substances have been investigated as 1,3-dipoles in the reactions with a number of mono and disubstituted alkynes (Scheme 2).

Scheme 2



(2-12) A — 14-21 — 13

(2-12) B

R_1 = H (**2a-12a**, **13a,b**, **14a-g**, **15a**, **16a-e**, **17a-e**, **18a-f**, **19a-c**),
OH (**2c**, **4c**, **6c**, **13c, 15b**, **17n**),
Me (**3b**, **5b**, **6b**, **9b**, **11b**, **14h-14j**, **16f**, **17f-m**, **18g-18m**);
R_2 = H (**2a**, **2c**, **13a-c**),
Me (**3a**, **3b**, **14a-j**),
CF_3 (**4a,c**, **15a,b**),
tert-Bu (**5a,b**, **16a-f**),
Ph (**6a-c**, **17a-17n**), 2,4-$(Me)_2$-C_6H_3 (**7a**),
2,4,6-$(Me)_3$-C_6H_2 (**8a**), 4-NO_2-C_6H_4 (**9a,b**, **18a-m**),
3-NO_2-C_6H_4 (**10a**, **19a-c**),
4-MeO-C_6H_4 (**11a,b**, **20a-f**),
CH=CHC_6H_5 (**12a**, **21a,b**)

R_3 = OMe (**13a-c**, **14d-f,i,j**, **15b**, **16d-f**, **17c-e,j-l,n**, **18d-f,k-m**, **19b,c**, **20b,c,e,f**, **21a,b**)
H (**14a,h**, **16a**, **17f,g**, **18a,g,h**, **20d**)
Me (**14b**, **16b**, **17a,h**, **18b,i**, **19a**, **20a**)
Ph (**14c**, **16c**, **17b,i**, **18c,j**)
OEt (**14g**, **17m**),

R_4 = H (**13a**, **14d,i**, **16d,f**, **17c,f,j**, **18d,g**)
CO_2Me (**13b,c**, **14f,j**, **15a,b**, **16e**, **17e,l,n**, **18f,m**, **19c**, **20c,f**, **21b**)
Ph (**14a-c,e,h**, **16a-c**, **17a,b,d,g-i,k**, **18a-c,e,h-j,l**, **19a, 20a,d**)
CF_3 (**14g**, **17m**)

The reaction was carried out in homogeneous (in solution) or heterogeneous (when crystal sample of nitrone was kept in dipolarophile vapours) modes. In the most cases the reaction in solution occurs very rapidly at room temperature (during several minutes) leading to compounds **13-21** with a high, often quantitative, yield. Since the reaction is exothermic, it was carried out on cooling in case of very active dipoles and dipolarophiles. The reaction in heterogeneous conditions was carried out at 50-70 °C during several days up to several weeks depending on dipolarophile vapours pressure. Cycloaddition products of the same structure and with a comparable yield are formed when the reaction is carried out both in heterogeneous and in homogeneous conditions.

It is important to note that the reaction of N-non-substituted derivatives of 4,5-dihydro-1*H*-imidazole 3-oxide with alkynes in heterogeneous conditions occurs exclusively as cycloaddition, despite these compounds exist in the solid state usually as tautomeric form **B** [24].

Alkynes containing no strong electron withdrawing substituents (dimethylacetylene, phenylacetylene, diphenylacetylene, propargyl alcohol) do not react even with the most active nitrones under investigation. Formation of cycloaddition products, for example, was not registered when **2a** was kept with the excess of dimethylacetylene as a solvent at 80 °C for 15 days.

The distinguishing feature of derivatives of 4,5-dihydro-1*H*-imidazole 3-oxide is their high regioselectivity in cycloaddition reactions with alkynes: in case of asymmetric alkynes, only one regioisomer containing more electron withdrawing substituent at position 4 of the 2,3-dihydroisoxazole cycle is formed (Scheme 2).

The structures of regioisomers **14-21** are proved by NMR (^{1}H and ^{13}C) data. Chemical shifts as well as multiplicity of the signals of carbon atom at positions 6 and 7 of the 1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazoles in NMR spectra unambiguously indicate positions of substituents in 2,3-dihydroisoxazole cycle for structures **14a, 14g, 17a** and **18e** (Figure 1). Position of the ester group in **14d** is determined by ^{13}C-NMR data (*J*-modulation). The signal at 153.5 ppm (C-6) is

doublet that corresponds to regioisomer structure **14d** (Figure1).

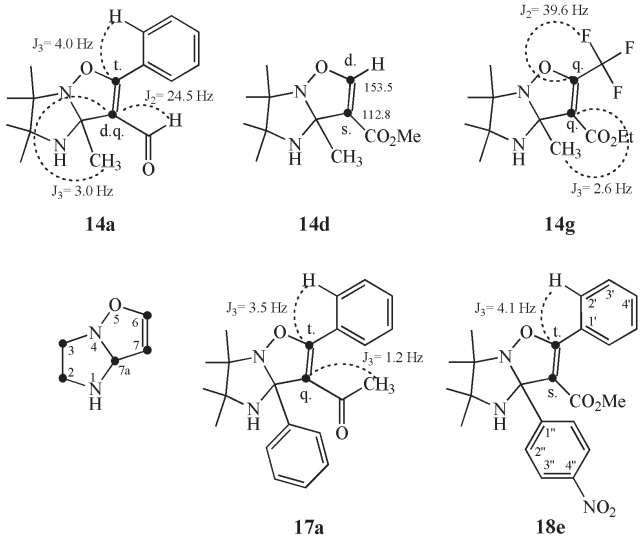
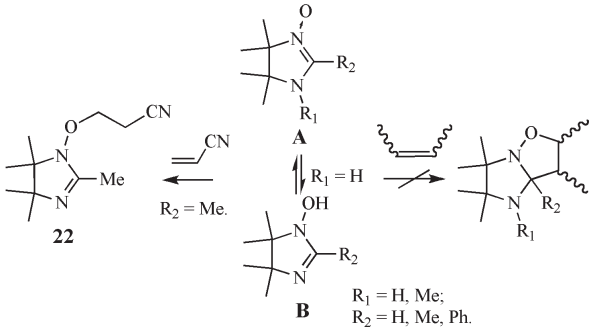


Figure 1. Spin-spin interaction and chemical shifts in ^{13}C-NMR spectra (mono resonance or *J*-modulation).

The structure of cycloadducts **14h, 16c, 17g** and **18j** is confirmed by X-ray diffraction analysis (Figure 2).

Examples of reaction of derivatives of 4,5-dihydro-1*H*-imidazole 3-oxide with alkenes are described in literature [20,21]. Our efforts to obtain cycloadducts by the reaction of **2a, 3a,b, 6a,b** with alkenes in different conditions were failed. Compounds containing a double bond which are the most active dipolarophiles towards the isolated nitrone group (acrylonitrile, phenylisocyanate, diethylazodicarboxylate, norboren, norbornadiene, maleic anhydride, N-phenylmaleimide) do not participate in the cycloaddition reaction with derivatives of 4,5-dihydro-1*H*-imidazole 3-oxide **2a, 3a,b, 6a,b** even upon prolonged heating in different solvents ($CHCl_3$, toluene or corresponding alkene) (Scheme 3). In most cases, the result of such interaction is the formation of products of

Scheme 3



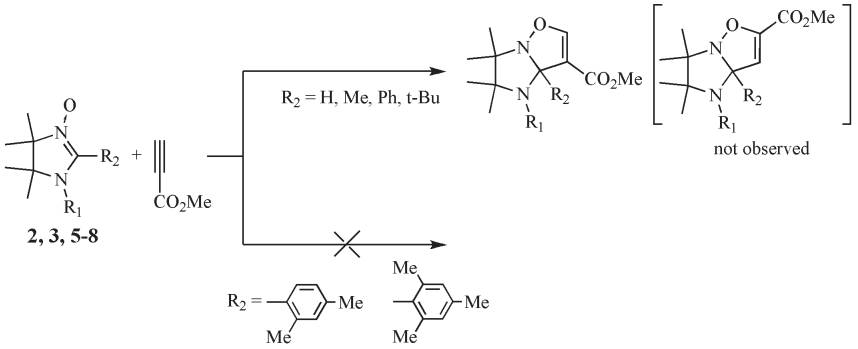
alkenes destruction and polymerization or products of nucleophilic addition of oxygen atom of the hydroxylamine group in tautomer **B** to the activated double bond of asymmetrically substituted alkene. Reaction of acrylonitrile with **3a** in chloroform, for example, results in formation of compound **22** (Scheme 3).

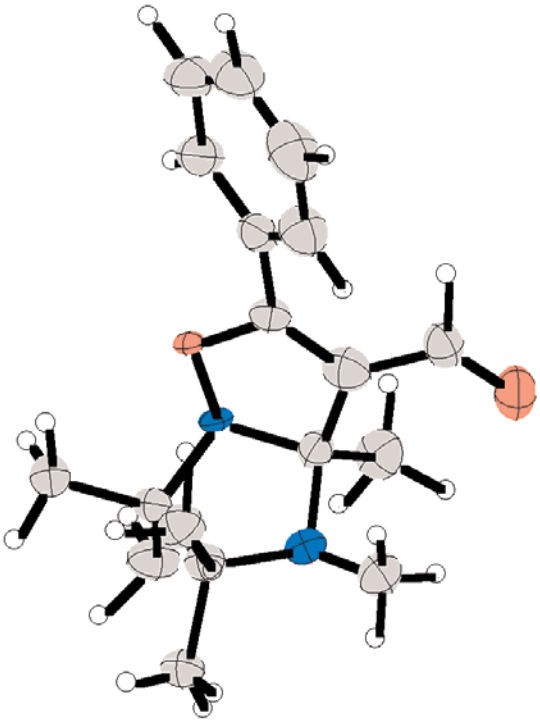
Product **22** is formed due to the peculiarity of N-non-substituted derivatives of 4,5-dihydro-1*H*-imidazole 3-oxide distinguishing them from the majority of nitrones and even from their N-substituted analogues. These compounds, as it is mentioned above, exist in solution as mixtures of two tautomeric forms - aminonitrone **A** and N-hydroxyaminoimine **B** (R_1 = H, scheme 3) [24]; form **B** plays the role of nucleophile towards the activated multiple bond. In spite of this fact, alkynes, unlike alkenes, react with N-non-substituted derivatives giving predominantly, and in most cases solely, corresponding cycloadducts.

Regioselectivity of the reaction is not changed even in the presence of considerable steric hindrance. Thus, although the reaction rate of imidazolines **2, 3, 5-8** with methyl propiolate noticeably decreases in the presence of a bulky substituent at position 2 of the 4,5-dihydro-1*H*-imidazole ring, the other - less hindered regioisomer is not formed (Scheme 4).

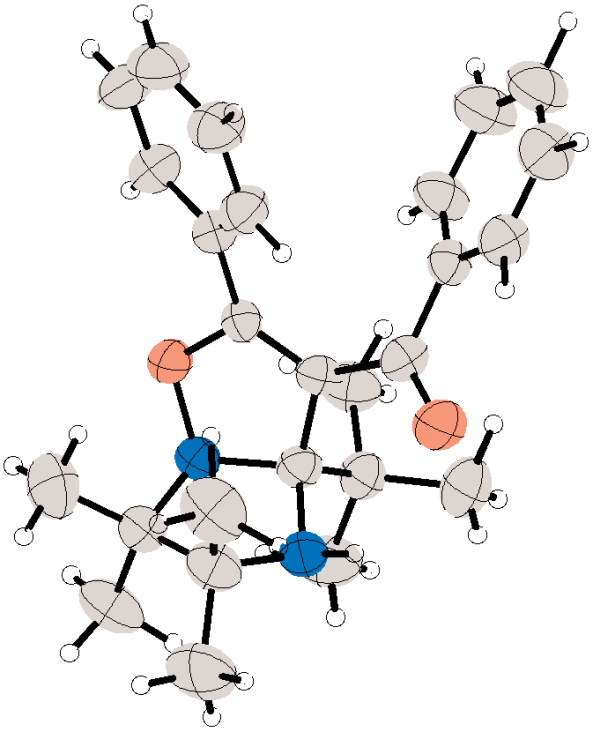
Introduction of one or two methyl groups in *ortho*-posi-

Scheme 4

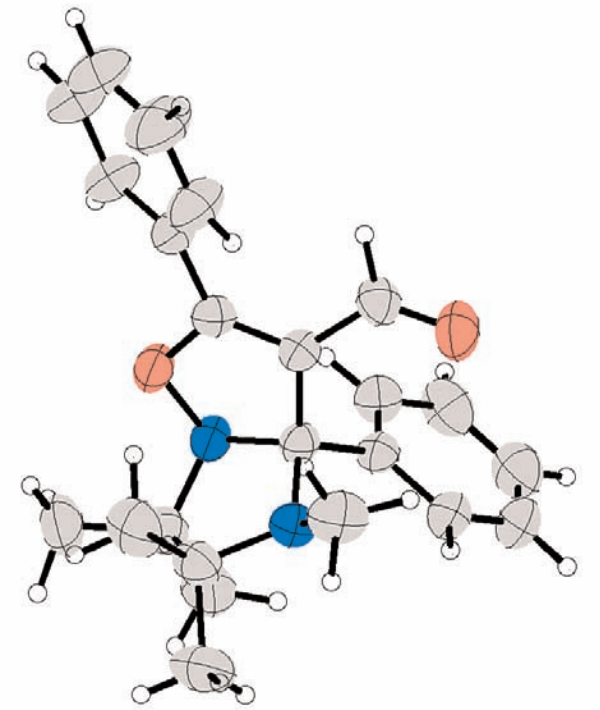




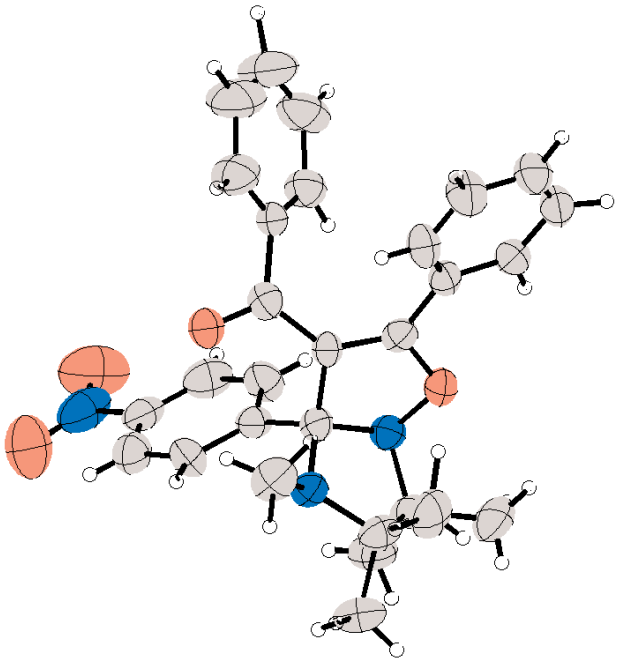
14h



16c



17g



18j

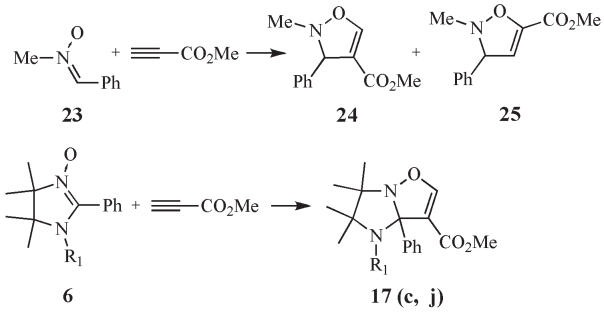
Figure 2. Crystal structure of **14h** (1,2,2,3,3,7a-hexamethyl-6-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carbaldehyde, CCDC 260688)**, 16c** ((7a-*tert*-butyl-2,2,3,3-tetramethyl-6-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)(phenyl)methanone, CCDC 260687)**, 17g** (6,7a-diphenyl-1,2,2,3,3-pentamethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carbaldehyde, CCDC 260355)**, 18j** ((1,2,2,3,3-pentamethyl-6-phenyl-7a-(4-nitrophenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)(phenyl)methanone, CCDC 260689).

tion of the phenyl ring in compounds **7** and **8** results in the twisting of the phenyl group from the plane of the 4,5-dihydro-1*H*-imidazole ring. As a result, the appreciable steric blocking of the nitrone group completely prevents the reaction with methyl propiolate. The introduction of two methyl groups in *ortho*-position of the phenyl ring leads to complete inactivation of the nitrone **8** even towards the most active dipolarophiles, such as dimethyl acetylenedicarboxylate (DMAD).

High regioselectivity of the reactions of the studied compounds with alkynes can be explained applying the theory of frontier molecular orbitals (FMO theory) widely used for the consideration of 1,3-dipolar cycloaddition reactions. In the overwhelming majority of the cases this reaction is the concerted process guided with the Woodward-Hoffman rule. According to *ab initio* HF/6-31G (d,p) calculations, the interaction of HOMO of 4,5-dihydro-1*H*-imidazole 3-oxide with LUMO of alkyne is determinative (Figure 3a). Thus, nitrone is donor and alkyne is acceptor of electrons. This is confirmed by the fact that the strengthening of the acceptor properties of substituents in alkyne is accompanied by the increase of the cycloaddition rate.

of nitrogen atom conjugated with the nitrone group. The nitrogen atom is π-donor that leads to raising the energy levels of frontier orbitals HOMO and LUMO in comparison with that of isolated nitrones. These increase the contribution of the interaction HOMO (nitrone) – LUMO (alkyne) and make less favourable the interaction LUMO (nitrone) – HOMO (alkyne). This fact stipulates higher regioselectivity of the studied system as compared to nitrones of similar structure. Thus, compounds **24** and **25** are formed in the reaction of N-methyl-C-phenylnitrone **23** with methyl in the ratio 58:42,

Scheme 5



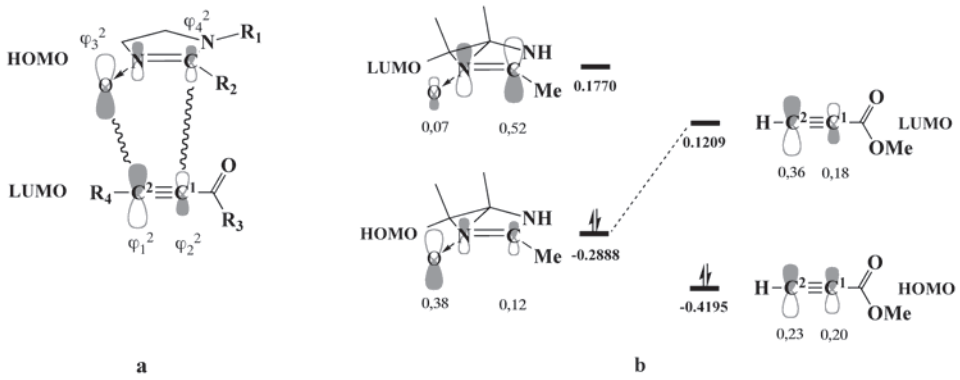


Figure 3. a - Interaction of HOMO of 4,5-dihydro-1*H*-imidazole 3-oxide with LUMO of alkyne; b - *ab initio* calculations in HF/6-31G (d,p) basis of the interaction of frontier orbitals of **3a** and methyl propiolate.

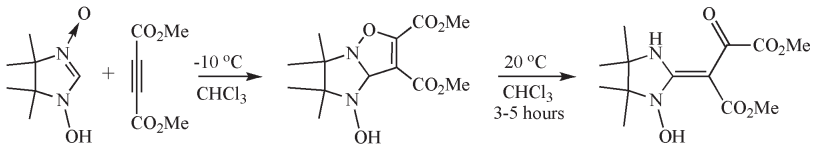
High regioselectivity of the studied reaction is the result of the significant difference of coefficients squares of atomic wave functions at reaction centres in LUMO of asymmetrically substituted alkynes (φ_1^2 and φ_2^2) and in HOMO of the nitrone group (φ_3^2 and φ_4^2). The results of *ab initio c*alculations of frontier orbitals interaction of **3a** and methyl propionate fulfilled on HF/6-31G(d,p) basis are represented on Figure 3b. Interaction of the centres with maximum values of φ_i^2 is preferred. Maximum atomic coefficients in the interacting molecular orbitals pertain to the oxygen atom of the nitrone group and to the carbon atom C^2 in alkyne (Figure 3b). Regioisomer **14d** is formed as a result of such overlapping, that is observed in the experiment.

As it is mentioned above, derivatives of 4,5-dihydro-1*H*-imidazole 3-oxide differ from acyclic nitrones by the presence

respectively [22], while compounds **6** give the only regioisomer **17(c, j)** (Scheme 5).

The cycloadducts synthesized are stable and capable of being stored for a long time at room temperature in the case of $R_2 \neq H$. When $R_2 = H$, cycloadducts initially formed spontaneously transform to enaminones **13** (Scheme 2). As a rule, this process is very fast but when cycloaddition reaction is carried out at about 0 °C, formation of the corresponding cycloadducts can be registered by ^1H NMR spectroscopy. The opening of 2,3-dihydroisoxazole ring in cycloadduct **26** (Scheme 6) is so kinetically hindered that cycloadduct **26** can be isolated by chromatography at 0 °C [23]. Cycloadduct **26** is quickly transformed at room temperature to enaminone **13C** with a quantitative yield.

Scheme 6



2c **26** **13c**

Conclusion.

Derivatives of 4,5-dihydro-1*H*-imidazole 3-oxide, both with and without substituents at the nitrogen atom at position 1, and with different substituents at position 2 of heterocycle have been demonstrated to react with acceptor-substituted alkynes giving corresponding cycloadducts, *i.e.* the derivatives of 1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole. High regioselectivity of this process is revealed, that is explained by the presence of the nitrogen atom conjugated with nitrone group. Alkenes are shown not to be dipolarophiles in the reaction with the studied substrates.

EXPERIMENTAL

NMR ^{1}H and ^{13}C spectra were recorded on Bruker AC–200, AM–400 (^{1}H, ^{13}C) and WP-200 (^{1}H, ^{19}F) spectrometers; solvents were used as internal standards. Hexafluorobenzene was used as internal standard for NMR ^{19}F. IR spectra were recorded with a Bruker IFS 66 spectrometer for KBr pellets (concentration 0.25%, pellet thickness 1 mm). UV spectra were measured with Specord M-40 spectrophotometer in EtOH. High-resolution mass spectra were recorded on a Finnigan MAT 8200 mass spectrometer with direct sample injection at a resolution of 10000 with ionisation power 70 eV. Melting points were measured in a sealed capillary. The yields are given for pure substances after recrystallization. Thin layer chromatography monitoring was carried out on alumina plates (Fluka, Switzerland) with chloroform and chloroform-MeOH mixtures (from 50:1 to 20:1) as eluents. The solutions were evaporated in *vacuo* in all cases. X-ray data were measured on a Bruker P4 and Smart Apex diffractometers with graphite monochromated Mo-Kα radiation. Atomic coordinates, thermal parameters, bond lengths and bond angles have been deposited at the Cambridge Crystallographic Data Centre; CCDC's contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

All computations were carried out with the GAMESS program package [25]. Full geometry optimization was carried out at the Hartree-Fock (HF) level of theory. The standard 6-31G (d, p) basis set was employed, which is 6-31G quality plus six d-like polarization functions on heavy atoms and three p-like polarization functions on hydrogen atoms. The basis set used (HF/6-31G (d, p)) was chosen by comparing of the experimental (X-ray) data with the geometrical characteristics and energies of compounds (cf. [24]). The harmonic vibration frequencies were determined by analytic second derivative methods at the 6-31G (d, p) level for equilibrium geometries **2-12**.

2-Substituted 4,4,5,5-tetramethylimidazolidine-1,3-diols - the precursors of 2-substituted 4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazol-1-ol 3-oxides were synthesized according to ref. [26,27] 2-Substituted 4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazol-1-ol 3-oxides were synthesized according to ref. [24] Synthesis of **13c** was published in ref. [23].

4,4,5,5-Tetramethyl-4,5-dihydro-1*H*-imidazol-1-ol 3-oxide (**2c**) [28].

MnO_2 (0.43 g, 5.0 mmol) was added to a solution of 0.20 g (1.25 mmol) of 4,4,5,5-tetramethylimidazolidine-1,3-diol in 10 ml $CHCl_3$ at –5-0 °C and the mixture was stirred at this temperature for 30 min (TLC monitoring). The oxidant was filtered off and filtrate was evaporated to dryness. The residue was treated with hexane and a precipitate of **2c** 0.15 g (75 %) was filtered off and was used without further purification; NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.14, 1.21 (s, 6H, 2-CH_3, 3-CH_3), 7.28 (s, 1H, N=C-H), 9.19 (broad s, 1H, NOH).

4,4,5,5-Tetramethyl-2-(trifluoromethyl)-4,5-dihydro-1*H*-imidazol-1-ol 3-oxide (**4c**).

This compound was synthesized similarly to that described above for **2c**. Reaction time was 40 min, the yield was 60%; NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.30 (s, 12H, 4,4,5,5-$(CH_3)_4$), 6.76 (broad s, 1H, NOH). NMR ^{19}F ($CDCl_3$, 188.28 MHz, δ, ppm): 95.4 (s. CF_3).

2-*tert*-Butyl-4,4,5,5-tetramethyl-4,5-dihydro-1H-imidazole 3-oxide (**5a**).

A solution of $NaNO_2$ (1.05 g, 15.2 mmol) in water (20 ml) was added to solution of 2-*tert*-butyl-4,4,5,5-tetramethyl-3-oxy-4,5-dihydroimidazole-1-oxyl (1.10 g, 5.05 mmol) in chloroform (30 ml). Hydrochloric acid (5 % aqueous solution, 1 ml) was added dropwise to the resulting mixture on vigorous stirring. After stirring for 30 min, the organic layer was separated, and the aqueous solution was extracted with chloroform (2×30 ml). The combined extracts were dried with $MgSO_4$, and the solvent was evaporated after removing of desiccant. The residue was dissolved in anhydrous tetrahydrofuran (10 ml), a catalyst (5% Pd on charcoal, 0.100 g) was added, and the mixture was hydrogenated with hydrogen upon stirring for 4 h at 20 °C. The catalyst was filtered off, and the solvent was removed to give 0.90 g (90 %) pure **5a**. The product can be additionally purified by recrystallization from the ethyl acetate – hexane mixture; NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.18, 1.19 (s, 6H, 4-CH_3, 5-CH_3), 1.32 (s, 9H, C-$(CH_3)_3$), 4.50 (broad s, 1H, NH). NMR ^{13}C ($CDCl_3$, 50.32 MHz, δ, ppm): 18.1, 23.2 (2-CH_3, 3-CH_3), 25.1 (C-(CH_3)$_3$), 32.0 (*C*-$(CH_3)_3$), 61.1 (C-5), 71.9 (C-4), 157.9 (C-2). λ_{max}, (ethanol), nm (lg ε): 264 (3.78). IR (KBr): ν = 3098, 2975, 2929, 2868, 2813,

1587, 1468, 1444, 1387, 1361, 1333, 1204, 1172, 1150, 1134, 1086, 743 cm^{-1}. m.p. 170-171 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{11}H_{22}N_2O$: C 66.62, H 11.18, N 14.23. Found: C 66.63, H 11.52, N 14.23.

2-*tert*-Butyl-1,4,4,5,5-pentamethyl-4,5-dihydro-1*H*-imidazole 3-oxide (**5b**).

Acetic anhydride (0.156 ml, 1.66 mmol) was added dropwise upon stirring to the solution of **5a** (0.109 g, 0.55 mmol) in anhydrous chloroform (10 ml). After stirring for 30 min, the reaction mixture was washed successively with aqueous solution of $KHCO_3$ and water and dried with $MgSO_4$. After filtration of desiccant and removal of the solvent, 1-(acetyloxy)-2-tert-butyl-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazole was obtained. The solution of this compound and dimethyl sulphate (0.157 ml, 1.66 mmol) in anhydrous ether (10 ml) was kept for 120 h at room temperature. The precipitate was collected by filtration and washed with anhydrous ether to give 0.060 g of 1-(acetyloxy)-2-*tert*-butyl-3,4,4,5,5-pentamethyl-4,5-dihydro-1*H*-imidazol-3-ium methylsulphate. The latter was dissolved in 5% water solution of NaOH (5 ml) and the resulting solution was kept for 10 min at 20 °C, then was extracted with chloroform (2×15 ml), and the combined extract was dried with $MgSO_4$. After filtration of desiccant the solvent was removed to give crude **5b**, which was purified by chromatography on alumina with chloroform as eluent to remove traces of the starting iminonitroxide and then with a (20:1) chloroform-methanol mixture. The eluate was evaporated to give 0.043 g (37 %) of nitrone **5b** as colourless oil; NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.04, 1.13 (s, 6H, 4-CH_3, 5-CH_3), 1.39 (s, 9H, C-$(CH_3)_3$), 2.74 (s, 3H, N-CH_3). NMR ^{13}C ($CDCl_3$, 50.32 MHz, δ, ppm): 19.2, 19.6 (2-CH_3, 3-CH_3), 26.9 (C-(CH_3)$_3$), 28.1 (*C*-$(CH_3)_3$), 31.3 (N-CH_3), 65.0 (C-5), 71.7 (C-4), 152.6 (C-2).

4,4,5,5-Tetramethyl-2-phenyl-4,5-dihydro-1H-imidazol-1-ol 3-oxide (**6c**) [26].

This compound was synthesized as it was pointed out for **2c**; reaction time was 20 min, the yield was 40%; NMR ^1H ([D_6]DMSO, 200.13 MHz, δ, ppm): 1.27 (s, 12H, 4,4,5,5-$(CH_3)_4$), 7.39-7.50 (m, 3H, Ph), 8.31-8.35 (m, 2H, Ph), 9.15 (broad s, 1H, N-OH).

4,4,5,5-Tetramethyl-2-(3-nitrophenyl)-4,5-dihydro-1H-imidazole 3-oxide (**10a**).

This compound was synthesized similarly to **5a** with the yield 90 %; NMR ^1H ([D_6]acetone, 200.13 MHz, δ, ppm): 1.30, 1.33 (s, 6H, 4-CH_3, 5-CH_3), 4.20 (broad s, 1H, NH), 7.56 (t, J_3=8.2 Hz, 1H, Ar), 8.21 (d.m, J_3=8.2 Hz, 1H, Ar), 8.75 (broad s, 1H, Ar), 8.85 (broad s, 1H, Ar). λ_{max}, (ethanol), nm (lg ε): 225 (4.35), 343 (3.58). IR (KBr): ν = 3089, 2982, 2791, 2677, 1627, 1597, 1534, 1441, 1347, 1159, 1063, 833, 812, 756, 729, 706 cm^{-1}. m.p. 192-194 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{13}H_{17}N_3O_3$: C 59.30, H 6.51, N 15.96. Found: C 59.37, H 6.49, N 15.64.

Reaction of 2-Substituted 4,4,5,5-Tetramethyl-4,5-dihydro-1*H*-imidazole 3-oxides with Alkynes in Solution (General Procedure, Method A).

Solution of 0.12 mmol of alkyne in 1 ml of $CHCl_3$ was added to cooled (-10 - 0 °C) solution of **2-12** (0.1 mmol) in 3 ml of $CHCl_3$. The reaction was carried out at room temperature up to the disappearance of starting **1** (TLC monitoring). After the completion of the reaction, the solvent was removed and a product was isolated by chromatography and purified by recrystallization.

Reaction of 2-Substituted 4,4,5,5-Tetramethyl-4,5-dihydro-1*H*-imidazole 3-oxides with Alkynes in Heterogeneous Conditions (General Procedure, Method B).

Finely powdered substrate **2-12** (0.1 mmol) was placed in one round-bottom flask (5 ml volume), and 1 mmol of alkyne was placed into another round-bottom flask (5 ml volume). These flasks were connected to two-joint cow receiver, supplied with stopcock. All the system was evacuated to 1 mm Hg and kept for 7-20 days at 60-70 °C (TLC monitoring). Reaction product was isolated by chromatography on alumina with $CHCl_3$ as eluent and then purified by recrystallization from hexane – ethyl acetate mixture.

Methyl 3-Oxo-2-(4,4,5,5-tetramethylimidazolidin-2-ylidene)-propanoate (**13a**).

Solution of 1.74 mmol methyl propiolate in 2 ml $CHCl_3$ was added to frozen solution (below -60 °C) of 0.21 g (1.45 mmol) of **2a** in 4 ml $CHCl_3$, and a mixture was allowed to warm slowly up to room temperature. After two hours the solvent was removed, and the residue was recrystallized to give 0.216 g **13a** (66 %); NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.17 (s, 12H, 4,4,5,5-$(CH_3)_4$), 3.65 (s, 3H, CO_2CH_3), 7.73, 9.13 (broad s, 1H, NH), 9.56 (s, 1H, CHO). λ_{max}, (ethanol), nm (lg ε): 232 (4.31), 268 (4.28). IR (KBr): ν = 3314, 3250, 2954, 2842, 1681, 1616, 1577, 1548, 1437, 1395, 1370, 1328, 1264, 1184, 1099 cm^{-1}. m.p. 132-133 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{11}H_{18}N_2O_3$: C 58.39, H 8.02, N 12.38. Found: C 57.85, H 8.13, N 12.08.

Dimethyl 2-oxo-3-(4,4,5,5-tetramethylimidazolidin-2-ylidene)succinate (**13b**).

This compound was synthesized similarly to **13a** with the yield 63%; NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.23 (s, 12H, 4,4,5,5-$(CH_3)_4$), 3.66, 3.80 (s, 3H, CO_2CH_3), 7.97, 9.16 (broad s, 1H, NH). λ_{max}, (ethanol), nm (lg ε): 233 (4.15), 272 (4.11). (KBr): ν = 3362, 3292, 2995, 2974, 2953, 1737, 1662, 1597, 1559, 1437, 1400, 1336, 1280, 1234, 1192, 1155, 1102 cm^{-1}. m.p. 168-170 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{13}H_{20}N_2O_5$: C 54.92, H 7.09, N 9.85. Found: C 54.93, H 7.00, N 9.87.

2,2,3,3,7a-Pentamethyl-6-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carbaldehyde (**14a**).

A solution of 3-phenylprop-2-ynal 0.167 ml (1.37 mmol) and **3a** 0.178 g (1.14 mmol) in 5 ml $CHCl_3$ was kept 3 h at room temperature and then the solvent was removed. Cycloadduct **14a** was isolated by flash chromatography on alumina with $CHCl_3$ as eluent and purified by recrystallization from hexane – ethyl acetate mixture. The yield was 0.186 g (57 %); NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.06, 1.11, 1.16, 1.31 (each s, 3H, 2-CH_3, 3-CH_3), 1.81 (s, 3H, 7a-CH_3), 2.33 (broad s, 1H, NH), 7.41-7.54 (m, 5H, Ph), 9.65 (s, 1H, CHO). NMR ^{13}C-mono ($CDCl_3$, 50.32 MHz, δ, ppm): 19.4, 25.1, 25.4, 25.6 (qqq, J_1=127.7 Hz, J_3=4.5 Hz, J_4=1.0 Hz, 2-CH_3 , 3-CH_3), 28.7 (q, J_1=128.6, 7a-CH_3), 64.0 (m, C-2), 71.9 (m, C-3), 89.9 (dq, J_3=5.5, J_2=5.0, C-7a), 118.7 (dq, J_2=24.5, J_3=3.0, C-7), 126.4 (t, J_2=7.4, Ph, C-1'), 128.7 (dm, J_1=163.0, Ph, C-2' , C-3'), 131.5 (dt, J_1=161.5, J_2=7.5, Ph, C-4'),

168.6 (t, J_3=4.0, C-6), 185.9 (d, J_1=174.3, -CHO). λ_{max}, (ethanol), nm (lg ε): 260 (3.91), 300 (3.88). IR (KBr): ν = 3314, 3007, 2989, 2969, 2941, 2837, 2764, 1648, 1631, 1596, 1492, 1477, 1397, 1371, 1346, 1167, 1112, 800, 771, 738, 699 cm^{-1}. m.p. 125-125 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{17}H_{22}N_2O_2$: C 71.30, H 7.74, N 9.78. Found: C 71.52, H 7.54, N 9.68.

1-(2,2,3,3,7a-Pentamethyl-6-phenyl-1,2,3,7a-tetrahydroimidazo-[1,2-*b*]isoxazol-7-yl)ethanone (**14b**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 60 %; NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.10, 1.20 (each s, 3H, 2-CH_3 , 3-CH_3), 1.07 (s, 6H, 2-CH_3 , 3-CH_3), 1.71 (s, 3H, $COCH_3$), 1.81 (s, 3H, 7a-CH_3), 2.90 (broad s, 1H, NH), 7.35 (s, 5H, Ph). NMR ^{13}C-mono ($CDCl_3$, 50.32 MHz, δ, ppm): 19.2, 25.3, 25.4, 25.8 (qqq, J_1=127.3 Hz, J_3=4.5 Hz, J_4=1.0 Hz, 2-CH_3 , 3-CH_3), 29.4 (q, J_1=127.9 Hz, 7a-CH_3), 29.8 (q, J_1=128.2 Hz, CO*C*H$_3$), 63.3 (m, C-2), 71.7 (m, C-3), 90.8 (q, J_2=4.5 Hz, C-7a), 118.7 (m, C-7), 128.9 (m, C-1'), 128.5, 128.7 (d.m, J_1=162.0 Hz, C-2' , C-3'), 130.5 (dt, J_1=162.0 Hz, J_2=7.5 Hz, C-4'), 162.8 (m, C-6), 193.9 (q, J_2=6.0 Hz, *C*OCH$_3$). λ_{max}, (ethanol), nm (lg ε): 239 (3.80), 291 (3.74). IR (KBr): ν = 3319, 3059, 3002, 2982, 2939, 1637, 1594, 1481, 1444, 1367, 1338, 1245, 1181, 1167, 1118, 792, 777, 710 cm^{-1}. m.p. 131.5-133.5 °C (from hexane).

Anal. Calcd. for $C_{18}H_{24}N_2O_2$: C 71.97, H 8.05, N 9.33. Found: C 71.82, H 8.07, N 9.34.

(2,2,3,3,7a-Pentamethyl-6-phenyl-1,2,3,7a-tetrahydroimidazo-[1,2-*b*]isoxazol-7-yl)(phenyl)methanone (**14c**).

This compound was synthesized similarly to **14a**; reaction time was 10 h, the yield was 30 %; NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.16, 1.19, 1.26, 1.34 (each s, 3H, 2-CH_3, 3-CH_3), 1.84 (s, 3H, 7a-CH_3), 1.96 (broad s, 1H, NH), 6.97-7.17 (m, 8H, Ph), 7.40 (d.m, J_3=7.5 Hz, 2H, Ph). λ_{max}, (ethanol), nm (lg ε): 248 (4.09), 319 (3.86). IR (KBr): ν = 3442, 3319, 3055, 3019, 2977, 2935, 1622, 1596, 1577, 1446, 1350, 1160, 883, 856 cm^{-1}. m.p. 125.5-126.5 °C (from heptane).

Anal. Calcd. for $C_{23}H_{26}N_2O_2$: C 76.21, H 7.23, N 7.73. Found: C 76.26, H 7.41, N 7.78.

Methyl 2,2,3,3,7a-pentamethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]-isoxazole-7-carboxylate (**14d**).

This compound was synthesized similarly to **14a**; reaction time was 24 h, the yield was 88 %; NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.03, 1.06, 1.09, 1.22 (each s, 3H, 2-CH_3, 3-CH_3), 1.68 (s, 3H, 7a-CH_3), 2.19 (broad s, 1H, NH), 3.67 (s, 3H, CO_2CH_3), 7.20 (s, 1H, C=CH). NMR ^{13}C ($CDCl_3$, 50.32 MHz, δ, ppm): 19.2, 24.9, 25.3, 25.8 (2-CH_3, 3-CH_3), 29.1 (7a-CH_3), 50.8 (CO_2CH_3), 64.2 (C-2), 71.6 (C-3), 88.0 (C-7a), 112.8 (C-7), 153.5 (C-6), 163.8 (*C*O$_2$CH$_3$). λ_{max}, (ethanol), nm (lg ε): 268 (4.00). IR (KBr): ν = 3318, 3074, 3019, 3003, 2987, 2968, 1689, 1632, 1440, 1329, 1182, 1164, 1135, 1093, 1070, 801 cm^{-1}. m.p. 90-91.5 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{12}H_{20}N_2O_3$: C 59.98, H 8.39, N 11.66. Found: C 60.15, H 8.16, N 11.57.

Methyl 2,2,3,3,7a-pentamethyl-6-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**14e**).

This compound was synthesized similarly to **14a**; reaction time was 24 h, the yield was 50; NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.13, 1.15, 1.19, 1.28 (each s, 3H, 2-CH_3, 3-CH_3), 1.80 (s, 3H, 7a-CH_3), 2.34 (broad s, 1H, NH), 3.63 (s, 3H, CO_2CH_3), 7.33-7.42 (m, 3H, Ph), 7.56 (d.m, J_3= 7.5 Hz, 2H, Ph). NMR ^{13}C ($CDCl_3$, 50.32 MHz, δ, ppm): 19.2, 25.2, 25.3, 25.8 (2-CH_3 , 3-CH_3), 29.9 (7a-CH_3), 50.8 (CO_2CH_3), 63.3 (C-2), 71.9 (C-3), 90.3 (C-7a), 107.0 (C-7), 127.7 (C-2', Ph), 128.2 (C-1', Ph), 128.8 (C-3', Ph), 130.3 (C-4', Ph), 162.3 (*C*O$_2$CH$_3$), 164.3 (C-6). λ_{max}, (ethanol), nm (lg ε): 233 (3.90), 244 (3.90). IR (KBr): ν = 3322, 3001, 2980, 2938, 1694, 1646, 1430, 1368, 1346, 1176, 1123, 1068, 796, 768, 702 cm^{-1}. m.p. 149-151 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{18}H_{24}N_2O_3$: C 68.33, H 8.65, N 8.85. Found: C 67.99, H 8.16, N 8.64.

Dimethyl 2,2,3,3,7a-pentamethyl-1,2,3,7a-tetrahydroimidazo-[1,2-*b*]isoxazole-6,7-dicarboxylate (**14f**).

This compound was synthesized similarly to **13a**; reaction time was 30 min, the yield was 71 %; NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.12, 1.14, 1.24, 1.28 (each s, 3H, 2-CH_3, 3-CH_3), 1.74 (s, 3H, 7a-CH_3), 2.24 (broad s, 1H, NH), 3.73, 3.86 (s, 3H, CO_2CH_3). NMR ^{13}C-mono ($CDCl_3$, 50.32 MHz, δ, ppm): 19.2, 25.2, 25.3, 25.8 (qqq, J_1=127.7 Hz, J_3=4.5 Hz, J_4=1.0 Hz, 2-CH_3, 3-CH_3), 29.1 (q, J_1=128.8, 7a-CH_3), 51.6 , 53.0 (q. J_1=147.2, CO_2CH_3), 63.9 (m, C-2), 72.3 (m, C-3), 89.9 (q, J_2=5.0, C-7a), 110.9 (q, J_3=2.8, C-7), 152.5 (s, C-6), 159.9, 162.8 (q, J_3=4.0, *C*O$_2$CH$_3$). λ_{max}, (ethanol), nm (lg ε): 274 (3.61). IR (KBr): ν = 3327, 3011, 2986, 2953, 1753, 1713, 1653, 1527, 1435, 1373, 1348, 1303, 1237, 1179, 1149, 1137, 1098, 1072, 823 cm^{-1}. m.p. 122-113 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{14}H_{22}N_2O_5$: C 56.36, H 7.43, N 9.39. Found: C 56.35, H 7.56, N 9.31.

Ethyl 2,2,3,3,6,7a-hexamethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**14g**).

A solution of 0.32 mmol methyl propiolate in 1 ml $CHCl_3$ was added to the frozen solution of 0.046 g (1.45 mmol) of **3a** in 5 ml $CHCl_3$. Reaction mixture turns colourless immediately. The mixture was allowed to warm slowly to room temperature, the solvent was removed, and cycloadduct **14g** was isolated from the residue by flash chromatography on alumina with $CHCl_3$ as eluent. The yield was 0.06 g (63 %). Compound **14g** can be additionally purified by sublimation in *vacuo* (2 mm Hg, 50 °C); NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.06, 1.11, 1.13, 1.27 (each s, 3H, 2-CH_3, 3-CH_3), 1.27 (t, J_3=7.1 Hz, 3H, OCH$_2$C*H*$_3$), 1.74 (s, 3H, 7a-CH_3), 2.19 (broad s, 1H, NH), 4.23 (q, 2H, OC*H*$_2$CH$_3$). NMR ^{19}F ($CDCl_3$, 188.28 MHz, δ, ppm): 99.6 (s. CF_3). NMR ^{13}C-mono ($CDCl_3$, 50.32 MHz, δ, ppm): 13.7 (qt, J_1=127.4, J_2=4.5, OCH$_2$*C*H$_3$), 18.9, 25.2, 25.3, 25.8 (qqq, J_1=127.7 Hz, J_3=4.5 Hz, J_4=1.0 Hz, 2-CH_3, 3-CH_3), 29.3 (q, J_1=129.0, 7a-CH_3), 60.8 (tq, J_1=148.3, J_2=4.5, O*C*H$_2$CH$_3$), 63.7 (m, C-2), 72.4 (m, C-3), 91.0 (q, J_2=4.8, C-7a), 112.1 (q, J_3=2.6, C-7), 117.7 (q, J_1(C-F)=275.0, CF_3), 148.6 (q, J_2(C-F)=39.6, C-6), 161.3 (t, J_3=4.1, *C*O$_2$Et). λ_{max}, (ethanol), nm (lg ε): 277 (3.69). IR (KBr): ν = 3343, 2984, 2939, 1715, 1666, 1469, 1448, 1394, 1374, 1346, 1311, 1234, 1176, 1096, 1069, 833 cm^{-1}. m.p. 29-30 °C (after sublimation). Found, m/z: 322,15068. Calculated for $C_{14}H_{21}F_3N_2O_3$, m/z: 322,15041.

1,2,2,3,3,7a-Hexamethyl-6-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carbaldehyde (**14h**).

This compound was synthesized similarly to **14a**; reaction time was 2 h, the yield was 59 %; NMR ^{1}H ($CDCl_3$, 200.13

MHz, δ, ppm): 0.80, 0.90, 1.17, 1.19 (each s, 3H, 2-CH_3, 3-CH_3), 1.64 (s, 3H, 7a-CH_3), 2.36 (s, 3H, N-CH_3), 3.63 (s, 3H, CO_2CH_3), 7.32-7.48 (m, 5H, Ph), 9.52 (s, 1H, CHO). m.p. 110-111 °C (from ethyl acetate – hexane mixture). Found: C 72.16, H 7.79, N 9.29. Calculated for $C_{18}H_{24}N_2O_2$: C 71.97, H 8.05, N 9.33; X-ray crystallography (CCDC 260688): $C_{18}H_{24}N_2O_2$, *FW* 300.39, triclinic, P^-1, *a* 6.747(2), *b* 10.585(4), *c* 12.164(4) Å, α 86.834(6), β 76.813(6), γ 76.165(5) °, *V* 821.3(5) Å^3, *Z* 2, D_C 1.215 g/cm^3 , μ(Mo-Kα) 0.079 mm^{-1}, θ 1.72-23.28°, 3555 reflections collected, 2356 unique, R_{int} = 0.0551, data/parameters 2356/296, *Goof* 0.983, *R* indices *(I*> 2σ(*I*)):R1 0.0411, *w*R2 0.1175; *R* indices (all data):R1 0.0449, *w*R2 0.1218.

Methyl 1,2,2,3,3,7a-hexamethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**14i**).

This compound was synthesized similarly to **14a**; reaction time was 4 h, the yield was 60 %.

NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.85, 0.91 (each s, 3H, 2-CH_3, 3-CH_3), 1.14 (s, 6H, 2-CH_3, 3-CH_3), 1.56 (s, 3H, 7a-CH_3), 2.33 (s, 3H, N-CH_3), 3.64 (s, 3H, CO_2CH_3), 7.26 (s, 1H, C=CH). λ_{max}, (ethanol), nm (lg ε): 266 (3.77). IR (KBr): ν = 3050, 3011, 2986, 2950, 2874, 2804, 1714, 1620, 1467, 1438, 1374, 1365, 1333, 1199, 1157, 1118, 1106, 1076, 867, 831 cm^{-1}. m.p. 83.5-84.5 °C (from heptane).

Anal. Calcd. for $C_{13}H_{22}N_2O_3$: C 61.39, H 8.72, N 11.01. Found: C 61.44, H 8.80, N 10.99.

Dimethyl 1,2,2,3,3,7a-hexamethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**14j**).

This compound was synthesized similarly to **14a**; reaction time was 1 h, the yield was 65 %; NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.89, 0.92, 1.13, 1.15 (each s, 3H, 2-CH_3, 3-CH_3), 1.57 (s, 3H, 7a-CH_3), 2.31 (s, 3H, N-CH_3), 3.66, 3.80 (s, 3H, CO_2CH_3). λ_{max}, (ethanol), nm (lg ε): 272 (3.62). IR (KBr): ν = 2995, 2953, 2848, 2803, 1750, 1717, 1646, 1436, 1371, 1343, 1309, 1221, 1156, 1103, 1072, 787 cm^{-1}. m.p. 40-42 °C (from heptane).

Anal. Calcd. for $C_{15}H_{24}N_2O_5$: C 57.68, H 7.74, N 8.97. Found: C 57.76, H 7.79, N 8.72.

Dimethyl 2,2,3,3-tetramethyl-7a-(trifluoromethyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**15a**).

This compound was synthesized similarly to **14g**; reaction time was 2 h, the yield was 58 %.

NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.16 (each s, 3H, 2-CH_3, 3-CH_3), 1.17 (s, 6H, 2-CH_3, 3-CH_3), 1.24 (s, 3H, 2-CH_3 , 3-CH_3), 2.74 (broad s, 1H, N-H), 3.78, 3.91 (s, 3H, CO_2CH_3). NMR ^{19}F ($CDCl_3$, 188.28 MHz, δ, ppm): 81.8 (s. CF_3). λ_{max}, (ethanol), nm (lg ε): 264 (3.72). IR (KBr): ν = 3360, 2994, 2961, 2928, 2859, 1758, 1721, 1655, 1441, 1380, 1347, 1295, 1216, 1190, 1167, 1136, 1114, 1055, 1030, 984, 788, 778, 735 cm^{-1}. m.p. 83-85 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{14}H_{19}F_3N_2O_5$: C 47.73, H 5.44, F 16.18, N 7.95. Found: C 47.85, H 5.53, F 15.77, N 7.65.

Dimethyl 1-hydroxy-2,2,3,3-tetramethyl-7a-(trifluoromethyl)-1,2,3,7a-tetrahydroimidazo [1,2-b]isoxazole-6,7-dicarboxylate (**15b**).

This compound was synthesized similarly to **13a**; reaction time was 10 h, the yield was 71 %; NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.12, 1.22 (each s, 6H, 2-CH_3, 3-CH_3), 3.76, 3.90 (s, 3H, CO_2CH_3), 5.31 (broad s, 1H, N-OH). NMR ^{19}F ($CDCl_3$, 188.28 MHz, δ, ppm): 87.2 (s. CF_3). λ_{max}, (ethanol), nm (lg ε): 267 (3.54). IR (KBr): ν = 3461, 3016, 2958, 2790, 1757, 1738, 1652, 1440, 1351, 1322, 1290, 1221, 1196, 1165, 1141, 1098, 1016, 983, 829, 800 cm^{-1}. m.p. 161-163 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{14}H_{19}F_3N_2O_6$: C 45.65, H 5.20, F 15.47, N 7.61. Found: C 45.65, H 4.96, F 15.67, N 8.00.

7a-*tert*-Butyl-2,2,3,3-tetramethyl-6-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carbaldehyde (**16a**).

This compound was synthesized by **Method B** with the 45% yield; NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm) 1.03 (s, 9H, $C(CH_3)_3$), 1.09 (s, 6H, 2-CH_3 , 3-CH_3), 1.23, 1.28 (s, 3H, 2-CH_3, 3-CH_3), 2.56 (broad s, 1H, N-H), 7.45-7.53 (m, 3H, Ph), 7.63-7.67 (m, 2H, Ph), 9.65 (s, 1H, CHO). λ_{max}, (ethanol), nm (lg ε): 227 (4.03), 273 (3.86), 309 (3.86). IR (KBr): ν = 3340, 3077,3013, 2993, 2978, 2960, 2870, 2768, 1635, 1615, 1595, 1479, 1464, 1449, 1401, 1379, 1336, 1256, 1226, 1156, 1046, 888, 835, 781, 755, 713 cm^{-1}. m.p. 118-120 °C (from hexane).

Anal. Calcd for $C_{20}H_{28}N_2O_2$: C 73.14, H 8.59, N 8.53. Found: C 73.04, H 8.37, N 8.32.

7a-*tert*-Butyl-1-(2,2,3,3-tetramethyl-6-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)ethanone (**16b**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 45 %; NMR ^{1}H ([D_6]acetone, 200.13 MHz, δ, ppm): 1.00 (s, 9H, $C(CH_3)_3$), 1.14 (s, 3H, 2,3-$(CH_3)_2$), 1.22 (s, 9H, 2,3-$(CH_3)_2$), 2.05 (s, 3H, $COCH_3$), 3.33 (s, 1H, NH), 7.50-7.60 (m, 5H, Ph). λ_{max}, (ethanol), nm (lg ε): 226 (3.89), 293 (3.80). IR (KBr): ν = 3335, 2995, 2958, 2864, 1642, 1479, 1447, 1386, 1362, 1326, 1151, 1109, 1073, 1054, 952, 800, 775, 762. 702 cm^{-1}. m.p. 104.5-105.5 °C (from hexane).

Anal. Calcd for $C_{21}H_{30}N_2O_2$: C 73.65, H 8.83, N 8.18. Found: C 73.69, H 8.99, N 8.28.

(7a-*tert*-Butyl-2,2,3,3-tetramethyl-6-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)(phenyl)methanone (**16c**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 43 %; NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.05 (s, 9H, $C(CH_3)_3$), 1.09, 1.15, 1.25, 1.27 (each s, 3H, 2-CH_3, 3-CH_3), 1.70 (broad s, 1H, N-H), 7.01-7.12 (m, 8H, Ph), 7.60 (d.m, J_3=7.5 Hz, 2H, Ph). λ_{max}, (ethanol), nm (lg ε): 255 (4.11), 322 (3.81). IR (KBr): ν = 3336, 3068, 3031, 3005, 2977, 2962, 1639, 1618, 1596, 1577, 1447, 1385, 1366, 1337, 1144, 1045, 873, 811 cm^{-1}. m.p. 147-148 °C (from hexane); X-ray crystallography (CCDC 260687): $C_{26}H_{32}N_2O_2$, *FW* 404.54, monoclinic, $P2_1/c$, *a* 12.011(8), *b* 10.767(7), *c* 17.986(11) Å, β 91.813(14) °, *V* 2325(3) Å^3, *Z* 4, D_C 1.155 g/cm^3 , μ(Mo-Kα) 0.073 mm^{-1}, θ 2.20-23.32°, 9597 reflections collected, 3332 unique, R_{int} = 0.1095, data/parameters 3332/400, *Goof* 0.940, *R* indices *(I*> 2σ(*I*)):R1 0.0653, *w*R2 0.1443; *R* indices (all data):R1 0.1108, *w*R2 0.1699.

Anal. Calcd. for $C_{26}H_{32}N_2O_2$: C 77.19, H 7.97, N 6.92. Found: C 77.21, H 8.09, N 6.95.

Methyl 7a-*tert*-Butyl-2,2,3,3-tetramethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**16d**).

This compound was synthesized similarly to **14a**; reaction time was 4 h, the yield was 52 %. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.99 (s, 9H, $C(CH_3)_2$), 1.12 (s, 3H, 2-CH_3 , 3-CH_3),

1.15 (s, 6H, 2-CH_3 , 3-CH_3), 1.20 (s, 3H, 2-CH_3 , 3-CH_3), 1.73 (broad s, 1H, N-H), 3.71 (s, 3H, CO_2CH_3), 7.37 (s, 1H, C=CH). λ_{max}, (ethanol), nm (lg ε): 223 (3.38), 265 (3.75). IR (KBr): ν = 3340, 3011, 2983, 2965, 2915, 1709, 1626, 1479, 1440, 1402, 1381, 1351, 1325, 1194, 1145, 1129, 1109, 1037, 927, 894, 879 cm^{-1}. m.p. 72-73 °C (from hexane).

Anal. Calcd. for $C_{15}H_{26}N_2O_3$: C 63.80, H 9.28, N 9.92. Found: C 63.94, H 9.66, N 9.59.

Dimethyl 7a-*tert*-Butyl-2,2,3,3-tetramethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**16e).**

This compound was synthesized similarly to **14a**; reaction time was 4 h, the yield was 74 %. NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.96 (s, 9H, $C(CH_3)_3$), 1.09, 1.15, 1.17, 1.18 (each s, 3H, 2-CH_3, 3-CH_3), 2.59 (broad s, 1H, N-H), 3.75, 3.84 (s, 3H, CO_2CH_3). λ_{max}, (ethanol), nm (lg ε): 225 (3.57), 273 (3.59). IR (KBr): ν = 3359, 3009, 2964, 2874, 1746, 1712, 1669, 1436, 1381, 1367, 1322, 1259, 1208, 1173, 1130, 1104, 1061 cm^{-1}. m.p. 49-50.5 °C (from hexane).

Anal. Calcd. for $C_{17}H_{28}N_2O_5$: C 59.98, H 8.29, N 8.23. Found: C 59.94, H 8.31, N 8.19.

Methyl 7a-*tert*-Butyl-1,2,2,3,3-pentamethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**16f**)**.**

This compound was synthesized similarly to **14a**; reaction time was 6 h, the yield was 60 %. NMR ^1H ([D_6]acetone, 200.13 MHz, δ, ppm): 0.94 (s, 6H, 2,3-$(CH_3)_2$), 1.04 (s, 9H, $C(CH_3)_3$), 1.14, 1.18 (each s, 3H, 2,3-$(CH_3)_2$), 2.66 (s, 3H, N-CH_3), 3.66 (s, 3H, CO_2CH_3), 7.65 (s, 1H, C=CH). λ_{max}, (ethanol), nm (lg ε): 269 (3.67). IR (KBr): ν = 3069, 3016, 2996, 2962, 1708, 1610, 1438, 1365, 1311, 1195, 1176, 1155, 1115, 1055, 1025, 878, 804 cm^{-1}. m.p. 47-48 °C (from hexane).

Anal. Calcd. for $C_{16}H_{28}N_2O_3$: C 64.83, H 9.52, N 9.45. Found: C 64.77, H 9.56, N 9.34.

1-(2,2,3,3-Tetramethyl-6,7a-diphenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)ethanone (**17a)**

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 56 %. NMR ^1H ([D_6]acetone, 200.13 MHz, δ, ppm): 1.04, 1.06, 1.28, 1.34 (each s, 3H, 2-CH_3, 3-CH_3), 1.71 (s, 3H, $COCH_3$), 3.33 (s, 1H, NH), 7.20-7.33 (m, 3H, Ph), 7.54-7.57 (m, 3H, Ph), 7.63-7.67 (m, 2H, Ph), 7.63-7.80 (m, 2H, Ph). NMR ^{13}C-mono ([D_6]acetone, 50.32 MHz, δ, ppm): 19.1, 24.9, 25.7, 26.5 (q. q. q, J_1 = 127.0 Hz, J_3 = 5.0 Hz, J_4 = 1.0 Hz, 2,3-$(CH_3)_2$), 29.7 (q. J_1 = 127.5 Hz, CO*C*H_3), 63.8 (m. C-2), 73.2 (m. C-3), 93.6 (t. q. J_3 = 4.0 Hz, J_4 = 1.0 Hz, C-7a), 121.3 (q. t. J_3 =1.1 Hz, C-7), 127.6 (t, J_1 = 162.6 Hz, C-1'), 127.8 (d.m, J_1 = 157.6 Hz, C-3"), 128.1 (dd, J_1 = 158.5 Hz, J_2 = 7.6 Hz, C-2"), 129.5 (dd, J_1 = 162.6 Hz, J_2 = 6.5 Hz, C-2'), 130.0 (dt, J_1 = 161.7 Hz, J_2 = 6.5 Hz, C-3'), 131.7 (d. t. t, J_1 = 162.6 Hz, J_2 = 7.1 Hz, J_3 =1.0 Hz, C-4'), 147.8 (t. J_2 = 7.1 Hz, C-1"), 162.7 (t. J_3 = 3.5 Hz, C-6), 192.9 (q. J_2 = 6.1 Hz, *C*OCH$_3$). λ_{max}, (ethanol), nm (lg ε): 245 (3.93), 300 (3.78). IR (KBr): ν = 3284, 3060, 2983, 1663, 1651, 1637, 1588, 1569, 1489, 1446, 1367, 1332, 1249, 1217, 1171, 1107, 1076, 770, 754, 702 cm^{-1}. m.p. 92.5-94.5 °C (from hexane).

Anal. Calcd. For $C_{23}H_{26}N_2O_2$: C 76.21, H 7.23, N 7.73. Found: C 76.06, H 7.49, N 7.59.

(2,2,3,3-Tetramethyl-6,7a-diphenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)(phenyl)methanone (**17b**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 67 %. NMR ^1H ([D_6]acetone, 200.13 MHz, δ, ppm): 1.04, 1.14, 1.31, 1.35 (each s, 3H, 2,3-$(CH_3)_2$), 3.50 (broad s, 1H, N-H), 7.00-7.37 (m, 13H, Ph), 7.86 (d.m, J_3 = 8.0 Hz, 2H, Ph). λ_{max}, (ethanol), nm (lg ε): 254 (4.17), 316 (3.81). IR (KBr): ν = 3356, 3336, 3059, 1634, 1614, 1597, 1577, 1490, 1447, 1367, 1344, 1217, 1151, 1073, 1024, 911, 884, 863, 816 cm^{-1}. m.p. 169-170 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{28}H_{28}N_2O_2$: C 79.22, H 6.65, N 6.60. Found: C 79.15, H 6.50, N 6.60.

Methyl 2,2,3,3-Tetramethyl-7a-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**17c**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 42 % or by **Method B** with the yield 20%. NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.84, 0.96, 1.10, 1.21 (each s, 3H, 2-CH_3, 3-CH_3), 2.74 (broad s, 1H, N-H), 3.47 (s, 3H, CO_2CH_3), 7.10-7.23 (m, 3H, Ph), 7.63 (d, J_3=7.5 Hz, 2H, Ph). λ_{max}, (ethanol), nm (lg ε): 255 (3.92). IR (KBr): ν = 3091, 3059, 2955, 1722, 1623, 1438, 1340, 1256, 1198, 1152, 1026, 760, 700 cm^{-1}. m.p. 76-77 °C (from hexane-benzene mixture).

Anal. Calcd. for $C_{17}H_{22}N_2O_3$: C 67.53, H 7.33, N 9.26. Found: C 67.43, H 7.61, N 9.15.

Methyl 2,2,3,3-Tetramethyl-6,7a-diphenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**17d**)**.**

This compound was synthesized similarly to **14a**; reaction time was 40 h, the yield was 53 %. NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.00, 1.10, 1.25, 1.34 (each s, 3H, 2-CH_3, 3-CH_3), 1.83 (broad s, 1H, N-H), 3.46 (s, 3H, CO_2CH_3), 7.17-7.45 (m, 6H, Ph), 7.64-7.66 (m, 4H, Ph). λ_{max}, (ethanol), nm (lg ε): 248 (4.00). IR (KBr): ν = 3349, 3056, 2978, 2948, 1688, 1629, 1598, 1492, 1435, 1366, 1346, 1218, 1187, 1165, 1115, 1090, 1074, 1028, 811 cm^{-1}. m.p. 100-101 °C (from heptane).

Anal. Calcd. for $C_{23}H_{26}N_2O_3$: C 72.99, H 6.92, N 7.40. Found: C 73.18, H 7.01, N 7.36.

Dimethyl 2,2,3,3-Tetramethyl-7a-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**17e**).

This compoundwas synthesized similarly to **14a**; reaction time was 20 h, the yield was 84 %. NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.90, 1.05, 1.20, 1.30 (each s, 3H, 2-CH_3, 3-CH_3), 3.55 3.84 (s, 3H, CO_2CH_3) 7.62-7.66 (m, 2H, Ph) 7.19-7.31 (m, 3H, Ph). λ_{max}, (ethanol), nm (lg ε): 273 (3.72). IR (KBr): ν = 3352, 3003, 2982, 2956, 1753, 1723, 1659, 1450, 1437, 1369, 1341, 1299, 1211, 1173, 1131, 1099, 1089, 1074, 971, 915, 876, 830 cm^{-1}.m.p 141-142 °C (from heptane).

Anal. Calcd. for $C_{19}H_{24}N_2O_5$: C 63.32, H 6.71, N 7.77. Found: C 63.42, H 6.88, N 7.60.

1,2,2,3,3-Pentamethyl-7a-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carbaldehyde (**17f**).

This compound was synthesized similarly to **13a**; reactants ratio was 1:2, reaction time was 2 h, the yield was 83 %. NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.92, 1.01, 1.09, 1.33 (each s, 3H, 2-CH_3, 3-CH_3), 2.42 (s, 3H, N-CH_3), 7.22 (s, 1H, C=CH), 7.25-7.34 (m, 2H, Ph), 7.53-7.57 (m, 3H, Ph), 9.45 (s, 1H, CHO). m.p 87-88 °C (from hexane).

Anal. Calcd. for $C_{17}H_{22}N_2O_2$: C 71,30, H 7.74, N 9.78. Found: C 71.02, H 8.09, N 9.60.

6,7a-Diphenyl-1,2,2,3,3-pentamethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carbaldehyde (**17g**).

This compound was synthesized by **Method B** with the 52% yield. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.96, 1.04, 1.12, 1.36 (each s, 3H, 2-CH_3, 3-CH_3), 2.54 (s, 3H, N-CH_3), 7.2-7.7 (m, 10H, Ph), 9.53 (s, 1H, CHO). λ_{max}, (ethanol), nm (lg ε): 206 (4.32), 255 (4.09). IR (KBr): ν = 3060, 2992, 2966, 2941, 2847, 2802, 2762, 1656, 1617, 1594, 1574, 1492, 1446, 1344, 1221, 1152, 1110, 1001, 984, 866, 840, 749, 699 cm^{-1}.m.p. 129-130 °C (from hexane). X-ray Crystallography (CCDC 260355): $C_{23}H_{26}N_2O_2$, *FW* 362.46, triclinic, P$^-$1, *a* 11.330(2), *b* 13.739(3), *c* 14.905(3) Å, α 66.66(1), β 80.89(1), γ 71.50(2)°, *V* 2018.7(7) Å^3, *Z* 4, D_C 1.193 g/cm^3, μ(Mo-Kα) 0.076 mm^{-1}, θ 1.79-24.99°, 7329 reflections collected, 6941 unique, R_{int} = 0.026, data/parameters 6941/643, *Goof* 0.959, *R* indices *(I*> 2σ(*I*)):R1 0.0537, *w*R2 0.1122; *R* indices (all data):R1 0.1139, *w*R2 0.1359.

Anal. Calcd. for $C_{23}H_{26}N_2O_2$: C 76.21, H 7.23, N 7.73. Found: C 75.72, H 7.17, N 7.51.

1-(1,2,2,3,3-Pentamethyl-6,7a-diphenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)ethanone (**17h**).

This compound was synthesized by **Method B** with the 73% yield. NMR ^{1}H ([D_6]acetone, 200.13 MHz, δ, ppm): 0.86, 1.14, 1.16, 1.29 (each s, 3H, 2-CH_3, 3-CH_3), 1.64 (s, 3H, $COCH_3$), 2.58 (s, 3H, NCH_3), 7.15-7.30 (m, 3H, Ph), 7.60-7.64 (m, 5H, Ph), 7.66-7.69 (m, 2H, Ph). λ_{max}, (ethanol), nm (lg ε): 245 (4.09). IR (KBr): ν = 3058, 3000, 2977, 2932, 2875, 2844, 2802, 1643, 1618, 1591, 1491, 1447, 1366, 1332, 1218, 1150, 1096, 981, 754, 706, 694 cm^{-1}. m.p. 160-161.5 °C (from hexane).

Anal. Calcd. for $C_{24}H_{28}N_2O_2$: C 76.56, H 7.50, N 7.44. Found: C 76.32, H 7.59, N 7.45.

(1,2,2,3,3-Pentamethyl-6,7a-diphenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)(phenyl)methanone (**17i**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 83 %. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.95, 1.15, 1.16, 1.42 (each s, 3H, 2-CH_3, 3-CH_3), 2.70 (s, 3H, N-CH_3), 6.91-7.37 (m, 13H, Ph), 7.75 (d.m, J_3 = 7.5 Hz, 2H, Ph). λ_{max}, (ethanol), nm (lg ε): 250 (4.14). IR (KBr): ν = 3059, 3022, 2959, 2867, 2841, 2800, 1613, 1592, 1575, 1491, 1446, 1346, 1218, 1166, 1148, 1001, 986, 889, 853, 814 cm^{-1}. m.p. 176.5-177.5 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{29}H_{30}N_2O_2$: C 79.42, H 6.89, N 6.39. Found: C 79.41, H 6.75, N 6.39.

Methyl 1,2,2,3,3-Pentamethyl-7a-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate(**17j**).

This compound was synthesized similarly to **14a**, reaction time was 5 h, the yield was 52 %. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.89, 1.04, 1.09, 1.32 (each s, 3H, 2-CH_3, 3-CH_3), 2.47 (s, 3H, N-CH_3), 3.52 (s, 3H, CO_2CH_3), 7.20-7.34 (m, 3H, Ph), 7.54 (s, 1H, C=CH), 7.57 (d.m, J_3 = 7.0 Hz, 2H, Ph). λ_{max}, (ethanol), nm (lg ε): 270 (3.58); IR (KBr): ν = 3063, 2990, 2952, 2846, 2802, 1719, 1617, 1442, 1366, 1332, 1225, 1195, 1166, 1123, 1032, 1001, 984 cm^{-1}. m.p. 89-90 °C (from hexane).

Anal. Calcd. for $C_{18}H_{24}N_2O_3$: C 68.33, H 7.65, N 8.85. Found: C 67.94, H 8.04, N 8.79.

Methyl 6,7a-Diphenyl-1,2,2,3,3-pentamethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**17k**).

This compound was synthesized by **Method B** with the 45% yield. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm) 0.90, 1.08, 1.10, 1.31 (each s, 3H, 2-CH_3, 3-CH_3), 2.56 (s, 3H, N-CH_3), 3.27 (s, 3H, CO_2CH_3), 7.24-7.29 (m, 2H, Ph), 7.38-7.44 (m, 5H, Ph), 7.61-7.64 (m, 3H, Ph). λ_{max}, (ethanol), nm (lg ε): 246 (4.08); IR (KBr): ν = 3086, 3058, 3011, 2995, 2959, 2871, 2846, 2801, 1704, 1636, 1598, 1492, 1464, 1446, 1342, 1219, 1189, 1150, 1119, 1075, 1027, 1001, 749, 697 cm^{-1}. m.p. 143-144 °C (from hexane).

Anal. Calcd. for $C_{24}H_{28}N_2O_3$: C 73.44, H 7.19, N 7.14. Found: C 73.64, H 7.24, N 7.15.

Dimethyl 1,2,2,3,3-Pentamethyl-7a-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**17l**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 56 %. NMR ^{1}H ([D_4]methanol, 200.13 MHz, δ, ppm): 0.92, 1.16, 1.18, 1.35 (each s, 3H, 2-CH_3, 3-CH_3), 2.52 (s, 3H, NCH_3), 3.51 , 3.95 (s, 3H, CO_2CH_3), 7.24-7.28 (m, 1H, Ph), 7,32-7,37 (m, 2H, Ph), 7,55-7,58 (m, 2H, Ph); NMR ^{13}C ([D_4]methanol, 50.32 MHz, δ, ppm): 19.7 , 21.2, 25.8, 26.2 (2-CH_3 , 3-CH_3), 30.6 (N-CH_3), 52.8, 54.8 (CO_2CH_3), 68.0 (C-2), 74.2 (C-3), 96.5 (C-7a), 112.0 (C-7), 129.3 (C-4"), 129.4, 129.7 (C-2" , C-3"), 145.0 (C-1"), 157.5 (C-6), 162.2, 165.0 (CO_2CH_3). λ_{max}, (ethanol), nm (lg ε): 276 (3.58). IR (KBr): ν = 2988, 2952, 2890, 2806, 1755, 1722, 1644, 1438, 1341, 1307, 1217, 1129, 1082, 1059, 1032, 989, 834, 810 cm^{-1}. m.p. 84.5-86 °C (from hexane).

Anal. Calcd. for $C_{20}H_{26}N_2O_5$: C 64.15, H 7.00, N 7.48. Found: C 64.47, H 7.30, N 7.49.

Methyl 1,2,2,3,3-Pentamethyl-7a-phenyl-6-(trifluoromethyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**17m**).

This compoundwas synthesized similarly to **14g**; reaction time was 20 min, the yield was 97 %. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.89 (s, 3H, 2-CH_3 , 3-CH_3), 1.01 (t, J_3 = 7.1 Hz, 3H, OCH_2CH_3), 1.09, 1.12, 1.34 (each s, 3H, 2-CH_3, 3-CH_3), 2.52 (s, 3H, N-CH_3), 3.98 (q, J_3 = 7.1 Hz, 2H, OCH_2CH_3), 7.23-7.25 (m, 1H, Ph), 7.31 (t, J_3 = 7.5 Hz, 2H, Ph), 7.55 (t, J_3 = 7.5 Hz, 2H, Ph). NMR ^{19}F ($CDCl_3$, 188.28 MHz, δ, ppm): 99.9 (s. CF_3). λ_{max}, (ethanol), nm (lg ε): 280 (3.56). IR (KBr): ν = 2983, 2945, 2810, 1714, 1647, 1467, 1447, 1392, 1370, 1340, 1306, 1258, 1224, 1175, 1113, 1080, 1039, 1005, 840 cm^{-1}. m.p. 43-44 °C (from hexane).

Anal. Calcd. for $C_{20}H_{25}F_3N_2O_3$: C 60.29, H 6.32, F 14.31, N 7.03. Found: C 59.96, H 6.77, F 14.77, N 7.20.

Dimethyl 1-Hydroxy-2,2,3,3-tetramethyl-7a-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**17n**).

This compound was synthesized similarly to **14g**; reaction time was 2 h, the yield was 25 %. NMR ^{1}H ([D_6]acetone, 200.13 MHz, δ, ppm): 0.97, 1.05, 1.25, 1.36 (each s, 3H, 2-CH_3, 3-CH_3), 3.45 , 3.88 (each s, 3H, CO_2CH_3), 7.27-7.31 (m, 3H, Ph), 7.37 (broad s, 1H, N-OH), 7.73 (dm, J_3 = 7.6 Hz, 2H, Ph). λ_{max}, (ethanol), nm (lg ε): 261 (3.52), 267 (3.53). IR (KBr): ν = 3418, 3014, 2992, 2951, 1756, 1713, 1650, 1436, 1367, 1347, 1307, 1210, 1173, 1145, 1088, 1070 cm^{-1}. m.p 124-126 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{19}H_{24}N_2O_6$: C 60.63, H 6.43, N 7.44. Found: C 60.70, H 6.41, N 7.41.

2,2,3,3-Tetramethyl-7a-(4-nitrophenyl)-6-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carbaldehyde (**18a**)

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 69 %. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.03, 1.06, 1.19, 1.35 (each s, 3H, 2-CH_3, 3-CH_3), 2.73 (broad s, 1H, NH), 7.44-7.63 (m, 5H, Ph), 8.00 (dt, J_3=9.0 Hz, J_4=2.1 Hz, 2H, Ar), 8.15 (dt, J_3=9.0 Hz, J_4=2.1 Hz, 2H, Ar), 9.53 (s, 1H, CHO). NMR ^{13}C-mono ($CDCl_3$, 50.32 MHz, δ, ppm): 18.4, 24.1, 25.0, 25.6 (qqq, J_1=127.7 Hz, J_3=4.5 Hz, J_4=1.0 Hz, 2-CH_3, 3-CH_3), 63.8 (m, C-2), 72.9 (m, C-3), 91.3 (dt, J_3=5.6 Hz, J_3=3.5 Hz, C-7a), 119.1 (d, J_2=25.9 Hz, C-7), 122.8 (d, J_1=169.0 Hz, C-3''), 125.7 (t, J_2=7.2 Hz, C-1'), 127.6 (dd, J_1=167.0 Hz, J_2=6.5 Hz, C-2''), 128.9 (d.m, J_1=165.4 Hz, C-2' or C-3'), 129.0 (dm, J_1=163.0 Hz, C-2' or C-3'), 132.1 (dtt, J_1=161.5 Hz, J_2=7.5 Hz, J_3=1.0 Hz, C-4'), 147.0 (m, C-4''), 151.9 (t, J_2=7.3 Hz, C-1''), 169.0 (t, J_3=4.0 Hz, C-6), 184.8 (d, J_1=176.4 Hz, CHO). λ_{max}, (ethanol), nm (lg ε): 273 (4.39). IR (KBr): ν = 3297, 3108, 3069, 2979, 2939, 2874, 1648, 1622, 1595, 1515, 1447, 1392, 1370, 1345, 1316, 1218, 1158, 1145, 862, 850 cm^{-1}. m.p. 156-157 °C (from hexane).

Anal. Calcd. for $C_{22}H_{23}N_3O_4$: C 67.16, H 5.89, N 10.68. Found: C 67.14, H 5.94, N 10.55.

1-(2,2,3,3-Tetramethyl-7a-(4-nitrophenyl)-6-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)ethanone (**18b**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 50 %. NMR ^{1}H ([D_6]acetone, 200.13 MHz, δ, ppm): 1.00, 1.08, 1.29, 1.37 (each s, 3H, 2-CH_3, 3-CH_3), 1.67 (s, 3H, $COCH_3$), 3.47 (s, 1H, NH), 7.58-7.69 (m, 5H, Ph), 8.05-8.09 (dt, J_3 = 9.0 Hz, J_4 = 2.0 Hz, 2H, Ar), 8.15-8.19 (dt, J_3 = 8.7 Hz, J_4 = 2.0 Hz, 2H, Ar). λ_{max}, (ethanol), nm (lg ε) 272 (4.19). IR (KBr): ν = 3355, 2984, 1631, 1605, 1593, 1516, 1490, 1446, 1370, 1347, 1160, 1107, 864, 850, 700 cm^{-1}. m.p. 144-146 °C (from hexane).

Anal. Calcd. for $C_{23}H_{25}N_3O_4$: C 67.80, H 6.18, N 10.31. Found: C 66.92, H 6.17, N 10.25.

(2,2,3,3-Tetramethyl-7a-(4-nitrophenyl)-6-phenyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)(phenyl)methanone (**18c**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 76 %. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.00, 1.13, 1.26, 1.35 (each s, 3H, 2-CH_3, 3-CH_3), 2.60 (s, 1H, N-H), 9.94-7.70 (m, 8H, Ar), 8.04-8.23 (m, 6H, Ar). λ_{max}, (ethanol), nm (lg ε): 262 (4.29); IR (KBr): ν = 3439, 3346, 3063, 2981, 2947, 2874, 1622, 1597, 1577, 1518, 1491, 1447, 1369, 1347, 1217, 1154, 887, 871, 849, 810 cm^{-1}. m.p. 129-130 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{28}H_{27}N_3O_4$: C 71.62, H 5.80, N 8.95. Found: C 71.42, H 5.45, N 9.27.

Methyl 2,2,3,3-Tetramethyl-7a-(4-nitrophenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**18d**).

This compound was synthesized similarly to **14a**; reaction time was 5 h, the yield was 76 %. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.93, 0.95, 1.14, 1.21 (**each** s, 3H, 2-CH_3, 3-CH_3), 3.00 (broad s, 1H, N-H), 3.53 (s, 3H, CO_2CH_3), 7.37 (s, 1H, C=CH), 7.87 (d, J_3 = 8.5 Hz, 2H, Ar), 8.09 (d, J_3 = 8.5 Hz, 2H, Ar). λ_{max}, (ethanol), nm (lg ε): 270 (4.15). IR (KBr): ν = 3312, 3056, 2991, 2956, 1710, 1616, 1603, 1513, 1438, 1372, 1345, 1217, 1166, 1129, 1106, 1081, 865, 853, 836 cm^{-1}. m.p. 141-143 °C (from hexane).

Anal. Calcd. for $C_{17}H_{21}N_3O_5$: C 58.78, H 6.09, N 12.10. Found: C 58.35, H 6.31, N 11.88.

Methyl 2,2,3,3-Tetramethyl-7a-(4-nitrophenyl)-6-phosphino-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**18e**).

This compound was synthesized similarly to **14a**; reaction time was 50 h at 60 °C, the yield was 61 %.

NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.03, 1.04, 1.25, 1.32 (each s, 3H, 2-CH_3, 3-CH_3), 2.87 (broad s, 1H, NH), 3.49 (s, 3H, CO_2CH_3), 7.41-7.48 (m, 3H, Ph), 7.65-7.70 (m, 2H, Ph), 7.96 (dt, J_3=9.0 Hz, J_4=2.1 Hz, 2H, Ar), 8.15 (dt, J_3=9.0 Hz, J_4=2.1 Hz, 2H, Ar). NMR ^{13}C-mono ($CDCl_3$, 50.32 MHz, δ, ppm): 18.5, 24.2, 25.3, 25.8 (qqq, J_1=127.7 Hz, J_3=4.5 Hz, J_4=1.0 Hz, 2-CH_3, 3-CH_3), 50.9 (q, J_1=147.2 Hz, CO_2CH_3), 63.1 (m, C-2), 72.8 (m, C-3), 91.8 (t, J_3=3.5 Hz, C-7a), 107.9 (s, C-7), 122.6 (d, J_1=168.8 Hz, C-3''), 127.2 (t, J_2=7.4 Hz, C-1'), 127.8 (d, J_1=172.1 Hz, C-2''), 128.0 (d.m, J_1=165.4 Hz, C-2'), 129.0 (d.m, J_1=163.0 Hz, C-3'), 131.1 (dtt, J_1=161.5 Hz, J_2=7.5 Hz, J_3=1.0 Hz, C-4'), 147.0 (m, C-4''), 153.2 (t, J_2=7.5 Hz, C-1''), 163.1 (t, J_3=4.1 Hz, C-6), 163.3 (q, J_3=4.1 Hz, CO_2CH_3). λ_{max}, (ethanol), nm (lg ε): 270 (4.27). IR (KBr): ν = 3354, 3068, 2978, 2951, 1688, 1635, 1599, 1516, 1492, 1437, 1347, 1188, 1175, 1112, 1073, 851 cm^{-1}. m.p. 126-128 °C (from hexane).

Anal. Calcd. for $C_{23}H_{25}N_3O_5$: C 65.24, H 5.95, N 9.92. Found: C 65.08, H 6.24, N 9.80.

Dimethyl 2,2,3,3-Tetramethyl-7a-(4-nitrophenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**18f**).

was synthesized similarly to **14a**; reaction time was 1 h, the yield was 49 %. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.92, 0.95, 1.16, 1.23 (each s, 3H, 2-CH_3, 3-CH_3), 2.81 (broad s, 1H, N-H), 3.52, 3.83 (each s, 3H, CO_2CH_3), 7.84 (dt, J_3=9.0 Hz, J_4=2.1 Hz, 2H, Ar), 8.08 (dt, J_3=9.0 Hz, J_4=2.1 Hz, 2H, Ar). λ_{max}, (ethanol), nm (lg ε): 269 (4.18). IR (KBr): ν = 3353, 2981, 2959, 1755, 1713, 1651, 1523, 1438, 1348, 1306, 1213, 1175, 1138, 1090, 851 cm^{-1}. m.p. 116-117 °C (from hexane).

Anal. Calcd. for $C_{19}H_{23}N_3O_7$: C 56.29, H 5.72, N 10.37. Found: C 56.43, H 5.91, N 10.30.

1,2,2,3,3-Pentamethyl-7a-(4-nitrophenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carbaldehyde (**18g**).

This compound was synthesized similarly to **13a**; the yield was 24 %. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.84, 1.01, 1.08, 1.33 (each s, 3H, 2-CH_3, 3-CH_3), 2.41 (s, 3H, N-CH_3), 7.58 (s, 1H, C=CH), 7.72 (dt, J_3=9.0 Hz, J_4=2.1 Hz, 2H, Ar), 8.14 (dt, J_3=9.0 Hz, J_4=2.1 Hz, 2H, Ar), 9.50 (s, 1H, CHO). m.p. 71.5-72.5 °C (from hexane).

Anal. Calcd. for $C_{17}H_{21}N_3O_4$: C 61.62, H 6.39, N 12.68. Found: C 61.58, H 6.67, N 12.67.

1,2,2,3,3-Pentamethyl-6-phenyl-7a-(4-nitrophenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carbaldehyde (**18h**).

This compound was synthesized by **Method B** with the 68% yield. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.88, 1.03, 1.12, 1.37 (each s, 3H, 2-CH_3, 3-CH_3), 2.54 (s, 3H, N-CH_3), 7.47-7.68 (m, 5H, Ph), 7.78-7.82 (d.m, J_3 = 8.7 Hz, 2H, Ar), 8.13-8.17 (d.m, J_3 = 8.7 Hz, 2H, Ar), 9.53 (s, 1H, CHO). λ_{max}, (ethanol), nm (lg ε): 271 (4.28). IR (KBr): ν = 3066, 2991, 2955, 2826, 2804, 2751, 1663, 1620, 1595, 1524, 1490, 1446, 1395, 1342, 1214, 1152, 1109, 985, 862, 851, 771, 702 cm^{-1}. m.p. 161-163 °C (from hexane).

Anal. Calcd. for $C_{23}H_{25}N_3O_4$: C 67.80, H 6.35, N 10.23. Found: C 67.82, H 6.35, N 10.23.

1-(1,2,2,3,3-Pentamethyl-6-phenyl-7a-(4-nitrophenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)ethanone (**18i**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 58 %. NMR ^{1}H ([D_6]acetone, 200.13 MHz, δ, ppm): 0.84, 1.16, 1.18, 1.32 (each s, 3H, 2-CH_3, 3-CH_3), 1.67 (s, 3H, $COCH_3$), 2.58 (s, 3H, NCH_3), 7.61-7.73 (m, 5H, Ph), 7.90-7.95 (dt, J_3 = 9.0 Hz, J_4 = 2.0 Hz, 2H, Ar), 8.13-8.18 (dt, J_3 = 8.7 Hz, J_4 = 2.0 Hz, 2H, Ar). λ_{max}, (ethanol), nm (lg ε): 275 (4.25). IR (KBr): ν = 3058, 2995, 2952, 2882, 2802, 1645, 1626, 1592, 1520, 1367, 1345, 1270, 1216, 1150, 1112, 1097, 1011, 983, 866, 846, 772, 698 cm^{-1}. m.p. 200-202 °C (from hexane).

Anal. Calcd. for $C_{24}H_{27}N_3O_4$: C 68.39, H 6.46, N 9.97. Found: C 68.21, H 6.50, N 9.62.

(1,2,2,3,3-Pentamethyl-6-phenyl-7a-(4-nitrophenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)(phenyl)methanone (**18j**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 79 %. NMR ^{1}H ([D_6]acetone, 200.13 MHz, δ, ppm): 0.91, 1.21, 1.25, 1.44 (each s, 3H, 2,3-$(CH_3)_2$), 2.70 (s, 3H, N-CH_3), 6.99-7.38 (m, 10H, Ph), 8.05 (dt, J_3 = 9.1 Hz, J_4 = 2.1 Hz, 2H, Ar), 8.19 (dt, J_3 = 9.1 Hz, J_4 = 2.1 Hz, 2H, Ar). λ_{max}, (ethanol), nm (lg ε): 271 (4.28). IR (KBr): ν = 3062, 3003, 2945, 2890, 2804, 1615, 1595, 1576, 1518, 1491, 1423, 1345, 1218, 1159, 988, 892, 865 cm^{-1}. m.p. 182.5-183.5 °C (from ethyl acetate – hexane mixture). X-ray crystallography (CCDC 260689): $C_{29}H_{29}N_3O_4$, *FW* 483.55, monoclinic, C2/c, *a* 26.144(3), *b* 13.2308(14), *c* 19.256(2) Å, β 129.236(2)°, *V* 5158.9(10) Å^3, *Z* 8, D_C 1.245 g/cm^3 , μ(Mo-Kα) 0.084 mm^{-1}, θ 1.84-23.28°, 10964 reflections collected, 3710 unique, R_{int} = 0.0857, data/parameters 3710/439, *Goof* 1.1100, *R* indices *(I*> 2σ(*I*)):R1 0.0761 *w*R2 0.1644; *R* indices (all data):R1 0.1274, *w*R2 0.1845.

Anal. Calcd. for $C_{29}H_{29}N_3O_4$: C 72.03, H 6.04, N 8.69. Found: C 71.74, H 5.99, N 8.65.

Methyl 1,2,2,3,3-Pentamethyl-7a-(4-nitrophenyl)--1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**18k**).

This compound was synthesized similarly to **14a**; reaction time was 40 h, the yield was 46 %. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.79, 1.02, 1.06, 1.29 (each s, 3H, 2-CH_3, 3-CH_3), 2.45 (s, 3H, N-CH_3), 3.51 (s, 3H, CO_2CH_3), 7.55 (s, 1H, C=CH), 7.73 (dt, J_3=9.0 Hz, J_4=2.1 Hz, 2H, Ar), 8.12 (dt, J_3=9.0 Hz, J_4=2.1 Hz, 2H, Ar). λ_{max}, (ethanol), nm (lg ε): 270 (4.17). IR (KBr): ν = 2987, 2949, 2850, 2804, 1719, 1618, 1522, 1439, 1367, 1346, 1214, 1196, 1156, 1123, 1032, 986, 862, 853 cm^{-1}. m.p. 108-110 °C (from hexane).

Anal. Calcd. for $C_{18}H_{23}N_3O_5$: C 59.82, H 6.41, N 11.63. Found: C 59.69, H 6.60, N 11.57.

Methyl 1,2,2,3,3-Pentamethyl-6-phenyl-7a-(4-nitrophenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**18l**).

This compound was synthesized by **Method B** with the 76% yield. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm) 0.85, 1.09, 1.12, 1.33 (each s, 3H, 2-CH_3, 3-CH_3), 2.57 (s, 3H, NCH_3), 3.32 (s, 3H, CO_2CH_3), 7.42-7.47 (m, 3H, Ph), 7.62-7.67 (m, 2H, Ph), 7.83 (d.m, J_3 = 9.0 Hz, 2H, Ar), 8.16 (dm, J_3 = 9.0 Hz, 2H, Ar). NMR ^{13}C ($CDCl_3$, 50.32 MHz, δ, ppm): 18.8, 20.1, 24.6, 24.9 (2-CH_3 , 3-CH_3), 29.2 (N-CH_3), 50.5 (CO_2CH_3), 66.1 (C-2), 71.7 (C-3), 94.8 (C-7a), 105.2 (C-7), 122.8 (C-3"), 127.8 (C-1'), 127.9 (C-2"), 128.2 (C-2'), 129.3 (C-3'), 131.0 (C-4'), 146.8 (C-4"), 152.5 (C-1"), 163.7 (C-6), 165.4 (-CO_2CH_3). λ_{max}, (ethanol), nm (lg ε): 270 (4.18). IR (KBr): ν = 3061, 2995, 2952, 2807, 1699, 1634, 1595, 1520, 1492, 1440, 1367,1346, 1273, 1218, 1198, 1124, 1037, 987, 865, 847, 792, 767, 750, 709 cm^{-1}. m.p. 169.5-171 °C (from hexane).

Anal. Calcd. for $C_{24}H_{27}N_3O_5$: C 65.89, H 6.22, N 9.60. Found: C 66.21, H 6.46, N 9.41.

Dimethyl 1,2,2,3,3-Pentamethyl-7a-(4-nitrophenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**18m**).

This compound was synthesized by **Method B** with the 61% yield. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm) 0.81, 1.32 (each s, 3H, 2-CH_3, 3-CH_3), 1.09, (s, 6H, 2-CH_3, 3-CH_3), 2.47 (s, 3H, N-CH_3), 3.50, 3.91 (each s, 3H, CO_2CH_3), 7.75 (dm, J_3 = 8.7 Hz, 2H, Ar), 8.15 (dm, J_3 = 8.7 Hz, 2H, Ar). λ_{max}, (ethanol), nm (lg ε): 271 (4.12). IR (KBr): ν = 3074, 2995, 2960, 1761, 1717, 1651, 1519, 1441, 1345, 1308, 1222, 1064, 864, 849, 794, 777, 742 cm^{-1}. m.p. 126.5-127.5 °C (from hexane).

Anal. Calcd. for $C_{20}H_{25}N_3O_7$: C 57.27, H 6.01, N 10.02. Found: C 56.91, H 6.26, N 9.87.

1-(2,2,3,3-Tetramethyl-6-phenyl-7a-(3-nitrophenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)ethanone (**19a**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 65 %. NMR ^{1}H ([D_6]acetone, 200.13 MHz, δ, ppm): 1.01, 1.08, 1.30, 1.38 (s, 3H, 2-CH_3, 3-CH_3), 1.67 (s, 3H, CO CH_3), 7.55-7.69 (m, 6H, Ph), 8.11 (dm, J_3 = 8.0 Hz, 1H, Ar), 8.21 (dm, J_3 = 8.0 Hz, 1H, Ar), 8.73 (t, J_4 = 1.8 Hz, 1H, Ar). λ_{max}, (ethanol), nm (lg ε): 263 (4.17). IR (KBr): ν = 3433, 3087, 2987, 2873, 1633, 1594, 1527, 1491, 1447, 1368, 1349, 1162, 1108, 1091, 770, 743, 728, 706 cm^{-1}. m.p. 146-148 °C (from hexane).

Anal. Calcd. for $C_{23}H_{25}N_3O_4$: C 67.80, H 6.18, N 10.31. Found: C 67.25, H 6.15, N 10.29.

Methyl 2,2,3,3-Tetramethyl-7a-(3-nitrophenyl)-1,2,3,7a-tetrahydroimidazo[1,2-b]isoxazole-7-carboxylate(**19b**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 80 %. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.95 (s, 6H, 2-CH_3 , 3-CH_3), 1.16, 1.22 (each s, 3H, 2-CH_3, 3-CH_3), 2.89 (broad s, 1H, N-H), 3.54 (s, 3H, CO_2CH_3), 7.38 (s, 1H, C=CH), 7.38-7.46 (m, 1H, Ar), 8.03-8.06 (m, 2H, Ar), 8.56 (s, 1H, Ar). λ_{max}, (ethanol), nm (lg ε): 265 (4.07). IR (KBr): ν = 3333, 3095, 3001, 2978, 2874, 1711, 1622, 1528, 1434, 1378, 1367, 1351, 1336, 1287, 1159, 1146, 1130, 1089, 1066, 903, 887, 808 cm^{-1}. m.p. 130.5-131.5 °C (from hexane).

Anal. Calcd. for $C_{17}H_{21}N_3O_5$: C 58.78, H 6.09, N 12.10. Found: C 58.39, H 6.01, N 11.95.

Dimethyl 2,2,3,3-Tetramethyl-7a-(3-nitrophenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**19c**).

This compound was synthesized similarly to **14a**; reaction time was 20 h, the yield was 76 %. NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.93, 0.97, 1.18, 1.25 (each s, 3H, 2-CH_3, 3-CH_3), 2.78 (broad s, 1H, N-H), 3.53, 3.84 (each s, 3H, CO_2CH_3), 7.43 (t, J_3 = 8.0 Hz, 1H, Ar), 8.01 (tm, J_3 = 8.0 Hz, 2H, Ar), 8.54 (s, 1H, Ar). λ_{max}, (ethanol), nm (lg ε): 265 (4.05). IR (KBr): ν =

3339, 2990, 2958, 1756, 1724, 1651, 1524, 1439, 1371, 1350, 1297, 1202, 1143, 1094, 1044, 897, 789, 774, 758, 738 cm^{-1}, 725. m.p. 118-119 °C (from hexane).

Anal. Calcd. for $C_{19}H_{23}N_3O_7$: C 56.29, H 5.72, N 10.37. Found: C 56.44, H 5.85, N 9.96.

1-(2,2,3,3-Tetramethyl-6-phenyl-7a-(4-methoxyphenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazol-7-yl)ethanone (**20a**).

This compound was synthesized similarly to **14a**; reaction time was 30 h, the yield was 54 %. NMR ^1H ([D_6]acetone, 200.13 MHz, δ, ppm): 1.03, 1.07, 1.27, 1.33 (each s, 3H, 2-CH_3, 3-CH_3), 1.73 (s, 3H, $COCH_3$), 3.78 (s, 3H, OCH_3), 6.82-6.87 (dm, J_3 = 8.7 Hz, 2H, Ar), 7.55-7.65 (m, 5H, Ph), 7.66-7.70 (dm, J_3 = 8.7 Hz, 2H, Ar). λ_{max}, (ethanol), nm (lg ε): 228 (4.26), 275 (3.89), 282 (3.89). IR (KBr): ν = 3059, 2980, 2933, 2839, 1633, 1609, 1593, 1511, 1489, 1444, 1372, 1335, 1302, 1248, 1171, 1101, 1067, 1031, 839, 770, 704, 611 cm^{-1}. m.p. 125-126.5 °C (from heptane).

Anal. Calcd. for $C_{24}H_{28}N_2O_3$: C 73.44, H 7.19, N 7.14. Found: C 73.42, H 7.39, N 7.19.

Methyl 7a-(4-Methoxyphenyl)-2,2,3,3-tetramethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**20b**).

This compound was synthesized similarly to **14a**; reaction time was 10 h, the yield was 40 %. NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.89, 1.00, 1.13, 1.24 (each s, 3H, 2-CH_3, 3-CH_3), 2.64 (broad s, 1H, N-H), 3.52 (s, 3H, CO_2CH_3), 3.70 (s, 3H, OMe), 6.77 (d, J_3 =9.0 Hz, 2H, Ar), 7.26 (s, 1H, C=CH), 7.58 (d, J_3=9.0 Hz, 2H, Ar). λ_{max}, (ethanol), nm (lg ε): 226 (3.99), 273 (3.82). IR (KBr): ν = 3311, 2998, 2960, 1701, 1630, 1619, 1439, 1344, 1247, 1178, 1163, 1127, 1107, 1084, 828, 766 cm^{-1}. m.p. 103-104 °C (from hexane).

Anal. Calcd. for $C_{18}H_{24}N_2O_4$: C 65.04, H 7.28, N 8.43. Found: C 65.18, H 7.52, N 8.41.

Dimethyl 7a-(4-Methoxyphenyl)-2,2,3,3-tetramethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**20c**).

This compound was synthesized similarly to **14a**; reaction time was 10 h, the yield was 58 %. NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.82, 0.96, 1.11, 1.20 (each s, 3H, 2-CH_3, 3-CH_3), 2.68 (broad s, 1H, N-H), 3.46, 3.63 (each s, 3H, CO_2CH_3), 3.74 (s, 3H, OMe), 6.71 (d, J_3=9.0 Hz, 2H, Ar), 7.47 (d, J_3=9.0 Hz, 2H, Ar). λ_{max}, (ethanol), nm (lg ε): 225 (4.09), 275 (3.78). IR (KBr): ν = 3321, 3011, 2973, 2955, 2833, 1748, 1727, 1651, 1609, 1510, 1439, 1343, 1312, 1248, 1213, 1177, 1134, 1076, 1030, 840 cm^{-1}. m.p. 114-115 °C (from hexane).

Anal. Calcd. for $C_{20}H_{26}N_2O_6$: C 61.53, H 6.71, N 7.18. Found: C 61.50, H 7.30, N 7.07.

1,2,2,3,3-Pentamethyl-6-phenyl-7a-(4-methoxyphenyl)-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carbaldehyde (**20d**).

This compound was synthesized by **Method B** with the 53% yield. NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.97, 1.02, 1.11, 1.35 (each s, 3H, 2-CH_3, 3-CH_3), 2.52 (s, 3H, N-CH_3), 3.76 (s, 3H, OMe), 6.80-6.85 (d.m, ^3J = 8.9 Hz, 2H, Ar), 7.50-7.54 (d.m, ^3J = 8.9 Hz, 2H, Ar), 7.50-7.54 (m, 3H, Ph), 7.63-7.68 (m, 2H, Ph), 9.53 (s, 1H, CHO). λ_{max}, (ethanol), nm (lg ε): 231 (4.28). IR (KBr): ν = 3058, 2938, 2833, 2803, 2765, 1652, 1619, 1508, 1462, 1445, 1342, 1243, 1169, 1108, 1040, 984, 845, 776, 704 cm^{-1}. m.p. 147-147.5 °C (from hexane).

Anal. Calcd. for $C_{24}H_{28}N_2O_3$: C 73.44, H 7.19, N 7.14. Found: C 72.90, H 7.32, N 6.92.

Methyl 7a-(4-Methoxyphenyl)-1,2,2,3,3-pentamethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**20e**).

This compound was synthesized similarly to **14a**; reaction time was 10 h, the yield was 50 %. NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 0.83, 0.96, 1.00, 1.24 (each s, 3H, 2-CH_3, 3-CH_3), 2.38 (s, 3H, N-CH_3), 3.47 (s, 3H, CO_2CH_3), 3.69 (s, 3H, OMe), 6.75 (d, J_3=9.0 Hz, 2H, Ar), 7.40 (d, J_3=9.0 Hz, 2H, Ar), 7.47 (s, 1H, C=CH). λ_{max}, (ethanol), nm (lg ε): 228 (4.11), 270 (3.83). IR (KBr): ν = 2997, 2949, 2844, 2802, 1715, 1618, 1512, 1464, 1439, 1331, 1243, 1194, 1160, 1122, 1034, 982, 847 cm^{-1}. m.p. 120-122 °C (from hexane).

Anal. Calcd. for $C_{19}H_{26}N_2O_4$: C 65.87, H 7.56, N 8.09. Found: C 66.08, H 7.90, N 8.04.

Dimethyl 7a-(4-Methoxyphenyl)-1,2,2,3,3-pentamethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**20f**).

This compound was synthesized similarly to **14a**; reaction time was 6 h, the yield was 60 %. NMR ^1H ([D_6]acetone, 200.13 MHz, δ, ppm): 0.89, 1.11, 1.13, 1.30 (each s, 3H, 2-CH_3, 3-CH_3), 2.48 (s, 3H, NCH_3), 3.49 (s, 3H, CO_2Me), 3.78 (s, 3H, OCH_3), 3.91(s, 3H, CO_2Me), 6.85-6.90 (dm, J_3 = 9.0 Hz, 2H, Ar), 7.42-7.47 (dm, J_3 = 9.0 Hz, 2H, Ar). λ_{max}, (ethanol), nm (lg ε): 227 (4.29), 275 (3.91). IR (KBr): ν = 3085, 3006, 2951, 2840, 2794, 1752, 1694, 1648, 1607, 1508, 1469, 1433, 1339, 1315, 1251, 1210, 1173, 1126, 1110, 1061, 847, 772 cm^{-1}. m.p. 105.5-107.5 °C (from hexane).

Anal. Calcd. for $C_{21}H_{28}N_2O_6$: C 62.36, H 6.98, N 6.93. Found: C 62.44, H 7.28, N 6.92.

Methyl 2,2,3,3-Tetramethyl-7a-[(*E*)-2-phenylvinyl]-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-7-carboxylate (**21a**).

This compound was synthesized similarly to **14a**; reaction time was 16 h, the yield was 33 %. NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.07 (s, 6H, 2-CH_3, 3-CH_3), 1.10, 1.29 (each s, 3H, 2-CH_3, 3-CH_3), 2.60 (broad s, 1H, N-H), 3.66 (s, 3H, CO_2CH_3), 6.67, 6.80 (each d, J_3=15.8 Hz, 2H, CH=CH-Ph), 7.15-7.37 (m, 5H, Ph). λ_{max}, (ethanol), nm (lg ε): 256 (4.32). IR (KBr): ν = 3309, 3079, 3055, 3022, 2978, 2954, 1687, 1648, 1629, 1477, 1441, 1332, 1199, 1160, 1132, 1060, 972 cm^{-1}. m.p. 127-129 °C (from hexane).

Anal. Calcd. for $C_{19}H_{24}N_2O_3$: C 69.49, H 7.37, N 8.53. Found: C 69.62, H 7.60, N 8.40.

Dimethyl 2,2,3,3-Tetramethyl-7a-[(*E*)-2-phenylvinyl]-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**21b**)

This compound was synthesized similarly to **14a**; reaction time was 10 h, the yield was 40 %. NMR ^1H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.04, 1.06, 1.11, 1.28 (each s, 3H, 2-CH_3, 3-CH_3), 2.64 (broad s, 1H, N-H), 3.65, 3.79 (each s, 3H, CO_2CH_3), 6.58, 6.81 (each d, J_3=15.8 Hz, 2H, CH=CH-Ph), 7.13-7.33 (m, 5H, Ph). λ_{max}, (ethanol), nm (lg ε): 256 (4.26). IR (KBr): ν = 3321, 3060, 3006, 2978, 2952, 1754, 1708, 1645, 1439, 1343, 1315, 1211, 1176, 1139, 1072, 987, 803 cm^{-1}. m.p. 138-139 °C (from hexane).

Anal. Calcd. for $C_{21}H_{26}N_2O_5$: C 65.27, H 6.78, N 7.25. Found: C 65.00, H 7.17, N 7.28.

3-[(2,4,4,5,5-Pentamethyl-4,5-dihydro-1*H*-imidazol-1-yl)oxy]-propanenitrile (**22**).

Solution of 0.326 g (2.09 mmol) of **3a** and 0.80 ml (12 mmol) acrylonitrile in 5 ml $CHCl_3$ was refluxed for 6 h. Then the solvent

was removed, and **22** was isolated by flash chromatography on alumina with ether as eluent. The yield was 0.081 g (19 %). NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.01, 1.06 (each s, 6H, 2-CH_3, 3-CH_3), 1.92 (s, 3H, 2-CH_3), 2.60 (t, J_3=6.0 Hz, 2H, CH_2CN), 3.97 (t, J_3=6.0 Hz, 2H, CH_2CN). NMR ^{13}C ($CDCl_3$, 50.32 MHz, δ, ppm): 14.3 (2-CH_3), 17.5 (*C*H_2-CN), 23.2 (2-CH_3, 3-CH_3), 66.6 (C-4), 70.1 (O-CH_2), 71.5 (C-5), 117.2 (-CN), 164.0 (C-2). λ_{max}, (ethanol), nm (lg ε): 228 (3.72). IR (KBr): ν = 2988, 2971, 2931, 2904, 2257, 1640, 1468, 1446, 1385, 1368, 1312, 1162, 1079, 1053, 760, 702, 652 cm^{-1}. m.p. 81-83 °C (from ethyl acetate – hexane mixture).

Anal. Calcd. for $C_{11}H_{19}N_3O$: C 63.13, H 9.15, N 20.08. Found: C 63.19, H 9.38, N 19.98.

Dimethyl 1-Hydroxy-2,2,3,3-tetramethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (**26**).

This compound was identified by NMR ^{1}H of reaction mixture formed in the reaction of imidazoline **2c** with DMAD in $CHCl_3$ at –10 °C. Warming to 25 °C of this reaction mixture during 3 h resulted in almost quantitative formation of **13c** (cf. [23]). NMR ^{1}H ($CDCl_3$, 200.13 MHz, δ, ppm): 1.25 (s, 12H, 4,4,5,5-$(CH_3)_4$), 3.58, 3.71 (each s, 1H, CO_2CH_3), 5.38 (s, 1H, C-H), 6.11 (broad s, 1H, N-OH).

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REFERENCES AND NOTES

† The details of the influence of tautomeric equilibrium state on the reaction path with dipolarophiles see in our next paper.

[1] A. Padwa, *Angew. Chem.*, **5**, 131 (1976).

[2] R. A. Firestone, *Tetrahedron*,, **33**, 3009 (1977).

[3] J. J. Tufariello in 1,3-Dipolar Cycloaddition Chemistry (Ed.: A. Padwa), Wiley-Interscience, New York, (1984), chapter 9, 83-167.

[4] R. Huisgen in Steric Course and Mechanism of 1,3-Dipolar Cycloadditions. Advances in Cycloaddition. (Ed.: D. P. Curran), Greenwich, CT, Jai Press Inc. Chapter 1 (1988).

[5] A. Padwa and A. M. Schoffstall in Intramolecular 1,3-Dipolar Cycloaddition Chemistry. Advances in Cycloaddition. (Ed.: D. P. Curran), Greenwich, CT, Jai Press Inc. chapter 2 (1990).

[6] P. A. Wade in Intramolecular 1,3-Dipolar Cycloadditions. Comprehensive Organic Synthesis. (Ed.: B. M. Trost and I. Fleming), Oxford, Pergamon Press. 4.10 (1991), 1111-1168.

[7] A. Padwa Intramolecular 1,3-Dipolar Cycloadditions. Comprehensive Organic Synthesis. (Ed.: B. M. Trost and I. Fleming), Oxford, Pergamon Press. 4.9 (1991), 1069-1109.

[8] L. Fisera, U. A. R. Altimari, et al. in Cycloaddition Reactions in Carbohydrate Chemistry. (Ed.: R. M. Giuliano), Washington, DC, Am. Chem. Soc. (1992), 158-171.

[9] L. Raimondi, *Gazz. Chim. Ital*., **4**, 167 (1997).

[10] K. V. Gothelf and K. A. Jorgensen, *Chem. Rev.*, **2**, 863-909 (1998).

[11] K. V. Gothelf, and K. A. Jorgensen, *J. Chem. Soc., Chem. Commun*., **16**, 1449-1458 (2000).

[12] R. C. F. Jones, J. N. Martin in *Nitrones* (Ed.: A. Padwa), John Wiley & Sons, Ltd (2002), 1-81.

[13] F. Saczewski, T. Debowski, M. Gdaniec, and Z. Gdaniec, *J. Org. Chem*., **61**, 5425-5429 (1996).

[14] S. P. Ashburn, and R. M. Coates, *J. Org. Chem*., **17**, 3127-3133 (1984).

[15] S.P. Ashburn, and R.M. Coates, *J. Org. Chem*., , **18**, 3076-3081 (1985).

[16] T. Hisano, K. Harano, T. Matsuoka, S. Watanabe, and T. Matsuzaki, *Chem. Pharm. Bull*., **4**, 907-911 (1989).

[17] S. Takahashi, and H. Kano, *Tetrahedron Lett*., **25**, 1687-1691 (1963).

[18] S. Takahashi, and H. Kano, *J. Org. Chem*., **4**, 1118-1122 (1965).

[19] R. C. F. Jones, J. N. Martin, P. Smith, T. Gelbrich, M. E. Light, and M. B. Hursthouse, *Chem. Commun*., **19**, 1949-1951 (2000).

[20] R. C. F. Jones, J. N. Martin, and P. Smith, *J. Heterocyclic Chem.*, **3**, 481-486 (2000).

[21] R. C. F. Jones, J. N. Martin, and P. Smith, *Synlett*., **7**, 967-970 (2000).

[22] R. Huisgen, H. Seidl, and I. Brüning, *Chem. Ber*., **102**, 1102-1116 (1969).

[23] V. A. Reznikov, G. I. Roshchupkina, D. G. Mazhukin, P. A. Petrov, S. A. Popov, S. V. Fokin, G. V. Romanenko, T. V. Rybalova, Y. V. Gatilov, Y. G. Shvedenkov, I. G. Irtegova, L. A. Shundrin, V. I. Ovcharenko, *Eur. J. Org. Chem.*, 749-765 (2004).

[24] S. A. Popov, R. V. Andreev, G. V. Romanenko, V. I. Ovcharenko, V. A. Reznikov, *Journal of Molecular Structure*, **697** *(1-3)*, 49 (2004).

[25] M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. J. Su, T. L. Windus, M. Dupuis, J. A. Montgomery, *J. Comput. Chem.*, **11**, 1347-1363 (1993).

[26] F. E. Ullman, J. H. Osiecki, D. G. B. Boocock and R. Darcy, *J. Am. Chem. Soc.*, **20**, 7049-7059 (1972).

[27] P. A. Petrov, S. V. Fokin, G. V. Romanenko, Y. G. Shvedenkov, V. A. Reznikov and V. I. Ovcharenko, *Mendeleev Commun.*, 179-181 (2001).

[28] R. Weiss, N. Kraut, F. Hampel, *J. Organomet. Chem*. **2001**, *617*, 473 - 482.