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SYNTHESIS OF 3-(ALK-2-YN-1-YL)-1,3-OXAZOLIDINES USING COPPER-CONTAINING CATALYSTS

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A selective method for the synthesis of 3-(alk-2-yn-1-yl)-1,3-oxazolidines has been developed by the reaction of bis(oxazolidin-3-yl)methanes with terminal acetylenes with copper-containing catalysts. The reaction of terminal acetylenes with optically active bis((4R)-4-ethyl-1,3-oxazolidin-yl)methane led to the formation of (4R)-3-(2-alkynyl)-4-ethyl-1,3-oxazolidines.

Keywords: 3-(alk-2-yn-1-yl)-1,3-oxazolidines, bis(1,3-oxazolidin-3-yl)methane, 3,8-dioxa-1,6-diazabicyclo[4.4.1]undecane, terminal acetylenes, catalysis.

One of the most widely known and used methods for the synthesis of propargylamines [1-4] is the Mannich three-component condensation of terminal acetylenes with amines under the influence of Cu(I) [5-9], Zn, Ni, Au(I), Au(III), Ag(I), Fe(III), In (III), and Hg salts, bimetallic Cu–Ru(II) systems, heterogeneous catalysts, for example, Cu-zeolite, Ni-Y-zeolite, LDH-$AuCl_4$, silver and copper nanoparticles, and copper catalysts on Al_2O_3 and SiO_2 [10]. Microwave [11] and ultrasound irradiation [12] are used to activate the three-component condensation mentioned above in the presence of Cu(I) salts. In addition, propargylamines are obtained by the reaction of metal acetylides with C=N electrophiles in anhydrous conditions at low temperatures [5]. The interest in polyfunctional propargylamines is explained by their wide use as universal precursors in fine organic synthesis [13-15] and also their use as biologically active compounds [16-25].

We have shown previously [26, 27] that it is possible to synthesize propargylamines by catalytic aminomethylation of terminal acetylenes with *gem*-diamines. With a continuation of the study of this reaction and also with objective of developing an effective method for the synthesis of 3-(alk-2-yn-1-yl)-1,3-oxazolidines, we have studied the aminomethylation of the terminal acetylenes **1a**-**c** with bis(oxazolidin-3-yl)-methanes **2a**-**d**. The latter were chosen because of the wide use of derivatives of oxazolidines in stereospecific organic synthesis [28-32].

We found that bis(oxazolidin-3-yl)methane (**2a**), obtained by method [33], was in a 1:4 mixture with 3,8-dioxa-1,6-diazabicyclo[4.4.1]undecane (**3a**), which is in agreement with other studies [34]. The reaction of terminal acetylenes **1a**-**c** with bis(oxazolidin-3-yl)methanes **2a**-**d** was carried out in conditions optimal for the aminomethylation of acetylenes with *gem*-diamines (5 mol% CuCl, 80°C, 6 h) [26, 27]. Under these conditions, the mixture of compounds **2a** and **3a** in reaction with 1-pentyne **1a**, 1-hexyne (**1b**), and phenylacetylene (**1c**) led to the selective formation of 3-(hex-2-yn-1-yl)-, 3-(hept-2-yn-1-yl)-, and 3-(3-phenylprop-2-yn-1-yl)-1,3-oxazolidines (**4a**-**c**) in 58, 71, and 81 yields, respectively.

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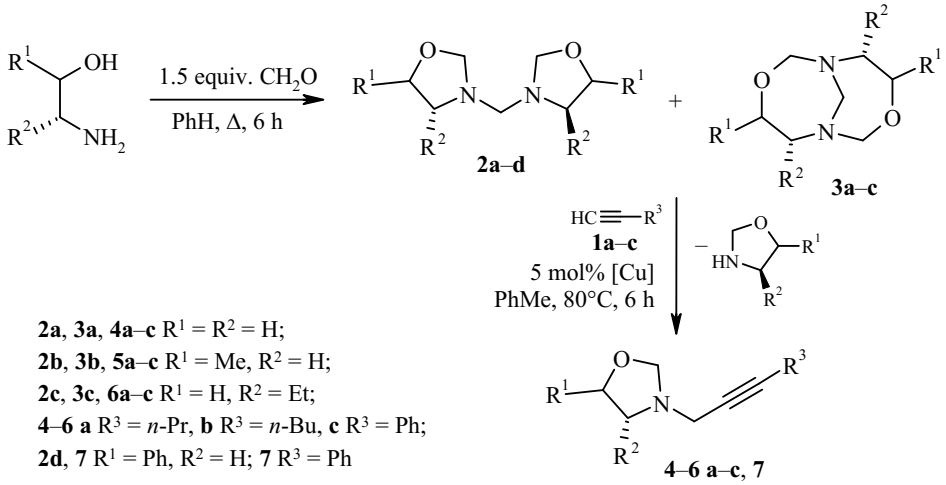
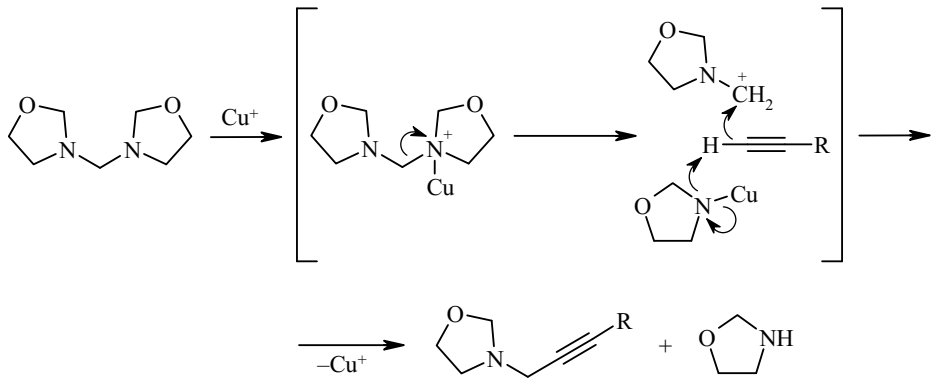
In the presence of other Cu-containing catalysts ($CuCl_2$, CuBr, CuI, $CuSO_4$, $Cu(CH_3CO_2)_2$, $CuCl_2 \cdot 2H_2O$–Al_2O_3) the yields of 3-(hept-2-yn-1-yl)-1,3-oxazolidine (**4b**) ranged from 24-72% (Table 1). The results obtained indicated that in the reaction with the acetylenes **1a-c** in the presence of copper catalyst, the isomer **2a** interacts with the formation of 3-(alk-2-yn-1-yl)-1,3-oxazolidines **4a-c**. It is possible that the high selectivity of the formation of compounds **4a-c** is explained by the shift of the equilibrium of the regioisomers **2a**+**3a** under the reaction conditions towards compound **2a** which is more reactive with the acetylenes. A similar isomerization **3a** → **2a** was observed in other studies [34] (conditions: 80-90°C, 1.5 h, toluene). According to the paper [34], the isomerization occurs through the stage of formation of the imine as determined by ^{13}C NMR spectra (164 ppm).



It might be suggested [35, 36] that in the conditions of aminomethylation of acetylenes, the first step is the coordination of the bis(oxazolidin-3-yl)methane molecule to the central atom of the catalyst [37], followed by nucleophilic addition of the acetylene to the carbocation formed, leading to the formation of the molecule of the 3-(alk-2-yn-1-yl)-1,3-oxazolidine.



It should be noted that we did not succeed in obtaining 3-(alk-2-yn-1-yl)-1,3-oxazolidines from the three-component condensation of terminal acetylenes with formaldehyde (or paraform) and 1,3-oxazolidine, obtained *in situ*, with CuCl as catalyst.

To broaden the scope of the method developed, and also the synthesis of new 3-(alk-2-yn-1-yl)-1,3-oxazolidines, we have studied the reaction of methyl-, ethyl-, and phenyl-substituted bis(oxazolidin-3-yl)methanes **2b-d** with terminal acetylenes in the presence of CuCl catalyst. The ratio of products **2**:**3** in the

TABLE 1. Effect of Catalyst on the Yield of 3-(Hept-2-yn-1-yl)-1,3-oxazolidine (**4b**)*

Experiment No.	Catalyst	Yield, %
1	CuCl	71
2	CuBr	56
3	CuI	43
4	$CuCl_2$	50
5	$CuCl_2 \cdot 2H_2O - Al_2O_3$	24
6	$CuSO_4$	54
7	$Cu(OAc)_2$	72

*Molar ratios of compound **2a** : 1-hexyne (**2b**) : catalyst = 1:1:0.05, PhMe, 80°C, 6 h, argon atmosphere.

reaction of substituted ethanolamines (amino-2-propanol, *R*-(-)-2-amino-1-butanol, and 2-amnio-1-phenylethanol) with formaldehyde depended on the substituent in the initial ethanolamine. As a result, mixtures of compounds **2b**+**3b** (ratio 4:1), **2c**+**3c** (ratio 9:1), whereas with 2-amino-1-phenylethanol only compound **2d** was obtained with a yield of 55%.

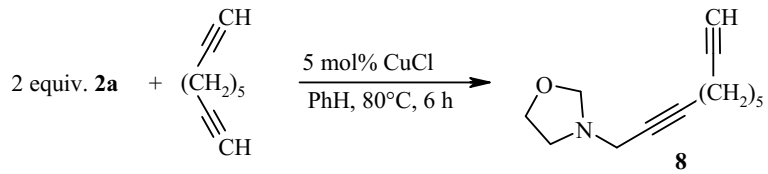
The synthesized bis(5-methyl-1,3-oxazolidin-yl)methane (**2b**) and bis(4-ethyl-1,3-oxazolidin-3-yl)-methane (**2c**) were isolated by column chromatography in pure form. The terminal acetylenes reacted with mixture of compounds **2b**+**3b** or **2c**+**3c** or with individual bis(oxazolidin-3-yl)methanes **2b**,**c** formed exclusively 3-(alk-2-yn-1-yl)-1,3-oxazolidines **5**,**6 a**-**c**.

In the ^{1}H NMR spectra of compounds **2c**,**d**, the protons of the CH_2 groups, which lie between the nitrogen and oxygen atoms, appear in the form AB system with coupling constants of 6.0 and 5.6 Hz, respectively, characteristic of bis(oxazolidin-3-yl)methanes, whereas the coupling constants for 3,8-dioxa-1,6-diazabicyclo[4.4.1]undecanes **3c**,**d** are >10 Hz [34]. The hydrogen atoms on the substituted carbon atom C-4 in compound **2c** and C-5 in compound **2d** appear as triplets at 2.79 and 5.01, respectively (J = 6.0 Hz).

We have established that the aliphatic acetylenes **1a**,**b** react with methyl- and ethyl-substituted bis(oxazolidin-3-yl)methanes **2b**,**c**, but do not react with bis(5-phenyl-1,3-oxazolidin-3-yl)methane (**2d**). The latter reacts only with phenylacetylene (**1c**) to give 5-phenyl-3-(3-phenylprop-2-yn-1-yl)-1,3-oxazolidine (**7**).

Propargylamines containing optically active substituents are effective intermediates in the synthesis of biologically active and natural compounds. However, methods for their synthesis are few and complex [29, 30]. We have proposed an effective method for the synthesis of optically active (4*R*)-3-(hex-2-yn-1-yl)-, (4*R*)-3-(hept-2-yn-1-yl)-, and (4*R*)-3-(phenylprop-2-yn-1-yl)-1,3-oxazolidines (**6a**-**c**) by the reaction of terminal acetylenes **1a**-**c** with optically active bis((4*R*)-4-ethyl-1,3-oxazolidin-3-yl)methane (**2c**). The reaction gave rise to (4*R*)-3-(alk-2-yn-1-yl)-4-ethyl-1,3-oxazolidines **6a**-**c** with yields of 24-83%.

Because of the presence of the asymmetric center C-4, in compounds **6a**-**c** the germinal methylene protons 5-CH_2 in the oxazolidine ring and the methylene group $\underline{CH_2}CH_3$ in the ethyl substituent are non-equivalent. In the ^{1}H NMR spectra, the diastereotopic protons of the 5-CH_2 methylene group appear as a multiplet and a triplet or two triplets with J = 7.5 Hz, and the protons of $CHC\underline{H_2}CH_3$ as two multiplets.



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To elucidate the possibility of the synthesis of bis(1,3-oxazolidin-3-yl)-substituted diynes, we carried out the reaction of bis(oxazolidin-3-yl)methane **2a** with 1,8-nonadiyne in a ratio of **2a** : 1,8-nonadiyne : CuCl = 2:1:0.05 (reaction conditions: 80°C, 6h, argon atmosphere). Under these conditions 3-(deca-2,9-diyn-1-yl)-1,3-oxazolidine (**8**) was obtained in 33% yield. Substituted bis(oxazolidin-3-yl)methanes **2b-d** did not react with 1,8-nonadiyne at all.

The mass spectra of the propargylamines **4-6 a-c**, **8** contain intense peaks for the $[M-H]^+$ ions, which are characteristic for mass spectra of higher amines [38]. It is probable that this is connected with the electronic factors of the amino groups, whereas in the spectrum of 5-phenyl-3-(3-phenylprop-2-yn-1-yl)-1,3-oxazolidine (**7**) the molecular ion $[M]^+$ with mass *m*/*z* 263 was observed with peaks of maximum intensity at 115 $[PhC{\equiv}CCH_2]^+$ and 104 $[PhCHCH_2]^+$ due to the aromatic rings influence. The fragment ions $[PhC{\equiv}CCH_2]^+$ (*m*/*z* 115) with maximum intensity are characteristic for 3-(3-phenylprop-2-yn-1-yl)-1,3-oxazolidines **4-6**.

So we have developed a new selective method for the synthesis of 3-(alk-2-yn-1-yl)-1,3-oxazolidines by the reaction of bis(oxazolidin-3-yl)methanes with terminal acetylenes in the presence of copper-containing catalysts. The reactions of terminal acetylenes with optically active bis((4*R)*-4-ethyl-1,3-oxazolidin-3-yl)-methanes led to the retention of the configuration of the chiral center with the formation of optically active (4*R*)-3-(hex-2-yn-1-yl)-, (4*R*)-3-(hept-2-yn-1-yl)-, and (4*R*)-4-ethyl-3-(3-phenylprop-2-yn-1-yl)-1,3-oxazolidines in 24-83 % yields.

EXPERIMENTAL

IR spectra of nujol mulls were recorded with a Bruker Vertex 70v spectrometer. ^1H and ^{13}C NMR spectra were recorded with Bruker Avance 400 (400 and 100 MHz, respectively, for compounds **4**, **5 a-c**, **7**, **8**) and Bruker Avance 500 spectrometers (500 and 125 MHz, respectively, for compounds **2c**,**d**, **6a-c**). The solvent was $CDCl_3$, the residual signals (7.26 ppm) of which were used as internal standard. ^{15}N NMR spectra were recorded with a Bruker Avance 500 (50 MHz) spectrometer with urea (77.0 ppm) as internal standard. Analysis of the reaction products was carried by GLC with a Chrom-5 chromatograph with a flame ionization detector, SE-30 (5%) stationary phase on Chromaton N-AW-HMDS carrier packed steel column, 2400×3 mm, programmer temperature 50-270°C, 8°C/min, helium carrier gas). Analysis by GC-MS was carried out on a Shimadzu GC 2010 chromatograph with a GCMS-QP2010 Ultra (Shimadzu, Japan) mass spectrometric detector, and a Supelco 5ms column (60 m×0.25mm×0.25μm). Carrier gas was helium, the temperature of the injector and interface 260°C, ion source 200°C. Method of ionization EI (70 eV). Mass spectra of compounds **7**, **8** were recorded on an Autoflex MALDI–TOF/TOF spectrometer (Bruker, Germany) with α-cyano-4-hydroxycinnamic and 2,5-dihydrobenzoic acids as matrix (samples were prepared as dried drops in chloroform, 1:10). Elemental analyses were carried out with a Karlo Erba 1106 apparatus. Special angles of rotation were measured with a Perkin-Elmer 341 polarimeter. Melting points were measured with a PHMK 80/2617 apparatus. The compounds prepared were purified by chromatography on KSK silica gel (50-160 μm). TLC was carried out on Sorbfil plates with detection in an iodine chamber.

Bis(1,3-oxazolidin-3-yl)methane (2a) and **3,8-dioxa-1,6-diazabicyclo[4.4.1]undecane (3a)** were prepared by the method described in paper [33]. A mixture of monoethanolamine (6 ml, 0.10 mol) and paraform (3.0 g, 0.10 mol) in PhH (100 ml) were heated in flask with a Dean-Stark condenser for 30 min. Then more paraform (1.5 g, 0.05 mol) was added, and the mixture was refluxed in the flask until water was no longer lost from the Dean and Stark condenser. The reaction mixture was filtered off, and the solvent was evaporated on a rotary evaporator. The colorless viscous liquid obtained consisted of a 1:4 mixture of compounds **2a** and **3a**. Yield 9.5 g (60%). The physicochemical and spectral characteristics of compounds **2a** and **3a** corresponded to the literature values [34].

Bis(5-methyl-1,3-oxazolidin-3-yl)methane (2b) and **6,9-dimethyl-3,8-dioxa-1,6-diazabicyclo-[4.4.1]undecane (3b**) were obtained analogously by the method described above [33]. A colorless liquid, consisting of a 4:1 mixture of compounds **2b** and **3b**, was obtained from 1-amino-2-propanol (3.80 g, 0.050 mol) and paraform (2.25 g, 0.075 mol). Yield 4.90 g (53%). Compound **2b** was isolated by column chromatography (R_f 0.20, 2:1 CCl_4–EtOAc). The physicochemical and spectroscopic properties of compound **2b** corresponded to the literature values [34].

Bis((4*R*)-4-ethyl-1,3-oxazolidin-3-yl)methane (2c) was obtained analogously to the method described above [33]. A colorless liquid consisting of a 9:1 mixture of compounds **2c** and **3c** was obtained from *R*-(-)-2-amino-1-butanol (4.7 ml, 0.05 mol). Yield 4.5 g (42%). Compound **2c** was isolated by column chromatography (R_f 0.40, 2:1 hexane–EtOAc). $[\alpha]_D^{18}$ -41.7° (*c* 4.05, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.79 (6H, t, *J* = 7.5, $CH_2C\underline{H}_3$); 1.18-1.25 (2H, m) and 1.36-1.42 (2H, m, $C\underline{H}_2CH_3$); 2.79 (2H, t, *J* = 6.0, 4-CH); 3.13-3.16 (2H, m) and 3.79 (2H, t, *J* = 6.5, 5-CH_2); 3.18 (2H, s, NCH_2N); 4.12 (2H, d, *J* = 6.0) and 4.42 (2H, d, *J* = 6.0, 2-CH_2). ^{13}H NMR spectrum, δ, ppm: 10.8 ($CH_2\underline{C}H_3$); 26.6 ($\underline{C}H_2CH_3$); 63.1 (C-4); 69.2 (C-5); 75.5 (NCH_2N); 84.2 (C-2). ^{15}N NMR spectrum, δ, ppm: 73.1. Found, %: C 61.59; H 10.40; N 13.12. $C_{11}H_{22}N_2O_2$. Calculated, %: C 61.65; H 10.35; N 13.07.

Bis(5-phenyl-1,3-oxazolidin-3-yl)methane (2d) was prepared by the method described above [33] from 2-amino-1-phenylethanol (0.690 g, 5.0 mmol) and paraform (0.225 g, 7.5 mmol). Yield 0.860 g, (55%), white crystals, mp 67-68°C. R_f 0.25 (hexane–CH_2Cl_2–EtOAc, 2:2:1). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.94-2.99 (2H, m) and 3.57-3.67 (2H, m, 4-CH_2); 3.61 (2H, s, NCH_2N); 4.77 (2H, d, *J* = 5.6) and 4.79 (2H, d, *J* = 5.6, 2-CH_2); 5.01 (2H, t, *J* = 6.0, 5-CH); 7.35-7.44 (10H, m, H Ph). ^{13}H NMR spectrum, δ, ppm: 59.0 (C-4); 74.8 (NCH_2N); 76.3 (C-5); 86.1 (C-2); 125.6 (C Ph); 127.5 (C Ph); 128.6 (C Ph); 142.3 (C Ph). Found, %: C 73.48; H 7.23; N 9.12. $C_{19}H_{22}N_2O_2$. Calculated, %: C 73.52; H 7.14; N 9.02.

Synthesis of 3-(Alk-2-yn-1-yl)-1,3-oxazolidines 4-6 a-c, 7. Compounds **4-6 a-c**, **7** were prepared by the method described in papers [26, 27]. A mixture of bis(oxazolidin-3-yl)methane (1 mmol) **2a-d** (compounds **2a-c** were used as a mixture with the isomeric 3,8-dioxa-1,6-diazabicyclo[4.4.1]undecane **3a-c**), terminal acetylene **1a-c** (1 mmol) and catalyst (0.05 mmol) in PhMe (3 ml) was stirred in an atmosphere of argon at 80°C for 6 h. The catalyst was separated from the reaction mixture, the solvent was evaporated, and the reaction mixture was purified by column chromatography.

3-(Hex-2-yn-1-yl)-1,3-oxazolidine (4a). Yield 0.09 g, (58%), colorless oil, R_f 0.22 (2:1 CCl_4-EtOAc). IR spectrum, ν, cm^{-1}: 1056 (C–O–C); 1450 (CH_2), 2253 (C≡C); 2932 (CH_3). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.98 (3H, t, *J* = 7.2, CH_3); 1.53 (2H, sextet, *J* = 7.2, $C\underline{H}_2CH_3$); 2.17 (2H, t, *J* = 7.2, $C\underline{H}_2CH_2CH_3$); 3.06 (2H, t, *J* = 6.8, 4-CH_2); 3.36 (2H, s, $NCH_2C{\equiv}C$); 3.80 (2H, t, *J* = 6.8, 5-CH_2); 4.37 (2H, s, 2-CH_2). ^{13}C NMR spectrum, δ, ppm: 13.5 (CH_3); 20.7 ($\underline{C}H_2CH_2CH_3$); 22.2 ($\underline{C}H_2CH_3$); 42.9 ($N\underline{C}H_2C{\equiv}C$); 51.3 (C-4); 63.6 (C-5); 76.1 ($NCH_2\underline{C}{\equiv}C$); 84.3 ($NCH_2C{\equiv}\underline{C}$); 85.9 (C-2). Mass spectrum, *m/z* (I_{rel}, %): 152 $[M\text{-}H]^+$ (100), 123 $[M\text{-}H\text{-}C_2H_5]^+$ (28), 110 $[M\text{-}C_3H_7]^+$ (31), 72 $[C_2H_4NCH_2O]^+$ (62). Found, %: C 70.47; H 9.95; N 9.21. $C_9H_{15}NO$. Calculated, %: C 70.55; H 9.87; N 9.14.

3-(Hept-2-yn-1-yl)-1,3-oxazolidine (4b). Yield 0.12 g (71%), colorless oil, R_f 0.22 (2:1 CCl_4–EtOAc). IR spectrum, ν, cm^{-1}: 1058 (C–O–C), 1458 (CH_2), 2250 (C≡C), 2930 (CH_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.93 (3H, t, *J* = 7.2, CH_3); 1.39-1.45 (2H, m, $C\underline{H}_2CH_3$); 1.45-1.52 (2H, m, $C\underline{H}_2CH_2CH_3$); 2.18-2.22 (2H, m, $C{\equiv}CC\underline{H}_2CH_2$); 3.07 (2H, t, *J* = 6.8, 4-CH_2); 3.37 (2H, s, $NCH_2C{\equiv}C$); 3.80 (2H, t, *J* = 6.8, 5-CH_2); 4.38 (2H, s, 2-CH_2). ^{13}C NMR spectrum, δ, ppm: 13.6 (CH_3); 18.4 ($C{\equiv}C\underline{C}H_2CH_2$); 21.9 ($\underline{C}H_2CH_3$); 30.8 ($\underline{C}H_2CH_2CH_3$); 42.8 ($N\underline{C}H_2C{\equiv}C$); 51.3 (C-4); 63.6 (C-5); 75.9 ($NCH_2\underline{C}{\equiv}C$); 84.5 ($NCH_2C{\equiv}\underline{C}$); 85.9 (C-2). Mass spectrum, *m/z* (I_{rel}, %): 166 $[M\text{-}H]^+$ (100), 137 $[M\text{-}H\text{-}C_2H_5]^+$ (22), 110 $[M\text{-}C_4H_9]^+$ (31), 72 $[C_2H_4NCH_2O]^+$ (33). Found, %: C 71.89; H 10.17; N 8.35. $C_{10}H_{17}NO$. Calculated, %: C 71.81; H 10.25; N 8.37.

3-(3-Phenylprop-2-yn-1-yl)-1,3-oxazolidine (4c). Yield 0.15 g (81%), colorless oil, n_D 1.3657 (at 28°C), R_f 0.23 (2:2:1 hexane–CH_2Cl_2–EtOAc). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.05 (2H, t, *J* = 6.8, 4-CH_2); 3.54-3.57 (2H, m, $NC\underline{H}_2C{\equiv}C$); 3.76 (2H, t, *J* = 6.8, 5-CH_2); 4.36-4.40 (2H, m, 2-CH_2); 7.22-7.25 (3H, m, H Ph); 7.37-7.41 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 43.2 ($NCH_2C{\equiv}C$); 51.4 (C-4); 63.7 (C-5); 84.0

($NCH_2\underline{C}\equiv C$); 85.6 ($NCH_2C\equiv\underline{C}$); 86.0 (C-2); 122.9 (C Ph); 128.2 (C Ph); 128.3 (C Ph); 131.7 (C Ph). Mass spectrum, *m/z* (I_{rel}, %): 186 $[M\text{-}H]^+$ (42), 156 $[M\text{-}CH_2O]^+$ (81), 115 $[PhC\equiv CCH_2]^+$ (100), 102 $[PhC\equiv CH]^+$ (17), 89 $[CPh]^+$ (64). Found, %: C 76.91; H 7.06; N 7.55. $C_{12}H_{13}NO$. Calculated, %: C 76.98; H 7.00; N 7.48.

3-(Hex-2-yn-1-yl)-5-methyl-1,3-oxazolidine (5a). Yield 0.09 g (45%), light-yellow transparent oil, R_f 0.40 (2:1 hexane–EtOAc). IR spectrum, ν, cm^{-1}: 1076 (C–O–C), 1457 (CH_2), 2250 (C≡C), 2932 (CH_2). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.91-0.94 (3H, m, $CH_2CH_2C\underline{H}_3$); 1.15-1.21 (3H, m, 5-CH_3); 1.43-1.49 (2H, m, $CH_2C\underline{H}_2CH_3$); 2.11-2.12 (2H, m, $C\underline{H}_2CH_2CH_3$); 2.44-2.48 (1H, m) and 3.11-3.16 (1H, m, 4-CH_2); 3.33 (2H, d, *J* = 2.0, $NCH_2C\equiv C$); 4.08-4.12 (1H, m, 5-CH); 4.33 (2H, d, *J* = 2.4, 2-CH_2). ^{13}C NMR spectrum, δ, ppm: 13.4 ($CH_2CH_2\underline{C}H_3$); 19.9 (5-CH_3); 20.6 ($\underline{C}H_2CH_2CH_3$); 22.1 ($CH_2\underline{C}H_2CH_3$); 42.8 ($N\underline{C}H_2C\equiv C$); 58.2 (C-4); 71.8 (C-5); 75.9 ($NCH_2\underline{C}\equiv C$); 84.5 ($NCH_2C\equiv\underline{C}$); 85.2 (C-2). Mass spectrum, *m/z* (I_{rel}, %): 166 $[M\text{-}H]^+$ (37), 123 $[M\text{-}H\text{-}C_3H_7]^+$ (100), 95 $[NCH_2C\equiv CC_3H_7]^+$ (63). Found, %: C 71.77; H 10.32; N 8.42. $C_{10}H_{17}NO$. Calculated, %: C 71.81; H 10.25; N 8.37.

3-(Hept-2-yn-1-yl)-5-methyl-1,3-oxazolidine (5b). Yield 0.14 g (70%), light-yellow oil, R_f 0.38 (2:1 hexane–EtOAc). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.83 (3H, t, *J* = 7.2, $CH_2C\underline{H}_3$); 1.17-1.19 (3H, m, 5-CH_3); 1.30-1.35 (2H, m, $C\underline{H}_2CH_2CH_3$); 1.37-1.40 (2H, m, $CH_2C\underline{H}_2CH_3$); 2.12 (2H, m, $C\equiv CC\underline{H}_2CH_2$); 2.42-2.47 (1H, m) and 3.09-3.16 (1H, m, 4-CH_2); 3.30-3.31 (2H, m, $NCH_2C\equiv C$); 4.01-4.10 (1H, m, 5-CH); 4.31-4.32 (2H, m, 2-CH_2). ^{13}C NMR spectrum, δ, ppm: 13.5 ($CH_2\underline{C}H_3$); 18.3 (5-CH_3); 19.9 ($C\equiv C\underline{C}H_2CH_2$); 21.8 ($\underline{C}H_2CH_3$); 30.7 ($\underline{C}H_2CH_2CH_3$); 42.8 ($N\underline{C}H_2C\equiv C$); 58.2 (C-4); 71.8 (C-5); 76.7 ($NCH_2\underline{C}\equiv C$); 84.4 ($NCH_2C\equiv\underline{C}$); 85.2 (C-2). Mass spectrum, *m/z* (I_{rel}, %): 180 $[M\text{-}H]^+$ (45), 137 $[M\text{-}H\text{-}C_3H_7]^+$ (53), 95 $[CH_2C\equiv CC_4H_9]^+$ (100). Found, %: C 72.79; H 10.61; N 7.78. $C_{11}H_{19}NO$. Calculated, %: C 72.88; H 10.56; N 7.73.

5-Methyl-3-(3-phenylprop-2-yn-1-yl)-1,3-oxazolidine (5c). Yield 0.06 g (28%), light-yellow oil, R_f 0.45 (2:1 hexane–EtOAc). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.29 (3H, d, *J* = 6.0, CH_3); 2.61 (1H, dd, *J* = 12.0, *J* = 7.2) and 3.27 (1H, dd, *J* = 12.0, *J* = 7.2, 4-CH_2); 3.65 (2H, s, $NCH_2C\equiv C$); 4.21 (1H, m, 5-CH); 4.48 (2H, s, 2-CH_2); 7.30-7.31 (3H, m, H Ph); 7.52-7.55 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 20.1 (CH_3); 43.4 ($N\underline{C}H_2C\equiv C$); 58.4 (C-4); 72.0 (C-5); 84.2 ($NCH_2\underline{C}\equiv C$); 85.3 ($NCH_2C\equiv\underline{C}$); 85.4 (C-2); 122.9 (C Ph); 128.3 (C Ph); 131.7 (C Ph); 132.2 (C Ph). Mass spectrum, *m/z* (I_{rel}, %): 200 $[M\text{-}H]^+$ (8), 157 $[M\text{-}CH_3CHO]^+$ (29), 115 $[PhC\equiv CCH_2]^+$ (100). Found, %: C 77.52; H 7.45; N 7.02. $C_{13}H_{15}NO$. Calculated, %: C 77.58; H 7.51; N 6.96.

(4*R*)-4-Ethyl-3-(hex-2-yn-1-yl)-1,3-oxazolidine (6a). Yield 0.13g (72%), light-yellow oil, R_f 0.56 (2:1 hexane–EtOAc), $[\alpha]_D^{21}$ -7.8° (*c* 0.40, $CHCl_3$). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.96 (3H, t, *J* = 7.5, 4-$CH_2C\underline{H}_3$); 0.99 (3H, t, *J* = 7.5, $CH_2CH_2C\underline{H}_3$); 1.41 (1H, quin, *J* = 7.0) and 1.64 (1H, quin, *J* = 7.0, 4-$C\underline{H}_2CH_3$); 1.54-1.56 (2H, m, $CH_2C\underline{H}_2CH_3$); 2.18 (2H, t, *J* = 7.0, $C\underline{H}_2CH_2CH_3$); 2.99 (1H, quin, *J* = 7.0, 4-CH); 3.40-3.43 (1H, m) and 4.06 (1H, t, *J* = 7.5, 5-CH_2); 3.43 (2H, s, $NCH_2C\equiv C$); 4.44 (2H, s, 2-CH_2). ^{13}C NMR spectrum, δ, ppm: 11.0 (4-$CH_2\underline{C}H_3$); 13.5 ($CH_2CH_2\underline{C}H_3$); 20.7 ($\underline{C}H_2CH_2CH_3$); 22.2 ($CH_2\underline{C}H_2CH_3$); 25.9 (4-$\underline{C}H_2CH_3$); 42.5 ($N\underline{C}H_2C\equiv C$); 63.8 (C-4); 70.3 (C-5); 76.9 ($NCH_2\underline{C}\equiv C$); 85.0 ($NCH_2C\equiv\underline{C}$); 85.3 (C-2). Mass spectrum, *m/z* (I_{rel}, %): 180 $[M\text{-}H]^+$ (38), 152 $[M\text{-}C_2H_5]^+$ (100), 124 $[M\text{-}C_4H_9]^+$ (45). Found, %: C 72.95; H 10.61; N 7.66. $C_{11}H_{19}NO$. Calculated, %: C 72.88; H 10.56; N 7.73.

(4*R*)-4-Ethyl-3-(hept-2-yn-1-yl)-1,3-oxazolidine (6b). Yield 0.17 g (83%), dark-yellow oil, R_f 0.50 (2:1 hexane–EtOAc). $[\alpha]_D^{20}$ -7.3 (*c* 2.39, $CHCl_3$). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.90 (3H, t, *J* = 7.5, $CH_2CH_2C\underline{H}_3$); 0.94 (3H, t, *J* = 7.5, 4-$CH_2C\underline{H}_3$); 1.31-1.37 (1H, m) and 1.57-1.64 (1H, m, 4-$C\underline{H}_2CH_3$); 1.38-1.44 (2H, m, $CH_2C\underline{H}_2CH_3$); 1.45-1.51 (2H, m, $C\underline{H}_2CH_2CH_3$); 2.18 (2H, t, *J* = 7.0, $C\equiv CC\underline{H}_2CH_2$); 2.94 (1H, q, *J* = 7.0, 4-CH); 3.36-3.39 (1H, m) and 4.02 (1H, t, *J* = 7.5, 5-CH_2); 3.37 (2H, s, $NCH_2C\equiv C$); 4.40 (2H, s, 2-CH_2). ^{13}C NMR spectrum, δ, ppm: 10.9 (4-$CH_2\underline{C}H_3$); 13.6 ($CH_2CH_2\underline{C}H_3$); 18.4 ($C\equiv C\underline{C}H_2CH_2$); 21.9 ($CH_2\underline{C}H_2CH_3$); 26.1 (4-$\underline{C}H_2CH_3$); 30.8 ($\underline{C}H_2CH_2CH_3$); 42.5 ($N\underline{C}H_2C\equiv C$); 63.7(C-4); 70.2 (C-5); 75.8 ($NCH_2\underline{C}\equiv C$); 84.4 ($NCH_2C\equiv\underline{C}$); 85.4 (C-2). ^{15}N NMR spectrum, δ, ppm: 65.1. Mass spectrum, *m/z* ($I_{rel,}$ %): 194 $[M\text{-}H]^+$ (6), 166 $[M\text{-}C_2H_5]^+$ (100), 138 $[M\text{-}C_4H_9]^+$ (50). Found, %: C 73.87; H 10.79; N 7.24. $C_{12}H_{21}NO$. Calculated, %: C 73.80; H 10.84; N 7.17.

(4*R*)-4-Ethyl-3-(3-phenylprop-2-yn-1-yl)-1,3-oxazolidine (6c). Yield 0.05 g (24%), light-yellow oil, R_f 0.53 (2:1 hexane–EtOAc), $[\alpha]_D^{18}$ -2.3° (*c* 1.01, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.01 (3H, t, *J* = 7.5, $CH_2C\underline{H}_3$); 1.41-1.49 (1H, m) and 1.64-1.73 (1H, m, $C\underline{H}_2CH_3$); 3.09 (1H, quin, *J* = 7.0, 4-CH); 3.45 (1H, t, *J* = 7.5) and 4.12 (1H, t, *J* = 7.5, 5-CH_2); 3.69 (2H, s, $NCH_2C{\equiv}C$); 4.50 (1H, d, *J* = 5.3) and 4.53 (1H, d, *J* = 5.3, 2-CH_2); 7.32-7.33 (3H, m, H Ph); 7.44-7.46 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 11.0 ($CH_2\underline{C}H_3$); 26.1 ($\underline{C}H_2CH_3$); 43.0 ($N\underline{C}H_2C{\equiv}C$); 64.0 (C-4); 70.4 (C-5); 84.0 ($NCH_2\underline{C}{\equiv}C$); 84.5 ($NCH_2C{\equiv}\underline{C}$); 85.5 (C-2); 122.9 (C Ph); 128.2 (C Ph); 128.3 (C Ph); 131.7 (C Ph). ^{15}N NMR spectrum, δ, ppm: 65.1. Mass spectrum, *m*/*z* (I_{rel}, %): 214 $[M\text{-}H]^+$ (55), 186 $[M\text{-}CHCH_3]^+$ (100), 115 $[PhC{\equiv}CCH_2]^+$ (100). Found, %: C 78.18; H 7.91; N 6.56. $C_{14}H_{17}NO$. Calculated, %: C 78.10; H 7.96; N 6.51.

5-Phenyl-3-(3-phenylprop-2-yn-1-yl)-1,3-oxazolidine (7). Yield 0.09 g (60%), light-yellow oil, R_f 0.50 (2:1:2 hexane–CCl_4–EtOAc). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.41 (1H, s) and 2.96-3.02 (1H, m, 4-CH_2); 3.77 (2H, s, $NCH_2C{\equiv}C$); 4.77 (2H, m, 2-CH_2); 5.13 (1H, t, *J* = 7.2, 5-CH); 7.22-7.52 (10H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 43.5 ($N\underline{C}H_2C{\equiv}C$); 61.4 (C-4); 77.4 (C-5); 83.4 ($NCH_2\underline{C}{\equiv}C$); 85.3 ($NCH_2C{\equiv}\underline{C}$); 86.9 (C-2); 122.9 (C Ph); 125.6 (C Ph); 127.2 (C Ph); 127.3 (C Ph); 128.1 (C Ph); 131.8 (C Ph); 141.8 (C Ph). Mass spectrum (EI, *m*/*z* (I_{rel}, %): 263 $[M]^+$ (65), 115 $[PhC{\equiv}CCH_2]^+$ (100), 104 $[PhCHCH_2]^+$ (100). Mass spectrum (MALDI–TOF/TOF), *m*/*z*: 264.318 $[M+H]^+$. Found, %: C 82.03; H 6.56; N 5.28. $C_{18}H_{17}NO$. Calculated, %: C 82.10; H 6.51; N 5.32.

3-(Deca-2,9-diyn-1-yl)-1,3-oxazolane (8) was prepared by the described method [26, 27] from a mixture of bis(1,3-oxazolidin-3-yl)methane (**2a**) (0.32 g, 2 mmol) and 3,8-dioxa-1,6-diazabicyclo[4.4.1]undecane (**3a**), 1,8-nonadiyne (0.12 g, 1 mmol), and CuCl (5 mg, 0.05 mmol) in PhMe (3 ml). The reaction mixture was stirred in an atmosphere of argon at 80°C for 6h, the catalyst was then separated, the solvent was evaporated, and the product was purified by column chromatography. Yield 0.10 g (33%), light-yellow oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.41-1.54 (6H, m, $CH_2(C\underline{H}_2)_3CH_2C{\equiv}CH$); 1.95 (1H, t, *J* = 2.6, C≡CH); 2.18-2.21 (4H, m, $C\underline{H}_2(CH_2)_3C\underline{H}_2C{\equiv}CH$); 3.07 (2H, t, *J* = 6.8, 4-CH_2); 3.35-3.37 (2H, m, $NCH_2C{\equiv}C$); 3.80 (2H, t, *J* = 6.8, 5-CH_2); 4.37 (2H, s, 2-CH_2). ^{13}C NMR spectrum, δ, ppm: 18.3 ($\underline{C}H_2C{\equiv}CH$); 18.6 ($NCH_2C{\equiv}C\underline{C}H_2$); 27.9 ($(CH_2)_2\underline{C}H_2(CH_2)_2$); 28.0 ($NCH_2C{\equiv}CCH_2\underline{C}H_2$); 28.2 ($\underline{C}H_2CH_2C{\equiv}CH$); 42.8 ($N\underline{C}H_2C{\equiv}C$); 51.2 (C-4); 63.6 (C-5); 68.3 ($C{\equiv}\underline{C}H$); 76.1 ($NCH_2\underline{C}{\equiv}C$); 84.2 ($\underline{C}{\equiv}CH$); 85.1 (C-2); 85.9 ($NCH_2C{\equiv}\underline{C}$). Mass spectrum (EI, 70 eV), *m*/*z* (I_{rel}, %): 204 $[M\text{-}H]^+$ (28), 119 $[C{\equiv}C(CH_2)_5C{\equiv}CH]^+$ (23), 72 $[NC_3H_6O]^+$ (100). Mass spectrum (MALDI–TOF/TOF), *m*/*z*: 206.445 $[M+H]^+$. Found, %: C 75.98; H 9.30; N 6.87. $C_{13}H_{19}NO$. Calculated, %: C 76.06; H 9.33; N 6.82.

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