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Expanding the chemical space of sp^3-enriched 4,5-disubstituted oxazoles *via* synthesis of novel building blocks

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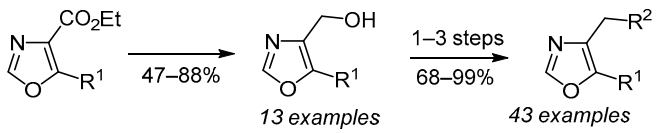


An efficient approach to the preparation of novel sp^3-enriched 4,5-disubstituted oxazoles bearing a functional group at the C-4 position is described. The method commenced with synthesis of ethyl oxazole-4-carboxylates (13 examples, 63–99% yield), with subsequent function insertion to the heterocyclic core by late-stage functional group transformation. The $LiBH_4$-mediated reduction of ethyl oxazole-4-carboxylates was the only method which could be optimized at multigram scale (up to 40 g), and its scope was demonstrated by preparation of 13 alcohols with (cyclo)alkyl, fluoroalkyl, or *N*-Boc-aminoalkyl moiety at the C-5 position (47–89% yield). The utility of these key intermediates was demonstrated by the preparation of chlorides (13 examples, 90–99% yield), azides (13 examples, 83–99% yield), amines (13 examples, 80–98% yield), and sulfonyl chlorides (4 examples, 68–97% yield) – advanced building blocks for synthetic and medicinal chemistry.

Keywords: alcohols, amines, azides, chlorides, esters, oxazoles, sulfonyl chlorides, building blocks.

Oxazoles represent an important class of heterocycles, occurring as the key substructural framework in numerous natural compounds (e.g., marine alkaloids)[1] and synthetic products,[2] featuring a broad range of biological activities, in particular, anticancer, antifungal, or antibacterial.[3–5] Whereas aryl-substituted oxazoles are widespread and well-studied, their sp^3-enriched counterparts have attracted much interest only in recent years (Fig. 1).[3] The known oxazoles with aliphatic moieties mainly included 2,4-di- and trisubstituted derivatives, e.g., protein kinase inhibitor mubritinib (**1**),[6] antimicrobial phenoxan (**2**),[7] peroxisome proliferator-activated receptor agonists muraglitazar (**3**),[8] darglitazone (**4**),[9] farglitazar (**5**),[10,11] or lipid peroxidation inhibitor martefragin A (**6**).[12]

Less common, but chemically and biologically interesting 4,5-disubstituted oxazoles are represented mainly by aryl-substituted derivatives, e.g., streptochlorin (**7**),[13] non-prostanoid partial IP receptor agonist BMY 45778 (**8**),[14] p38 kinase inhibitor CP-808844 (**9**).[15]

Synthetic approaches and chemical properties of substituted oxazoles are well studied and surveyed in a number of reviews or books.[1–4,16–18] Most of the literature methods relies on the late-stage oxazole ring construction, which limits the scope of the substituents that can be introduced into the target molecule. This is especially the case for sp^3-enriched 4,5-disubstituted derivatives. An alternative approach to such compounds could rely on appropriate oxazole-containing building blocks, which could be used for further functionalization. Recently, it has been pointed out that above-mentioned strategy is often overlooked in synthetic and medicinal chemistry.[19] It should be noted that sp^3-enriched low-molecular weight building blocks derived from the 4,5-disubstituted oxazole framework are less known in the literature. Typically, an entry into this chemotype is provided by 5-alkyl-substituted oxazole-4-carboxylates **10**, which in turn are obtained by condensation of carboxylic acids **11**[20–29] or their activated derivatives, e.g., acyl chlorides,[30–33] anhydrides,[34–45] or

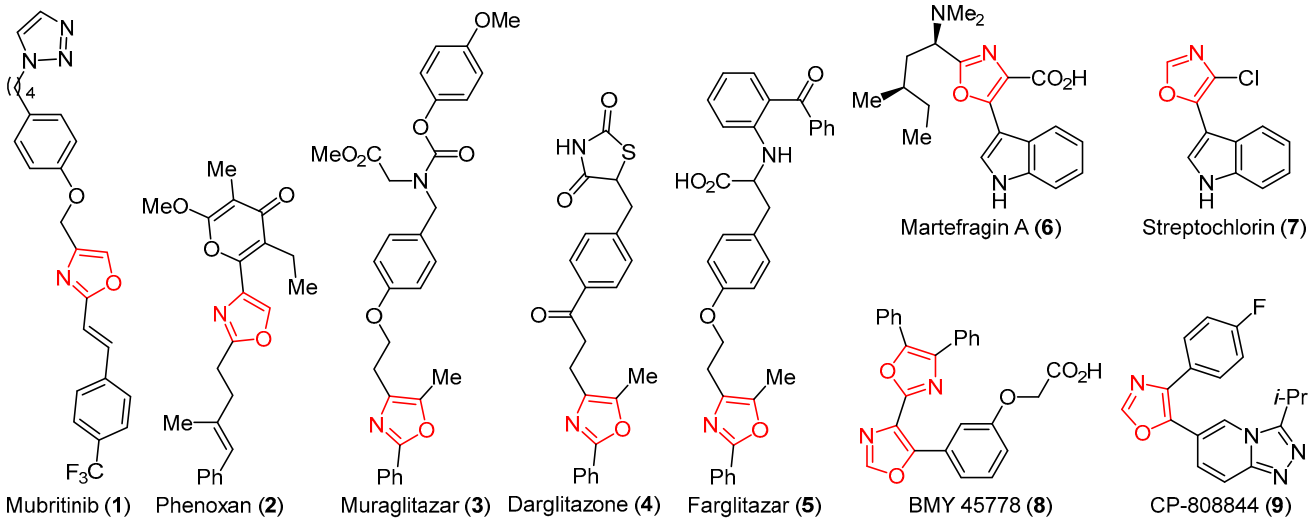


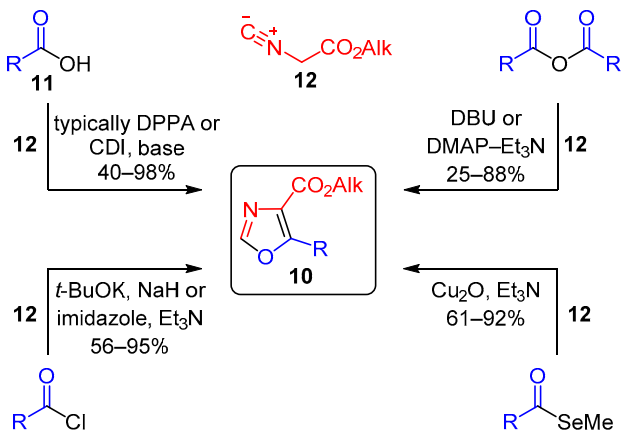
Figure 1. Some important representatives of di- and trisubstituted oxazoles.

methyl selenoates,[46] with alkyl 2-isocyanoacetates **12** (Scheme 1).

In this work, we have aimed at multigram preparation of novel sp^3-enriched 4,5-disubstituted oxazoles bearing a functional group at the C-4 position, i.e., alcohols **13** (13 examples), chlorides **14** (13 examples), azides **15** (13 examples), amines **16** (13 examples), and sulfonyl chlorides **17** (4 examples) (Fig. 2). All building blocks **13**–**17** were obtained *via* modification of the key intermediates **10a**–**m**.

Esters **10a**–**m** were obtained by a CDI-promoted reaction of carboxylic acids **11a**–**m** with ethyl 2-isocyanoacetate **12** in the presence of DBU as a base in THF.[21] Products **10a**–**m** were isolated in 63–99% yield (Table 1). It is interesting to note that the procedure gave the best results in the case of *N*-Boc-protected amino acids **11h**–**l** and methoxymethyl derivative **11m** (86–99% yield), good yields (75–89%) – with simple (cyclo)alkyl carboxylic acids **11a**–**e**, while the corresponding fluoroalkyl-substituted derivatives **10f**,**g** were obtained in moderate yields (63–65%). This might be related to the volatility of the corresponding esters.

Scheme 1. Known approaches to 5-substituted oxazole-4-carboxylates **10** with aliphatic substituents



Reduction of esters **10** with complex metal hydrides was found to be challenging due to the high hydrophilicity of the target alcohols **13**, which made the isolation of the products extremely complicated. It should be noted that this reaction was described in the literature for compound **10a** at less than 1 g scale; product **13a** was used in the next step without purification.[37] In addition to that, several aryl-substituted counterparts were introduced into such transformations.

The reported methods relied on the use of DIBAL,[37] $LiAlH_4$,[47,48] or $NaBH_4$,[49–51] and the corresponding products were obtained in 67–87% yields. We have tested all these methods with compound **10a** at 10 g scale (Table 2, entries 1–5); it was found that although the product was formed, it could not be isolated in pure form with satisfactory yield. The use of $LiBH_4$ in THF at room temperature (entry 6), as well as changing the solvent to MeOH also appeared to be unfruitful; in the latter case, the corresponding methyl ester was formed as a byproduct. Only when ester **10a** was

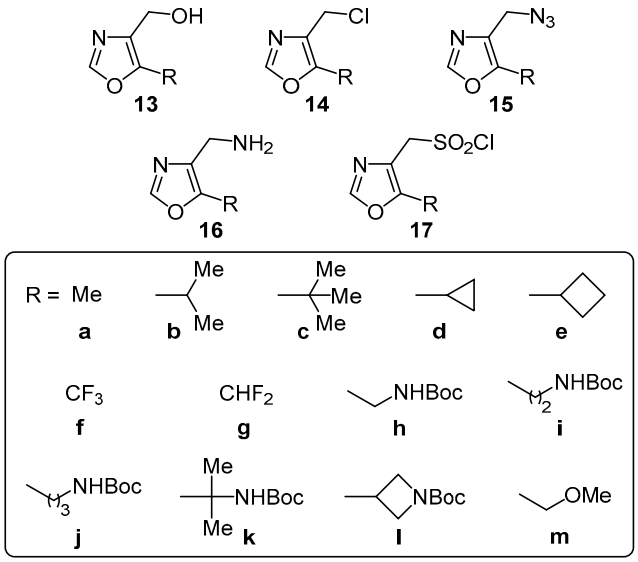
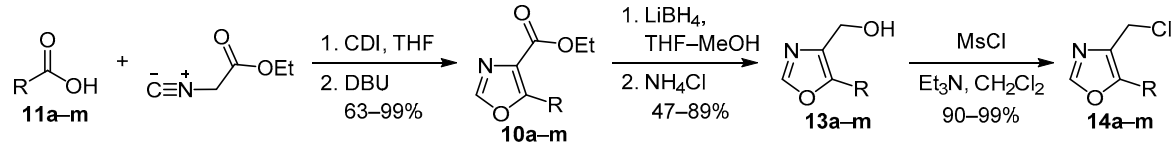
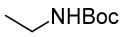
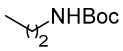
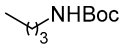
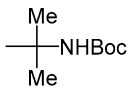
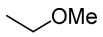


Figure 2. sp^3-Enriched 4,5-disubstituted oxazoles **13**–**17**.

Table 1. Synthesis of esters **10a**–**m**, alcohols **13a**–**m**, and chlorides **14a**–**m**



Entry	Compound **11**	R	Ester **10**	Yield, %	Alcohol **13**	Yield, %	Chloride **14**	Yield, %
1	**11a**	Me	**10a**	75	**13a**	69	**14a**	92
2	**11b**		**10b**	86	**13b**	60	**14b**	95
3	**11c**		**10c**	89	**13c**	71	**14c**	96
4	**11d**		**10d**	86	**13d**	76	**14d**	98
5	**11e**		**10e**	78	**13e**	89	**14e**	93
6	**11f**	CF_3	**10f**	63	**13f**	68	**14f**	90
7	**11g**	CHF_2	**10g**	65	**13g**	47	**14g**	92
8	**11h**		**10h**	97	**13h**	62	**14h**	99
9	**11i**		**10i**	95	**13i**	85	**14i**	96
10	**11j**		**10j**	97	**13j**	78	**14j**	97
11	**11k**		**10k**	86	**13k**	80	**14k**	98
12	**11l**		**10l**	99	**13l**	75	**14l**	96
13	**11m**		**10m**	98	**13m**	72	**14m**	92

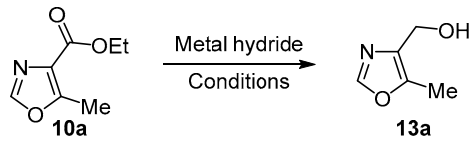
refluxed with $LiBH_4$ in THF–MeOH, 2:1 (entry 8), and the reaction mixture was quenched with saturated aq NH_4Cl and then solid NH_4Cl, the target derivative **13a** could be obtained in good yield (69%).

The developed protocol was applied successfully for the preparation of all the target alcohols **13a**–**m** at up to 40 g scale (47–89% yield, after column chromatography) (Table 1). It should be noted that chromatographic purification of alcohols **13** prior to their use in further transformations is strongly advised in order to ensure high yields and purity of the target products.

In the next step, chlorides **14a**–**m** were obtained by reaction of alcohols **13a**–**m** with mesyl chloride and Et_3N (Table 1). Under these reaction conditions, mesylation of compounds **13** was immediately followed by nucleophilic substitution with chlorine anion leading to the target compounds **14a**–**m** in excellent yields (90–99%). Such reaction outcome is unusual, but not unprecedented for various hetarylmethanols.[52–54]

Preparation of azides **15a**–**m** relied on the nucleophilic substitution of compounds **14a**–**m** with NaN_3 in refluxing

Table 2. Reduction step optimization for the preparation of alcohol **13a**

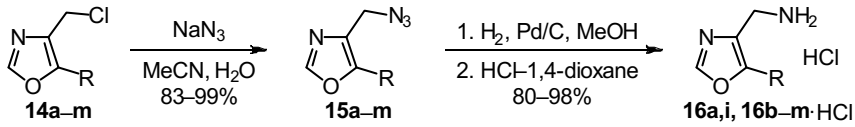


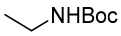
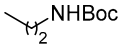
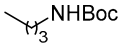
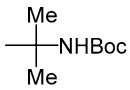
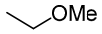
Entry	Metal hydride	Conditions	Isolated yield of the target alcohol **13a**, %
1	DIBAL	Hexanes, –78°C to 0 °C, 2 h	48
2	$LiAlH_4$	THF	34
3	$NaBH_4$	THF, reflux	–*
4	$NaBH_4$	MeOH, reflux	28**
5	$NaBH_4$	THF–MeOH (2:1), reflux	45
6	$LiBH_4$	THF, rt	–*
7	$LiBH_4$	MeOH, rt	6**
8	$LiBH_4$	THF–MeOH (2:1), reflux	69

* No reaction was observed.

** The corresponding methyl ester was obtained as byproduct.

Table 3. Synthesis of azides **15a**–**m** and amines **16a**–**m**·HCl



Entry	Chloride **14**	R	Azide **15**	Yield, %	Amine **16**	Yield, %
1	**14a**	Me	**15a**	86	**16a**	93*
2	**14b**		**15b**	96	**16b**·HCl	90
3	**14c**		**15c**	98	**16c**·HCl	87
4	**14d**		**15d**	89	**16d**·HCl	80
5	**14e**		**15e**	98	**16e**·HCl	96
6	**14f**	CF_3	**15f**	85	**16f**·HCl	83
7	**14g**	CHF_2	**15g**	83	**16g**·HCl	81
8	**14h**		**15h**	99	**16h**·HCl	87
9	**14i**		**15i**	92	**16i**	95*
10	**14j**		**15j**	94	**16j**·HCl	98
11	**14k**		**15k**	95	**16k**·HCl	95
12	**14l**		**15l**	96	**16l**·HCl	95
13	**14m**		**15m**	98	**16m**·HCl	92

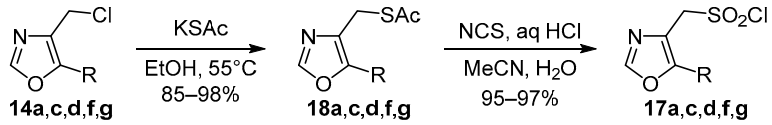
* The compound was isolated as a base.

$MeCN–H_2O$ (ca. 70:1). The reaction proceeded smoothly and gave excellent yields (83–99%) of the target building blocks **15a**–**m** (Table 3). Subsequent catalytic reduction of azides **15a**–**m** under 1 atm of H_2 in the presence of 10% Pd/C in MeOH, followed by acidification with 10% HCl in 1,4-dioxane (for compounds **16a**–**g**,**m**, entries 1–7 and 13) or NH_4Cl in MeOH (for *N*-Boc-monoprotected diamines **16h**–**l**, entries 8–12) led to the corresponding amines **16a**–**m**·HCl (80–98% yield).

Chlorides **14a**,**c**,**d**,**f**,**g** were transformed into sulfonyl chlorides **17a**,**c**,**d**,**f**,**g**. The corresponding thioacetates **18** were obtained from compound **14** in 85–98% yields upon treatment with KSAc in EtOH at 55°C (Table 4). Subsequent oxidative chlorination with *N*-chlorosuccinimide in the presence of aq HCl in $MeCN–H_2O$ (10:1) gave the target sulfonyl chlorides **17a**,**c**,**d**,**f**,**g**. It should be noted that most of the synthesized compounds **17** were found to be unstable upon any isolation or storage conditions. This was not the case with derivatives **17f**,**g** bearing electron-withdrawing tri- or difluoromethyl groups, which were stable and could be isolated in 95–97% yield. Nevertheless, unlike cyclopropyl derivative **17d**, alkyl-substutituted oxazoles **17a**,**c** were also obtained and characterized (68–72% yield); they should be subjected to further transformations immediately after isolation. It was found that sulfonyl chlorides **17a**,**c** decomposed to the corresponding chlorides **14a**,**c**, respectively, at room temperature after 48 h (established by ^{1}H NMR spectroscopy). When a sample of sulfonyl chloride **17c** had been stored at –24°C for 2 months, the ratio **14c**:**17c** was found to be 1:3.

Despite numerous literature examples of using alkyl-substituted oxazoles in organic synthesis and drug discovery, their preparation and the scope of the known methods have been largely underrepresented to date, especially for functionalized sp^3-enriched 4,5-disubstituted derivatives. In this work, general, efficient, and scalable methods for the preparation of novel 4,5-disubstituted oxazoles bearing a functional group at the C-4 position were developed. The synthesized building blocks also

Table 4. Synthesis of thioacetates **18** and sulfonyl chlorides **17**



Entry	Chloride **14**	R	Thioacetate **18**	Yield, %	Sulfonyl chloride **17**	Yield, %
1	**14a**	Me	**18a**	89	**17a**	72
2	**14c**		**18c**	93	**17c**	68
3	**14d**		**18d**	85	**17d**	0
4	**14f**	CF_3	**18f**	96	**17f**	97
5	**14g**	CHF_2	**18g**	98	**17g**	95

contained alkyl, cycloalkyl, di/trifluoromethyl, *N*-Boc-aminoalkyl, or methoxymethyl substituent at the C-5 atom of the heteroaromatic ring. The proposed approach commenced from ethyl oxazole-4-carboxylates **10a**–**m**, which were obtained from aliphatic carboxylic acids **11a**–**m** and ethyl isocyanoacetate **12**. Reduction of esters **10a**–**m** was challenging in these series due to the high hydrophilicity of the corresponding alcohols **13a**–**m**. It was found that using $LiBH_4$ in THF–MeOH (2:1) followed by quenching of the reaction mixture with saturated aq NH_4Cl and then solid NH_4Cl was very efficient, and products **13** were obtained in 47–88% yield (13 examples; 12 novel).

The utility of alcohols **13** was demonstrated by the preparation of four other compound classes. In particular, mesylation of alcohols **13** was accompanied by nucleophilic substitution with chlorine anion leading to chlorides **14a**–**m** (90–99% yield). Reaction of compounds **14** with NaN_3 gave azides **15a**–**m** (83–99% yield), which were transformed to amines **16a**–**m** by catalytic reduction (80–98% yield). Alternatively, sulfonyl chlorides **17** were obtained *via* oxidative chlorination with NCS of the corresponding thioacetates **18** (4 examples, 68–97% yield). These functionalized low-molecular weight hydrophilic oxazole derivatives were prepared on up to 40 g scale; therefore, they can be considered as promising building blocks for organic synthesis and drug discovery, which are readily available to scientific community and can significantly expand the currently accessible lead-like chemical space (Fig. 3).

An efficient approach to the preparation of novel sp^3-enriched 4,5-disubstituted oxazoles bearing different functional groups at the C-4 position is described, i.e., alcohols, chlorides, azides, amines, and sulfonyl chlorides. All compounds were obtained *via* modification of the key intermediate ethyl oxazole-4-carboxylate.

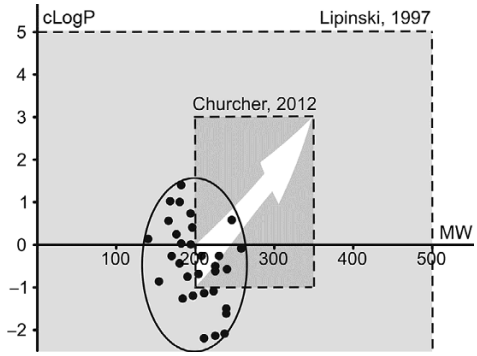


Figure 3. The simplest derivatives of building blocks **14**, **16**, and **17** shown in MW (molecular weight) – cLogP (calculated octanol – water partition coefficient logarithm) (black dots within an ellipse). Structures of the derivatives were obtained by *in silico* coupling with dimethylamine (for compounds **14** and **17**) or acetyl chloride (for compounds **16**); the Boc protective groups were also transformed into acetyl. Dotted lines show limits imposed by Lipinski rule-of-five (light gray)[55] and criteria for lead-likeness by Churcher et al. (dark gray).[56] The white arrow shows that there is enough space left for the design of lead-like compounds based on the building blocks synthesized.

Experimental

^1H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker 170 Avance 500 spectrometer (500, 126, and 470 MHz, respectively) and a Varian Unity Plus 400 spectrometer (400, 101, and 376 MHz, respectively). TMS or residual solvent peaks used as internal standards (7.26 and 77.2 ppm for ^1H and ^{13}C nuclei, respectively, in $CDCl_3$, 2.50 and 39.5 ppm for ^1H and ^{13}C nuclei, respectively, in DMSO-d_6). Mass spectra were recorded on an Agilent 1100 LCMSD SL instrument (chemical ionization (CI), CF_3CO_2H) and an Agilent 5890 Series II 5972 GCMS instrument (electron impact ionization (EI)). Elemental analyses were performed at the Laboratory of Organic Analysis, Department of Chemistry, Taras Shevchenko National University of Kyiv. Melting points were measured on a MPA100 OptiMelt automated melting point system. Analytical TLC was performed using Polychrom SI F254 plates. Column chromatography was performed using silica gel (230–400 mesh) as the stationary phase. Instant JChem version 17.2.27.0 was used for the calculation of physicochemical parameters, Chemaxon, Hungary, www.chemaxon.com.

Solvents were purified according to the standard procedures.[57] Compounds **11a**–**m** and **12** were available from Enamine Ltd.

Synthesis of esters 10a–m (General method). The corresponding carboxylic acid **11a**–**m** (0.307 mol) was dissolved in THF (350 ml), and CDI (59.7 g, 0.368 mol) was added in portions to the solution. The resulting mixture was heated at 55°C for 1 h and then cooled to 0°C. Ethyl 2-isocyanoacetate **12** (41.6 g, 0.368 mol) was added in one portion, then DBU (56.0 g, 0.368 mol) was added dropwise at 0°C, and the resulting mixture was stirred at room temperature for 12 h. Then THF was evaporated under reduced pressure, the residue was dissolved in EtOAc (500 ml) and washed with 10% aq solution of citric acid (300 ml), H_2O (500 ml), and brine (300 ml). The organic phase was dried over Na_2SO_4 and evaporated under reduced pressure.

Ethyl 5-methyloxazole-4-carboxylate (10a). Yield 35.7 g (75%), yellowish liquid. For physical and spectral data, see ref.[25,32,33,36]

Ethyl 5-isopropyloxazole-4-carboxylate (10b).[32] Yield 48.4 g (86%), brown oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.70 (1H, s, H oxazole); 4.31 (2H, q, *J* = 7.2, OC$\underline{H}_2$CH$_3$); 3.74 (1H, sept, *J* = 7.0, C$\underline{H}$(CH$_3$)$_2$); 1.33 (3H, t, *J* = 7.2, OCH$_2$C$\underline{H}_3$); 1.23 (6H, d, *J* = 7.0, CH(C$\underline{H}_3$)$_2$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 164.2; 162.0; 148.6; 125.3; 60.8; 25.9; 20.4; 14.2. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 184 $[M+H]^+$ (100). Found, %: C 59.01; H 7.16; N 7.73. $C_9H_{13}NO_3$. Calculated, %: C 59.00; H 7.15; N 7.65.

Ethyl 5-(*tert*-butyl)oxazole-4-carboxylate (10c).[58] Yield 53.9 g (89%), brown oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.66 (1H, s, H oxazole); 4.32 (2H, q, *J* = 7.1, OC$\underline{H}_2$CH$_3$); 1.40 (9H, s, C(C$\underline{H}_3$)$_3$); 1.35 (3H, t, *J* = 7.1, OCH$_2$C$\underline{H}_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 165.9; 162.0; 147.2; 125.9; 61.0; 33.2; 28.1; 14.2. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 198 $[M+H]^+$ (100). Found, %: C 61.15; H 7.27; N 7.03. $C_{10}H_{15}NO_3$. Calculated, %: C 60.90; H 7.67; N 7.10.

Ethyl 5-cyclopropyloxazole-4-carboxylate (10d).[31] Yield 47.8 g (86%), brown oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.54 (1H, s, H oxazole); 4.30 (2H, q, *J* = 7.1, OC$\underline{H}_2$CH$_3$); 2.68 (1H, tt, *J* = 8.4, *J* = 5.1, CH cyclopropane); 1.31 (3H, t, *J* = 7.1, OCH$_2$C$\underline{H}_3$); 1.07–1.03 (2H, m, CH$_2$ cyclopropane); 1.00–0.97 (2H, m, CH$_2$ cyclopropane). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 162.3; 160.9; 147.3; 126.6; 60.8; 14.3; 8.9; 7.7. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 182 $[M+H]^+$ (42), 136 $[M–OEt]^+$ (100). Found, %: C 60.04; H 5.82; N 7.43. $C_9H_{11}NO_3$. Calculated, %: C 59.66; H 6.12; N 7.73.

Ethyl 5-cyclobutyloxazole-4-carboxylate (10e) was purified by column chromatography on silica gel, eluent hexanes–EtOAc, 2:1, R_f 0.37. Yield 46.7 g (78%), colorless liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.73 (1H s, H oxazole); 4.29 (2H, q, *J* = 7.1, OC$\underline{H}_2$CH$_3$); 4.20 (1H, quintet, *J* = 8.8, CH cyclobutane); 2.35–2.23 (4H, m, 2CH$_2$ cyclobutane); 2.05–1.94 (1H, m, CH$_2$ cyclobutane); 1.91–1.83 (1H, m, CH$_2$ cyclobutane); 1.32 (3H, t, *J* = 7.1, OCH$_2$C$\underline{H}_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 162.0; 161.4; 148.7; 125.6; 60.8; 30.9; 27.4; 18.3; 14.2. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 196 $[M+H]^+$ (50), 150 $[M–OEt]^+$ (100). Found, %: C 61.77; H 6.52; N 7.11. $C_{10}H_{13}NO_3$. Calculated, %: C 61.53; H 6.71; N 7.18.

Ethyl 5-(trifluoromethyl)oxazole-4-carboxylate (10f) was purified by column chromatography on silica gel, eluent hexanes–EtOAc, 4:1, R_f 0.44. Yield 40.4 g (63%), colorless liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 8.02 (1H, s, H oxazole); 4.35 (2H, q, *J* = 7.2, OC$\underline{H}_2$CH$_3$); 1.31 (3H, t, *J* = 7.1, OCH$_2$C$\underline{H}_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 158.8; 150.9; 142.6 (q, *J* = 44.6); 132.1 (q, *J* = 2.3); 118.0 (q, *J* = 270.0); 62.2; 13.7. ^{19}F NMR spectrum (470 MHz, $CDCl_3$), δ, ppm: –61.6. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 210 $[M+H]^+$ (42), 182 $[M–CH_2=CH(CH_3)+H]^+$ (77), 164 $[M–OEt]^+$ (100). Found, %: C 40.10; H 2.99; N 7.01. $C_7H_6F_3NO_3$. Calculated, %: C 40.20; H 2.89; N 6.70.

Ethyl 5-(difluoromethyl)oxazole-4-carboxylate (10g) was purified by column chromatography on silica gel, eluent hexanes–EtOAc, 4:1, R_f 0.42. Yield 38.1 g (65%), colorless liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.99 (1H, s, H oxazole); 7.23 (1H, t, *J* = 52.1, CHF_2); 4.40 (2H, q, *J* = 7.2, OC$\underline{H}_2$CH$_3$); 1.37 (3H, t, *J* = 7.2, OCH$_2$C$\underline{H}_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 160.0; 151.4; 147.6 (t, *J* = 24.6); 132.1 (t, *J* = 5.8); 106.0 (t, *J* = 238.0); 62.2; 14.0. ^{19}F NMR spectrum (470 MHz, $CDCl_3$), δ, ppm (*J*, Hz): –118.1 (d, *J* = 52.1). Mass spectrum (CI), *m*/*z* (I_{rel}, %): 210 $[M+H]^+$ (30), 164 $[M–CH_2=CH(CH_3)+H]^+$ (29), 146 $[M–OEt]^+$ (100). Found, %: C 44.01; H 3.51; N 6.95. $C_7H_7F_2NO_3$. Calculated, %: C 43.99; H 3.69; N 7.33.

Ethyl 5-{[(*tert*-butoxycarbonyl)amino]methyl}oxazole-4-carboxylate (10h).[32] Yield 80.5 g (97%), beige crystals, mp 63–65°C. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.77 (1H, s, H oxazole); 5.34 (1H, br. s, NH); 4.63 (2H, d, *J* = 6.2, C$\underline{H}_2$NHBoc); 4.34 (2H, q, *J* = 7.1, OC$\underline{H}_2$CH$_3$); 1.39 (9H, s, C(C$\underline{H}_3$)$_3$); 1.36 (3H, t, *J* = 7.1, OCH$_2$C$\underline{H}_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 161.7; 156.1; 155.5; 149.4; 128.2; 80.1; 61.4; 35.5; 28.3; 14.2. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 215 $[M–(H_3C)_2C=CH_2+H]^+$ (68), 171 $[M–CO_2–(H_3C)_2C=CH_2+H]^+$ (100). Found, %: C 53.46; H 6.52; N 10.37. $C_{12}H_{18}N_2O_5$. Calculated, %: C 53.33; H 6.71; N 10.36.

Ethyl 5-{2-[(*tert*-butoxycarbonyl)amino]ethyl}oxazole-4-carboxylate (10i).[59] Yield 82.9 g (95%), brown oil. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 7.78 (1H s, H oxazole); 4.80 (1H, s, NH); 4.36 (2H, q, *J* = 7.1, OC$\underline{H}_2$CH$_3$); 3.45 (2H, q, *J* = 6.0, CH$_2$C$\underline{H}_2$NHBoc); 3.24 (2H, t, *J* = 6.5, C$\underline{H}_2$CH$_2$NHBoc); 1.38 (9H, s, C(C$\underline{H}_3$)$_3$); 1.38 (3H, t, *J* = 7.1, CH$_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 162.0; 157.3; 155.7; 149.4; 128.3; 79.4; 61.2; 38.7; 28.3; 26.7; 14.3. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 307 $[M+Na]^+$ (7), 229 $[M–(H_3C)_2C=CH_2+H]^+$ (72), 185 $[M–CO_2–(H_3C)_2C=CH_2+H]^+$ (100). Found, %: C 55.12; H 7.14; N 9.69. $C_{13}H_{20}N_2O_5$. Calculated, %: C 54.92; H 7.09; N 9.85.

Ethyl 5-{3-[(*tert*-butoxycarbonyl)amino]propyl}oxazole-4-carboxylate (10j) was purified by column chromatography on silica gel, eluent hexanes–EtOAc, 2:1, R_f 0.34.

Yield 88.8 g (97%), yellowish liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.74 (1H, s, H oxazole); 4.88 (1H, br. s, NH); 4.35 (2H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 3.11 (2H, q, *J* = 6.0, $CH_2CH_2C\underline{H}_2NHBoc$); 3.06 (2H, t, *J* = 7.3, $C\underline{H}_2CH_2CH_2NHBoc$); 1.85 (2H, quint, *J* = 7.1, $CH_2C\underline{H}_2CH_2NHBoc$); 1.40 (9H, s, $C(C\underline{H}_3)_3$); 1.37 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 162.1; 159.1; 155.9; 149.1; 127.4; 61.1; 39.4; 28.4; 28.0; 27.9; 23.0; 14.3. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 321 $[M+Na]^+$ (7), 243 $[M–(H_3C)_2C=CH_2+H]^+$ (87), 199 $[M–CO_2–(H_3C)_2C=CH_2+H]^+$ (100). Found, %: C 56.16; H 7.09; N 9.17. $C_{14}H_{22}N_2O_5$. Calculated, %: C 56.36; H 7.43; N 9.39.

Ethyl 5-{2-[(*tert*-butoxycarbonyl)amino]propan-2-yl}-oxazole-4-carboxylate (10k).[32] Yield 78.8 g (86%), beige crystals, mp 60–62°C. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.70 (1H, s, H oxazole); 5.60 (1H, br. s, NH); 4.33 (2H, q, *J* = 7.2, $OC\underline{H}_2CH_3$); 1.68 (6H, s, $C(C\underline{H}_3)_2$); 1.35 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 1.27 (9H, s, $C(C\underline{H}_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 163.3; 161.8; 154.9; 147.5; 125.7; 79.5; 61.3; 51.4; 28.2; 26.7; 14.2. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 183 $[M–NHCO_2t\text{-}Bu+H]^+$ (100). Found, %: C 56.21; H 7.08; N 9.32. $C_{14}H_{22}N_2O_5$. Calculated, %: C 56.36; H 7.43; N 9.39.

Ethyl 5-[1-(*tert*-butoxycarbonyl)azetidin-3-yl]oxazole-4-carboxylate (10l). Yield 90.1 g (99%), brown crystals, mp 78–80°C. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.84 (1H, s, H oxazole); 4.49 (1H, tt, *J* = 8.7, *J* = 6.3, CH azetidine); 4.35 (2H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 4.30–4.25 (2H, m, CH_2 azetidine); 4.10 (2H, dd, *J* = 8.7, *J* = 6.3, CH_2 azetidine); 1.43 (9H, s, $C(C\underline{H}_3)_3$); 1.36 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 161.6; 157.6; 156.1; 149.4; 127.9; 79.9; 61.3; 53.3; 28.3; 25.1; 14.2. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 241 $[M–(H_3C)_2C=CH_2+H]^+$ (100), 197 $[M–CO_2–(H_3C)_2C=CH_2+H]^+$ (27). Found, %: C 57.03; H 7.02; N 9.20. $C_{14}H_{20}N_2O_5$. Calculated, %: C 56.75; H 6.80; N 9.45.

Ethyl 5-(methoxymethyl)oxazole-4-carboxylate (10m).[60] Yield 55.7 g (98%), brown oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.82 (1H, s, H oxazole); 4.69 (2H, s, $C\underline{H}_2OCH_3$); 4.27 (2H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 3.29 (3H, s, OCH_3); 1.28 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 161.3; 154.3; 150.4; 129.6; 63.3; 61.3; 58.5; 14.1. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 186 $[M+H]^+$ (25), 154 $[M–OMe]^+$ (100). Found, %: C 51.56; H 6.24; N 7.47. $C_8H_{11}NO_4$. Calculated, %: C 51.89; H 5.99; N 7.56.

Synthesis of alcohols 13a–m (General method). The corresponding ester **10a–m** (0.194 mol) was dissolved in THF–MeOH (2:1, 450 ml), and $LiBH_4$ (10.6 g, 0.485 mol) was added in small portions at room temperature. The resulting mixture was heated at 55°C overnight and then cooled to room temperature. Saturated aq NH_4Cl (30 ml) and solid NH_4Cl (30.0 g) were added to the reaction mixture. Then most of the solvent was evaporated under reduced pressure, the residue was diluted with EtOAc (500 ml), and the formed precipitate was filtered off and washed with hot EtOAc (2×100 ml). The filtrate was dried over Na_2SO_4 and evaporated under reduced pressure.

(5-Methyloxazol-4-yl)methanol (13a)[37] was purified by column chromatography on silica gel, eluent $CHCl_3$–MeOH, 25:1, R_f 0.36. Yield 15.1 g (69%), yellowish powder, mp 47–49°C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 7.71 (1H, s, H oxazole); 4.48 (2H, s, $C\underline{H}_2OH$); 4.20 (1H, br. s, OH); 2.29 (3H, s, CH_3). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 149.4; 145.4; 133.7; 55.5; 10.0. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 114 $[M+H]^+$ (58), 96 $[M–OH]^+$ (100). Found, %: C 53.11; H 6.32; N 12.28. $C_5H_7NO_2$. Calculated, %: C 53.09; H 6.24; N 12.38.

(5-Isopropyloxazol-4-yl)methanol (13b) was purified by column chromatography on silica gel, eluent $CHCl_3$–MeOH, 14:1, R_f 0.40. Yield 16.3 g (60%), colorless liquid. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.71 (1H, s, H oxazole); 4.51 (2H, s, $C\underline{H}_2OH$); 4.11 (1H, br. s, OH); 3.10 (1H, sept, *J* = 6.9, $C\underline{H}(CH_3)_2$); 1.23 (6H, d, *J* = 6.9, $CH(C\underline{H}_3)_2$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 153.6; 149.2; 132.0; 55.5; 25.2; 21.3. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 142 $[M+H]^+$ (100), 124 $[M–OH]^+$ (86). Found, %: C 59.67; H 8.02; N 10.24. $C_7H_{11}NO_2$. Calculated, %: C 59.56; H 7.85; N 9.92.

[5-(*tert*-Butyl)oxazol-4-yl]methanol (13c) was triturated with cold pentane. Yield 21.4 g (71%), yellowish crystals, mp 54–56°C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 7.68 (1H, s, H oxazole); 4.63–4.59 (2H, m, $C\underline{H}_2OH$); 3.81 (1H, br. s, OH); 1.32 (9H, s, $C(C\underline{H}_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 155.4; 148.4; 131.9; 56.7; 32.6; 29.3. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 156 $[M+H]^+$ (32), 138 $[M–OH]^+$ (100). Found, %: C 61.73; H 8.72; N 8.66. $C_8H_{13}NO_2$. Calculated, %: C 61.91; H 8.44; N 9.03.

(5-Cyclopropyloxazol-4-yl)methanol (13d) was purified by column chromatography on silica gel, eluent $CHCl_3$–MeOH, 10:1, R_f 0.32. Yield 21.5 g (76%), colorless liquid. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.62 (1H, s, H oxazole); 4.55 (2H, s, $C\underline{H}_2OH$); 4.06 (1H, br. s, OH); 1.90 (1H, tt, *J* = 8.5, *J* = 5.2, CH cyclopropane); 0.95–0.89 (2H, m, CH_2 cyclopropane); 0.87–0.82 (2H, m, CH_2 cyclopropane). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 149.8; 148.5; 133.5; 55.5; 6.5; 5.8. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 140 $[M+H]^+$ (34), 122 $[M–OH]^+$ (100). Found, %: C 60.69; H 6.75; N 9.95. $C_7H_9NO_2$. Calculated, %: C 60.42; H 6.52; N 10.07.

(5-Cyclobutyloxazol-4-yl)methanol (13e). Yield 26.4 g (89%), colorless oil. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.74 (1H, s, H oxazole); 4.47 (2H, s, $C\underline{H}_2OH$); 3.99 (1H, br. s, OH); 3.60 (1H, quint, *J* = 8.8, CH cyclobutane); 2.36–2.23 (4H, m, $2CH_2$ cyclobutane); 2.03–1.94 (1H, m, CH_2 cyclobutane); 1.92–1.85 (1H, m, CH_2 cyclobutane). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ ppm: 151.2; 149.4; 132.4; 55.5; 30.3; 28.1; 18.6. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 154 $[M+H]^+$ (23), 136 $[M–OH]^+$ (100). Found, %: C 62.62; H 6.91; N 9.38. $C_8H_{11}NO_2$. Calculated, %: C 62.73; H 7.24; N 9.14.

[5-(Trifluoromethyl)oxazol-4-yl]methanol (13f) was purified by column chromatography on silica gel, eluent $CHCl_3$–MeOH, 25:1, R_f 0.22. Yield 22.0 g (68%), yellowish liquid. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm

(*J*, Hz): 8.66 (1H, s, H oxazole); 5.49 (1H, t, *J* = 5.8); 4.46 (2H, d, *J* = 5.8, C$\underline{H}_2$OH). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 153.3; 142.0 (q, *J* = 2.2); 133.6 (q, *J* = 42.4); 119.4 (q, *J* = 267.0); 54.1. ^{19}F NMR spectrum (376 MHz, DMSO-d_6), δ, ppm: –62.4. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 150 $[M–F+H]^+$ (100). Found, %: C 35.85; H 2.30; N 8.05. $C_5H_4F_3NO_2$. Calculated, %: C 35.94; H 2.41; N 8.38.

[5-(Difluoromethyl)oxazol-4-yl]methanol (13g) was purified by column chromatography on silica gel, eluent $CHCl_3$–MeOH, 14:1, R_f 0.36. Yield 13.6 g (47%), yellowish liquid. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.91 (1H, s, H oxazole); 6.92 (1H, t, *J* = 53.1, CHF_2); 4.76 (2H, s, C$\underline{H}_2$OH); 2.53 (1H, s, OH). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 151.6; 140.0 (t, *J* = 4.4); 139.6 (t, *J* = 28.0); 107.5 (t, *J* = 236.0); 56.6. ^{19}F NMR spectrum (376 MHz, $CDCl_3$), δ, ppm: –116.1. Mass spectrum (EI), *m*/*z* (I_{rel}, %): 149 $[M]^+$ (21), 119 $[M–H_2CO]^+$ (100). Found, %: C 40.67; H 3.52; N 8.99. $C_5H_5F_2NO_2$. Calculated, %: C 40.28; H 3.38; N 9.39.

***tert*-Butyl {[4-(hydroxymethyl)oxazol-5-yl]methyl}-carbamate (13h)** was triturated with cold pentane. Yield 27.5 g (62%), white solid, mp 83–85°C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.73 (1H, s, H oxazole); 5.32 (1H, s, NH); 4.61 (2H, s, C$\underline{H}_2$OH); 4.32 (2H, d, *J* = 6.2, C$\underline{H}_2$NHBoc); 4.06 (1H, br. s, OH); 1.37 (9H, s, C(C$\underline{H}_3$)$_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 156.3; 150.0; 145.1; 136.6; 80.6; 57.0; 34.4; 28.3. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 173 $[M–(H_3C)_2C=CH_2+H]^+$ (80), 129 $[M–CO_2–(H_3C)_2C=CH_2+H]^+$ (100). Found, %: C 52.37; H 7.15; N 12.62. $C_{10}H_{16}N_2O_4$. Calculated, %: C 52.62; H 7.07; N 12.27.

***tert*-Butyl {2-[4-(hydroxymethyl)oxazol-5-yl]ethyl}-carbamate (13i)**. Yield 40.0 g (85%), brownish oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.76 (1H, s, H oxazole); 5.03 (1H, s, NH); 4.51 (2H, s, C$\underline{H}_2$OH); 3.68 (1H, br. s, OH); 3.35 (2H, t, *J* = 6.6, $CH_2C\underline{H}_2$NHBoc); 2.90 (2H, t, *J* = 6.6, C$\underline{H}_2CH_2$NHBoc); 1.39 (9H, s, C(C$\underline{H}_3$)$_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 155.9; 149.8; 146.7; 135.2; 79.6; 55.8; 39.0; 28.3; 25.4. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 170 $[M–O$*t*$-Bu+H]^+$ (47), 143 $[M–CO_2–(H_3C)_2C=CH_2+H]^+$ (27), 127 $[M–NHCO_2$*t*$-Bu+H]^+$ (100). Found, %: C 54.89; H 7.35; N 11.34. $C_{11}H_{18}N_2O_4$. Calculated, %: C 54.53; H 7.49; N 11.56.

***tert*-Butyl {3-[4-(hydroxymethyl)oxazol-5-yl]propyl}-carbamate (13j)** was purified by column chromatography on silica gel, eluent $CHCl_3$–MeOH, 14:1, R_f 0.42. Yield 38.8 g (78%), colorless oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.75 (1H, s, H oxazole); 4.92 (1H, s, NH); 4.51 (2H, s, C$\underline{H}_2$OH); 3.95 (1H, br. s, OH); 3.09 (2H, q, *J* = 6.7, $CH_2CH_2C\underline{H}_2$NHBoc); 2.74 (2H, t, *J* = 7.0, C$\underline{H}_2CH_2CH_2$NHBoc); 1.82 (2H, quint, *J* = 6.7, $CH_2C\underline{H}_2CH_2$NHBoc); 1.42 (9H, s, C(C$\underline{H}_3$)$_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 156.2; 149.6; 148.2; 134.4; 79.4; 55.8; 39.2; 28.4; 28.3; 21.6. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 279 $[M+Na]^+$ (3), 201 $[M–(H_3C)_2C=CH_2+H]^+$ (3), 140 $[M–NHCO_2$*t*$-Bu+H]^+$ (100). Found, %: C 56.60; H 7.66; N 11.09. $C_{12}H_{20}N_2O_4$. Calculated, %: C 56.24; H 7.87; N 10.93.

***tert*-Butyl {2-[4-(hydroxymethyl)oxazol-5-yl]propan-2-yl}carbamate (13k)** was triturated with cold hexanes. Yield 39.8 g (80%), yellowish solid, mp 107–109°C. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.69 (1H, s, H oxazole); 5.28 (1H, br. s, NH); 4.60 (2H, s, C$\underline{H}_2$OH); 3.85 (1H, br. s, OH); 1.64 (6H, s, C(C$\underline{H}_3$)$_2$); 1.32 (9H, s, C(C$\underline{H}_3$)$_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 154.4; 150.8; 148.3; 133.6; 79.9; 56.6; 51.1; 28.2; 27.4. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 279 $[M+Na]^+$ (3), 257 $[M+H]^+$ (40), 201 $[M–(H_3C)_2C=CH_2+H]^+$ (30), 183 $[M–O$*t*$-Bu]^+$ (100), 142 $[M–NHCO_2$*t*$-Bu+H]^+$ (7). Found, %: C 55.93; H 7.55; N 11.30. $C_{12}H_{20}N_2O_4$. Calculated, %: C 56.24; H 7.87; N 10.93.

***tert*-Butyl 3-[4-(hydroxymethyl)oxazol-5-yl]azetidine-1-carboxylate (13l)** was crystallized from hexanes–*t*-BuOMe, 50:1. Yield 37.0 g (75%), white solid, mp 136–138°C. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.85 (1H, s, H oxazole); 4.87 (1H, br. s, NH); 4.52 (2H, s, C$\underline{H}_2$OH); 4.22–4.17 (2H, m, CH_2 azetidine); 4.08–4.04 (2H, m, CH_2 azetidine); 3.99–3.92 (1H, m, CH azetidine); 1.43 (9H, s, C(C$\underline{H}_3$)$_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 156.2; 150.2; 147.2; 134.9; 121.3; 79.9; 55.6; 54.1; 28.3; 24.1. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 199 $[M–(H_3C)_2C=CH_2+H]^+$ (10), 155 $[M–CO_2–(H_3C)_2C=CH_2+H]^+$ (3), 126 $[M–H_2CNHBoc+H]^+$ (21), 108 $[M–H_2CNHBoc–OH]^+$ (100). Found, %: C 57.05; H 6.79; N 10.89. $C_{12}H_{18}N_2O_4$. Calculated, %: C 56.68; H 7.14; N 11.02.

[5-(Methoxymethyl)oxazol-4-yl]methanol (13m) was purified by column chromatography on silica gel, eluent $CHCl_3$–MeOH, 14:1, R_f 0.30. Yield 20.0 g (72%), yellowish oil. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 7.82 (1H, s, H oxazole); 4.58 (2H, s) and 4.48 (2H, s, C$\underline{H}_2$OCH$_3$, CH$_2$OH); 3.73 (1H, s, OH); 3.34 (3H, s, OCH$_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 150.8; 144.8; 137.6; 63.2; 58.2; 56.0. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 144 $[M+H]^+$ (100). Found, %: C 50.51; H 6.43; N 10.12. $C_6H_9NO_3$. Calculated, %: C 50.35; H 6.34; N 9.79.

Synthesis of chlorides 14a–m (General method). The corresponding alcohol **13a**–**m** (0.132 mol) was dissolved in CH_2Cl_2 (250 ml), and Et_3N (27.6 ml, 20.0 g, 0.198 mol) was added. The solution was cooled to 0°C, and MsCl (18.1 g, 0.158 mol) was added dropwise. The resulting mixture was stirred at room temperature overnight, then washed with saturated aq solution of $NaHCO_3$ (200 ml), H_2O (200 ml), and brine (100 ml). The organic phase was dried over Na_2SO_4 and evaporated under reduced pressure.

4-(Chloromethyl)-5-methyloxazole (14a). Yield 16.0 g (92%), yellowish liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.67 (1H, s, H oxazole); 4.42 (2H, s, CH_2Cl); 2.27 (3H, s, CH_3). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 149.3; 146.7; 131.1; 36.9; 10.0. Mass spectrum (EI), *m*/*z* (I_{rel}, %): 133 $[M]^+$ (9), 131 $[M]^+$ (27), 96 $[M–Cl]^+$ (100). Found, %: C 45.93; H 4.30; N 11.01; Cl 27.31. C_5H_6ClNO. Calculated, %: C 45.65; H 4.60; N 10.65; Cl 26.95.

4-(Chloromethyl)-5-isopropyloxazole (14b). Yield 20.0 g (95%), yellowish liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.74 (1H, s,

H oxazole); 4.54 (2H, s, CH_2Cl); 3.15 (1H, sept, J = 6.9, C<u>H</u>$(CH_3)_2$); 1.31 (6H, d, J = 6.9, CH(C<u>H</u>$_3)_2$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 154.9; 149.1; 129.4; 37.1; 25.5; 21.0. Mass spectrum (EI), *m/z* (I_{rel}, %): 161 $[M]^+$ (12), 159 $[M]^+$ (36), 146 $[M–CH_3]^+$ (20), 144 $[M–CH_3]^+$ (60), 124 $[M–Cl]^+$ (100). Found, %: C 52.46; H 5.95; N 8.66; Cl 21.94. $C_7H_{10}ClNO$. Calculated, %: C 52.68; H 6.32; N 8.78; Cl 22.21.

5-(*tert*-Butyl)-4-(chloromethyl)oxazole (14c). Yield 22.0 g (96%), yellowish liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.66 (1H, s, H oxazole); 4.58 (2H, s, CH_2Cl); 1.34 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 156.7; 148.4; 129.3; 38.5; 32.8; 29.0. Mass spectrum (CI), *m/z* (I_{rel}, %): 176 $[M+H]^+$ (33), 174 $[M+H]^+$ (100). Found, %: C 55.35; H 6.96; N 7.92; Cl 20.81. $C_8H_{12}ClNO$. Calculated, %: C 55.34; H 6.97; N 8.07; Cl 20.42.

4-(Chloromethyl)-5-cyclopropyloxazole (14d). Yield 20.4 g (98%), yellowish liquid. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.66 (1H, s, H oxazole); 4.55 (2H, s, CH_2Cl); 1.90 (1H, tdd, J = 8.4, J = 6.8, J = 4.2, CH cyclopropane); 1.04–0.95 (2H, m, CH_2 cyclopropane); 0.94–0.86 (2H, m, CH_2 cyclopropane). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 151.2; 148.5; 130.8; 37.0; 6.7; 5.8. Mass spectrum (EI), *m/z* (I_{rel}, %): 159 $[M]^+$ (12), 157 $[M]^+$ (36), 122 $[M–Cl]^+$ (100). Found, %: C 53.02; H 5.13; N 8.50; Cl 22.23. C_7H_8ClNO. Calculated, %: C 53.35; H 5.12; N 8.89; Cl 22.49.

4-(Chloromethyl)-5-cyclobutyloxazole (14e). Yield 21.1 g (93%), brownish oil. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 8.06 (1H, s, H oxazole); 4.49 (2H, s, CH_2Cl); 3.62 (1H, quint, J = 8.7, CH cyclobutane); 2.39–2.28 (4H, m, $2CH_2$ cyclobutane); 2.09–2.00 (1H, m, CH_2 cyclobutane); 1.97–1.89 (1H, m, CH_2 cyclobutane). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 153.1; 149.7; 128.8; 36.1; 30.2; 27.8; 18.7. Mass spectrum (EI), *m/z* (I_{rel}, %): 173 $[M]^+$ (3), 171 $[M]^+$ (9), 143 $[M–H_2C=CH_2]^+$ (73), 136 $[M–Cl]^+$ (100). Found, %: C 55.78; H 5.97; N 7.96; Cl 20.86. $C_8H_{10}ClNO$. Calculated, %: C 55.99; H 5.87; N 8.16; Cl 20.66.

4-(Chloromethyl)-5-(trifluoromethyl)oxazole (14f). The CH_2Cl_2 solution of compound was evaporated under reduced pressure. Yield 22.0 g (90%), yellowish liquid. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 7.95 (1H, s, H oxazole); 4.57 (2H, s, CH_2Cl). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 151.7; 137. 9; 136.3 (q, J = 43.5); 118.8 (q, J = 268.0); 34.7. ^{19}F NMR spectrum (376 MHz, $CDCl_3$), δ, ppm: –117.1. Mass spectrum (EI), *m/z* (I_{rel}, %): 187 $[M]^+$ (5), 185 $[M]^+$ (15), 150 $[M–Cl]^+$ (100). Found, %: C 32.60; H 1.34; N 7.46; Cl 19.17. $C_5H_3ClF_3NO$. Calculated, %: C 32.37; H 1.63; N 7.55; Cl 19.11.

4-(Chloromethyl)-5-(difluoromethyl)oxazole (14g). The solution of compound in CH_2Cl_2 was evaporated under reduced pressure. Yield 20.3 g (92%), colorless liquid. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.90 (1H, s, H oxazole); 6.81 (1H, t, J = 53.4, CHF_2); 4.58 (2H, s, CH_2Cl). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 151.4; 140.4 (t, J = 30.6); 136.8; 107.6 (t, J = 237.0); 35.2. ^{19}F NMR spectrum (376 MHz, $CDCl_3$), δ, ppm: –117.1. Mass spectrum (EI), *m/z* (I_{rel}, %): 169 $[M]^+$ (7), 167 $[M]^+$ (21), 150 $[M–Cl]^+$ (100). Found, %: C 35.98; H 2.27; N 8.28; Cl 21.47. $C_5H_4ClF_2NO$. Calculated, %: C 35.85; H 2.41; N 8.36; Cl 21.16.

***tert*-Butyl {[4-(chloromethyl)oxazol-5-yl]methyl}-carbamate (14h)**. Yield 32.2 g (99%), white solid, mp 92–94°C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.75 (1H, s, H oxazole); 5.01 (1H, s, NH); 4.57 (2H, s, CH_2Cl); 4.36 (2H, d, J = 6.1, C<u>H</u>$_2$NHBoc); 1.41 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 155.5; 150.1; 146.6; 133.2; 80.3; 36.4; 34.3; 28.3. Mass spectrum (EI), *m/z* (I_{rel}, %): 248 $[M]^+$ (<1), 246 $[M]^+$ (3), 193 $[M–H_2C=C(CH_3)+H]^+$ (20), 191 $[M–H_2C=C(CH_3)+H]^+$ (60), 175 $[M–O$*t*$-Bu]^+$ (33), 173 $[M–O$*t*$-Bu]^+$ (100). Found, %: C 48.64; H 6.21; N 11.02; Cl 14.39. $C_{10}H_{15}ClN_2O_3$. Calculated, %: C 48.69; H 6.13; N 11.36; Cl 14.37.

***tert*-Butyl {2-[4-(chloromethyl)oxazol-5-yl]ethyl}-carbamate (14i)**. Yield 33.0 g (96%), brown oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.75 (1H, s, H oxazole); 4.95 (1H, s, NH); 4.44 (2H, s, CH_2Cl); 3.38–3.30 (2H, m, CH_2C<u>H</u>$_2$NHBoc); 2.88 (2H, t, J = 6.5, C<u>H</u>$_2CH_2$NHBoc); 1.37 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 155.7; 150.0; 147.8; 132.7; 79.5; 38.8; 36.6; 28.3; 25.5. Mass spectrum (CI), *m/z* (I_{rel}, %): 263 $[M+H]^+$ (33), 261 $[M+H]^+$ (100). Found, %: C 50.34; H 6.88; N 10.94; Cl 13.29. $C_{11}H_{17}ClN_2O_3$. Calculated, %: C 50.68; H 6.57; N 10.74; Cl 13.60.

***tert*-Butyl {3-[4-(chloromethyl)oxazol-5-yl]propyl}-carbamate (14j)**. Yield 35.2 g (97%), brown oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.71 (1H, s, H oxazole); 4.87 (1H, s, NH); 4.45 (2H, s, CH_2Cl); 3.13–3.04 (2H, m, CH_2CH_2C<u>H</u>$_2$NHBoc); 2.69 (2H, t, J = 7.3, C<u>H</u>$_2CH_2CH_2$NHBoc); 1.80 (2H, quint, J = 7.3, CH_2C<u>H</u>$_2CH_2$NHBoc); 1.37 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 156.0; 149.6; 131.4; 79.2; 39.6; 36.8; 28.3; 28.2; 21.9. Mass spectrum (CI), *m/z* (I_{rel}, %): 275 $[M+H]^+$ (<1), 219 $[M–(H_3C)_2C=CH_2+H]^+$ (100), 219 $[M–(H_3C)_2C=CH_2+H]^+$ (33). Found, %: C 52.61; H 7.02; N 10.15; Cl 12.71. $C_{12}H_{19}ClN_2O_3$. Calculated, %: C 52.46; H 6.97; N 10.20; Cl 12.90.

***tert*-Butyl {2-[4-(chloromethyl)oxazol-5-yl]propan-2-yl}carbamate (14k)**. Yield 35.5 g (98%), yellowish solid, mp 119–121°C. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.71 (1H, s, H oxazole); 5.10 (1H, br. s, NH); 4.61 (2H, s, CH_2Cl); 1.65 (6H, s, $C(CH_3)_2$); 1.35 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 154.0; 152.5; 148.3; 130.2; 79.9; 51.3; 37.7; 28.2; 27.5. Mass spectrum (CI), *m/z* (I_{rel}, %): 277 $[M+H]^+$ (33), 275 $[M+H]^+$ (100). Found, %: C 52.41; H 6.58; N 10.37; Cl 13.24. $C_{12}H_{19}ClN_2O_3$. Calculated, %: C 52.46; H 6.97; N 10.20; Cl 12.90.

***tert*-Butyl 3-[4-(chloromethyl)oxazol-5-yl]azetidine-1-carboxylate (14l)**. Yield 34.6 g (96%), white solid, mp 67–69°C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 7.81 (1H, s, H oxazole); 4.45 (2H, s, CH_2Cl); 4.26–4.21 (2H, m, CH_2 azetidine); 4.10–4.06 (2H, m, CH_2 azetidine); 3.93–3.87 (1H, m, CH azetidine); 1.43 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 156.1; 150.0; 148.4; 132.4; 80.0; 53.9; 36.4; 28.3; 24.2. Mass spectrum

(CI), *m*/*z* (I_{rel}, %): 275 $[M+H]^+$ (11), 273 $[M+H]^+$ (33), 219 $[M–H_2C=C(CH_3)+H]^+$ (33), 217 $[M–H_2C=C(CH_3)+H]^+$ (100). Found, %: C 53.16; H 6.32; N 10.58; Cl 13.00. $C_{12}H_{17}ClN_2O_3$. Calculated, %: C 52.85; H 6.28; N 10.27; Cl 13.00.

4-(Chloromethyl)-5-(methoxymethyl)oxazole (14m). Yield 19.6 g (92%), brown oil. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 7.83 (1H, s, H oxazole); 4.55 (2H, s, $C\underline{H}_2OCH_3$); 4.50 (2H, s, CH_2Cl); 3.38 (3H, s, OCH_3). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 150.8; 145.9; 134.6; 63.1; 58.4; 36.2. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 164 $[M+H]^+$ (33), 162 $[M+H]^+$ (100). Found, %: C 44.26; H 4.76; N 8.92; Cl 21.69. $C_6H_8ClNO_2$. Calculated, %: C 44.60; H 4.99; N 8.67; Cl 21.94.

Synthesis of azides 15a–m (General method). The corresponding chloride **14a**–**m** (0.119 mol) and NaN_3 (38.6 g, 0.594 mol) were dissolved in MeCN (250 ml) with H_2O (3.50 ml). The resulting mixture was refluxed overnight, then cooled to room temperature, and the precipitate was filtered off and washed with EtOAc (100 ml). The filtrate was evaporated under reduced pressure, the residue was dissolved in EtOAc (200 ml), washed with H_2O (100 ml) and brine (100 ml). The organic phase was dried over Na_2SO_4 and evaporated under reduced pressure.

4-(Azidomethyl)-5-methyloxazole (15a). Yield 14.1 g (86%), brown liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.75 (1H, s, H oxazole); 4.21 (2H, s, CH_2N_3); 2.34 (3H, s, CH_3). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 149.6; 146.7; 129.5; 45.6; 10.0. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 96 $[M–HN_3]^+$ (100). Found, %: C 43.75; H 4.17; N 40.81. $C_5H_6N_4O$. Calculated, %: C 43.48; H 4.38; N 40.56.

4-(Azidomethyl)-5-isopropyloxazole (15b). Yield 19.0 g (96%), yellowish liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.75 (1H, s, H oxazole); 4.23 (2H, s, CH_2N_3); 3.09 (1H, hept, J = 7.0, $C\underline{H}(CH_3)_2$); 1.28 (6H, d, J = 7.0, $CH(C\underline{H}_3)_2$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 155.1; 149.4; 127.4; 45.6; 25.3; 21.4. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 124 $[M–HN_3]^+$ (100). Found, %: C 50.54; H 6.23; N 33.84. $C_7H_{10}N_4O$. Calculated, %: C 50.59; H 6.07; N 33.71.

4-(Azidomethyl)-5-(*tert*-butyl)oxazole (15c). Yield 21.0 g (98%), yellowish liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.69 (1H, s, H oxazole); 4.30 (2H, s, CH_2N_3); 1.33 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 157.0; 148.6; 127.2; 46.7; 32.6; 29.3. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 138 $[M–HN_3]^+$ (100). Found, %: C 53.08; H 6.92; N 31.40. $C_8H_{12}N_4O$. Calculated, %: C 53.32; H 6.71; N 31.09.

4-(Azidomethyl)-5-cyclopropyloxazole (15d). Yield 17.4 g (89%), yellowish liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.66 (1H, s, H oxazole); 4.29 (2H, s, CH_2N_3); 1.90 (1H, tdd, J = 13.4, J = 8.4, J = 5.0, CH cyclopropane); 1.03–0.97 (2H, m, CH_2 cyclopropane); 0.93–0.87 (2H, m, CH_2 cyclopropane). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 151.2; 148.6; 129.2; 45.6; 6.8; 5.7. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 122 $[M–HN_3]^+$ (100). Found, %: C 50.97; H 5.26; N 33.79. $C_7H_8N_4O$. Calculated, %: C 51.21; H 4.91; N 34.13.

4-(Azidomethyl)-5-cyclobutyloxazole (15e). Yield 20.8 g (98%), brown liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.76 (1H, s, H oxazole); 4.16 (2H, s, CH_2N_3); 3.57 (1H, quint, J = 8.8, CH cyclobutane); 2.37 –2.29 (2H, m, CH_2 cyclobutane); 2.28–2.23 (2H, m, CH_2 cyclobutane); 2.06–1.95 (1H, m, CH_2 cyclobutane); 1.94–1.87 (1H, m, CH_2 cyclobutane). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 152.6; 149.6; 127.8; 45.6; 30.2; 28.2; 18.5. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 151 $[M–N_2+H]^+$ (5), 136 $[M–HN_3]^+$ (3). Found, %: C 54.10; H 5.89; N 31.38. $C_8H_{10}N_4O$. Calculated, %: C 53.92; H 5.66; N 31.44.

4-(Azidomethyl)-5-(trifluoromethyl)oxazole (15f). Yield 19.4 g (85%), colorless liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 8.00 (1H, s, H oxazole); 4.38 (2H, s, CH_2N_3). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 151.8; 136.6 (q, J = 43.5); 136.5 (q, J = 1.6); 118.9 (q, J = 268.0); 44.6. ^{19}F NMR spectrum (470 MHz, $CDCl_3$), δ, ppm: –61.9. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 150 $[M–HN_3]^+$ (100). Found, %: C 31.61; H 1.96; N 28.99. $C_5H_3F_3N_4O$. Calculated, %: C 31.26; H 1.57; N 29.17.

4-(Azidomethyl)-5-(difluoromethyl)oxazole (15g). Yield 17.2 g (83%), colorless liquid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.93 (1H, s, H oxazole); 6.84 (1H, t, J = 53.3, CHF_2); 4.40 (2H, s, CH_2N_3). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 151.7; 140.6 (t, J = 30.1); 135.4; 107.6 (t, J = 237.0); 45.3. ^{19}F NMR spectrum (470 MHz, $CDCl_3$), δ, ppm: –115.7; –115.8. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 147 $[M–N_2+H]^+$ (100). Found, %: C 34.31; H 1.96; N 31.99. $C_5H_4F_2N_4O$. Calculated, %: C 34.49; H 2.32; N 32.18.

***tert*-Butyl {[4-(azidomethyl)oxazol-5-yl]methyl}-carbamate (15h)**. Yield 29.8 g (99%), yellow solid. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.79 (1H, s, H oxazole); 5.10 (1H, s, NH); 4.35 (2H, s, $C\underline{H}_2NH$); 4.33 (2H, s, CH_2N_3); 1.41 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 155.4; 150.4; 146.9; 131.4; 80.2; 45.3; 34.2; 28.3. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 226 $[M–N_2+H]^+$ (25), 170 $[M–N_2–H_2C=C(CH_3)+H]^+$ (30), 123 $[M–N_2–NHBoc]^+$ (100). Found, %: C 47.76; H 6.20; N 27.69. $C_{10}H_{15}N_5O_3$. Calculated, %: C 47.43; H 5.97; N 27.65.

***tert*-Butyl {2-[4-(azidomethyl)oxazol-5-yl]ethyl}-carbamate (15i)**. Yield 29.3 g (92%), yellow oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.79 (1H, s, H oxazole); 4.85 (1H, s, NH); 4.21 (2H, s, CH_2N_3); 3.36 (2H, q, J = 6.6, $CH_2C\underline{H}_2NHBoc$); 2.89 (2H, t, J = 6.6, $C\underline{H}_2CH_2NHBoc$); 1.40 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 155.7; 150.1; 147.8; 130.9; 79.6; 45.4; 39.0; 28.3; 25.3. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 226 $[M–N_2+H]^+$ (25), 166 $[M–N_2–Ot\text{-}Bu+H]^+$ (25), 109 $[M–N_2+H]^+$ (100). Found, %: C 49.81; H 6.81; N 25.85. $C_{11}H_{17}N_5O_3$. Calculated, %: C 49.43; H 6.41; N 26.20.

***tert*-Butyl {3-[4-(azidomethyl)oxazol-5-yl]propyl}-carbamate (15j)**. Yield 31.5 g (94%), yellowish oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.74 (1H, s, H oxazole); 4.82 (1H, s, NH); 4.19 (2H, s, CH_2N_3); 3.10 (2H, d, J = 7.0, $CH_2CH_2C\underline{H}_2NHBoc$); 2.74–2.63 (2H, m, $C\underline{H}_2CH_2CH_2.NHBoc$); 1.79 (2H, quint, J = 7.0,

$CH_2C\underline{H}_2CH_2NHBoc$); 1.39 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 156.0; 149.8; 149.7; 129.6; 79.2; 45.5; 39.6; 28.6; 28.3; 21.8. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 254 $[M–N_2+H]^+$ (17), 139 $[M–N_2–NBoc+H]^+$ (100). Found, %: C 51.32; H 7.06; N 24.95. $C_{12}H_{19}N_5O_3$. Calculated, %: C 51.23; H 6.81; N 24.90.

***tert*-Butyl {2-[4-(azidomethyl)oxazol-5-yl]propan-2-yl}-carbamate (15k)**. Yield 31.8 g (95%), yellow solid. ^1H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.72 (1H, s, H oxazole); 5.08 (1H, br. s, NH); 4.33 (2H, s, CH_2N_3); 1.63 (6H, s, $C(CH_3)_2$); 1.35 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 154.0; 152.7; 148.4; 128.6; 79.9; 51.2; 46.2; 28.2; 27.9. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 254 $[M–N_2+H]^+$ (31), 138 $[M–N_2–NHBoc]^+$ (50), 123 $[M–N_2–CH_3–NHBoc]^+$ (100). Found, %: C 50.97; H 7.06; N 24.61. $C_{12}H_{19}N_5O_3$. Calculated, %: C 51.23; H 6.81; N 24.90.

***tert*-Butyl 3-[4-(azidomethyl)oxazol-5-yl]azetidine-1-carboxylate (15l)**. Yield 31.9 g (96%), white solid. ^1H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.85 (1H, s, H oxazole); 4.28–4.15 (4H, m, CH_2N_3, CH_2 azetidine); 4.11–4.03 (2H, m, CH_2 azetidine); 3.92–3.85 (1H, m, CH azetidine); 1.43 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 156.1; 150.3; 148.4; 130.6; 79.9; 54.0; 45.5; 28.3; 24.2. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 252 $[M–N_2+H]^+$ (5), 108 $[M–N_2–CH_2CH_2NHBoc+H]^+$ (100). Found, %: C 51.49; H 6.16; N 25.00. $C_{12}H_{17}N_5O_3$. Calculated, %: C 51.60; H 6.14; N 25.08.

4-(Azidomethyl)-5-(methoxymethyl)oxazole (15m). Yield 19.6 g (98%), yellow liquid. ^1H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.82 (1H, s, H oxazole); 4.44 (2H, s, CH_2OCH_3); 4.26 (2H, s, CH_2N_3); 3.32 (3H, s, OCH_3). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 150.9; 146.1; 133.0; 63.1; 58.3; 45.3. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 141 $[M–N_2+H]^+$ (8), 109 $[M–N_2–OMe]^+$ (58), 96 $[M–N_2–CH_2OMe+H]^+$ (100). Found, %: C 43.11; H 4.73; N 33.03. $C_6H_8N_4O_2$. Calculated, %: C 42.86; H 4.80; N 33.32.

Synthesis of amines 16a–m (General method). The corresponding azide **15a**–**m** (0.101 mol) and 10% Pd/C (2.00 g) were placed in MeOH (200 ml) under H_2 (1 atm). After the reaction was complete (monitored by ^1H NMR spectroscopy, ca. 12 h), the precipitate was filtered off and carefully washed with MeOH (50 ml). The filtrate was evaporated under reduced pressure, and the residue was dissolved in 1,4-dioxane (200 ml). The resulting solution was cooled to 15°C, and NH_4Cl (5.13 g, 960 mmol) in MeOH (100 ml) (for *N*-Boc amines **16h**–**l**) or 10% HCl in 1,4-dioxane (20 ml) (for the rest of the compounds) was added, the precipitate formed was filtered off and dried under reduced pressure.

(5-Methyloxazol-4-yl)methanamine (16a). Yield 10.5 g (93%), yellowish liquid. ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 7.64 (1H, s, H oxazole); 3.61 (2H, s, $C\underline{H}_2NH_2$); 2.23 (3H, s, CH_3); 1.62 (2H, br. s, NH_2). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 149.2; 143.4; 135.2; 37.2; 9.9. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 113 $[M+H]^+$ (100). Found, %: C 53.83; H 7.14; N 24.84. $C_5H_8N_2O$. Calculated, %: C 53.56; H 7.19; N 24.98.

(5-Isopropyloxazol-4-yl)methanamine hydrochloride (16b·HCl). Yield 16.1 g (90%), beige solid, mp 184–186°C. ^1H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 8.54 (3H, s, $NH_2·HCl$); 8.34 (1H, s, H oxazole); 3.87 (2H, d, *J* = 5.9, $C\underline{H}_2NH_2$); 3.25 (1H, sept, *J* = 6.8, $C\underline{H}(CH_3)_2$); 1.20 (6H, d, *J* = 6.8, $CH(C\underline{H}_3)_2$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 154.9; 151.0; 126.1; 33.9; 24.6; 21.6. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 141 $[M+H–HCl]^+$ (100). Calculated, %: $C_7H_{13}ClN_2O$: C 47.60; H 7.42; N 15.86; Cl 20.07. Found, %: C 47.32; H 7.28; N 15.98; Cl 20.37.

[5-(*tert*-Butyl)oxazol-4-yl]methanamine hydrochloride (16c·HCl). Yield 16.8 g (87%), white crystals, mp 216–218°C. ^1H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 8.62 (3H, s, $NH_2·HCl$); 8.34 (1H s, H oxazole); 3.95 (2H, s, $C\underline{H}_2NH_2$); 1.31 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 155.8; 150.5; 125.8; 35.2; 32.7; 29.3. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 155 $[M+H–HCl]^+$ (16), 136 $[M+H–NH_4Cl]^+$ (100). Found, %: C 50.39; H 8.13; N 15.03; Cl 18.21. $C_8H_{15}ClN_2O$. Calculated, %: C 50.39; H 7.93; N 14.69; Cl 18.59.

(5-Cyclopropyloxazol-4-yl)methanamine hydrochloride (16d·HCl). The hydrogenation was performed in an autoclave under 40 atm of H_2. Yield 14.1 g (80%), white crystals, mp 197–199°C. ^1H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 8.54 (3H, br. s, $NH_2·HCl$); 8.25 (1H, s, H oxazole); 3.92 (2H, s, $C\underline{H}_2NH_2$); 2.19 (1H, tt, *J* = 8.6, *J* = 5.1, CH isopropane); 1.01–0.94 (2H, m, CH_2 cyclopropane); 0.86–0.78 (2H, m, CH_2 cyclopropane). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 151.0; 150.3; 127.7; 34.0; 7.1; 5.9. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 139 $[M+H–HCl]^+$ (3), 122 $[M+H–NH_4Cl]^+$ (100). Found, %: C 48.01; H 6.18; N 15.76; Cl 20.45. $C_7H_{11}ClN_2O$. Calculated, %: C 48.15; H 6.35; N 16.04; Cl 20.30.

(5-Cyclobutyloxazol-4-yl)methanamine hydrochloride (16e·HCl). Yield 18.3 g (96%), beige solid, mp 175–177°C. ^1H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 8.49 (3H, s, $NH_2·HCl$); 8.37 (1H, s, H oxazole); 3.86–3.75 (3H, m, $C\underline{H}_2NH_2$, CH cyclobutane); 2.27–2.16 (4H, m, $2CH_2$ cyclobutane); 1.99–1.93 (1H, m, CH_2 cyclobutane); 1.87–1.81 (1H, m, CH_2 cyclobutane). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 152.4; 151.3; 126.7; 33.9; 29.6; 28.0; 18.5. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 153 $[M+H–HCl]^+$ (9), 136 $[M+H–NH_4Cl]^+$ (100). Found, %: C 50.85; H 7.25; N 15.19; Cl 18.62. $C_8H_{13}ClN_2O$. Calculated, %: C 50.93; H 6.95; N 14.85; Cl 18.79.

[5-(Trifluoromethyl)oxazol-4-yl]methanamine hydrochloride (16f·HCl). Yield 17.0 g (83%), white solid, mp 171–173°C. ^1H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 8.92 (1H, s, H oxazole); 8.83 (3H, s, $NH_2·HCl$); 4.08 (2H, s, $C\underline{H}_2NH_2$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 154.8; 135.8 (q, *J* = 1.7); 134.9 (q, *J* = 42.6); 119.4 (q, *J* = 268.0); 33.7. ^{19}F NMR spectrum (376 MHz, DMSO-d_6), δ, ppm: –61.6. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 167 $[M+H–HCl]^+$ (100). Found, %: C 30.05; H 2.80; N 14.03; Cl 17.58. $C_5H_6ClF_3N_2O$. Calculated, %: C 29.65; H 2.99; N 13.83; Cl 17.50.

[5-(Difluoromethyl)oxazol-4-yl]methanamine hydrochloride (16g·HCl). Yield 15.1 g (81%), beige solid, mp 157–159°C. ^1H NMR spectrum (400 MHz, DMSO-d_6),

δ, ppm (*J*, Hz): 8.73 (1H, s, H oxazole); 8.24 (3H, br. s, NH_2·HCl); 7.48 (1H, t, *J* = 51.3, CHF_2); 4.11 (2H, s, $C\underline{H}_2NH_2$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 154.1; 140.5 (t, *J* = 25.6); 134.6 (t, *J* = 5.5); 107.6 (t, *J* = 233.0); 33.4. ^{19}F NMR spectrum (376 MHz, DMSO-d_6), δ, ppm: –116.6. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 149 $[M+H–HCl]^+$ (100). Found, %: C 32.75; H 3.86; N 15.38; Cl 19.52. $C_5H_7ClF_2N_2O$. Calculated, %: C 32.54; H 3.82; N 15.18; Cl 19.21.

***tert*-Butyl {[4-(aminomethyl)oxazol-5-yl]methyl}-carbamate hydrochloride (16h·HCl)**. Yield 20.0 g (87%), white solid, mp 204–206°C. ^1H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 8.38 (4H, br. s, NH_2·HCl, H oxazole); 7.43 (1H, s, NHBoc); 4.24 (2H, s, $C\underline{H}_2$NHBoc); 3.93 (2H, s, $C\underline{H}_2NH_2$); 1.36 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 155.9; 151.8; 148.0; 129.9; 78.8; 34.0; 33.9; 28.6. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 228 $[M+H–HCl]^+$ (42), 172 $[M–H_2C=C(CH_3)_2–HCl+H]^+$ (100). Found, %: C 45.81; H 7.05; N 16.21; Cl 13.45. $C_{10}H_{18}ClN_3O_3$. Calculated, %: C 45.54; H 6.88; N 15.93; Cl 13.44.

***tert*-Butyl {2-[4-(aminomethyl)oxazol-5-yl]ethyl}-carbamate (16i)**. Yield 26.7 g (95%), brown oil. ^1H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.71 (1H, s, H oxazole); 5.10 (1H, br. s, NHBoc); 4.61 (2H, s, $C\underline{H}_2NH_2$); 1.78–1.52 (6H, m, $2CH_2$, NH_2); 1.35 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 154.0; 152.5; 148.3; 130.2; 79.9; 51.3; 37.7; 28.2; 27.5. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 242 $[M+H–HCl]^+$ (50), 186 $[M–H_2C=C(CH_3)_2–HCl+H]^+$ (100). Found, %: C 54.88; H 8.15; N 17.73. $C_{11}H_{19}N_3O_3$. Calculated, %: C 54.76; H 7.94; N 17.42.

***tert*-Butyl {3-[4-(aminomethyl)oxazol-5-yl]propyl}-carbamate hydrochloride (16j·HCl)**. Yield 28.9 g (98%), white solid, mp 157–459°C. ^1H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 8.56 (3H, s, NH_2·HCl); 8.33 (1H, s, H oxazole); 6.90 (1H, s, NHBoc); 3.86 (2H, s, $C\underline{H}_2NH_2$); 2.92 (2H, q, *J* = 6.5, $CH_2CH_2C\underline{H}_2$NHBoc); 2.70 (2H, t, *J* = 7.4, $C\underline{H}_2CH_2CH_2$NHBoc); 1.68 (2H, quint, *J* = 7.4, $CH_2C\underline{H}_2CH_2$NHBoc); 1.35 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 156.1; 151.3; 150.4; 128.0; 78.0; 39.7; 33.9; 28.7; 28.1; 21.7. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 256 $[M+H–HCl]^+$ (66), 200 $[M–H_2C=C(CH_3)_2–HCl+H]^+$ (100). Found, %: C 49.45; H 7.41; N 14.28; Cl 12.11. $C_{12}H_{22}ClN_3O_3$. Calculated, %: C 49.40; H 7.60; N 14.40; Cl 12.15.

***tert*-Butyl {2-[4-(aminomethyl)oxazol-5-yl]propan-2-yl}carbamate hydrochloride (16k·HCl)**. Yield 28.0 g (95%), white solid, mp 189–191°C. ^1H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 8.41 (3H, br. s, NH_2·HCl); 8.34 (1H, s, H oxazole); 7.41 (1H, s, NHBoc); 3.89 (2H, s, $C\underline{H}_2NH_2$); 1.53 (6H, s, $C(CH_3)_2$); 1.32 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 154.6; 150.1; 126.4; 78.6; 50.9; 39.5; 34.8; 28.6; 27.6. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 256 $[M+H–HCl]^+$ (60), 200 $[M–H_2C=C(CH_3)_2–HCl+H]^+$ (100). Found, %: C 49.01; H 8.00; N 14.35; Cl 11.97. $C_{12}H_{22}ClN_3O_3$. Calculated, %: C 49.40; H 7.60; N 14.40; Cl 12.15.

***tert*-Butyl 3-[4-(aminomethyl)oxazol-5-yl]azetidine-1-carboxylate hydrochloride (16l·HCl)**. Yield 27.8 g (95%), gray solid, mp 175–177°C. ^1H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 8.49 (3H, s, NH_2·HCl); 8.47 (1H, s, H oxazole); 4.27–4.07 (3H, m, $C\underline{H}_2NH_2$, CH azetidine); 3.87 (4H, s, $2CH_2$ azetidine); 1.39 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 155.9; 152.0; 149.4; 129.0; 79.4; 54.3; 33.8; 28.5; 23.9. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 254 $[M+H–HCl]^+$ (20), 198 $[M–H_2C=C(CH_3)_2–HCl+H]^+$ (100). Found, %: C 49.38; H 6.94; N 14.73; Cl 12.31. $C_{12}H_{20}ClN_3O_3$. Calculated, %: C 49.74; H 6.96; N 14.50; Cl 12.23.

[5-(Methoxymethyl)oxazol-4-yl]methanamine hydrochloride (16m·HCl). Yield 16.6 g (92%), beige solid, mp 125–127°C. ^1H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 8.65 (3H, s, NH_2·HCl); 8.48 (1H, s, H oxazole); 4.53 (2H, s, CH_2OCH_3); 3.95 (2H, q, *J* = 5.6, $C\underline{H}_2NH_2$); 3.25 (3H, s, OCH_3). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 152.7; 146.7; 131.5; 62.4; 57.9; 33.7. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 143 $[M+H–HCl]^+$ (100). Found, %: C 40.43; H 5.85; N 15.66; Cl 19.48. $C_6H_{11}ClN_2O_2$. Calculated, %: C 40.35; H 6.21; N 15.68; Cl 19.85.

Synthesis of thioacetates 18a,c,d,f,g (General method). The corresponding chloride **14** (0.119 mol) and KSAc (20.4 g, 0.179 mol) were added to EtOH (250 ml), and the resulting mixture was heated at 55°C overnight. Then the reaction mixture was cooled to room temperature, the solvent was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 (200 ml), washed with H_2O (100 ml) and brine (100 ml). The organic phase was dried over Na_2SO_4 and evaporated under reduced pressure.

***S*-[(5-Methyloxazol-4-yl)methyl]ethanethioate (18a)**. Yield 18.1 g (89%), brown oil. ^1H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.65 (1H, s, H oxazole); 3.93 (2H, s, CH_2SAc); 2.32 (3H, s, CH_3CO); 2.29 (3H, s, CH_3). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 195.0; 149.2; 145.4; 130.4; 30.3; 24.5; 10.0. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 172 $[M+H]^+$ (17), 130 $[M–COCH_2+H]^+$ (58), 96 $[M–SAc]^+$ (100). Found, %: C 48.84; H 5.52; N 8.50; S 18.96. $C_7H_9NO_2S$. Calculated, %: C 49.11; H 5.30; N 8.18; S 18.73.

***S*-{[5-(*tert*-Butyl)oxazol-4-yl]methyl}ethanethioate (18c)**. Yield 23.6 g (93%), brown oil. ^1H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.64 (1H, s, H oxazole); 4.14 (2H, s, CH_2SAc); 2.31 (3H, s, CH_3CO); 1.33 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 194.9; 155.1; 148.4; 127.5; 32.5; 30.2; 29.2; 26.1. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 214 $[M+H]^+$ (100), 172 $[M–COCH_2+H]^+$ (50), 138 $[M–SAc]^+$ (28). Found, %: C 56.51; H 7.11; N 6.97; S 15.04. $C_{10}H_{15}NO_2S$. Calculated, %: C 56.31; H 7.09; N 6.57; S 15.03.

***S*-[(5-Cyclopropyloxazol-4-yl)methyl]ethanethioate (18d)**. Yield 20.0 g (85%), brown oil. ^1H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.57 (1H, s, H oxazole); 4.06 (2H, s, CH_2SAc); 2.33 (3H, s, CH_3CO); 2.01 (1H, ttd, *J* = 9.8, *J* = 6.6, *J* = 3.4, CH cyclopropane); 0.98–0.94 (2H, m, CH_2 cyclopropane); 0.87–0.83 (2H, m, CH_2 cyclopropane). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 195.0; 149.6; 148.2; 130.0; 30.3; 24.6; 6.6; 5.8. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 198 $[M+H]^+$ (50), 156 $[M–COCH_2+H]^+$

(67), 122 $[M–SAc]^+$ (28). Found, %: C 54.51; H 5.45; N 6.73; S 16.43. $C_9H_{11}NO_2S$. Calculated, %: C 54.80; H 5.62; N 7.10; S 16.25.

***S*-{[5-(Trifluoromethyl)oxazol-4-yl]methyl}ethanethioate (18f)**. Yield 25.7 g (96%), brown oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.90 (1H, s, H oxazole); 4.16 (2H, s, CH_2SAc); 2.36 (3H, s, CH_3CO). ^{13}C NMR spectrum (101 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 193.6; 151.5; 137.7; 135.6 (q, *J* = 43.2); 119.1 (q, *J* = 268.0); 30.1; 23.7. ^{19}F NMR spectrum (376 MHz, $CDCl_3$), δ, ppm: –62.5. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 224 $[M+H]^+$ (6), 184 $[M–COCH_2+H]^+$ (100), 150 $[M–SAc]^+$ (67). Found, %: C 37.08; H 2.64; N 6.14; S 14.62. $C_7H_6F_3NO_2S$. Calculated, %: C 37.34; H 2.69; N 6.22; S 14.24.

***S*-{[5-(Difluoromethyl)oxazol-4-yl]methyl}ethanethioate (18g)**. Yield 24.2 g (98%), brown oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 7.87 (1H, s, H oxazole); 6.99 (1H, t, *J* = 52.7, CHF_2); 4.05 (2H, s, CH_2SAc); 2.33 (3H, s, CH_3CO). ^{13}C NMR spectrum (101 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 194.6; 151.5; 139.6 (t, *J* = 27.0); 136.9 (t, *J* = 5.0); 107.1 (t, *J* = 236.0); 30.2; 23.8. ^{19}F NMR spectrum (376 MHz, $CDCl_3$), δ, ppm: –116.6. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 224 $[M+H]^+$ (11), 166 $[M–COCH_2+H]^+$ (100), 132 $[M–SAc]^+$ (78). Found, %: C 40.20; H 3.64; N 6.61; S 15.14. $C_7H_7F_2NO_2S$. Calculated, %: C 40.58; H 3.41; N 6.76; S 15.47.

Synthesis of sulfonyl chlorides 17a,c,f,g (General method). NCS (102 g, 0.764 mol) was dissolved in MeCN (430 ml) with H_2O (43.0 ml), and saturated aq HCl (10.8 ml) was added. The solution was cooled to 10°C, and the corresponding thioacetate **18** (0.191 mol) was added in portions. Then the resulting mixture was stirred at 10 to 20°C for 1 h, the solvent was evaporated under reduced pressure. The residue was dissolved in *t*-BuOMe (450 ml), washed with H_2O (200 ml) and brine (100 ml). The organic phase was dried over Na_2SO_4 and evaporated under reduced pressure.

(5-Methyloxazol-4-yl)methanesulfonyl chloride (17a). Yield 26.9 g (72%), yellowish oil. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 8.10 (1H, s, H oxazole); 4.51 (2H, s, CH_2SO_2Cl); 2.35 (3H, s, CH_3). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 150.0; 147.5; 130.1; 35.9; 10.2. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 196 $[M+H]^+$ (100), 198 $[M+H]^+$ (100). Found, %: C 30.65; H 2.91; N 7.54; S 16.56; Cl 17.91. $C_5H_6ClNO_3S$. Calculated, %: C 30.70; H 3.09; N 7.16; S 16.39; Cl 18.12.

[5-(*tert*-Butyl)oxazol-4-yl]methanesulfonyl chloride (17c). Yield 30.9 g (68%), yellowish oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 7.83 (1H, s, H oxazole); 5.02 (2H, s, CH_2SO_2Cl); 1.41 (9H, s, $C(CH_3)_3$). ^{13}C NMR spectrum (101 MHz, $CDCl_3$), δ, ppm: 160.6; 149.3; 119.8; 63.9; 33.3; 28.8. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 238 $[M+H]^+$ (100), 240 $[M+H]^+$ (100). Found, %: C 40.62; H 4.88; N 5.86; S 13.17; Cl 14.54. $C_8H_{12}ClNO_3S$. Calculated, %: C 40.42; H 5.09; N 5.89; S 13.49; Cl 14.91.

[5-(Trifluoromethyl)oxazol-4-yl]methanesulfonyl chloride (17f). Yield 46.2 g (97%), yellow crystals, mp 50–52°C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 8.07 (1H, s, H oxazole); 4.97 (2H, s, CH_2SO_2Cl). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 152.2; 140.1 (q, *J* = 43.8); 128.8; 118.4 (q, *J* = 269.0); 60.8. ^{19}F NMR spectrum (376 MHz, $CDCl_3$), δ, ppm: –63.0. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 252 $[M+H]^+$ (22), 250 $[M+H]^+$ (67), 150 $[M–SO_2Cl]$+ (100). Found, %: C 24.21; H 0.89; N 5.89; S 12.47; Cl 14.46. $C_5H_3ClF_3NO_3S$. Calculated, %: C 24.06; H 1.21; N 5.61; S 12.85; Cl 14.20.

[5-(Difluoromethyl)oxazol-4-yl]methanesulfonyl chloride (17g). Yield 42.0 g (95%), brownish oil. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 8.02 (1H, s, H oxazole); 6.86 (1H, t, *J* = 53.6, CHF_2); 4.98 (2H, s, CH_2SO_2Cl). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 152.0, 144.2 (t, *J* = 31.2); 127.4; 107.7 (t, *J* = 239.0); 61.1. ^{19}F NMR spectrum (376 MHz, $CDCl_3$), δ, ppm: –118.6. Mass spectrum (CI), *m*/*z* (I_{rel}, %): 234 $[M+H]^+$ (10), 232 $[M+H]^+$ (30), 214 $[M–F]^+$ (25), 212 $[M–F]^+$ (75), 132 $[M–SO_2Cl]^+$ (100). Found, %: C 26.10; H 1.67; N 5.76; S 13.45; Cl 15.70. $C_5H_4ClF_2NO_3S$. Calculated, %: C 25.93; H 1.74; N 6.05; S 13.84; Cl 15.31.

Supplementary information file containing ^{1}H, ^{13}C and ^{19}F NMR spectra of the synthesized compounds is available at the journal website at http://link.springer.com/journal/10593.

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