A Copper-Catalyzed Multicomponent Reaction and 'Click Strategy' for the Stereoselective Synthesis of a New Series of Oxazolone Peptidomimetics with α-Acylamino Amide and β-Amido Ketone Structures

by **Biny Balan** and **Damodaran Bahulayan***

Department of Chemistry, University of Calicut, Malappuram-673635, Kerala, India (phone: +91-9995538062; fax: +91-494-2400269; e-mail: bahulayan@yahoo.com)

A novel 'click ligation' strategy for the stereoselective synthesis of a medium-size library of structurally complex and functionally diverse oxazolone peptidomimetics, which contain α-acylamino carboxamide or β-amido ketone residues, is presented. Most of these molecules have lipophilicity constant values (log P) in the qualifying range for cell permeability, and that indicates the possibilities of these new molecules to be used in the search for potential inhibitors for a broad spectrum of enzymes.

Introduction. – The focus of modern drug discovery is the identification of structurally complex and functionally diverse compounds that can target clinically relevant pathways [1]. A recent method for the introduction of diversity and complexity in a drug lead is the fragment-based assembly of diversity elements, allowing the construction of small-molecule inhibitors with core and peripheral binding sites [2]. The core functionality usually consists of a heterocyclic molecule, and the peripheral functionality is made up of a peptidic or non-peptidic fragment. The fragments are usually prepared in short reaction sequences, and are then assembled by a mild reaction as ligation tool. An emerging trend in this concept is the use of multicomponent reactions (MCRs) [3] for scaffold generation and the Cu^{I}-catalyzed azide–alkyne [3 + 2] cycloaddition (CuAAC) [4], leading to the formation of a 1,2,3-triazole between two structural scaffolds. Several drug molecules developed by this strategy are now commercially available, and many are in the final stages of clinical trials [5]. In addition, due to the bioisosteric nature of amide bonds and 1,2,3-triazoles, it is possible to convert a non-peptidic molecule to a peptidomimetic [6] with higher stability and better bioavailability [7].

Oxazoles and its derivatives [8] represent an important heterocyclic class that shows affinity to bind at the primary binding pockets of enzymes and are present in many pharmacologically active molecules [9]. Among the oxazole derivatives, oxazolones exhibit a wide spectrum of pharmacological features such as anticancer, antimicrobial, antifungal, and sedative activities [10]. The functional groups at C(4) and C(2) of an oxazolone are crucial for its enzyme-inhibitory activity. Many potential inhibitors of enzymes such as tyrosinase [11], (11β)-hydrosteroid dehydrogenase type 1 (11β-HSD1) [12], herpes protease [13], *etc.*, are based on the structural modifications of oxazolones at C(2) and C(4) with simple substituents such as Ph or naphthyl groups.

The α-acylamino amide group is a functional motif present in many commercially available drug molecules such as telaprevir, used for the treatment of hepatitis C,

bortezomib, a threonine protease inhibitor, and parziquantel used for the treatment of schistosomiasis (*Fig. 1*) [14]. Similarly, β-amido ketones are important building blocks for the synthesis of 1,3-amino alcohols and β-lactams. The former are structural parts of peptidyl nucleoside antibiotics such as nikkomycins and polyoxins [15], and the latter occur in β-lactamase inhibitors such as 6-β-bromopenicillinic acid [16].

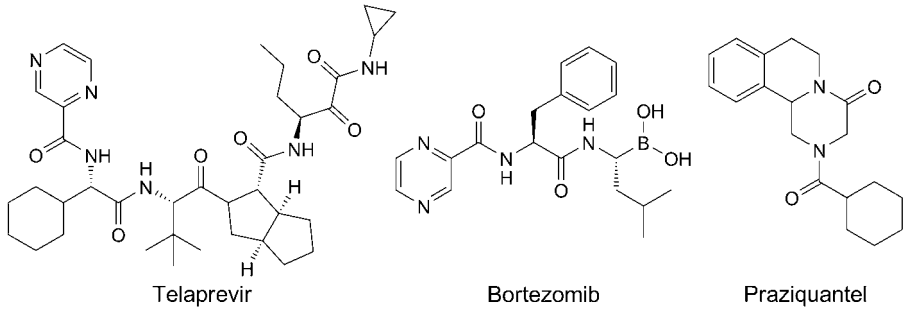


Fig. 1. *Commercial drug molecules with α-acylaminoamide core structure*

We have recently developed a series of novel protocols for the synthesis of peptidomimetics based on α-acylamino amides and β-amido ketones [17][18].

As part of our ongoing studies in MCRs and 'click chemistry', we decided to search for possibilities of functionalizing the oxazolone core structure with an α-acylamino amide or a β-amido ketone group to generate a series of new peptidomimetic structures **A** and **B** (*cf. Fig. 2*), which may be useful for development of new drug leads.

Results and Discussion. – We started our studies by functionalizing oxazolones with α-acylaminoamide moieties. The oxazolones **1a**–**1f** (*Scheme 1*) were obtained in good-

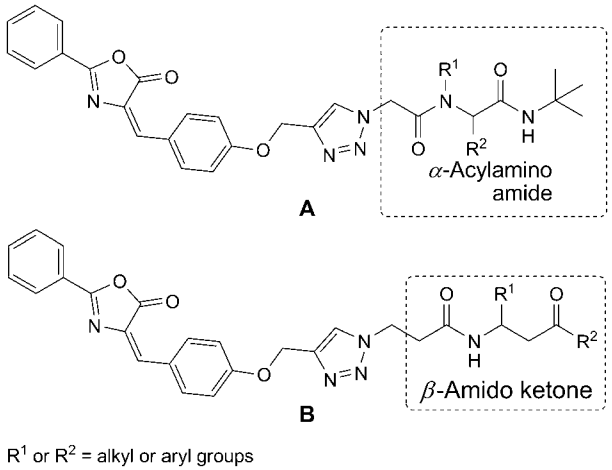
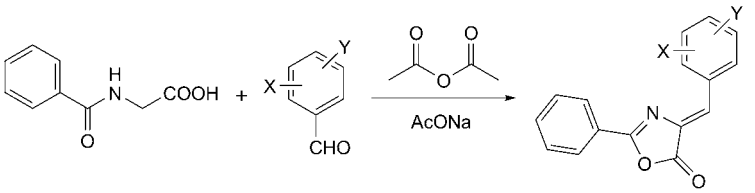


Fig. 2. *Oxazolone peptidomimetics*

to-excellent yields from the reactions of *N*-benzoylglycine with propargylated benzaldehyde derivatives under *Erlenmeyer–Perkin* conditions [19]. All six oxazolone derivatives, containing (alkynyloxy)phenyl and -napthyl substituents, were characterized by standard spectroscopic techniques [11].

Scheme 1. *Oxazolones with [(Alkynyloxy)arenyl]methylidene Substituents Used in the Present Study*

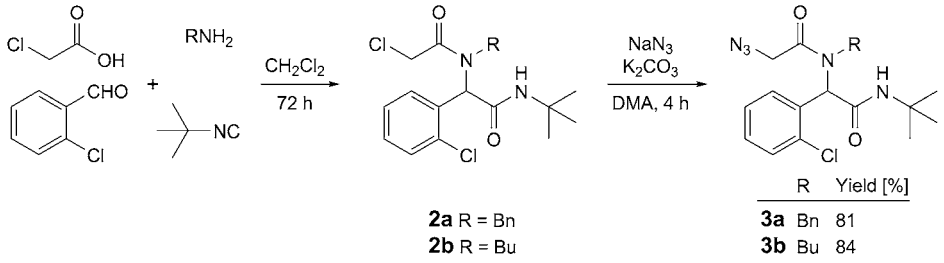


	X	Y	Yield [%]	log *P*
1a	2-(Prop-2-yn-1-yloxy)	H	81	3.48
1b	4-(Prop-2-yn-1-yloxy)	H	81	3.52
1c	4-(Prop-2-yn-1-yloxy)	3-MeO	75	3.11
1d	4-(Prop-2-yn-1-yloxy)	2-(Prop-2-yn-1-yloxy)	91	3.67
1e	4-(Prop-2-yn-1-yloxy)	3-(Prop-2-yn-1-yloxy)	80	3.27
1f	2-(Prop-2-yn-1-yloxy)	[5,6]Benzo	63	4.64

The α-(azidoacyl)amino amides **3a** and **3b** used in this study were prepared *via* an *Ugi* four-component reaction between $ClCH_2COOH$, chlorobenzaldehyde, a primary amine, and ^{t}BuNC (*Scheme 2*). The reaction afforded the chloro derivatives **2a** and **2b**, respectively, and subsequent replacement of the Cl-substituent by N_3 by treating with NaN_3 in dimethylacetamide (DMA) afforded **3a** and **3b**, respectively, in excellent yields. The assembly of the components **1** and **3** by a Cu^I-catalyzed [3 + 2] azide–alkyne cycloaddition was carried out in different solvents using different Cu^I sources. After several attempts, an optimized condition was established based on the use of *t*-BuOH/H_2O/DMSO 4:2:1 in the presence of a catalytic amount of $CuSO_4$ and sodium ascorbate at room temperature (*cf. Scheme 3*).

The cycloaddition reactions took place with almost quantitative formation of the 1,2,3-triazole derivatives **4**, and the precipitated products were collected and purified by simple washing with solvent. The resulting products are collected in *Fig. 3*. The cycloaddition reactions of **1d** and **1e** (both contain two alkynyloxy substituents) with 2

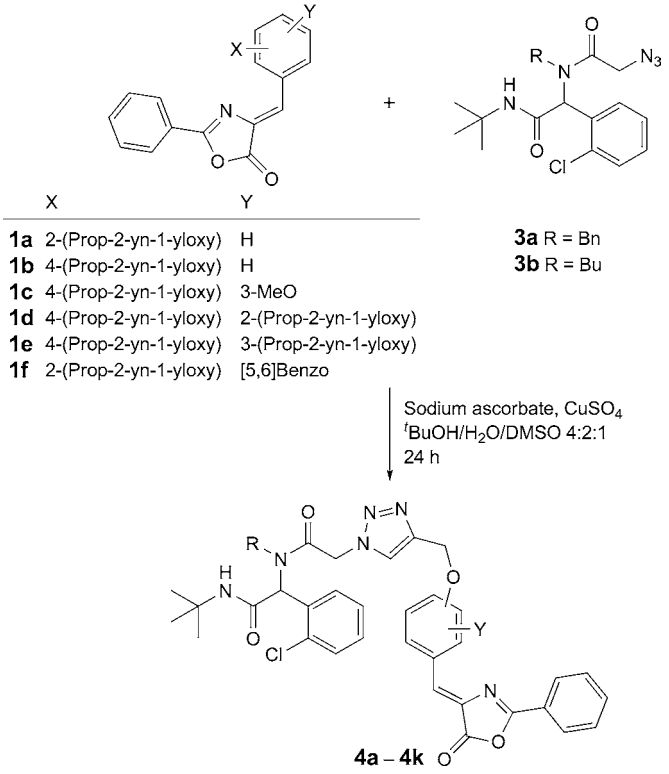
Scheme 2. *α-Acylamino Acetamides Obtained from* Ugi-*4CR*



2a R = Bn
2b R = Bu

	R	Yield [%]
3a	Bn	81
3b	Bu	84

Scheme 3. *Cu^{I}-Promoted [3+2] Cycloaddition Reactions of Oxazolones* **1** *with α-Acylamino Acetamides* **3**

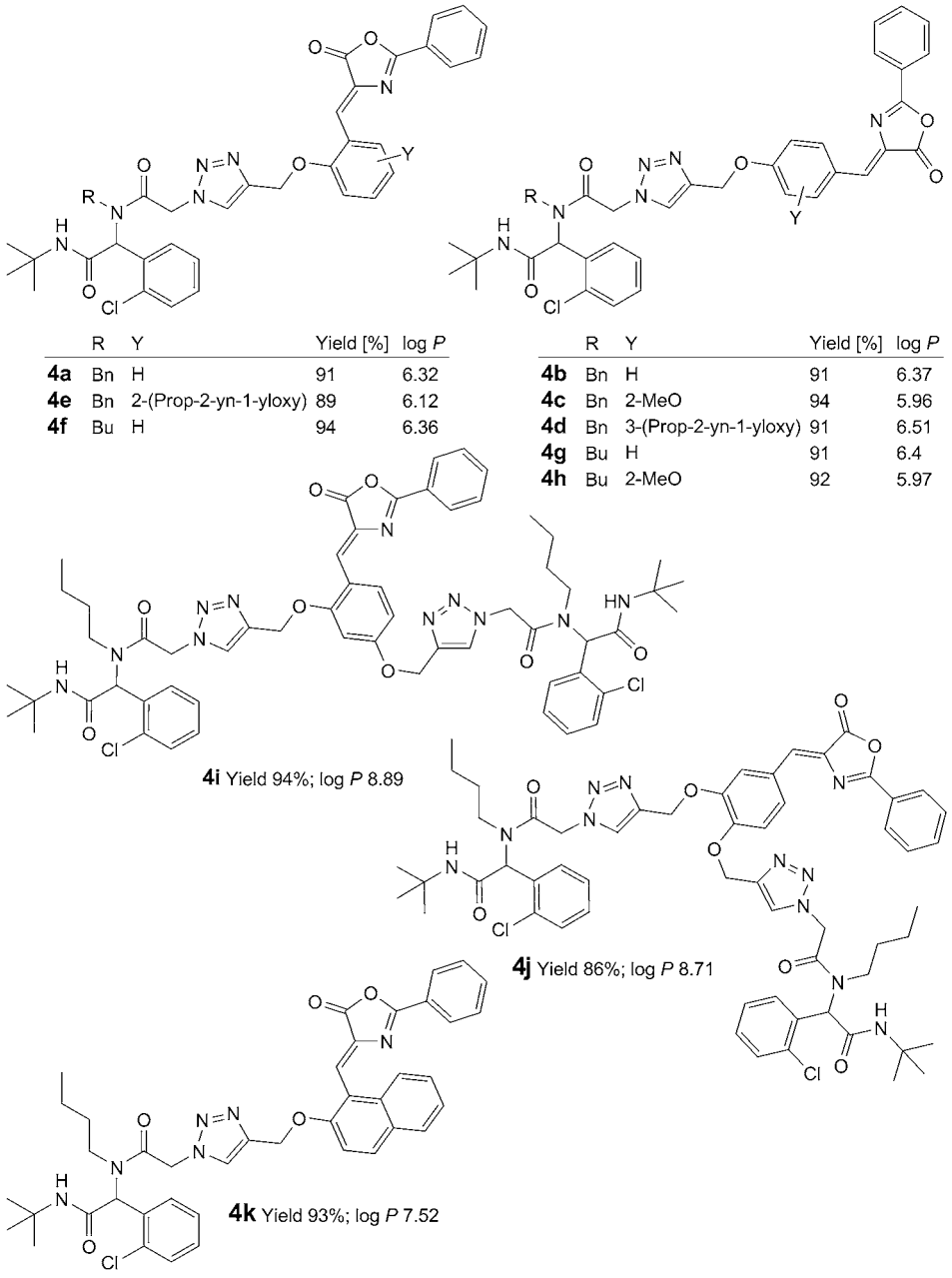


equiv. of azido derivatives **3a** afforded the corresponding monocycloaddition products **4d** and **4e**, with one alkyne group remaining intact. On the other hand, when the same alkynes were treated with 2 equiv. of azide **3b**, the reaction afforded **4i** and **4j**, in which both alkynyloxy groups participated in cycloaddition reactions.

The former reactions were repeated in different concentrations of the azido derivative **3a**, and no change in the nature of the product was observed. The presence of a free prop-2-yn-1-yloxy group in **4d** and **4e** provides an additional binding handle and is expected to increase the possibilities of these two compounds to be considered as potent inhibitors of different enzyme classes.

To evalue the regio- and stereoselectivity in the triazole formation, we compared the spectroscopic data of the peptidomimetics with literature values. The ^{1}H-NMR spectra showed a downfield shifted signal at *ca.* 8.8 ppm in all the 'click products', which corresponds to the ethylenic H-atom of an *anti*-1,4-disubstituted 1,2,3-triazole isomer. This value is in agreement with those in [20].

The success of this method prompted us to study the outcome of the functionalization of oxazolones with *β*-amino acid derivatives, and we decided to prepare a series of azido derivatives with *β*-amido ketone structures. A recent development in the synthesis of *N*-substituted *β*-amino ketone derivatives is the emergence of a *Mannich*-



	R	Y	Yield [%]	log *P*
4a	Bn	H	91	6.32
4e	Bn	2-(Prop-2-yn-1-yloxy)	89	6.12
4f	Bu	H	94	6.36

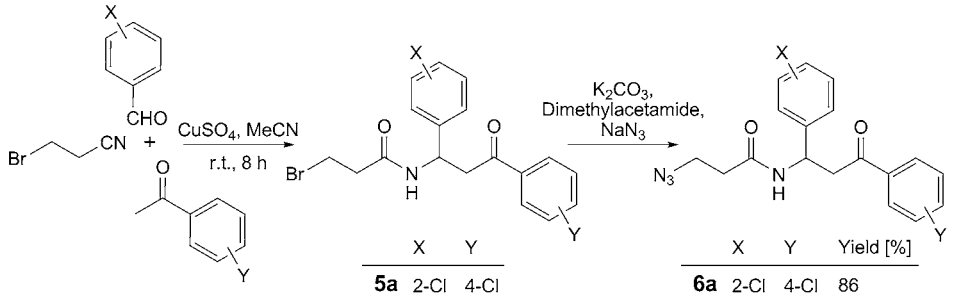
	R	Y	Yield [%]	log *P*
4b	Bn	H	91	6.37
4c	Bn	2-MeO	94	5.96
4d	Bn	3-(Prop-2-yn-1-yloxy)	91	6.51
4g	Bu	H	91	6.4
4h	Bu	2-MeO	92	5.97

Fig. 3. *Peptidomimetics obtained from Cu^{I}-catalyzed [3 + 2] cycloaddition reactions of oxazolones* **1** *with α-aminoacyl amides*

type MCR, which involves a one-pot condensation of a non-enolizable aldehyde, an enolizable ketone, and MeCN in the presence of AcCl [21] (*Scheme 4*). Several new

catalysts have been reported over the years, but many of them suffer from poor stereoselectivity, and the scope of the nitrile component was limited to MeCN [22]. To use a halogen-substituted nitrile instead of MeCN in this reaction to obtain a Br-bearing amido group in the final product, we decided to investigate the reaction with 3-bromopropionitrile in the presence of various catalysts. At room temperature, the reaction in the presence of a catalytic amount of $CuSO_4$ was suitable to introduce a halogen-substituted moiety. The β-(bromo-amido) ketone derivatives **5a** – **5e** were then quantitatively converted to the β-(azido-amido) ketones **6a** – **6e** in almost quantitative yields by treatment with NaN_3 in DMA (*Scheme 4*).

Scheme 4. *β-Propanamido Ketone Scaffolds Used in the Present Study*



	X	Y
5a	2-Cl	4-Cl
5b	2-Br	4-Br
5c	4-Cl	4-Cl
5d	4-Cl	4-Br
5e	2-Cl	4-Br

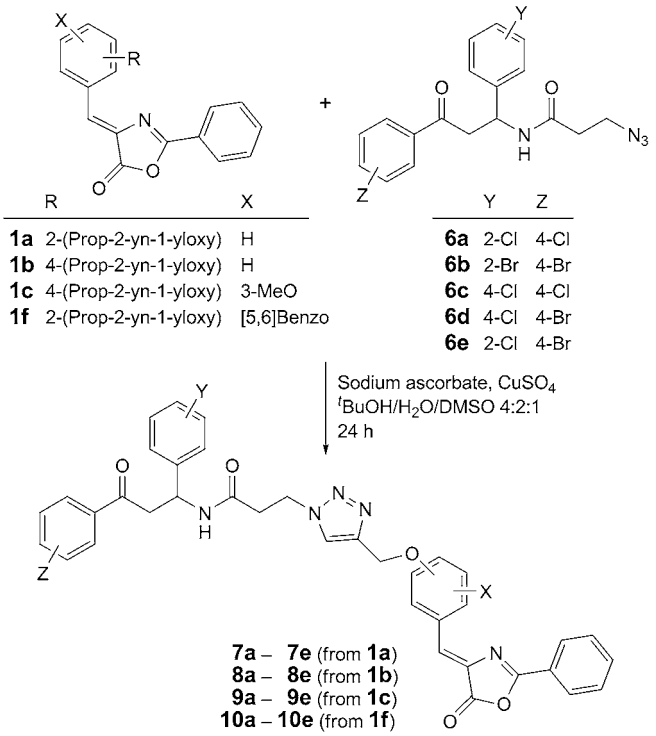
	X	Y	Yield [%]
6a	2-Cl	4-Cl	86
6b	2-Br	4-Br	98
6c	4-Cl	4-Cl	98
6d	4-Cl	4-Br	99
6e	2-Cl	4-Br	99

Ligations of oxazolones **1** with β-amido ketones **6** were carried out by Cu^I-catalyzed azide–alkyne [3 + 2] cycloaddition reactions outlined in *Scheme 5*. The reactions of **1a** – **1f** with **6a** – **6e** afforded the (1-substituted 1,2,3-triazol-4-yl)methoxy-carrying oxazolone peptidomimetics **7a** – **10e** in more than 90% yield (*Fig. 4*). The reactions did not display any significant change in yields with respect to the nature of the substituents in the β-amido ketone residue.

Compounds **4a** – **4k** and **7a** – **10e** represent oxazolone peptidomimetics with more than one amide-bond isosteres. Groups such as 1,2,3-triazoles, esters, and alkenes have the ability to participate in non-covalent interactions, and the extent of interaction is comparable with that of amide bonds [23]. Peptide-bond isosteres can enable a detailed evaluation of the structure and function of the peptidic molecules by amplifying or attenuating biochemical properties. The oxazolone ring resembles a cyclic ester, and, since the geometric parameters of an ester functionality is comparable to those of an amide bond, the oxazolone ring can also be considered as a peptide-bond isostere [23].

In compounds **4a** – **4k**, the diversity elements such as oxazolone ring, 1,2,3-triazole, and other isosteres are placed in alternate positions, and, therefore, these molecules can be considered as conjugated acyclic oxazolone mimics with an α-acylamino amide-type secondary binding group. Compounds **7a** – **10e** contain an additional β-oxo-alkyl group, and there is a possibility for this keto group to form a tetrahedral adduct with nucleophilic residues present in the target enzymes during the inhibition process.

Scheme 5. *Cu^{I}-Promoted [3 + 2] Cycloaddition Reactions of Oxazolones* **1** *with β-Propanamido Ketones* **6a – 6e**



This possibility renders the second category of mimics **7a – 10e** slightly more promising than the first category of α-acylamino oxazolone derivatives **4a – 4k**.

This assumption is further supported by the calculated lipophilicity constant (log *P*) values of both categories of peptidomimetics. log *P* is a measure of cell permeability and central nervous system-distribution capability of a molecule. It has been recognized that lipophilic molecules have greater access to central nervous system than hydrophilic molecules [24]. Drug-like molecules usually have log *P* values between −0.4 and 5.6 [25]. As compiled in *Fig. 4* , the log *P* values[1]) obtained for the β-amido ketone-containing oxazolone mimics **7a – 10e** are close to the upper limit of the qualifying range of membrane-permeable drug classes [27].

Conclusions. – In conclusion, we have developed a medium-size library of structurally complex and functionally diverse oxazolone peptide mimics based on the 'click ligation' of oxazolone derivatives with α-acylamino amide or β-amido ketone moieties. Preliminary calculations on biological activity providing descriptors such as log *P* indicate the future perspectives for these new scaffolds as efficient cell-permeable molecules.

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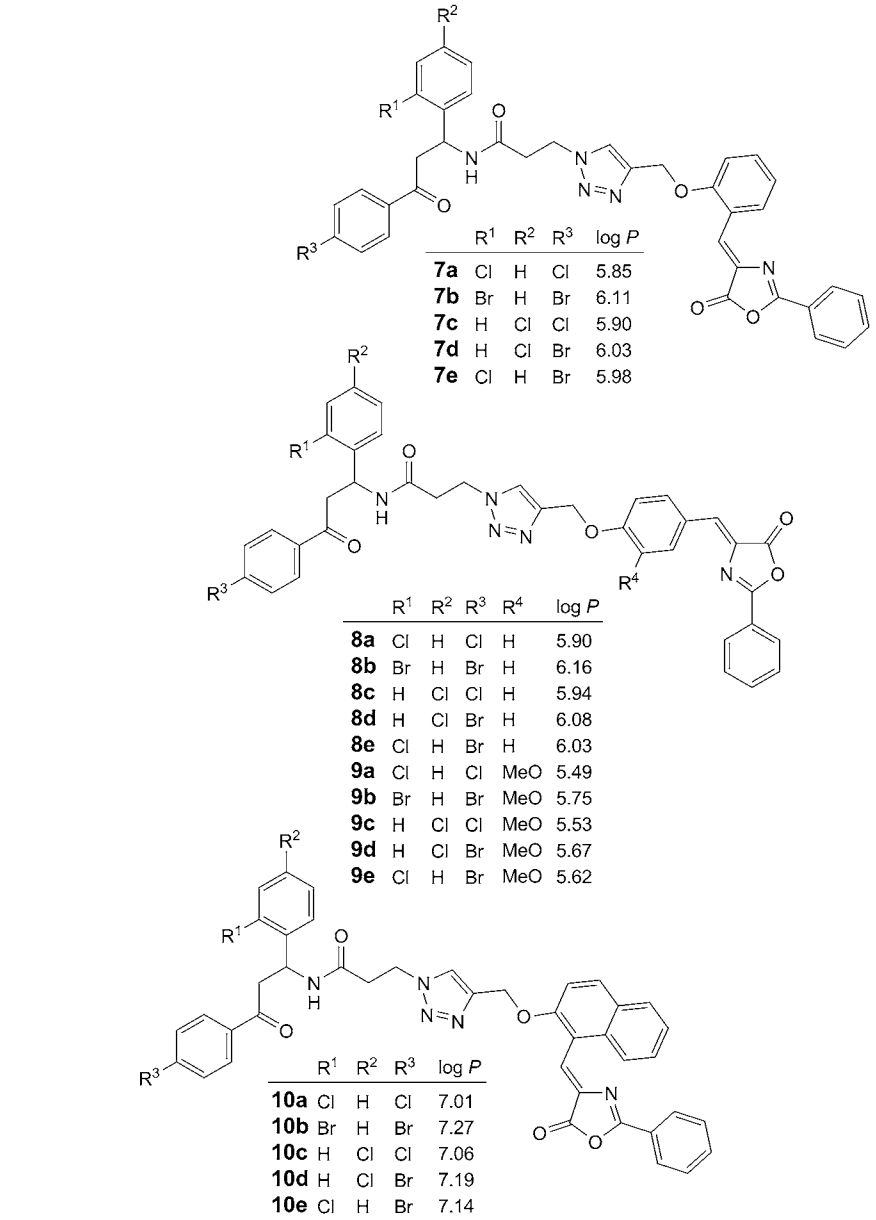
[1]) Calculated by using *Molinspiration* calculation service [26].



	R^1	R^2	R^3	log *P*
7a	Cl	H	Cl	5.85
7b	Br	H	Br	6.11
7c	H	Cl	Cl	5.90
7d	H	Cl	Br	6.03
7e	Cl	H	Br	5.98

	R^1	R^2	R^3	R^4	log *P*
8a	Cl	H	Cl	H	5.90
8b	Br	H	Br	H	6.16
8c	H	Cl	Cl	H	5.94
8d	H	Cl	Br	H	6.08
8e	Cl	H	Br	H	6.03
9a	Cl	H	Cl	MeO	5.49
9b	Br	H	Br	MeO	5.75
9c	H	Cl	Cl	MeO	5.53
9d	H	Cl	Br	MeO	5.67
9e	Cl	H	Br	MeO	5.62

	R^1	R^2	R^3	log *P*
10a	Cl	H	Cl	7.01
10b	Br	H	Br	7.27
10c	H	Cl	Cl	7.06
10d	H	Cl	Br	7.19
10e	Cl	H	Br	7.14

Fig. 4. *Selected peptidomimetics obtained from Cu^I-catalyzed [3+2] cycloaddition reactions of oxazolones* **1** *with β-propanamido ketones* **6a**–**6e**

Experimental Part

General. The chemicals were obtained from the *Sigma–Aldrich* and *Merck*, and were used without further purification. M.p.: *Toshini Wall* apparatus; uncorrected. IR Spectra (KBr): *JASCO FT-IR 4100*;

in cm^{-1}. ^1H- and ^{13}C-NMR spectra: *Bruker-DRX-500-Avance*; at 500 (^1H) and 125 MHz (^{13}C) in (D_6)DMSO and $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. EI-MS (70 eV): *Finnigan-MAT-8430*; in *m*/*z*.

Representative Procedure for the Synthesis of (4Z)-2-Phenyl-4-[2-(prop-2-yn-1-yloxy)benzylidene]-1,3-oxazol-5(4H)-one (**1a**). A soln. of *2-(prop-2-yn-1-yloxy)benzaldehyde*; 0.3 g, 2 mmol), hippuric acid (0.354 g, 2 mmol), Ac_2O (0.532 g, 6 mmol), and anh. AcONa (0.152 g, 2 mmol) was heated at reflux with constant stirring for 3 h. Then, the mixture was cooled, 20 ml of EtOH was added slowly, and the mixture was allowed to stand overnight. The crystallized crude product was filtered, washed with hot H_2O, and then with a small volume of an ice cold H_2O/MeOH 1:1 mixture. The crude product obtained was dried and recrystallized from abs. EtOH to yield **1a** (0.465 g, 81%). M.p. 160–162°. IR (KBr): 3257, 2115, 1583, 1556. ^1H-NMR: 3.66 (*s*, 1 H); 4.99 (*s*, 2 H); 7.17–8.81 (*m*, 9 H). ^{13}C-NMR: 56.3; 78.7; 78.8; 113.1; 121.8; 123.2; 125.0; 127.9; 129.3. 132.1; 133.1; 133.7, 156.7; 163.0; 167.0. EI-MS: 304 (M^+).

(4Z)-2-Phenyl-4-[4-(prop-2-yn-1-yloxy)benzylidene]-1,3-oxazol-5(4H)-one (**1b**). Yield: 0.465 g (81%). M.p. 165–166°. IR (KBr): 3310, 1782, 1572, 1557. ^1H-NMR: 3.63 (*s*, 1 H); 4.92 (*s*, 2 H); 7.14–9.88 (*m*, 9 H). ^{13}C-NMR: 55.8; 78.5; 78. 8; 115.2; 115.4; 127.7; 129.3; 130.9; 131.0; 131.6; 133.4; 134.4; 159.7; 162.1; 167.0. EI-MS: 304 (M^+).

(4Z)-4-[3-Methoxy-4-(prop-2-yn-1-yloxy)benzylidene]-2-phenyl-1,3-oxazol-5(4H)-one (**1c**). Yield: 0.397g (75%). M.p. 165–167°. IR (KBr): 3312, 1780, 1584, 1556. ^1H-NMR: 2.56 (*s*, 1 H); 4.03 (*s*, 3 H); 4.86 (*s*, 2 H); 7.10–8.17 (*m*, 9 H). ^{13}C-NMR: 46.7; 56.3; 78.7; 78.8; 113.1; 121.8; 122.1; 123.2; 125.0; 127.9; 129.3; 132.1; 132.7; 133.1; 133.7; 156.7; 167.0. EI-MS: 334 (M^+).

(4Z)-4-[2,4-Bis(prop-2-yn-1-yloxy)benzylidene]-2-phenyl-1,3-oxazol-5(4H)-one (**1d**). Yield: 0.458 g (91%). M.p. 160–162°. IR: 3247, 2119, 1783, 1583, 1556, 946, 865, 696. ^1H-NMR: 3.66 (*s*, 2 H); 4.94–5.00 (*m*, 4 H); 6.83–8.83 (*m*, 9 H). ^{13}C-NMR: 56.6; 78.1; 78.4; 100.6; 108.4; 115.9; 123.6; 125.3; 127.8; 128.3; 130.5; 133.4; 133.6; 158.4; 162.0; 167.2. EI-MS: 358 (M^+).

(4Z)-4-[3,4-Bis(prop-2-yn-1-yloxy)benzylidene]-2-phenyl-1,3-oxazol-5(4H)-one (**1e**). Yield: 0.396 g (80%). M.p. 161–163°. IR: 3244, 3074, 2119, 1789, 1585. ^1H-NMR: 2.57 (*s*, 4 H); 4.86 (*s*, 4 H); 7.17–9.88 (*m*, 9 H). ^{13}C-NMR: 46.7; 56.3; 78.6; 78.7; 78.8; 78.9; 113.1; 121.8; 122.1; 123.2; 125.0; 127.9; 129.3; 132.1; 132.7; 133.1; 133.7; 156.7; 163.0; 167.0. EI-MS: 358 (M^+).

(4Z)-2-Phenyl-4-{[2-(prop-2-yn-1-yloxy)naphthalen-1-yl]methylidene}-1,3-oxazol-5(4H)-one (**1f**). Yield: 0.321 g (63%). M.p. 155–159°. IR: 3255, 3058, 2117, 1576. ^1H-NMR: 2.58 (*s*, 1 H); 4.96 (*s*, 2 H); 7.26–10.90 (*m*, 12 H). ^{13}C-NMR: 56.3; 78.7; 78.8; 113.1; 121.8; 123.2; 123.8; 125.0; 126.8; 127.9; 128.5; 129.3; 132.1; 132.7; 133.1; 133.7; 156.7; 163.0; 167.0. EI-MS: 353.2 (M^+).

Representative Procedure for the Synthesis of N-*Benzyl*-N-*{2-[*tert-*butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}-2-chloroacetamide* (**2a**). Equimolar amount of 2-chlorobenzaldehyde (1.41 g, 0. 01 mol) and $PhCH_2NH_2$ (1.07 g, 0.01 mol) were dissolved in CH_2Cl_2 (8 ml) and stirred in r.t. for 20 min. Then, 1 equiv. of *t*-BuNC (0.83 g, 0.01 mol) and $ClCH_2COOH$ (0.95 g, 0.01 mol) were added, and the mixture was stirred at r.t. The reaction was monitored by TLC and was complete after 72 h. The solvent was evaporated under vacuum, and the crude product was obtained after repeated washings with petroleum ether (5 × 15 ml) to afford **2a** (3.58 g, 88%). IR: 3334, 2963, 1690, 1658, 1540, 1485, 1455, 1382, 1363, 1256, 1232. 1014, 759, 629. ^1H-NMR: 1.27 (*s*, 9 H); 4.36 (*s*, 2 H); 4.86 (*s*, 2 H); 5.75 (*s*, 1 H); 8.06 (*s*, 1 H); 7.04–7.42 (*m*, 9 H). ^{13}C-NMR: 28.3; 43.1; 43.4; 50. 4; 63.9; 64.1; 115.4; 121.2; 121.5; 130.9; 131.6; 131.7; 132.1; 133.1; 137.5; 137.8; 165.2; 168.2. EI-MS: 407.1 (M^+).

N-*Butyl*-N-*{2-[(*tert-*butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}-2-chloroacetamide* (**2b**). Yield: 3.62 g (84%). M.p. 160–162°. IR: 3297, 3070, 1677, 1648, 750. ^1H-NMR: 1.01–1.04 (*t*, *J* = 14.5, 3 H); 1.05–1.09 (*m*, 2 H); 1.34 (*s*, 9 H); 1.38–1.46 (*m*, 2 H); 3.23–3.35 (*m*, 3 H); 4.22 (*s*, 2 H); 5.98 (*s*, 1 H); 7.27–7.60 (*m*, 4 H); 8.16 (*s*, 1 H). ^{13}C-NMR: 28.3; 30.6; 30.8; 30.9; 43.1; 43.4; 50.4; 63.9; 63.9; 64.1; 129.9; 130.9; 131.6; 131.7; 137.5; 137.8; 165.2; 168.2. EI-MS: 373.3 ($[M+1]^+$).

Representative Procedure for the Synthesis of 2-Azido-N-*benzyl*-N-*{2-[(*tert-*butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}acetamide* (**3a**). Compound **2a** (1.02g, 0.0025 mol) and NaN_3 (700 mg) were dissolved in dimethylacetamide (DMA; 4 ml). Then, K_2CO_3 (1 g) was added, the mixture was stirred at r.t. for 4 h, and was then diluted with H_2O. The white precipitate obtained was filtered and washed repeatedly with H_2O to afford **3a** (0.83 g, 81%). IR: 3304, 3072, 2100, 1649. ^1H-NMR: 1.16 (*s*, 9 H); 2.50 (*s*, 2 H); 4.72 (*s*, 2 H); 5.60 (*s*, 1 H); 6.84–7.37 (*m*, 9 H); 8.09 (*s*, 1 H). ^{13}C-NMR: 26.3; 30.6; 30.8; 31.9;

43.1; 46.4; 49.4; 63.9; 63.9; 65.1; 129.9; 129.9; 131.6; 131.7; 136.5; 136.8.; 169.2; 169.8. EI-MS: 414.4 ([$M+1$]$^+$).

2-Azido-N-*butyl*-N-*{2-[(*tert-*butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}acetamide* (**3b**). Yield: 0.82 g (83%). IR: 3310, 3071, 2107, 1678, 1643. ^{1}H-NMR: 0.64–0.67 (*t*, $J=15$, 3 H); 0.94–0.97 (*m*, 2 H); 1.35 (*s*, 9 H); 1.60–1.69 (*m*, 2 H); 3.10 (*s*, 2 H); 3.22–3.28 (*m*, 2 H); 6.08 (*s*, 1 H); 7.26–7.59 (*m*, 4 H); 7.60 (*s*, 1 H). ^{13}C-NMR: 26.3; 29.6; 30.1; 30.6; 43.1; 44.8; 50.1; 64.1; 64.3; 66.1; 129.8; 129.9; 131.6; 131.7; 136.5; 136.8; 169.9; 170. 2. EI-MS: 380.1 ([$M+1$]$^+$).

Representative Procedure for the Cu^I-Promoted 1,3-Dipolar Cycloaddition Reactions. Equimolar amounts of **3a** (60 mg, 2 mmol) and **1** (83 mg, 2 mmol) were dissolved in minimum amount of DMSO. Then, 2 ml of *t*-BuOH, 1 ml of H_2O, 70 mg of $CuSO_4 \cdot 5\ H_2O$, and 83 mg of sodium ascorbate were added, and the mixture was stirred at r.t. After 24 h, the mixture was poured into cold H_2O. The precipitated 'click product' was filtered, washed with H_2O, and dried under vacuum.

N-*Benzyl*-N-*{2-[(*tert-*butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}-2-[4-({2-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]acetamide* (**4a**). Yield: 128 mg (91%). IR: 3258, 3060, 2965, 2926, 1780, 1583, 1556. ^{1}H-NMR: 1.19–1.23 (*m*, 9 H); 4.82 (*s*, 2 H); 4.97 (*s*, 2 H); 5.88 (*s*, 2 H); 6.32 (*s*, 1 H); 6.86–8.35 (*m*, 20 H); 8.79–8.81 (*d*, $J=7.6$, 1 H). ^{13}C-NMR: 26.3; 30.6; 30.8; 31.9; 43.1; 46.4; 49.4; 56.3; 63.9; 63.9; 65.1; 78.7; 78.8; 113.1; 121.8; 122.1; 123.2; 125.0; 127.9; 129.3; 129.8; 131.6; 131.7; 132.1, 132.7; 136.5; 136.8; 156.7; 163.0; 167.0; 169.2; 169. 8. EI-MS: 717 (M^+).

N-*Benzyl*-N-*{2-[(*tert-*butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}-2-[4-({4-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]acetamide* (**4b**). Yield: 128 mg (91%). IR: 3258, 3060, 2965, 2926, 1780, 1583, 1556. ^{1}H-NMR: 1.19 (*s*, 9 H); 4.82 (*s*, 2 H); 4.97 (*s*, 2 H); 5.88 (*s*, 2 H); 6.32 (*s*, 1 H); 6.86–8.35 (*m*, 20 H); 8.81 (*s*, 1 H). ^{13}C-NMR: 26.3; 30.6; 30.8; 31.9; 43.1; 46.4; 49.4; 55.4; 63.9; 63.9; 65.1; 78.5; 78.8; 115.2; 115.4; 127.7; 129.3; 129.8; 129.9; 130.9; 131.0; 131.5; 131.6; 131.7; 133.4; 136.5; 136.8; 159.7; 162.1; 167.0; 169.2; 169.8. EI-MS: 717 (M^+).

N-*Benzyl*-N-*{2-[(*tert-*butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}-2-[4-({2-methoxy-4-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]acetamide* (**4c**). Yield: 106 mg (94%). IR: 3252, 3064, 2958, 2922, 1782, 1586, 1556. ^{1}H-NMR: 1.19 (*s*, 9 H); 3.64 (*s*, 3 H); 3.89 (*s*, 2 H); 4.92 (*s*, 2 H); 5.27 (*s*, 2 H); 6.20 (*s*, 1 H); 7.15–8.15 (*m*, 19 H); 9.85 (*s*, 1 H). ^{13}C-NMR: 26.0; 30.6; 30.8; 31.9; 43.1; 46.4; 46.7; 49.4; 56.3; 63.9; 65.1; 78.7; 78.8; 113.1; 121.8; 122.1; 122.2; 125.0; 129.9; 129.9; 129.9; 131.6; 131.7; 132.1; 132.7; 133.1; 133.7; 136.5; 136.8; 156.7; 163.0; 167.0, 169.2; 169. 8. EI-MS: 747.1 (M^+).

N-*Benzyl*-N-*{2-[(tert-butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}-2-[4-({4-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]-3-(prop-2-yn-1-yloxy)phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]acetamide* (**4d**). Yield: 99 mg (89%). IR: 3289, 3065, 2965, 2928, 2120, 1783, 1583, 1556. ^{1}H-NMR: 1.23 (*s*, 9 H); 3.67 (*s*, 1 H); 4.76 (*s*, 2 H); 4.90 (*s*, 2 H); 4.94 (*s*, 2 H); 5.86 (*s*, 2 H); 6.31 (*s*, 1 H); 6.84–8.28 (*m*, 19 H); 8.82–8.84 (*m*, 1 H). ^{13}C-NMR: 26.0; 30.6; 30.8; 31.9; 43.1; 46.4; 49.4; 56.6; 63.9; 65.1; 78.1; 78.4; 100.6; 108.4; 115.9; 123.6; 125.3; 127.8; 128.3; 129.9; 12.9; 130.5; 131.6; 131.7; 133.4; 133.6; 136.5; 136.8; 158.4; 162.0; 167.2; 169.2; 169. 8. EI-MS: 771 (M^+).

N-*Benzyl*-N-*{2-[(tert-butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}-2-[4-({2-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]-6-(prop-2-yn-1-yloxy)phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]acetamide* (**4e**). Yield: 96 mg (89%). IR: 3079, 2965, 2925, 2117, 1789, 1597, 1557. ^{1}H-NMR: 1.16 (*s*, 9 H); 3.62 (*s*, 1 H); 4.73–4.77 (*s*, 2 H); 4.89–4.91 (*s*, 2 H); 5.25 (*s*, 2 H); 6.27 (*s*, 1 H); 6.82–8.30 (*m*, 19 H); 9.80 (*s*, 1 H). ^{13}C-NMR: 26.0; 30.6, 30. 8; 31.9; 43.1; 46.4; 46.7; 49.4; 56.3; 63.9; 65.1; 78.6; 78.7; 78.8; 78.9; 113.1; 121.8; 122.1; 123.2; 125.0; 127.9; 129.3; 129.9; 129.9; 131.6; 131.7; 132.1; 132.7; 133.1; 133.7; 136.5; 136.8; 156.7; 163.0; 167.0; 169.2; 169.8. EI-MS: 771.0 (M^+).

N-*Butyl*-N-*{2-[(tert-butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}-2-[4-({2-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]acetamide* (**4f**). Yield: 64 mg (94%). IR: 3258, 3074, 2962, 2932, 1790, 1596, 1557. ^{1}H-NMR: 0.60–0.64 (*m*, 3 H); 0.91–1.02 (*m*, 2 H); 1.32–1.47 (*m*, 2 H); 1.25 (*s*, 9 H); 5.36 (*s*, 2 H); 5.66 (*s*, 2 H); 6.11 (*s*, 1 H); 7.16–8.31 (*m*, 15 H); 8.80–8.82 (*m*, 1 H).^{13}C-NMR: 26.3; 29.6; 30.1; 30.6; 43.1; 44.8; 50.1; 56.3; 64.1; 64.3; 66.1; 78.7; 78.8; 113.1; 121.8; 122.1; 123.2; 125.0; 127.9; 129.3; 129.8; 129.9; 131.6; 131.7; 132.1; 132.7; 133.1; 133.7; 136.5; 136.8; 156.7; 163.0; 166.9; 167.0; 170.2. EI-MS: 683.1 (M^+).

N-*Butyl*-N-*{2-[(tert-butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}-2-[4-({4-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]acetamide* (**4g**). Yield: 103 mg (91%). IR: 2962, 1767, 1650, 1556. ^{1}H-NMR: 0.60–0.64 (*m*, 3 H); 0.91–1.02 (*m*, 2 H); 1.25 (*s*, 9 H); 1.32–1.47 (*m*, 2 H); 5.36 (*s*, 2 H); 5.66 (*s*, 2 H); 6.11 (*s*, 1 H); 7.16–8.31 (*m*, 15 H); 8.82–8.80 (*m*, 1 H). ^{13}C-NMR: 26.3; 29.6; 30.1; 30.6; 43.1; 44.8; 50.1; 55.8; 64.1; 64.3; 66.1; 78.5; 78.8; 115.2; 115.4; 127.7; 129.3; 129.8; 129.9; 130.9; 131.0; 131.5; 131.6; 131.7; 133.4; 133.4; 136.5; 136.8; 159.7; 162.1; 166.9; 167.0; 170. 2. EI-MS: 683.1 (M^+).

N-*Butyl*-N-*{2-[(tert-butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}-2-[4-({2-methoxy-4-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]acetamide* (**4h**). Yield: 59 mg (92%). IR: 3311, 3069, 2960, 2932, 1780, 1585, 1555. ^{1}H-NMR: 0.58–0.68 (*m*, 3 H); 0.91–0.96 (*m*, 2 H); 1.24 (*s*, 9 H); 1.33–1.48 (*m*, 2 H); 3.82–3.85 (*m*, 2 H); 3.89 (*s*, 3 H); 4.92 (*s*, 2 H); 5.29 (*s*, 2 H); 6.10 (*s*, 1 H); 7.18–8.28 (*m*, 14 H); 9.86 (*s*, 1 H). ^{13}C-NMR: 26.3; 29.6; 30.1; 30.6; 43.1; 44.8; 46.7; 50.1; 56.3; 64.1; 66.1; 78.7; 78.8; 113.1; 121.8; 122.1; 123.2; 125.0; 127.9; 129.3; 129.8; 129.9; 131.6; 131.7; 132.1; 132.7; 133.1; 133.7; 136.5; 136.8; 156.7; 163.0; 166.9; 167.0; 170.2. EI-MS: 713.1 (M^+).

*2,2′-[{4-[(*Z*)-(5-Oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]benzene-1,3-diyl}bis(oxymethanediyl-1*H*-1,2,3-triazole-4,1-diyl)]bis(*N-*butyl*-N-*{2-[(tert-butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}acetamide)* (**4i**). Yield: 89 mg (94%). IR: 3069, 2962, 2932, 1786, 1556. ^{1}H-NMR: 0.56–0.69 (*m*, 6 H); 0.91–1.01 (*m*, 4 H); 1.28 (*s*, 18 H); 1.33–1.47 (*m*, 4 H); 4.94 (*s*, 4 H); 5.38 (*s*, 4 H); 6.12 (*s*, 2 H); 6.84–8.33 (*m*, 19 H); 8.82–8.85 (*m*, 2 H). ^{13}C-NMR: 26.3; 29.6; 30.1; 30.6; 43.1; 44.8; 52.4; 56.3; 64.1; 64.3; 66.1; 77.8; 78.8; 113.1; 121.8; 122.1; 123.2; 125.0; 127.9; 129.3; 129.7; 129.8; 131.6; 131.7; 132.1; 132.7; 133.1; 133.7; 136.5; 136.8; 156.7; 163.9; 167.0; 170.2. EI-MS: 1116.1 ($[M+1]^+$).

*2,2′-[{4-[(*Z*)-(5-Oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]benzene-1,2-diyl}bis(oxymethanediyl-1*H*-1,2,3-triazole-4,1-diyl)]bis(*N-*butyl*-N-*{2-[(tert-butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}acetamide)* (**4j**). Yield: 78 mg (86%). IR: 3281, 2929, 1655, 1542. ^{1}H-NMR: 0.56–0.69 (*m*, 6 H); 0.91–1.01 (*m*, 4 H); 1.28 (*s*, 18 H); 1.33–1.47 (*m*, 4 H); 4.94 (*s*, 4 H); 5.38 (*s*, 4 H); 6.12 (*s*, 2 H); 6.84–8.33 (*m*, 19 H); 8.82–8.85 (*m*, 2 H). ^{13}C-NMR: 26.3; 29.6; 30.1; 30.6; 43.1; 44.8; 50.1; 56.3; 64.1; 64.3; 66.1; 78.1; 78.8; 113.1; 121.8; 122.1; 123.2; 125.0; 127.9; 129.3; 129.7; 129.8; 129.9; 131.6; 131.7; 132.1; 132.7; 133.1; 133.7; 136.5; 136.8; 156.7; 163.0; 166.9; 167.0; 170.2. EI-MS: 1116.1 ($[M+1]^+$).

N-*Butyl*-N-*{2-[(tert-butyl)amino]-1-(2-chlorophenyl)-2-oxoethyl}-2-{4-[({1-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]naphthalen-2-yl}oxy)methyl]-1*H*-1,2,3-triazol-1-yl}acetamide* (**4k**). Yield: 81 mg (93%). IR: 3080, 1667, 1590, 2929. ^{1}H-NMR: 0.85–0.97 (*m*, 3 H); 1.15–1.18 (*m*, 2 H); 1.23 (*s*, 9 H); 1.52–1.53 (*m*, 2 H); 2.21 (*s*, 2 H); 3.18–3.19 (*m*, 2 H); 5.20 (*s*, 2 H); 6.30 (*s*, 1 H); 7.05–8.07 (*m*, 16 H); 8.23 (*s*, 1 H); 9.09 (*s*, 1 H). ^{13}C-NMR: 26.5; 29.9; 31.4; 41.4; 48.3; 56.0; 62.4; 66.2; 77.8; 78.4; 115.5; 120.3; 127.2; 128.1; 128.4; 129.0; 129.1; 129.6; 129.7; 130.1; 130.5; 133.7; 134.5; 137.7; 156.2; 166.2; 166.4; 169.5. EI-MS: 732.3 (M^+).

*Representative Procedure for the Synthesis of 3-Azido-*N*-[1-(2-chlorophenyl)-3-(4-chlorophenyl)-3-oxopropyl]propanamide* (**6a**). A mixture of 4-chloroacetophenone (0.352 g, 2 mmol), 2-chlorobenzaldehyde (0.282 g, 2 mmol), and 3-bromopropanenitrile (0.268 g, 2 mmol) in MeCN (3 ml) was stirred in the presence of 5 mol-% $CuSO_4$ at r.t. for 8 h. After completion of the reaction (TLC), the mixture was poured into ice-cold H_2O and extracted with CH_2Cl_2 (15 ml). Evaporation of the solvent, followed by purification on silica gel (SiO_2; 100–200 mesh, AcOEt/hexane 3 : 1) afforded pure functionalized bromo β-acetamido ketone **5** (0.678 g, 79%). One mmol of **5** (0.428 g), 3 mmol of K_2CO_3, and 1 mmol of NaN_3 were dissolved in DMA. The mixture was stirred for 6–8 h; after the completion of the reaction, it was poured into ice-cold H_2O, and the precipitate was filtered, washed, and dried in vacuum to afford **6a** (0.385 g, 86%). IR: 3282, 3070, 1685, 1654. ^{1}H-NMR: 2.68–2.71 (*m*, 2 H); 2.81–2.83 (*m*, 1 H); 3.41–3.45 (*m*, 1 H); 3.74–3.78 (*m*, 2 H); 5.84–5.83 (*m*, 1 H); 7.13–7.97 (*m*, 8 H); 8.17 (*s*, 1 H). ^{13}C-NMR: 39.6; 39.7; 41.4; 48.2; 76.8; 77.0; 127.1; 127.9; 128.3; 128.4; 128.9; 129.0; 130.0; 130.3; 132.4; 134.7; 137.6; 141.1; 169.1; 197.5.

*3-Azido-*N*-[1-(2-bromophenyl)-3-(4-bromophenyl)-3-oxopropyl]propanamide* (**6b**). Yield: 0.523 g (98%). IR: 3296, 3066, 2107, 1682, 1645. ^{1}H-NMR: 2.32–2.38 (*m*, 2 H); 3.34 (*t*, J = 19.2, 2 H); 3.35 (*d*, J = 12.4, 1 H); 3.71–3.74 (*m*, 1 H); 5.61–5.66 (*m*, 1 H); 7.18–8.54 (*m*, 8 H); 8.57 (*s*, 1 H). ^{13}C-NMR: 36.1; 39.2; 39.5; 39.7; 43.1; 47.3; 123.9; 125.1; 128.7; 129.4; 129.8; 133.6; 136.0; 140.4; 148.4; 150.6; 172.9; 196.6. EI-MS: 480.8 ($[M+1]^+$).

3-Azido-N-*[1,3-bis(4-chlorophenyl)-3-oxopropyl]propanamide* (**6c**). Yield: 0.455 g (98%). IR: 3296, 3066, 2107, 1682, 1645. ^{1}H-NMR: 2.46 (*t*, *J* = 20, 2 H); 2.67 (*t*, *J* = 15, 2 H); 3.38–3.42 (*m*, 1 H); 5.54 (*s*, 1 H); 6.89–7.84 (*m*, 9 H). ^{13}C-NMR: 35.9; 39.6; 40.1; 42.8; 47.3; 49.4; 76.7; 77.0; 77.2; 133.4; 134.7; 138.9; 139.0; 140.3; 169.0; 169.4; 197.0.

3-Azido-N-*[3-(4-bromophenyl)-1-(4-chlorophenyl)-3-oxopropyl]propanamide* (**6d**). Yield: 0.455 g (99%). IR: 3299, 3067, 2109, 1683, 1649. ^{1}H-NMR: 2.46–2.48 (*m*, 2 H); 2.67–2.69 (*m*, 2 H); 3.37–3.42 (*m*, 1 H); 5.52–5.57 (*m*, 1 H); 6.83–7.77 (*m*, 9 H). ^{13}C-NMR: 36.0; 39.6; 40.1; 42.7; 47.3; 49.4; 77.0; 127.8; 128.8; 128.9; 129.1; 129.6; 132.1; 135.1; 169.8; 197.3.

3-Azido-N-*[3-(4-bromophenyl)-1-(2-chlorophenyl)-3-oxopropyl]propanamide* (**6e**). Yield: 0.456 g (99%). IR: 3296, 3066, 2107, 1682, 1645. ^{1}H-NMR: 2.46–2.48 (*m*, 2 H); 2.67–2.69 (*m*, 2 H); 3.40–3.44 (*m*, 1 H); 5.80–5.85 (*m*, 1 H); 7.09–7.75 (*m*, 9 H). ^{13}C-NMR: 35.9; 39.5; 47.3; 48.1; 76.7; 77.0; 127.1; 127.2; 128.2; 128.3; 128.9; 129.8; 131.4; 131.9; 132.4; 135.1; 137.6; 168.8; 197.7.

Representative Procedure for the Cu^I-Promoted 1,3-Dipolar Cycloaddition Reactions of **1a**–**1c** *and* **1f** *with* **6a**–**6e**. *Synthesis of* N-*[1-(2-Chlorophenyl)-3-(4-chlorophenyl)-3-oxopropyl]-3-[4-({2-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**7a**). Equimolar amounts of **6a** (78 mg, 2 mmol) and **1a** (83 mg, 2 mmol) were dissolved in minimum amount of DMSO. Then, 2 ml of *t*-BuOH, 1 ml of H_2O, 70 mg of $CuSO_4 \cdot 5\ H_2O$, and 83 mg of sodium ascorbate were added, and the mixture was stirred at r.t. After 24 h, the mixture was poured into ice-cold H_2O. The precipitated 'click product' **7a** was filtered, washed with H_2O, and dried under vacuum. Yield: 126 mg (68%). IR: 3297, 3067, 1789, 1684, 1640, 1589, 1557. ^{1}H-NMR: 2.68–2.70 (*m*, 2 H); 3.31–3.33 (*m*, 2 H); 4.74 (*t*, *J* = 13.5, 2 H); 5.10–5.30 (*s*, 2 H); 5.81 (*s*, 1 H); 7.10–7.83 (*m*, 18 H); 8.14–8.16 (*m*, 1 H); 8.81–8.83 (*m*, 1 H). ^{13}C-NMR: 39.6; 39.7; 41.4; 48.2; 56.3; 76.8; 77.0; 78.7; 78.8; 113.1; 121.8; 122.1; 123.2; 125.0; 127.1; 127.9; 128.1; 128.3; 128.4; 129.0; 129.3; 130.0; 130.3; 132.1; 132.4; 132.7; 133.1; 133.7; 134.7; 137.6; 141.1; 156.7; 163.0; 167.0; 169.1; 197.5. EI-MS: 694.2 (M^+).

N-*[1-(2-Bromophenyl)-3-(4-bromophenyl)-3-oxopropyl]-3-[4-({2-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**7b**). Yield: 84 mg (65%). IR: 3298, 3069, 1789, 1681, 1650, 1595, 1557. ^{1}H-NMR: 2.67–2.70 (*m*, 2 H); 3.27–3.31 (*m*, 2 H); 4.71 (*t*, *J* = 11, 2 H); 5.20 (*s*, 2 H); 5.76 (*s*, 1 H); 7.06–7.75 (*m*, 18 H); 8.14–8.16 (*m*, 1 H); 8.82–8.83 (*m*, 1 H). ^{13}C-NMR: 36.1; 39.2; 39.5; 39.7; 43.1; 47.3; 56.3; 78.7; 78.8; 113.1; 121.8; 122.1; 123.2; 123.9; 125.0, 125.1; 127.9; 128.7; 129.3; 129.4; 129.8; 132.1; 132.7; 133.1; 133.6; 133.7; 136.0; 140.4; 148.4; 150.6; 156.7; 163.0; 167.0; 172.9; 196.6. EI-MS: 782.3 (M^+).

N-*[1,3-Bis(4-chlorophenyl)-3-oxopropyl]-3-[4-({2-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)-methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**7c**). Yield: 89 mg (86%). M.p. 80–83°. IR: 3284, 3068, 1580, 1557. ^{1}H-NMR: 2.62–2.68 (*m*, 2 H); 3.26–3.41 (*m*, 2 H); 4.75 (*t*, *J* = 12, 2 H); 5.20 (*s*, 2 H); 5.49–5.53 (*m*, 1 H), 6.84–7.83 (*m*, 17 H); 8.14–8.16 (*m*, 1 H); 8.83–8.84 (*m*, 1 H). ^{13}C-NMR: 55.1; 76.6; 76.9; 77.1; 96.1; 115.3; 128.2; 128.8; 131.4; 133.0; 134.4; 159.9; 167.3. EI-MS: 694.2 ($[M+1]^+$).

N-*[3-(4-Bromophenyl)-1-(4-chlorophenyl)-3-oxopropyl]-3-[4-({2-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**7d**). Yield: 86 mg (85%). M.p. 79–82°. IR: 3296, 3068, 1584, 1557. ^{1}H-NMR: 2.67–2.68 (*m*, 2 H); 3.20–3.40 (*m*, 2 H); 4.60–4.80 (*m*, 2 H); 5.20–5.30 (br. *s*, 2 H); 5.40–5.60 (*m*, 1 H); 6.80–7.77 (*m*, 17 H); 8.14–8.16 (*d*, 1 H); 8.82–8.83 (*m*, 1 H). ^{13}C-NMR: 55.7; 76.8; 77.1; 76.8; 96.0; 115.2; 125.8; 128.1; 128.8; 129.6; 131.3; 131.9; 132.9; 134.3; 159.8. EI-MS: 737.4 (M^+).

N-*[3-(4-Bromophenyl)-1-(2-chlorophenyl)-3-oxopropyl]-3-[4-({2-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**7e**). Yield: 87 mg (85%). M.p. 78–84°. IR: 1649, 1585, 1557. ^{1}H-NMR: 2.62–2.69 (*m*, 2 H); 3.32–3.34 (*m*, 2 H); 4.75 (*t*, *J* = 11, 2 H); 5.21–5.26 (*m*, 1 H); 5.80 (*s*, 2 H); 7.18–7.74 (*m*, 18 H); 8.16 (*s*, 1 H); 8.83 (*s*, 1 H). ^{13}C-NMR: 55.7; 76.6; 76.8; 77.1; 96.0; 115.2; 125.8; 128.1; 128.8; 129.6; 131.3; 131.9; 132.9; 134.3; 159.8. EI-MS: 737.4 (M^+).

N-*[1-(2-Chlorophenyl)-3-(4-chlorophenyl)-3-oxopropyl]-3-[4-({4-[(*Z*)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**8a**). Yield: 113 mg (98%). IR: 3308, 3067, 2916, 1788, 1685, 1652, 1588, 1555. ^{1}H-NMR: 2.59–2.70 (*m*, 2 H); 2.71–2.91 (*m*, 1 H); 3.32–3.33 (*m*, 1 H); 4.69–4.78 (*m*, 2 H); 5.18 (*s*, 2 H); 5.79–5.78 (*m*, 1 H); 7.05–8.23 (*m*, 19 H); 9.89 (*s*, 1 H). ^{13}C-NMR: 39.6; 39.7; 41.4; 48.2; 55.8; 76.8; 77.0; 78.5; 78.8; 115.2; 115.4; 127.1; 127.7; 127.9; 128.3;

128.4; 128.9; 129.0; 129.3; 130.0; 130.3; 130.9; 131.0; 131.6; 132.4; 133.4; 134.4; 134.7; 137.6; 141.1; 159.7; 162.1; 167.0; 169.1; 197.5. EI-MS: 694.2 (M^+).

N-*[1-(2-Bromophenyl)-3-(4-bromophenyl)-3-oxopropyl]-3-[4-({4-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**8b**). Yield: 99 mg (76%). IR: 1785, 1649, 1585, 1556. ^{1}H-NMR: 2.55–2.62 (*m*, 2 H); 3.30–3.40 (*m*, 2 H); 4.77–4.78 (*m*, 2 H); 5.10–5.20 (br. *s*, 2 H); 5.70–5.80 (*m*, 1 H); 7.07–7.60 (*m*, 19 H); 8.17–8.22 (*m*, 1 H). ^{13}C-NMR: 55.7; 76.1; 76.6; 76.9; 77.1; 77.8; 96.1; 115.3; 125.8; 127.3; 128.2; 128.8; 129.6; 131.3; 131.6; 132.0; 132.9; 134.4; 159.9; 167.6. EI-MS: 782.3 (M^+).

N-*[1,3-Bis(4-chlorophenyl)-3-oxopropyl]-3-[4-({4-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)-methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**8c**). Yield: 87 mg (86%). M.p. 142–144°. IR: 3309, 3082, 2923, 1683, 1646, 1556. ^{1}H-NMR: 2.59–2.70 (*m*, 2 H); 2.71–2.91 (*m*, 1 H); 3.32–3.33 (*m*, 1 H); 4.69–4.78 (*m*, 2 H); 5.18 (*s*, 2 H); 5.78–5.79 (*m*, 1 H); 7.05–8.23 (*m*, 19 H); 9.89 (*s*, 1 H). ^{13}C-NMR: 55.1; 76.6; 76.9; 77.1; 96.1; 115.3; 128.2; 128.8; 131.4; 133.0; 134.4; 159.9; 167.3. EI-MS: 694.2 ($[M+1]^+$).

N-*[3-(4-Bromophenyl)-1-(4-chlorophenyl)-3-oxopropyl]-3-[4-({4-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**8d**). Yield: 84 mg (83.5%). M.p. 141–144°. IR: 2919, 1653, 1598, 1585. ^{1}H-NMR: 2.58–2.68 (*m*, 2 H); 3.29–3.30 (*m*, 2 H); 4.69–4.79 (*m*, 2 H); 5.17 (*s*, 2 H); 5.46–5.55 (*m*, 1 H); 6.88–8.18 (*m*, 17 H); 8.21–8.23 (*m*, 1 H), 9.89 (*s*, 1 H). ^{13}C-NMR: 55.7; 76.6; 76.8; 77.1; 96.0; 115.2; 125.8; 128.1; 128.8; 129.6; 131.3; 131.9; 132.9; 134.3; 159.8. EI-MS: 737.4 (M^+).

N-*[3-(4-Bromophenyl)-1-(2-chlorophenyl)-3-oxopropyl]-3-[4-({4-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**8e**). Yield: 86 mg (84%). M.p. 140–142°. IR: 3309, 2924, 1784, 1648, 1585, 1557. ^{1}H-NMR: 2.59–2.68 (*m*, 2 H); 3.28–3.30 (*m*, 2 H); 4.69–4.78 (*m*, 2 H); 5.17 (*s*, 2 H); 5.46–5.55 (*m*, 1 H); 6.88–8.18 (*m*, 17 H); 8.21–8.23 (*m*, 1 H); 9.89 (*s*, 1 H). ^{13}C-NMR: 55.7; 76.6; 76.8; 77.1; 96.0; 115.2; 125.8; 128.1; 128.8; 129.6; 131.3; 131.9; 132.9; 134.3; 159.8. EI-MS: 737.4 (M^+).

N-*[1-(2-Chlorophenyl)-3-(4-chlorophenyl)-3-oxopropyl]-3-[4-({2-methoxy-4-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**9a**). Yield: 104 mg (96%). IR: 3307, 2930, 1788, 1681, 1588. ^{1}H-NMR: 2.67–2.69 (*m*, 2 H); 2.71–2.90 (*m*, 1 H); 3.30 (*d*, *J* = 23, 1 H); 3.96 (*s*, 3 H); 4.85–4.86 (*m*, 2 H); 5.20–5.30 (br. *s*, 2 H); 5.70–5.80 (*m*, 1 H); 7.07–8.13 (*m*, 18 H); 9.80 (*s*, 1 H). ^{13}C-NMR: 36.4; 39.7; 41.4; 56.0; 76.8; 77.1; 109.3; 112.5; 126.8; 127.2; 128.1; 128.4; 129.0; 129.1; 129.2; 129.6; 129.7; 130.1; 130.5; 130.7; 132.5; 134.7; 137.7; 140.4; 197.2. EI-MS: 723.2 (M^+).

N-*[1-(2-Bromophenyl)-3-(4-bromophenyl)-3-oxopropyl]-3-[4-({2-methoxy-4-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**9b**). Yield: 88 mg (81%). M.p. 85–89°. IR: 3296, 2930, 1681, 1651, 1585. ^{1}H-NMR: 2.69–2.91 (*m*, 2 H); 3.77–3.78 (*m*, 1 H); 4.66 (*s*, 3 H); 4.85–4.86 (*t*, 2 H); 5.25 (*s*, 2 H); 5.70–5.80 (*m*, 1 H); 7.07–8.14 (*m*, 18 H); 9.84 (*s*, 1 H). ^{13}C-NMR: 36.4; 39.7; 40.1; 41.4; 50.2; 50.4; 56.0; 77.1; 77.4; 76.8; 112.5; 122.7; 127.8; 128.2; 129.1; 129.2; 129.3; 129.7; 129.8; 132.1; 133.2; 133.4; 135.1; 139.3; 197.5. EI-MS: 811.1 (M^+).

N-*[1,3-Bis(4-chlorophenyl)-3-oxopropyl]-3-[4-({2-methoxy-4-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**9c**). Yield: 87 mg (89%). M.p. 120–124°. IR: 2930, 1677, 1654, 1589. ^{1}H-NMR: 2.66–2.69 (*m*, 2 H); 3.41–3.43 (*m*, 2 H); 3.87 (*s*, 3 H); 4.66–4.86 (*m*, 2 H); 5.24 (*s*, 2 H); 5.40–5.60 (*m*, 1 H); 6.91–8.15 (*m*, 18 H); 9.84 (*s*, 1 H). ^{13}C-NMR: 36.4; 39.6; 40.1; 42.8; 42.9; 46.2; 49.4; 55.9; 76.7; 77.0; 77.3; 126.6; 127.8; 127.9; 128.1; 128.5; 128.8; 129.0; 129.1; 129.4; 129.5; 139.0; 190.9. EI-MS: 723.2 (M^+).

N-*[3-(4-Bromophenyl)-1-(4-chlorophenyl)-3-oxopropyl]-3-[4-({2-methoxy-4-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5*H*)-ylidene)methyl]phenoxy}methyl)-1*H*-1,2,3-triazol-1-yl]propanamide* (**9d**). Yield: 82 mg (81%). M.p. 122–125°. IR: 3297, 3083, 2932, 1681, 1651, 1585. ^{1}H-NMR: 2.66–2.69 (*m*, 2 H); 3.31 (*dd*, *J* = 23, 21, 2 H); 4.03 (*s*, 3 H); 4.66–4.86 (*m*, 2 H); 5.23 (*s*, 2 H); 5.54–5.55 (*m*, 1 H); 6.86–8.17 (*m*, 18 H); 9.84 (*s*, 1 H). ^{13}C-NMR: 36.6; 39.7; 40.2; 42.9; 43.0; 49.5; 55.9; 56.0; 56.6; 77.1; 76.8; 77.4; 113.2; 114.6; 125.8; 127.3; 127.6; 127.9; 128.2; 128.9; 129.1; 129.4; 129.6; 129.7; 130.1; 131.9; 132.2; 133.2; 133.5; 135.0; 139.1; 167.9; 191.0. EI-MS: 768.2 ($[M+1]^+$).

N-*[3-(4-Bromophenyl)-1-(2-chlorophenyl)-3-oxopropyl]-3-[4-({2-methoxy-4-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5H)-ylidene)methyl]phenoxy}methyl)-1H-1,2,3-triazol-1-yl]propanamide* (**9e**). Yield: 84 mg (82%). M.p. 78–80°. IR: 3091, 3069, 2963, 1681, 1651, 1585. ^{1}H-NMR: 2.68–2.71 (*m*, 2 H); 2.88 (*d*, *J* = 21, 1 H); 3.36 (*d*, *J* = 20, 1 H); 4.03 (*s*, 3 H); 4.65–4.86 (*m*, 2 H); 5.25 (*s*, 2 H); 5.76–5.84 (*m*, 1 H); 7.09–8.40 (*m*, 18 H); 9.84 (*s*, 1 H). ^{13}C-NMR: 36.4; 39.7; 40.1; 41.4; 46.2; 48.1; 48.3; 56.0; 56.6; 76.6; 76.8; 77.1; 77.3; 77.4; 112.4; 113.2; 127.2; 128.2; 128.4; 129.0; 129.1; 129.7; 129.8; 130.1; 132.0; 132.1; 132.2; 132.5; 133.2; 135.1; 137.7; 168.6; 191.1; 197.3; 197.9. EI-MS: 768.2 ([*M* + 1]$^+$).

N-*[1-(2-Chlorophenyl)-3-(4-chlorophenyl)-3-oxopropyl]-3-{4-[({1-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5H)-ylidene)methyl]naphthalen-2-yl}oxy)methyl]-1H-1,2,3-triazol-1-yl}propanamide* (**10a**). Yield: 88 mg (83%). IR: 3297, 3247, 3063, 1775, 1671, 1589. ^{1}H-NMR: 2.56 (*t*, *J* = 12.5, 2 H); 3.20–3.30 (*m*, 2 H); 4.85–4.95 (*m*, 2 H); 5.20 (*s*, 2 H); 5.70–5.80 (*m*, 1 H); 7.26–8.07 (*m*, 20 H); 9.26–9.28 (*m*, 1 H); 10.89 (*s*, 1 H). ^{13}C-NMR: 57.3; 76.6; 76.9; 77.1; 96.1; 113.9; 125.2; 125.2; 128.1; 129.8; 137.0; 159.7; 191.6. EI-MS: 743.2 (M^+).

N-*[1-(2-Bromophenyl)-3-(4-bromophenyl)-3-oxopropyl]-3-{4-[({1-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5H)-ylidene)methyl]naphthalen-2-yl}oxy)methyl]-1H-1,2,3-triazol-1-yl}propanamide* (**10b**). Yield: 80 mg (79%). M.p. 80–84°. IR: 2916, 1665, 1587, 1567. ^{1}H-NMR: 2.59–2.69 (*m*, 2 H); 2.71–2.92 (*m*, 2 H); 4.70–4.96 (*m*, 2 H); 5.74 (*s*, 2 H); 5.75–5.78 (*m*, 1 H); 7.05–8.09 (*m*, 20 H); 9.21–9.28 (*m*, 1 H); 10.90 (*s*, 1 H). ^{13}C-NMR: 57.3; 70.1; 76.6; 76.9; 77.1; 96.1; 113.9; 125.2; 125.2; 128.1; 129.1; 129.8; 131.5; 137.0; 161.7; 191.6. EI-MS: 831.4 (M^+).

N-*[1,3-Bis(4-chlorophenyl)-3-oxopropyl]-3-{4-[({1-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5H)-ylidene)methyl]naphthalen-2-yl}oxy)methyl]-1H-1,2,3-triazol-1-yl}propanamide* (**10c**). Yield: 84 mg (86%). M.p. 105–107°. IR: 3255, 2892, 1656, 1590. ^{1}H-NMR: 2.56 (*t*, *J* = 13, 2 H); 3.20–3.34 (*m*, 2 H); 4.87–4.95 (*m*, 2 H); 5.20 (*s*, 2 H); 5.70–5.80 (*m*, 1 H); 7.26–8.07 (*m*, 20 H); 9.26–9.28 (*m*, 1 H); 10.89 (*s*, 1 H). ^{13}C-NMR: 57.3; 70.1; 76.6; 76.9; 77.1; 96.1; 113.9; 125.2; 125.2; 128.1; 129.1; 129.8; 131.5; 137.0; 161.7; 191.6. EI-MS: 743.2 (M^+).

N-*[3-(4-Bromophenyl)-1-(4-chlorophenyl)-3-oxopropyl]-3-{4-[({1-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5H)-ylidene)methyl]naphthalen-2-yl}oxy)methyl]-1H-1,2,3-triazol-1-yl}propanamide* (**10d**). Yield: 79 mg (81%). M.p. 110–113°. IR: 3297, 3083, 1666, 1586. ^{1}H-NMR: 2.56 (*t*, *J* = 12, 2 H); 4.82–4.95 (*m*, 2 H); 5.30 (*s*, 2 H); 5.70–5.80 (*m*, 1 H); 7.26–8.07 (*m*, 20 H); 9.26–9.28 (*m*, 1 H); 10.89 (*s*, 1 H). ^{13}C-NMR: 57.3; 70.1; 76.6; 76.9; 77.1; 96.1; 113.9; 125.2; 125.2; 128.1; 129.1; 129.8; 131.5; 137.0; 161.7; 191.6. EI-MS: 787.2 (M^+).

N-*[3-(4-Bromophenyl)-1-(2-chlorophenyl)-3-oxopropyl]-3-{4-[({1-[(Z)-(5-oxo-2-phenyl-1,3-oxazol-4(5H)-ylidene)methyl]naphthalen-2-yl}oxy)methyl]-1H-1,2,3-triazol-1-yl}propanamide* (**10e**). Yield: 80 mg (80%). M.p. 100–103°. IR: 3295, 3086, 1671, 1589. ^{1}H-NMR: 2.56 (*t*, *J* = 12, 2 H); 4.77–4.95 (*m*, 2 H); 5.30 (*s*, 2 H); 5.70–5.80 (*m*, 1 H); 7.26–8.07 (*m*, 20 H); 9.26–9.28 (*m*, 1 H); 10.89 (*s*, 1 H). ^{13}C-NMR: 57.3; 70.1; 76.6; 77.1; 96.1; 113.9; 125.2; 125.2; 128.1; 129.1; 129.8; 131.5; 137.0; 161.7; 191.6. EI-MS: 787.2 (M^+).

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