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PAPER

Azide–alkyne cycloaddition *en route* towards 1*H*-1,2,3-triazole-tethered β-lactam–ferrocene and β-lactam–ferrocenylchalcone conjugates: synthesis and *in vitro* anti-tubercular evaluation†

Kewal Kumar,[a] Séverine Carrère-Kremer,[b] Laurent Kremer,[b,c] Yann Guérardel,[d,e] Christophe Biot[d,e] and Vipan Kumar*[a]

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A diverse range of triazoles were prepared following well established, Cu-mediated azide–alkyne cycloaddition reactions with the aim of probing the anti-tubercular structure–activity relationships (SAR) within the β-lactam–ferrocene–triazole conjugate family. The anti-tubercular evaluation studies of the synthesized conjugates revealed that none of the scaffolds exhibited any activity that restricted mycobacterial growth even at high doses. The introduction of various substituents onto the N-1 of the β-lactam ring, introducing mono- or di-ferrocenylchalcone substituents at the C-3 position as well as introducing a spacer of varying chain length failed to produce any significant enhancement in the activity profiles. The described protocol was a successful attempt on the inclusion of a ferrocene nucleus in the β-lactam family tethered *via* triazole linkers having metabolic stability and physicochemical favourability.

Despite the availability of highly efficacious treatments and the recent progress in global efforts, tuberculosis (TB) is more prevalent in the world today than at any other time in human history and is still one of the leading causes of morbidity and mortality worldwide. According to the World Health Organization (WHO) report, there were an estimated 8.5–9.2 million cases and 1.2–1.5 million deaths (including deaths from TB among HIV-positive people) in 2010.[1] TB is the second leading cause of death from an infectious disease worldwide (after HIV, which caused an estimated 1.8 million deaths in 2008) in India and China accounting for 40% of the world's notified cases of TB in 2010.[1] *Mycobacterium tuberculosis*, the pathogen responsible for TB, uses diverse strategies to survive in a variety of host lesions and to evade immune surveillance. Even though improved methods of prevention, detection, diagnosis and treatment have greatly reduced the number of people who contract the disease, the emergence of multidrug resistant (MDR), extensively drug-resistant (XDR) tuberculosis as well as its synergism with HIV have amplified the incidence of TB.[2] A recent study by Cegielski *et al*. has revealed that the previous treatment with second line anti-tubercular drugs increased the risk of XDR-TB by more than four times.[3] The slow moving pipeline of anti-tubercular agents and the threat posed by the emergence of MDR- and XDR-TB call for intensified research efforts, not only for the development of new molecular scaffolds but also for the re-engineering and repositioning of some old drug families.

Over the past few years, bioorganometallic chemistry has developed as a rapidly growing and maturing area which links classical organometallic chemistry to biology, medicine, and molecular biotechnology.[4] Organometallic analogues of biologically active compounds have emerged as an important strategy since metallopharmaceuticals offer potential advantages which include the preparation of stable transition metal complexes with predictable structures, the ability to tune ligand affinities according to their electron transfer properties, substitution rates and reduction potentials along with efficient biological targeting.[5] Advances in the rational design of metal-based therapeutic agents have increased after the discovery of cisplatin, which has been the main impetus for the expansion of metal complexes in cancer and other pathologies.[6] The introduction of a ferrocenyl (Fc) moiety into a drug molecule has now been recognized as a useful approach for the development of more effective therapeutic applications *viz.* ferrocenyl-conjugates of commercial anti-estrogen tamoxifen and anti-androgen nilutamide exhibited higher cytotoxicity on breast or prostate cancer cells with respect to the reference drugs.[7] Nolte and co-workers have recently utilized the click chemistry protocol for the insertion of the ferrocenyl moiety into the peptide nucleic acid backbone as well as for the synthesis of ferrocenyl triazole amino acid conjugates.[8,9]

[a]*Department of Chemistry, Guru Nanak Dev University, Amritsar-143005, Punjab, India. E-mail: vipan_org@yahoo.com; Fax: +91-183-2258819-20; Tel: +91-183-2258802 extn.3320*
[b]*Laboratoire de Dynamique des Interactions Membranaires Normales et Pathologiques, UMR 5235 CNRS, Université Montpellier 2I, Place Eugène Bataillon, 34095 Montpellier Cedex 05, France*
[c]*INSERM, DIMNP, Place Eugène Bataillon, 34095 Montpellier Cedex 05, France*
[d]*Université Lille Nord de France, Université de Lille 1, Unité de Glycobiologie Structurale et Fonctionnelle, F-59650 Villeneuve d'Ascq, France*
[e]*CNRS, UMR 8576, F-59650 Villeneuve d'Ascq, France*
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Indeed, the most emblematic example of the contribution of the Fc moiety to the improvement of a drug is that of ferroquine (FQ), a chloroquine (CQ) isostere with an Fc-based side chain that is 22 times more potent than CQ itself and is now under clinical trials.[10] Recently, we have been engaged in the synthesis of quinoline–ferrocene hybrids displaying significant activity (MIC = 2.5–5 μg ml^{-1}) against *M. tuberculosis* while the evaluation of ferroquine (FQ, SSR97193), mainly because of its structural similarity with the synthesized hybrids, revealed moderate inhibitory activity (MIC of 10–15 μg ml^{-1}).[11]

Pélinski *et al*. in a recent report has shown the synthesis and *in vitro* evaluation of a series of twenty five ferrocenyl derivatives including ferrocenyl amides derived from nicotinamide and pyrazinamide, ferrocenyl pyridinyl, quinolyl and acridinylhydrazones displaying interesting antimycobacterial profiles.[12] These examples illustrate that the use of ferrocene-based structural chimeras targeting *M. tuberculosis* may have the prospective of having entirely new metal-specific modes of action that will introduce intricacies for the organism to develop the mechanism of resistance.

Chalcones are naturally occurring derivatives of the parent compound 1,3-diphenyl-2-propen-1-one and belong to the flavonoid family of organic compounds. The appeal of working with chalcones stems from their synthetic accessibility, the various ways the core structure can be diversified and their ability to confer drug-like properties to compound libraries modelled on them.[13] A recent report by Chauhan and co-workers on the synthesis and *in vitro* screenings of quinolinyl chalcones has shown them to possess promising activities with an MIC in the range of 3.12–12.5 μg ml^{-1} against *M. tuberculosis*.[14] The introduction of a ferrocene scaffold into chalcone compounds can add significant changes in biological effects. For example, modification of the structural profiles of ferrocenyl chalcones resulted in enhanced antimalarial activity.[15] Moreover, some ferrocenyl chalcones containing glycoside units have been observed to show *in vitro* antitumor activity on HL-60 human leukemia cells.[16]

β-Lactam antibiotics have continued to be chemotherapeutics of incomparable effectiveness since their introduction, conjugating a broad spectrum of activities with low toxicity.[17] The great vivacity of interest in this field has led to the development of classical β-lactam substrates such as penicillins and cephalosporins together with the non-classical ones such as carbapenems and monobactams.[18] In recent years, the renewed interest is focussed on the synthesis and modification of the β-lactam ring to obtain compounds with diverse pharmacological activities such as cholesterol absorption inhibitory activity; human tryptase, thrombin and chymase inhibitory activity; vasopressin V1a antagonist activity; antidiabetic, antimalarial, anti-inflammatory, antiparkinsonian, anti-tubercular and anti-HIV activity.[17] They are also found to be potent inhibitors of serine protease, human leukocyte elastase and human cytomegalovirus protease, and some of these derivatives are effective on central nervous system and moderately active against several types of cancers.[19]

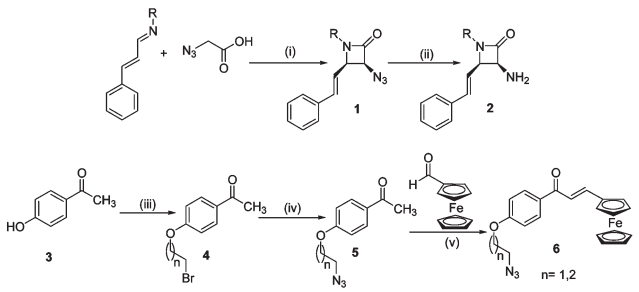
After the introduction of 'click chemistry', the incorporation of 1,2,3-triazoles as attractive linker units between two pharmacophores to give an innovative bifunctional drug has become increasingly useful and important in constructing bioactive molecules and functional molecules.[20] Additionally, many investigations showed that the incorporation of a suitable spacer length as well as variable aromatic substituents have an important effect on the antimicrobial activities.[21]

In continuation of our interest in the synthesis of novel molecular frameworks with biological potentials utilizing molecular hybridization protocols,[22] we have recently disclosed the synthesis and anti-tubercular evaluation of ferrocene–β-lactam and ferrocenylchalcone–β-lactam hybrids.[23] Herein, we provide a detailed insight on the inclusion of a ferrocene nucleus in the well established β-lactam family by exploring Huisgen's azide–alkyne cycloaddition reaction.

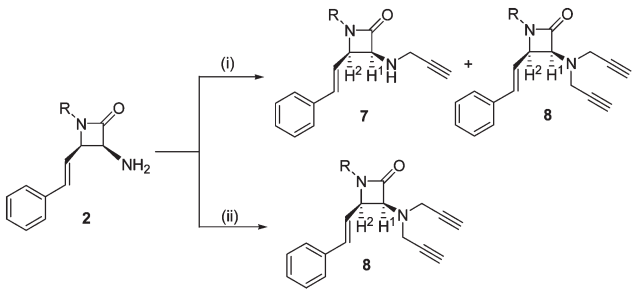
Results and discussion

The desired precursor **2** was prepared *via* our recently reported protocol involving Zn/NH_4Cl mediated reduction of 3-azido-2-azetidinones **1**, which in turn were synthesized by the Staudinger reaction of 1-azadiene with azidoketene, generated *in situ* from azidoacetic acid and *p*-toluenesulphonyl chloride in the presence of triethylamine. The second precursor *viz*. *o*-alkylazido ferrocenylchalcone **6** was prepared following standard synthetic protocols involving base-mediated *o*-alkylation of 4-hydroxyacetophenone **3** with dibromoalkanes followed by treatment with sodium azide in dry DMF resulting in the formation of *o*-alkylazido acetophenones **5** which were subsequently condensed with ferrocene-carboxaldehyde as depicted in Scheme 1.

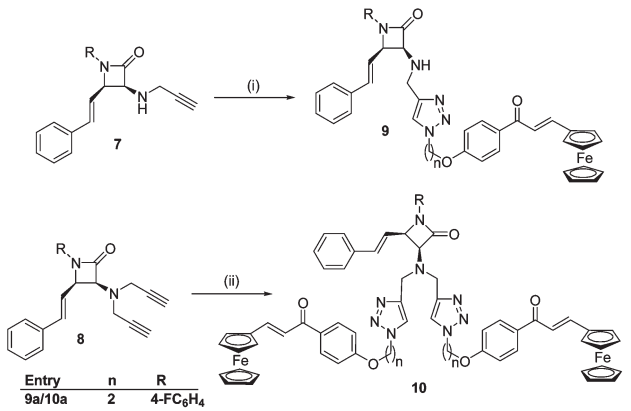
3-Amino-2-azetidinone **2**, required for the synthesis of the desired hybrids, was synthesized through a previously reported procedure.[22] The *N*-alkylation of **2** was carried out using propargyl bromide in anhydrous DMF in the presence of potassium carbonate as a base. Interestingly, the use of 1.1 equiv. of propargyl bromide resulted in the isolation of mono- as well as di-propargylated products in the ratio of 75 : 25, as evidenced by the ^1H NMR analysis of the crude reaction mixture. Both products were isolated using column chromatography eluting with a mixture of EtOAc : hexane (1 : 9 for compound **8** and 3 : 7 for compound **7**). The treatment of **2** with 2.1 equiv. of propargyl bromide resulted in the exclusive isolation of di-propargylated product **8** in good yields. The *cis*-stereochemistry of the products was assigned on the basis of observed coupling constant J = 5.4 Hz between H^1 and H^2 (Scheme 2).



Scheme 1 Reagents and conditions: (i) *p*-toulenesulfonyl chloride (1.2 mmol), Et_3N (2.5 mmol), dry DCM; (ii) Zn, (1.2 mmol)/NH_4Cl (2.1 mmol), $C_2H_5OH : H_2O$ (3 : 1), 60 °C, 2 h; (iii) dibromoalkanes (1.1 mmol), K_2CO_3 (1.5 mmol), acetone, rt, overnight; (iv) NaN_3 (2.2 mmol), DMF, 60 °C, 3 h; (v) 10% NaOH, $C_2H_5OH : H_2O$ (9 : 1), rt, overnight.



Scheme 2 Reagents and conditions: (i) K_2CO_3 (1.2 mmol), propargyl bromide (1.1 mmol), DMF, rt, 6 h; (ii) K_2CO_3 (2.2 mmol), propargyl bromide (2.5 mmol), DMF, rt, 6 h.



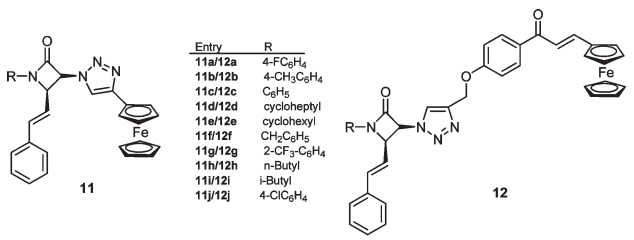
Entry	n	R
9a/10a	2	4-FC_6H_4
9b/10b	2	4-$CH_3C_6H_4$
9c/10c	2	4-ClC_6H_4
9d/10d	2	C_6H_5
9e/10e	2	Cycloheptyl
9f/10f	2	Cyclohexyl
9g/10g	3	4-FC_6H_4
9h/10h	3	4-$CH_3C_6H_4$
9i/10i	3	4-ClC_6H_4
9j/10j	3	C_6H_5
9k/10k	3	Cycloheptyl
9l/10l	3	Cyclohexyl

Scheme 3 Reagents and conditions: (i) **6** (1 mmol), $CuSO_4{\cdot}5H_2O$ (0.05 mmol), sodium ascorbate (0.13 mmol), EtOH : H_2O, rt, 8 h; (ii) **6** (2 mmol), sodium ascorbate (0.26 mmol), $CuSO_4{\cdot}5H_2O$ (0.1 mmol), EtOH : H_2O, rt, 8 h.

Further, precursors **7** and **8** were utilized in the synthesis of desired mono- and bis-1*H*-1,2,3-triazole-tethered β-lactam–ferrocenylchalcone conjugates with a well modulated alkyl chain length as a spacer. Thus the reaction of **7** with **6** (1 mmol) in the presence of copper sulphate and sodium ascorbate in an ethanol–water mixture led to the isolation of **9**, while the reaction of **8** with **6** (2 mmol) under similar conditions led to the formation of **10** in good to excellent yields (Scheme 3). The structures of hybrids **9** and **10** were assigned based on spectral data and analytical evidence. Compound **9b**, for example, showed a molecular ion peak $[M + H]^+$ 718.5275 along with the characteristic peaks in ^1H and ^{13}C NMR spectra. The ^1H NMR spectrum exhibited the presence of a singlet at δ 2.28 corresponding to methyl protons, a singlet at δ 4.16 corresponding to 5H (cyclopentadiene ring of ferrocene), a doublet of doublets at δ 5.72 (J = 5.7, 7.2 Hz) corresponding to H^2 of β-lactam ring proton, another doublet of doublets at δ 6.17 (J = 7.2, 15.9 Hz) corresponding to H^3 of styryl group proton along with a characteristic singlet at δ 7.75 corresponding to the triazole ring proton. The presence of a requisite number of carbons in the ^{13}C NMR spectrum further corroborates the assigned structure.

Table 1 *In vitro* antimycobacterial activity of compounds **9a–l/10a–l** and **11a–j/12a–j** against *M. tuberculosis* mc^{2}7000

Compound	MIC (μg ml^{-1})
9a/10a	>100
9b/10b	>100
9c/10c	>100
9d/10d	>100
9e/10e	>100
9f/10f	>100
9g/10g	>100
9h/10h	>100
9i/10i	>100
9j/10j	>100
9k/10k	>100
9l/10l	>100
11a/12a	>100
11b/12b	>100
11c/12c	>100
11d/12d	>100
11e/12e	>100
11f/12f	>100
11g/12g	>100
11h/12h	>100
11i/12i	>100
11j/12j	>100
Cephalexin	10–25



Entry	R
11a/12a	4-FC_6H_4
11b/12b	4-$CH_3C_6H_4$
11c/12c	C_6H_5
11d/12d	cycloheptyl
11e/12e	cyclohexyl
11f/12f	$CH_2C_6H_5$
11g/12g	2-CF_3-C_6H_4
11h/12h	n-Butyl
11i/12i	i-Butyl
11j/12j	4-ClC_6H_4

Fig. 1 β-lactam–ferrocene **11** and β-lactam–ferrocenylchalcone **12** conjugates.

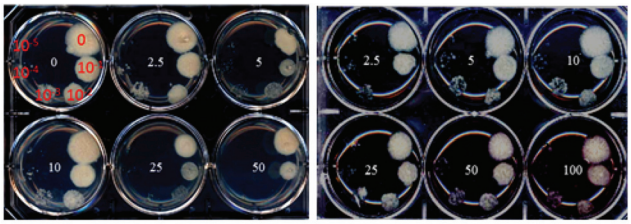
The synthesized chimeric scaffolds were then evaluated for their anti-tubercular profiles and the results are summarized in Table 1. The anti-tubercular evaluation data of our previously reported[23] β-lactam–ferrocene **11** and β-lactam–ferrocenylchalcone **12** conjugates as shown in Fig. 1 have also been included in Table 1 for comparison purposes.

Cephalexin, a β-lactam antimicrobial, was included as a positive control, and found to exhibit an MIC value of 10–25 μg ml^{-1}, consistent with previous findings.[24]

The effects of cephalexin and one representative of the series of the tested chimeric molecules **9i** are depicted in Fig. 2.

Conclusions

The evaluation studies clearly revealed the inability of the synthesized conjugates to restrict the mycobacterial growth even at 100 μg ml^{-1}, the highest doses tested. The introduction of various substituents from aryl to alkyl on the N-1 position of the β-lactam ring, mono-or di-ferrocenylchalcone substituted 1*H*-1,2,3-triazoles at the C-3 position and spacer of varied alkyl



Cephalexin **Ferrocenylchalcone-β-lactam 9i**

Fig. 2 Cephalexin, but neither β-lactam–ferrocene hybrids[23] nor β-lactam–ferrocenylchalcone based hybrids (9i), inhibit *M. tuberculosis* growth. The susceptibility of *M. tuberculosis* was determined on Middlebrook 7H11 solid medium containing OADC enrichment, pantothenic acid with increasing inhibitor concentrations (indicated in white, μg ml^{-1}). Serial 10-fold dilutions (indicated in red on the control plate) of actively growing culture were plated and incubated at 37 °C for 2–3 weeks. The synthesized hybrids were dissolved in DMSO for the assay.

chain length (n = 2 or 3) failed to improve the activity profiles of these structural chimeras. In conclusion, the present manuscript is an extension of our recently reported protocol,[23] providing a detailed insight into the synthesis of mono and bis-1*H*-1,2,3-triazole-tethered β-lactam–ferrocenylchalcone hybrids using click chemistry and their anti-tubercular evaluation. The described protocol is a successful attempt on the inclusion of a ferrocene nucleus in the β-lactam family tethered *via* triazole linkers having metabolic stability and physicochemical favourability.

Experimental

General

Melting points were determined by open capillary using a Veego Precision Digital Melting Point apparatus (MP-D) and are uncorrected. IR spectra were recorded on a Shimadzu D-8001 spectrophotometer. ^{1}H NMR spectra were recorded in deuterochloroform with Jeol 300 (300 MHz) spectrometers using TMS as an internal standard. Chemical shift values are expressed as parts per million downfield from TMS and J values are in hertz. Splitting patterns are indicated as s: singlet, d: doublet, t: triplet, m: multiplet, dd: double of doublets, ddd: doublet of a doublet of doublets, and br: broad peak. ^{13}C NMR spectra were recorded on Jeol 300 (75 MHz) spectrometers in deuterochloroform using TMS as an internal standard. Mass spectra were recorded on a BRUCKER high resolution mass spectrometer (micrOTOF-QII). Column chromatography was performed on silica gel (60–120 mesh) using an ethyl acetate–hexane mixture as an eluent. The precursors for the synthesis of desired molecular conjugates *viz.* **2**,[25] **7** and **8**[22] were prepared *via* our recently reported protocols.

In vitro anti-tubercular activity

Bacterial strains and growth conditions: *M. tuberculosis* mc^{2}7000 an unmarked version[26] of mc^{2}6030 was grown at 37 °C in Sauton's medium supplemented with 20 μg ml^{-1} of pantothenic acid.

Materials and methods

Drug susceptibility testing. The susceptibility of *M. tuberculosis* mc^{2}7000 to the various compounds was determined as reported previously.[27] In brief, Middlebrook 7H10 solid medium containing oleic-albumin-dextrose-catalase enrichment (OADC) and 20 μg ml^{-1} of pantothenic acid was supplemented with increasing concentrations of the chemical analogues. Serial 10-fold dilutions of each actively growing culture were plated and incubated at 37 °C for 2–3 weeks. The MIC was defined as the minimum concentration required to inhibit 99% of the growth.

Procedure for the preparation of β-lactam–ferrocenylchalcone hybrids (9 and 10)

To a stirred solution of azide **6** (1 mmol for **9** and 2 mmol for **10**) in ethanol : water (10 : 1) were added in succession appropriate acetylenic lactam **7** or **8** (1 mmol), copper sulphate (0.055 mmol for **9** and 0.1 mmol for **10**) and sodium ascorbate (0.13 mmol for **9** and 0.26 for **10**) at room temperature. On completion, as monitored by tlc, water (15 ml) was added to the reaction mixture and extracted with chloroform (2 × 50 ml). Combined organic layers were dried over anhydrous sodium sulphate and concentrated under reduced pressure to result in a crude product which was purified by silica gel chromatography using 4 : 6 (EtOAc : hexane) for **9** and 5.5 : 4.5 (EtOAc : hexane) for **10**.

3-[(1-{2-[4-(3-Ferrocenyl-acryloyl)-phenoxy]-ethyl}-1*H* [1,2,3]-triazol-4-ylmethyl)-amino]-1-(4-fluoro-phenyl)-4-styryl-azetidin-2-one (9a). Yield 80%; brick red solid; mp. 112–113 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.16 (s, 5H, H^{13}), 4.37 (s, 2H, H^5), 4.47 (s, 2H, H^{12}), 4.57 (s, 2H, H^{11}), 4.64 (s, 2H, H^7), 4.89 (t, J = 6.0 Hz, –NH, exchangeable with D_2O), 5.16–5.30 (m, 3H, H^1 + H^8), 5.75 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.19 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.71 (d, J = 15.9 Hz, 1H, H^4), 6.93–7.71 (m, 13H, 11ArH + H^9 + H^{10}), 7.76 (s, 1H, triazole-H^6), 7.94 (d, J = 8.4 Hz, 2H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 49.6, 58.6, 60.5, 61.2, 63.3, 69.0, 69.8, 71.4, 79.3, 114.3, 115.8, 115.9, 116.2, 118.7, 118.8, 122.2, 125.1, 126.7, 126.8, 128.7, 128.8, 130.7, 132.4, 135.4, 135.5, 143.1, 146.5, 161.8, 188.4. HRMS (ESI-micrOTOF-QII) calcd for $C_{41}H_{36}FFeN_5O_3$ [M + H]$^+$ 722.3751, found 722.3749.

3-[(1-{2-[4-(3-Ferrocenyl-acryloyl)-phenoxy]-ethyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-4-styryl-1-*p*-tolyl-azetidin-2-one (9b). Yield 81%; brick red solid; mp. 114–115 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.28 (s, 3H, –CH_3), 4.16 (s, 5H, H^{13}), 4.37 (s, 2H, H^5), 4.47 (s, 2H, H^{12}), 4.57 (s, 2H, H^{11}), 4.65 (s, 2H, H^7), 4.90 (t, J = 6.0 Hz, –NH, exchangeable with D_2O), 5.16–5.29 (m, 3H, H^1 + H^8), 5.72 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.17 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.72 (d, J = 15.9 Hz, 1H, H^4), 6.90–7.69 (m, 13H, 11ArH + H^9 + H^{10}), 7.75 (s, 1H, triazole-H^6), 7.95 (d, J = 8.6 Hz, 2H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 21.0, 49.7, 58.6, 60.1, 61.1, 66.3, 69.0, 69.8, 71.4, 79.3, 114.3, 117.2, 118.7, 122.4, 125.3, 126.7, 126.8, 128.8, 128.9, 129.6, 129.7, 130.7, 131.3, 132.4, 134.3, 136.5, 146.3, 146.4, 161.1, 188.6. HRMS (ESI-micrOTOF-QII) calcd for $C_{42}H_{39}FeN_5O_3$ [M + H]$^+$ 718.5279, found 718.5275.

3-[(1-{2-[4-(3-Ferrocenyl-acryloyl)-phenoxy]-ethyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-(4-chloro-phenyl)-4-styryl-azetidin-2-one (9c). Yield 79%; brick red solid; mp. 117–118 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.14 (s, 5H, H^{13}), 4.36 (s, 2H, H^5), 4.46 (s, 2H, H^{12}), 4.58 (s, 2H, H^{11}), 4.63 (s, 2H, H^7), 4.88 (t, J = 6.0 Hz, –NH, exchangeable with D_2O), 5.14–5.31 (m, 3H, H^1 + H^8), 5.71 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.17 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.73 (d, J = 15.9 Hz, 1H, H^4), 6.89–7.67 (m, 13H, 11ArH + H^9 + H^{10}), 7.76 (s, 1H, triazole-H^6), 7.96 (d, J = 8.4 Hz, 2H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 49.4, 58.5, 60.3, 61.1, 63.5, 69.2, 69.6, 71.5, 79.7, 114.4, 115.6, 115.8, 116.5, 118.4, 118.6, 122.4, 125.2, 126.6, 128.3, 128.5, 128.9, 130.5, 132.3, 135.2, 135.4, 143.5, 146.3, 161.2, 188.9. HRMS (ESI-micrOTOF-QII) calcd for $C_{41}H_{36}ClFeN_5O_3$ $[M + H]^+$ 738.6192, found 738.6184.

3-[(1-{2-[4-(3-Ferrocenyl-acryloyl)-phenoxy]-ethyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-phenyl-4-styryl-azetidin-2-one (9d). Yield 82%; brick red solid; mp. 116–117 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.14 (s, 5H, H^{13}), 4.35 (s, 2H, H^5), 4.48 (s, 2H, H^{12}), 4.55 (s, 2H, H^{11}), 4.63 (s, 2H, H^7), 4.92 (t, J = 6.0 Hz, –NH, exchangeable with D_2O), 5.14–5.28 (m, 3H, H^1 + H^8), 5.70 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.19 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.74 (d, J = 15.9 Hz, 1H, H^4), 6.93–7.66 (m, 14H, 12ArH + H^9 + H^{10}), 7.78 (s, 1H, triazole-H^6), 7.93 (d, J = 8.6 Hz, 2H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 49.4, 58.8, 60.6, 66.3, 69.8, 69.9, 71.5, 76.8, 79.6, 114.9, 117.3, 118.6, 126.7, 126.8, 126.9, 128.3, 128.5, 128.7, 129.5, 129.7, 130.5, 131.9, 132.7, 134.8, 136.8, 146.4, 146.6, 161.8, 188.4. HRMS (ESI-micrOTOF-QII) calcd for $C_{41}H_{37}FeN_5O_3$ $[M + H]^+$ 704.6415, found 704.6411.

3-[(1-{2-[4-(3-Ferrocenyl-acryloyl)-phenoxy]-ethyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-cycloheptyl-4-styryl-azetidin-2-one (9e). Yield 79%; brick red solid; mp. 115–116 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.33–2.26 (m, 12H, cycloheptyl); 3.55–3.59 (m, 1H, cycloheptyl H), 4.16 (s, 5H, H^{13}), 4.39 (s, 2H, H^5), 4.46 (s, 2H, H^{12}), 4.58 (s, 2H, H^{11}), 4.63 (s, 2H, H^7), 4.92 (t, J = 6.0 Hz, –NH, exchangeable with D_2O), 5.14–5.29 (m, 3H, H^1 + H^8), 5.71 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.16 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.72 (d, J = 15.9 Hz, 1H, H^4), 6.93–7.68 (m, 9H, 7ArH + H^9 + H^{10}), 7.77 (s, 1H, triazole-H^6), 7.94 (d, J = 8.6 Hz, 2H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 23.6, 28.4, 32.7, 48.6, 49.7, 58.5, 60.2, 66.7, 69.2, 69.5, 71.1, 76.4, 79.7, 114.9, 117.4, 118.6, 126.3, 126.5, 126.8, 128.2, 129.5, 131.9, 132.5, 134.8, 136.6, 146.4, 146.8, 161.9, 188.5. HRMS (ESI-micrOTOF-QII) calcd for $C_{42}H_{45}FeN_5O_3$ $[M + H]^+$ 724.5272, found 724.5267.

3-[(1-{2-[4-(3-Ferrocenyl-acryloyl)-phenoxy]-ethyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-cyclohexyl-4-styryl-azetidin-2-one (9f). Yield 82%; brick red solid; mp. 116–117 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.43–2.25 (m, 10H, cyclohexyl); 3.52–3.55 (m, 1H, cyclohexyl H), 4.17 (s, 5H, H^{13}), 4.37 (s, 2H, H^5), 4.45 (s, 2H, H^{12}), 4.58 (s, 2H, H^{11}), 4.67 (s, 2H, H^7), 4.91 (t, J = 6.0 Hz, –NH, exchangeable with D_2O), 5.11–5.27 (m, 3H, H^1 + H^8), 5.74 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.17 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.71 (d, J = 15.9 Hz, 1H, H^4), 6.91–7.66 (m, 9H, 7ArH + H^9 + H^{10}), 7.75 (s, 1H, triazole-H^6), 7.94 (d, J = 8.4 Hz, 2H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 22.1, 27.3, 31.5, 47.4, 49.6, 58.7, 60.4, 66.5, 69.6, 69.8, 71.2, 76.7, 79.3, 114.8, 117.1, 118.5, 126.2, 126.4, 126.7, 128.6, 129.2, 131.8, 132.4, 134.6, 136.9, 146.1, 146.9, 161.4, 188.3. HRMS (ESI-micrOTOF-QII) calcd for $C_{41}H_{43}FeN_5O_3$ $[M + H]^+$ 710.7537, found 710.7531.

3-[(1-{3-[4-(3-Ferrocenyl-acryloyl)-phenoxy]-propyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-(4-fluoro-phenyl)-4-styryl-azetidin-2-one (9g). Yield 85%; brick red solid; mp. 118–119 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.34–2.36 (m, 2H, H^8), 4.00 (s, 2H, H^5), 4.16 (s, 5H, H^{13}), 4.46 (s, 4H, H^7 + H^{14}), 4.58 (s, 2H, H^{12}), 4.89 (t, J = 6.0 Hz, –NH, exchangeable with D_2O), 5.15–5.28 (m, 3H, H^1 + H^9), 5.81 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.20 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.74 (d, J = 15.9 Hz, 1H, H^4), 6.89–6.98 (m, 4H, –ArH), 7.14 (d, J = 15.9 Hz, 1H, H^{10}), 7.25–7.55 (m, 7H, –ArH), 7.64 (s, 1H, triazole-H^6), 7.72 (d, J = 15.9 Hz, 1H, H^{11}), 7.98 (d, J = 8.9 Hz, 2H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.2, 47.0, 58.7, 60.5, 64.3, 69.0, 69.8, 71.3, 71.8, 79.4, 114.2, 115.9, 116.2, 118.7, 118.8, 122.5, 124.4, 126.7, 126.8, 128.7, 128.8, 130.7, 131.9, 132.7, 135.5, 136.8, 143.0, 146.2, 161.9, 188.2. HRMS (ESI-micrOTOF-QII) calcd for $C_{42}H_{38}FFeN_5O_3$ $[M + H]^+$ 736.1041, found 736.1037.

3-[(1-{3-[4-(3-Ferrocenyl-acryloyl)-phenoxy]-propyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-4-styryl-1-p-tolyl-azetidin-2-one (9h). Yield 84%; brick red solid; mp. 112–113 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.30–2.34 (m, 2H, H^8), 2.32 (s, 3H, $–CH_3$), 4.01 (s, 2H, H^5), 4.17 (s, 5H, H^{13}), 4.44 (s, 4H, H^7 + H^{14}), 4.59 (s, 2H, H^{12}), 4.88 (t, J = 6.0 Hz, –NH, exchangeable with D_2O), 5.16–5.27 (m, 3H, H^1 + H^9), 5.80 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.22 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.75 (d, J = 15.9 Hz, 1H, H^4), 6.86–6.95 (m, 4H, –ArH), 7.13 (d, J = 15.9 Hz, 1H, H^{10}), 7.23–7.53 (m, 7H, –ArH), 7.62 (s, 1H, triazole-H^6), 7.71 (d, J = 15.9 Hz, 1H, H^{11}), 7.98 (d, J = 8.9Hz, 2H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.5, 21.4, 47.6, 58.4, 60.3, 64.7, 69.3, 69.5, 71.6, 71.8, 79.7, 114.1, 115.5, 116.4, 118.6, 118.7, 122.3, 124.5, 126.6, 126.9, 128.5, 128.9, 130.5, 131.8, 132.4, 135.6, 136.9, 143.2, 146.1, 161.4, 188.1. HRMS (ESI-micrOTOF-QII) calcd for $C_{43}H_{41}FeN_5O_3$ $[M + H]^+$ 732.0409, found 732.0401.

3-[(1-{3-[4-(3-Ferrocenyl-acryloyl)-phenoxy]-propyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-(4-chloro-phenyl)-4-styryl-azetidin-2-one (9i). Yield 80%; brick red solid; mp. 119–120 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.32–2.36 (m, 2H, H^8), 4.02 (s, 2H, H^5), 4.14 (s, 5H, H^{13}), 4.48 (s, 4H, H^7 + H^{14}), 4.59 (s, 2H, H^{12}), 4.88 (t, J = 6.0 Hz, –NH, exchangeable with D_2O), 5.17–5.29 (m, 3H, H^1 + H^9), 5.80 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.21 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.73 (d, J = 15.9 Hz, 1H, H^4), 6.88–6.96 (m, 4H, –ArH), 7.14 (d, J = 15.9 Hz, 1H, H^{10}), 7.23–7.54 (m, 7H, –ArH), 7.66 (s, 1H, triazole-H^6), 7.74 (d, J = 15.9 Hz, 1H, H^{11}), 7.96 (d, J = 8.9 Hz, 2H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.1, 47.4, 58.5, 60.3, 64.7, 69.3, 69.9, 71.5, 71.9, 79.6, 114.3, 115.8, 116.3, 118.6, 118.9, 122.3, 124.5, 126.6, 126.9, 128.5, 128.9, 130.5, 131.7, 132.6, 135.4, 136.6, 143.3, 146.4, 161.8, 188.1. HRMS (ESI-micrOTOF-QII) calcd for $C_{42}H_{38}ClFeN_5O_3$ $[M + H]^+$ 752.0713, found 752.0710.

3-[(1-{3-[4-(3-Ferrocenyl-acryloyl)-phenoxy]-propyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-phenyl-4-styryl-azetidin-2-one (9j). Yield 80%; brick red solid; mp. 110–111 °C; ^{1}H NMR ($CDCl_3$,

300 MHz): δ 2.31–2.37 (m, 2H, H^8), 4.01 (s, 2H, H^5), 4.14 (s, 5H, H^{13}), 4.47 (s, 4H, H^7 + H^{14}), 4.57 (s, 2H, H^{12}), 4.87 (t, J = 6.0 Hz, –NH, exchangeable with D_2O), 5.15–5.27 (m, 3H, H^1 + H^9), 5.83 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.21 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.72 (d, J = 15.9 Hz, 1H, H^4), 6.88–6.96 (m 4H, –ArH), 7.12 (d, J = 15.9 Hz, 1H, H^{10}), 7.23–7.51 (m, 8H, –ArH), 7.63 (s, 1H, triazole-H^6), 7.75 (d, J = 15.9 Hz, 1H, H^{11}), 7.97 (d, J = 8.9 Hz, 2H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.4, 47.3, 58.6, 60.1, 64.8, 69.2, 69.8, 71.4, 71.8, 79.2, 114.6, 115.5, 116.7, 118.1, 118.5, 122.6, 124.2, 126.6, 126.8, 128.3, 128.8, 130.3, 131.5, 132.8, 135.7, 136.9, 143.4, 146.2, 161.6, 188.2. HRMS (ESI-micrOTOF-QII) calcd for $C_{42}H_{39}FeN_5O_3$ $[M + H]^+$ 718.4291, found 718.4288.

3-[(1-{3-[4-(3-Ferrocenyl-acryloyl)-phenoxy]-propyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-cycloheptyl-4-styryl-azetidin-2-one (9k). Yield 81%; brick red solid; mp. 118–119 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.37–2.33 (m, 14H, H^8 + cycloheptyl); 3.53–3.55 (m, 1H, cycloheptyl H), 4.01 (s, 2H, H^5), 4.16 (s, 5H, H^{13}), 4.45 (s, 4H, H^7 + H^{14}), 4.56 (s, 2H, H^{12}), 4.87 (t, J = 6.0 Hz, –NH, exchangeable with D_2O), 5.16–5.29 (m, 3H, H^1 + H^9), 5.83 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.21 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.75 (d, J = 15.9 Hz, 1H, H^4), 6.87–6.95 (m, 2H, –ArH), 7.16 (d, J = 15.9 Hz, 1H, H^{10}), 7.24–7.49 (m, 5H, –ArH), 7.62 (s, 1H, triazole-H^6), 7.70 (d, J = 15.9 Hz, 1H, H^{11}), 7.97 (d, J = 8.4 Hz, 2H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.2, 22.5, 27.7, 31.9, 47.3, 49.4, 58.7, 60.2, 66.5, 69.6, 69.9, 71.2, 76.6, 79.8, 114.2, 117.1, 118.7, 126.2, 126.5, 126.7, 128.5, 129.9, 131.5, 132.0, 134.2, 136.4, 146.2, 146.6, 161.2, 188.6. HRMS (ESI-micrOTOF-QII) calcd for $C_{43}H_{47}FeN_5O_3$ $[M + H]^+$ 738.2419, found 738.2416.

3-[(1-{3-[4-(3-Ferrocenyl-acryloyl)-phenoxy]-propyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-cyclohexyl-4-styryl-azetidin-2-one (9l). Yield 83%; brick red solid; mp. 113–114 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.46–2.32 (m, 12H, H^8 + cyclohexyl), 3.54–3.55 (m, 1H, cyclohexyl H), 4.02 (s, 2H, H^5), 4.17 (s, 5H, H^{13}), 4.47 (s, 4H, H^7 + H^{14}), 4.59 (s, 2H, H^{12}), 4.88 (t, J = 6.0 Hz, –NH, exchangeable with D_2O), 5.14–5.28 (m, 3H, H^1 + H^9), 5.81 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.22 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.72 (d, J = 15.9 Hz, 1H, H^4), 6.87–6.99 (m, 2H, –ArH), 7.13 (d, J = 15.9 Hz, 1H, H^{10}), 7.26–7.49 (m, 5H, –ArH), 7.64 (s, 1H, triazole-H^6), 7.73 (d, J = 15.9 Hz, 1H, H^{11}), 7.99 (d, J = 8.9 Hz, 2H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.4, 22.2, 27.4, 31.6, 47.4, 49.7, 58.3, 60.5, 66.9, 69.0, 69.8, 71.5, 76.2, 79.5, 114.5, 117.1, 118.0, 126.0, 126.1, 126.6, 128.1, 129.7, 131.9, 132.2, 134.7, 136.8, 146.5, 146.6, 161.6, 188.1. HRMS (ESI-micrOTOF-QII) calcd for $C_{42}H_{45}FeN_5O_3$ $[M + H]^+$ 724.1053, found 724.1047.

3-[Bis-(1-{2-[4-(3-ferrocenyl-acryloyl)-phenoxy]-ethyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-(4-fluoro-phenyl)-4-styryl-azetidin-2-one (10a). Yield 82%; brick red solid; mp. 107–108 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.01 (s, 4H, H^5), 4.14 (s, 10H, H^{13}), 4.36 (s, 4H, H^7), 4.48 (s, 4H, H^{12}), 5.51–5.24 (m, 4H, H^8), 4.56 (s, 4H, H^{11}), 4.75 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 4.96 (d, J = 5.1 Hz, 1H, H^1) 6.24 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.66 (d, J = 15.9 Hz, 1H, H^4), 6.90 (d, J = 8.6 Hz, 4H, –ArH), 7.10 (d, J = 15.9 Hz, 2H, H^9), 7.23–7.37 (m, 9H, –ArH), 7.71 (d, J = 15.9 Hz, 2H, H^{10}), 7.87 (s, 2H, triazole-H^6), 7.95 (d, J = 8.6 Hz, 4H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 45.4, 49.6, 58.3, 62.2, 66.1, 69.3, 69.4, 71.8, 79.4, 114.1, 117.7, 118.5, 124.8, 126.9, 128.5, 129.7, 130.4, 132.6, 133.3, 134.7, 135.3, 135.6, 138.2, 138.5, 139.9, 143.5, 146.4, 161.2, 188.7. HRMS (ESI-micrOTOF-QII) calcd for $C_{65}H_{57}FFe_2N_8O_5$ $[M + H]^+$ 1161.3211, found 1161.3206.

3-[Bis-(1-{2-[4-(3-ferrocenyl-acryloyl)-phenoxy]-ethyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-4-styryl-1-p-tolyl-azetidin-2-one (10b). Yield 83%; brick red solid; mp. 105–106 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.27 (s, 3H, $–CH_3$), 4.00 (s, 4H, H^5), 4.16 (s, 10H, H^{13}), 4.34 (s, 4H, H^7), 4.46 (s, 4H, H^{12}), 4.50–4.52 (m, 4H, H^8), 4.57 (s, 4H, H^{11}), 4.76 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 4.97 (d, J = 5.1 Hz, 1H, H^1), 6.26 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.64 (d, J = 15.9 Hz, 1H, H^4), 6.91 (d, J = 8.6 Hz, 4H, –ArH), 7.09 (d, J = 15.9 Hz, 2H, H^9), 7.25–7.34 (m, 9H, –ArH), 7.72 (d, J = 15.9 Hz, 2H, H^{10}), 7.86 (s, 2H, triazole-H^6), 7.97 (d, J = 8.6 Hz, 4H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 21.0, 45.3, 49.4, 58.5, 62.2, 66.3, 69.0, 69.8, 71.3, 79.3, 114.3, 117.2, 118.8, 124.9, 126.7, 128.8, 129.6, 130.7, 132.3, 133.8, 134.9, 135.0, 135.4, 138.5, 138.6, 139.8, 143.9, 146.7, 161.3, 188.0. HRMS (ESI-micrOTOF-QII) calcd for $C_{66}H_{60}Fe_2N_8O_5$ $[M + H]^+$ 1157.1352, found 1157.1348.

3-[Bis-(1-{2-[4-(3-ferrocenyl-acryloyl)-phenoxy]-ethyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-(4-chloro-phenyl)-4-styryl-azetidin-2-one (10c). Yield 83%; brick red solid; mp. 102–103 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.02 (s, 4H, H^5), 4.15 (s, 10H, H^{13}), 4.33 (s, 4H, H^7), 4.47 (s, 4H, H^{12}), 4.50–4.53 (m, 4H, H^8), 4.57 (s, 4H, H^{11}), 4.74 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 4.98 (d, J = 5.1 Hz, H^1), 6.27 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.63 (d, J = 15.9 Hz, 1H, H^4), 6.93 (d, J = 8.6 Hz, 4H, –ArH), 7.07 (d, J = 15.9 Hz, 2H, H^9), 7.24–7.37 (m, 9H, –ArH), 7.74 (d, J = 15.9 Hz, 2H, H^{10}), 7.84 (s, 2H, triazole-H^6), 7.96 (d, J = 8.6 Hz, 4H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 45.2, 49.4, 58.2, 62.3, 66.4, 69.5, 69.7, 71.6, 79.3, 114.4, 117.6, 118.3, 124.6, 126.7, 128.3, 129.6, 130.2, 132.4, 133.1, 134.4, 135.2, 135.5, 138.1, 138.5, 139.6, 143.2, 146.6, 161.5, 188.4. HRMS (ESI-micrOTOF-QII) calcd for $C_{65}H_{57}ClFe_2N_8O_5$ $[M + H]^+$ 1177.5307, found 1177.5302.

3-[Bis-(1-{2-[4-(3-ferrocenyl-acryloyl)-phenoxy]-ethyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-phenyl-4-styryl-azetidin-2-one (10d). Yield 85%; brick red solid; mp. 114–115 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.03 (s, 4H, H^5), 4.17 (s, 10H, H^{13}), 4.36 (s, 4H, H^7), 4.45 (s, 4H, H^{12}), 4.51–4.54 (m, 4H, H^8), 4.57 (s, 4H, H^{11}), 4.77 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 4.95 (d, J = 5.1 Hz, 1H, H^1), 6.23 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.75 (d, J = 15.9 Hz, 1H, H^4), 6.90 (d, J = 8.6 Hz, 4H, –ArH), 7.08 (d, J = 15.9 Hz, 2H, H^9), 7.23–7.37 (m, 10H, –ArH), 7.73 (d, J = 15.9 Hz, 2H, H^{10}), 7.87 (s, 2H, triazole-H^6), 7.98 (d, J = 8.4 Hz, 4H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 49.6, 58.7, 60.3, 66.7, 69.5, 69.6, 71.4, 76.6, 79.3, 114.7, 117.2, 118.7, 126.2, 126.4, 126.7, 128.1, 128.4, 128.9, 129.4, 129.9, 130.8, 131.7, 132.8, 134.6, 136.4, 146.6, 146.8, 161.7, 188.9. HRMS (ESI-micrOTOF-QII) calcd for $C_{65}H_{58}Fe_2N_8O_5$ $[M + H]^+$ 1143.6244, found 1143.6437.

3-[Bis-(1-{2-[4-(3-ferrocenyl-acryloyl)-phenoxy]-ethyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-cycloheptyl-4-styryl-azetidin-2-one

(10e). Yield 78%; brick red solid; mp. 102–103 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.34–2.24 (m, 12H, cycloheptyl); 3.51–3.56 (m, 1H, cycloheptyl H), 4.03 (s, 4H, H^5), 4.18 (s, 10H, H^{13}), 4.35 (s, 4H, H^7), 4.46 (s, 4H, H^{12}), 4.52–4.55 (m, 4H, H^8), 4.55 (s, 4H, H^{11}), 4.73 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 4.95 (d, J = 5.1 Hz, 1H, H^1), 6.25 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.66 (d, J = 15.9 Hz, 1H, H^4), 6.90 (d, J = 8.6 Hz, 4H, –ArH), 7.10 (d, J = 15.9 Hz, 2H, H^9), 7.23–7.32 (m, 5H, –ArH), 7.75 (d, J = 15.9 Hz, 2H, H^{10}), 7.83 (s, 2H, triazole-H^6), 7.95 (d, J = 8.6 Hz, 4H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 23.5, 28.7, 32.6, 48.8, 49.5, 58.7, 60.1, 66.4, 69.3, 69.7, 71.0, 76.2, 79.5, 114.6, 117.1, 118.3, 126.3, 126.5, 126.6, 128.1, 129.3, 131.4, 132.2, 134.6, 136.8, 146.1, 146.5, 161.6, 188.7. HRMS (ESI-micrOTOF-QII) calcd for $C_{66}H_{67}Fe_2N_8O_5$ $[M + H]^+$ 1162.8946, found 1162.8940.

3-[Bis-(1-{2-[4-(3-ferrocenyl-acryloyl)-phenoxy]-ethyl}-1*H*-[1,2,3]-triazol-4-ylmethyl)-amino]-1-cyclohexyl-4-styryl-azetidin-2-one (10f). Yield 81%; brick red solid; mp. 103–104 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.44–2.23 (m, 10H, cyclohexyl); 3.51–3.53 (m, 1H, cyclohexyl H), 4.00 (s, 4H, H^5), 4.15 (s, 10H, H^{13}), 4.33 (s, 4H, H^7), 4.47 (s, 4H, H^{12}), 4.51–4.54 (m, 4H, H^8), 4.55 (s, 4H, H^{11}), 4.75 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 4.96 (d, J = 5.1 Hz, 1H, H^1), 6.27 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.62 (d, J = 15.9 Hz, 1H, H^4), 6.94 (d, J = 8.6 Hz, 4H, –ArH), 7.08 (d, J = 15.9 Hz, 2H, H^9), 7.24–7.36 (m, 5H, –ArH), 7.69 (d, J = 15.9 Hz, 2H, H^{10}), 7.83 (s, 2H, triazole-H^6), 7.96 (d, J = 8.6 Hz, 4H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 22.3, 27.6, 31.7, 47.5, 49.8, 58.4, 60.3, 66.8, 69.2, 69.7, 71.0, 76.3, 79.6, 114.7, 117.3, 118.4, 126.2, 126.3, 126.7, 128.2, 129.6, 131.7, 132.6, 134.4, 136.6, 146.3, 146.8, 161.1, 188.8. HRMS (ESI-micrOTOF-QII) calcd for $C_{65}H_{64}Fe_2N_8O_5$ $[M + H]^+$ 1148.1147, found 1148.1142.

3-[Bis-(1-{3-[4-(3-ferrocenyl-acryloyl)-phenoxy]-propyl}-1*H*-[1,2,3]triazol-4-ylmethyl)-amino]-1-(4-fluoro-phenyl)-4-styryl-azetidin-2-one (10g). Yield 81%; brick red solid; mp. 104–105 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.32–2.37 (m, 4H, H^8), 4.03 (s, 4H, H^5), 4.14 (s, 10H, H^{13}), 4.47 (s, 8H, H^7 + H^{14}), 4.57 (s, 4H, H^{12}), 5.13–5.29 (m, 5H, H^1 + H^9), 5.82 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.22 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.76 (d, J = 15.9 Hz, 1H, H^4), 6.88–6.99 (m, 8H, –ArH), 7.12 (d, J = 15.9 Hz, 2H, H^{10}), 7.27–7.58 (m, 5H, –ArH), 7.65 (s, 2H, triazole-H^6), 7.73 (d, J = 15.9 Hz, 2H, H^{11}), 7.97 (d, J = 8.9 Hz, 4H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.5, 45.3, 49.4, 58.6, 62.7, 66.4, 69.1, 69.6, 71.9, 79.8, 114.3, 117.5, 118.4, 124.7, 126.5, 128.4, 129.4, 130.6, 132.5, 133.3, 134.6, 135.5, 135.7, 138.1, 138.6, 139.8, 143.2, 146.7, 161.2, 188.3. HRMS (ESI-micrOTOF-QII) calcd for $C_{67}H_{61}FFe_2N_8O_5$ $[M + H]^+$ 1189.2590, found 1189.2584.

3-[Bis-(1-{3-[4-(3-ferrocenyl-acryloyl)-phenoxy]-propyl}-1*H*-[1,2,3]triazol-4-ylmethyl)-amino]-4-styryl-1-p-tolyl-azetidin-2-one (10h). Yield 80%; brick red solid; mp. 104–105 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.91–2.24 (m, 2H, H^8), 2.35 (s, 3H, $-CH_3$), 4.02 (s, 4H, H^5), 4.14 (s, 10H, H^{13}), 4.45 (s, 8H, H^7 + H^{14}), 4.51 (s, 4H, H^{12}), 5.12–5.28 (m, 5H, H^1 + H^9), 5.76 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.24 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.74 (d, J = 15.9 Hz, 1H, H^4), 6.89–6.97 (m, 5H, –ArH), 7.14 (d, J = 15.9 Hz, 2H, H^{10}), 7.25–7.56 (m, 8H, –ArH), 7.73 (d, J = 15.9 Hz, 2H, H^{11}), 7.91 (s, 2H, triazole-H^6), 7.93 (d, J = 9.0 Hz, 4H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.3, 21.5, 47.4, 58.5, 60.1, 64.8, 69.2, 69.5, 71.7, 71.9, 79.6, 114.4, 115.7, 116.6, 118.2, 118.8, 122.2, 124.2, 126.1, 126.3, 128.6, 128.8, 130.7, 131.6, 132.3, 135.4, 136.4, 143.1, 146.4, 161.5, 188.5. HRMS (ESI-micrOTOF-QII) calcd for $C_{68}H_{64}Fe_2N_8O_5$ $[M + H]^+$ 1185.6373, found 1185.6369.

3-[Bis-(1-{3-[4-(3-ferrocenyl-acryloyl)-phenoxy]-propyl}-1*H*-[1,2,3]triazol-4-ylmethyl)-amino]-1-(4-chloro-phenyl)-4-styryl-azetidin-2-one (10i). Yield 84%; brick red solid; mp. 101–102 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.33–2.39 (m, 4H, H^8), 4.04 (s, 4H, H^5), 4.12 (s, 10H, H^{13}), 4.45 (s, 8H, H^7 + H^{14}), 4.56 (s, 4H, H^{12}), 5.11–5.31 (m, 5H, H^1 + H^9), 5.81(dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.21 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.78 (d, J = 15.9 Hz, 1H, H^4), 6.86–6.97 (m, 8H, –ArH), 7.14 (d, J = 15.9 Hz, 2H, H^{10}), 7.26–7.55 (m, 5H, –ArH), 7.66 (s, 2H, triazole-H^6), 7.74 (d, J = 15.9 Hz, 2H, H^{11}), 7.98 (d, J = 8.9 Hz, 4H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.3, 45.4, 49.6, 58.5, 62.4, 66.7, 69.3, 69.5, 71.8, 79.9, 114.2, 117.4, 118.1, 124.6, 126.4, 128.6, 129.5, 130.3, 132.2, 133.7, 134.3, 135.5, 135.7, 138.5, 138.8, 139.6, 143.0, 146.5, 161.5, 188.9. HRMS (ESI-micrOTOF-QII) calcd for $C_{67}H_{61}ClFe_2N_8O_5$ $[M + H]^+$ 1205.8463, found 1205.8459.

3-[Bis-(1-{3-[4-(3-ferrocenyl-acryloyl)-phenoxy]-propyl}-1*H*-[1,2,3]triazol-4-ylmethyl)-amino]-1-phenyl-4-styryl-azetidin-2-one (10j). Yield 78%; brick red solid; mp. 106–107 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.29–2.35 (m, 4H, H^8), 4.01 (s, 4H, H^5), 4.15 (s, 10H, H^{13}), 4.47 (s, 8H, H^7 + H^{14}), 4.56 (s, 4H, H^{12}), 5.13–5.26 (m, 5H, H^1 + H^9), 5.80 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.24 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.74 (d, J = 15.9 Hz, 1H, H^4), 6.89–6.98 (m, 8H, –ArH), 7.11 (d, J = 15.9 Hz, 2H, H^{10}), 7.24–7.55 (m, 6H, –ArH), 7.65 (s, 2H, triazole-H^6), 7.74 (d, J = 15.9 Hz, 2H, H^{11}), 7.98 (d, J = 8.9 Hz, 4H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.2, 47.5, 58.2, 60.7, 64.3, 69.7, 69.9, 71.5, 71.6, 79.3, 114.1, 115.7, 116.2, 118.6, 118.9, 122.3, 124.5, 126.6, 126.9, 128.1, 128.4, 130.4, 131.2, 132.5, 135.8, 136.8, 143.3, 146.4, 161.1, 188.6. HRMS (ESI-micrOTOF-QII) calcd for $C_{67}H_{62}Fe_2N_8O_5$ $[M + H]^+$ 1171.5113, found 1171.5117.

3-[Bis-(1-{3-[4-(3-ferrocenyl-acryloyl)-phenoxy]-propyl}-1*H*-[1,2,3]triazol-4-ylmethyl)-amino]-1-cycloheptyl-4-styryl-azetidin-2-one (10k). Yield 80%; brick red solid; mp. 102–103 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.32–2.32 (m, 16H, H^8 + cycloheptyl); 3.54–3.58 (m, 1H, cycloheptyl H), 4.01 (s, 4H, H^5), 4.15 (s, 10H, H^{13}), 4.46 (s, 8H, H^7 + H^{14}), 4.55 (s, 4H, H^{12}), 5.14–5.27 (m, 5H, H^1 + H^9), 5.84 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.24 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.76 (d, J = 15.9 Hz, 1H, H^4), 6.88–6.97 (m, 6H, –ArH), 7.13 (d, J = 15.9 Hz, 2H, H^{10}), 7.26–7.54 (m, 3H, –ArH), 7.63 (s, 2H, triazole-H^6),7.71 (d, J = 15.9 Hz, 2H, H^{11}), 7.97 (d, J = 8.9 Hz, 4H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.4, 22.1, 27.4, 31.5, 47.7, 49.2, 58.4, 60.5, 66.7, 69.5, 69.7, 71.3, 76.7, 79.7, 114.6, 117.2, 118.6, 126.3, 126.7, 126.9, 128.4, 129.7, 131.4, 132.3, 134.1, 136.6, 146.4, 146.5, 161.5, 188.8. HRMS (ESI-micrOTOF-QII) calcd for $C_{68}H_{71}Fe_2N_8O_5$ $[M + H]^+$ 1190.1983, found 1190.1978.

3-[Bis-(1-{3-[4-(3-ferrocenyl-acryloyl)-phenoxy]-propyl}-1*H*-[1,2,3]triazol-4-ylmethyl)-amino]-1-cyclohexyl-4-styryl-azetidin-2-one (10l). Yield 84%; brick red solid; mp. 104–105 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.45–2.35 (m, 14H, H^8 + cyclohexyl), 3.51–3.53 (m, 1H, cyclohexyl H), 4.00 (s, 4H, H^5), 4.15 (s, 10H, H^{13}), 4.46 (s, 8H, H^7 + H^{14}), 4.57 (s, 4H, H^{12}), 5.13–5.27 (m, 5H, H^1 + H^9), 5.81 (dd, J = 5.7 Hz, 7.2 Hz, 1H, H^2), 6.21 (dd, J = 7.2 Hz, 15.9 Hz, 1H, H^3), 6.75 (d, J = 15.9 Hz, 1H, H^4), 6.87–6.97 (m, 6H, –ArH), 7.14 (d, J = 15.9 Hz, 2H, H^{10}), 7.26–7.59 (m, 3H, –ArH), 7.63 (s, 2H, triazole-H^6), 77.2 (d, J = 15.9 Hz, 2H, H^{11}), 7.98 (d, J = 8.9 Hz, 4H, –ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.2, 22.4, 27.5, 31.7, 47.2, 49.6, 58.1, 60.7, 66.8, 69.5, 69.9, 71.3, 76.4, 79.2, 114.2, 117.6, 118.3, 126.2, 126.3, 126.7, 128.2, 129.8, 131.8, 132.1, 134.8, 136.9, 146.2, 146.5, 161.4, 188.0. HRMS (ESI-micr-OTOF-QII) calcd for $C_{67}H_{68}Fe_2N_8O_5$ $[M + H]^+$ 1176.4863, found 1176.4858.

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