Articles

Synthesis, Molecular Modeling, and Structure−Activity Relationship of Benzophenone-Based CAAX-Peptidomimetic Farnesyltransferase Inhibitors†

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Received March 7, 2001

Because of the involvement of farnesylated proteins in oncogenesis, inhibition of the protein-modifying enzyme farnesyltransferase is considered a major emerging strategy in cancer therapy. Here, we describe the structure−activity relationship of a novel class of CAAX-peptidomimetic farnesyltransferase inhibitors based on the benzophenone scaffold. 4′-Methyl, 4′-chloro, 4′-bromo, and 4′-nitrophenylacetic acid as substituents at the 2-amino group of the benzophenone core structure yield farnesyltransferase inhibitors active in the nanomolar range. Using diphenylacetic acid in this position further improves activity. SEAL superimposition of inhibitor **12a** to the enzyme-bound conformation of a CAAX-peptide shows a markedly good resemblance of the molecular properties of the peptide. FlexX docking of **12a** confirms the good fit of the molecule into the peptide binding site of farnesyltransferase. The novel benzophenone-based AAX-peptidomimetic substructure described here will be useful for the design of some novel types of farnesyltransferase inhibitors.

Cancer is caused by a stepwise accumulation of mutations that affect growth control, differentiation, and cell survival.[1] Ras proteins play a central role in the signal transduction cascades controlling these processes.[2,3] Mutated forms of Ras, which are constitutively active, are found in approximately 30% of all cancers in man. Several post-transformational modifications occur before Ras aquires its full biological activity. The crucial step is the transfer of a farnesyl residue from farnesylpyrophosphate to the thiol of a cysteine side chain of the C-terminal CAAX-tetrapeptide sequence (C, cysteine; A, aliphatic amino acid; X, serine or methionine) catalyzed by the enzyme farnesyltransferase.[4] Therefore, inhibition of farnesyltransferase has received considerable interest in recent years as a strategy for the development of novel potential cancer therapeutics.[5−7] However, there is accumulating evidence that Ras may not be the only substrate of farnesyltransferase involved in oncogenesis.[8] Focus has shifted to RhoB, another member of the class of small GTPases that is involved in receptor trafficking.[9,10] Irrespective of the unresolved issue of the mechanism by which farnesyltransferase inhibitors exert their antiproliferative effects, the efficacy of these compounds and their low toxicity have been demonstrated,[11] and their use is, therefore, regarded as a major emerging strategy in cancer therapy.

Farnesyltransferase recognizes and binds only the last four C-terminal amino acids of the CAAX-consensus sequence of its substrate proteins. This tetrapeptide is therefore a primary template for the development of non-peptide farnesyltransferase inhibitors.[5−7] We have described[12] compound **1** as the lead structure of a novel class of peptidomimetic farnesyltransferase inhibitors based on the benzophenone scaffold. Our initial design idea was to use the 2,5-diaminobenzophenone as a core structure in which the unsubstituted phenyl residue should mimic the lipophilic side chain of the A_2 (e.g. Ile in the CVIM-tetrapeptide) amino acid. The central benzene should carry the cysteinyl residue at its 5-amino group and a second acyl substituent at its 2-amino function, which was intended to replace the X amino acid. Here, we describe our research effort, which was solely directed toward the optimization of the AAX-peptidomimetic substructure of **1**. This improved 2-acylaminobenzophenone is then used in further studies as a AAX-peptidomimetic partial structure of different kinds of farnesyltransferase inhibitors as for instance bisubstrate analogue inhibitors.[13] Accordingly, in the first line, we left the *N*-terminal cysteine unchanged, which has been shown to be a valuable building block of CAAX-peptidomimetics.

Chemistry

Synthesis of the target compounds started with the acylation of commercially available 2-amino-5-nitrobenzophenone (**2**) with the appropriate carboxylic acid chlorides in hot toluene. Then, the nitro group of the resulting compound **3** was reduced using tin(II) chloride. The amine **4** was acylated with *N*-Boc-*S*-tritylcysteine, which was activated as a mixed anhydride. The *N*-Boc as well as the *S*-trityl protecting groups were cleaved from **5** using trifluoroacetic acid/triethylsilane. In the case of the carboxylic acid derivatives **7b**,**d**, alkaline

† Dedicated to Prof. Dr. Wolfgang Hanefeld on the occasion of his 60th birthday

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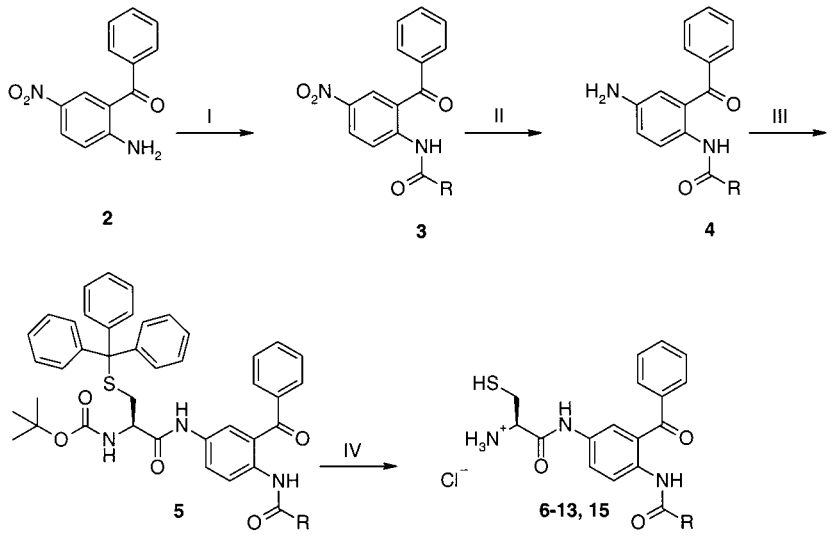
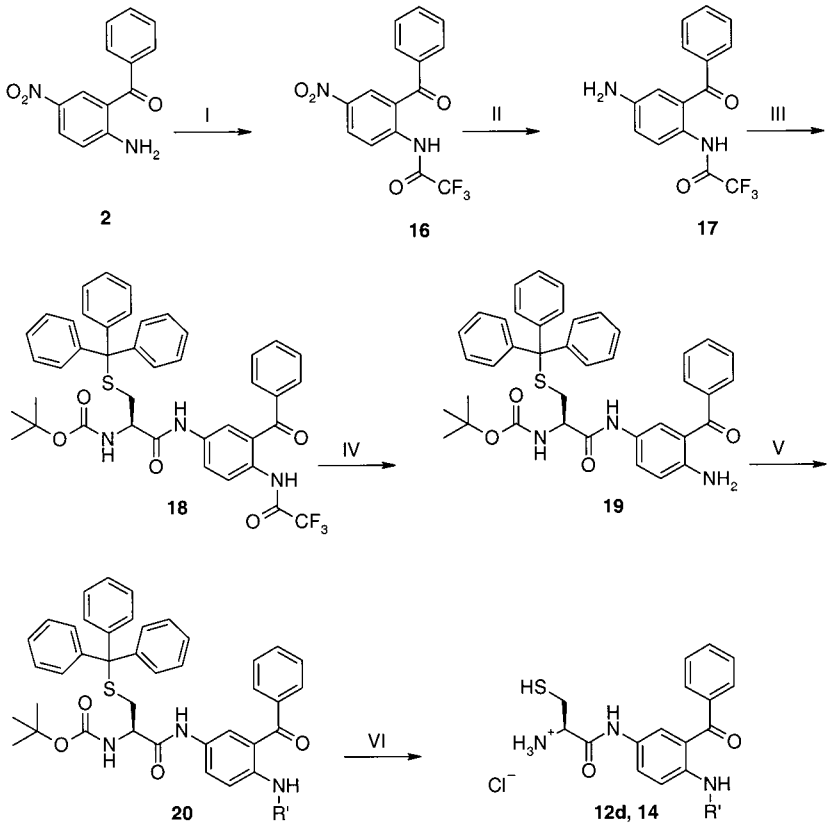
10.1021/jm010872r CCC: $20.00
Published on Web 08/07/2001

Scheme 1[a]



[a] (I) R-COCl, toluene, reflux, 2 h; (II) $SnCl_2 \cdot 2H_2O$, ethyl acetate, reflux, 2 h; (III) (a) *N*-Boc-*S*-trityl-Cys-OH, isobutyl chloroformate, NMM, DMF, −15 °C, 5 min, (b) then **4**, DMF, −15 °C → rt, overnight; (IV) (a) TFA, Et_3SiH, dichloromethane, rt, 1 h, (b) HCl(g) in diethyl ether.

Scheme 2[a]



[a] (I) TFAA, pyridine, dichloromethane, 0 °C, 1 h; (II) $SnCl_2 \cdot 2H_2O$, ethyl acetate, reflux, 2h; (III) (a) *N*-Boc-*S*-trityl-Cys-OH, isobutyl chloroformate, NMM, DMF, −15 °C, 5 min, (b) then **4**, DMF, −15 °C → rt, overnight; (IV) K_2CO_3, water/dioxane, reflux 2 h; (V) R-SO_2Cl or R-COCl, toluene, reflux 2 h; (VI) (a) TFA, Et_3SiH, dichloromethane, rt, 2 h, (b) HCl(g) in diethyl ether.

hydrolysis of the methyl ester was performed prior to acidic removal of the *N*- and *S*-protective groups. The target compounds were precipitated as hydrochloride salts with HCl(g) in diethyl ether (Scheme 1). This scheme could not be followed for the preparation of the nitro compound **12d**, because of the reduction step involved early in the sequence, and for the synthesis of the sulfonamides **14**, because of the insufficient reactivity of the 2-amino group of compound **2**. Therefore, first the amino group of **2** was protected as a trifluoroacetate. Then, the nitro group was reduced and acylated by *N*-Boc-*S*-tritylcysteine, as described above. Alkaline hydrolysis yielded the amine **19**, which was reactive enough to be sulfonylized. Alternatively, **19** was reacted with 4-nitrophenylacetyl chloride to obtain **12d**. The sequence was completed by removal of the protection groups and the precipitation of the hydrochloride salts as described above (Scheme 2).

Chart 1. Structures of the Lead Compound **1** and Novel Benzophenone-Based Farnesyltransferase Inhibitors **6**−**15**

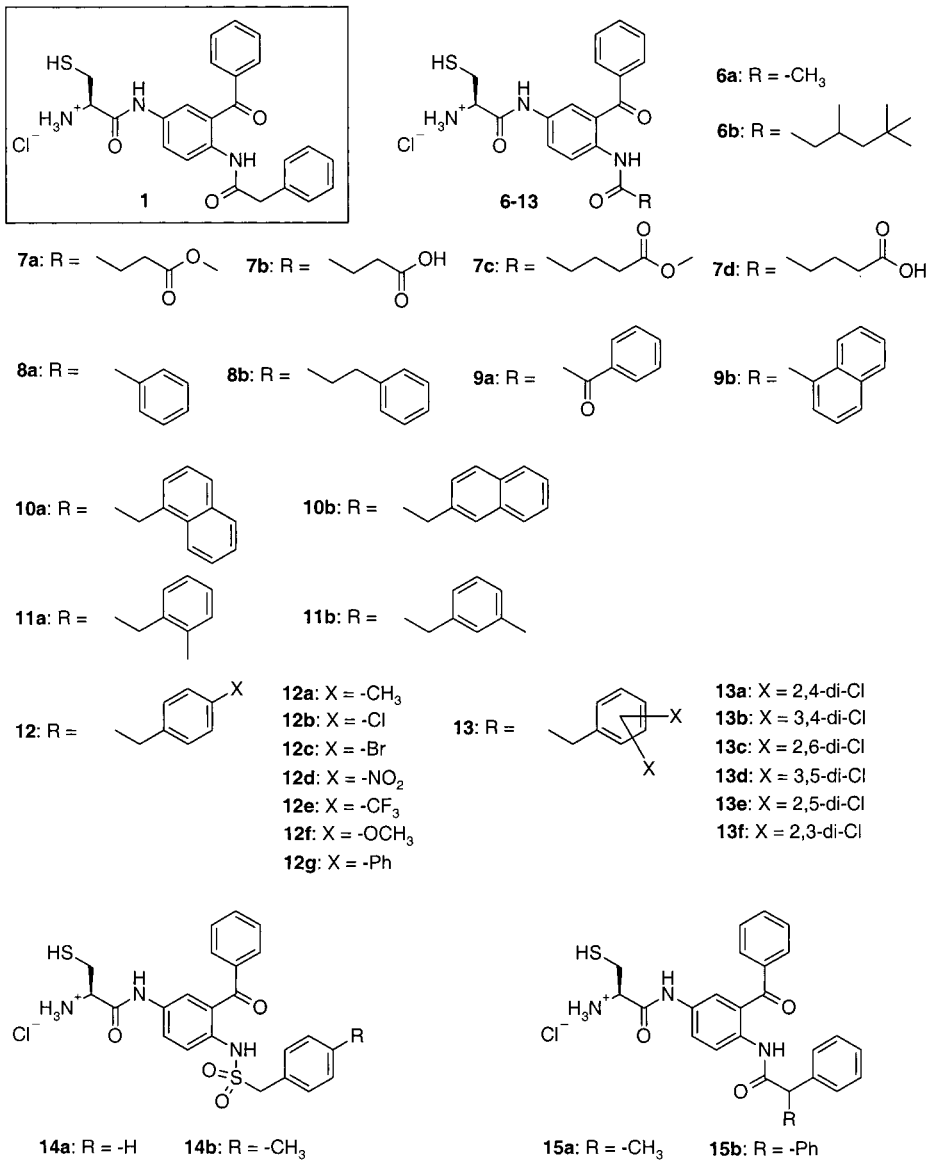


Table 1. Farnesyltransferase Inhibitory Activity of Compounds **1** and **6**−**15**

compd	IC_{50} (nM)	compd	IC_{50} (nM)	compd	IC_{50} (nM)
1	650 ± 50	**10a**	380 ± 55	**13a**	120 ± 50
6a	7600 ± 2000	**10b**	460 ± 50	**13b**	480 ± 75
6b	8600 ± 2000	**11a**	400 ± 130	**13c**	340 ± 55
7a	1800 ± 120	**11b**	540 ± 60	**13d**	535 ± 55
7b	700 ± 65	**12a**	77 ± 25	**13e**	2400 ± 400
7c	2400 ± 150	**12b**	105 ± 30	**13f**	420 ± 70
7d	550 ± 50	**12c**	76 ± 25	**14a**	85 ± 15
8a	4780 ± 220	**12d**	115 ± 30	**14b**	100 ± 10
8b	1290 ± 105	**12e**	725 ± 50	**15a**	650 ± 60
9a	1420 ± 135	**12f**	545 ± 75	**15b**	36 ± 10
9b	4600 ± 210	**12g**	1980 ± 180		

Results and Discussion

In the present study we focused our attention on the variation of the acyl substituent at the 2-amino group of our lead structure **1** (Chart 1, Table 1). First, we removed the phenyl residue from the phenylacetic acid substituent (compound **6a**). This resulted, not entirely unexpectedly, in a drop in farnesyltransferase inhibitory activity of about 1 order of magnitude. Introduction of a branched alkyl residue as in **6b** caused further reduction in activity. Since the CAAX peptides terminate with a carboxyl group, we prepared the acid derivatives **7a**−**d**. From these four compounds only the glutaric acid derivative **7d** was slightly more active (IC_{50} = 550 nM) than the lead structure. Because of the ease of preparation and their obvious activity, we returned to aryl derivatives as substituents in this position.

First, to determine the correct distance between the phenyl residue and the rest of the molecule in **1**, we varied this distance by either removing or adding a methylene group between the phenyl and the amide moiety. Both alterations (compounds **8a**,**b**) resulted in a considerable drop in activity, proving our initial design idea correct. The phenylacetic acid moiety was initially selected because of its length, which resembles that of the methionine side chain. Next, we reduced the conformational flexibility at the α-position by transforming the α-carbon from an sp^3 center to an sp^2 center (compound **9a**) or embedding it into a rigid ring structure as in **9b**. Both variations showed markedly reduced activity, while this reduction was more pronounced in the rigid ring structure. This demonstrated that a

certain degree of conformational flexibility in the α-position is necessary for farnesyltransferase inhibitory activity.

Upon enlargement of the aryl substituent by the replacement of phenyl by 1- and 2-naphthyl, respectively, an improvement in activity could be observed (**10a**, IC_{50} = 380 nM; **10b**, IC_{50} = 460 nM). However, this effect could also be obtained by simply adding a methyl group to the ortho-position of the lead structure's phenyl (**11a**, IC_{50} = 400 nM). Shifting the methyl group to the meta-position caused a slight reduction in activity (**11b**, IC_{50} = 540 nM). However, shifting the methyl group even one position further to the para-position resulted in compound **12a** (IC_{50} = 77 nM), which was nearly 1 order of magnitude more active against the farnesyltransferase than the initial lead structure **1** (IC_{50} = 650 nM). In the next step, various substituents were introduced into the para-position. The bromo-substituted derivative **12c** turned out to be as equally potent as the methyl derivative **12a**, whereas the chloro derivative **12b** and nitro compound **12d** were only slightly less potent than the methyl derivative **12a**. Surprisingly, the trifluoromethyl-substituted compound **12e** showed a 10-fold reduction in activity. The bulky phenyl residue (**12g**) caused an even more pronounced drop in activity (IC_{50} = 1.98 μM).

Since a methyl group at any position of the phenyl residue has caused an increased activity, we prepared all six disubstituted phenyl derivatives searching for a possible additive effect. Because of compound availibility, we chose the chloro substituent for this series (**13a**−**f**). Unfortunately, none of the disubstituted phenyl derivatives showed any improved activity. In contrast, most of them were considerably less active than the 4-monosubstituted chloro derivative **12b**.

Replacement of the amide moiety in **1** by a sulfonamide group resulted in a markedly increased activity (**14a**, IC_{50} = 85 nM). Again, our hopes for an additive effect of different structural variations were disappointed since the 4′-methyl derivative **14b** was even slightly less active than **14a**.

Finally, we introduced a second substituent into the α-position of our initial lead structure **1**. While a methyl group made no difference (**15a**), a phenyl residue (**15b**) resulted in an IC_{50} value of 36 nM, which represents a 20-fold improvement compared to the initial lead structure **1** and a 2-fold increase of activity compared to the 4′-monosubstituted phenyl derivatives **12a,c**.

The recently published[14] crystal structure of a ternary complex of farnesyltransferase, a farnesylpyrophosphate analogue and *N*-acetyl-Cys-Val-Ile-selenoMetOH (PDB 1QBQ) has resolved the issue of the enzyme-bound conformation of the CAAX-peptide substrate. The crystal structure shows the peptide bound to the active site of farnesyltransferase in an extended conformation with its cysteine sulfur coordinated to the zinc ion. We used this enzyme-bound conformation of the *N*-acetyl-Cys-Val-Ile-selenoMetOH peptide for an alignment of our inhibitor **12a** to the CAAX-peptide. Hereby, the program SEAL[15] tries to superimpose the two molecules in such a way that their physicochemical properties (steric, electrostatic, hydrophobic, and hydrogen-bond donor/acceptor) show the best fit (Figure 1). Not surprisingly, the two cysteinyl residues are fitted exactly to each other. But also the remainder of the inhibitor shows a markedly good resemblance of the molecular properties of the CAAX-peptide. The side chain of the isoleucine is mimicked by the terminal phenyl residue of the benzophenone core structure, while the keto carbonyl oxygen occupies the position of the C-terminal amide moiety of the CAAX-peptide. The amide nitrogen of this moiety is mimicked by the amide nitrogen in the 2-position of the benzophenone scaffold, while the carbonyl oxygen of this benzophenone amide moiety acts as a surrogate of the terminal carboxyl group of the terminal methionine. The side chain of methionine is mimicked by the tolyl residue of the 2-acylaminosubstituent of the benzophenone core structure.

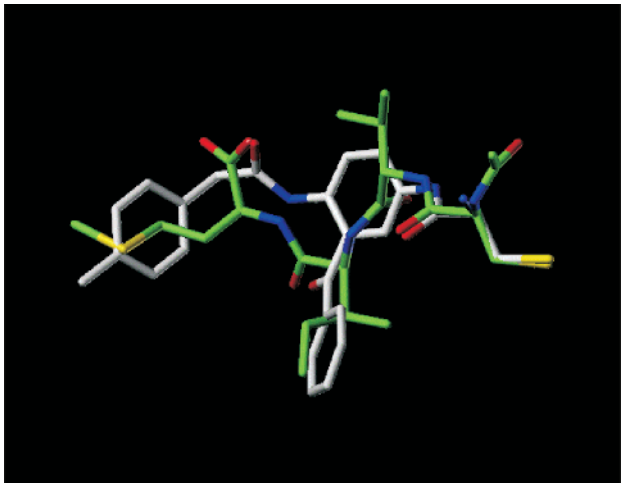


Figure 1. SEAL superimposition of the enzyme-bound conformation of *N*-acetyl-Cys-Val-Ile-selenoMetOH and the benzophenone-based inhibitor **12a**. Colors: carbon, white (**12a**) and light green (*N*-Ac−CVI(seleno)M); nitrogen, blue; oxygen, red; sulfur, yellow.

The benzophenone derivative **12a** has been docked into the active site of farnesyltransferase using the flexible docking program FlexX.[16] The position of the zinc coordinated $-SCH_2CH_\alpha-$ cysteine substructure from the crystal structure has been used for the positioning of the base fragment of the benzophenone **12a**. The docking of the remainder of the inhibitor was performed fragment by fragment while the program searches for favorable interactions between the inhibitor and the enzyme, trying to avoid steric overlaps at each step. Figure 2 shows the docking result of **12a** into the active site of farnesyltransferase, confirming the good fit of the molecule into the peptide binding site of the enzyme. Figure 3 eludicates possible interactions between **12a** and the amino acids of the active site as found by FlexX. These interactions are mainly hydrophobic in nature, with the exception of hydrogen bonds between the backbone amide nitrogen of Tyr-166α and the side chain of Gln-167α, respectively, and the arylacyl amide oxygen of **12a**. A second hydrogen bond is predicted between the hydroxyl group of Ser-99β and the keto carbonyl oxygen of the benzophenone core structure. In addition to the hydrophobic interaction with amino acid side chains, there is also predicted such an interaction between the core phenyl residue and the terminus of the prenyl residue. In summary, most interactions predicted for **12a** by FlexX are in good agreement with the interactions seen for the corre-

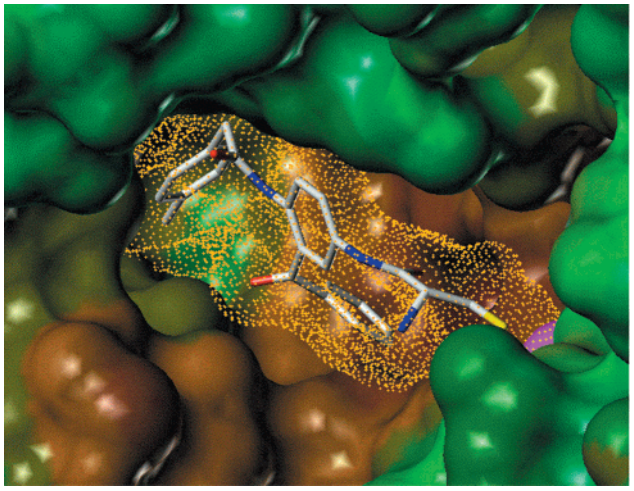


Figure 2. Docking of inhibitor **12a** displayed with its connolly surface (yellow dots) into the active site of farnesyltransferase. The molecular surface of the active site has been calculated using the program MOLCAD (implemented in the molecular modeling software package SYBYL[17]). FPP is included in the surface. Hydrophobic properties are indicated in brown and hydrophilic in green to blue colors. The enzyme-bound zinc is show as a magenta sphere.

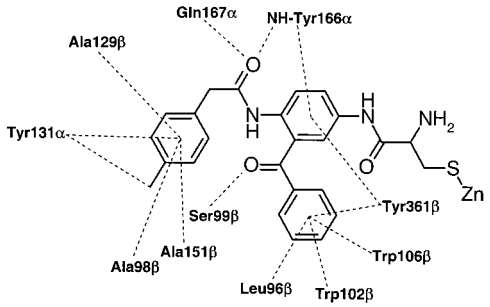


Figure 3. Schematic representation of possible interactions between inhibitor **12a** and active site amino acids as found by FlexX.

Table 2. Antiproliferative Effect (GI_{50} (μM)) of Selected Benzophenone Inhibitors

compd	HL-60	THP-1	K-562
12a			8.1
12c	4.2	14.9	7.9

sponding elements of the *N*-acetyl-Cys-Val-Ile-seleno-MetOH peptide in the crystal structure,[14] proving the usefulness of predictions made by the modeling programs SEAL and FlexX. Docking of the inhibitor **15b** shows mainly the same interactions as described for **12a**. In addition, there is a hydrophobic interaction between the additional terminal phenyl residue of **15b** and Tyr-166α that easily explains the 2-fold enhancement in farnesyltransferase inhibitory activity.

Our benzophenone-based farnesyltransferase inhibitors are not intended to be used as cancer therapeutic in the present form but were investigated to identify an optimized AAX-peptidomimetic to be used as partial structure of different kinds of farnesyltransferase inhibitors,[13] although some initial cell culture experiments have been performed with compounds **12a** and **12b**. Both compounds showed antiproliferative effects at low micromolar concentrations (Table 2).

In summary, we have developed and optimized a novel AAX-peptidomimetic substructure useful for the design of some novel types of farnesyltransferase inhibitors, as will be reported in due course.

Experimental Section

Melting points were determined on a Leitz HM-LUX melting point apparatus and are uncorrected. ^{1}H- and ^{13}C NMR spectra were recorded on a JEOL JMN-GX-400 and a JEOL JMN-LA-500 spectrometer. Mass spectra were obtained with a Vacuum Generators VG 7070 H using a Vector 1 data acquisition system from Teknivent or an AutoSpec mass spectrometer from Micromass. IR spectra were recorded on a Nicolet 510P FT-IR-spectrometer. Microanalyses were obtained from a CH analyzer according to Dr. Salzer from Labormatic and from a Hewlett-Packard CHN-analyzer type 185. Column chromatography was carried out using silica gel 60 (0.062−0.200 mm) from Merck. Solvents and reagents were used as purchased from commercial source unless otherwise noted. Quoted yields are of purified material.

General Procedures. General Procedure A: Preparation of *N*-(2-Benzoyl-4-nitrophenyl)amides 3. To a solution of 2-amino-5-nitrobenzophenone (**2**) (1.2 g, 5 mmol) in hot toluene (50 mL) was added the appropriate acid chloride (5 mmol), dissolved in toluene (10 mL). The mixture was refluxed for 2 h. Then, most of the solvent was removed in vacuo. The products crystallized upon cooling and were recrystallized from EtOH.

General Procedure B: Reduction of *N*-(2-Benzoyl-4-nitrophenyl)amides 3 to *N*-(4-Amino-2-benzoylphenyl)-amides 4. To a solution of the *N*-(2-benzoyl-4-nitrophenyl)-amides **3** in EtOAc (approximately 5 mL per mmol) was added $SnCl_2 \cdot 2H_2O$ (1.125 g per mmol nitro compound). Then, the solution was refluxed for 2 h. The cooled solution was diluted with water and the pH was adjusted to 7−8 by addition of saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (3 × 100−200 mL), and the combined organic extracts were thoroughly washed with brine and dried over $MgSO_4$. The products obtained after the removal of the solvent were used without further purification.

General Procedure C: Acylation of *N*-(4-Amino-2-benzoylphenyl)amides 4 Using Mixed Anhydride Activation. *N*-Boc-*S*-trt-cysteine was dissolved in dry dimethylformamide (DMF) in a flame-dried flask under an atmosphere of Ar. After addition of *N*-methylmorpholine (0.25 mL per mmol acid), the solution was cooled to −15 °C and isobutyl chloroformate (0.13 mL per mmol acid) was added. A solution of the *N*-(4-amino-2-benzoylphenyl)amides **4** (1 equiv) in dry DMF was added after 5 min. The mixture was left to warm to room temperature overnight and then poured into brine (400−800 mL). The aqueous mixture was extracted with EtOAc (3 × 100 mL), and the combined organic extracts were washed successively with 0.67 M citric acid, saturated $NaHCO_3$ solution, and brine and dried with $MgSO_4$. The residue obtained after removal of the solvent was purified by flash chromatography using ethyl acetate:*n*-hexane 2:3 as eluents.

General Procedure D: *N*-Boc-S-trt-cysteine N,S-Deprotection. The *N*-Boc-*S*-trt protected derivatives **6** and **20** were dissolved in dry dichloromethane (DCM) (6 mL per mmol). Upon addition of trifluoroacetic acid (3 mL per mmol), the color of the solution turned brown. Triethylsilane was added until the solution became colorless. Stirring was continued for 1 h. After removal of the volatiles in vacuo, the solid residue was washed several times with *n*-hexane to remove most of the triphenylmethane. Then, the solid was dissolved in a minimal amount of EtOAc and an excess of diethyl ether, saturated with HCl(g), was added. The precipitate was collected and washed with dry diethyl ether.

General Procedure E: Hydrolysis of Methyl Esters. Compounds **5c** and **5d** were dissolved in a mixture of THF/methanol. After addition of 1 N NaOH (1 equiv), the mixture was stirred at room temperature for 12 h. Then, most of the solvent was removed in vacuo and diluted with water, and the pH was adjusted to 1−2 by addition of concentrated HCl. The aqueous phase was extracted with EtOAc (3 × 50−100 mL),

and the combined organic extracts were thoroughly washed with brine, dried over $MgSO_4$, and evaporated to dryness.

***N*-(2-Benzoyl-4-nitrophenyl)acetamide (3a).** The compound was prepared by following general procedure A. Compound **3a** is a yellow solid (1.307 g, 92% yield): mp 146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.22 (s, 3H), 7.48 (m, 2H), 7.63 (m, 3H), 8.37 (m, 1H), 8.41 (m, 1H), 8.84 (m, 1H), 11.04 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)acetamide (4a).** The compound was prepared from **3a** (0.995 g, 3.5 mmol) by following general procedure B. Compound **4a** is a yellow oil (0.86 g, 96% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.09 (s, 3H), 6.73 (m, 1H), 6.84 (m, 1H), 7.41(m, 3H), 7.65 (m, 2H), 8.23 (m, 1H), 10.12 (s, 1H).

***N*-[4-(Acetylamino)-3-benzoylphenyl]-N^{α}-tert-butyloxycarbonyl-S-tritylcysteinamide (5a).** The compound was prepared from **4a** (0.284 g, 1.0 mmol) by following general procedure C. Compound **5a** is a yellow solid (0.16 g, 23% yield): mp 104 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (s, 9H), 2.13 (s, 2H), 2.54 (m, 1H), 2.70 (m, 1H), 3.82 (m, 1H), 4.68 (m, 1H), 7.13 (m, 2H), 7.20 (m, 7H), 7.34 (m, 6H), 7.42 (m, 3H), 7.54 (m, 1H), 7.65 (m, 2H), 7.71 (m, 1H), 8.47 (m, 1H), 10.47 (s, 1H).

***N*-[4-(Acetylamino)-3-benzoylphenyl]cysteinamide Hydrochloride (6a).** The compound was prepared from **5a** (0.13 g, 0.18 mmol) by following general procedure D. Compound **6a** is a yellow solid (0.059 g, 84% yield): mp 131 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.70 (s, 3H), 3.02 (m, 2H), 4.14 (s, 1H), 7.47 (m, 3H), 7.58 (m, 1H), 7.63 (m, 2H), 7.69 (m, 1H), 7.77 (m, 1H), 8.43 (s, 2H), 9.90 (s, 1H), 10.89 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.7, 51.9, 54.6, 120.5, 120.6, 122.5 124.2, 127.9, 128.0, 128.4, 129.2, 129.7, 132.3, 132.3, 133.8, 133.9, 136.9, 136.9, 165.2, 167.8, 194.5; ESI-MS m/z = 44 (100), 60 (49), 84 (49), 73 (29), 377 (28), 327 (20), 212 (19), 395 (19, M^+ + 2H). Anal. ($C_{18}H_{20}ClN_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-3,5,5-trimethylhexanoylamide (3b).** The compound was prepared by following general procedure A. Compound **3b** is a yellow solid (1.85 g, 66% yield): mp 91 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.90 (s, 9H), 1.03 (m, 3H), 1.16 (m, 1H), 1.28 (m, 1H), 2.17 (m, 1H), 2.26 (m, 1H), 2.47 (m, 1H), 7.3 (m, 2H), 7.66 (m, 3H), 8.39 (m, 1H), 8.47 (m, 1H), 8.93 (m, 1H), 11.14 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-3,5,5-trimethylhexanoylamide (4b).** The compound was prepared from **3b** (0.97 g, 2.54 mmol) by following general procedure B. Compound **4b** is a yellow oil (0.795 g, 89% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.82 (s, 9H), 0.94 (m, 3H), 1.06 m, 1H), 1.22 (m, 1H), 2.07 (m, 2H), 2.29 (m, 1H), 6.73 (m, 1H), 6.84 (m, 1H), 7.39 (m, 2H), 7.52 (m, 1H), 7.65 (m, 2H), 8.30 (m, 1H), 10.17 (s, 1H).

***N*-[3-Benzoyl-4-(3,5,5-trimethylhexanoylamino)phenyl]-N^{α}-*tert*-butyloxycarbonyl-S-tritylcysteinamide (5b).** The compound was prepared from **5b** (0.528 g, 1.5 mmol) by following general procedure C. Compound **5b** is a yellow solid (0.466 g, 39% yield): mp 87 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (s, 9H), 0.95 (m, 3H), 1.07 (m, 1H), 1.23 (m, 1H), 1.32 (s, 9H), 2.33 (m, 1H), 2.52 (m, 1H), 2.67 (m, 1H), 3.63 (m, 1H), 3.77 (m, 1H), 4.68 (m, 1H), 7.13 (m, 3H), 7.19 (m, 1H), 7.20 (m, 6H), 7.33 (m, 6H), 7.40 (m, 2H), 7.45 (m, 1H), 7.52 (m, 1H), 7.64 (m, 2H), 7.69 (m, 1H), 8.51 (m, 1H), 10.51 (s, 1H).

***N*-[3-Benzoyl-4-(3,5,5-trimethylhexanoylamino)phenyl]cysteinamide Hydrochloride (6b).** The compound was prepared from **5b** (0.16 g, 0.2 mmol) by following general procedure D. Compound **6b** is a yellow solid (0.09 g, 91% yield): mp 238 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.75 (m, 3H), 0.80 (s, 9H), 0.96 (m, 1H), 1.13 (m, 1H), 1.82 (m, 1H), 1.99 (m, 1H), 4.24 (s, 1H), 7.49 (m, 3H), 7.61 (m, 1H), 7.68 (m, 2H), 7.80 (m, 2H), 8.78 (s, 2H), 9.96 (s, 1H), 11.23 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 22.1, 24.8, 29.7, 30.5, 45.2, 50.0, 54.3, 109.2, 120,3, 122.2, 124.2, 128.0, 129.4, 132.4, 134.2, 136.5, 165.4, 169.9, 194.8; ESI-MS m/z = 212 (100), 352 (59), 213 (26), 211 (26), 492 (4.8, M^+), 456 (0.03, base). Anal. ($C_{25}H_{34}ClN_3O_3S$) C, H, N.

3-[*N*-(2-Benzoyl-4-nitrophenyl)carbamoyl]propionic Acid Methyl Ester (3c). The compound was prepared by following general procedure A. Compound **3c** is a yellow solid (1.58 g, 88% yield): mp 158 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.69 (m, 2H), 2.76 (m, 2H), 3.64 (s, 3H), 7.48 (m, 2H), 7.63 (m, 3H), 8.34 (m, 1H), 8.42 (m, 1H), 8.83 (m, 1H), 11.15 (s, 1H).

3-[*N*-(4-Amino-2-benzoylphenyl)carbamoyl]propionic acid methyl ester (4c). The compound was prepared from **3c** (1.068 g, 3.0 mmol) by following general procedure B. Compound **4c** is a yellow oil (0.899 g, 92% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64 (m, 4H), 3.56 (s, 2H), 3.62 (s, 3H), 6.73 (m, 1H), 6.81 (m, 1H), 7.39 (m, 2H), 7.52 (m, 1H), 7.64 (m, 2H), 8.23 (m, 1H), 10.23 (s, 1H).

3-[*N*-[2-Benzoyl-4-(*N*-*tert*-butyloxycarbonyl-S-tritylcysteinylamino)phenyl]carbamoyl]propionic Acid Methyl Ester (5c). The compound was prepared from 4c (0.49 g, 1.5 mmol) by following general procedure **C**. Compound **5c** is a yellow solid (0.439 g, 38% yield): mp 91 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (s, 9H), 2.52 (dd, J = 13, 6 Hz, 1H), 2.66 (m, 5H), 3.61 (s, 3H), 3.80 (m, 1H), 4.71 (m, 1H), 7.13 (m, 3H), 7.20 (m, 6H), 7.32 (m, 6H), 7.40 (m, 2H), 7.45 (m, 2H), 7.51 (m, 1H), 7.64 (m, 2H), 7.67 (m, 1H), 8.45 (m, 1H), 10.57 (s, 1H).

3-[*N*-[2-Benzoyl-4-(cysteinylamino)phenyl]carbamoyl]-propionic Acid Methyl Ester Hydrochloride (7a). The compound was prepared from **5c** (0.15 g, 0.19 mmol) by following general procedure D. Compound **7a** is a yellow solid (0.026 g, 32% yield): mp 81 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.27 (m, 2H), 2.31 (m, 2H), 3.05 (m, 2H), 3.53 (s, 3H), 4.17 (m, 1H), 7.49 (m, 3H), 7.63 (m, 3H), 7.74 (m, 1H), 7.78 (m, 1H), 8.47 (s, 2H), 10.02 (s, 1H), 10.94 (s, 1H). Anal. ($C_{21}H_{24}ClN_3O_5S$) C, H, N.

3-[*N*-[2-Benzoyl-4-(*N*-*tert*-butyloxycarbonyl-S-tritylcysteinylamino)phenyl]carbamoyl]propionic Acid. The compound was prepared from **5c** (0.125 g, 0.16 mmol) by following general procedure E. This compound is a yellow solid (0.08 g, 66% yield): mp 95 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.31 (s, 9H), 2.45 (m, 1H), 2.66 (m, 5H), 3.91 (m, 1H), 4.82 (m, 1H), 7.11 (m, 3H), 7.19 (m, 12H), 7.32 (m, 6H), 7.40 (m, 1H), 7.64 (m, 1H), 8.43 (m, 1H), 10.62 (s, 1H).

3-[*N*-[2-Benzoyl-4-(cysteinylamino)phenyl]carbamoyl]-propionic Acid Hydrochloride (7b). The compound was prepared from 3-[*N*-[2-benzoyl-4-(*N*-*tert*-butyloxycarbonyl-*S*-tritylcysteinylamino)phenyl]carbamoyl]propionic acid (0.06 g, 0.08 mmol) by following general procedure D. Compound **7b** is a yellow solid (0.028 g, 83% yield): mp 112 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.22 (m, 4H), 3.05 (m, 2H), 4.15 (m, 1H), 7.48 (m, 4H), 7.63 (m, 3H), 7.78 (m, 1H), 8.49 (s, 2H), 10.01 (s, 1H), 10.99 (s, 1H); ESI-MS m/z = 294 (100), 212 (38), 105 (24), 295 (20), 416 (0.8, base). Anal. ($C_{20}H_{22}ClN_3O_3S$) C, H, N.

4-[*N*-(4-Nitro-2-benzoylphenyl)carbamoyl]butyric Acid Methyl Ester (3d). The compound was prepared by following general procedure A. Compound **3d** is a yellow solid (1.85 g, 99% yield): mp 70 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.06 (m, 2H), 2.43 (t, J = 7 Hz, 2H), 2.55 (t, J = 7 Hz, 2H), 3.65 (s, 3H), 7.53 (m, 2H), 7.67 (m, 3H), 8.39 (m, 1H), 8.46 (m, 1H), 8.90 (m, 1H), 11.13 (s, 1H).

4-[*N*-(4-Amino-2-benzoylphenyl)carbamoyl]butyric Acid Methyl Ester (4d). The compound was prepared from **3d** (1.068 g, 3.0 mmol) by following general procedure B. Compound **4d** is a yellow oil (0.979 g, 96% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.97 (m, 2H), 2.35 (m, 4H), 3.55 (s, 2H), 3.58 (s, 3H), 6.74 (m, 1H), 6.84 (m, 1H), 7.41 (m, 2H), 7.52 (m, 1H), 7.64 (m, 2H), 8.27 (m, 1H), 10.20 (s, 1H).

4-[*N*-[2-Benzoyl-4-(*N*-*tert*-butyloxycarbonyl-S-tritylcysteinylamino)phenyl]carbamoyl]butyric Acid Methyl Ester (5d). The compound was prepared from **5d** (0.51 g, 1.5 mmol) by following general procedure C. Compound **5d** is a yellow solid (0.43 g, 37% yield): mp 79 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (s, 9H), 1.98 (q, J = 7 Hz, 2H), 2.35 (t, J = 7 Hz, 2H), 2.40 (t, J = 7 Hz, 2H), 2.52 (dd, J = 14, 8 Hz, 1H), 2.67 (dd, J = 14, 5 Hz, 1H), 3.59 (s, 3H), 3.80 (m, 1H), 4.70 (m, 1H), 7.13 (m, 3H), 7.19 (m, 6H), 7.32 (m, 7H), 7.45 (m, 2H), 7.45 (m, 2H), 7.50 (m, 1H), 7.64 (m, 1H), 7.69 (1H), 8.47 (m, 1H), 10.52 (s, 1H).

4-[*N*-[2-Benzoyl-4-(cysteinylamino)phenyl]carbamoyl]-butyric Acid Methyl Ester Hydrochloride (7c). The compound was prepared from **5d** (0.18 g, 0.23 mmol) by following general procedure D. Compound **7c** is a yellow solid (0.091 g, 82% yield): mp 101 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.53 (m, 2H), 2.03 (t, J = 7 Hz, 2H), 2.15 (t, J = 7 Hz, 2H), 3.05 (m, 2H), 3.55 (s, 3H), 4.18 (m, 1H), 7.47 (m, 3H), 7.59 (m, 1H), 7.65 (m, 2H), 7.72 (m, 1H), 7.78 (m, 1H), 8.47 (s, 2H), 9.96 (s, 1H), 10.97 (s, 1H); ESI-MS m/z =212 (100), 340 (59), 211 (37), 238 (34), 435 (25), 307 (24), 300 (19), 237 (17), 309 (16), 428 (15), 341 (13). Anal. ($C_{22}H_{26}ClN_3O_5S$) C, H, N, S.

4-[*N*-[2-Benzoyl-4-(*N*-*tert*-butyloxycarbonyl-*S*-tritylcysteinylamino)phenyl]carbamoyl] butyric acid. The compound was prepared from **5d** (0.167 g, 0.21 mmol) by following general procedure E. This compound is a yellow solid (0.156 g, 96% yield): mp 69 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.32 (s, 9H), 2.00 (m, 2H), 2.38 (m, 4H), 2.52 (m, 1H), 2.65 (m, 1H), 3.81 (m, 1H), 4.76 (m, 1H), 7.14 (m, 3H), 7.20 (m, 6H), 7.33 (m, 6H), 7.49 (m, 3H), 7.54 (m, 3H), 7.67 (m, 2H), 8.54 (s, 1H), 10.60 (s, 1H).

4-[*N*-[2-Benzoyl-4-(cysteinylamino)phenyl]carbamoyl]-butyric Acid Hydrochloride (7d). The compound was prepared from 4-[*N*-[2-benzoyl-4-(*N*-*tert*-butyloxycarbonyl-*S*-tritylcysteinylamino)phenyl]carbamoyl]butyric acid (0.13 g, 0.18 mmol) by following general procedure D. Compound **7d** is a yellow solid (0.066 g, 86% yield): mp 88 °C; ^{1}H NMR (400 MHz,DMSO-d_6) δ 1.53 (m, 2H), 2.04 (m, 2H), 2.15 (m, 2H), 3.05 (s, 2H), 4.36 (m, 1H), 7.48 (m, 3H), 7.62 (m, 3H), 7.79 (m, 2H), 8.62 (s, 2H), 9.99 (s, 1H), 11.22 (s, 1H); ESI-MS m/z = 212 (100), 211 (43), 340 (36), 308 (31), 309 (26), 235 (26), 326 (20), 428 (4.4, base − 2), 430 (1.5, base). Anal. ($C_{21}H_{24}ClN_3O_5S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)benzamide (3e).** The compound was prepared by following general procedure A. Compound **3a** is a yellow solid (1.489 g, 86% yield): mp 184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.57 (m, 5H), 7.59−7.64 (m, 1H), 7.66−7.69 (m, 2H), 8.00−8.02 (m, 2H), 8.41 (m, 1H), 8.50 m, 1H), 9.09 (m, 1H), 12.17 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)benzamide (4e).** The compound was prepared from **3e** (0.488 g, 1.4 mmol) by following general procedure B. Compound **4e** is a yellow oil (0.34 g, 77% yield);^{1}H NMR (400 MHz, $CDCl_3$) δ 3.58 (s, 2H), 6.82 (m, 1H), 6.92 m, 1H), 7.39−7.48 (m, 5H), 7.50−7.54 (m, 1H), 7.65−7.68 (m, 2H), 7.93−7.96 (m, 2H), 8.56 (m, 1H), 11.37 (s, 1H).

***N*-(3-Benzoyl-4-benzoylaminophenyl)-N^{α}-*tert*-butyloxycarbonyl-S-tritylcysteinamide (5e).** The compound was prepared from **4e** (0.232 g, 0.75 mmol) by following general procedure C. Compound **5e** is a yellow solid (0.321 g, 54% yield): mp 112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 9H), 2.54 (m, 1H), 2.69 (m, 1H), 3.81 (m, 1H), 4.71 (m, 1H), 7.16 (m, 9H), 7.34 (m, 14H), 7.66 (m, 2H), 7.77 (m, 1H), 7.96 (m, 2H), 8.74 (m, 1H), 11.66 (s, 1H).

***N*-(3-Benzoyl-4-benzoylaminophenyl)cysteinamide Hydrochloride (8a).** The compound was prepared from **5e** (0.15 g, 0.2 mmol) by following general procedure D. Compound **8a** is a yellow solid (0.078 g, 94% yield): mp 129 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.07 (s, 2H), 4.20 (s, 1H), 7.50 (m, 6H), 7.68 (m, 4H), 7.76 (m, 1H), 7.85 (s, 1H), 7.89 (m, 1H), 8.50 (2H), 10.61 (s, 1H), 11.05 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.8, 54.6, 121.0, 122.8, 124.7, 127.1, 128.0, 128.2, 129.4, 131.0, 131.5, 132.4, 132.7, 134.0, 134.3, 137.1, 165.1, 165.5, 194.3; ESI-MS m/z = 105 (100), 316 (82), 297 (41), 296 (27), 211 (25), 317 (20), 420 (11, base). Anal. ($C_{23}H_{22}ClN_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-3-phenylpropionylamide (3f).** The compound was prepared by following general procedure A. Compound **3f** is white solid (1.217 g, 65% yield): mp 76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.75 (t, J = 7 Hz, 2H), 3.01 (t, J = 7 Hz, 2H), 7.08 (m, 2H), 7.16 (m, 3H), 7.48 (m, 2H), 7.60 (m, 3H), 8.35 (m, 1H), 8.39 (m, 1H), 8.85 (m, 1H), 11.00 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-3-phenylpropionylamide (4f).** The compound was prepared from **3f** (1.2 g, 3.2 mmol) by following general procedure B. Compound **4f** is a yellow solid (0.933 g, 85% yield): mp 142−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.60 (t, J = 8 Hz, 2H), 2.96 (t, J = 8 Hz, 2H), 3.52 (s, 2H), 6.72 (m, 1H), 6.84 (m, 1H), 7.04 (m, 1H), 7.16 (m, 4H), 7.40 (m, 2H), 7.52 (m, 1H), 7.63 (m, 2H), 8.27 (m, 1H), 10.13 (s, 1H).

***N*-[3-Benzoyl-4-(3-phenylpropionylamino)phenyl]-N^{α}-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5f).** The compound was prepared from **4f** (0.374 g, 1.0 mmol) by following general procedure C. Compound **5f** is a yellow solid (0.342 g, 43% yield): mp 96 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (s, 9H), 2.60 (m, 2H), 2.64 (t, J = 8 Hz, 2H), 2.97 (t, J = 8 Hz, 2H), 3.79 (m, 1H), 4.70 (m, 1H), 7.04 (m, 1H), 7.16 (m, 15H), 7.34 (m, 5H), 7.40 (m, 2H), 7.44 (m, 1H), 7.52 (m, 1H), 7.61 (m, 2H), 7.66 (m, 1H), 8.46 (d, J = 9 Hz, 1H), 10.47 (s, 1H).

***N*-[3-Benzoyl-4-(3-phenylpropionylamino)phenyl]-cysteinamide Hydrochloride (8b).** The compound was prepared from **5f** (0.158 g, 0.2 mmol) by following general procedure D. Compound **8b** is yellow solid (0.062 g, 66% yield): mp 109 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.27 (t, J = 8 Hz, 2H), 2.55 (t, J = 8 Hz, 2H), 3.06 (s, 2H), 4.19 (s, 1H), 7.12 (m, 3H), 7.22 (m, 2H), 7.48 (m, 3H), 7.65 (m, 3H), 7.75 (m, 1H), 7.79 (m, 1H), 8.49 (s, 2H), 9.99 (s, 1H), 11.01 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 28.0, 30.3, 37.3, 54.5, 120.2, 120.5, 122.5, 122.8, 125.7, 126.0, 127.8, 128.0, 128.1, 129.3, 130.4, 131.2, 132.1, 132.6, 133.8, 137.1, 140.0, 141.1, 166.8, 167.9, 194.1; ESI-MS m/z = 212 (100), 344 (88), 211 (39), 238 (34), 447 (3, base − H). Anal. ($C_{25}H_{26}ClN_3O_3S$) C, H, N, S.

***N*-(2-Benzoyl-4-nitrophenyl)phenylglyoxylic Amide (3g).** The compound was prepared by following general procedure A. Compound **3g** is a yellow solid (1.58 g, 84% yield): mp 204 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53(m, 4H), 7.67 (m, 2H), 7.77 (m, 2H), 8.39 (m, 2H), 8.49 (m, 1H), 8.54 (m, 1H), 9.02 (m, 1H), 12.34 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)phenylglyoxylicamide (4g).** The compound was prepared from **3g** (1.122 g, 3.0 mmol) by following general procedure B. Compound **4g** is a yellow solid (0.897 g, 87% yield): mp 58 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66 (s, 2H), 6.82 (m, 1H), 6.88 (m, 1H), 7.47(m, 7H), 7.69 (m, 2H), 8.29 (m, 1H), 8.43 (m, 1H), 11.50 (s, 1H).

[3-Benzoyl-4-(2-oxy-3-phenylpropanoylamino)phenyl]-N^{α}-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5g). The compound was prepared from **4g** (0.516 g, 1.5 mmol) by following general procedure C. Compound **5g** is a yellow solid (0.236 g, 20% yield): mp 73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 9H), 2.55 (m, 1H), 2.69 (m, 1H), 3.63 (s, 2H), 7.13 (m, 3H), 7.22 (m, 5H), 7.33 (m, 6H), 7.41 (m, 4H), 7.53 (m, 5H), 7.71 (m, 3H), 8.30 (m, 2H), 8.62 (m, 1H), 11.80 (s, 1H).

***N*-[3-Benzoyl-4-(2-oxy-3-phenylpropanoylamino)phenyl]cysteinamide Hydrochloride (9a).** The compound was prepared from **5g** (0.112 g, 0.14 mmol) by following general procedure D. Compound **9a** is a yellow solid (0.06 g, 88% yield): mp 133 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.03 (s, 2H), 4.17 (m, 1H), 7.31 (m, 2H), 7.39 (m, 1H), 7.53 (m, 3H), 7.73 (m, 4H), 7.88 (m, 2H), 8.30 (m, 1H), 8.47 (s, 2H), 10.99 (s, 1H), 11.17 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 41.6, 51.5, 118.5, 120.8, 121.1, 122.0, 125.9, 127.9, 128.0, 128.7, 129.2, 130.2, 130.9, 131.9, 132.1, 132.4, 134.1, 137.7, 143.1, 165.4, 166.9, 194; ESI-MS m/z = 239 (100), 346 (47), 212 (67), 105 (59), 211 (47), 240 (33), 44 (31), 310 (22), 107 (22), 327 (20), 446 (1.47, base − 2H), 448 (0.2, base). Anal. ($C_{24}H_{22}ClN_3O_4S$) C, H, N, S.

***N*-(2-Benzoyl-4-nitrophenyl)-1-naphthoylamide (3h).** The compound was prepared by following general procedure A. Compound **3h** is a yellow solid (0.99 g, 50% yield): mp 160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (m, 8H), 7.84 (m, 2H), 7.96 (m, 1H), 8.46 (m, 2H), 9.16 (m, 1H), 11.74 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-1-naphthoylamide (4h).** The compound was prepared from **3h** (0.97 g, 2.4 mmol) by following general procedure B. Compound **4h** is a yellow solid (0.745 g, 83% yield): mp 77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 (s, 2H), 6.80 (m, 1H), 6.93 (m, 1H), 7.45 (m, 6), 7.65 (m, 2H), 7.72 (m, 1H), 7.79 (m, 1H), 7.86 (m, 1H), 8.44 (m, 1H), 8.57 (m, 1H), 10.78 (s, 1H).

***N*-[[3-Benzoyl-4-(1-naphthoylamino)phenyl]-N^{α}-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5h).** The compound was prepared from **4h** (0.36 g, 1.0 mmol) by following general procedure C. Compound **5h** is a yellow solid (0.556 g, 71% yield): mp 98 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34 (s, 9H), 2.55 (dd, J = 13, 5 Hz, 1H), 2.66 (dd, J = 13, 8 Hz, 1H), 3. 81 (m, 1H), 4.67 (m, 1H), 7.14 (m, 2H), 7.20 (m, 7H), 7.35 (m, 7H), 7.45 (m, 5H), 7.57 (m, 1H), 7.65 (m, 2H), 7.76 (m, 2H), 7.81 (m, 1H), 7.89 (m, 1H), 8.45 (m, 1H), 8.79 (m, 1H), 11.14 (s, 1H).

***N*-[[3-Benzoyl-4-(1-naphthoylamino)phenyl]cysteinamide Hydrochloride (9b).** The compound was prepared from **5h** (0.52 g, 0.64 mmol) by following general procedure D. Compound **9b** is a yellow solid (0.269 g, 83% yield): mp 133 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.05 (s, 2H), 4 0.16 (s, 1H), 7.24 (m, 1H), 7.48 (m, 5H), 7.62 (m, 2H), 7.75 (m, 2H), 7.86 (m, 2H), 7.95 (m, 3H), 8.49 (s, 2H), 10.63 (s, 1H), 11.05 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 25.2, 54.6, 120.9, 125.1, 125.5, 125.6, 126.6, 128.3, 128.7, 129.3, 129.5, 130.0, 130.5, 132.7, 133.0, 133.5, 134.0, 135.1, 137.3, 165.9, 166.2, 194.8; ESI-MS m/z = 155 (100), 64 (62), 127 (60), 44 (25), 192 (14), 366 (12), 507 (0.26, $M^+ + H$). Anal. ($C_{27}H_{24}ClN_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(1-naphthyl)acetamide (3i).** The compound was prepared by following general procedure A. Compound **3i** is a yellow solid (0.53 g, 26% yield): mp 117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.18 (s, 2H), 7.38 (m, 9H), 7.79 (m, 2H), 7.96 (m, 1H), 8.28 (m, 2H), 8.79 (m, 1H), 10.87 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(1-naphthyl)acetamide (4i).** The compound was prepared from **3i** (0.475 g, 1.15 mmol) by following general procedure B. Compound **4i** is a yellow solid (0.42 g, 96% yield): mp 63 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (s, 2H), 6.59 (m, 2H), 6.75 (m, 1H), 7.35 (m, 11), 7.76 (m, 2H), 7.96 (m, 1H), 8.14 (m, 1H), 9.86 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(1-naphthyl)acetylamino]phenyl]-N^{α}-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5i).** The compound was prepared from **4i** (0.42 g, 1.1 mmol) by following general procedure C. Compound **5i** is a yellow solid (0.572 g, 63% yield): mp 93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (s, 9H), 2.49 (dd, J = 13, 6 Hz, 1H), 2.65 (dd, J = 13, 7 Hz, 1H), 3.76 (m, 1H), 4.09 (s, 2H), 4.65 (m, 1H), 7.11 (m, 5H), 7.41 (m, 21H), 7.54 (m, 1H), 7.76 (m, 2H), 7.96 (m, 1H), 8.39 (m, 1H), 10.27 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(1-naphthyl)acetylamino]phenyl]-cysteinamide Hydrochloride (10a).** The compound was prepared from **5i** (0.17 g, 0.2 mmol) by following general procedure D. Compound **10a** is a yellow solid (0.092 g, 95% yield): mp 118 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.04 (s, 2H), 3.89 (s, 2H), 4.17 (s, 1H), 7.28 (m, 1H), 7.42 (m, 5H), 7.62 (m, 4H), 7.72 (m, 1H), 7.77 (m, 2H), 7.89 (m, 2H), 8.45 (s, 2H), 10.31 (s, 1H), 10.94 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 27.8, 42.6, 52.4, 109. 2, 120.5, 123.9, 125.3, 125.5, 127. 7, 128.1, 129.4, 132.3, 133.9, 139.4, 165.5, 169.1, 188.9; ESI-MS m/z = 380 (100), 212 (83), 361 (48), 141 (45), 239 (38), 211 (34), 381 (29), 360 (24), 142 (23), 168 (20), 484 (0.6, Base). Anal. ($C_{28}H_{26}ClN_3O_3S$) C, H, N, S.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(2-naphthyl)acetamide (3j).** The compound was prepared by following general procedure A. Compound **3j** is a yellow solid (1.106 g, 67% yield): mp 138 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.89 (s, 2H), 7.43 (m, 5H), 7.57 (m, 3H), 7.78 (m, 4H), 8.32 (m, 2H), 8.83 (m, 1H), 11.11 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(2-naphthyl)acetamide (4j).** The compound was prepared from **3j** (1.054 g, 2.6 mmol) by following general procedure B. Compound **4j** is a yellow solid (0.964 g, 98% yield): mp 55 °C; ^{1}H NMR (400 MHz,$CDCl_3$) δ 3.76 (s, 1H), 6.67 (m, 1H), 7.79 (m, 1H), 7.39 (m, 5H), 7.50 (m, 2H), 7.62 (m, 3H), 7.76 (m, 4H), 8.20 (m, 1H),10.10 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(2-naphthyl)acetylamino]phenyl]-N^{α}-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5j).** The compound was prepared from **4j** (0.57 g, 1.5 mmol) by following general procedure C. Compound **5j** is a yellow solid (0.674 g, 54% yield): mp 105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (s, 9H), 2.40 (dd, J = 13, 6 Hz, 1H), 2.65 (dd, J = 13, 7 Hz, 1H), 3.76 (m, 1H), 3.79 (s, 2H), 4.67 (m, 1H), 7.15 (m, 10H), 7.37 (m, 13H), 7.48 (m, 1H), 7.56 (m, 2H), 7.63 (m, 1H), 7.73 (m, 3H), 8.42 (m, 1H), 10.51 (s, 1H).

***N*-[3-Benzoyl-4-[2-(2-naphthyl)acetylamino]phenyl]cysteinamide Hydrochloride (10b).** The compound was prepared from **5j** (0.13 g, 0.16 mmol) by following general procedure D. Compound **10b** is a yellow solid (0.07 g, 85% yield): mp 112 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.05 (s, 2H), 3.49 (s, 2H), 4.14 (s, 1H), 7.22 (m, 1H), 7.45 (m, 4H), 7.56 (m, 4H), 7.56 (m, 2H), 7.63 (m, 3H), 7.76 (m, 4H), 7.85 (m, 1H), 8.46 (s, 1H), 10.26 (s, 1H), 10.98 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.8, 42.1, 54.6, 120.1, 122.5, 125.1, 125.8, 127.2, 127.3, 127.44, 127.46, 128.0, 129.3, 131.3, 132.1, 132.7, 134.0, 137.0, 165.4, 168.7, 194.4; ESI-MS m/z = 212 (100), 380 (83), 361 (60), 141 (50), 360 (44), 211 (43), 239 (27), 381 (24), 300 (21), 142 (20), 484 (0.2, base). Anal. ($C_{28}H_{26}ClN_3O_3S$) C, H, N, S.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(2-methylphenyl)acetamide (3k).** The compound was prepared by following general procedure A. Compound **3k** is a yellow solid (1.19 g, 64% yield): mp 119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (s, 3H), 3.75 (s, 2H), 7.18 (m, 3H), 7.23 (m, 1H), 7.45 (m, 2H), 7.57 (m, 3H), 8,31 (m, 1H), 8.34 (m, 1H), 8.83 (m, 1H), 10.86 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(2-methylphenyl)acetamide (4k).** The compound was prepared from **3k** (1.13 g, 3.0 mmol) by following general procedure B. Compound **4k** is a yellow solid (1.005 g, 97% yield): mp 182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24 (s, 3H), 3.63 (s, 2H), 6.66 (m, 1H), 6.80 (m, 1H), 7.16 (m, 4H), 7.39 (m, 2H), 7.50 (m, 1H), 7.60 (m, 2H), 8.18 (m, 1H), 9.80 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(2-methylphenyl)acetylamino]-phenyl]-N^{α}-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5k).** The compound was prepared from **4k** (0.344 g, 1.0 mmol) by following general procedure C. Compound **5k** is a yellow solid (0.307 g, 39% yield): mp 87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.25 (s, 3H), 2.51 (dd, J = 13, 5 Hz, 1H), 2.62 (dd, J = 13, 7 Hz, 1H), 3.66 (s, 2H), 3.84 (m, 1H), 4.79 (m, 1H), 7.16 (m, 14H), 7.33 (m, 6H), 7.37 (m, 2H), 7.44 (m, 1H), 7.49 (m, 1H), 7.59 (m, 3H), 8.43 (d, J = 9 Hz), 10.23 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(2-methylphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (11a).** The compound was prepared from **5k** (0.21 g, 0.26 mmol) by following general procedure D. Compound **11a** is a yellow solid (0.096 g, 76% yield): mp 106 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.11 (s, 3H), 3.05 (d, J = 5 Hz, 2H), 3.41 (s, 2H), 4.16 (s, 1H), 7.00 (m, 2H), 7.08 (m, 2H), 7.45 (m, 2H), 7.61 (m, 4H), 7.71 (m, 1H), 7.79 (m, 1H), 8.46 (s, 2H), 10.14 (s, 1H), 10.97 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 18.3, 24.1, 39.5, 53.9, 118.5, 119.9 121.8, 123.4, 124.8, 125.8, 127.3, 128.6, 128.9, 129.2, 131.5, 131.8, 133.0, 133.3, 135.7, 136.1, 164.6, 168.0, 193.9; ESI-MS m/z = 105 (100),212 (34), 239 (20), 344 (15), 448 (0.71, base). Anal. ($C_{25}H_{26}ClN_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(3-methylphenyl)acetamide (3l).** The compound was prepared by following general procedure A. Compound **3l** is a yellow solid (1.33 g, 71% yield): mp 94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.74 (s, 2H), 7.13 (m, 3H), 7.25 (m, 1H), 7.52 (m, 2H), 7.64 (m, 3H), 8,36 (m, 1H), 8.41 (m, 1H), 8.87 (m, 1H), 11.02 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(3-methylphenyl)acetamide (4l).** The compound was prepared from **3l** (1.272 g, 3.4 mmol) by following general procedure B. Compound **4l** is a yellow oil (1.067 g, 92% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.25 (s, 3H), 3.54 (s, 2H), 6.68 (m, 1H), 6.79 (m, 1H), 7.04 (m, 3H), 7.16 (m, 1H), 7.38 (m, 2H), 7.52 (m, 1H), 7.61 (m, 2H), 8.19 (m, 1H), 9.98 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(3-methylphenyl)acetylamino]phenyl]-N^{α} -*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5l).** The compound was prepared from **4l** (0.344 g, 1.0 mmol) by following general procedure C. Compound **5l** is a yellow solid (0.282 g, 36% yield): mp 93 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.26 (s, 3H), 2.51 (dd, J = 13, 5 Hz, 1H), 2.62 (dd,

J = 13, 7 Hz, 1H), 3.60 (s, 2H), 3.84 (m, 1H), 4.79 (m, 1H), 7.03 (m, 1H), 7.09 (m, 2H), 7.13 (m, 3H), 7.19 (m, 8H), 7.33 (m, 6H), 7.39 (m, 2H), 7.44 (m, 1H), 7.51 (m, 1H), 7.61 (m, 2H), 7.64 (m, 1H), 8.43 (d, J = 9 Hz), 10.38 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(3-methylphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (11b).** The compound was prepared from **5k** (0.213 g, 0.26 mmol) by following general procedure D. Compound **11b** is a yellow solid (0.079 g, 63% yield): mp 109 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.22 (s, 3H), 3.04 (d, J = 5 Hz, 2H), 3.34 (s, 2H), 4.16 (s, 1H), 6.87 (m, 1H), 6.91 (s, 1H), 6.98 (m, 1H), 7.10 (m, 1H), 7.46 (m, 2H), 7.57 (m, 2H), 7.64 (m, 2H), 7.71 (m, 1H), 7.77 (m, 1H), 8.45 (s, 2H), 10.13 (s, 1H), 10.94 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 20.7, 24.7, 41.9, 54.7, 120.5, 122.4, 124.1, 125.9, 126.9, 127.9, 128.0, 128.6, 129.3, 129.5, 131.0, 132.4, 132.5, 134.9, 135.3, 130.1, 165.3, 167.9, 195.9; ESI-MS m/z = 212 (100), 344 (66), 105 (43), 211 (38), 239 (24), 238 (21), 449 (0.83, base). Anal. ($C_{25}H_{26}ClN_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(4-methylphenyl)acetamide (3m).** The compound was prepared by following general procedure A. Compound **3m** is a yellow solid (1.75 g, 93% yield): mp 95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.74 (s, 2H), 7.17 (m, 2H), 7.24 (m, 2H), 7.51 (m, 2H), 7.65 (m, 3H), 8,37 (m, 1H), 8.41 (m, 1H), 8.88 (m, 1H), 11.05 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(4-methylphenyl)acetamide (4m).** The compound was prepared from **3m** (1.75 g, 4.67 mmol) by following general procedure B. Compound **4m** is a yellow solid (1.053 g, 65% yield): mp 159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 3H), 3.55 (s, 2H), 6.66 (m, 1H), 6.78 (m, 1H), 7.07 (m, 2H), 7.13 (m, 2H), 7.38 (m, 2H), 7.51 (m, 1H), 7.61 (m, 2H), 8.18 (m, 1H), 9.97 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-methylphenyl)acetylamino]phenyl]-N^{α}-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5m).** The compound was prepared from **4m** (0.861 g, 2.3 mmol) by following general procedure C. Compound **5m** is a yellow solid (1.104 g, 61% yield): mp 107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.26 (s, 3H), 2.51 (dd, J = 13, 5 Hz, 1H), 2.62 (dd, J = 13, 7 Hz, 1H), 3.59 (s, 2H), 3.84 (m, 1H), 4.81 (m, 1H), 7.14 (m, 14H), 7.32 (m, 6H), 7.38 (m, 2H), 7.49 (m, 2H), 7.60 (m, 2H), 7.66 (m, 1H), 8.42 (d, J = 9 Hz), 10.39 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-methylphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (12a).** The compound was prepared from **5m** (0.18 g, 0.23 mmol) by following general procedure D. Compound **12a** is a yellow solid (0.093 g, 84% yield): mp 114 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.23 (s, 3H), 3.05 (d, J = 5 Hz, 2H), 3.55 (s, 2H), 4.18 (s, 1H), 6.96 (m, 2H), 7.02 (m, 2H), 7.47 (m, 2H), 7.61 (m, 4H), 7.72 (m, 1H), 7.79 (m, 1H), 8.48 (s, 2H), 10.15 (s, 1H), 11.01 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.5, 24.5, 41.9, 51.9, 54.6, 120.5, 122.2, 124.2, 128.0, 128.6, 128.8, 129.3, 131.0, 132.1, 132.5, 134.1, 135.3, 137.1, 165.7, 168.9, 198.9; ESI-MS m/z = 212 (100), 344 (66), 211 (38), 105 (27), 239 (24), 238 (24), 449 (0.5, base + H). Anal. ($C_{25}H_{26}ClN_3O_3S$) C, H, N, S.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(4-chlorphenyl)acetamide (3n).** The compound was prepared by following general procedure A. Compound **3n** is a yellow solid (1.506 g, 76% yield): mp 130 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.71 (s, 2H), 7.25 (m, 2H), 7.29 (m, 2H), 7.24 (m, 2H), 7.61 (m, 3H), 8.33 (m, 1H), 8.39 (m, 1H), 8.82 (m, 1H), 11.10 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(4-chlorphenyl)acetamide (4n).** The compound was prepared from **3n** (1.48 g, 3.74 mmol) by following general procedure B. Compound **4n** is a yellow solid (1.124 g, 82% yield): mp 172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.53 (s, 2H), 3.58 (s, 2H), 6.71 (m, 1H), 6.81 (m, 1H), 7.23 (m, 4H), 7.40 (m, 2H), 7.52 (m, 1H), 7.62 (m, 2H), 8.22 (m, 1H), 10.15 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-chlorphenyl)acetylamino]phenyl]-N^{α}-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5n).** The compound was prepared from **4n** (0.547 g, 1.5 mmol) by following general procedure C. Compound **5n** is a yellow solid (0.62 g, 51% yield): mp 104 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.51 (dd, J = 13, 5 Hz, 1H), 2.65 (dd, J = 13, 7 Hz, 1H), 3.61 (s, 2H), 3.78 (m, 1H), 4.69 (m, 1H), 7.11 (m, 3H), 7.19 (m, 12H), 7.32 (m, 5H), 7.39 (m, 2H), 7.43 (m, 1H), 7.49 (m, 1H), 7.60 (m, 2H), 7.65 (m, 1H), 8.41 (m, 1H), 10.52 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-chlorphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (12b).** The compound was prepared from **5n** (0.15 g, 0.19 mmol) by following general procedure D. Compound **12b** is a yellow solid (0.08 g, 86% yield): mp 117 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.04 (s, 2H), 3.38 (s, 2H), 4.18 (s, 1H), 7.07 (m, 2H), 7.26 (m, 2H), 7.45 (m, 2H), 7.52 (m, 1H), 7.61 (m, 3H), 7.71 (m, 1H), 7.78 (m, 1H), 8.46 (s, 2H), 10.20 (s, 1H), 10.98 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.8, 42.1, 54.6, 119.2, 120.5, 122.4, 124.4, 127.9, 128.1, 129.3, 130.8, 131.0, 132.5, 134.1,134.2 136.7, 165.4, 168.3, 194.4; ESI-MS m/z = 212 (100), 364 (87), 211 (52), 239 (33), 366 (31), 238 (29), 345 (27), 452 (26), 300 (23), 365 (21); 467 (0.5, base). Anal. ($C_{24}H_{22}Cl_2N_3O_3S$) C, H, N,S.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(4-bromphenyl)acetamide (3o).** The compound was prepared by following general procedure A. Compound **3o** is a yellow solid (1.91 g, 87% yield): mp 138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 2H), 7.25 (m, 2H), 7.29 (m, 2H), 7.24 (m, 2H), 7.61 (m, 3H), 8.39 (m, 1H), 8.45 (m, 1H), 8.88 (m, 1H), 11.17 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(4-bromphenyl)acetamide (4o).** The compound was prepared from **3o** (1.89 g, 4.3 mmol) by following general procedure B. Compound **4o** is a yellow oil (1.146 g, 65% yield); ^{1}H NMR (400 MHz, $CDCl_3$): 3.58 (s, 4H), 6.71(d, J = 3 Hz, 1H), 6.80 (m, 1H), 7.15 (d, J = 9 Hz, 1H), 7.19 (m, 1H), 7.40 (m, 4H), 7.52 (m, 1H), 7.61 (m, 2H), 8.21 (d, J = 9 Hz, 1H), 10.16 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-bromphenyl)acetylamino]phenyl]-N^{α}-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5o).** The compound was prepared from **4o** (0.409 g, 1.0 mmol) by following general procedure C. Compound **5o** is a yellow solid (0.448 g, 52% yield): mp 103 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.51 (dd, J = 13, 5 Hz, 1H), 2.65 (dd, J = 13, 7 Hz, 1H), 3.59 (s, 2H), 3.79 (m, 1H), 4.69 (m, 1H), 7.15 (m, 12H), 7.32 (m, 6H), 7.38 (m, 3H), 7.43 (m, 2H), 7.51 (m, 1H), 7.61 (m, 2H), 7.80 (m, 1H), 7.65 (m, 1H), 8.42 (m, 1H), 10.52 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-bromphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (12c).** The compound was prepared from **5o** (0.42 g, 0.49 mmol) by following general procedure D. Compound **12c** is a yellow solid (0.206 g, 81% yield): mp 112 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.05 (s, 2H), 3.35 (s, 2H), 4.16 (s, 1H), 7.00 (m, 2H), 7.46 (m, 4H), 7.50 (m, 1H), 7.61 (m, 3H), 7.71 (m, 1H), 7.79 (m, 1H), 8.46 (s, 2H), 10.22 (s, 1H), 10.99 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 25.7, 42.4, 55.5, 119.4, 120.5, 121.3, 123.3, 125.4, 129.0, 130.3, 131.8, 132.1,132.4, 132.7, 133.5, 135.2, 135.5 137,6, 166.4, 169.2, 195.2; ESI-MS m/z = 58 (100), 212 (44), 105 (34), 211 (33), 169 (31), 239 (23), 281 (21); 513 (0.34, base). Anal. ($C_{24}H_{23}BrClN_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(4-trifluoromethylphenyl)acetamide (3p).** The compound was prepared by following general procedure A. Compound **3p** is a yellow solid (1.866 g, 86% yield): mp 109 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.80 (s, 2H), 7.44 (m, 2H), 7.48 (m, 2H), 7.59 (m, 5H), 8.33 (m, 1H), 8.41 (m, 1H), 8.82 (m, 1H), 11.17 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(4-trifluoromethylphenyl)acetamide (4p).** The compound was prepared from **3p** (0.51, 1.2 mmol) by following general procedure B. Compound **4p** is a yellow solid (0.434 g, 91% yield): mp 169 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.67 (s, 2H), 6.72 (m, 1H), 6.81 (m, 1H), 7.41 (m, 4H), 7.52 (m, 3H), 7.61 (m, 2H), 8.23 (m, 1H), 10.26 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-trifluoromethylphenyl)acetylamino]phenyl]-N^{α}-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5p).** The compound was prepared from **4p** (0.398 g, 1.0 mmol) by following general procedure C. Compound **5p** is a yellow solid (0.342 g, 41% yield): mp 85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.51 (dd, J = 13, 5 Hz, 1H), 2.65 (dd, J = 13, 6 Hz, 1H), 3. 07 (s, 2H), 3.79 (m, 1H), 4.68 (m, 1H), 6.81 (m, 2H), 7.12 (m, 3H), 7.18 (m, 7H), 7.33 (m, 6H),

7.41 (m, 5H), 7.53 (m, 3H), 7.60 (m, 2H), 7.66 (m, 1H), 8.43 (d, J = 9 MHz, 1H), 10.60 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-trifluoromethylphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (12e).** The compound was prepared from **5p** (0.32 g, 0.38 mmol) by following general procedure D. Compound **12e** is a yellow solid (0.197 g, 95% yield): mp 129 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.06 (s, 2H), 3.50 (s, 2H), 4.19 (s, 1H), 7.29 (m, 2H), 7.44 (m, 2H), 7. 56 (m, 4H), 7.63 (m, 2H), 7.74 (m, 1H), 7.81 (m, 1H), 8.49 (s, 2H), 10.23 (s, 1H), 11.03 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 22.3, 27.9, 39.5, 52.2, 52.8, 118.1 120.0, 120.7, 122.0, 122.3, 122.3, 122.8, 124.5, 124.8, 125.6, 126.8, 127.3, 129.1, 129.3, 130.0, 132.0, 134.3, 137.5, 162.9, 165.6, 191.9; ESI-MS m/z = 398 (100), 212 (92), 105 (28), 211 (48), 379 (43), 378 (25), 239 (19), 105 (18), 501 (1.33, base − H). Anal. ($C_{25}H_{23}ClF_3N_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(4-methoxyphenyl)acetamide (3q).** The compound was prepared by following general procedure A. Compound **3q** is a yellow solid (1.341 g, 69% yield): mp 120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (s, 2H), 3.72 (s, 3H), 6.85 (m, 2H), 7.22 (m, 2H), 7.46 (m, 2H), 7.59 (m, 3H), 8.32 (m, 1H), 8.36 (m, 1H), 8.83 (m, 1H), 10.99 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(4-methoxyphenyl)acetamide (4q).** The compound was prepared from **3q** (1.32 g, 3.3 mmol) by following general procedure B. Compound **4q** is a yellow solid (1.162 g, 95% yield): mp 129 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.54 (s, 2H), 3.71 (s, 3H), 6.68 (m, 1H), 6.81 (m, 1H), 7.18 (m, 2H), 7.38 (m, 2H), 7.49 (m, 1H), 7.52 (m, 1H), 7.61 (m, 2H), 8. 91 (m, 1H), 9.98 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-methoxyphenyl)acetylamino]phenyl]-*N*$^\alpha$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5q).** The compound was prepared from **4q** (0.36 g, 1.0 mmol) by following general procedure C. Compound **5q** is a yellow solid (0.367 g, 46% yield): mp 105 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.51 (dd, J = 13, 5 Hz, 1H), 2.65 (dd, J = 13, 7 Hz, 1H), 3.57 (s, 2H), 3.71 (s, 3H), 3.77 (m, 1H), 4.68 (m, 1H), 6.81 (m, 2H), 7.12 (m, 3H), 7.18 (m, 9H), 7.32 (m, 6H), 7. 83 (m, 2H), 7.43 (m, 1H), 7.50 (m, 1H), 7.59 (m, 2H), 7.63 (m, 1H), 8.43 (d, J = 9 MHz, 1H), 10.38 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-methoxyphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (12f).** The compound was prepared from **5q** (0.32 g, 0.39 mmol) by following general procedure D. Compound **12f** is a yellow solid (0.14 g, 72% yield): mp 95 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.04 (s, 2H), 3.30 (s, 2H), 3.69 (s, 3H), 4.16 (s, 1H), 6.77 (m, 2H), 6.99 (m, 2H), 7.45 (m, 2H), 7.60 (m, 4H), 7.72 (m, 1H), 7.79 (m, 1H), 8.47 (s, 2H), 10.13 (d, J = 4 Hz, 1H), 10.99 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 24.7, 39.5, 52.6, 52.8, 111.5, 118.6 120.4, 122.1, 125.0, 126.0, 126.1, 126.8, 127.3, 127.9, 130.1, 130.5, 132.1, 134.8, 155.8, 163.4, 167.0, 192.5; ESI-MS m/z = 121 (100), 44 (55), 148 (50), 212 (33), 105 (28), 239 (13), 281 (11), 501 (1.25, base). Anal. ($C_{25}H_{26}ClN_3O_4S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(4-biphenylyl)acetamide (3r).** The compound was prepared by following general procedure A. Compound **3r** is a yellow solid (1.5 g, 68% yield): mp 106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 2H), 7.44 (m, 14H), 8.38 (m, 1H), 8.43 (m, 1H), 8.90 (m, 1H), 11.14 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(4-biphenylyl)acetamide (4r).** The compound was prepared from **3r** (1.63 g, 3.7 mmol) by following general procedure B. Compound **4r** is a yellow solid (1.097 g, 72% yield): mp 67 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (s, 2H), 3.70 (s, 2H), 6.75 (m, 1H), 6.87 (m, 1H), 7.54 (m, 14), 8.29 (m, 1H), 10.19 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-biphenyl)acetylamino]phenyl]-*N*$^\alpha$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5r).** The compound was prepared from **4r** (0.813 g, 2.0 mmol) by following general procedure C. Compound **5r** is a yellow solid (0.954 g, 56% yield): mp 105 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.51 (dd, J = 13, 5 Hz, 1H), 2.66 (dd, J = 13, 8 Hz, 1H), 3.68 (s, 2H), 3.78 (m, 1H), 4.67 (m, 1H), 7.12 (m, 4H), 7.18 (m, 6H), 7.26 (m, 1H), 7.35 (m, 12H), 7.44 (m, 1H), 7.50 (m, 5H), 7.60 (m, 2H), 7.65 (m, 1H), 8.46 (m, 1H), 10.51 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-biphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (12g).** The compound was prepared from **5r** (0.16 g, 0.19 mmol) by following general procedure D. Compound **12g** is a yellow solid (0.1 g, 95% yield): mp 116 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.05 (s, 2H), 3.43 (s, 2H), 4.16 (s, 1H), 7.16 (m, 2H), 7.33 (m, 1H), 7.59 (m, 14H), 8.46 (s, 2H), 10.22 (s, 1H), 10.97 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 24.8, 41.9, 54.6, 120.4, 122.6, 124.3, 126.3, 126.4, 127.1, 128.1, 128.7, 129.3, 129.5, 132.5, 134.4, 137.6, 138.2, 165.4, 168.7, 194.5; ESI-MS m/z = 212 (100), 406 (99), 167 (62), 211 (51), 378 (47), 194 (33), 407 (30), 239 (27), 386 (26), 238 (25), 168 (21). Anal. ($C_{30}H_{28}ClN_3O_3S$) C, H, N, S.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(2,4-dichlorphenyl)acetamide (3s).** The compound was prepared by following general procedure A. Compound **3s** is a yellow solid (1.109 g, 52% yield): mp 159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.69 (s, 2H), 7.15 (m, 1H), 7.39 (m, 2H), 7.48 (m, 2H), 7.62 (m, 3H), 8.34 (m, 1H), 8.41 (m, 1H), 8.81 (m, 1H), 11.16 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(2,4-dichlorphenyl)acetamide (4s).** The compound was prepared from **3s** (1.087 g, 2.5 mmol) by following general procedure B. Compound **4s** is a yellow solid (0.908 g, 93% yield): mp 152 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.56 (s, 2H), 6.71(m, 1H), 6.81 (m, 1H), 7.11 (m, 1H), 7.33 (m, 1H), 7.39 (m, 3H), 7.52 (m, 1H), 7.62 (m, 2H), 8.21 (m, 1H), 10.23 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(2,4-dichlorphenyl)acetylamino]phenyl]-*N*$^\alpha$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5s).** The compound was prepared from **4s** (0.399 g, 1.0 mmol) by following general procedure C. Compound **5s** is a yellow solid (0.359 g, 43% yield): mp 91 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.52 (dd, J = 13, 5 Hz, 1H), 2.67 (dd, J = 13, 7 Hz, 1H), 3.59 (s, 2H), 3.78 (m, 1H), 4.66 (m, 1H), 7.13 (m, 4H), 7.19 (m, 8H), 7.33 (m, 7H), 7.39 (m, 2H), 7.44 (m, 1H), 7.51 (m, 1H), 7.61 (m, 2H), 7.68 (m, 1H), 8.41 (m, 1H), 10.59 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(2,4-dichlorphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (13a).** The compound was prepared from **5s** (0.325 g, 0.38 mmol) by following general procedure D. Compound **13a** is a yellow solid (0.156 g, 76% yield): mp 126 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.05 (s, 2H), 3.41 (s, 2H), 4.17 (m, 1H), 7.04 (m, 1H), 7.32 (m, 1H), 7.43 (m, 3H), 7.53 (m, 2H), 7.60 (m, 2H), 7.71 (m, 1H), 7.78 (m, 1H), 8.45 (s, 2H), 10.16 (s, 1H), 10.94 (s, 1H); ^{13}C NMR (100 MHz,DMSO-d_6) δ 24.7, 40.9, 54.5, 122.3, 124.2, 124.5, 125.2, 127.9, 129.1, 129.2, 129.9, 130.4, 130.8, 131.4, 132.3, 134.2, 136,0, 165.3, 167.8, 194.2; ESI-MS m/z = 44 (100), 212 (60), 105 (48), 211 (33), 159 (31), 239 (23), 237 (21); 538 (0.83, base). Anal. ($C_{24}H_{22}Cl_3N_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(3,4-dichlorphenyl)acetamide (3t).** The compound was prepared by following general procedure A. Compound **3t** is a yellow solid (1.153 g, 54% yield): mp 134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 2H), 7.24 (m, 1H), 7.28 (m, 1H), 7.38 (m, 1H), 7.47 (m, 2H), 7.61 (m, 3H), 8.33 (m, 1H), 8.39 (m, 1H), 8.82 (m, 1H), 11.07 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(3,4-dichlorphenyl)acetamide (4t).** The compound was prepared from **3t** (1.14 g, 2.6 mmol) by following general procedure B. Compound **4t** is a yellow solid (0.986 g, 96% yield): mp 146 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 3.57 (s, 2H), 3.72 (s, 2H), 6.70(m, 1H), 6.80 (m, 1H), 7.18 (m, 1H), 7.24 (m, 1H), 7.33 (m, 1H), 7.40 (m, 2H), 7.51 (m, 1H), 7.61 (m, 2H), 8.22 (m, 1H), 10.14 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(3,4-dichlorphenyl)acetylamino]phenyl]-*N*$^\alpha$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5t).** The compound was prepared from 5t (0.399 g, 1.0 mmol) by following general procedure C. Compound **5t** is a yellow solid (0.384 g, 45% yield): mp 89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.53 (dd, J = 13, 5 Hz, 1H), 2.68 (dd, J = 13, 7 Hz, 1H), 3.76 (s, 2H), 3.78 (m, 1H), 4.68 (m, 1H), 7.13 (m, 3H), 7.19 (m, 9H), 7.24 (m, 1H), 7.33 (m, 6H), 7.39 (m, 2H), 7.46 (m, 1H), 7.51 (m, 1H), 7.61 (m, 2H), 7.66 (m, 1H), 8.43 (m, 1H), 10.50 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(3,4-dichlorphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (13b).** The compound was

prepared from **5t** (0.33 g, 0.39 mmol) by following general procedure D. Compound **13b** is a yellow solid (0.155 g, 74% yield): mp 116 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.05 (s, 2H), 3.53 (s, 2H), 4.17 (m, 1H), 7.18 (m, 1H), 7.30 (m, 1H), 7.48 (m, 3H), 7.58 (m, 2H), 7.63 (m, 2H), 7.73 (m, 1H), 7.79 (m, 1H), 8.46 (s, 2H), 10.20 (s, 1H), 11.00 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.7, 40.7, 54.5, 122.3, 124.2, 124.5, 125.2, 128.0, 128.2, 129.3, 129.9, 130.4, 130.8, 131.4, 132.3, 132.5, 132.9, 134.4, 136,0, 165.8, 167.3, 195.2; ESI-MS m/z = 398 (100), 400 (68), 424 (32), 159 (53), 55 (52), 123(45), 105 (41), 212 (37), 211 (27), 538 (0.72, M^+). Anal. ($C_{24}H_{22}Cl_3N_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(2,6-dichlorphenyl)acetamide (3u).** The compound was prepared by following general procedure A. Compound **3u** is a yellow solid (1.264 g, 64% yield): mp 172 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.15 (s, 2H), 7.18 (m, 1H), 7.32 (m, 2H), 7. 64 (m, 2H), 7.60 (m, 3H), 8.32 (m, 1H), 8.38 (m, 1H), 8.83 (m, 1H), 11.06 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(2,6-dichlorphenyl)acetamide (4u).** The compound was prepared from **3u** (1.225 g, 2.85 mmol) by following general procedure B. Compound **4u** is a yellow solid (1.012 g, 89% yield): mp 148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.52 (s, 2H), 4.03 (s, 1H), 6.69(m, 1H), 6.80 (m, 1H), 7.14 (m, 1H), 7.28 (m, 2H), 7.39 (m, 2H), 7.51 (m, 1H), 7.61 (m, 2H), 8.26 (m, 1H), 10.12 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(2,6-dichlorphenyl)acetylamino]phenyl]-*N*$^\alpha$-*tert*-butyloxycarbonyl-S-tritylcysteinamide (5u).** The compound was prepared from **4u** (0.399 g, 1.0 mmol) by following general procedure C. Compound **5u** is a yellow solid (0.334 g, 40% yield): mp 83 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.51 (dd, J = 13, 5 Hz, 1H), 2.65 (dd, J = 13, 7 Hz, 1H), 3.77 (m, 1H), 4.06 (s, 2H), 4.67 (m, 1H), 7.13 (m, 3H), 7.19 (m, 8H), 7.29 (m, 2H), 7.33 (m, 6H), 7.39 (m, 2H), 7.44 (m, 1H), 7.51 (m, 1H), 7.60 (m, 2H), 7.65 (m, 1H), 8.48 (m, 1H), 10.50 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(2,6-dichlorphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (13c).** The compound was prepared from **5u** (0.3 g, 0.35 mmol) by following general procedure D. Compound **13c** is a yellow solid (0.157 g, 77% yield): mp 143 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.06 (s, 2H), 3.33 (m, 1H), 3.73 (s, 2H), 4.18 (s, 1H), 7.26 (m, 1H), 7.38 (m, 2H), 7.47 (m, 2H), 7.62 (m, 4H), 7.74 (m, 1H), 7.79 (m, 1H), 8.49 (s, 2H), 10.16 (s, 1H), 10.97 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.6, 37.7, 54.5, 120.7, 122.6, 124.2, 127.8, 128.0, 129.1, 131.4, 132.4, 135.3, 137,4, 165.3, 166.3, 194.6; ESI-MS m/z = 105 (100), 212 (44), 44 (34), 211 (33), 159 (31), 237 (23), 424 (21); 502 (0.54, base). Anal. ($C_{24}H_{22}Cl_3N_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(3,5-dichlorphenyl)acetamide (3v).** The compound was prepared by following general procedure A. Compound **3v** is a yellow solid (1.76 g, 57% yield): mp 145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.85 (s, 2H), 7.21 (m, 1H), 7.29 (m, 1H), 7.34 (m, 1H), 7.48 (m, 2H), 7.61 (m, 3H), 8.34 (m, 1H), 8.41 (m, 1H), 8.82 (m, 1H), 11.11 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(3,5-dichlorphenyl)acetamide (4v).** The compound was prepared from **3v** (1.0 g, 2.3 mmol) by following general procedure B. Compound **4v** is a yellow solid (0.882 g, 96% yield): mp 146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 2H), 6.71 (m, 1H), 6.81 (m, 1H), 7.15 (m, 1H), 7.24 (m, 1H), 7.31 (m, 1H), 7.41 (m, 2H), 7.54 (m, 1H), 7.63 (m, 2H), 8.23 (m, 1H), 10.18 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(3,5-dichlorphenyl)acetylamino]phenyl]-*N*$^\alpha$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5v).** The compound was prepared from **4v** (0.399 g, 1.0 mmol) by following general procedure C. Compound **5v** is a yellow solid (0.29 g, 34% yield): mp 91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.51 (dd, J = 13, 5 Hz, 1H), 2.66 (dd, J = 13, 7 Hz, 1H), 3.76 (s, 2H), 3.78 (m, 1H), 4.69 (m, 1H), 7.13 (m, 3H), 7.19 (m, 8H), 7.25 (m, 1H), 7.33 (m, 7H), 7.43 (m, 2H), 7.48 (m, 1H), 7.52 (m, 1H), 7.62 (m, 2H), 7.67 (m, 1H), 8.43 (m, 1H), 10.54 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(3,5-dichlorphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (13d).** The compound was prepared from **5v** (0.270 g, 0.32 mmol) by following general procedure D. Compound **13d** is a yellow solid (0.295 g, 87% yield): mp 86 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.05 (s, 2H), 3.57 (s, 2H), 4.17 (m, 1H), 7.31 (m, 2H), 7.39 (m, 1H), 7.47 (m, 2H), 7.62 (m, 2H), 7.65 (m, 2H), 7.74 (m, 1H), 7.80 (m, 1H), 8.44 (s, 2H), 10.18 (s, 1H), 10.91 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.6, 54.5, 120.6, 122.5, 124.2, 125.9, 127.9, 128.0, 128.1, 128.7, 129.2, 130.2, 130.9, 131.1,131.2, 131.9, 132.1, 132.4, 134.1, 135.1, 136.7, 143.5, 165.2, 167.0, 194.5; ESI-MS m/z = 41 (100), 55 (92), 105 (86), 43 (86), 159 (64), 212 (49), 37 (45), 211 (43), 539 (0.81, M^+ + H). Anal. ($C_{24}H_{22}Cl_3N_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(2,5-dichlorphenyl)acetamide (3w).** The compound was prepared by following general procedure A. Compound **3w** is a yellow solid (1.239 g, 58% yield): mp 143 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.85 (s, 2H), 7.21 (m, 1H), 7.30 (m, 1H), 7.35 (m, 1H), 7.49 (m, 2H), 7.61 (m, 3H), 8.34 (m, 1H), 8.40 (m, 1H), 8.82 (m, 1H), 11.11 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(2,5-dichlorphenyl)acetamide (4w).** The compound was prepared from **3w** (1.2 g, 2.8 mmol) by following general procedure B. Compound **4w** is a yellow solid (0.928 g, 83% yield): mp 132 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.59 (s, 2H), 3.72 (s, 2H), 6.71 (m, 1H), 6.80 (m, 1H), 7.16 (m, 1H), 7.22 (m, 1H), 7.31 (m, 1H), 7.39 (m, 2H), 7.55 (m, 1H), 7.62 (m, 2H), 8.22 (m, 1H), 10.18 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(2,5-dichlorphenyl)acetylamino]phenyl]-*N*$^\alpha$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5w).** The compound was prepared from **4w** (0.2 g, 0.5 mmol) by following general procedure C. Compound **5w** is a yellow solid (0.215 g, 51% yield): mp 91 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.51 (dd, J = 13, 5 Hz, 1H), 2.66 (dd, J = 13, 7 Hz, 1H), 3.63 (s, 1H), 3.76 (m, 2H), 4.68 (m, 1H), 7.13 (m, 4H), 7.19 (m, 8H), 7.25 (m, 1H), 7.33 (m, 6H), 7.41 (m, 2H), 7.46 (m, 1H), 7.52 (m, 1H), 7.62 (m, 2H), 7.67 (m, 1H), 8.45 (m, 1H), 10.55 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(2,5-dichlorphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (13e).** The compound was prepared from **5w** (0.49 g, 0.57 mmol) by following general procedure D. Compound **13e** is a yellow solid (0.295 g, 96% yield): mp 117 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.07 (s, 2H), 3.42 (s, 2H), 4.18 (m, 1H), 7.31 (m, 2H), 7.39 (m, 1H), 7.48 (m, 2H), 7.61 (m, 2H), 7.66 (m, 2H), 7.74 (m, 1H), 7.80 (m, 1H), 8.48 (s, 2H), 10.21 (s, 1H), 11.00 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 25.2, 39.5, 55.1, 121.1, 121.2, 123.0, 123.1, 124.8, 126.5, 128.5, 128.6, 128.7, 129.3, 129.8, 130.8, 131.6,131.7, 131.7, 132.4, 132.5, 132.7, 133.0, 134.7, 135,7, 137.2, 165.8, 167.6, 195.0; ESI-MS m/z = 398 (100), 44 (73), 105 (59), 159 (53), 55 (52), 212 (37), 211 (27), 539 (0.64, M^+ + H). Anal. ($C_{24}H_{22}Cl_3N_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2-(2,3-dichlorphenyl)acetamide (3x).** The compound was prepared by following general procedure A. Compound **3x** is a yellow solid (1.328 g, 62% yield): mp 78 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.90 (s, 2H), 7.25 (m, 1H), 7.34 (m, 1H), 7.39 (m, 1H), 7.52 (m, 2H), 7.65 (m, 3H), 8.38 (m, 1H), 8.44 (m, 1H), 8.86 (m, 1H), 11.16 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-(2,3-dichlorphenyl)acetamide (4x).** The compound was prepared from **3x** (1.295 g, 3.0 mmol) by following general procedure B. Compound **4x** is a yellow solid (1.134 g, 94% yield): mp 152 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.67 (s, 2H), 3.80 (s, 2H), 6.79 (m, 1H), 6.89 (m, 1H), 7.24 (m, 1H), 7.32 (m, 1H), 7.39 (m, 1H), 7.47 (m, 2H), 7.59 (m, 1H), 7.70 (m, 2H), 8.30 (m, 1H), 10.26 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(2,3-dichlorphenyl)acetylamino]phenyl]-*N*$^\alpha$ -*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5x).** The compound was prepared from **4x** (0.399 g, 1.0 mmol) by following general procedure C. Compound **5x** is a yellow solid (0.528 g, 63% yield): mp 94 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.51 (dd, J = 13, 5 Hz, 1H), 2.66 (dd, J = 13, 7 Hz, 1H), 3.76 (s, 2H), 3.78 (m, 1H), 4.68 (m, 1H), 7.13 (m, 3H), 7.19 (m, 8H), 7.25 (m, 1H), 7.33 (m, 7H), 7.42 (m, 2H), 7.46 (m, 1H), 7.52 (m, 1H), 7.62 (m, 2H), 7.67 (m, 1H), 8.44 (m, 1H), 10.55 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(2,3-dichlorphenyl)acetylamino]phenyl]cysteinamide Hydrochloride (13f).** The compound was prepared from **5x** (0.49 g, 0.57 mmol) by following general procedure D. Compound **13f** is a yellow solid (0.295 g, 96% yield): mp 123 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.07 (s, 2H), 3.42 (s, 2H), 4.18 (m, 1H), 7.31 (m, 2H), 7.39 (m, 1H), 7.48 (m, 2H), 7.61 (m, 2H), 7.66 (m, 2H), 7.74 (m, 1H), 7.80 (m, 1H), 8.48 (s, 2H), 10.21 (s, 1H), 11.00 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 25.2, 39.5, 55.1, 121.1, 121.2, 123.0, 123.1, 124.8, 126.5, 128.5, 128.6, 128.7, 129.3, 129.8, 130.8, 131.6,131.7, 131.7, 132.4, 132.5, 132.7, 133.0, 134.7, 135,7, 137.2, 165.8, 167.6, 195.0; ESI-MS *m*/*z* = 44 (100), 55 (86), 105 (70), 69 (53), 212 (43), 237(42), 159 (38), 502 (0.21, base). Anal. ($C_{24}H_{22}Cl_3N_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2-phenylpropionylamide (3y).** The compound was prepared by following general procedure A. Compound 3y is a yellow solid (1.098 g, 59% yield): mp 130 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.55 (d, *J* = 7 Hz, 3H), 3.74 (q, *J* = 7 Hz, 1H), 7.19 (m, 1H), 7.30 (m, 2H), 7.34 (m, 2H), 7.45 (m, 2H), 7.58 (m, 3H), 8.30 (m, 1H), 8.35 (m, 1H), 8.85 (m, 1H), 11.11 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2-phenylpropionylamide (4y).** The compound was prepared from **3y** (1.02 g, 2.75 mmol) by following general procedure B. Compound **4y** is a yellow oil (0.937 g, 98% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.50 (d, *J* = 7 Hz, 3H), 3.63 (q, *J* = 7 Hz, 1H), 6.69 (m, 1H), 6.80 (m, 1H), 7.17 (m, 1H), 7.25 (m, 2H), 7.31 (m, 2H), 7.38 (m, 2H), 7.51 (m, 1H), 7.59 (m, 2 H), 8.25 (m, 1H), 10.21 (s, 1H).

***N*-[[3-Benzoyl-4-(2-phenylpropylamino)]phenyl]-*N*$^\alpha$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5y).** The compound was prepared from **4y** (0.344 g, 1.0 mmol) by following general procedure C. Compound **5y** is a yellow solid (0.12 g, 15% yield): mp 97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 9H), 1.53 (m, 3H), 2.51 (dd, *J* = 13, 5 Hz, 1H), 2.62 (dd, *J* = 13, 7 Hz, 1H), 3.65 (m, 3H), 3.76 (m, 1H), 4.79 (m, 1H), 7.12 (m, 3H), 7.19 (m, 7H), 7.28 (m, 2H), 7.33 (m, 9H), 7.39 (m, 2H), 7.46 (m, 2H), 7.59 (m, 2H), 7.63 (m, 1H), 8.48 (m, 1H), 10.57 (s, 1H).

***N*-[[3-Benzoyl-4-(2-phenylpropylamino)]phenyl]cysteinamide Hydrochloride (15a).** The compound was prepared from **5y** (0.09 g, 0.11 mmol) by following general procedure D. Compound **15a** is a yellow solid (0.048 g, 93% yield): mp 114 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.12 (d, *J* = 7 Hz, 3H), 3.05 (d, *J* = 5 Hz, 2H), 3.44 (m, 1H), 3.59 (m, 1H), 4.17 (s, 1H), 7.20 (m, 5H), 7.46 (m, 2H), 7.54 (m, 1H), 7.63 (m, 3H), 7.76 (m, 2H), 8.46 (s, 2H), 10.13 (s, 1H), 10.96 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 18.5, 25.3, 45.8, 55.1, 121.5, 123.0, 126.9, 127.2, 128.0, 128.5, 128.5, 129.7, 131.0, 132.7, 132.9, 134.1, 137.4, 141.5, 166.3, 172.2, 195.9; ESI-MS *m*/*z* = 105 (100), 44 (65), 212 (50), 77 (49), 132 (26), 344 (24), 238 (22), 484 (0.42, M^+). Anal. ($C_{25}H_{26}ClN_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)-2,2-diphenylacetamide (3z).** The compound was prepared by following general procedure A. Compound **3z** is a yellow solid (1.98 g, 91% yield): mp 159 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.11 (s, 1H), 7.27 (m, 2H), 7.35 (m, 8H), 7.51 (m, 2H), 7.64 (m, 3H), 7.39 (m, 1H), 7.43 (m, 1H), 8.98 (m, 1H), 11.28 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)-2,2-phenylacetamide (4z).** The compound was prepared from **3z** (1.93 g, 4.5 mmol) by following general procedure B. Compound **4z** is a yellow solid (1.64 g, 90% yield): mp 162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.58 (s, 2H), 5.00 (s, 1H), 6.75 (m, 1H), 6.86 (m, 1H), 7.22 (m, 2H), 7.31 (m, 8H), 7.44 (m, 2H), 7.57 (m, 1H), 7.67 (m, 2H), 8.38 (m, 1H), 10.35 (s, 1H).

***N*-[3-Benzoyl-4-(2,2-diphenylacetylamino)phenyl]-*N*$^\alpha$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (5z).** The compound was prepared from **4z** (0.406 g, 1.0 mmol) by following general procedure C. Compound **5z** is a yellow solid (0.38 g, 45% yield): mp 103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 9H), 2.58 (m, 1H), 2.72 (m, 1H), 3.84 (m, 1H), 4.75 (m, 1H), 5.03 (s, 1H), 7.19 (m, 3H), 7.26 (m, 10H), 7.35 (m, 10H), 7.45 (m, 2H), 7.54 (m, 2H), 7.64 (m, 2H), 7.71 (m, 1H), 8.60 (m, 1H), 10.71 (s, 1H).

***N*-[3-Benzoyl-4-(2,2-diphenylacetylamino)phenyl]cysteinamide Hydrochloride (15b).** The compound was prepared from **5z** (0.36 g, 0.42 mmol) by following general procedure D. Compound **15b** is a yellow solid (0.242 g, 97% yield): mp 118 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.02 (m, 2H), 4.13 (s, 1H), 4.98 (s, 1H), 7.09 (m, 4H), 7.21 (m, 6H), 7.42 (m, 2H), 7.56 (m, 2H), 7.63 (m, 2H), 7.69 (m, 1H), 7.76 (m, 1H), 8.40 (s, 2H), 10.34 (s, 1H), 10.86 (s, 1H); ^{13}C NMR (125 MHz,DMSO-d_6) δ 25.1, 55.1, 57.1, 121.0, 122.6 124.7, 126.4, 126.9, 128.4, 128.5, 128.5, 128.9, 129.2, 129.7, 132.1, 132.9, 137.1, 139.8, 165.8, 170.1, 194.8; ESI-MS *m*/*z* = 239 (100), 406 (95), 387 (93), 167 (64), 265 (49), 168 (32), 386 (28), 212 (24), 388 (21), 336 (20), 512 (1.02, base M+2H). Anal. ($C_{30}H_{28}ClN_3O_3S$) C, H, N.

***N*-(2-Benzoyl-4-nitrophenyl)trifluoroacetamide (16).** 2-Amino-5-nitrobenzophenone (**2**) (1.2 g, 5 mmol) was dissolved in a mixture of DCM (50 mL) and dry pyridine (0.45 mL). The solution was cooled to 0 °C and trifluoroacetic anhydride (0.75 mL) was added dropwise. The mixture was left to warm to room temperature for 2 h. Then, the solution was diluted with DCM, washed with water, brine, saturated $NaHCO_3$ solution, and dried over $MgSO_4$. The residue obtained after removal of the solvent was recrystallized from EtOH. Compound **16** is a yellow solid (1.42 g, 83% yield): mp 135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (m, 2H), 7.71 (m, 3H), 8.50 (m, 1H), 8.57 (m, 1H), 8.87 (m, 1H), 12.27 (s, 1H).

***N*-(4-Amino-2-benzoylphenyl)trifluoroacetamide (17).** The compound was prepared from **16** (1.4 g, 4.1 mmol) by following general procedure B. Compound **17** is a yellow solid (1.205 g, 95% yield): mp 108 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (m, 1H), 6.87 (m, 1H), 7.43 (m, 2H), 7.55 (m, 1H), 7.65 (m, 2H), 8.31 (m, 1H), 1.141 (s, 1H).

***N*-[3-Benzoyl-4-(trifluoroacetylamino)phenyl]-*N*$^\alpha$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (18).** The compound was prepared from **17** (1.025 g, 3.3 mmol) by following general procedure C. Compound **18** is a yellow solid (1.455 g, 58% yield): mp 104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (s, 9H), 2.54 (dd, *J* = 13, 6 Hz, 1H), 2.67 (dd, *J* = 13, 6 Hz, 1H), 3.86 (m, 1H), 4.70 (m, 1H), 7.13 (m, 3H), 7.20 (m, 7H), 7.34 (m, 6H), 7.43 (m, 2H), 7.55 (m, 2H), 7.65 (m, 2H), 7.82 (m, 1H), 8.46 (m, 1H), 11.74 (s, 1H).

***N*-[4-Amino-3-benzoylphenyl]-*N*$^\alpha$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (19).** Compound **18** (1.96 g, 2.6 mmol) was dissolved in a mixture of dioxane/saturated K_2CO_2 solution (1:1, 40 mL) and refluxed for 3 h. Then, the solution was diluted with water and extracted with EtOAc (3 × 50 mL), and the combined organic extracts were thoroughly washed with water and brine and dried over $MgSO_4$. The residue obtained after removal of the solvent was purified flash chromatography (eluents ethyl acetate:*n*-hexane 2:3). Compound **19** is a yellow solid (1.725 g, 88% yield): mp 103 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.30 (s, 9H), 2.49 (dd, *J* = 13, 6 Hz, 1H), 2.64 (dd, *J* = 13, 6 Hz, 1H), 3.80 (m, 1H), 4.78 (m, 1H), 7.07 (m, 1H), 7.11 (m, 3H), 7.18 (m, 9H), 7.32 (m, 8H), 7.39 (m, 2H), 7.43 (m, 2H), 7.67 (m, 2H). Anal. ($C_{40}H_{39}N_3O_4S$) C, H, N.

***N*-[[3-Benzoyl-4-[2-(4-nitrophenyl)acetylamino]phenyl]-*N*$^\alpha$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (20a).** The compound was prepared from **19** (0.23 g, 0.35 mmol) by following general procedure A. Compound **20a** is a yellow solid (0.155 g, 54% yield): mp 103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (s, 9H), 2.51 (dd, *J* = 13, 5 Hz, 1H), 2.65 (dd, *J* = 13, 7 Hz, 1H), 3.78 (m, 1H), 3.80 (s, 2H), 4.69 (m, 1H), 7.12 (m, 3H), 7.18 (m, 7H), 7.32 (m, 6H), 7.39 (m, 2H), 7.44 (m, 3H), 7.52 (m, 1H), 7.59 (m, 2H), 7.69 (m, 1H), 8.13 (m, 2H), 8.40 (m, 1H), 10.67 (s, 1H).

***N*-[[3-Benzoyl-4-[2-(4-nitrophenyl)acetylamino]phenyl]cysteinamide Hydrochloride (12d).** The compound was prepared from **20a** (0.14 g, 0.17 mmol) by following general procedure D. Compound **12d** is a yellow solid (0.078 g, 90% yield): mp 139 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.05 (s, 2H), 3.56 (s, 2H), 4.18 (s, 1H), 7.33 (m, 2H), 7.43 (m, 2H), 7.52 (m, 1H), 7.56 (m, 1H), 7.62 (m, 2H), 7.72 (m, 1H), 7.80 (m, 1H), 8.07 (m, 2H), 8.46 (s, 2H), 10.28 (s, 1H), 10.98 (s, 1H);

^{13}C NMR (125 MHz, DMSO-d_6) δ 25.5, 42.5, 55.3, 121.1, 121.2, 123.1 123.7, 125.3, 128.7, 128.8, 129.5, 129.9 130.9, 132.3, 132.4, 133.2, 135.1,135.2 137.4, 137.4, 143.8, 146.9, 166.1, 168.3, 195.0; ESI-MS m/z = 105 (100), 133 (75), 77 (74), 212 (57), 498 (55), 44 (48), 237 (45), 514 (8, M^+)480 (6, base + H). Anal. ($C_{24}H_{23}ClN_4O_5S$) C, H, N.

***N*-[3-Benzoyl-4-(phenylmethansulfonylamino)phenyl]-*N*$^{\alpha}$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (20b).** The compound was prepared from **19** (0.326 g, 0.4 mmol) by following general procedure A using the sulfonyl chloride instead of the carboxylic acid chloride. Compound **20b** is a yellow solid (0.29 g, 89% yield): mp 93 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (s, 9H), 2.53 (dd, J = 13, 5 Hz, 1H), 2.71 (dd, J = 13, 7 Hz, 1H), 3.79 (m, 1H), 4.29 (s, 2H), 4.69 (m, 1H), 7.08 (m, 2H), 7.13 (m, 6H), 7.20 (m, 6H), 7.34 (m, 6H), 7.43 (m, 3H), 7.54 (m, 1H), 7.61 (m, 3H), 7.69 (m, 1H), 9.88 (s, 1H).

***N*-[[3-Benzoyl-4-(phenylmethansulfonylamino)phenyl]-cysteinamide Hydrochloride (14a).** The compound was prepared from **20b** (0.19 g, 0.23 mmol) by following general procedure D. Compound **14a** is a yellow solid (0.092 g, 78% yield): mp 136 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.06 (s, 2H), 4.15 (s, 1H), 4.47 (s, 2H), 7.26 (m, 5H), 7.45 (m, 1H), 7.53 (m, 2H), 7.66 (m, 3H), 7.78 (m, 1H), 7.83 (m, 1H), 8.45 (s, 2H), 9.67 (s, 1H), 10.98 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 28.0, 41.1, 55.3, 119.6, 122.8, 124.3, 128.8, 128.8, 128.9, 129.4, 129.7, 130.2, 131.3, 132.0, 133.4, 133.6, 134.8, 137.8 139.6, 154.4, 166.2, 197.4; ESI-MS m/z = 91 (100), 435 (83), 211 (55), 237 (42), 301 (33), 371 (32), 508 (11, base + H + HCl). Anal. ($C_{23}H_{24}ClN_3O_4S_2$) C, H, N.

***N*-[3-Benzoyl-4-(4-methylphenylmethansulfonylamino)-phenyl]-*N*$^{\alpha}$-*tert*-butyloxycarbonyl-*S*-tritylcysteinamide (20c).** The compound was prepared from **19** (0.329 g, 0.5 mmol) by following general procedure A. Compound **20c** is a yellow solid (0.272 g, 66% yield): mp 87 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (s, 9H), 2.25 (s, 3H), 2.47 (dd, J = 13, 5 Hz, 1H), 2.65 (dd, J = 13, 7 Hz, 1H), 3.79 (m, 1H), 4.36 (s, 2H), 4.72 (m, 1H), 6.60 (m, 1H), 7.07 (m, 2H), 7.11 (m, 3H), 7.18 (m, 7H), 7.34 (m, 10H), 7.43 (m, 3H), 7.54 (m, 2H), 8.74(m, 1H), 9.89 (s, 1H).

***N*-[[3-Benzoyl-4-(4-methylphenylsulfonylamino]phenyl]-cysteinamide Hydrochloride (14b).** The compound was prepared from **20c** (0.24 g, 0.29 mmol) by following general procedure D. Compound **14b** is a yellow solid (0.134 g, 89% yield): mp 131 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.27 (s, 3H), 2.98 (s, 2H), 4.04 (s, 1H), 4.46 (s, 2H), 6.83 (m, 1H), 7.15 (m, 2H), 7.45 (m, 1H), 7.26 (m, 2H), 7.50 (m, 2H), 7.57 (m, 5H), 7.79 (m, 1H), 8.39 (s, 2H), 10.49 (s, 1H); ESI-MS m/z = 105 (100), 385 (63), 211 (49), 315 (33), 237 (26), 487 (6, base + 3H), 521 (2, base + H + HCl). Anal. ($C_{24}H_{26}ClN_3O_4S_2$) C, H, N.

Enzyme Preparation. Yeast farnesyltransferase (FTase) was fused to glutathione S-transferase at the N-terminus of the β-subunit. FTase was expressed in *Escherichia coli* DH5α grown in LB media containing ampicillin and chloramphenicol for coexpression of pGEX-DPR1 and pBC-RAM2 for FTase production.[18] The enzyme was purified by standard protocol using glutathione-agarose beads for selective binding of the target protein.

Farnesyltransferase Assay. The assay was carried out as described.[19] FPP was obtained as an ammonium salt solution in methanol:10 mM aqueous NH_4Cl (7:3) from Sigma-Aldrich. Dansyl-GCVLS was custom synthesized by ZMBH, Heidelberg, Germany. The assay mixture (100 μL volume) contained 50 mM Tris/HCl pH 7.4, 5 mM $MgCl_2$, 10 μM, $ZnCl_2$, 5 mM DTT, 7 μM Ds-GCVLS, 20 μM FPP and approximately 5 nmol yeast GST-FTase[13] and 1% of various concentrations of the test compounds dissolved in DMSO. The progress of the enzyme reaction was followed by the enhancement of the fluorescence emission at 505 nm (excitation at 340 nm). The reaction was started by addition of the enzyme and run in a quartz cuvette thermostated at 30 °C. Fluorescence emission was recorded with a Perkin-Elmer LS50B spectrometer. IC_{50} values were calculated from the initial velocity of three independent measurements of typically four or five inhibitor concentrations and expressed as mean ± SD.

Cells and Culture Conditions. Established suspended human leukaemic cell lines K-562 cells, a chronic myeloid leukaemic cell line; HL-60 cells, an acute myeloid leukaemic cell line; and THP-1 cells, an acute monocytic leukaemic cell line, were cultured in RPMI 1640 medium (Gibco, cat.-no. 15140-114), supplemented with 100 U/mL penicillin, 100 μg/mL streptomycin, and 10% FBS.

Test Conditions. For each experiment, approximately 10 000 cells were seeded with 0.1 mL culture medium, containing sodium bicarbonate, but without HEPES, into 96-well microplates (NUNC). The plates were previously prepared with dilutions of 1:2, 1:4, 1:8, 1:16, 1:32, 1:64, 1:128, 1:256, 1:512, and 1:1024 of test substances in 0.1 mL of medium. The cells were incubated for 72 h at 37 °C in a humidified atmosphere and 5% CO_2.

Methods of Evaluation. After incubation suspension cultures fo K-562, HL-60, and THP-1 cells were analyzed by the Cell Counter + Analyzer System CASY 1 (SCHÄRFE, Reutlingen, Germany). The 0.2 mL content of each well in the microplate was diluted 1:50 with CASYTON (SCHÄRFE). Every count/mL was automatically calculated from the arithmetic mean of three successive counts of 0.4 mL each. The software for data evaluation (CASYSTAT, SCHÄRFE) offers a fast graphical evaluation of the measurement parameters, for example, as diagrams of cell diameter distribution, overlays of different curves, and cell volume distributions.

The essential parameters for the estimation of growth inhibition (GI) and for changes in diameter distribution curves are expressed as diagrams. The GI_{50} value was defined as being where the concentration−response curve intersected the 50% line, determined by means of the cell counts/mL, compared to control.

Molecular Modeling. All molecular modeling was performed using SYBYL[16] version 6.6 running on a Silicon Graphics O2 (R10000). The alignment procedure was done with SEAL[14] using default parameters. Flexible docking was performed using FlexX[15] version 1.7.6. The cysteinyl partial structure of the inhibitor **12a** was used as the base fragment that was manually placed on the position of the zinc coordinated $-SCH_2CH_\alpha-$ cysteine substructure of the CVI(seleno)M peptide taken from the crystal structure (PDB 1QBQ).[13] For these calculations the FlexX command MAPREF and the manual mode of the PLACEBAS command were used. Default paramaters were employed except the MAX·ENERGY parameter, which was set to 10 kJ mol^{-1}.

Acknowledgment. The authors gratefully thank Prof. Gerhard Klebe who provided us with all facilities needed for the modeling and also for helpful discussions. The pGEX-DPR1 and pBC-RAM2 plasmids were kindly provided by Prof. F. Tamanoi (UCLA). I.S.wishes to thank Prof. Dr. S. Grabley and PD Dr. R. Thiericke for generous support and Ms. S. Egner for excellent technical assistance. Financial support by the German Pharmaceutical Society is gratefully acknowledged.

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JM010872R