

Supporting Information

Irreversible Inhibition of the Epidermal Growth Factor Receptor by 3-Aminopropanamides

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Experimental procedures.

Synthesis. Ethyl 4-(3-bromoanilino)quinazolin-6-ylcarbamate (25). Ethyl chloroformate (133 μ L, 1.40 mmol) was added dropwise to a stirred solution of 6-amino-4-(3-bromoanilino)quinazoline **4** (400 mg, 1.27 mmol) in anhydrous pyridine (10 mL) at 0 °C. The mixture was warmed to room temperature and stirred for 5 h. Pyridine was removed under reduced pressure and the solid residue was washed with 10% acetic acid solution and water until neutrality. The crude product **25** was dried in vacuo and used in the next step without further purification: MS (APCI) m/z 387.1; 1 H NMR (CD₃OD, 300 MHz) δ 1.37 (t, J = 7.1 Hz, 3H), 4.30 (q, J = 7.2 Hz, 2H), 7.40 (t, J = 8.0 Hz, 1H), 7.49 (m, 1H), 7.75 (ddd, J = 7.9, 2.3, 1.2 Hz, 1H), 7.80 (d, J = 9.0 Hz, 1H), 7.95 (dd, J = 9.1, 2.3 Hz, 1H), 8.07 (t, J = 1.9 Hz, 1H), 8.63 (d, J = 2.1 Hz, 1H), 8.68 (s, 1H).

4-(3-Bromoanilino)-6-methylaminoquinazoline (26). Ethyl carbamate **25** was dissolved in anhydrous THF (30 mL) and cooled in an ice bath. Red-Al (1.17 mL, 5.08 mmol) was added by small portions and the resulting mixture was heated at reflux overnight. The reaction was then cooled to 0 °C and quenched with 30% KOH solution (1.2 mL). The crude product was purified by silica gel chromatography (AcOEt/n-hexane, 60:40 to 99:1) to give **26** as a yellow solid (60%): mp 145 °C; MS (APCI) m/z 329.1, 331.3; 1 H NMR (CD₃OD, 300 MHz) δ 2.89 (s, 3H), 7.09 (d, J = 2.4 Hz, 1H), 7.23 (m, 3H), 7.51 (d, J = 9.0 Hz, 1H), 7.70 (m, 1H), 8.04 (br s, 1H), 8.28 (s, 1H).

N-(4-(3-Bromoanilino)quinazolin-6-yl)-3-chloropropanamide (27a). A stirring suspension of amine **4** (300 mg, 0.95 mmol) and 3-chloropropionyl chloride (3 mL, 31.3 mmol) was heated to 50 °C and stirred for 5 h. Methanol (6 mL) was then added dropwise and the mixture was evaporated under reduced pressure. The solid residue was washed with Et₂O and water, dried under reduced pressure and purified by silica gel chromatography (CH₂Cl₂/MeOH, 98:2 to 95:5) to afford **27a** as a white solid (86%): MS (APCI) m/z 409.3, 407.4; 1 H NMR (CDCl₃, 300 MHz) δ 2.96 (t, J = 6.2 Hz, 2H), 3.95 (t, J = 6.2 Hz, 2H), 7.31-7.33 (m, 2H), 7.78 (m, 3H), 8.14 (s, 1H), 8.55 (s, 1H), 8.72 (s, 1H).

N-(4-(3-Bromoanilino)quinazolin-6-yl)-3-chloro-N-methylpropanamide (27b). 4-(3-Bromoanilino)-6-methylaminoquinazoline **26** was reacted with 3-chloropropionyl chloride as described for compound **27a**. The product **27b** obtained as a pale yellow solid (75%) was used in the next step without further purification: mp 176-179 °C; MS (APCI): m/z 419.1, 420.3, 421.2, 422.2; 1 H NMR (CD₃OD, 300 MHz) δ 2.67 (br s, 2H), 3.42 (s, 3H), 3.78 (m, 2H), 7.33 (m, 2H), 7.78 (m, 1H), 7.83 (dd, J = 8.9, 2.2 Hz, 1H), 7.92 (d, J = 8.7 Hz, 1H), 8.17 (s, 1H), 8.42 (br s, 1H), 8.66 (s, 1H).

7-Chloroquinazolin-4(1H)-one (29). 2-Amino-4-chlorobenzoic acid **28** (5.0 g, 29.1 mmol) and formamidine acetate (6.1 g, 58.3 mmol) in methoxyethanol (35 mL) were stirred at reflux overnight. The clear reaction mixture was then cooled to rt, the solvent was removed under vacuum and the solid residue was washed several times with aqueous NH₃ (0.01M) to yield a light brown powder (94%): mp 254-255 °C; MS (APCI) m/z 181.3, 183.1; 1 H NMR (DMSO-*d*6, 300 MHz) δ 7.54 (dd, J = 8.5, 1.9 Hz, 1H), 8.72 (d, J = 1.9 Hz, 1H), 8.11 (d, J = 8.5 Hz, 1H), 8.14 (s, 1H), 12.40 (br s, 1H).

7-Chloro-6-nitroquinazolin-4(1H)-one (30). A solution of **29** (1.18 g, 6.5 mmol) in conc. H₂SO₄ (3.5 mL, 65 mmol) and fuming HNO₃ (3.5 mL) was heated at 100 °C for 1 h. After cooling to rt, the solution was poured onto ice-water and the precipitant was collected by filtration. The light yellow solid was crystallized twice from AcOH to give **30** as a bright yellow solid (70%): mp (AcOH) >230 °C; MS (APCI) m/z 224.1, 226.0; 1 H NMR (DMSO-*d*6, 300 MHz) δ 8.05 (s, 1H), 8.32 (s, 1H), 8.69 (s, 1H), 12.79 (br s, 1H).

7-Ethoxy-6-nitroquinazolin-4(1H)-one (31). 7-Chloroquinazoline derivative **30** (700 mg, 3.10 mmol) was added to a solution of Na (422 mg, 18.6 mmol) in anhydrous EtOH (110 mL) and the mixture was stirred at reflux for 3 days. The dark solution was neutralized with AcOH, the solvent was removed under reduced pressure, and residue was extracted from AcOEt/H₂O. The organic layer was

evaporated to dryness and the crude product was purified by silica gel chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}/\text{AcOH}$, 96:3:1) to afford **31** as a white solid (50%): mp (EtOH) >230 °C; MS (APCI) m/z 236.3; ^1H NMR ($\text{DMSO}-d_6$, 300 MHz) δ 1.43 (t, J = 7.0 Hz, 3H), 4.38 (q, J = 7.0 Hz, 2H), 8.26 (s, 1H), 8.44 (s, 1H), 8.55 (s, 1H), 12.54 (br s, 1H).

4-Chloro-7-ethoxy-6-nitroquinazoline (32). A suspension of **31** (314 mg, 1.34 mmol) in POCl_3 (15 mL) was heated to reflux for 30 min. The clear solution was then evaporated under reduced pressure and the residue was dissolved in CH_2Cl_2 and washed with aqueous NaHCO_3 . The organic layer was dried and the solvent removed to obtain **32** (99%) that was used the next step without further purification: ^1H NMR (CDCl_3 , 300 MHz) δ 1.57 (t, J = 7.0 Hz, 3H), 4.37 (q, J = 7.0 Hz, 2H), 7.54 (s, 1H), 8.62 (s, 1H), 9.07 (s, 1H).

4-(3-Chloro-4-fluoroanilino)-7-ethoxy-6-nitroquinazoline (33). 4-Chloro-7-ethoxy-6-nitroquinazoline **32** (381 mg, 1.51 mmol) and 3-chloro-4-fluoroaniline (438 mg, 3.01 mmol) in *i*-PrOH (16 mL) were heated to reflux and conc HCl (3 drops) was added. The mixture was stirred and refluxed for 30 min and then basified by addition of Et_3N . The solvent was removed under reduced pressure, the solid residue was dissolved in Et_2O and filtered, then the solvent was removed under reduced pressure and the residue was further dissolved in AcOEt and washed with H_2O . The organic layer was evaporated to dryness giving **33** (99%) that was used in the next step without further purifications: MS (APCI) m/z 363.2, 365.3; ^1H NMR ($\text{DMSO}-d_6$, 400 MHz) δ 1.43 (t, J = 7.0 Hz, 3H), 4.09 (q, J = 7.0 Hz, 2H), 7.51 (s, 1H), 7.53 (t, J = 9.1 Hz, 1H), 7.77 (ddd, J = 9.1, 4.0, 2.8 Hz, 1H), 8.11 (dd, J = 6.7, 2.4 Hz, 1H), 8.83 (s, 1H), 9.34 (s, 1H), 10.85 (br s, 1H).

6-Amino-4-(3-chloro-4-fluoroanilino)-7-ethoxyquinazoline (34). Iron powder (225 mg, 4.04 mmol) and AcOH (0.33 mL, 5.77 mmol) were added to a solution of 6-nitroquinazoline **33** (488 mg, 1.35 mmol) in $\text{EtOH}/\text{H}_2\text{O}$ 7:3 (60 mL) and the mixture was heated to reflux for 2 h. 30% NH_3 solution was added to basify the solution, then the solvent was removed under reduced pressure. The residue was dissolved in AcOEt and washed with H_2O . The organic layer was evaporated to give the reduced product **34** (89%): mp 206-208 °C; MS (APCI) m/z 333.4, 335.3; ^1H NMR (MeOD , 400 MHz) δ 1.57 (t, J = 6.9 Hz, 3H), 4.34 (q, J = 6.9 Hz, 2H), 7.11 (s, 1H), 7.33 (t, J = 8.9 Hz, 1H), 7.48 (s, 1H), 7.64 (ddd, J = 8.8, 4.1, 2.7 Hz, 1H), 7.93 (dd, J = 6.6, 2.5 Hz, 1H), 8.56 (s, 1H).

3-Chloro-N-(4-(3-Chloro-4-fluoroanilino)-7-ethoxyquinazolin-6-yl)propanamide (35). 6-aminoquinazoline **34** was reacted with 3-chloropropionil chloride as described for compound **27a**. The resulting solid residue (99%) was used in the next step without no further purification: MS (APCI) m/z 425.3, 427.4; ^1H NMR (MeOD , 300 MHz) δ 1.59 (t, J = 7.0 Hz, 3H), 3.06 (t, J = 6.2 Hz, 2H), 3.93 (t, J = 6.2 Hz, 2H), 4.40 (q, J = 7.0 Hz, 2H), 7.28 (s, 1H), 7.35 (t, J = 8.9 Hz, 1H), 7.63 (ddd, J = 8.9, 4.1, 2.8 Hz, 1H), 7.91 (dd, J = 6.6, 2.6 Hz, 1H), 8.73 (s, 1H), 9.13 (s, 1H).

N-(4-(3-Chloro-4-(pyridin-2-ylmethoxy)anilino)-3-cyano-7-ethoxyquinolin-6-yl)acetamide (41b). A mixture of *N*-(4-chloro-3-cyano-7-ethoxyquinolin-6-yl)acetamide **40** (400 mg, 1.39 mmol), 3-chloro-4-(pyridine-2-ylmethoxy)aniline **45** (295 mg, 1.25 mmol), and pyridine hydrochloride (145 mg, 1.25 mmol) in *i*-PrOH (3.5 mL) was refluxed overnight. The solid was filtered, washed with H_2O and Et_2O to afford the coupling product **41b** (99%): ^1H NMR ($\text{DMSO}-d_6$, 300 MHz) δ 1.50 (t, J = 6.9 Hz, 3H), 2.19 (s, 3H), 4.33 (q, J = 6.9 Hz, 2H), 5.35 (s, 2H), 7.38 (m, 3H), 7.51 (s, 1H), 7.61 (m, 2H), 7.92 (td, J = 7.8, 1.9 Hz, 1H), 8.62 (d, J = 4.1 Hz, 1H), 8.93 (s, 1H), 9.03 (s, 1H), 9.60 (s, 1H), 10.91 (br s, 1H).

6-Amino-4-(3-chloro-4-(pyridin-2-ylmethoxy)anilino)-7-ethoxyquinoline-3-carbonitrile (42b). Acetamide **41b** was suspended in conc HCl (1.22 mL) and H_2O (0.6 mL), and the mixture was stirred at reflux for 5 h. The solvent was then evaporated and the residue was treated with aqueous NaHCO_3 , filtered, washed with H_2O and dried. Silica gel chromatography purification ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 96:4) afforded **42b** (78%): MS (APCI) m/z 446.1; ^1H NMR ($\text{DMSO}-d_6$, 300 MHz) δ 1.43 (t, J = 6.9 Hz, 3H), 4.21 (q, J = 6.9 Hz, 2H), 5.24 (s, 2H), 5.41 (s, 2H), 7.03 (d, J = 8.7 Hz, 1H), 7.21 (m, 4H), 7.36 (m, 1H), 7.57 (d, J = 7.7 Hz, 1H), 7.87 (td, J = 7.7, 1.5 Hz, 1H), 8.24 (s, 1H), 8.58 (d, J = 4.4 Hz, 1H), 9.13 (s, 1H).

3-Chloro-N-(4-(3-chloro-4-fluoroanilino)-3-cyano-7-ethoxyquinolin-6-yl)propanamide (43a). 6-Amino-4-(3-chloro-4-fluoroanilino)-7-ethoxyquinoline-3-carbonitrile **42a** was reacted with 3-

chloropropionil chloride as described for compound **27a**. Silica gel chromatography purification ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 98:2 to 95:5) afford **43a** as a pale yellow solid (99%): MS (APCI) m/z 536.3, 538.5; ^1H NMR (DMSO-*d*6, 300 MHz) δ 1.47 (t, J = 7.1 Hz, 3H), 3.01 (t, J = 6.5 Hz, 2H), 3.90 (t, J = 6.3 Hz, 2H), 4.31 (q, J = 7.4 Hz, 2H), 5.29 (s, 2H), 7.19-7.27 (m, 2H), 7.36-7.39 (m, 3H), 7.59 (d, J = 7.8 Hz, 1H), 7.88 (t, J = 7.7 Hz, 1H), 8.48 (s, 1H), 8.73 (d, J = 4.0 Hz, 1H), 8.87 (s, 1H), 9.52 (s, 1H), 9.64 (s, 1H).

3-Chloro-N-(4-(3-chloro-4-(pyridin-2-ylmethoxy)anilino)-3-cyano-7-ethoxyquinolin-6-yl)propanamide (**43b**). 6-Amino-4-(3-chloro-4-(pyridine-2-ylmethoxy)anilino)-7-ethoxyquinoline-3-carbonitrile **42b** was reacted with 3-chloropropionil chloride as described for compound **27a**. Silica gel chromatography purification ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 98:2 to 95:5) gave **43b** as a pale yellow solid (99%): MS (APCI) m/z 536.3, 538.5; ^1H NMR (DMSO-*d*6, 300 MHz) δ 1.47 (t, J = 7.1 Hz, 3H), 3.01 (t, J = 6.5 Hz, 2H), 3.90 (t, J = 6.3 Hz, 2H), 4.31 (q, J = 7.4 Hz, 2H), 5.29 (s, 2H), 7.19-7.27 (m, 2H), 7.36-7.39 (m, 3H), 7.59 (d, J = 7.8 Hz, 1H), 7.88 (t, J = 7.7 Hz, 1H), 8.48 (s, 1H), 8.73 (d, J = 4.0 Hz, 1H), 8.87 (s, 1H), 9.52 (s, 1H), 9.64 (s, 1H).

3-Chloro-4-(pyridine-2-ylmethoxy)aniline (**45**). 4-Anilino-2-chlorophenol **44** (200 mg, 1.39 mmol) was dissolved in anhydrous DMF (1.6 mL), benzaldehyde (155 μL , 1.53 mmol) and the mixture was stirred at rt for 10 min. Potassium carbonate was then added (768 mg, 5.56 mmol) followed by picolyl chloride hydrochloride (273 mg, 1.67 mmol). The reaction was stirred at 50 $^{\circ}\text{C}$ for 24 h, then the solvent was removed under reduced pressure and the residue was carefully added of 2N HCl. Upon complete dissolution, the product was extracted with EtOAc and the aqueous layer was basified with 2N NaOH. The resulting precipitate was washed with water and dried to give **45** (95%) that was used in the next step without further purification: MS (APCI) m/z 235.3; ^1H NMR (DMSO-*d*6, 300MHz) δ 4.94 (s, 2H), 5.07 (s, 2H), 6.45 (dd, J = 8.7, 2.7 Hz, 1H), 6.65 (d, J = 2.7 Hz, 1H), 6.91 (d, J = 8.7 Hz, 1H), 7.33 (m, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.84 (td, J = 7.7, 1.8 Hz, 1H), 8.55 (d, J = 4.2 Hz, 1H).

In vitro Stability assays. Chemical stability was tested at fixed ionic strength (μ = 0.15 M), under physiological (0.01 M PBS, pH 7.4), and alkaline (0.01 M borate buffer, pH 9.0) pH conditions, at 37 $^{\circ}\text{C}$. Stock solutions of **3** and **5** were prepared in DMSO, and each sample was incubated at a final concentration of 1 μM in prewarmed buffered solutions (final concentration of DMSO: 1% v/v). At regular time points, aliquots were sampled and immediately injected into the HPLC system. For rat plasma stability assays, rat plasma was quickly thawed and diluted to 80% (v/v) with 0.1 M PBS, pH 7.4. Compound stock solution in DMSO was added (final compound concentration: 1 μM , DMSO concentration: 1% v/v) and maintained at 37 $^{\circ}\text{C}$. Aliquots of solution were sampled, two volumes of acetonitrile were added and the mixture was centrifuged (4 $^{\circ}\text{C}$, 8,000 g, 10 min) and analyzed by RP-HPLC.

Analytical Method. HPLC column used was a RP-C18 Supelco Discovery (Supelco, Bellefonte, PA, USA), 5 μm , 150 x 4.6 mm i.d. Mobile phases consisted of water and methanol, both additioned with trifluoroacetic acid (TFA) at 0.05% v/v and at a flow rate of 1 mL min^{-1} . Conditions chosen were the following: Eluent A: methanol + 0.05% TFA; Eluent B: water + 0.05% TFA. T(0 min): 40% A: 60% B; T(10 min) 90% A:10% B returning to initial conditions after 0.5 min, followed by 5 min re-equilibration time. Injection volume: 10 μL . Single ions at m/z $[\text{M}+\text{H}]^+$ = 414.3 amu (**5**); 315.2 (**4**); 369.2 (**3**); 468.1 (**45**) were monitored. MS potentials were optimized by Flow Injection Analysis (FIA) of stock solutions of compounds in 1:1 water:methanol additioned with 0.05% trifluoroacetic acid. The following parameters were retained for optimal analyte detection: nebulizer gas: 13 psi; turbo ion spray gas: 13 psi; curtain gas: 10 psi; cone voltage: 45 V; skimmer voltage: 295 V; entrance potential: 4.6 V; ion source temperature: 450 $^{\circ}\text{C}$. The dwell time used for acquiring data for each SIM analysis was 1000 ms. For HR-MS analysis, HPLC column was a RP-C18 Supelco Discovery (Supelco, Bellefonte, PA, USA), 5 μm , 150 x 4.6 mm i.d. thermostated at 30 $^{\circ}\text{C}$. Mobile phases consisted of water and methanol, both additioned with formic acid (FA) at 0.1% v/v and at a flow rate of 1 mL min^{-1} . Conditions chosen were the following: Eluent A: methanol + 0.1% FA; Eluent B: water + 0.1% FA. T(0 min): 30% A: 70% B; T(2 min) 30% A:70% B; T(12 min) 95% A:5% B; T(14 min) 95% A:5% B returning to initial

conditions after 0.5 min, followed by 5 min re-equilibration time. LTQ-Orbitrap mass analyzer operated in scan mode in the 200-600 m/z range (scan mode). Detection was in positive polarity. Tuning parameters for ESI source were chosen as follows: Source Voltage (kV): 3; Sheath Gas Flow Rate: 25; Aux Gas Flow Rate: 10; Sweep Gas Flow Rate: 10; Capillary Voltage (V): 9; Capillary Temperature ($^{\circ}\text{C}$): 275; Tube Lens Voltage (V): 105

Figure S1. HPLC-MS chromatogram of compound **5** (UPR1157) after 24 h incubation under alkaline conditions (pH 9.0) at 37 °C. Mass balance studies revealed 77% of **5** (blue) recovered after 24 h, with acrylamide **3** (19%, in red) and amine **4** (4%, in green) as degradation products.

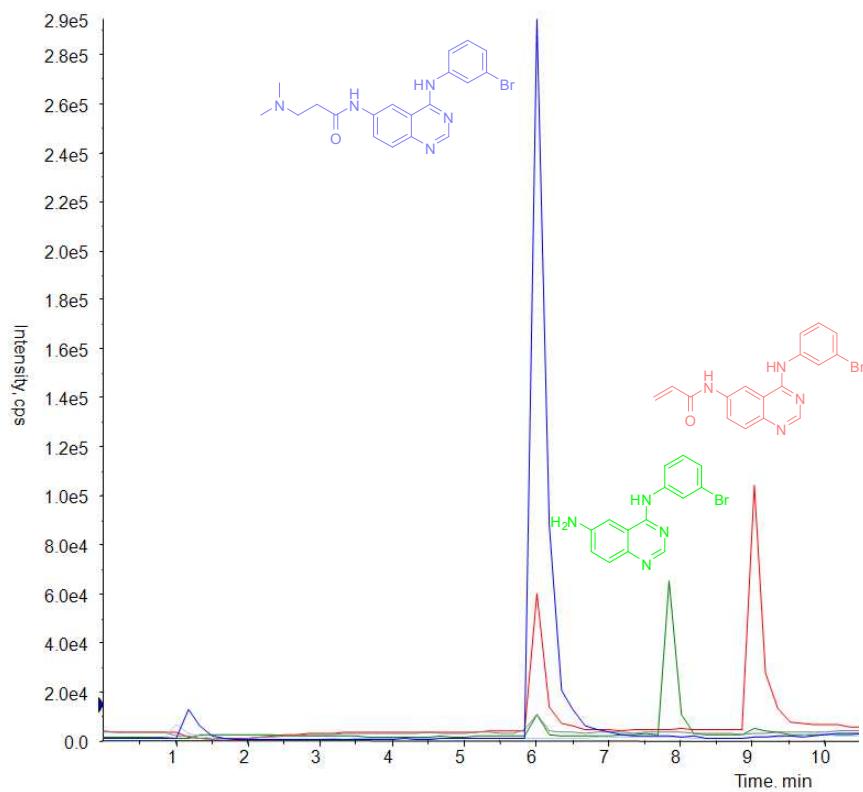


Figure S2. HPLC-MS chromatograms of compound **3** incubated in the presence of LMW thiols cysteamine and GSH. As a title of example, reported in Figure S2 are LC/MS traces corresponding to the formation of GSH- ($m/z = 676.10$) and cysteamine- ($m/z = 446.06$) conjugates by compound **3** ($m/z = 369.03$) after 1 h incubation at 37 °C. (A) Acrylamide **3** incubated in the presence of cysteamine ($t = 0$, $m/z = 369.03$); (B) Acrylamide **3** incubated in the presence of GSH ($t = 0$, $m/z = 369.03$); (C) Acrylamide **3** incubated in the presence of cysteamine ($t = 1$ h, $m/z = 446.06$); (D) Acrylamide **3** incubated in the presence of GSH ($t = 1$ h, $m/z = 676.10$).

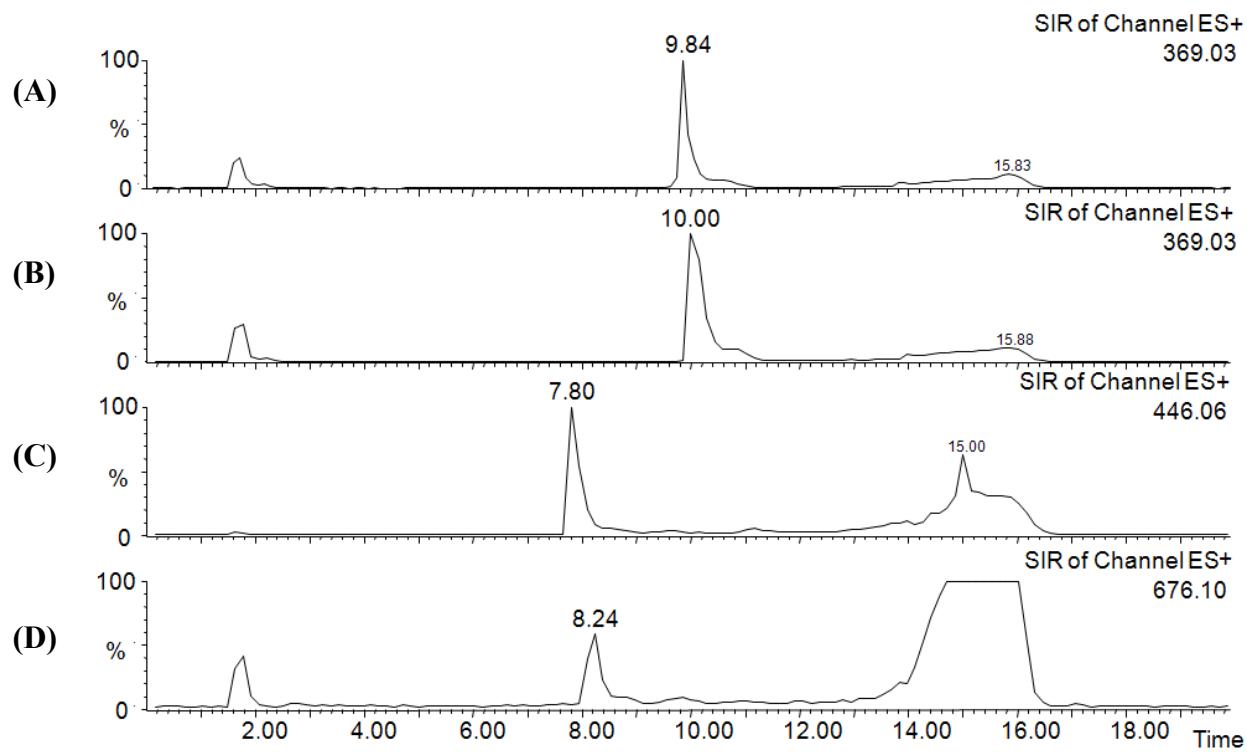


Figure S3. The unique identity of the conjugate formed by compounds **3** and **5** with cysteine in A549 cell lysate was confirmed by high resolution mass spectrometry employing a LTQ Orbitrap mass analyzer (Thermo). Below is the comparison between the calculated (first row) and experimental (second row) high resolution spectrum of the observed cysteine conjugate of compound **5** in cell lysates.

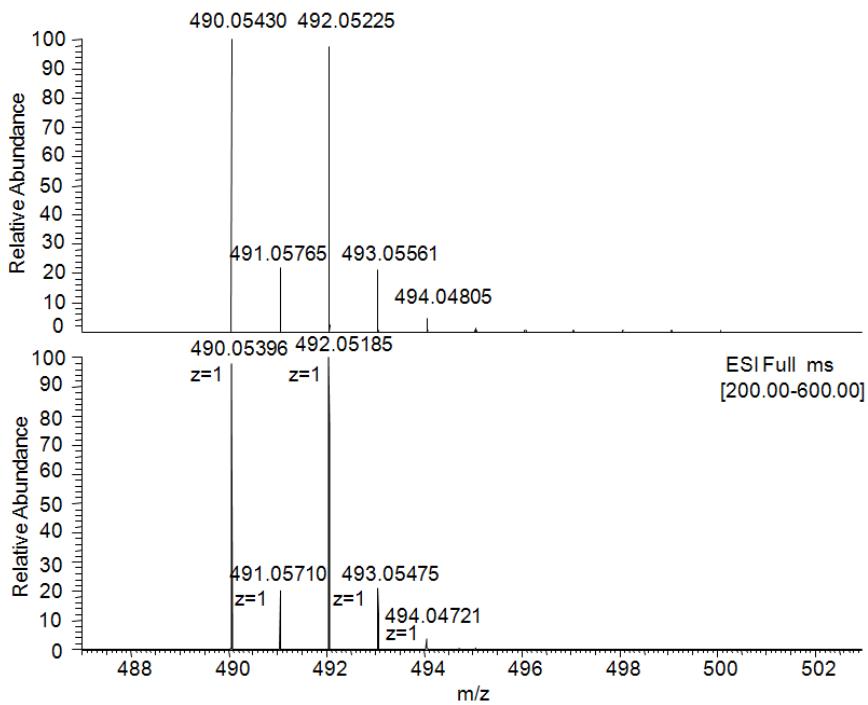


Figure S4. Total Ion Chromatogram (TIC) of A549 cell lysate control (A) compared to incubation in the presence of compound **5** (B). The peak at $t_R = 4.10$ min corresponds to **5** and has the HRMS spectrum reported below: the calculated (C-first row) and experimental (C-second row).

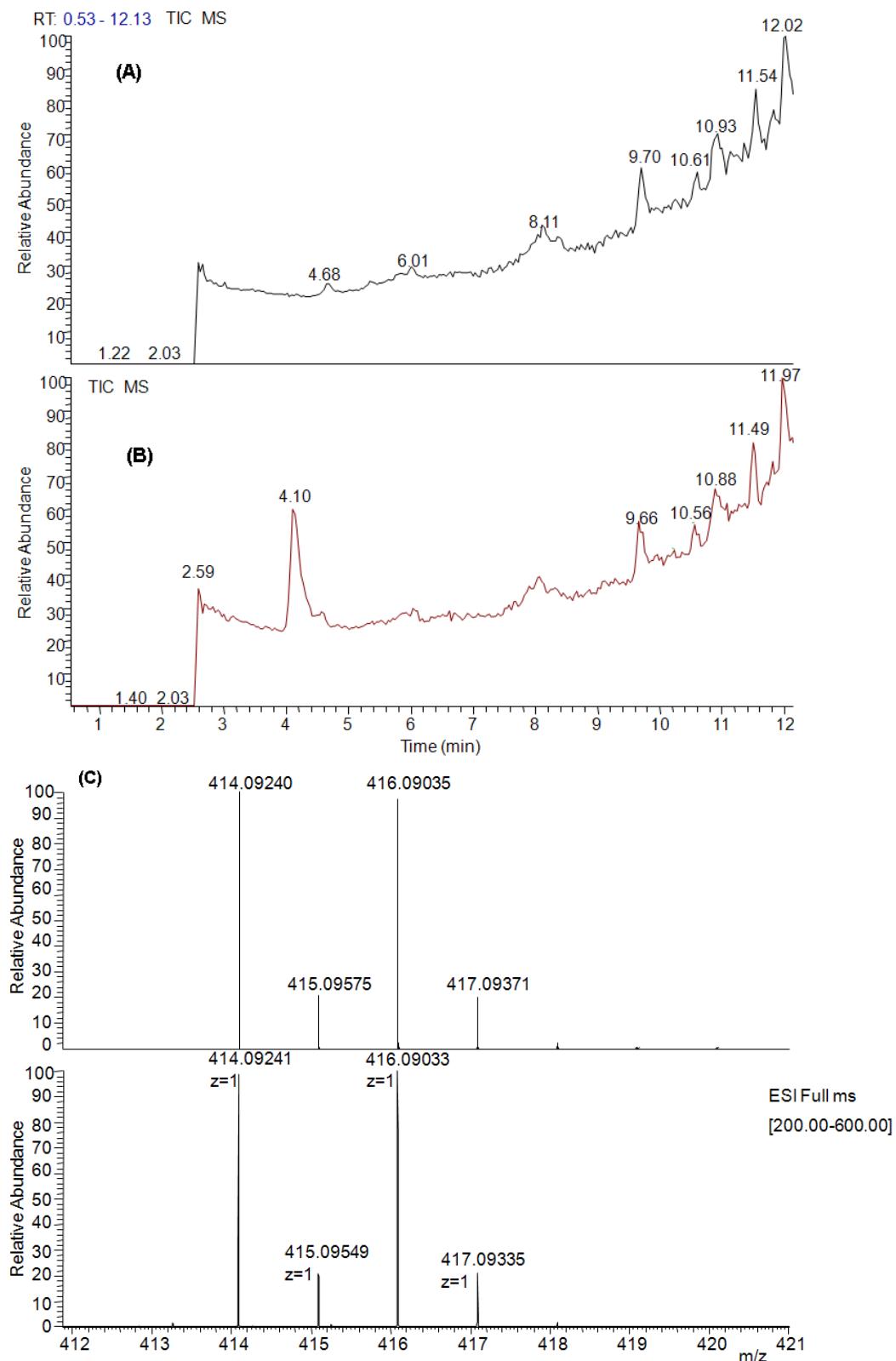


Table S1. Quantification of intracellular concentration of compounds **3**, **4** and **5** in A549 cells.

Compound	nmol/mg prot ^a mean (± SEM)	
	1 h	8 h
3	< LOD ^b	< LOD ^b
4	0.050 ± 0.01	< LOD ^b
5	0.105 ± 0.01	< LOD ^b

^a Intracellular nmol of compound per mg of protein detected 1 h or 8 h after 1 h incubation with the compound (1 μM); data were normalized for the protein content in each cellular sample; mean ± SEM, n = 3. ^b limit of detection (LOD) = 20 pmol/mL.

Table S2. ErbB2 tyrosine kinase inhibition.

Compd	Series	R	ErbB2	
			kinase assay	IC ₅₀ (μM) ^a
5	A			>10
20	D			0.97 ± 0.05
21	D			0.98 ± 0.01

^a Concentration to inhibit by 50% ErbB2 tyrosine kinase activity. IC₅₀ values were measured by the phosphorylation of a peptide substrate using homogeneous time resolved fluorescence (see Experimental Section in the main text). Mean values of three independent experiments ± SEM are reported.

Table S3. Elemental Analysis Data.

Compound	Formula	C	H	N
		Calcd % Found %	Calcd % Found %	Calcd % Found %
3	C ₁₇ H ₁₃ BrN ₄ O	55.30 54.96	3.55 3.83	15.17 14.98
4	C ₁₄ H ₁₁ BrN ₄ ·3/2H ₂ O	49.92 49.73	3.65 3.92	16.63 16.23
5	C ₁₉ H ₂₀ BrN ₅ O	55.08 54.69	4.87 4.89	16.90 16.53
6	C ₂₂ H ₂₄ BrN ₅ O·3/4H ₂ O	56.47 56.46	5.49 5.43	14.96 14.77
7	C ₂₁ H ₂₂ BrN ₅ O ₂ ·1/3H ₂ O	54.56 54.75	4.94 4.99	15.15 14.88
8	C ₂₂ H ₂₅ BrN ₆ O·1/2H ₂ O	55.23 55.22	5.48 5.54	17.57 17.28
9	C ₂₀ H ₂₂ BrN ₅ O	56.08 56.48	5.18 5.15	16.35 16.13
10	C ₁₉ H ₁₆ ClFN ₄ O ₂ ·2/3CH ₃ CH ₂ OH	58.49 58.31	4.83 4.75	13.42 13.09
11	C ₂₁ H ₂₃ ClFN ₅ O ₂ ·2/3H ₂ O	56.81 56.92	5.53 5.58	15.78 15.47
12	C ₂₄ H ₂₇ ClFN ₅ O ₂ ·1H ₂ O	58.83 59.20	5.97 5.97	14.29 14.08
13	C ₂₃ H ₂₅ ClFN ₅ O ₃ ·2/3H ₂ O	56.85 57.22	5.46 5.44	14.41 14.09
14	C ₂₁ H ₁₆ ClFN ₄ O ₂ ·1/2H ₂ O	60.07 60.09	4.08 3.95	13.35 13.15
15	C ₂₃ H ₂₃ ClFN ₅ O ₂ ·1H ₂ O	58.29 57.93	5.35 5.32	14.78 14.69
16	C ₂₆ H ₂₇ ClFN ₅ O ₂ ·1/2CH ₃ CH ₂ OH	62.48 62.15	5.83 5.58	13.50 13.82
17	C ₂₅ H ₂₅ ClFN ₅ O ₃ ·1/2CH ₃ CH ₂ OH	59.94 60.22	5.42 5.47	13.44 13.23
18	C ₂₇ H ₂₂ ClFN ₅ O ₃ ·2/3CH ₃ OH	63.74 64.04	4.99 4.76	13.42 13.04
19	C ₂₉ H ₂₉ ClFN ₆ O ₃ ·1/2H ₂ O	62.81 62.81	5.23 5.40	15.41 15.10
20	C ₃₂ H ₃₃ ClFN ₆ O ₃ ·3/2H ₂ O	62.79 63.08	5.93 6.12	13.73 13.35
21	C ₃₁ H ₃₁ ClFN ₆ O ₄	63.42 63.08	5.32 6.48	14.32 13.92