SUPPLEMENTARY MATERIALS

Preliminary discovery of small molecule inhibitors of Epidermal Growth Factor Receptor (EGFR) that bind to the extracellular domain

Rosa Di Liddo [1], Marco Verona [1], Christian Vaccarin [1,2], Laura Acquasaliente [1], Sandra Schrenk [1], Monica Piccione [1], Carola Cenzi [1], Michele De Franco [1], Matteo Dal Prà[1], Giovanni Ribaudo [3], Maria Grazia Ferlin [1,†], Maria Teresa Conconi [1], Adriana Chilin [1], Valentina Gandin [1] and Giovanni Marzaro [1,*]

[1] Department of Pharmaceutical and Pharmacological Sciences, University of Padova, Via Marzolo 5, I-35131 Padova, Italy; rosa.diliddo@unipd.it (R.D.L.); marco.verona@phd.unipd.it (M.V.); christian.vaccarin@phd.unipd.it (C.V.); laura.acquasaliente@unipd.it (L.A.); sandra89.schrenk@gmail.com (S.S.); monica.piccione@studenti.unipd.it (M.P.); carola.cenzi@iov.veneto.it (C.C.); miky_defra@hotmail.com (M.D.F.); matteo.dal-pra@autifony.com (M.D.P.); mariagrazia.ferlin@unipd.it (M.G.F.); mariateresa.conconi@unipd.it (M.T.C.); adriana.chilin@unipd.it (A.C.); valentina.gandin@unipd.it (V.G.)

[2] Center for Radiopharmaceutical Sciences, ETH-PSI-USZ, Paul Scherrer Institute, 5232 Villigen-PSI, Switzerland

[3] Department of Molecular and Translational Medicine, University of Brescia, Viale Europa 11, I-25123 Brescia, Italy; giovanni.ribaudo@unibs.it

* Correspondence: Correspondence: giovanni.marzaro@unipd.it; Tel.: +39-049-827-5024

† Retired.

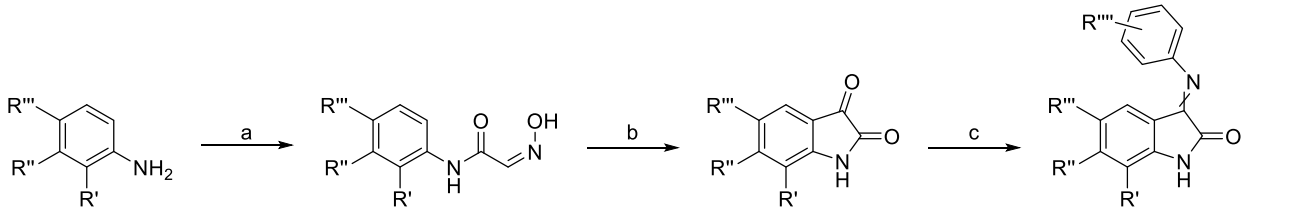
Experimental details:

Supplementary Table and Figures:

1. Synthesis and characterization of isatin Schiff bases

All solvent and starting materials were purchased from commercial suppliers (Sigma Aldrich and Carlo Erba) and used without further purifications. Thin layer chromatography (TLC) was performed on pre-coated plates of silica gel 60 with fluorescent indicator UV254 (0.2 mm, Merck); column chromatography was done with silica gel 60 (0.063-0.100 mm, Merck). The microwave-assisted synthetic procedures were conducted on a CEM Discover monomode reactor with the temperature monitored by a built-in infrared sensor and the automatic control of the power; all the reactions were performed in closed devices with pressure control. The ^{1}H- and ^{13}C-NMR spectra were recorded at room temperature on a Bruker 300 spectrometer; chemical shifts are reported in ppm and are referred to residual solvent peaks. Coupling constants (J) are given in Hz. The ratio E/Z was determined on the basis of 1H-NMR peak areas. The purity of the compounds (higher than 99.5% for all the compounds) was checked by HPLC. HRMS spectra were obtained using a Applied Biosystem Mariner system 5220 with direct injection of the sample.

Compounds were synthesized according to the following general scheme:



1 (R' = R'' = R''' = H)
2 (R' = R'' = H, R''' = Br)
3 (R' = H, R'' = R''' = -OCH_2CH_2O-)
4 (R' = H, R'' = Cl, R''' = F)
5 (R' = R'' = H, R''' = CH_3)
6 (R' =CH_3, R'' = H, R''' = CH_3)
7 (R' = R'' = H, R''' = NO_2)
8 (R' = R'' = H, R''' = OCH_3)

9 (R' = R'' = R''' = H)
10 (R' = R'' = H, R''' = Br)
11 (R' = H, R'' = R''' = -OCH_2CH_2O-)
12 (R' = H, R'' = Cl, R''' = F)
13 (R' = R'' = H, R''' = CH_3)
14 (R' =CH_3, R'' = H, R''' = CH_3)
15 (R' = R'' = H, R''' = NO_2)
16 (R' = R'' = H, R''' = OCH_3)

17 (R' = R'' = R''' = H)
18 (R' = R'' = H, R''' = Br)
19 (R' = H, R'' = R''' = -OCH_2CH_2O-)
20 (R' = H, R'' = Cl, R''' = F)
21 (R' = R'' = H, R''' = CH_3)
22 (R' =CH_3, R'' = H, R''' = CH_3)
23 (R' = R'' = H, R''' = NO_2)
24 (R' = R'' = H, R''' = OCH_3)

Reaction conditions: a) chloral hydrate, NH_2OH·HCl, Na_2SO_4, 1M HCl, 80°C, 2h; b) conc. H_2SO_4, 60°C, 15 min; c) (4-aminophenyl)acetic acid or 3-aminobenzotrifluoride, AcOH, ethanol, reflux or MW irradiation.

Compounds **9-24** were synthesized according to literature methods[1,2,3]

Compounds **DSF-067/-069** and **DSF-091/-103** are herein reported in detail.

ID	Starting isatin	R′	R″	R‴	R⁗
DSF-067	**17**	H	H	H	*p*-CH_2COOH
DSF-068	**18**	H	H	Br	*p*-CH_2COOH
DSF-069	**17**	H	H	H	*m*-CF_3
DSF-091	**19**	H	-OCH_2CH_2O-		*p*-CH_2COOH
DSF-092	**20**	H	Cl	F	*p*-CH_2COOH
DSF-093	**21**	H	H	Me	*p*-CH_2COOH
DSF-094	**22**	Me	H	Me	*p*-CH_2COOH
DSF-095	**23**	H	H	NO_2	*p*-CH_2COOH
DSF-096	**24**	H	H	OMe	*p*-CH_2COOH
DSF-097	**18**	H	H	Br	*m*-CF_3
DSF-098	**19**	H	-OCH_2CH_2O-		*m*-CF_3
DSF-099	**20**	H	Cl	F	*m*-CF_3
DSF-100	**21**	H	H	Me	*m*-CF_3
DSF-101	**22**	Me	H	Me	*m*-CF_3
DSF-102	**23**	H	H	NO_2	*m*-CF_3
DSF-103	**24**	H	H	OMe	*m*-CF_3

General Procedure for the Synthesis of Isatin Schiff-bases. In a round-bottomed flask, isatin derivative **17-24** (1.0 mmol) was dissolved in hot absolute ethanol (3 mL), and then an equimolar amount of suitable substituted aniline was added. The mixture is acidified with glacial acetic acid (100 μL) and refluxed overnight. The obtained precipitate was filtered, washed with ethanol and re-crystallised from ethanol. In some cases, the reaction was performed under microwave irradiation at 200W, 115 °C for 30 minutes, dispersing equimolar amounts of reagents (1 mmol each) in 3 mL of ethanol and adding 100 μL of glacial acetic acid.

(E,Z)-2-(4-(2-oxoindolin-3-ylideneamino)phenyl)acetic acid (**DSF-067**). Compound **DSF-067** was prepared by reacting compound **17** with 2-(4-aminophenyl)acetic acid under conventional heating. Yield 34%.
Ratio E/Z: 85:15; mp = 227-229°C; IR (KBr): $\tilde{\nu}$ (cm^{-1}) = 3244 (NH), 1719 (C=O), 1201 (C=O); HRMS (ESI-TOF) for $C_{16}H_{13}N_2O_3$ $(M+H)^+$: calcd = 281.0921, found = 281.1003
Isomer E: ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.34 (broad s, 1H), 10.96 (broad s, 1H), 7.37-7.32 (m, 3H), 6.95-6.92 (m, 2H), 6.90 (dd, J=7.8, J=0.8, 1H), 6.73 (td, J=7.8, J=0.8, 1H), 6.45 (dd, J=7.8, J=0.8, 1H), 3.64 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.2, 164.0, 155.4, 149.4, 147.4, 134.9, 132.3, 131.0, 125.8, 122.1, 117.8, 116.2, 112.0, 40.6
Isomer Z: ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.34 (broad s, 1H), 10.85 (broad s, 1H), 7.58 (dd, J=7.5, J=0.9, 1H), 7.47 (td, J=7.5, J=0.9, 1H), 7.22-7.18 (m, 2H), 7.06 (td, J=7.5, J=0.9, 1H), 7.00-9.62 (m, 2H), 6.86 (dd, J=7.5, J=0.9, 1H), 3.56 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.8, 158.9, 153.2, 147.8, 146.0, 134.6, 131.8, 129.7, 123.2, 122.8, 122.0, 119.9, 111.2, 40.6

(E,Z)-2-(4-(5-bromo-2-oxoindolin-3-ylideneamino)phenyl)acetic acid (**DSF-068**). Compound **DSF-068** was prepared by reacting compound **18** with 2-(4-aminophenyl)acetic acid under conventional heating. Yield 31%.
Ratio E/Z: 81:19; mp = 235-237°C; IR (KBr): $\tilde{\nu}$ (cm^{-1}) = 3231 (NH), 1726 (C=O), 1232 (C=O); HRMS (ESI-TOF) for $C_{16}H_{12}BrN_2O_3$ $(M+H)^+$: calcd = 359.0026, found = 359.0018
Isomer E: ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.35 (broad s, 1H), 11.12 (broad s, 1H), 7.53 (dd, J=8.4, J=2.0, 1H), 7.40-7.36 (m, 2H), 6.98-6.94 (m, 2H), 6.88 (d, J=8.4, 1H), 6.50 (d, J=2.0, 1H), 3.65 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.2, 163.5, 158.5, 154.4, 149.0, 146.5, 137.0, 131.1, 128.0, 117.8, 114.0, 113.4, 40.6
Isomer Z: ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.35 (broad s, 1H), 11.00 (broad s, 1H), 7.69 (d, J=2.0, 1H), 7.62 (dd, J=8.3, J=2.0, 1H), 7.23-7.20 (m, 2H), 7.04-7.01 (m, 2H), 6.83 (d, J=8.3, 1H), 3.57 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.5, 163.6, 159.0, 152.3, 147.2, 145.0, 136.6, 129.7, 125.5, 120.2, 117.8, 114.4, 113.3, 40.6

(E,Z)-3-(3'-(trifluoromethyl)phenylimino)indolin-2-one (**DSF-069**). Compound **DSF-069** was prepared by reacting compound **17** with 3-(trifluoromethyl)aniline under conventional heating. Yield 27%.
Ratio E/Z: 69:31; mp = 251-254°C; IR (KBr): $\tilde{\nu}$ (cm^{-1}) = 3424 (NH), 1713 (C=O), 1330 (C-F); HRMS (ESI-TOF) for $C_{15}H_{10}F_3N_2O$ $(M+H)^+$: calcd = 291.0740, found = 291.0728
Isomer E: ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.01 (broad s, 1H), 7.70 (t, J=7.2, 1H), 7.62-7.58 (m, 1H), 7.39-7.33 (m, 3H), 6.92 (d, J=7.2, 1H), 6.73 (td, J=7.6, J=1.0, 1H), 6.25 (dd, J=7.6, J=1.0, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.1, 156.8, 152.2, 148.2, 135.8, 131.8, 131.3, 126.1, 125.6, 122.7, 122.5, 122.2, 116.5, 115.1, 112.6
Isomer Z: ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.88 (broad s, 1H), 7.62-7.58 (m, 2H), 7.47 (td, J=7.2, J=1.2, 1H), 7.44 (dd, J=7.2, J=1.2, 1H), 7.32 (s, 1H), 7.28 (dd, J=7.2, J=1.2, 1H), 7.07 (td, J=7.2, J=1.2, 1H), 6.88 (d, J=7.8, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 159.4, 155.0, 150.8, 147.0, 135.5, 130.3, 130.1, 124.0, 125.3, 124.0, 123.8, 123.3, 121.9, 121.4, 111.8

(E,Z)-2-(4-(5,6-dioxane-2-oxoindoline-3-ylideneamino)phenyl)acetic acid (**DSF-091**). Compound **DSF-091** was prepared by reacting compound **19** with 2-(4-aminophenyl)acetic acid under microwave irradiation. Yield 18%.

Ratio E/Z: >95:5; mp = 266-268°C; IR (KBr): ṽ (cm^{-1}) = 3434 (NH), 1719 (C=O), 1327 (C=N), 1165 (C-O); HRMS (ESI-TOF) for $C_{18}H_{15}N_2O_5$ $(M+H)^+$: calcd = 339.0975, found = 339.1000
Isomer E: ^1H NMR (300 MHz, DMSO-d_6) δ = 12.35 (broad s, 1H), 10.69 (broad s, 1H), 7.36-7.31 (m, 2H), 6.90-6.86 (m, 2H), 6.34 (s, 1H), 5.89 (s, 1H), 4.24-4.19 (m, 2H), 4.08-4.05 (m, 2H), 3.61 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.7, 164.9, 156.2, 150.2, 148.2, 147.0, 137.8, 132.4, 132.2, 117.0, 114.8, 113.5, 102.7, 65.8, 64.0, 40.3
Isomer Z was not characterized due the very low percentage in the mixture (less than 5%)

(E,Z)-2-(4-(6-chloro-5-fluoro-2-oxoindolin-3-ylideneamino)phenyl)acetic acid (**DSF-092**). Compound **DSF-092** was prepared by reacting compound **20** with 2-(4-aminophenyl)acetic acid under microwave irradiation. Yield 19%.
Ratio E/Z: 78:22; mp = 247-250°C; IR (KBr): ṽ (cm^{-1}) = 3319 (NH), 1718 (C=O), 1471 (C-F); HRMS (ESI-TOF) for $C_{16}H_{11}ClFN_2O_3$ $(M+H)^+$: calcd = 333.0437, found = 333.0444
Isomer E: ^1H NMR (300 MHz, DMSO-d_6) δ 12.34 (broad s, 1H), 11.15 (broad s, 1H), 7.41-7.36 (m, 2H), 7.06 (d, J=6.1, 1H), 7.00-6.95 (m, 2H), 6.23 (d, J=8.9, 1H), 3.65 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.2, 163.8, 154.1, 152.5, 148.6, 144.4, 133.0, 131.2, 125.7, 117.8, 115.3, 113.4, 113.3, 40.6
Isomer Z: ^1H NMR (300 MHz, DMSO-d_6) δ 12.34 (broad s, 1H), 11.02 (broad s, 1H), 7.65 (d, J=8.1, 1H), 7.24-7.20 (m, 2H), 7.05-7.02 (m, 2H), 7.01 (d, J=6.4, 1H), 3.65 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.2, 163.8, 158.2, 154.0, 148.6, 145.4, 134.5, 129.7, 126.2, 120.2, 115.4, 112.5, 111.4, 40.6

(E,Z)-2-(4-(5-methyl-2-oxoindolin-3-ylideneamino)phenyl)acetic acid (**DSF-093**). Compound **DSF-093** was prepared by reacting compound **21** with 2-(4-aminophenyl)acetic acid under conventional heating. Yield 52%.
Ratio E/Z: 85:15; mp = 231-232°C; IR (KBr): ṽ (cm^{-1}) = 3283 (NH), 1709 (C=O), 1220 (C=O); HRMS (ESI-TOF) for $C_{17}H_{15}N_2O_3$ $(M+H)^+$: calcd = 295.1077, found = 295.1054
Isomer E: ^1H NMR (300 MHz, DMSO-d_6) δ 12.34 (broad s, 1H), 10.86 (broad s, 1H), 7.37-7.33 (m, 2H), 7.16 (dd, J=8.0, J=1.8, 1H), 6.93-6.88 (m, 2H), 6.78 (d, J=8.0, 1H), 6.14 (d, J=1.8, 1H), 3.64 (s, 2H), 1.94 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.3, 164.0, 155.8, 149.7, 145.1, 135.2, 132.3, 131.7, 131.1, 126.3, 122.0, 117.7, 111.7, 40.6, 20.9
Isomer Z: ^1H NMR (300 MHz, DMSO-d_6) δ 12.34 (broad s, 1H), 10.76 (broad s, 1H), 7.41 (d, J=1.1, 1H), 7.25 (dd, J=7.9, J=1.1, 1H), 7.21-7.18 (m, 2H), 6.98-6.94 (m, 2H), 6.75 (d, J=7.9, 1H), 3.55 (s, 2H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.3, 159.1, 153.3, 147.8, 143.7, 134.9, 131.8, 130.9, 129.7, 123.5, 121.4, 119.8, 110.9, 40.6, 19.0

(E,Z)-2-(4-(5,7-dimethyl-2-oxoindolin-3-ylideneamino)phenyl)acetic acid (**DSF-094**). Compound **DSF-094** was prepared by reacting compound **22** with 2-(4-aminophenyl)acetic acid under conventional heating. Yield 26%.
Ratio E/Z: 84:16; mp = 240-242°C; IR (KBr): ṽ (cm^{-1}) = 3180 (NH), 1725 (C=O), 1617 (C=C), 1319 (C-N); HRMS (ESI-TOF) for $C_{18}H_{17}N_2O_3$ $(M+H)^+$: calcd = 309.1234, found = 309.1212
Isomer E: ^1H NMR (300 MHz, DMSO-d_6) δ 10.89 (broad s, 1H), 7.36-7.32 (m, 2H), 7.00 (s, 1H), 6.90-6.86 (m, 2H), 5.99 (s, 1H), 3.62 (s, 2H), 2.14 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.5, 164.6, 156.1, 149.6, 143.7, 140.6, 136.5, 131.0, 130.9, 130.8, 123.7, 118.0, 117.6, 40.6, 20.2, 16.3
Isomer Z: ^1H NMR (300 MHz, DMSO-d_6) δ 10.81 (broad s, 1H), 7.24 (s, 1H), 7.22-7.18 (m, 2H), 7.09 (s, 1H), 6.96-6.92 (m, 2H), 3.54 (s, 2H), 2.25 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.7, 160.5, 159.7, 147.5, 142.3, 136.5, 136.3, 131.8, 130.1, 129.7, 120.9, 119.8, 114.3, 40.7, 20.8, 16.0

(E,Z)-2-(4-(5-nitro-2-oxoindolin-3-ylideneamino)phenyl)acetic acid (**DSF-095**). Compound **DSF-095** was prepared by reacting compound **23** with 2-(4-aminophenyl)acetic acid under microwave irradiation. Yield 38%.
Ratio E/Z: 75:25; mp = 235-238°C; IR (KBr): ṽ (cm^{-1}) = 3225 (NH), 1735 (C=O), 1617 (C=C), 1343 (N=O); HRMS (ESI-TOF) for $C_{16}H_{12}N_3O_5$ $(M+H)^+$: calcd = 326.0771, found = 326.0785

Isomer E: ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.27 (dd, J=8.7, J=2.4, 1H), 7.44-7.40 (m, 2H), 7.36 (d, J=2.4, 1H), 7.09 (d, J=8.7, 1H), 7.05-7.01 (m, 2H), 3.66 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.0, 164.3, 152.8, 151.2, 148.4, 142.0, 133.2, 131.1, 130.6, 128.7, 120.9, 118.1, 112.2, 40.6
Isomer Z: ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.37 (dd, J=8.6, J=2.4, 1H), 8.28 (d, J=2.4, 1H), 7.27-7.23 (m, 2H), 7.14-7.10 (m, 2H), 7.07 (d, J=8.6, 1H), 3.58 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.1, 159.2, 153.6, 151.5, 146.8, 143.0, 133.0, 130.3, 129.8, 128.9, 120.6, 117.5, 111.5, 40.6

(E,Z)-2-(4-(5-methoxy-2-oxoindolin-3-ylideneamino)phenyl)acetic acid (**DSF-096**). Compound **DSF-096** was prepared by reacting compound **24** with 2-(4-aminophenyl)acetic acid under conventional heating. Yield 52%.
Ratio E/Z: 86:14; mp = 223-225°C; IR (KBr): ῡ (cm^{-1}) = 3235 (NH), 1742 (C=O), 1484 (C=C), 1306 (C-N); HRMS (ESI-TOF) for $C_{17}H_{15}N_2O_4$ $(M+H)^+$: calcd = 311.1026, found = 311.1038
Isomer E: ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.34 (broad s, 1H), 10.78 (broad s, 1H), 7.38-7.34 (m, 2H), 6.98-6.90 (m, 3H), 6.81 (d, J=8.5, 1H), 5.91 (d, J=2.6, 1H), 3.62 (s, 2H), 3.39 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.3, 164.1, 154.4, 149.5, 140.9, 132.4, 131.0, 127.0, 120.5, 116.5, 112.6, 111.5, 55.6, 40.9
Isomer Z: ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.34 (broad s, 1H), 10.67 (broad s, 1H), 7.22-7.18 (m, 2H), 7.08 (d, J=2.6, 1H), 7.03 (dd, J=8.5, J=2.6, 1H), 6.99-6.95 (m, 2H), 6.78 (d, J=8.5, 1H), 3.76 (s, 3H), 3.55 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.3, 163.4, 154.4, 149.5, 139.7, 131.8, 130.5, 129.8, 123.8, 120.9, 120.8, 112.5, 111.9, 55.6, 40.9

(E,Z)-3-(3-(trifluoromethyl)benzylidene)-5-bromoindolin-2-one (**DSF-097**). Compound **DSF-097** was prepared by reacting compound **18** with 3-(trifluoromethyl)aniline under conventional heating. Yield 30%.
Ratio E/Z: 73:27; mp = 151-153°C; IR (KBr): ῡ (cm^{-1}) = 3433 (NH), 1732 (C=O), 1316 (C-F); HRMS (ESI-TOF) for $C_{15}H_9BrF_3N_2O$ $(M+H)^+$: calcd = 368.9845, found = 368.9839
Isomer E: ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.05 (broad s, 1H), 7.76-7.74 (m, 1H), 7.63-7.59 (m, 1H), 7.58 (dd, J=8.2, J=2.1, 1H), 7.39-7.37 (m, 1H), 7.25-7.23 (m, 1H), 6.99 (d, J=8.2, 1H), 6.54 (d, J=2.1, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.9, 158.2, 151.6, 146.7, 137.4, 132.7, 131.4, 128.5, 125.6, 122.3, 121.5, 118.0, 115.2, 114.0, 113.2
Isomer Z: ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.95 (broad s, 1H), 7.78 (d, J=2.1, 1H), 7.68 (dd, J=8.2, J=2.1, 1H), 7.54 (dt, J=7.9, J=0.7, 1H), 7.45 (dt, J=7.9, J=0.7, 1H), 7.36-7.34 (m, 1H), 7.31-7.27 (m, 1H), 7.03 (d, J=8.2, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.2, 157.7, 150.3, 145.4, 137.1, 130.3, 130.3, 126.0, 125.8, 123.9, 121.4, 123.8, 117.9, 114.0, 113.8

(E,Z)-3-(3-(Trifluoromehyl)phenylimino)-5,6-dioxanoindolin-2-one (**DSF-098**). Compound **DSF-098** was prepared by reacting compound **19** with 3-(trifluoromethyl)aniline under microwave irradiation. Yield 15%.
Ratio E/Z: 69:31; mp = 279-281°C; IR (KBr): ῡ (cm^{-1}) = 3431 (NH), 1733 (C=O), 1322 (C-F); HRMS (ESI-TOF) for $C_{17}H_{12}F_3N_2O_3$ $(M+H)^+$: calcd = 349.0795, found = 349.0801
Isomer E: ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.24 (broad s, 1H), 7.74-7.72 (m, 1H), 7.63 (d, J=7.9, 1H), 7.41 (s, 1H), 7.37 (d, J=7.9, 1H), 6.23 (s, 1H), 5.89 (s, 1H), 4.22-4.20 (m, 2H), 4.08-4.06 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 158.0, 150.2, 147.2, 146.6, 146.2, 137.8, 131.4, 130.9, 129.9, 124.5, 114.8, 114.7, 113.5, 112.5, 102.4, 65.8, 64.0
Isomer Z: ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.15 (broad s, 1H), 7.54-7.52 (m, 1H), 7.44 (d, J=7.9, 1H), 7.33 (s, 1H), 7.28 (d, J=7.9, 1H), 6.25 (s, 1H), 5.72 (s, 1H), 4.72-4.70 (m, 2H), 4.25-4.23 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 158.0, 149.3, 147.0, 146.2, 145.3, 136.3, 129.7, 124.6, 122.6, 122.1, 121.9, 121.5, 115.3, 112.9, 102.6, 66.8, 63.2

(E,Z)-3-(3-(trifluoromethyl)benzylidene)-6-chloro-5-fluoroindolin-2-one (**DSF-099**). Compound **DSF-099** was prepared by reacting compound **20** with 3-(trifluoromethyl)aniline under conventional heating. Yield 30%.

RatioE/Z: 73:27; mp = 152-154°C; IR (KBr): ṽ (cm^{-1}) = 3178 (NH), 1741 (C=O), 1618 (C=N), 1473 (C=C), 1330 (C-F); HRMS (ESI-TOF) for $C_{15}H_8ClF_4N_2O$ $(M+H)^+$: calcd = 343.0256, found = 343.0251
Isomer E: ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.15 (broad s, 1H), 7.78-7.76 (t, J=7.7, 1H), 7.70 (d, J=7.7, 1H), 7.46 (s, 1H), 7.39 (d, J=7.7, 1H), 7.16 (d, J=6.1, 1H), 6.18 (d, J=8.9, 1H);^{13}C NMR (75 MHz, DMSO-d_6) δ 164.2, 155.2, 153.5, 148.6, 145.4, 131.6, 130.9, 126.7, 124.6, 122.4, 122.2, 116.3, 114.8, 113.3, 112.5
Isomer Z: ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.03 (broad s, 1H), 7.65 (d, J=8.1, 1H), 7.59-7.57 (t, J=8.2, 1H), 7.49 (d, J=8.2, 1H), 7.44 (s, 1H), 7.36 (d, J=8.2, 1H), 7.01 (d, J=6.4, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.0, 158.2, 154.0, 148.6, 145.4, 130.8, 129.7, 126.2, 124.4, 123.0, 121.7, 116.3, 115.4, 112.5, 111.4

(E,Z)-3-(3-(trifluoromethyl)phenylimino)-5-methylindolin-2-one (**DSF-100**). Compound **DSF-100** was prepared by reacting compound **21** with 3-(trifluoromethyl)aniline under conventional. Yield 33%.
Ratio E/Z: 64:36; mp = 230-232°C; IR (KBr): ṽ (cm^{-1}) = 3268 (NH), 1739 (C=O), 1617 (C=N), 1333 (C-F); HRMS (ESI-TOF) for $C_{16}H_{12}F_3N_2O$ $(M+H)^+$: calcd = 305.0896, found = 305.0900
Isomer E: ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.91 (broad s, 1H), 7.71 (t, J=7.8, 1H), 7.63 (d, J=7.8, 1H), 7.39 (s, 1H), 7.26 (d, J=7.8, 1H), 7.19 (dd, J=8.0, J=1.0, 1H), 6.81 (d, J=8.0, 1H), 6.05 (d, J=1.0, 1H), 1.94 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.8, 156.6, 151.6, 145.6, 135.7, 131.9, 131.4, 131.2, 126.0, 124.5, 123.4, 121.9, 116.1, 114.9, 112.0, 20.2
Isomer Z: ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.79 (broad s, 1H), 7.53 (t, J=7.8, 1H), 7.42-7.40 (m, 1H), 7.34-7.30 (m, 2H), 7.27-7.25 (m, 2H), 6.77 (d, J=8.0, 1H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 159.2, 154.8, 150.5, 144.3, 135.5, 130.9, 130.8, 129.9, 124.7, 123.4, 122.7, 122.4, 121.6, 114.8, 111.2, 20.2

(E,Z)-3-(3-(trifluoromethyl)phenylimino)-5,7-dimethylindolin-2-one (**DSF-101**). Compound **DSF-101** was prepared by reacting compound **22** with 3-(trifluoromethyl)aniline under conventional heating. Yield 29%.
Ratio E/Z: 64:36; mp = 240-242°C; IR (KBr): ṽ (cm^{-1}) = 3432 (NH), 1725 (C=O), 1334 (C-F); HRMS (ESI-TOF) for $C_{17}H_{14}F_3N_2O$ $(M+H)^+$: calcd = 319.1053, found = 319.1061
Isomer E: ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.94 (broad s, 1H), 7.71 (t, J=7.9, 1H), 7.62 (d, J=7.9, 1H), 7.36 (s, 1H), 7.31 (d, J=7.9, 1H), 7.04 (s, 1H), 5.89 (s, 1H), 2.15 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.3, 156.9, 151.6, 144.2, 136.9, 131.8, 131.4, 129.2, 123.5, 122.7, 121.3, 115.8, 114.8, 20.7, 16.3
Isomer Z: ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.82 (broad s, 1H), 7.53 (t, J=7.9, 1H), 7.43 (d, J=7.9, 1H), 7.31 (d, J=7.9, 1H), 7.26 (s, 1H), 7.24 (s, 1H), 7.13 (s, 1H), 2.26 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 159.7, 155.2, 150.6, 142.9, 136.8, 130.9, 130.8, 130.0, 129.9, 123.8, 123.4, 121.7, 121.3, 120.5, 115.9, 20.7, 16.1

(E,Z)-3-(3-(trifluoromethyl)benzylidene)-5-nitroindolin-2-one (**DSF-102**). Compound **DSF-102** was prepared by reacting compound **23** with 3-(trifluoromethyl)aniline under microwave irradiation. Yield 27.8%.
Ratio E/Z: 65:35; mp = 250-252°C; IR (KBr): ṽ (cm^{-1}) = 3297 (NH), 1751 (C=O), 1618 (C=N), 1328 (C-F), 1164 (C-O), 1125 (N=O) cm-1.; HRMS (ESI-TOF) for $C_{15}H_9F_3N_3O_3$ $(M+H)^+$: calcd = 336.0591, found = 336.0579
Isomer E: ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.30 (dd, J=8.8, J=2.3, 1H), 7.78 (t, J=7.8, 1H), 7.72 (d, J=7.8, 1H), 7.48 (s, 1H), 7.39 (d, J=7.8, 1H), 7.12-7.07 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.4, 155.8, 150.9, 141.4, 139.7, 131.6, 131.0, 130.9, 124.6, 122.4, 122.0, 120.7, 114.8, 112.7
Isomer Z: ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.40 (dd, J=8.7, J=2.5, 1H), 8.27 (d, J=2.5, 1H), 7.58 (t, J=7.9, 1H), 7.51 (d, J=7.9, 1H), 7.48-7.46 (m, 1H), 7.36 (d, J=7.9, 1H), 7.10-7.06 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 160.6, 155.5, 149.7, 142.5, 137.5, 130.9, 130.8, 129.7, 124.6, 124.4, 123.0, 121.7, 118.3, 116.3, 111.9

(E,Z)-3-(3-(trifluoromethyl)phenylimino)-5-methoxyindolin-2-one (**DSF-103**). Compound **DSF-103** was prepared by reacting compound **24** with 3-(trifluoromethyl)aniline under conventional. Yield 58%.
Ratio E/Z: 66:34; mp = 236-239°C; IR (KBr): ṽ (cm^{-1}) = 3448 (NH), 1749 (C=O), 1629 (C=N), 1476 (C=C), 1339 (C-F), 1302 (C-N); HRMS (ESI-TOF) for $C_{16}H_{12}F_3N_2O_2$ $(M+H)^+$: calcd = 321.0845, found = 321.0829
Isomer E: ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.82 (broad s, 1H), 7.73 (t, J=7.8, 1H), 7.63 (d, J=7.8, 1H), 7.41 (s, 1H), 7.33 (d, J=7.8, 1H), 6.99 (dd, J=8.5, J=2.6, 1H), 6.84 (d, J=8.5, 1H), 5.72 (d, J=2.6, 1H), 3.40 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.8, 154.4, 151.5, 141.3, 131.4, 130.8, 123.0, 124.5, 122.1, 120.6, 114.7, 112.8, 112.4, 108.3, 55.5
Isomer Z: ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.69 (broad s, 1H), 7.53 (t, J=7.9, 1H), 7.44 (d, J=7.9, 1H), 7.33 (s, 1H), 7.28 (d, J=7.9, 1H), 7.18 (d, J=2.6, 1H), 7.06 (dd, J=8.5, J=2.6, 1H), 6.81 (d, J=8.5, 1H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 159.2, 156.9, 150.3, 140.3, 129.9, 129.7, 124.6, 122.6, 122.1, 122.1, 121.9, 121.5, 115.9, 111.4, 56.2

2. Surface Plasmonic Resonance (SPR) experiments

2.1. EGFR-EGF interaction: SPR measurements were carried out at 25 °C on a dual flow-cell Biacore-X100 instrument (GE-Healthcare, Chicago IL). EGFR (SinoBiological, Beijing China) was immobilized (3360 RU) on a carboxymethylated-dextran chip (CM5), using the amide coupling chemistry at pH 4.0. Increasing concentrations of recombinant EGF (DiscoverX inc) were injected over the EGFR-coated sensor chip at a flow rate of 10 μL/min, with a contact time of 180 sec, in 10 mM Hepes pH 7.4, 150 mM NaCl, 3 mM EDTA, 0.005% polyoxyethylene sorbitan

Each binding curve was subtracted for the corresponding baseline obtained on the reference flow cell and accounting for nonspecific binding, which was found <2% of RU_{max}. The dissociation constant (K_d) relative to the binding of the ligand (L), *i.e.* EGF, to the immobilized receptor (R), *i.e.* EGFR, was obtained as a fitting parameter by plotting the value of the response units at the steady state (RU_{eq}), after reaching equilibrium at each ligand concentration (Figure S2), and fitting the data points with an equation describing the one-site binding model:

$$RUeq = RUmax \cdot \frac{[L]_F}{[L]_F + K_d}$$

where RU_{max} is the RU value at saturating L concentrations and $[L]_F$ is the concentration of the free ligand in equilibrium with the receptor-ligand (RL) complex present on the sensor chip surface. When $[R] << K_d$, then $[L]_F$ can be approximated to $[L]_T$, i.e. the total ligand concentration in the mobile phase. Data analysis was performed using the BIAevaluation software and OriginPro 2018b.

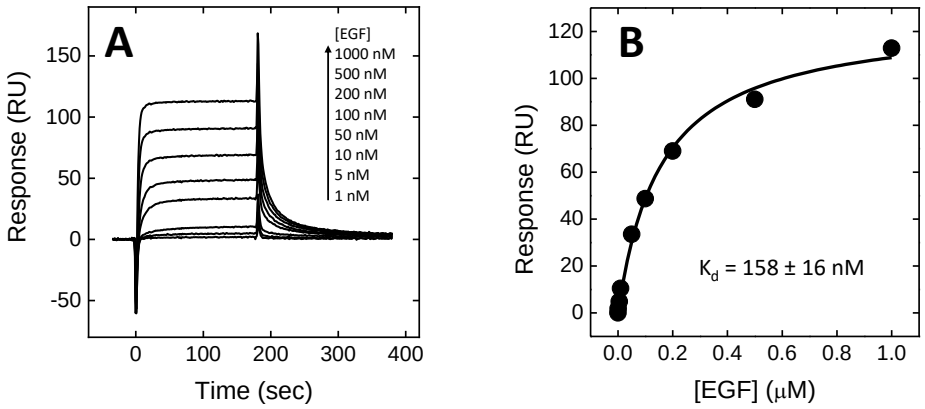


Figure S1. Binding of EGF to EGFR monitored by surface plasmon resonance. (**A**) Sensograms relative to EGF binding. (**B**) Plot of RU_{max} versus EGF concentration. The fitting of data points with one-binding equation yields a K_d value of 158 ± 16 nM.

2.2. DSF-102 competition experiments: Competition assays with **DSF-102** in solution were carried out by incubating a constant concentration of EGF (1 μM) with increasing amounts of **DSF-102** up to 100 μM for 30 min, followed by injection over the EGFR sensor chip. All measurements were carried out at a flow rate of 10 μl/min, at 25°C using 10 mM Hepes pH 7.4, 150 mM NaCl, 3 mM EDTA, 0.005% polyoxyethylene sorbitan as running buffer. The SPR signal was taken at the end of the association phase and plotted against **DSF-102** concentration in order to visualize the effect of competition.

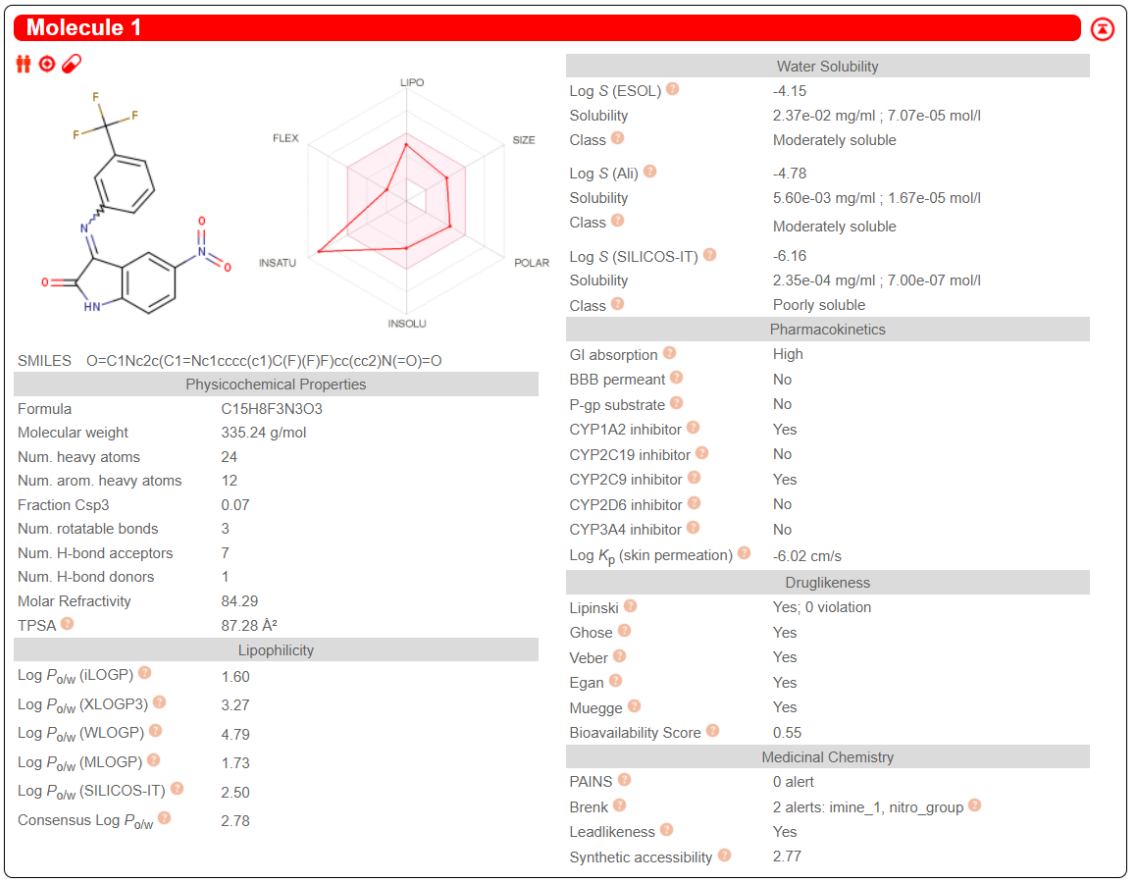


Figure S2. Drug likeness properties of DSF-102. Drug likeness properties have been computed using the SwissADME online tool [5].

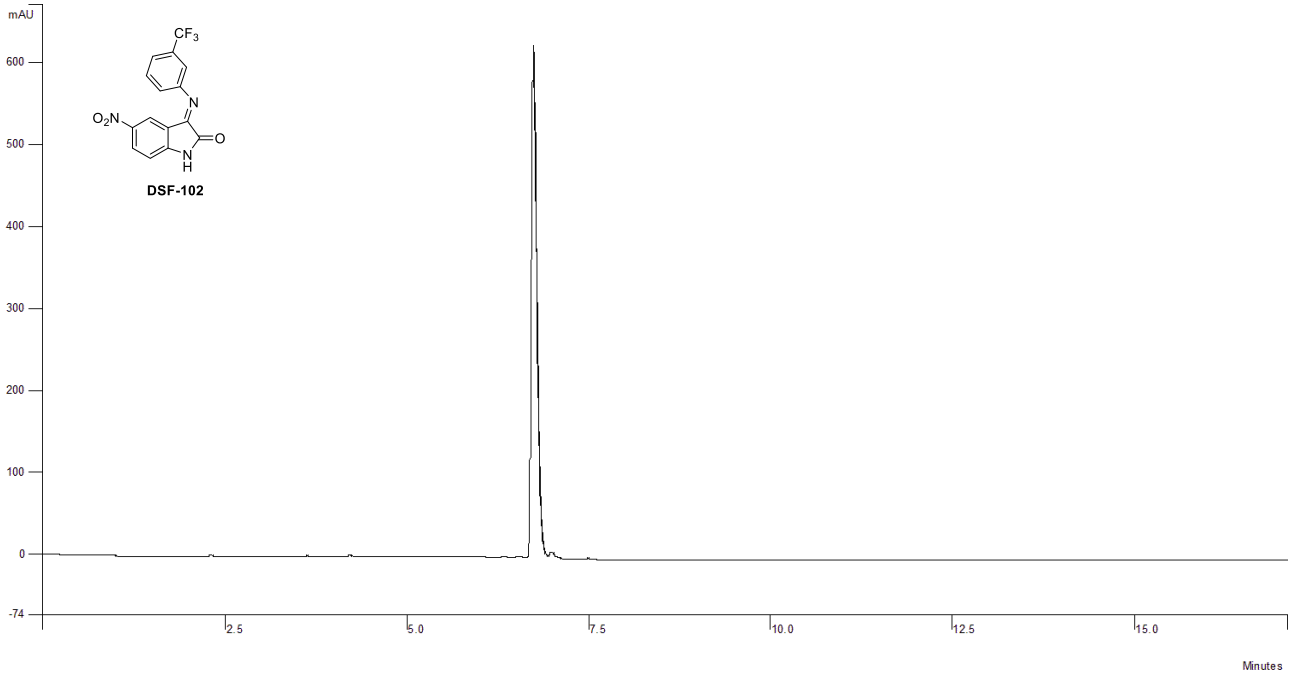


Figure S3. HPLC analysis of DSF-102

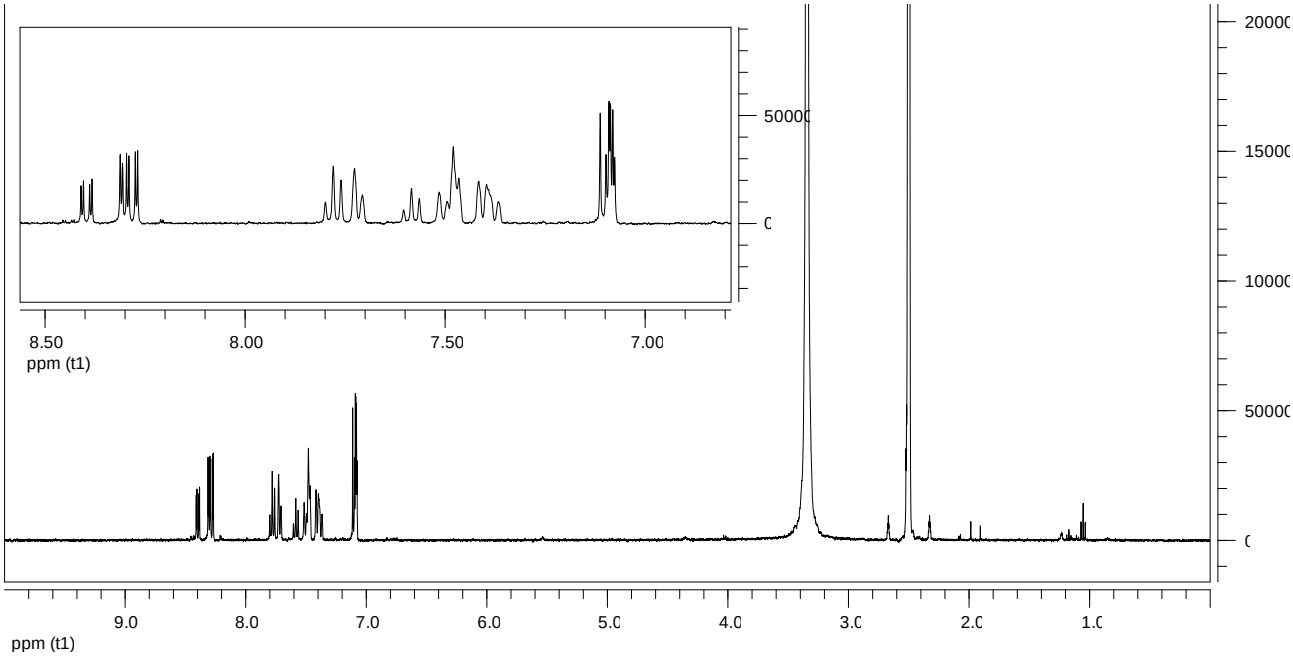


Figure S4. 1H-NMR of DSF-102

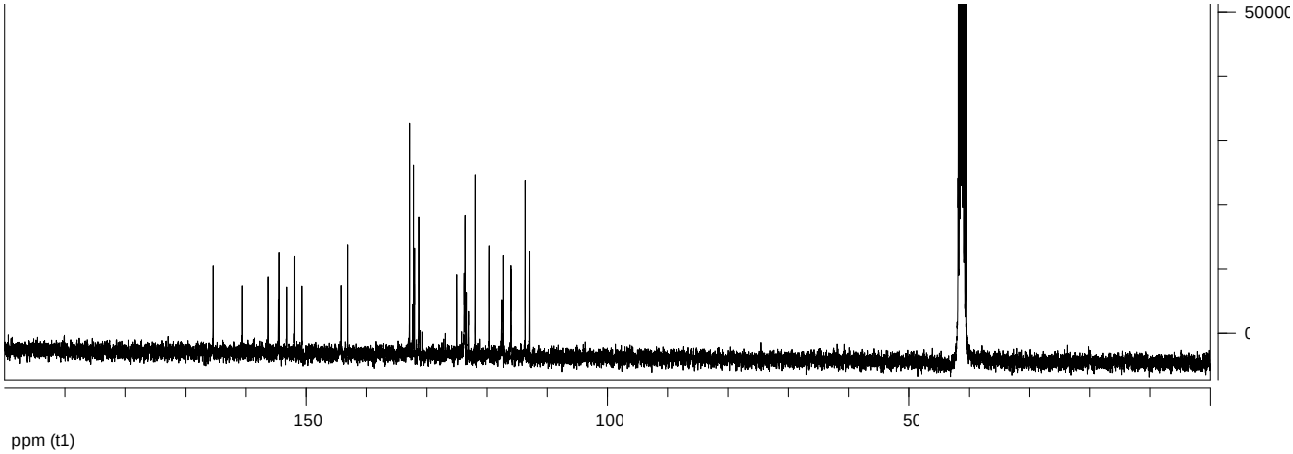


Figure S5. 13C-NMR of DSF-102

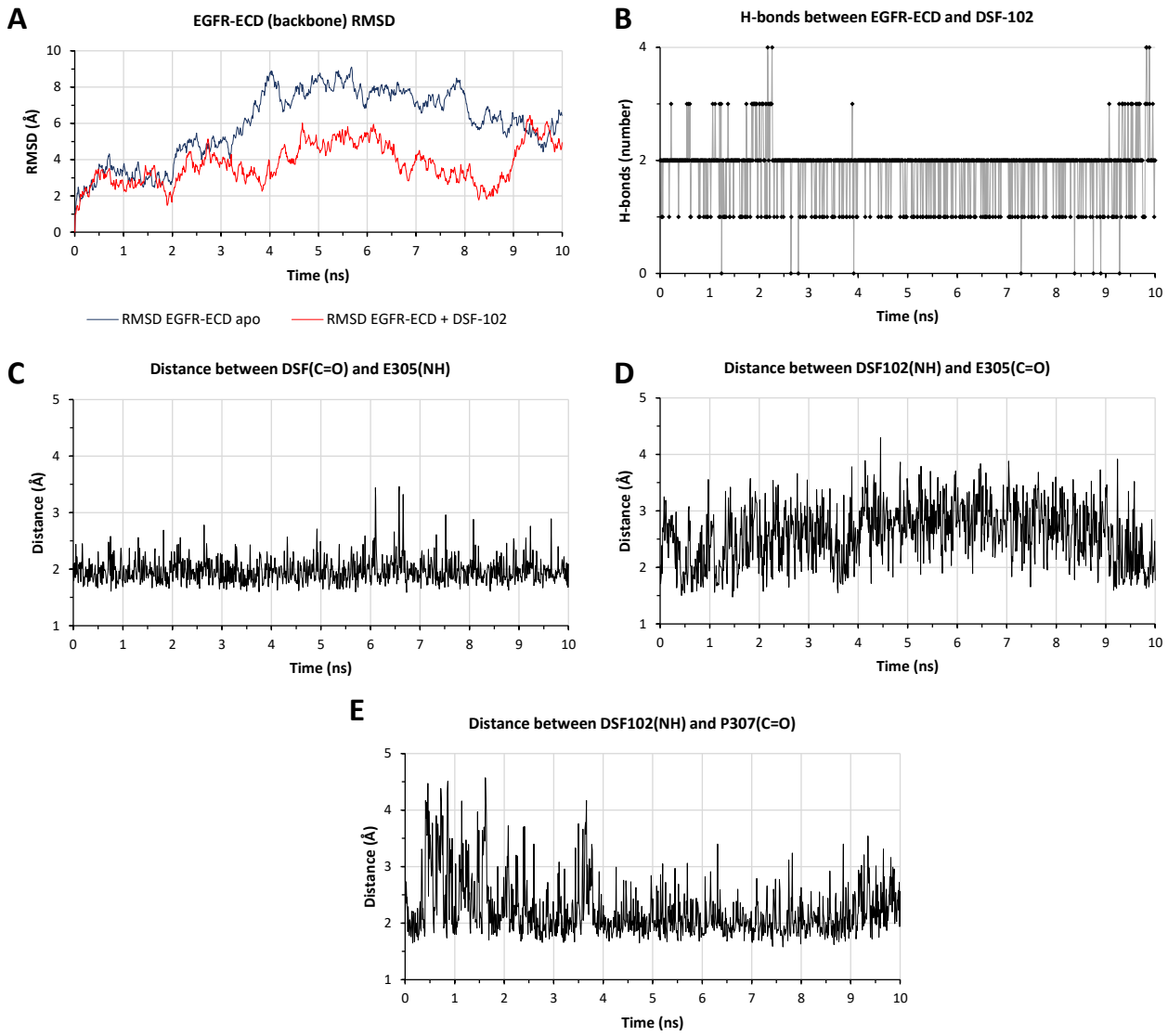


Figure S6. Results from MD studies. (**A**) RMSD (Å) of apo (blue line) and **DSF-102** bound (red line) EGFR-ECD during 10 ns of simulations. (**B**) Number of H-bonds formed between **DSF-102** and EGFR-ECD calculated through the hbond utility of Gromacs software. (**C**) Distance (Å) between **DSF-102** C=O and ^{305}Glu amide-NH. The distance was computed between the oxygen and the hydrogen atoms. (**D**) Distance (Å) between **DSF-102** NH and ^{305}Glu amide-C=O. The distance was computed between the hydrogen and the oxygen atoms. (**E**) Distance (Å) between **DSF-102** NH and ^{307}Pro amide-C=O. The distance was computed between the hydrogen and the oxygen atoms.

Table S1. List of screened compounds, SMILES code and % of inhibition at 50 and 10 μM (mean ± SD of three independent experiments)

Compound	SMILES	% inhibition @ 50 uM	% inhibition @ 10 uM
DSF001	NC1=CC2=CC3=C(C=C(N)C=C3)C=C2C=C1	0 ± 2	0 ± 2
DSF002	CC(C1=CC=CC2=C1C=C(C=CC=C3C(C)=O)C3=C2)=O	0 ± 2	0 ± 3
DSF003	ClCC1=C2C(C=CC=C2)=C(CCl)C3=C1C=CC=C3	50 ± 1	35 ± 5
DSF004	N#CCC1=C2C(C=CC=C2)=C(CC#N)C3=C1C=CC=C3	1 ± 1	0 ± 2
DSF005	O=C(C1=CC=CC2=C1C=C(C=CC=C3C(O)=O)C3=C2)O	1 ± 4	0 ± 5
DSF006	C1(C=CC=C2)=C2C(CN3CCOCC3)=C4C=CC=CC4=C1CN5CCOCC5	27 ± 4	19 ± 1
DSF007	C1(C=CC=C2)=C2C(CN3CCCCC3)=C4C=CC=CC4=C1CN5CCCCC5	16 ± 4	16 ± 4
DSF008	O=C(C1=C2C=CC=C1)C3=C(C(NC(C)=O)=CC=C3O)C2=O	14 ± 2	0 ± 5
DSF009	O=C(C1=C2C(NCCOCCN)=CC=C1NCCOCCN)C3=C(C=CC(C(NC4=CC=C(NS(=O)(C)=O)C=C4)=O)=C3)C2=O	48 ± 1	8 ± 1
DSF010	O=C(C1=C2C(NCCN3CCNCC3)=CC=C1NCCN4CCNCC4)C5=C(C=CC(C(NC6=CC=C(NS(=O)(C)=O)C=C6)=O)=C5)C2=O	34 ± 2	28 ± 3
DSF011	O=C(C1=C2C=CC=C1O)C3=C(C=C(COC(COCC(O)=O)=O)C=C3O)C2=O	39 ± 1	9 ± 5
DSF012	O=C(C1=C2C=CC=C1)C3=C(C(NCCCCCOC(C(C)NC(C(C(C)C)NC(OCC4=CC=CC=C4)=O)=O)=O)=CC=C3NCCCCCOC(C(C)NC(C(C(C)C)NC(OCC5=CC=CC=C5)=O)=O)=O)C2=O	20 ± 5	0 ± 1
DSF013	O=C(C1=C2C=CC=C1)C3=C(C(NCCCCCO)=CC=C3NCCCCCOC(C(C)NC(C(C(C)C)NC(OCC4=CC=CC=C4)=O)=O)=O)C2=O	0 ± 2	0 ± 5
DSF014	O=C(C1=C2C=CC=C1OCC=C)C3=C(C(OCC=C)=CC=C3)C2=O	0 ± 1	0 ± 3
DSF015	O=C(C1=C2C=CC=C1)C3=C(C(F)=CC=C3NCCN(C)C)C2=O	48 ± 1	39 ± 4
DSF016	O=C(C1=C2C=CC=C1)C3=C(C(F)=CC=C3NCCNCCO)C2=O	25 ± 3	33 ± 5
DSF017	O=C(C1=C2C=CC=C1)C3=C(C(NC(CN4CCCCC4)=O)=CC=C3NC(CN5CCCCC5)=O)C2=O	14 ± 1	9 ± 2
DSF018	O=C(C1=C2C=CC=C1)C3=C(C(NC(CN4CCOCC4)=O)=CC=C3NC(CN5CCOCC5)=O)C2=O	38 ± 5	16 ± 3
DSF019	O=C(C1=C2C(O)=CC=C1O)C3=C(C(NC(CN4CCCCC4)=O)=CC=C3NC(CN5CCCCC5)=O)C2=O	33 ± 1	35 ± 5
DSF020	O=C(C1=C2C(O)=CC=C1O)C3=C(C(NC(CN4CCOCC4)=O)=CC=C3NC(CN5CCOCC5)=O)C2=O	29 ± 1	33 ± 5
DSF021	O=C(C1=C2C=CC=C1)C3=C(C(NC(CCN4CCOCC4)=O)=CC=C3NC(CCN5CCOCC5)=O)C2=O	30 ± 5	16 ± 4
DSF022	NC1=CC=CC(C2=NC=NC(C3=CC=CC=C3)=C2)=C1	4 ± 4	0 ± 2
DSF023	NC1=CC=CC(C2=NC=NC(C3=CC=C(C(O)=O)C=C3)=C2)=C1	8 ± 2	22 ± 1
DSF024	OC1=NC(C2=CC=C(C(O)=O)C=C2)=CC(C3=CC(C(F)(F)F)=CC=C3)=N1	5 ± 3	16 ± 1
DSF025	FC(C1=CC=CC(C2=NC=NC(C3=CC=C(C(O)=O)C=C3)=C2)=C1)(F)F	34 ± 1	6 ± 5
DSF026	FC(C1=CC=CC(C2=NC=NC(C3=CC=CC=C3)=C2)=C1)(F)F	0 ± 1	0 ± 5
DSF027	C1(C2=CC=CC=C2)=CC(C3=CC(C4=CC=CC=C4)=CC=C3)=NC=N1	0 ± 1	0 ± 2
DSF028	BrC1=CC=CC(C2=NC=NC(C3=CC=CC=C3)=C2)=C1	0 ± 1	0 ± 4
DSF029	OC1=CC(C2=CC=CC=C2)=CC=C1C3=CC=C(C(O)=O)C=C3	0 ± 3	1 ± 4
DSF030	OC1=CC(C2=CC=CC=C2)=CC=C1C3=CC=C(C(NCC4=CC=CC=C4)=O)C=C3	0 ± 1	0 ± 5
DSF031	O=C1OC2=C(C=CC(NC3=CC=CC(OC)=C3)=N2)C=C1C4=CC=CS4	19 ± 1	0 ± 1
DSF032	O=C1OC2=C(C=CC(NC3=CC=CC(SC)=C3)=N2)C=C1C4=CC=CS4	3 ± 5	0 ± 3

DSF033	O=C1OC2=C(C(N(C)C)=NC(NC3=CC=CC(OC)=C3)=N2)C=C1C4=C(Cl)C=CC=C4Cl	12 ± 3	0 ± 2
DSF034	O=C1OC2=C(C(O)=NC(NC3=CC=CC(OC)=C3)=N2)C=C1C4=C(Cl)C=CC=C4Cl	0 ± 1	14 ± 2
DSF035	O=C1OC2=C(C(O)=NC(NC3=CC=CC(OC)=C3)=N2)C=C1C4=CC(OC)=CC(OC)=C4	0 ± 2	0 ± 5
DSF036	O=C1OC2=C(C(O)=NC(NC3=CC=CC(OC)=C3)=N2)C=C1C4=CC=CC=C4	0 ± 5	0 ± 3
DSF037	O=C1OC2=C(C(NC3=CC=CC(C4=CC=CC=C4)=C3)=NC=N2)C=C1C5=C(Cl)C=CC=C5Cl	40 ± 5	12 ± 4
DSF038	O=C1OC2=C(C(NC3=CC=CC(C)=C3)=NC=N2)C=C1C4=C(Cl)C=CC=C4Cl	24 ± 5	0 ± 1
DSF039	O=C1OC2=C(C(N3CCN(C)CC3)=NC=N2)C=C1C4=C(Cl)C=CC=C4Cl	10 ± 2	0 ± 2
DSF040	O=C1OC2=NC(O)=NC=C2C=C1C(OCC)=O	0 ± 5	0 ± 1
DSF041	O=C1OC2=NC(NC3=CC=CC(C4=CC=CC=C4)=C3)=NC(O)=C2C=C1C5=CC=CC(Br)=C5	0 ± 4	0 ± 1
DSF042	OC1=CC=C2C(OC(C(CC(OC)=O)=C2C)=O)=C1	0 ± 2	0 ± 4
DSF043	O=C1OC2=CC(OC)=CC=C2C(C)=C1CC(NC3=CC=C(C(O)=O)C=C3)=O	0 ± 2	0 ± 2
DSF044	O=C1OC2=C(C)C(OC)=CC=C2C(C)=C1CCC(NC3=CC=C(C(O)=O)C=C3)=O	0 ± 1	0 ± 2
DSF045	O=C1OC2=CC(OC)=CC=C2C(C)=C1CCC(NC3=CC=C(C(O)=O)C=C3)=O	0 ± 5	0 ± 3
DSF046	O=C1OC2=CC(OCCOC)=CC=C2C(C)=C1CC(NC3=CC=C(C(O)=O)C=C3)=O	0 ± 1	0 ± 2
DSF047	O=C1OC2=C(C)C(OC)=CC=C2C(C)=C1CC(NC3=CC=CC(C(O)=O)=C3)=O	0 ± 1	0 ± 4
DSF048	O=C1OC2=CC(OCCOC)=CC=C2C(C)=C1CCC(NC3=CC=C(C(O)=O)C=C3)=O	3 ± 4	9 ± 3
DSF049	O=C1OC2=NC3=C(C(CCCC4)=C4O3)C=C2C(C)=C1CCC(NC5=CC(C(O)=O)=CC=C5)=O	36 ± 3	35 ± 2
DSF050	O=C1OC2=C(C)C3=C(C(CCCC4)=C4O3)C=C2C(C)=C1CC(NC5=CC=CC(O)=C5)=O	32 ± 2	24 ± 4
DSF051	O=C1OC2=C(C)C3=C(C(CCCC4)=C4O3)C=C2C(C)=C1CC(NC5=CC=C(NS(=O)(C)=O)C=C5)=O	50 ± 1	40 ± 1
DSF052	O=C1OC2=C(C)C3=C(C(CCCC4)=C4O3)C=C2C(C)=C1CC(NC5=CC=C(NC(C)=O)C=C5)=O	49 ± 2	41 ± 4
DSF053	O=C1OC2=C(C)C3=C(C(CCCC4)=C4O3)C=C2C(C)=C1CC(NC5=CC=C(C(N)=O)C=C5)=O	43 ± 1	39 ± 5
DSF054	O=C1OC2=C(O)C3=C(C(CCCC4)=C4O3)C=C2C(C)=C1C	46 ± 4	8 ± 4
DSF055	CC1=C(C)OC2=C1C=C3C(OC(C(CC(NCC4=CC=CC=C4Cl)=O)=C3C)=O)=C2C	46 ± 5	46 ± 1
DSF056	O=C(NC1=CC=C(C)C=C1)NC(C=C2)=CC=C2NC3=NC=NC(C4=CC=CC=C4)=C3	22 ± 5	0 ± 1
DSF057	O=C(NC1=CC=C(C(O)=O)C=C1)NC(C=C2)=CC=C2NC3=NC=NC(C4=CC=CC=C4)=C3	44 ± 5	17 ± 2
DSF058	OC1=NC(NC2=CC(OC)=CC=C2)=NC=C1C(O)=O	5 ± 5	12 ± 2
DSF059	CC1=CC=C([N+]([O-])=O)C=C1NC2=NC=CC(C3=CN=CC=C3)=N2	0 ± 5	0 ± 5
DSF060	ClC1=NC(C)=NC(NC2=NC=C(C(O)=O)S2)=C1	0 ± 2	0 ± 1
DSF061	ClC1=CN=C(OC2=CC=CC(NC(NC(C3=CC=CC=C3)=O)=O)=C2)N=C1	1 ± 1	20 ± 4
DSF062	ClC1=CN=C(OC2=CC=CC(NC(NC(C3=CC=CC=C3)=O)=S)=C2)N=C1	21 ± 2	9 ± 3

DSF063	ClC1=CN=C(OC2=CC=CC(NC(NC(C3=CC=CC=C3[N+]([O-])=O)=O)=O)=C2)N=C1	5 ± 5	0 ± 4
DSF064	O=C(C1=CC=CC=C1)NC(NC2=CC(OC3=NC=C(CC)C=N3)=CC=C2)=O	0 ± 2	0 ± 5
DSF065	O=C(C1=CC=CC=C1)NC(NC2=CC(OC3=NC=C(CC)C=N3)=CC=C2)=S	22 ± 5	0 ± 5
DSF066	O=C(C1=CC=CC=C1[N+]([O-])=O)NC(NC2=CC(OC3=NC=C(CC)C=N3)=CC=C2)=O	0 ± 4	0 ± 4
DSF067	O=C1NC2=CC=CC=C2/C1=N\C3=CC=C(CC(O)=O)C=C3	42 ± 1	42 ± 5
DSF068	O=C1NC2=CC=C(Br)C=C2/C1=N\C3=CC=C(CC(O)=O)C=C3	56 ± 4	37 ± 5
DSF069	O=C1NC2=CC=CC=C2/C1=N\C3=CC(C(F)(F)F)=CC=C3	56 ± 2	27 ± 5
DSF070	O=C1NC2=CC=C(Br)C=C2/C1=N\C3=C(OC)C=CC(OC)=C3	41 ± 1	20 ± 5
DSF071	O=C1OC(C2=CC(C(O)=O)=CC=C2)=N/C1=C/C3=CC=C(NC(C)=O)C=C3	0 ± 5	0 ± 3
DSF072	O=C1OC(C2=CC=CC=C2)=N/C1=C/C3=CC(OC)=C(OC(C)=O)C=C3	39 ± 2	16 ± 4
DSF073	O=C1OC(C2=CC=CC=C2)=N/C1=C/C3=CC=C(N(C)C)C=C3	36 ± 3	23 ± 1
DSF074	O=C1OC(C2=CC=CC=C2)=N/C1=C/C3=CN=C(C=CC=C4)C4=C3	48 ± 2	10 ± 3
DSF075	O=C1OC(C2=CC=CC=C2)=N/C1=C/C3=CC=CN3	34 ± 4	18 ± 5
DSF076	O=C1OC(C2=CC=CC=C2)=N/C1=C/C3=CC=C(OC)C=C3	18 ± 4	25 ± 2
DSF077	O=C1OC(C2=CC=CC=C2)=N/C1=C/C3=CN(C(C)=O)C4=C3C=CC=C4	39 ± 1	7 ± 1
DSF078	O=C1OC(C2=CC=CN=C2Cl)=N/C1=C/C3=CC=C(NC(C)=O)C=C3	37 ± 4	7 ± 1
DSF079	O=C1OC(C2=CC(OC)=CC=C2[N+]([O-])=O)=N/C1=C/C3=CC=C(NC(C)=O)C=C3	41 ± 2	3 ± 1
DSF080	O=C1OC(C2=CC=C([N+]([O-])=O)C=C2O)=N/C1=C/C3=CC=C(NC(C)=O)C=C3	28 ± 3	11 ± 5
DSF081	O=S(C1=CC=C(CC(O)=O)C=C1)(NC2=CC=CC=C2)=O	26 ± 1	21 ± 5
DSF082	CC(C=CC=C1C)=C1NS(C2=CC=C(CC(O)=O)C=C2)(=O)=O	19 ± 5	16 ± 1
DSF083	CC(C=CC=C1C)=C1NS(C2=CC=C(CC(O)=O)C=C2)(=O)=O	49 ± 3	36 ± 4
DSF084	ClC1=CC([N+]([O-])=O)=C(S(NC2=CC=C(C(O)=O)C=C2)(=O)=O)C=C1	29 ± 3	19 ± 2
DSF085	ClC1=CC([N+]([O-])=O)=C(S(NC2=CC=C(C(O)=O)C(O)=C2)(=O)=O)C=C1	36 ± 5	0 ± 4
DSF086	ClC1=CC([N+]([O-])=O)=C(S(NC2=CC=CC(Cl)=C2)(=O)=O)C=C1	19 ± 4	0 ± 3
DSF087	ClC1=CC([N+]([O-])=O)=C(S(NC2=CC=C(C(OCC)=O)C=C2)(=O)=O)C=C1	36 ± 4	2 ± 3
DSF088	ClC1=CC([N+]([O-])=O)=C(S(NC2=CC(OC)=CC=C2OC)(=O)=O)C=C1	22 ± 3	0 ± 3
DSF089	ClC1=CC([N+]([O-])=O)=C(S(N2CCOCC2)(=O)=O)C=C1	22 ± 4	20 ± 5
DSF090	ClC1=CC([N+]([O-])=O)=C(S(N2CCCCC2)(=O)=O)C=C1	19 ± 1	12 ± 2

Supplementary Bibliography

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