Supporting Information

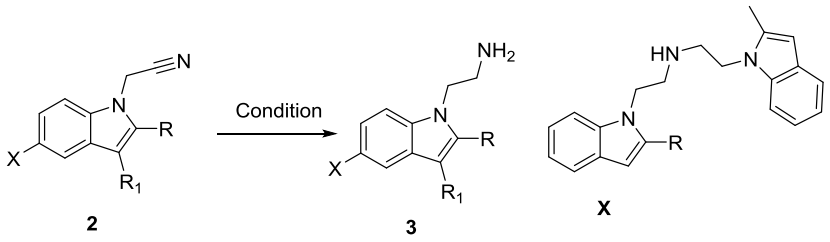
Lead optimization studies of cinnamic amide EP2 antagonists

Thota Ganesh[†,], Jianxiong Jiang[†], Myung-Soon Yang[†] and Ray Dingledine[†]*

[†]Department of Pharmacology, School of Medicine, Emory University, 1510 Clifton Rd;

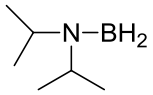
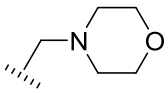
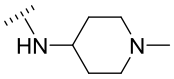
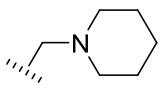
Atlanta, GA, 30322, United States of America.

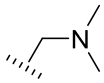
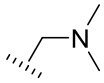
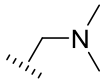
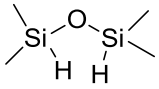
Supporting Table S1: Optimization of 2-(2-(trifluoromethyl)-1H-indol-1-yl)acetonitrile and analogs reduction reaction.[a]



2 **3** **X**

Entry	Starting material	Condition used	Product Isolated yield 3a-e	**X**	Observation of byproducts. Additional notes
1	**2a** R = CH_3, R_1, X = H	2.5 eq. LAH, THF, 0 ^{0}C-RT, 2-12 hr	**3a**: 32-42 % (n = 3)	0	Inseparable complex mixture
2	**2b** R = CF_3, R_1, X = H	2.5 eq. LAH,THF 0 ^{0}C-RT, 6-12h	**3b**: 32-57 % (n = 8)	0	Inseparable complex mixture
3	**2b** R = CF_3, R_1, X = H	H_2, 10% Pd/C, 1:1 EtoAc:MeoH, 35 psi, 24h, RT	**3b**. 17.5 % (n = 1)	35 %	Only **3b** and **X** are observed

4	**2b** R = CF_3, R_1, X = H	2 eq.  cat. $LiBH_4$, THF overnight,	**3b**. 0 % n = 1	0	95% of the starting material was recovered after 24h. Reagent was prepared as reported in References[1, 2]
5	**2b** R = CF_3, R_1, X = H	$InCl_3$, $NaBH_4$, (1:1 eq), THF	**3b**. 53 % n = 1	0	Clean product is obtained after work up as reported in Reference[3]
6	**2c** R = CH_3, R_1 = H, X = F	2.5 eq. LAH,THF 0 ^{0}C-RT, 6-12h	**3c:** 31-47 % (n = 2)	0	Complex inseparable mixture of byproducts observed
7	**2e** R_1, X = H, R = 	2.5 eq. LAH,THF 0 ^{0}C-RT, 6-12h	**3e**: 55 % (n = 1)	0	Complex inseparable mixture of byproducts observed
8	**2f** R_1, X = H, R = 	2.5 eq. LAH,THF 0 ^{0}C-RT, 6-12h	**3f**: 20 % (n = 1)		Complex inseparable mixture of byproducts observed. The product isolated was only reagent grade (> 85% pure)
9	**2i** R = CH_3, X = H, R_1 = 	2.5 eq. LAH,THF 0 ^{0}C-RT, 6-12h	**3i:** 55 % (n = 1)	0	Complex inseparable mixture of byproducts observed
10	**2j** R = CH_3,	2.5 eq. LAH,THF 0 ^{0}C-RT, 6-12h	**3j:** 0 (n = 1)	0	SM or product decomposition

	X = H, R_1 = 				
11	**2j** R, X = H, R_1 = 	1 eq. KBH_4, excess Raney Ni, EtOH,	**3j:** 5 % (n = 1)	0	Reaction was carried out as reported in reference.[4] Poor conversion is observed
12	**2j** R, X = H, R_1 = 	 $Ti(OPr)_4$, Toluene, reflux	**3j:** 0 % (n = 1)	0	No conversion is observed. Only, SM was recovered. Reaction was carried out as reported in reference [5]

[a] Reactions were carried out in an oven dried round bottom flask under nitrogen atmosphere as described in literature precedents, by using commercially available dry solvents.

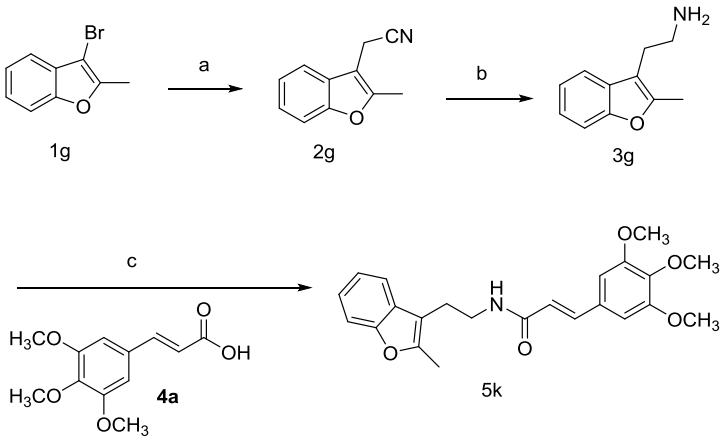
Discussion about the reduction of cyanide reaction: The low yields in the reduction of indole acetonitrile to corresponding amine are presumably duo to the presence of active methylene group. As previously suggested by Singaram group,[1, 2] the reducing agents may have been acting competitively as bases to abstract the proton from active methylene group leading to ketimine type of reactive intermediates, which could undergo self dimerization or polymerization leading to inseparable mixture of byproducts. As a result, the yield of expected amine products was low to moderate. Further optimization is needed to improve the yield of this reaction.

Supporting Table S2. Predicted ADMET properties of the selected four compounds by QikProp 3.5 (http://www.schrodinger.com)

Compd.	Mol wt	QP logS	QP LogP o/w	QP LogBB	QP Log HERG	# met ab	QPP-Caco	Rule of five	# rtv -fg	HOA
5d (TG6-10-1)	448	-7.16	6.08	-0.257	-6.485	3	3592.7	1	1	1
6a (TG8-4)	424	-5.56	4.06	-1.99	-6.952	5	374.9	0	1	3
6c (TG8-21)	424	-5.44	3.67	-2.26	-6.844	6	226.8	0	1	3
6f (TG8-27)	424	-5.65	4.78	-1.11	-6.374	5	1428.5	0	1	3
6k (TG8-57)	451	-5.80	5.41	-0.381	-7.52	5	761.8	1	1	3
6l (TG8-53)	405	-6.40	5.71	-0.345	-8.16	3	762.8	1	1	1
6m (TG8-56)	391	-5.79	5.29	0.259	-7.85	3	758.8	1	1	3

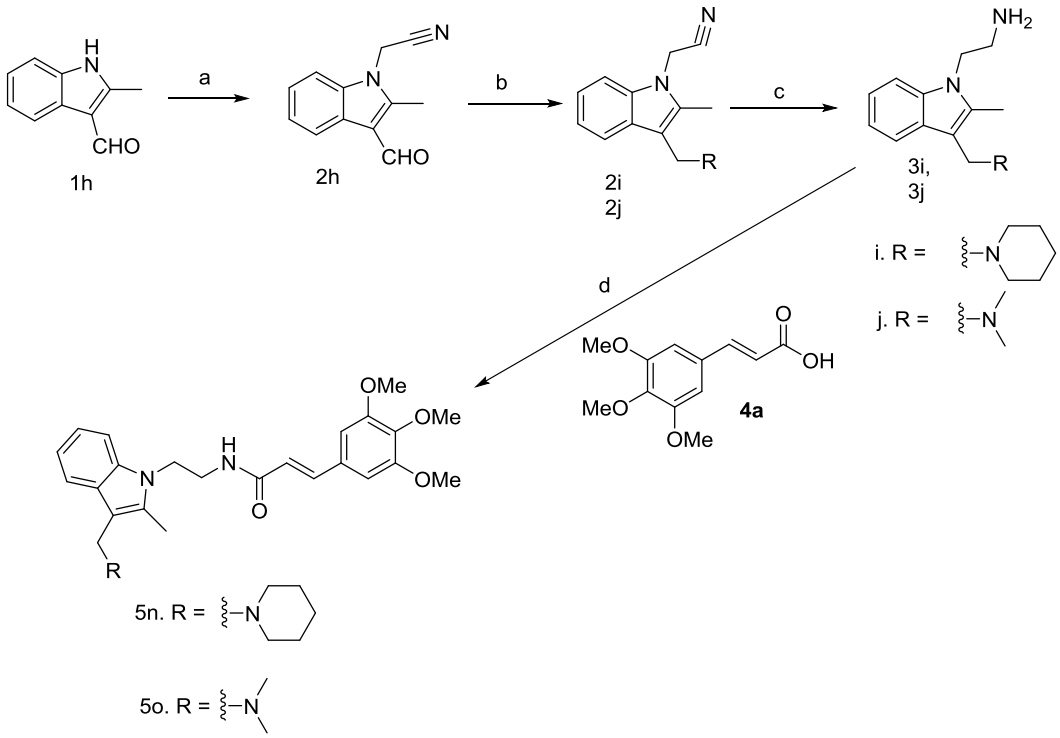
[a] QPlog S – aqueous solubility (log M) (favorable range -6.5-0.5)
QPlogPo/w –octanol/water partition coefficient (favorable range -2.0-6.5)
QPLogBB –brain/blood partition coefficient (-3.0-1.2)
QPlog HERG – IC_{50} for blocking HERG channels (concern below -5.0)
metab – number of likely metabolic reactions (1-8)
QPPCaco – Gut-blood barrier permeability (<25 poor, >500 great)
Rule of Five – number of violations of Lipinski's rule of five (fewer is better)
rtvfg – number of reactive functional groups (fewer is better)
Human oral absorption (HOA) – qualitative metric (1, 2 or 3, low, medium or high)

Supporting Scheme S1. Synthesis of (*E*)-*N*-(2-(2-methylbenzofuran-3-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)acrylamide.[a]



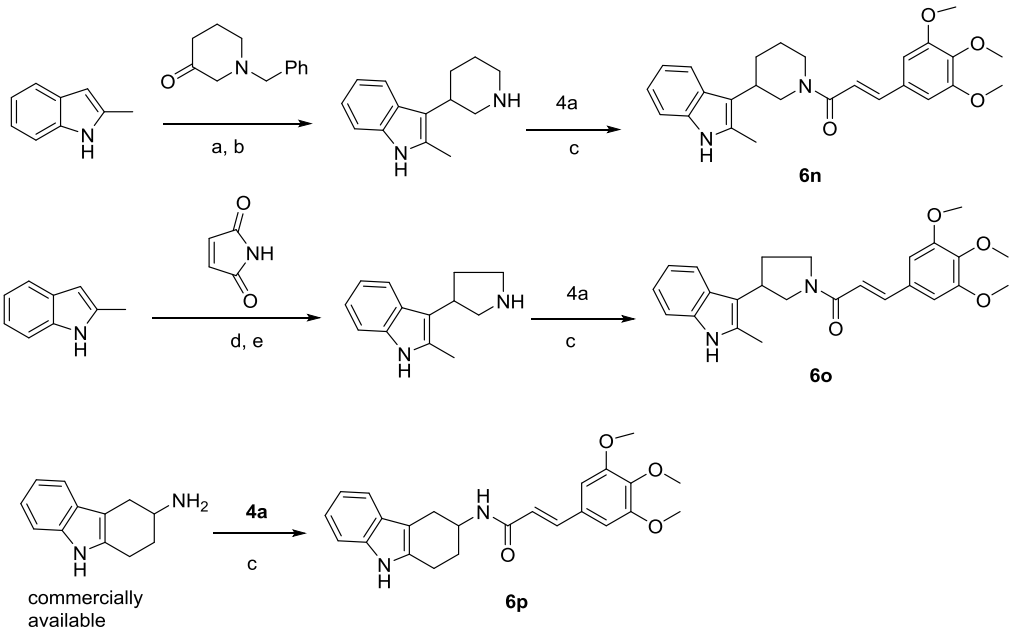
[a]*Reagents and conditions*. a. *n*-Buli, bromoacetonitrile, THF, 30%. b. LAH, THF, 20%, c. EDCI, DMAP, DCM, 65%. *Yields reported are from one repetition and are not optimised.*

Supporting Scheme S2. Synthesis of more soluble cinnamic amide EP2 antagonists for SAR study.[a]



[a]*Reagents and conditions*. a. NaH, bromoacetonitrile, DMF 75% b. piperidine, or N,N-dimethylamine, $Na(OAc)_3BH$, AcOH, DCM, 70%. c. LAH, THF, 55% (for **3i**), KBH_4, Raney-Ni, EtOH, 5% (for **3j**). d. EDCI, DMAP, DCM, 75%. *Yields reported are from one repetition and are*

Supporting Scheme S3. Synthesis of constrained linker cinnamic amide EP2 antagonists.[a]



[a]Reagents and conditions: a, H_3PO_4, AcOH, reflux, b, H_2, 20% wet Pd $(OH)_2$, 50 PSI, 25% (two steps). c. **4a**, EDCI, DMAP, DCM, 75%. d. AcOH, reflux, e, LAH, THF, 20% (two steps).

Supporting information text

Compound Synthesis.

Intermediates **2a, c-f** were synthesized by the method described for **2b** in the main text.

*2-(2-Methyl-1H-indol-1-yl)acetonitrile (**2a**):* ^{1}H NMR ($CDCl_3$): δ 7.55 (d, *J* = 7.6 Hz, 1H), 7.25 (m, 2H), 7.16 (m, 1H), 6.33 (s, 1H), 4.80 (s, 2H), 2.45 (s, 3H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 171 [M+H].

*2-(5-Fluoro-2-methyl-1H-indol-1-yl)acetonitrile (**2c**).* ^{1}H NMR ($CDCl_3$): δ 7.16 (dd, *J* = 9.2, 3.2 Hz, 2H), 6.94 (t x d, J = 9.2, 2.4 Hz, 1H), 6.27 (t, *J* = 1.2 Hz, 1H), 4.89 (s, 2H), 2.45 (s, 3H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 189 [M+H].

*2-(2-Formyl-1H-indol-1-yl)acetonitrile (**2d**)*. ^{1}H NMR ($CDCl_3$): δ 9.8 (s, 1H), 7.77 (d x t, *J* = 8, 0.8 Hz, 1H), 7.53 (t x d, *J* = 7.2, 1.2 Hz, 1H), 7.45 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.36 (d, *J* = 0.8 Hz, 1H), 7.28 (t x d, *J* = 7.6, 0.8 Hz, 1H), 5.62 (s, 2H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 185 [M+H].

*2-(2-(Morpholinomethyl)-1H-indol-1-yl)acetonitrile (**2e**)*. ^{1}H NMR ($CDCl_3$): δ 7.58 (d, *J* = 7.6 Hz, 1H), 7.29 (m, 2H), 7.18 (t x d, *J* = 7.2, 1.2 Hz, 1H), 6.44 (s, 1H), 5. 24 (s, 2H), 3.71 (t, *J* = 4.4 Hz, 4H), 3.68 (s, 2H), 2.52 (bs, 4H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 256 [M+H].

*2-(2-(((1-Methylpiperidin-4-yl)amino)methyl)-1H-indol-1-yl)acetonitrile (**2f**)*. ^{1}H NMR ($CDCl_3$): δ 7.55 (d, *J* = 8 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.24 (m, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.38 (s, 1H), 5. 33 (s, 2H), 3.99 (s, 2H), 2.78 (bs, 2H), 2.48 m, 1H), 2.23 (s, 3H), 1. 93 (m, 4H), 1.40 (m, 2H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 283 [M+H].

*2-(3-Formyl-2-methyl-1H-indol-1-yl)acetonitrile (**2h**)*: ^{1}H NMR ($CDCl_3$): δ 10.2 (s, 1H), 8.28 (dd x t, *J* = 8, 2.4 Hz, 1H), 7.34 (m, 3H), 4.98 (s, 2H), 2.77 (s, 3H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 199 [M+H].

*2-(2-Methyl-3-(piperidin-1-ylmethyl)-1H-indol-1-yl)acetonitrile (**2i**)*: ^{1}H NMR ($CDCl_3$): δ 7.59 (d, *J* = 7.6 Hz, 1H), 7.27-7.20 (m, 2H), 7.16 (t x d, *J* = 7.6, 1.6 Hz, 1H), 4. 91 (s,

2H), 3.87 (s, 2H), 2.69 (bs, 4H), 2.46 (s, 3H), 1.64 (m, 4H), 1.39 (bs, 2H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 268 [M+H].

*2-(3-((Dimethylamino)methyl)-2-methyl-1H-indol-1-yl)acetonitrile (**2j**):* ^{1}H NMR ($CDCl_3$): δ 7.64 (d, *J* = 7.6 Hz, 1H), 7.23 (m, 3H), 7.15 (t x d, *J* = 6.4, 1.2 Hz, 1H), 4. 94 (s, 2H), 3.52 (s, 2H), 2.47 (s, 3H), 2.24 (s, 6H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 228 [M+H].

*2-(2-Methylbenzofuran-3-yl)acetonitrile (**2g**)*. 3-Bromo-2-methyl furan (**1g**)[6] (1.17g, 5.5 mmol) in THF (15 mL) was added *n*-BuLi (6.4 mmol, 1.4 eq) at -78 ^{o}C, dropwise and resulting reaction mixture was stirred for 10 minutes. Then bromoacetonitrile (0.93 mL, 1.4 eq) was introduced dropwise and the reaction mixture was stirred at -78 ^{o}C for 8hrs. Saturated brine solution was added to quench the reaction and product was extracted with ethyl acetate (3 x 20 mL). Organics were dried over Na_2SO_4 and concentrated. The crude on silica gel chromatography eluting with 0-20% ethyl acetate provided starting material (50%), 2-methyl-furan (20%, debrominated) and **2g** (~10% yield). ^{1}H NMR ($CDCl_3$): δ 7.40 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.27 (t x d, *J* = 7.8, 1.6 Hz, 1H), 7.03 (t x d, *J* = 7.6, 1.2 Hz, 1H), 6. 98 (d, *J* = 8.4 Hz, 1H), 4.84 (s, 2H), 2.09 (s, 3H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 172 [M+H].

*Synthesis of compounds **2k, 2l** and **2m** are described in the main text.*

*Methyl (E)-3-(4-hydroxy-3,5-dimethoxyphenyl)acrylate (**2o**).* A solution of 3,5-dimethoxy-4-hydroxy-cinnamic acid (**2n**) (560 mg) was refluxed in excess methanol (25 mL) in the presence of catalytic H_2SO_4 for 24 hrs. Cooled the reaction mixture and then removed the methanol under vacuum. The crude was disolved in ethyl acetate (50 ml) and washed with water and brine (15 mL). Ethyl acetate was concentrated to provide **2o** in quantitative yield (600 mg), used for next reaction without purification. ^{1}H NMR ($CDCl_3$): δ 7.57 (d, *J* = 16 Hz, 1H), 6.74 (s, 2H), 6.28 (d, *J* = 16 Hz, 1H), 3. 89 (s, 6H), 3.77 (s, 3H).

*Methyl (E)-3-(4-(2-(dimethylamino)ethoxy)-3,5-dimethoxyphenyl)acrylate (**2p**). This was synthesized by the procedure described for **2l*** in the main text*, from compounds **2o** and 2-dimethylaminoethylethanol.* ^{1}H NMR ($CDCl_3$): δ 7.57 (d, *J* = 16 Hz, 1H), 6.75 (s, 2H), 6.30 (d, *J* = 16 Hz, 1H), 4. 04 (t, *J* = 5.2 Hz, 2H), 3.83 (s, 6H), 3.77 (s, 3H). (2.67 (t, *J* = 6 Hz, 2H), 2.31 (s, 6H).

*(E)-3-(4-(2-(Dimethylamino)ethoxy)-3,5-dimethoxyphenyl)acrylic acid (**2q**).* This was synthesized by the procedure described for **2m**. But, upon completion of the hydrolysis of ester, reaction mixture was adjusted to pH 5, then concentrated to dryness and used for next reaction to synthesize **6k** (see below). Likewise, starting materials, *(E)-3-(4-(3-(dimethylamino)propoxy)phenyl)acrylic acid,* and *(E)-3-(4-(2-(dimethylamino)ethoxy)-phenyl)acrylic acid* were prepared and used for synthesis of **6l** and **6m** (see below).

Synthesis of intermediates 3a-i. These intermediates were prepared by the following procedure as described for **3b** in the main text.

Characterization data

*2-(2-Methyl-1H-indol-1-yl)ethanamine (**3a**)*: ^{1}H NMR ($CDCl_3$): δ 7.51 (d, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 8 Hz, 1H), 7.12 (t x d, *J* = 7.2, 1.2 Hz, 1H), 7.06 (t x d, *J* = 7.2, 1.2 Hz, 1H) 6.25 (s, 2H), 4.13 (t, *J* = 6.4 Hz, 2H) 3.06 (t, *J* = 6.4 Hz, 2H) 2.45 (s, 3H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 175 [M+H].

*2-(5-Fluoro-2-methyl-1H-indol-1-yl)ethanamine (**3c**)*. ^{1}H NMR ($CDCl_3$): δ 7.17 (dd, *J* = 9,4 Hz, 1H), 7.14 (dd, *J* = 9.6, 2.4 Hz, 1H), 6.85 (t x d, *J* = 8.8, 2.4 Hz, 1H), 6.19 (t, *J* = 0.8 Hz, 1H), 4.11 (t, *J* = 6.4 Hz, 2H) 3.05 (t, *J* = 6.4 Hz, 2H) 2.42 (s, 3H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 193 [M+H].

*2-(2-(Morpholinomethyl)-1H-indol-1-yl)ethanamine (**3e**)*: ^{1}H NMR ($CDCl_3$): δ 7.56 (t, *J* = 6,6 Hz, 1H), 7.34 (m, 1H), 7.18 (m, 1H), 7.08 (m, 1H), 6.37 (d, *J* = 10.8 Hz, 1H), 4.27 (t, *J* = 6.8 Hz, 2H) 3.65 (m, 6H), 3.13 (t, *J* = 6.4 Hz, 2H), 2.47 (s, 4H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 260 [M+H].

*N-((1-(2-Aminoethyl)-1H-indol-2-yl)methyl)-1-methylpiperidin-4-amine (**3f**)*. ^{1}H NMR ($CDCl_3$): δ 7.53 (m, 1H), 7.27 (m, 1H), 7.11 (m, 2H), 6.35 (m, 1H), 4.21 (t, *J* = 6.4 Hz, 2H) 3.92 (s, 2H), 3.08 (t, *J* = 6.4 Hz, 2H), 2.80 (bs, 2H), 2.50 (m, 1H), 2.27 (s, 3H), 2.22(m, 2H), 1.98 (m, 4H). LCMS (ESI): ~ 85% purity at λ 254, MS; m/z, 287 [M+H].

*2-(2-Methylbenzofuran-3-yl)ethanamine (**3g**).* ^{1}H NMR ($CDCl_3$): δ 7.34 (dd, *J* = 7.4, 2Hz, 1H), 7.20 (t x d, *J* = 8, 2 Hz, 1H), 6.87 (t x d, *J* = 7.4, 0.8 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 1H) 4.04 (t, *J* = 4.8 Hz, 2H) 3.67 (t, *J* = 5. 6 Hz, 2H), 2.15 (s, 3H). LCMS (ESI): ~ 95% purity at λ 254, MS; m/z, 176 [M+H].

*2-(2-Methyl-3-(piperidin-1-ylmethyl)-1H-indol-1-yl)ethanamine (**3i**):* NMR indicated mixture of two compounds, but it was used for next reaction as it is. LCMS (ESI): ~ 60% purity at λ 254, MS; m/z, 272 [M+H].

*2-(3-((Dimethylamino)methyl)-2-methyl-1H-indol-1-yl)ethanamine (**3j**):* A solution of KBH_4 (192 mg, 3.55 mmol) and Raney nickel (0.23g excess) in ethanol (8 mL) was added compound **2j** (202 mg, 0.9 mmol) and resulting was stirred over 48 hrs. Conversion of the reactant to product is very poor, even with excess addition of the reagents. Filtered the solids and filtrate was concentrated and subjected to silica gel chromatography, eluting with 0-30% ethyl acetate in hexane to recover starting material (65% yield) and product **3j** (~ 5% yield). ^{1}H NMR ($CDCl_3$): δ 7.60 (d, *J* = 8 Hz, 1H), 7.28 (d, *J* = 8 Hz, 1H), 7.12 (t x d, *J* = 7.6, 1.2 Hz, 1H), 7.07 (t x d, *J* = 7.8, 1.2 Hz, 1H) 4.14 (t, *J* = 6.4 Hz, 2H) 3.54 (s, 2H), 3.04 (t, *J* = 6 Hz, 2H), 2.42 (s, 3H), 2.24 (s, 6H). LCMS (ESI): ~ 95% purity at λ 254, MS; m/z, 232 [M+H].

*Starting materials **3k, 3l** and 3,4,5-trimethoxycinnamic acid (**4a**) and derivatives (**4b-d**), were purchased from commercial sources.*

*Synthesis of compounds **5b-z** and **6a-q*** is carried out by the method described for **5d** in the main text.

Characterization data

*(E)- N-(2-(2-Methyl-1H-indol-1-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**5a**).*

Characterization data for this compound has been described before.[7]

*(E)-3-(3,5-Dimethoxyphenyl)-N-(2-(2-methyl-1H-indol-1-yl)ethyl)acrylamide (**5b**).* ^{1}H NMR ($CDCl_3$): δ 7.51 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 15.6 Hz, 1H), 7.29 (d, *J* = 8 Hz, 1H), 7.10 (m, 2H), 6.56 (d, *J* = 2 Hz, 2H), 6.45 (d, *J* = 2.4 Hz, 1H), 6.24 (s, 1H), 6.19 (d, *J* = 15.6 Hz, 1H), 5.63 (1H, NH), 4.3 (t, *J* = 6 Hz, 2H), 3.79 (s, 6H), 3.71 (q, *J* = 6.4 Hz, 2H), 2.3 (s, 3H). LCMS (ESI): 97% purity at λ 254, MS; m/z, 365 [M+H].

*(E)-3-(4-Fluoro-3,5-dimethylphenyl)-N-(2-(2-methyl-1H-indol-1-yl)ethyl)acrylamide (**5c**).* ^{1}H NMR ($CDCl_3$): δ 7.51 (d, *J* = 7.2 Hz, 1H), 7.49 (d, *J* = 15.6 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.09 (m, 4H), 6.24 (s, 1H), 6.10 (d, *J* = 15.6 Hz, 1H), 5.57 (1H, NH), 4.3 (t, *J* = 6.4 Hz, 2H), 3.69 (q, *J* = 6 Hz, 2H), 2.39 (s, 3H), 2.38 (s, 6H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 351 (M+H). Anal. Calcd for $C_{22}H_{23}FN_2O$; C, 75.40; H, 6.62; N, 7.99; found; C, 74.85; H, 6.63; N, 8.00

*(E)-3-(4-Methoxyphenyl)-N-(2-(2-(trifluoromethyl)-1H-indol-1-yl)ethyl)acrylamide (**5e**).* ^{1}H NMR ($CDCl_3$): δ 7.64 (d, *J* = 8 Hz, 1H), 7.6 (s, 1H), 7.57 (d, *J* = 5.6 Hz, 1H), 7.39 (d, *J* = 8 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.15 (d, *J* = 7.2 Hz, 1H), 6.95 (s, 1H), 6.86 (d, *J* =

7.6 Hz, 1H), 6.14 (d, *J* = 15.6 Hz, 1H), 5.82 (1H, NH), 4.45 (t, *J* = 6.4 Hz, 2H), 3.8 (s, 3H), 3.74 (q, *J* = 6.4 Hz, 2H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 389 [M+H].

*(E)-3-(4-Fluoro-3,5-dimethylphenyl)-N-(2-(2-(trifluoromethyl)-1H-indol-1-yl)ethyl)-acrylamide (**5f**).* ^{1}H NMR ($CDCl_3$): δ 7.65 (d, *J* = 8.4 Hz, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.52 (d, *J* = 15.6 Hz, 1H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.16 (t, *J* = 7.2 Hz, 1H), 7.10 (d, *J* = 6.8 Hz, 2H), 6.96 (s, 1H), 6.14 (d, *J* = 15.6 Hz, 1H), 5.7 (1H, NH), 4.46 (t, *J* = 6.4 Hz, 2H), 3.76 (q, *J* = 6.4 Hz, 2H), 2.24 (s, 3H), 2.23 (s, 3H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 405 [M+H].

*(E)-N-(2-(2-Methyl-1H-indol-3-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)-acrylamide (**5g**)*. ^{1}H NMR($CDCl_3$): δ 7.93 (bs, NH), 7.52 (d, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 16 Hz, 1H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.10 (m, 2H), 6.65 (s, 2H), 6.15 (d, *J* = 15.6 Hz, 1H), 5.66 (t, *J* = 5.6 Hz, NH), 3.84 (s, 9H), 3.63 (q, *J* = 6 Hz, 2H), 2.97 (t, *J* = 6.8Hz, 2H), 2.37 (s, 3H). LCMS (ESI): > 97% purity at λ 254, MS: m/z, 395 [M+H]. Anal. Calcd for $C_{23}H_{26}N_2O_4$; C, 70.03; H, 6.64; N, 7.10; found; C, 69.24; H, 6.76; N, 7.03

*(E)-3-(3,4-Dimethoxyphenyl)-N-(2-(2-methyl-1H-indol-3-yl)ethyl)acrylamide (**5h**).* ^{1}H NMR $CDCl_3$+MeOH-d_4). δ 7.43 (d, *J* = 7.2 Hz, 1H), 7.4 (d, *J* = 15.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 6.99 (m, 3H), 6.90 (d, *J* = 1.6 Hz, 1H), 6.75 (d, *J* = 8Hz, 1H), 6.12 (d, *J* = 15.6 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.51 (t, *J* = 6.8 Hz, 2H), 2.89 (t, *J* = 6.4 Hz, 2H), 2.28 (s, 3H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 365 [M+H].

*(E)-N-(2-(5,7-Difluoro-2-methyl-1H-indol-3-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)-acrylamide (**5i**).* ^{1}H NMR ($CDCl_3$): δ 7.42 (d, *J* = 15.2 Hz, 1H), 6.91 (dd, *J* = 9.2, 2.4 Hz, 1H), 6.65 (s, 2H), 6.54 (m, 1H), 6.19 (d, *J* = 15.6 Hz, 1H), 3.81 (s, 6H), 3.80 (s, 3H), 3.50 (t, *J* = 6.8 Hz, 2H), 2.86 (t, *J* = 6.4 Hz, 2H), 2.32 (s, 3H). Mass calcd for $C_{23}H_{24}F_2N_2O_4$, 430.17; LCMS (ESI): > 97% purity at λ 254, MS; m/z, 431 [M+H].

*(E)-3-(4-Fluoro-3,5-dimethylphenyl)-N-(2-(2-methyl-1H-indol-3-yl)ethyl)acrylamide (**5j**)* . ^{1}H NMR ($CDCl_3$): δ 8.45 (s, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 15.6 Hz, 1H), 7.26 (d, *J* = 7.2 Hz, 1H), 7.05 (m, 4H), 6.11 (d, *J* = 15.2 Hz, 1H), 3.56 (t, *J* = 6.8 Hz, 2H), 2.92 (t, *J* = 6.4 Hz, 2H), 2.41 (s, 3H), 2.19 (s, 6H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 351 [M+H]. Anal. Calcd. for $C_{22}H_{23}FN_2O$; C, 75.40; H, 6.62; N, 7.99; found; C, 75.45; H, 6.57; 7.95.

*(E)-N-(2-(2-Methylbenzofuran-3-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**5k**)*. ^{1}H NMR ($CDCl_3$): δ 7.53 (d, *J* = 16 Hz, 1H), 7.36 (dd, *J* = 7.6 Hz, 1H), 7.25 (m, 1H), 6.9 (m, 2H), 6.71 (s, 2H), 6.31 (d, *J* = 15.6 Hz, 1H), 6.29 (t, *J* = 5.6 Hz, NH), 4.16 (t, *J* = 4.8 Hz, 2H), 3.86 (s, 6H), 3.85 (s, 3H), 3.81 (q, *J* = 3.2 Hz, 2H), 2.11 (s, 3H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 396 [M+H].

*(E)-N-(2-(2-(Morpholinomethyl)-1H-indol-1-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)-acrylamide (**5l**).* ^{1}H NMR ($CDCl_3$): δ 7.53 (d, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 15.6 Hz, 1H), 7.36 (d, *J* = 8 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.6 (s, 2H), 6.37 (t, *J* = 4.4 Hz, 2H), 6.27 (d, *J* = 15.6 Hz, 1H), 4.4 (t, *J* = 6 Hz, 2H), 3.83 (s, 6H), 3.76 (q,

J = 5.6 Hz, 2H), 3.67 (t, *J* = 4.4 Hz, 4H), 3.58 (s, 2H), 2.48 (t, *J* = 4.4 Hz, 4H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 480 [M+H].

*(E)-N-(2-(2-(((1-Methylpiperidin-4-yl)amino)methyl)-1H-indol-1-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**5m**).* ^{1}H NMR ($CDCl_3$): δ 7.73 (s, 1H), 7.54 (d, *J* = 8 Hz, 1H), 7.44 (d, *J* = 15.2 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.08 (t, *J* = 7.2 Hz, 1H), 6.63 (s, 2H), 6.39 (s, 1H), 6.17 (d, *J* = 15.2 Hz, 1H), 4.38 (t, *J* = 5.6 Hz, 2H), 3.93 (s, 2H), 3.83 (m, 4H), 3.8 (s, 9H), 2.8 (m, 2H), 2.23 (s, 3H), 2.0 (m, 5H). LCMS (ESI): > 97% purity at λ 254, MS; m/z 507 [M+H].

*(E)-N-(2-(2-Methyl-3-(piperidin-1-ylmethyl)-1H-indol-1-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**5n**).* ^{1}H NMR ($CDCl_3$): δ 7.64 (d, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 15.6 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.10 (m, 2H), 6.6 (s, 2H), 6.14 (d, *J* = 15.6 Hz, 1H), 5.67 (t, *J* = 5.6 Hz, NH), 4.31 (t, *J* = 6 Hz, 2H), 3.85 (s, 9H), 3.75 (q, *J* = 6 Hz, 2H), 3.59 (s, 2H), 2.40 (bs, 4H), 2.38 (s, 3H), 1.5 (m, 4H), 1.6 (m, 2H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 492 [M+H].

*(E)-N-(2-(3-((Dimethylamino)methyl)-2-methyl-1H-indol-1-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**5o**).* ^{1}H NMR ($CDCl_3$): δ 7.6 (d, *J* = 7.2 Hz, 1H), 7.47 (d, *J* = 15.6 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.10 (m, 2H), 6.66 (s, 2H), 6.16 (d, *J* = 15.6 Hz, 1H), 5.73 (t, *J* = 5.4 Hz, NH), 4.3 (t, *J* = 6 Hz, 2H), 3.84 (s, 9H), 3.68 (q, *J* = 6 Hz, 2H), 3.54 (s, 2H), 2.39 (s, 3H), 2.25 (s, 6H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 452 [M+H].

*(E)-N-(2-(2-Oxoindolin-3-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**5p**).* ^{1}H NMR ($CDCl_3$): δ 8.0 (s, 1H), 7.49 (d, *J* = 15.6 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.04 (d, *J* = 7.2 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.69 (s, 2H), 6.6 (t, *J* = 5 Hz, NH), 6.28 (d, *J* = 15.6 Hz, 1H), 3.87 (m, 1H), 3.85 (s, 9H), 3.63 (q, *J* = 6 Hz, 2H), 3.52 (d, *J* = 6.4 Hz, 2H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 397 [M+H].

*(E)-N-(3,4-Dimethoxyphenethyl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**5q**).* ^{1}H NMR ($CDCl_3$): δ 7.51 (d, *J* = 15.6 Hz, 1H), 6.81 (d, *J* = 8 Hz, 1H), 6.75 (m, 2H), 6.9 (s, 2H), 6.2 (d, *J* = 15.6 Hz, 1H), 5.57 (t, *J* = 5.4 Hz, 1H), 3.85 (s, 9H), 3.84 (s, 6H), 3.62 (m, 2H), 3.82 (t, *J* = 6.8 Hz, 2H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 402 [M+H].

*(E)-N-(3-(4-Methoxyphenyl)propyl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**5r**).* ^{1}H NMR ($CDCl_3$): δ 7.45 (d, *J* = 15.6 Hz, 1H), 7.09 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 6.69 (s, 2H), 6.2 (d, *J* = 15.6 Hz, 1H), 5.5 (t, *J* = 5.4 Hz, NH), 3.86 (s, 6H), 3.85 (s, 3H), 3.41 (q, *J* = 6.4 Hz, 2H), 2.62 (t, *J* = 7.2 Hz, 2H), 1.85 (m, 2H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 386 [M+H].

*(E)-N-((2-Methyl-1H-indol-3-yl)methyl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**5s**).* ^{1}H NMR (DMSO-d_6): δ 10.9 (s, 1H), 8.11 (t, *J* = 5.2 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 15.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 6.96 (t, *J* = 7.2 Hz, 1H), 6.89 (t, *J* = 7.2 Hz, 1H), 6.81 (s, 2H), 6.55 (d, *J* = 16 Hz, 2H), 4.42 (d, *J* = 5.6 Hz, 2H), 3.74 (s, 6H), 3.63 (s,

3H), 2.36 (s, 3H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 403 [M+Na], 784 [M_2+ Na].

*(E)-N-((1,2-Dimethyl-1H-indol-3-yl)methyl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**5t**)*. ^{1}H NMR ($CDCl_3$): δ 7.56 (d, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 15.6 Hz, 1H), 7.27 (d, *J* = 8 Hz, 1H), 7.18 (t x d, *J* = 7.2, 1.2 Hz, 1H), 7.13 (t x d, *J* = 7.2, 1.2 Hz, 1H), 6.66 (s, 2H), 6.21 (d, *J* = 15.6 Hz, 1H), 5.6 (t, *J* = 5 Hz, NH), 4.70 (d, *J* = 4.8 Hz, 2H), 3.83 (s, 9H), 3.66 (s, 3H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 395 [M+H].

*N-(3,4-Dimethoxyphenethyl)-3-(2-methyl-1H-indol-1-yl)propanamide (**5u**).* ^{1}H NMR ($CDCl_3$): δ 7.5 (d, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 8 Hz, 1H), 7.09 (m, 2H), 6.62 (d, *J* = 8 Hz, 1H), 6.53 (d, *J* = 2 Hz, 1H), 6.38 (dd, *J* = 8 Hz, 1H), 6.2 (bs, 1H), 5.2 (bs, 1H), 4.38 (t, *J* = 6.8 Hz, 2H), 3.80 (s, 3H), 3.78 (s, 3H), 3.31 (q, *J* = 5.6 Hz, 2H), 2.49 (q, *J* = 6.8 Hz, 4H), 2.04 (s, 3H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 367 [M+H].

*N-(2-(2-Methyl-1H-indol-1-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)propanamide (**5v**) .* Characterization data for this compound has been described before.[7]

*3-Amino-N-(2-(2-methyl-1H-indol-1-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)propanamide (**5w**).* ^{1}H NMR ($CDCl_3$): δ 7.48 (m, 1H), 7.3o (m, 1H), 7.14 (t, *J* = 7.2 Hz, 1H), 7.0 (t, *J* = 7.2, 1.2 Hz, 1H), 6.40 (d, *J* = 3.2 Hz, 2H), 6.24 (s, 1H), 4.38 (m, 1H), 4.23 (m, 1H), 3.98 (m, 1H), 3.82 (m, 2H), 3.8 (s, 6H), 3.79 (s, 3H), 3.59 (m, 2H), 2.48 (s, 3H). Mass calcd for $C_{23}H_{29}N_3O_4$, 411.22; LCMS (ESI): > 95% purity at λ 254, MS; m/z, 412 [M+H].

*N-(2-(2-Methyl-1H-indol-1-yl)ethyl)-2-(3,4,5-trimethoxyphenyl)acetamide (**5x**).* ^{1}H NMR ($CDCl_3$): δ 7.46 (d, *J* = 7.6 Hz, 1H), 7.23 (dd, *J* = 8.8, 1.6Hz, 1H), 7.11 (t x d, *J* = 7.2, 1.2 Hz, 1H), 7.03 (t x d, *J* = 7.2, 1.2 Hz, 1H), 6.18 (s, 1H), 6.16 (s, 2H), 5.5 (t, *J* = 5 Hz, NH), 4.20 (t, *J* = 6 Hz, 2H), 3.77 (s, 3H), 3.67 (s, 6H), 3.52 (q, *J* = 6 Hz, 2H), 3.3 (s, 2H), 2.3 (s, 3H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 383 [M+H].

*(S, E)-Methyl 3-(2-methyl-1H-indol-3-yl)-2-(3-(3,4,5-trimethoxyphenyl)-acrylamido)propanoate (**5y**).* ^{1}H NMR ($CDCl_3$): δ 8.1 (s, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 15.6 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.17 (d, *J* = 8 Hz, 1H), 7.11 (t, *J* = 8 Hz, 1H), 6.99 (d, *J* = 2.4 Hz, 1H), 6.25 (d, *J* = 15.2 Hz, 1H), 6.16 (d, *J* = 7.6 Hz, 1H), 5.09 (m, 1H), 3.85 (s, 9H), 3.71 (s, 3H), 3.39 (m, 2H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 453 [M+H].

*(R, E)-Methyl 3-(2-methyl-1H-indol-3-yl)-2-(3-(3,4,5-trimethoxyphenyl)acrylamido)-propanoate (**5z**).* ^{1}H NMR ($CDCl_3$): δ 8.18 (bs, 1H), 7.53 (d, *J* = 9.2 Hz, 1H), 7.50 (d, *J* = 15.6 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.17 (t x d, *J* = 7.2, 1.2 Hz, 1H), 7.09 (t x d, *J* = 8, 1 Hz, 1H), 6.99 (d, *J* = 2.4 Hz, 1H), 6.25 (d, *J* = 15.6 Hz, 1H), 6.15 (d, *J* = 7.6 Hz, 1H), 5.09 (m, 1H), 3.85 (s, 9H), 3.71 (s, 3H), 3.39 (m, 2H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 453 [M+H].

*Synthesis and characterization data of **6a** and **6c** are described in the main text.*

*(E)-3-(3,4-bis(2-Hydroxyethoxy)phenyl)-N-(2-(2-(trifluoromethyl)-1H-indol-1-yl)ethyl)acrylamide (**6b**).* ^{1}H NMR ($CDCl_3$): δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H) 7.38 (d, *J* = 15.6 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 8 Hz, 2H), 6.97 (s, 1H), 6.84 (s, 1H), 6.77 (d, *J* = 8 Hz, 1H), 6.13 (d, *J* = 15.6 Hz, 1H), 4. 34 (t, *J* = 6 Hz, 1H), 3.99 (t, *J* = 4.4 Hz, 4H), 3.81 (q, *J* = 3.6 Hz, 4H), 3.58 (t, *J* = 6.8 Hz, 2H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 479 [M + H]. Anal. Calcd for $C_{24}H_{25}F_3N_2O_5$; C, 60.25; H, 5.27; N, 5.85; found; C, 60.28; H, 5.30; N, 5.92

*(E)-3-(4-(2-Hydroxyethoxy)phenyl)-N-(2-(2-methyl-1H-indol-1-yl)ethyl)acrylamide (**6d**).* ^{1}H NMR ($CDCl_3$): δ 7.54 (d, *J* = 15.6 Hz, 1H), 7.51 (d, *J* = 7.6 Hz, 1H) 7.39 (d, *J* = 8.8 Hz, 2H), 7.29 (d, *J* = 8 Hz, 1H), 7.11 (t, *J* = 7.2 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.24 (s, 1H), 6.10 (d, *J* = 15.6 Hz, 1H), 5.58 (d, *J* = 6 Hz, 1H), 4. 30 (t, *J* = 6 Hz, 2H), 4.08 (t, *J* = 4 Hz, 2H), 3.95 (d, *J* = 3.6 Hz, 2H), 3.68 (q, *J* = 6 Hz, 2H), 2.39 (s, 3H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 365 [M + H].

*(E)-3-(4-(3-Hydroxypropoxy)phenyl)-N-(2-(2-methyl-1H-indol-1-yl)ethyl)acrylamide (**6e**)* ^{1}H NMR ($CDCl_3$): δ 7.54 (d, *J* = 15.6 Hz, 1H), 7.51 (d, *J* = 8 Hz, 1H) 7.38 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8 Hz, 1H), 7.11 (t, *J* = 8 Hz, 1H), 7.05 (t, *J* = 8 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.24 (s, 1H), 6.09 (d, *J* = 15.6 Hz, 1H), 5.56 (t, *J* = 5 Hz, 1H), 4. 30 (t, *J* = 6 Hz, 2H), 4.12 (t, *J* = 5.6 Hz, 2H), 3.84 (t, *J* = 6 Hz, 2H), 3.68 (q, *J* = 6.4 Hz, 2H), 2.39 (s, 3H), 2.0 (m, 2H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 379 [M + H].

*(E)-3-(4-(2-Hydroxyethoxy)-3,5-dimethoxyphenyl)-N-(2-(2-methyl-1H-indol-1-yl)ethyl)acrylamide (**6f**).* ^{1}H NMR ($CDCl_3$): δ 7.51 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 15.6 Hz, 1H) 7.28 (d, *J* = 8 Hz, 1H), 7.11 (d, *J* = 8 Hz, 1H), 7.07 (d, *J* = 8 Hz, 1H), 6.67 (s, 2H), 6.24 (s, 1H), 6.14 (d, *J* = 15.2 Hz, 1H), 5.64 (t, *J* = 5 Hz, 1H), 4. 30 (t, *J* = 6 Hz, 2H), 4.12 (t, *J* = 4 Hz, 2H), 3.85 (s, 6H), 3.70 (t, *J* = 6 Hz, 4H), 2.39 (s, 3H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 425 [M + H]. HRFABMS: Calcd for $C_{24}H_{28}N_2O_5Na$, 447.18904; found 447.18886.

*(E)-3-(4-(2-Hydroxyethoxy)-3,5-dimethoxyphenyl)-N-(2-(2-(trifluoromethyl)-1H-indol-1-yl)ethyl)acrylamide (**6g**).* ^{1}H NMR ($CDCl_3$): δ 7.65 (d, *J* = 8 Hz, 1H), 7.56 (d, *J* = 8.8 Hz, 1H) 7.52 (d, *J* = 15.6 Hz, 1H), 7.33 (t, *J* = 7 Hz, 1H), 7.17 (t, *J* = 7.2 Hz, 1H), 6.96 (s, 2H), 6.86 (s, 2H), 6.17 (d, *J* = 15.6 Hz, 1H), 5.71 (t, *J* = 6 Hz, 1H), 4.47 (t, *J* = 6.4 Hz, 2H), 4.13 (t, *J* = 4.4 Hz, 2H), 3.86 (s, 6H), 3.76 (q, *J* = 6 Hz, 2H), 3.70 (bs, 2H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 479 [M + H].

*2-(2-Methyl-1H-indol-1-yl)ethyl (E)-3-(3,4,5-trimethoxyphenyl)acrylate (**6h**).* ^{1}H NMR ($CDCl_3$): δ 7.51 (d, *J* = 8 Hz, 1H), 7.46 (d, *J* = 16.4 Hz, 1H) 7.33 (d, *J* = 8.4 Hz, 1H), 7.15 (t x d, *J* = 7.2, 1.2 Hz, 1H), 7.08 (t x d, *J* = 8, 0.8 Hz, 1H), 6.65 (s, 2H), 6.27 (s, 1H), 6.23 (d, *J* = 15.6 Hz, 1H), 4.50 (t, *J* = 5.2 Hz, 2H), 4.39 (t, *J* = 5.2 Hz, 2H), 3.87 (s, 6H), 3.86 (s, 3H), 2.45 (s, 3H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 396 [M + H].

*2-(4-Fluorophenyl)-N-(2-(2-methyl-1H-indol-1-yl)ethyl)cyclopropane-1-carboxamide (**6i**).*

^{1}H NMR ($CDCl_3$): δ 7.49 (dd, *J* = 7.4, 0.4 Hz, 1H), 7.26 (dd, *J* = 7.4, 0.4 Hz, 1H) 7.07-6.90 (m, 6H), 4.25 (t, *J* = 6 Hz, 2H), 3.59 (q, *J* = 6 Hz, 2H), 2.49 (m, 1H), 2.40 (s, 3H), 1.58 (m, 1H), 1.39 (m, 1H), 1.19 (m, 1H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 337 [M + H].

*(E)-N-(2-(2-Methylpiperidin-1-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**6j**).* Characterization data for this compound has been reported previously [7]

*(E)-3-(4-(2-(Dimethylamino)ethoxy)-3,5-dimethoxyphenyl)-N-(2-(2-methyl-1H-indol-1-yl)ethyl)acrylamide (**6k**).* ^{1}H NMR ($CDCl_3$): δ 7.50 (d, *J* = 8 Hz, 1H), 7.47 (d, *J* = 15.6 Hz, 1H), 7.29 (d, *J* = 8 Hz, 1H) 7.12 (t, *J* = 7.2 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.64 (s, 2H), 6.13 (d, *J* = 15.6 Hz, 1H), 5.6 (t, *J* = 5 Hz, 1H), 4.31 (t, *J* = 5.6 Hz, 2H), 4.05 (t, *J* = 6 Hz, 2H), 3.82 (s, 6H), 3.71 (q, *J* = 6 Hz, 2H), 2.69 (t, *J* = 6 Hz, 2H), 2.39 (s, 3H), 2.32 (s, 6H). LCMS (ESI): > 95% purity at λ 254, MS; m/z, 452 [M + H].

*(E)-3-(4-(3-(Dimethylamino)propoxy)phenyl)-N-(2-(2-methyl-1H-indol-1-yl)ethyl)acrylamide (**6l**).* ^{1}H NMR ($CDCl_3$): δ 7.54 (d, *J* = 15.6 Hz, 1H), 7.51 (d, *J* = 8 Hz, 1H), 7.37 (d, *J* = 8.8 Hz, 2H) 7.29 (d, *J* = 8 Hz, 1H), 7.11 (t, *J* = 7.2 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.24 (s, 1H), 6.09 (d, *J* = 15.6 Hz, 1H), 5.58 (t, *J* = 6 Hz, 1H), 4.29 (t, *J* = 6 Hz, 2H), 4.01 (t, *J* = 6.4 Hz, 2H), 3.68 (q, *J* = 6 Hz, 2H), 2.43 (t, *J* = 6.8 Hz, 2H), 2.39 (s, 3H), 2.24 (s, 6H), 1.94 (q, *J* = 6.8 Hz, 2H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 406 [M + H].

*(E)-3-(4-(2-(Dimethylamino)ethoxy)phenyl)-N-(2-(2-methyl-1H-indol-1-yl)ethyl)acrylamide (**6m**).* ^{1}H NMR ($CDCl_3$): δ 7.54 (d, *J* = 15.6 Hz, 1H), 7.50 (d, *J* = 8 Hz, 1H), 7.37 (d, *J* = 8.8 Hz, 2H) 7.30 (d, *J* = 8 Hz, 1H), 7.11 (t, *J* = 7.2 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.27 (s, 1H), 6.08 (d, *J* = 15.6 Hz, 1H), 5.63 (t, *J* = 6 Hz, 1H), 4.28 (t, *J* = 5.6 Hz, 2H), 4.05 (t, *J* = 5.6 Hz, 2H), 3.67 (q, *J* = 6 Hz, 2H), 2.70 (t, *J* = 5.2 Hz, 2H), 2.39 (s, 3H), 2.31 (s, 6H). LCMS (ESI): > 96% purity at λ 254, MS; m/z, 392 [M + H].

*(E)-1-(3-(2-Methyl-1H-indol-1-yl)piperidin-1-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (**6n**).* ^{1}H NMR ($CDCl_3$) indicates every signal is split including methoxy groups on the phenyl ring, and methyl group on the indole ring. Most other peaks appeared as multiplets, suggesting it is a mixture of isomers possibly due to tertiary nitrogen. However, since it is a inactive compound we have not made any efforts to separate this mixture further. LCMS (ESI): > 95% purity at λ 254, MS; m/z, 435 [M + H].

*(E)-1-(3-(2-Methyl-1H-indol-1-yl)pyrrolidin-1-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (**6o**).* Like the above compound this compound NMR spectrum also showed similar splitting pattern of signals, but we are able write the data as follows. ^{1}H NMR ($CDCl_3$): δ 8.60 (s, 1H), 7.66 (d, *J* = 15.2 Hz, 1H), 7.64 (d, *J* = 15.6 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 2H) 7.52 (d, *J* = 7.6 Hz, 1H), 7.28 (m, 1H), 7.07 (m, 2H), 6.76 (s, 1H), 6.94 (s, 1H), 6.60 (d, *J* = 15.6 Hz, 1H), 4.05 (m, 2H), 3.88 (s, 3H), 3.83 (s, 3H), 3.82 (s, 3H), 3.80 (m, 2H), 2.54 (m, 1H), 2.41 (s, 3H).2.30 (m, 1H), 2.18 (m, 1H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 421 [M + H].

*(E)-N-(2,3,4,9-Tetrahydro-1H-carbazol-3-yl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**6p**).* ^{1}H NMR (DMSO-d_6): δ 10.8 (s, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 16 Hz, 1H), 7.30 (d, *J* = 8 Hz, 1H), 7.21 (d, *J* = 8 Hz, 2H) 6.90 (t, *J* = 7.2 Hz, 1H), 6.89 (t, *J* = 7.2 Hz, 1H), 6.85 (s, 2H), 6.61 (d, *J* = 16 Hz, 2H), 4.18 (bs, 1H), 3.77 (s, 6H), 3.64 (s, 3H), 2.94 (dd, *J* = 15.2, 5.2 Hz, 1H), 2.79 (t, *J* = 5.6 Hz, 2H), 2.51 (dd, *J* = 15.2,7.6 Hz, 1H), 1.99 (m, 1H), 1.83 (m, 1H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 307 [M + H].

*(E)-3-(4-Methoxyphenyl)-N-(2-(2-methyl-1H-indol-1-yl)ethyl)acrylamide (**6q**)*. Characterization data for this compound has been reported previously.[7]

*(E)-3-(3-Methoxyphenyl)-N-(2-(2-methyl-1H-indol-1-yl)ethyl)acrylamide (**6r**).* ^{1}H NMR ($CDCl_3$): δ 7.55 (d, *J* = 15.6 Hz, 1H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.12 (m, 3H), 6.90 (s, 1H), 6.88 (dd, *J* = 8, 2.4 Hz, 1H), 6.21 (d, *J* = 15.6 Hz, 1H), 5.64 (bs, 1H), 4.30 (t, *J* = 6 Hz, 2H), 3.79 (s, 3H), 3.69 (q, *J* = 6 Hz, 2H), 2.39 (s, 3H). LCMS (ESI): > 98% purity at λ 254, MS; m/z, 335 [M + H].

*(E)-3-(2-Methoxyphenyl)-N-(2-(2-methyl-1H-indol-1-yl)ethyl)acrylamide (**6s**).* ^{1}H NMR ($CDCl_3$): δ 7.85 (d, *J* = 16 Hz, 1H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.41 (dd, *J* = 7, 2 Hz, 2H), 7.28 (m, 2H), 7.01 (m, 2H), 6.92 (m, 2H), 6.38 (d, *J* = 16 Hz, 1H), 5.68 (bs, 1H), 4.30 (t, *J* = 6.4 Hz, 2H), 3.81 (s, 3H), 3.68 (q, *J* = 6 Hz, 2H), 2.40 (s, 3H). LCMS (ESI): > 98% purity at λ 254, MS; m/z, 335 [M + H].

*(E)-N-(2-(1H-Indazol-3-yl)ethyl)-3-(3,4,5-trimethoxyphenyl)acrylamide (**6t**).* ^{1}H NMR ($CDCl_3$): δ 7.75 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 8 Hz, 1H), 7.45 (dd, *J* = 15.6 Hz, 1H), 7.22 (m, 1H), 6.65 (s, 2H), 6.31 (d, *J* = 16 Hz, 1H), 3.88 (m, 2H), 3.82 (s, 3H), 3.81 (s, 6H), 3.37 (t, *J* = 6 Hz, 2H). LCMS (ESI): > 97% purity at λ 254, MS; m/z, 382 [M + H].

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